The effect of age on electromyographic and kinematic responses to electrical stimulation of the distal tibial nerve during walking

by

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BPT, Maharshi Dayanand University, 2009

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University of Victoria

Supervisory Committee

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Abstract

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In young healthy adults, characteristic obstacle avoidance reflexes (stumble corrective) were elicited with electrical stimulation during walking that were dependent on the anatomical location of cutaneous afferents stimulated (sole versus dorsum of the foot). We previously demonstrated an age-related erosion of these stumble corrective responses when the perturbation was applied to the dorsum of the foot. However, it is unknown whether similar age-related reflex erosion is present with stimulation to the sole of the foot. The purpose of this study was to identify age-dependent differences in stumbling reactions to electrically evoked stimulation of the tibial nerve at the ankle during walking in healthy young (19-39) and older adult (70 years and older) groups. Electromyograms (EMG) of the tibialis anterior (TA), soleus (SOL), medial gastrocnemius (MG), biceps femoris (BF) and vastus lateralis (VL) were recorded along with gait kinematics including angular displacement and velocity at the ankle and knee joint as well as toe clearance relative to the walking surface. The main finding of this study was the significant erosion of the kinematic and EMG stumbling reactions seen in the older adults compared to the young. Specifically, during mid-swing phase, there was reduced peak toe clearance and significantly smaller amplitudes in ankle dorsiflexion and knee flexion angular displacement as well as absent responses in TA and MG in older adults compared to the young. Further, these degraded responses were superimposed on altered mid-swing phase kinematics during unstimulated walking in the older adults showing reduced toe clearance, knee flexion and increased ankle dorsiflexion compared to the young. This combination of degraded reflexes and altered unstimulated kinematics resulted in significantly reduced toe clearance in the older adults and could suggest that these adults are in the prodromal stage of fall risk.

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Chapter 1. Introduction and Literature review

1.1 General Introduction

Aging is related to multifarious neural and mechanical changes that result in quantifiable modifications to mobility and specifically to gait. Key factors have been associated with alterations in healthy locomotion such as muscle weakness (i.e. sarcopenia), reduced joint range of motion, decreased postural and dynamic balance, lower visual acuity, decreased number of sensory receptors, lower nerve conduction velocity (Wagman & Lesse, 1952), as well as proprioceptive decline (Riva et al., 2013). Such age-related changes in sensorimotor function could result in an altered response to a sensory stimulus. An example of this altered reflex control was seen by Chalmers and Knutzen who found a significant decrease in muscle afferent reflex amplitudes during the stance phase (Chalmers & Knutzen, 2000). A reduced ability to effectively respond to an obstacle or disturbance during walking could result in an unfortunate event such as a trip or a fall. Indeed, the incidence of falls tends to increase with age (Rubenstein, 2006). Falls account for 74% of injury-related hospitalizations for older adults (Canadian Institute for Health Information, 2011) and cause more than 90% of all hip fractures in this age group (Zuckerman, 1996). Thus it is imperative to understand the many age-related risk factors associated with this potentially harmful event to improve our understanding of mobility decline associated with the normal aging process versus pathological changes associated with fall risk. Further an improved understanding could inform early detection of mobility decline and potentially contribute to fall prevention interventions.

Studies of reflexes during locomotion in healthy young subjects have demonstrated that reflexes serve an important functional role in response to a disturbance to gait (Zehr & Stein, 1999). Perturbations to the top and bottom of the foot during walking in young healthy subjects results in neural and mechanical stumble corrective outcomes that assist in removing the limb from the disturbance and enable the progression of walking (Eng et al., 1994; Zehr, Komiyama & Stein, 1997). Evaluating changes in these reflexes in different clinical populations during locomotion has been effective in probing the integrity of neural control and characterizing changes associated with disease or injury (Hundza & Zehr, 2006; Zehr & Loadman, 2012).

While stumble corrective reflexes have been extensively studied in a younger population in humans (for review see Zehr, Stein & Loeb, 2000) there have been only a few studies directly investigating changes in stumble corrective responses in older adults (Schillings et al., 2005). Additionally, these studies have primarily investigated neural responses with limited focus on key fall-related kinematic measures such as toe clearance. Previous studies investigating age-related changes to stumble corrective reflexes during walking have used mechanical perturbation to elicit reflexes (Eng et al., 1994; Schillings et al., 2005). Though the responses to perturbations evoked mechanically and electrically are similar (Eng et al., 1994; Zehr et al., 1997), the age-related changes in response to electrical stimulation of cutaneous afferents require further study. Zehr and Loadman (2012) did evoke cutaneous reflexes by stimulating the superficial peroneal (SP) nerve in an older adult group that was an age-matched control group for a cohort of participants who experienced a stroke. However, this older adult group ranged in age from 37-88 years (mean age of 64 years) and there was no direct comparison to reflexes in young adults. Recently, our lab directly compared reflexes evoked with electrical stimulation of the superficial peroneal (SP) nerve in young and older adults (Brodie et al., in preparation). In this study, we found that in older adults the kinematic stumble corrective reflexes were eroded with significant reductions in the magnitude of ankle plantarflexion displacement, plantarflexion velocity, knee flexion displacement and angular velocity reflexes during swing. These differences contributed to a blunted toe clearance reflex in the older adults compared to the young in mid swing (Brodie et al., in preparation). To the best of our knowledge, no known research has comparatively quantified muscle and mechanical reflexes to tibial nerve electrical stimulation in young versus the older adults to determine whether these reflexes are eroded with age as seen in our earlier study on SP nerve stimulation. Thus, the purpose of this study is to examine age-related changes in neuromechanical reflexes elicited with tibial nerve stimulation during walking. Knowledge of changes in stumble corrective reflex function due to ageing would provide critical insight into understanding age-related changes in locomotor function including the ability to respond to perturbations during walking.

In chapter 1of this manuscript-based thesis, I will present relevant background information and rationale supporting the evaluation of age-related changes in muscle and mechanical reflexes to electrical stimulation of cutaneous pathways of the foot during locomotion. A brief review will be presented on the role of afferent feedback in the neural control of locomotion, as well as the functional role of cutaneous reflexes during locomotion including nerve, task and phase specificity of reflexes. Finally a summary of research on age-related changes in reflexes and gait parameters will be presented. Using a manuscript style presentation, Chapter 2 will outline my thesis research project.

1.2 Role of afferent feedback during human locomotion

In the early 2000s, the neural control of rhythmic activities such as walking was described as a tripartite system (Zehr, 2005). This model puts CPGs at the core of rhythmic locomotor activities (see Figure 1). However, there are complex neurological interactions between supraspinal inputs, CPGs and afferent feedback to effectively regulate the rhythmic activity to meet environmental demands. This complex interaction depicts the important role of sensory feedback in the neural control of human locomotion and the integrated role that reflexes play.

Skin receptors in the foot provide useful tactile information during human walking. Either mechanical or electrical stimulation of Aβ, Aδ and C nerve axons from specialized skin mechanoreceptors such as Merkel disks, Pacinian and Meissner corpuscles, Ruffini endings and free nerve endings (Zehr & Stein, 1999) result in functionally relevant neural and mechanical cutaneous reflexes (Van Wezel, Ottenhoff & Duysens, 1997 ; Zehr et al., 1997). These cutaneous receptors when stimulated alter the muscle activation patterns during walking as well as change the locomotor rhythm itself (as cited in DeSerres et al., 1995). Van Wezel et al. (2000) studied participants with sensory polyneuropathy and postulated that Aβ fibers, specifically, mediate reflexes evoked by non-nociceptive stimuli. Maki et al. (1999) established that plantar pressure sensation plays an important role in controlling balancing reactions that involve rapid compensatory stepping movements.

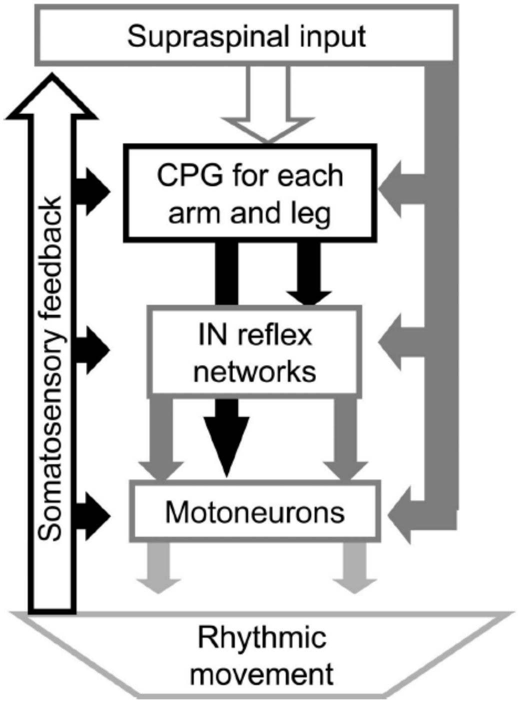


Figure.1 Model representing role of CPG, supraspinal input and sensory feedback in generating rhythmic movement

(From Zehr, 2005. *Exercise and sport sciences reviews*)

1.3 Reflex control during locomotion

Electrically evoked reflexes

To elucidate the role of reflexes during human locomotion, electrically evoked Hoffmann (H-) reflex and cutaneous reflexes are the commonly used methods. The H-reflex is the electrical analogue of the natural, monosynaptic stretch reflex. It is a simple tool to analyze reflex behavior in which electrical stimulation is applied percutaneously to a mixed nerve fiber, resulting in recruitment of several sensory afferents such as group Ia, Ib and II as well as α-motor neuron axons, (Capaday & Stein, 1986; Zehr, 2002). The H-reflex is more easily used during static conditions; using the H-relfex during dynamic movements such as walking is more challenging because changes in muscle characteristics such as length and background motor activity can alter the reflex amplitude (Zehr, 2002).

Cutaneous reflexes provide another approach to probe the integrity of the nervous system as well as the role of afferent feedback during walking. Cutaneous reflexes have some advantages over H-reflex in that they are minimally sensitive to peripheral feedback and the level background muscle activity (bEMG) during rhythmic movement (Zehr, Hesketh & Chua, 2001; Hundza & Zehr, 2006). Further, cutaneous reflex pathways are functionally relevant to human locomotion, playing key roles in autoregulation of balance control during walking (Zehr, Komiyama & Stein, 1997). The cutaneous reflex pathways are polysynaptic, i.e. contain a numerous interneuronal connections modulating the excitability of the motor neuron pool in the spinal cord (Burke, 1999). The result is that a single volley of cutaneous stimuli can produce reflexes of different latencies. Cutaneous afferent input produces a stumble corrective response that has a short latency component, which has been observed in intact as well as chronic spinalized cats (Forssberg et al., 1975; Forssberg et al., 1976; Forsberg et al., 1977). Given the duration of this short latency response, it must be mediated by spinal circuits.

Electrically versus mechanical evoked reflexes

Scientists have compared reflexes evoked with electrical or mechanical stimulation. A review of studies by Zehr and Stein (1999) concluded that both modalities involve similar pathways and electrically evoked reflexes are qualitatively similar to natural cutaneous activation. For example, Perrier and colleagues (2000) while studying post-synaptic potentials in peroneal motoneurons observed that reflexes to electrical stimulation of SP nerve are similar in sign and latency to natural skin stimulation of SP nerve innervation field. Buford and Smith

(1993) observed some differences between the two modes of evoking cutaneous reflexes in cats. They observed that the amplitude of kinematic responses elicited by electrical pulses was typically less than that evoked by physical taps. However, the taps that did not disturb the path of the swing leg produced similar magnitude of responses to electrical stimulation. Thus, a fundamental difference between mechanical and electrical stimulation is that the muscle afferents and potentially joint receptors are not activated in the latter. The role of these afferents has been thought to have limited effect on the stumble correction response (Forsberg et al., 1977; Prochazka et al., 1978). Further, it can be argued that electrical stimulation bypasses the cutaneous receptors (Caruso, 1995), which are known to show degenerative changes with age (as reviewed in Shaffer & Harrison, 2007). Nevertheless, an advantage of using electrically-evoked cutaneous perturbations is that they afford more rigorous control of stimulus intensity and location compared to mechanical perturbations (Burke, 1999).

1.4 Phase and task dependence of cutaneous reflexes

Conventionally, to evoke cutaneous reflexes, trains of non-noxious electrical stimuli are applied to the skin superficial to a peripheral cutaneous nerve, such as the SP, sural or tibial nerve innervating receptors on the dorsum and sole of the foot respectively. Despite the tibial nerve being a mixed nerve, reflexes evoked with electrical stimulation of the tibial nerve are typically considered “cutaneous reflexes” because they are very similar to those seen with sural nerve stimulation (a cutaneous nerve) (Yang & Stein, 1990; Zehr, Stein &Komiyama, 1998a) and are likely largely dominated by influence from cutaneous afferents. In order to quantify a cutaneous reflex average background muscle activity and kinematics from unstimulated walking are subtracted from average stimulated trials to yield a subtracted trace of the ‘reflex’ whose functional relevance can be interpreted by studying the corresponding task and phase of the movement (Brooke et al., 1997).

The numerous interneuronal connections in cutaneous reflex pathways result in modulation of the input onto the motor neuron pool in the spinal cord (Burke, 1999; Zehr, 2005). Phase dependent reflex modulation during walking occurs when the same stimulus evokes a different reflex in terms of amplitude or sign during different phases of the gait cycle (Forsberg et al., 1975; Duysens & Stein, 1978; Forssberg, 1979; Duysens et al., 1990; Duysens et al., 1992; DeSerres et al., 1995; Van Wezel et al., 1997; Zehr & Kido, 2001). Forssberg et al. (1975) first described the phenomenon of "phase-dependent reflex reversal" during walking as an excitation of a set of muscles by a stimulus during one phase and inhibition in the other phase. They showed that a non-noxious stimulus to the foot increased flexor activation during swing while it enhanced extensor activity during stance in spinalized animals. This phase dependent reflex reversal has been shown in response to both electrical and mechanical stimuli (Duysens & Stein, 1978; Forssberg, 1979).

The cutaneous reflexes are also shown to be task-dependent, i.e. influenced by the state of activation of the muscles which may be different among tasks such as between standing versus walking versus running (Burke, Dickson & Skuse, 1991; Burke, 1999). This feature points to the useful function of reflexes during different behaviors (Zehr & Stein, 1999). Burke (1999) showed that following non-noxious stimulation of the sural nerve, the early and middle reflexes in tibialis anterior (TA), biceps femoris (BF) and vastus lateralis (VL) were different among tasks such as sitting, standing normally or standing on an unstable platform. Abbruzzese et al. (1996) observed task dependent reflexes when low intensity cutaneous input to the sole of the foot produced facilitation of soleus while prone, but inhibition during standing. Yang and

Stein (1990) showed that subsequent to tibial nerve stimulation, the middle latency excitatory response seen in TA during the swing phase changes to an inhibition response during the swing to stance transition (see Figure 2-A). This reflex reversal was not seen during standing. Thus, it can be argued that cutaneous reflex modulation is both phase and task dependent. Similar task-dependent reflex reversal was seen by Zehr, Hesketh and Chua (2001) in VL, SOL and MG muscles after distal tibial nerve stimulation. The middle latency responses in these muscles reversed from excitatory under static conditions to suppressive during leg cycling.

DeSerres et al. (1995) argue that PSTH (Post Stimulus Time Histograms) data from single motor units during walking prove possible existence of parallel inhibitory and excitatory pathways to TA motor units (see Figure 2-B). This supports the probability of reflex reversals during different phases of gait cycle. Moreover, these phase dependent reflexes are independent of the background EMG activity during walking indicating premotoneuronal gating of these reflexes (Duysens et al., 1990).

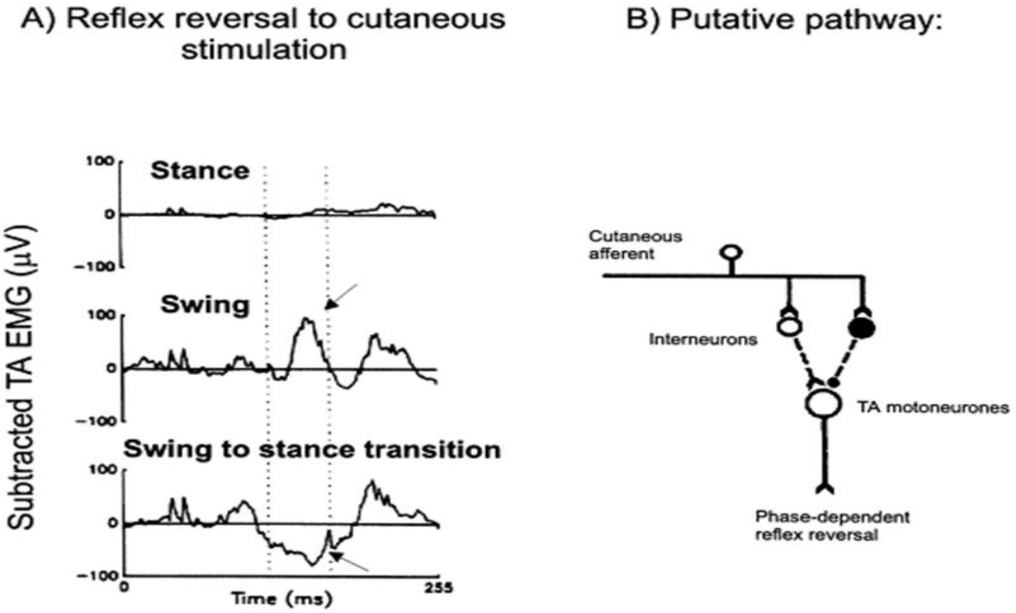


Figure 1: Reflex reversal and the involved pathway. (From Zehr &Stein, 1999. *Progress in Neurobiology*, 58(2), 185-205) Figure 2 (A) shows phase dependent reflex modulation including a reflex reversal in TA after tibial nerve stimulation. The arrows note excitation in swing and inhibition in swing and stance transition. The probable mechanism responsible for this reflex modulation is shown in Figure 2 (B). The parallel pathways of a group of excitatory and inhibitory interneurons project on the motorneurons in turn affecting the TA activity.

1.5 Nerve specificity of cutaneous reflexes

In addition to displaying phase and task dependence, cutaneous reflexes are also specific to the sensory area being stimulated. Cutaneous reflexes produce a nerve specific response dependent on the anatomical region innervated by the nerve (Van Wezel et al., 1997; Zehr et al., 1997; Zehr & Kido, 2001). Van Wezel et al. (1997) showed that stimulation of the three cutaneous nerves in the lower limb (i.e. sural, superficial peroneal and tibial nerves) produced differential activation patterns in the BF muscle. Nonetheless, the function of these different reflexes is the same which is to avoid or overcome a destabilizing stumble during the gait cycle. For example, cutaneous reflexes elicited during SP nerve stimulation in the foot during swing are shown to be associated with inhibition of TA (i.e. decreased dorsiflexion), activation of BF (increased knee flexion) and activation of hip flexors to cause increase hip flexion. This is a typical obstacle avoidance reflex, in which, if one happens to hit an object on the dorsum of their foot, the flexor reflex helps in clearing the obstacle and avoiding the stumble. Similarly, tibial nerve stimulation (i.e. stimulation along the medial border and arch of sole of the foot) elicits a withdrawal reflex during the swing phase, and stability enhancement or foot placement response during early stance (Zehr et al., 1997). Sural nerve stimulation (lateral border of the foot) during swing phase shows typical obstacle avoidance reflex with increased ankle dorsiflexion and knee flexion (Zehr, Stein & Komiyama, 1998a). These nerve specific reflexes were present during rhythmic activities like walking, but not observed during static postures such as standing (Komiyama, Zehr & Stein, 2000).

1.6 Functional relevance of cutaneous reflexes

Modulation of cutaneous reflexes has been studied using several methods to understand their functional relevance. Reflexes can be evaluated at specific latencies or using the average cumulative reflex expression (ACRE) (Baken et al., 2005; Zehr et al., 2000). Specifically latencies are categorized as early or P1 (occurring ~50ms) which are generally smaller in magnitude and middle latency or P2 (peak around 80ms) which are larger in magnitude and more consistent (Baken et al., 2005). The average cumulative reflex EMG ($ACRE_{125}$) is defined as the average of subtracted motor output for the 125ms post stimulus. This measure gives a “net” effect determining how modulated muscle reflexes may correspond with kinematic or mechanical outcomes during movement (similar to Zehr & Chua, 2000). The ACRE is more directly related to the kinematics and therefore is often used when studying reflexes from a functional relevance perspective (Zehr & Stein, 1999).

A functional reflex will involve EMG and kinematic responses that are behaviorally relevant to the gait pattern (Zehr & Stein, 1999). Berger and colleagues (1984) studied the ipsilateral and contralateral effects of supra-maximal tibial nerve stimulation during different phases of human gait cycle. The researchers concluded that the activation of TA during walking was primarily to hold the body center of gravity constant to maintain balance. These responses were highly dependent on the phase of the gait cycle and helped in rapid correction of ipsilateral foot position, with the strongest responses noticed in the beginning of stance and swing phase (see Figure 3 below).

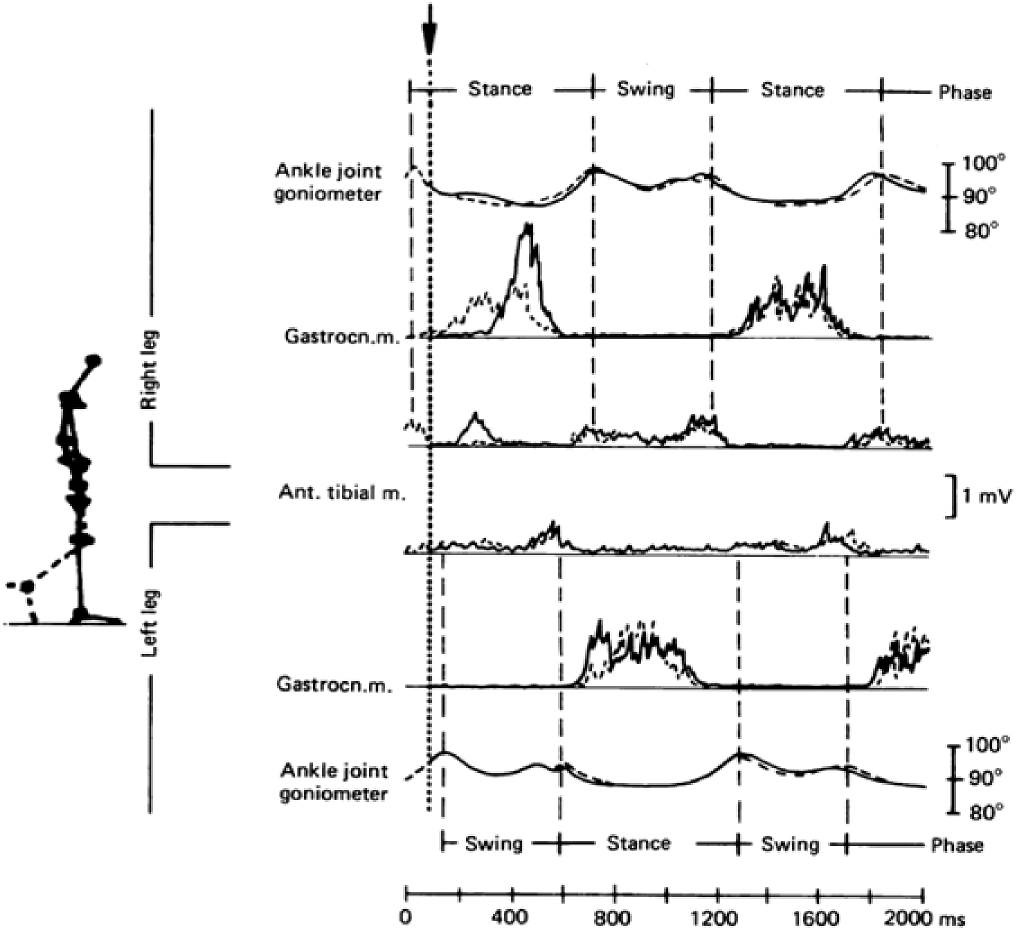


Figure 3. Rectified and averaged (n= 10) EMG and ankle kinematics after right tibial nerve stimulation during walking

(From Berger, Dietz & Quintern, 1984. *Journal of Physiology*)

Yang and Stein (1990) studied EMG reflexes in leg muscles to non-noxious stimulation of tibial nerve during walking. Looking at the middle latency reflexes in TA, they observed excitation during swing contributing to increased dorsiflexion, and inhibition during swing to stance transition contributing to earlier foot placement on the ground. They postulated two functional implications of these reflexes- 1) withdrawal response to stimuli and 2) preserve balance or stability during walking. These results are similar to that observed in other studies (Duysens et al., 1990; Zehr et al., 1997). Zehr et al. (1997) showed that electrical stimulation of tibial nerve (sole of the foot) elicits increased dorsiflexion at the stance to swing transition. This response helps to prevent scuffing of the foot to an object on the floor, thus preventing tripping. Also, at late swing, this response is reversed resulting in increased plantar-flexion (Figure 4 right panel). This helps in placing the foot on the floor as well as stability during the transition (Zehr et al., 1997). Thus, a functional reversal, with dorsiflexion during the transition from stance to swing and a plantarflexion during late swing helps in smooth movement of the swing leg so as to prevent tripping during swing and to assist placing and weight acceptance at the beginning of stance.

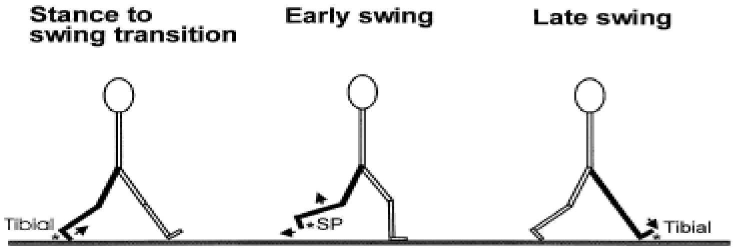


Figure 4. Cutaneous reflexes during gait cycle for SP and tibial nerves

(From Zehr et al., 1997. *Journal of Neurophysiology*)

Zehr et al. (1997) and Van Wezel et al. (1997) have both shown that electrical stimulation of the dorsum of the foot (SP nerve innervation area) during swing phase produces a suppression of ankle flexor activity and excitation of both VL and BF throughout swing. Kinematically, it results in plantarflexion in swing and an increase in knee flexion during early-swing. This “stumble corrective response” is similar to that observed in cats by Forssberg (1979) during both mechanical and electrical stimulation of the dorsum of the paw. Similar stumble corrective responses were noticed by Schillings and colleagues (2005) during mechanical tripping in humans using a novel approach of inducing reflexes by unexpected perturbations to the swing foot by using obstacles on a treadmill.

Zehr, Stein and Komiyama (1998a) evaluated the muscle and functional kinematic outcomes of electrical stimulation of the sural nerve during walking. Medium intensity stimulation during stance produced ankle eversion and dorsiflexion responses with corresponding activity in MG and TA. Functionally, it helps in accommodating an uneven terrain that may put pressure on the lateral side of the foot (sural nerve innervation area). Swing phase showed a typical obstacle avoidance response where there was an increased ankle dorsiflexion and knee flexion in response to both medium and high intensity electrical stimulation. In summary, sensory feedback from the foot has location or nerve specific information which is sculpted to have a functional role during human walking. These reflexes primarily modify the trajectory of the swing limb to overcome the perturbation and induce stabilization during stance to maintain gait stability (Zehr & Stein, 2000).

1.7 Effects of aging in older adults

Age-related changes in sensory and motor function

There are several age-related systemic changes such as sarcopenia and sensorimotor decline that directly or indirectly affect gait patterns in humans. Sarcopenia leads to decreased physical function and an overall low quality of life (Rizzoli et al., 2013). This may cause deterioration of essential motor skills such as gait. Biomechanical age-related changes occurring in gait patterns are reduced stride length as well as increased stride frequency and double support duration (Winter, 1991; Judge, Davis & Ounpuu, 1996). Judge and colleagues (1996) argued that changes in step length in older subjects was due to lower ankle plantarflexor power during the late stance phase of gait which was compensated by increasing the hip flexor power. Nigg and

Skleryk (1988) showed that elderly participants had slower walking speed and decreased joint range of motion (ROM) at foot and ankle joints during mid-stance than their younger counterparts. This reduced joint ROM is possibly due to increased stiffness in ankle and subtalar joints. Moreover, Meskers and colleagues (2007) found that ankle stiffness among the elderly was higher during dorsiflexion than plantarflexion. Interestingly, Christ et al. (1992) showed that age-related decrease in muscle strength was more prominent in plantarflexors than dorsiflexor muscle group. This age-related strength and power loss in plantar flexors can reduce the necessary push-off force in older adults. (Winter et al., 1990; Christ et al., 1992; Judge et al., 1996)

Other studies have examined toe clearance differences between young and old. Mills, Barrett and Morrison (2001) and Barrett et al., (2010) found higher variability in toe clearance in the older adults which is associated with an increased fall risk. Winter et al. (1990) found lower but insignificant differnces in toe clearance in older adults (1.11 cm) as compare to the young adults (1.27 cm). These age-related changes are detrimental to dynamic balance and put the elderly at an increased fall risk which becomes imminent with environmental constraints. The previous examination of toe clearance, however, was restricted to minimum toe clearance and did not examine differences in gait parametres across multiple positions across the swing phase.

The age-related changes seen in somatosensory function possibly contributes to an increased risk for falls (Lord, Clark & Webster, 1991). Decreased sensitivity on the plantar surface of the foot can lead to alterations in gait. Eils et al. (2004) using ice immersion technique on the plantar surface in young adults showed significant gait variations such as decreased dorsiflexion at ground contact and decreased plantar flexion at push-off and attributed this to decreased activation of lower leg muscles. Moreover, kinematic changes at the knee and hip led to a more smooth initial contact and weight bearing for the whole leg, producing a cautious walking pattern (Eils et al., 2004). Such decreased sensitivity of the plantar skin is common with aging (Maki et al., 1999) and can possibly lead to alterations in gait, with probable effects on cutaneous reflex behavior among the elderly. Numerous other age-related physiological factors such as muscle weakness, increased reaction time, reduced vestibular and visual function are known to contribute to fall risk in older adults (Lord & Sturnieks, 2005).

Comparative gait analysis among fallers and non-fallers shows increased stride-to-stride variability in kinematic measures such as ankle plantar flexion, hip extension, and hip flexion in elderly fallers compared with non-fallers (Barak, Wagenaar & Holt, 2006). Kerrigan et al. (1998) and Kerrigan et al. (2000) list age-related changes in gait as reduced peak hip extension, increased anterior pelvic tilt, and reduced plantarflexion as well as reduced ankle power in terminal stance. In those predisposed to falls, a further reduction in peak hip extension, knee flexion and knee power is seen. Furthering this work, healthy young, old non-fallers and old fallers were found to have a progressive reduction in peak hip extensor moment, indicating a progressive reduction of the hip joint range of motion and commensurate limitation on gait function (Kerrigan et al., 2001).

Effects of aging on reflexes

Aging affects the nervous system through several changes such as decreased nerve conduction velocity in efferent motor fibers (Dorfman & Bosley, 1979), decreased number and density of sensory receptors (Kenshalo, 1986), and slower nerve conduction velocity (Sato, Sato & Suzuki, 1985) leading to proprioceptive decline (Riva et al.). These age-related changes could influence reflex expression in older adults. For example, Hoffman reflex (H-reflex) amplitude decreases with age (Burke & Kamen, 1996; Brooke et al. 1997), suggesting a general decrease in the excitability of spinal reflexes with age. Chalmers and Knutzen (2000) demonstrated a decrease in amplitude of H-reflex in soleus muscle during stance phase in older adults as compared to the young. This may be indicative of age-related alterations in the central reflex mechanisms affecting stretch reflex contribution to ankle extensor neural drive

The age-related changes seen in somatosensory function possibly contribute to an increased risk for falls (Lord, Clark & Webster, 1991). Decreased sensitivity on the plantar surface of the foot can lead to alterations in gait. Eils et al. (2004) using ice immersion technique on the plantar surface in young adults showed significant gait variations such as decreased dorsiflexion at ground contact and decreased plantar flexion at push-off and attributed this to decreased activation of lower leg muscles. Moreover, kinematic changes at the knee and hip led to a more smooth initial contact and weight bearing for the whole leg, producing a cautious walking pattern (Eils et al., 2004). Such decreased sensitivity of the plantar skin is common with aging (Maki et al., 1999) and can lead to alterations in gait, with probable effects on cutaneous reflex behavior among the elderly. Numerous other age-related physiological factors such as muscle weakness, increased reaction time, reduced vestibular and visual function are known to contribute to fall risk in older adults (Lord & Sturnieks, 2005).

Cutaneous reflexes have been used to study certain pathological states as a means to probe the integrity of the nervous system and specifically the neural control of walking which has added to the knowledge and understanding of the functionality of these reflexes during the human gait cycle (Jones & Yang, 1994; Zehr et al., 1998b; Hundza & Zehr, 2007; Zehr & Loadman, 2012). Jones and Yang (1994) studied tibial nerve reflexes in spinal cord injury patients during walking. They noticed mild reflex modulation during different phases of the gait cycle, but the responses were predominantly excitatory. Following stimulation of SP nerve during walking in stroke participants, Zehr and Loadman (2012) found that the general reflex modulation pattern is preserved after stroke; however significant differences are seen in the more affected side such as during stance-swing transition, showed facilitation in VL instead of suppression and TA showed suppression instead of facilitation.

Tripping occurs when the swing foot encounters an obstacle during walking. One third of adults over 65 fall at least once per year (O'Loughlin et al., 1993). Tripping has been reported to be a major contributor of falls among community dwelling seniors (Blake et al., 1988). To overcome a perturbation to the dorsum of the foot, the body produces a characteristic "stumble correction response". In the cat, Forssberg (1979) documented passive planterflexion (i.e. inhibition of dorsiflexion), combined with hip and knee flexor excitation in response to the perturbation applied to the dorsum of the paw during swing phase of walking. Perturbation paradigms used by Schillings and colleagues (2000) involved a mechanical perturbation to the sole of the foot during walking and the corresponding responses elicited were referred to as "stumbling reactions". In our study, we electrically stimulated the distal tibial nerve which is qualitatively similar to mechanical perturbations used by Schillings et al. (2000). So we will refer to the responses elicited with electrical stimulation of distal tibial nerve as "stumbling reactions".

Studying stumbling reactions is a useful and functionally relevant medium to explore age and fall-risk related changes in neural control of walking. There are limited studies directly investigating changes in stumbling reactions in the older adults (Schillings et al., 2005). Additionally, previous studies have used mechanical perturbations and primarily investigated neural responses with limited focus on key fall-related kinematic measure such as toe clearance (Eng et al., 1994; Schillings et al., 2005). Zehr and Loadman (2012) studied superficial peroneal

(SP) nerve reflexes in an older adult group that was an age-matched control group for a clinical cohort. However, this older adult group had a heterogeneous age range (37-88 years) and there was no direct comparison with the reflexes of young adults. While there has been some investigation on the effect of aging on stumble corrective reflexes to SP nerve stimulation (Brodie et al., in preparation) there remains to be an investigation of the neural and mechanical outcomes (or the “stumbling reactions”) associated with electrical stimulation of the distal tibial nerve.

1.8 Summary

Cutaneous reflexes play an important functional role in human locomotion. These stumble corrective or stability related reflexes are phase, context and nerve dependent (Zehr et al., 1997; Van Wezel et al., 1997). Aging is associated with deteriorative changes in the neuromuscular system. This predisposes seniors to an increased risk for falls. Age-related changes in gait parameters have been studied and certain biomechanical variants have been identified (Winter, 1991).

While cutaneous reflex modulation has been widely studied in a young population, the effects of age on these crucial neuromechanical reflexes, is yet to be determined. Electrically evoked stumble corrective reflexes provide a useful medium to explore age-related and fall-risk related changes in neural control walking. Specifically, “stumbling reactions” evoked by stimulating the distal tibial nerve have not been comparatively studied in the elderly population. This is the rationale for undertaking this study and comparing the responses elicited with electrical stimulation of the tibial nerve at the ankle among young and healthy older adults.

Chapter 2. Manuscript

2.1 Introduction

The normal aging process has multifarious influences on the sensorimotor system and is associated with alterations in gait as well as a decrease in dynamic postural stability (Granta & Lockhart, 2008; Kang & Dingwell, 2008). Some examples of these age-related changes which affect locomotion and postural balance include muscle weakness (i.e. sarcopenia), decreased joint range of motion and increased joint stiffness, slower nerve conduction velocity (Sato, Sato & Suzuki, 1985), proprioceptive decline (Riva et al., 2013), loss of cutaneous mechanoreceptors (Kenshalo, 1986), as well as decreased amplitude of muscle afferent reflexes (Burke & Kamen, 1996). Concurrently, age-related changes in walking mechanics include reduced peak hip extension, increased anterior pelvic tilt, reduced plantarflexion as well as reduced ankle power (Kerrigan et al., 1998; Kerrigan et al., 2000). Age-related changes in motor control can also alter the response to an obstacle or disturbance during walking (Schillings et al., 2005), which can result in the occurrence of falls for some older adults while not for others (O’Loughlin et al., 1993). As such, the relationship between normal age-related changes in motor control and increased fall risk is currently not clear. To better understand these relationships it is imperative to investigate alterations in electromyographic (EMG) and kinematic responses to disturbances during walking in healthy younger adults compared to healthy older adults with no fall history.

Studying reflexes elicited in response to perturbations to the foot during walking has provided a useful medium to probe the integrity in the neural control of walking (Zehr & Loadman, 2012; Zehr, Fujita & Stein, 1998b). Given that for older adults 59% of falls during walking result from tripping (Berg et al., 1997), examining reactions to perturbations to the foot during walking is particularly relevant to understand age-related changes in the integrity of the neuromechanical control of walking. In young healthy adults, previous work has demonstrated that characteristic stumble reactions were elicited with mechanically and electrically evoked perturbations to the dorsum of the foot during walking with both resulting in similar obstacle avoidance strategies (Zehr & Stein, 1999). Further, the reflexes resulted from coordinated muscle and kinematic outcomes that produced functional responses that were specific to the anatomical location of the perturbation on the foot (i.e. nerve stimulated) as well as the phase of gait cycle during human locomotion (Duysens et al., 1992; Zehr et al., 1997). Perturbation to the dorsum of the foot resulted in reduced ankle dorsiflexion and greater knee flexion during swing phase (Eng et al., 1994; Zehr et al., 1997). In contrast, perturbations to the sole of the foot produced an ankle dorsiflexion response during stance to swing transition as well as a knee flexion response during mid-swing (Zehr et al., 1997).

Previous work by Schillings and colleagues (2005) comparing healthy younger and older adults, found that mechanical perturbation applied to the foot during walking evoked smaller amplitude muscle reflexes and more failures to clear the obstacles in older adults. However no significant kinematic differences were observed (Schillings et al., 2005). Further, in this work toe clearance was not measured and toe clearance is an important measure of fall risk (Mills et al., 2008). The minimum toe clearance (MTC) during normal walking is about 13mm (Levinger et al., 2012), and it is known to decrease with age (Tinetti, Speechley & Ginter, 1988). The lack of significant kinematic differences between age groups could possibly be explained by the sensitivity of the kinematic measurement tool and lower resolution due to larger divisions of the gait cycle. Further the type of mechanical perturbation employed activated a relatively smaller portion of the cutaneous afferents compared to using electrically-evoked cutaneous perturbations, which has the ability to activate a larger portion of cutaneous afferents. In addition cutaneous reflexes afford more rigorous control of stimulus intensity and location compared to mechanical perturbations (Burke, 1999). Previous work in our lab employed high-resolution kinematic analysis to investigate cutaneous reflexes evoked with electrical stimulation to the dorsum of the foot during walking in healthy younger and older adults (Brodie et al., submitted). We found that in older adults the kinematic responses to the perturbation were eroded with significant reductions in the magnitude of ankle plantarflexion displacement, plantarflexion velocity, knee flexion displacement and angular velocity responses during swing. These differences contributed to a blunted toe clearance elevation response in mid swing in the older adults compared to the young. (Brodie et al., in preparation).

It is currently unclear if the age-related erosion of responses seen with stimulation to the dorsum of the foot would present similarly with perturbation to the sole of the foot. To that end this study sought to determine if stumble reactions, evoked with electrical stimulation of the distal tibial nerve innervating the sole of the foot during walking were reduced in magnitude in older adults compared to young adults. Based on previous findings of age-related changes to stumble reactions evoked with stimulation to superficial peroneal nerve, we hypothesized that there would be an age-related degradation in both the EMG and kinematic responses to tibial nerve stimulation during walking whereby healthy older adults will have reduced amplitude of reflexes compared to young adults. Further we hypothesize that there will be a decreased toe clearance elevation response to perturbation which reflects an inability to remove the end point effector, the foot, from the perturbation during walking.

2.2 Methods

2.2.1 Participants and Procedure

Fourteen healthy young adults (YOUNG) below the age of 40 years (7 males, 7 females, and mean age 25.4±5.4) and twelve healthy older adults (OLD) above the age of 70 years (8 males, 4 females, and mean age 76.7±4.8) free of any known neurological, musculoskeletal or metabolic conditions participated in the study. Participants walked for approximately 10 minutes on a treadmill at an average walking speed of 2.5 m/s. Participants wore an overhead supported safety harness and an automatic shut off mechanism that would stop the treadmill and support the participant in case of an accidental fall. The harness was loosely suspended so that it did not provide extra stability during the experiment and allowed for natural arm swing. The study protocol was approved from Human Research Ethics Committee at the University of Victoria and participants provided written consent.

2.2.2 Nerve stimulation

Surface electrodes (Thought Technology, Ltd., Montreal, PQ, CAN) applied over the distal tibial nerve at the right ankle. Throughout the walking cycle electrical stimulation was delivered psuedorandomly with trains of 5 X 1.0 ms pulses at 300Hz (Grass S88, Grass Instruments, AstroMed Inc) with no more than one stimulation per gait cycle and up to 3 gait cycles without simulation for a total of 240 stimulated cycles. The tibial nerve was stimulated at approximately 2 times radiating threshold (RT) (where a clear radiating parasthesia was reported in the nerve innervation area) with a mean stimulation intensity of 2.0 ±.4 and 2.2.± 0.4 times RT for the OLD and YOUNG respectively.

2.2.3 Electromyography

Bipolar surface EMG was recorded from ipsilateral (right) soleus (SOL), medial gastrocnemius (MG), tibialis anterior (TA), vastus lateralis (VL) and biceps femoris (BF) using disposable Ag-AgCl surface electrodes (Thought Technology (Uni-GelTM, T3425). Recording sites were shaved, gently abraded and cleansed using an alcohol swab. Ground electrodes for EMG recordings were placed on nearby electrically neutral areas such as the patella. EMG recordings from all muscles were pre-amplified and band pass filtered at 100-300 Hz (P511 Grass Instruments, AstroMed Inc.) and full-wave rectified.

2.2.4 Kinematics

Lower limb kinematics and gait parameters were measured using eight Vicon® MX-T20S 3-D motion analysis cameras (Vicon Motion Systems, Oxford, UK). Reflective markers were placed bilaterally on the pelvis, knee, ankle, head of fifth metatarsal and heel, and clustered makers were placed on thigh, shank and feet. Reconstruction of anatomical landmarks was based on the 6-degrees of freedom model (Collins et al., 2009) and used to determine joint angle, angular velocity and toe height. Sagittal plane joint angles were calculated for the ankle and knee bilaterally from segment markers for the foot, shank, thigh and pelvis. Joint angular velocity was calculated as the time-differential of joint angular displacement. Toe clearance was determined as the vertical height of the 5th metatarsal head marker relative to the walking surface. The beginning of each gait cycle, corresponding to the timing of heel-strike, was based on the time index when the ipsilateral heel maker reached its lowest vertical point.

2.2.5 Data Acquisition and Analysis

EMG data were sampled at 1000 Hz using a 16 bit A/D converter connected to a computer running custom-written LabView software (National Instruments, Austin, TX) while kinematic data was sampled at 100Hz using the Vicon Nexus 1.7.2 software and analyzed using the Visual 3D software. Kinematic data were interpolated, synchronized with EMG data and Butterworth filtered at 10Hz data using custom-written Matlab (Mathworks, Natick, MA) software. Post-acquisition, all data was partitioned into 16 equal time bins based on division of the gait cycle, beginning with initiation of stance at heel strike. EMG and kinematic reflexes to the stimuli occurring in each bin were averaged. EMG and kinematic data recorded without stimulation (i.e. background) for each bin were also averaged. EMG and kinematic responses to stimulation were subtracted from background data for the corresponding bin yielding subtracted reflex traces for each bin of the gait cycle (~10-20 observations per bin).

2.2.6 EMG Analysis

Stimulation artifact was removed and the EMG data were filtered using a dual-pass third-order Butterworth low pass filter at 40Hz. EMG reflexes were only considered significant if their amplitude was over a 2 S.D. band calculated from pre-stimulus subtracted values. The reflexes for each participant were analyzed for “net reflex effect” using the average cumulative reflex activity for 125ms post stimulation ($ACRE_{125}$) (adapted from Zehr et al., 1997; Zehr et al., 2000). This sum was then divided by the time interval (i.e. 125ms) (adapted from Zehr, et al., 1997; Zehr et al., 2000). A window of 125ms was chosen to capture the majority of response necessary to relate the net EMG reflex effect with the net mechanical outcome (i.e. movement kinematics; see below), while minimizing significant voluntary contributions (see Zehr et al., 1995). Mean reflex and background EMG (bEMG) were normalized to the percentage maximum average bEMG during the unstimulated walking cycle.

2.2.7 Kinematic analysis

Angular displacement reflexes were taken as the maximal excursion in mean subtracted traces from 70ms-220ms window. This window was chosen to reflect the delays between the EMG response and the peak mechanical response based on an electromechanical delay in human skeletal muscle (Cavanagh & Komi, 1979) as well as the presence of the peak response in both the YOUNG and OLD. Angular velocity responses were taken as the peak amplitude of mean subtracted velocity within this window. Toe clearance was the vertical height of the 5th metatarsal head marker relative to the walking surface.

2.2.8 Statistical analysis

Using Statistica 10.0 (STATISTICA™, StatSoft Inc.) a 2 X 16 repeated measures analysis of variance was conducted separately for unstimulated background EMG and kinematics (joint angular displacement and velocity and toe clearance), as well as for reflex (subtracted) EMG and kinematics to determine significant main effects for age and statistically significant age-bin interactions. A Fisher's LSD post-hoc analysis was done for significant interactions to determine significant differences between age groups at each bin. These post hoc analyses were also used to determine the presence of significant EMG and kinematic reflexes within each age group. Each bin was compared to the bin closest to a zero to determine significant reflexes from background. Planned comparisons were conducted on toe clearance reflexes during swing phase to determine differences between the two age groups on this a priori defined variable which is critically relevant to fall risk. Peak kinematics measures were compared between age groups using a one-tailed t-test. Descriptive statistics include mean, and standard error of the mean (SEM). Statistical significance level was set at $p \leq .05$

2.3 Results

Background walking pattern

Background toe clearance

OLD and YOUNG group averages for toe height during unstimulated walking are shown in Figure 5A. While there was no significant main effect for age, there was a significant interaction (F(15, 345)=1.9855, p=.02). At bins 11, 12 and 16, the OLD the toe was positioned significantly closer to the ground compared to the YOUNG.

Background ankle kinematics and lower leg EMG

OLD and YOUNG group averages of joint angular displacement and angular velocities for the ankle during unstimulated walking are shown in 5B and 5C. For ankle angular displacement, there was a significant main effect (F(15,360)=11.922 $p<0.002$) for age as well as significant bin by age interaction(F(15,360)=5.0110 $p<0.000$). The OLD had greater dorsiflexion at the stance-swing transition at bin 10 with peak ankle dorsiflexion of 13.68±1.35°, while the YOUNG were at 11.78 ± 1.03° (see Table 1). The OLD also had reduced plantarflexion in early swing at bins 11 – 13 compared to the YOUNG; with peak plantarflexion of 7.05 ± 1.58° as compared to 16.05 ± 1.11° in the young (see Table 1). Therefore the OLD held the ankle in more dorsiflexion throughout swing. The OLD had reduced plantarflexion velocity at bins 10 and 11 and reduced dorsiflexion velocity at bins 12 and 13 compared to the YOUNG (F(15, 360)=3.61, $p<0.001$).

The pattern of muscle activity in the lower limb during unstimulated steps of the walking trials was similar for the two groups. There were no significant differences across muscles except for in MG, which showed a significant main effect for age (F(15,360)=6.65, p=0.02) indicating a greater level of overall activity in the OLD compared to the YOUNG (Figure 6B).

Table 1. Peak background values (mean±SEM) for toe clearance joint angular displacement and velocity at the ankle and knee joints during unstimulated walking. (*) indicates significantly lower in the OLD compared to the YOUNG (p<0.05).

	OLD	**YOUNG**
Peak toe clearance	81.41 ± 2.76mm	81.16 ± 3.27mm
Peak Range of Motion		
Ankle Dorsiflexion	13.68 ± 1.35°	*11.78 ± 1.03°*
Ankle Plantarflexion	*7.05 ± 1.58°*	*16.05 ± 1.11°* *
Knee Flexion	*57.21 ± 1.18°*	*57.89 ± 1.39°*
Peak Joint Velocity		
Ankle PF	*165.57± 12.95 °/s*	*194.51 ± 38.2 °/s* *
Ankle DF	*80.46 ± 12.68 °/s*	*124.34 ± 6.52 °/s* *
Knee Flexion	*281.65.0 ± 9.36 °/s*	*289.32 ± 8.12 °/s*
Knee Extension	*288.49 ± 19.65 °/s*	*354.11 ± 9.98 °/s* *

Background knee kinematics and EMG

Group averages of joint angular displacement and angular velocities for the knee during unstimulated walking are shown in Figure 7(A-B). Despite the direction of knee displacement and angular velocity being in the same direction across the gait cycle between YOUNG and OLD, in the OLD the knee was less extended at bins 1, 15, and 16 compared to the YOUNG (F(15,360)=3.92, p<0.00). Additionally the OLD had reduced knee extension velocity at mid to late swing bins (13-15) and at heel strike (bin 1) compared to the YOUNG (F(15,360)=3.29, p<0.00*)*.

BF and VL muscles showed higher activation levels during stance and lower during terminal swing in the OLD compared to the YOUNG. VL activity was higher in the OLD than the YOUNG during stance (bin 4) and lower in the OLD at terminal swing (bin 16) (F(15,360)=1.73, p=0.04,). BF activity was higher in the OLD than the YOUNG during stance bins 2-4 and again leading into heel-strike at bin 16 (F(15,360)=3.65, p<0.00, Fisher's LSD *post hoc*).

Cutaneous reflexes during walking

Toe elevation response

Representative single subject reflex traces for toe height during stimulated walking from an OLD and YOUNG participant are displayed in Figure 8A. Group averages displayed similar results and are shown in Figure 5D. While there was no significant main effect for age or interaction between age and bin, planned comparisons across swing phase (bin 9-16) showed a significant difference in toe clearance responses at terminal stance (bin 9) in the OLD compared to the YOUNG. Interestingly, the response in the OLD reduced the toe height by 4.0 mm, while in the YOUNG it increased the toe height by 3.0 mm (see Figure 5D). Significantly lower peak toe clearance response was seen in the OLD (7.8±2.6 mm) compared to the YOUNG (15.4±3.4 mm) at mid swing (bin 12). Bins 11, 12 and 13 showed significant responses from zero (bin 3) in OLD, while bins 12, 13 and 15 were significant in the YOUNG.

Ankle kinematic and lower leg EMG responses

Representative single subject reflex traces of an OLD and YOUNG participant for ankle kinematics during stimulated walking are displayed in Figure 8B with similar group averages displayed in Figure 5E and 5F. Upon direct comparison between the age groups, there was a main effect for age for angular displacement and angular velocity of the ankle. A reduced amplitude of dorsiflexion displacement response was found in the OLD compared to the YOUNG during terminal stance, toe off and swing (bins 8, 9, 10 and 12) with mean differences of 3.24°, 4.24°, 3.78 and 2.15° respectively (F(15, 360)=2.48, p<0.002, Fisher's LSD *post hoc*). Peak angular dorsiflexion displacement for the OLD (2.78 ± 0.71°) was significantly lower than the YOUNG (7.02 ± 1.26°). In OLD, bin 9 was significantly different from zero (bin 3), while in YOUNG, bins 8, 9, 10, 12, 13 and 15 had significant responses.

Ankle angular velocity group comparisons showed significant main effect for age (F(15, 360)=7.17, p<0.013); however there was no significant interaction. Peak angular dorsiflexion velocity for the OLD (59.67±9.55°/s) was significantly lower than the YOUNG (122.32±25.18 °/s). In the OLD there was significant angular velocity response from zero (bin 5) in bin 9 for dorsiflexion and bin 11 for plantarflexion. In YOUNG, there were significant responses from zero (bin5) in both dorsiflexion and plantarflexion direction. The significant dorsiflexion angular velocity responses were seen during swing and heel strike (bins 9, 12, 13, 16 and 1) and a significant plantarflexion response in bin 11.

Table 2. Peak response values (mean±SEM) for toe clearance, joint angular displacement and velocity at the ankle and knee joints during walking. (*) indicates significantly reduced reflex in the OLD compared to the YOUNG (p<0.05).

	OLD	**YOUNG**
Peak toe clearance	7.8± 2.6mm	15.4 ± 3.4mm *
Peak Range of Motion		
Ankle Dorsiflexion	2.78 ± 0.71°	7.02 ± 1.26° *
Knee Flexion	*4.50* ± 1.38 °	*8.35* ± 1.47 ° *
Peak Joint Velocity		
Ankle PF	*26.16 ± 11.71°/s*	*34.48 ± 28.71 °/s*
Ankle DF	*59.67 ± 9.55 °/s*	*122.32 ± 25.18 °/s* *
Knee Flexion	*48.99 ± 22.31 °/s*	*101.59 ± 25.61 °/s*
Knee Extension	*22.22 ± 17.0 °/s*	*36.15 ± 19.11 °/s*

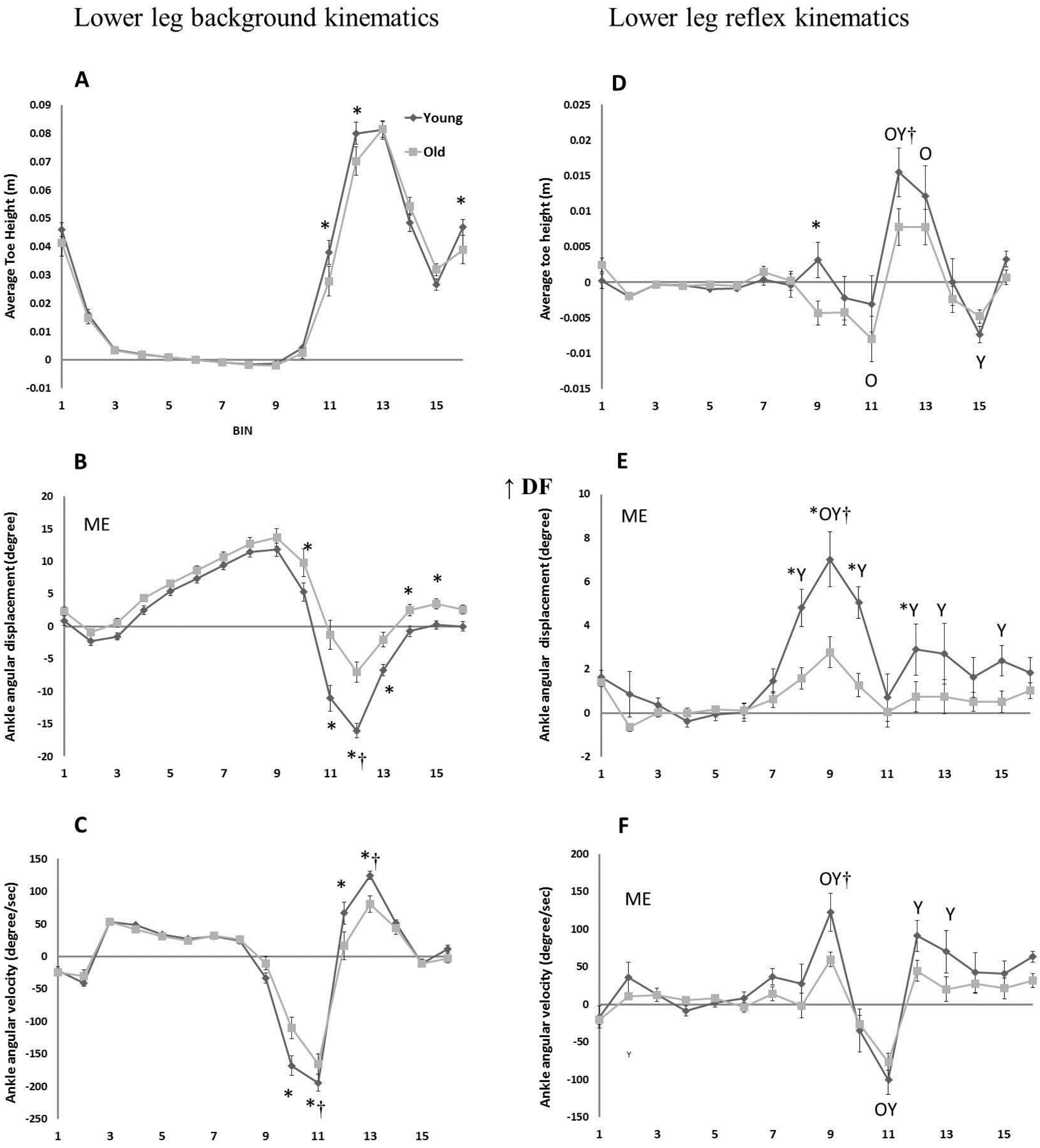


Figure 5 (A-F) Group data for background kinematics (A-C) and changes in kinematics in response to stimulation (D-F) throughout the step cycle for old (grey) and young (black). * shows significant group differences, O and Y indicates a response significantly different from zero in the Old and the Young respectively,. ME indicates a significant main-effect for age across the gait cycle. † represents significant difference in peak values. Bins 1-9 represent stance, 10-16 swing phase of gait cycle. DF=dorsiflexion

In TA, there was a significant main effect for age and interaction (see Figure 9D). Representative single subject reflex traces for an OLD and YOUNG participant are displayed in Figure 11D. The OLD had a significantly lower amplitude EMG response in TA compared to the YOUNG in swing-stance transition (bin 9-10), mid swing (bin 12-13) and terminal swing (bin 16). In MG there was a significant interaction, with the OLD showing an inhibition at mid swing (bins 12-13), while the YOUNG had an excitation reflex response. The pattern of reflex in SOL was similar for age both groups, with no main effect for age or interactions. Reflexes in TA were significantly different from zero (bin 6) in the YOUNG at the stance-swing transition (8-11) and throughout swing (12-14 and 16), while no significant responses were noticed in the OLD. Reflexes in MG were significantly different from zero (bin 2) in the YOUNG in stance at bins (3-7) and in swing at bins (12 and 13); and in the OLD in stance at bins (5 and 6). In SOL, the reflexes were significantly different from zero (bin 2) in the YOUNG in stance at bins (5-7) and in swing at bins (14 and 16); and in the OLD (zero bin was bin 9) in stance at bins (1-2, 4-7) and during swing at bin 14.

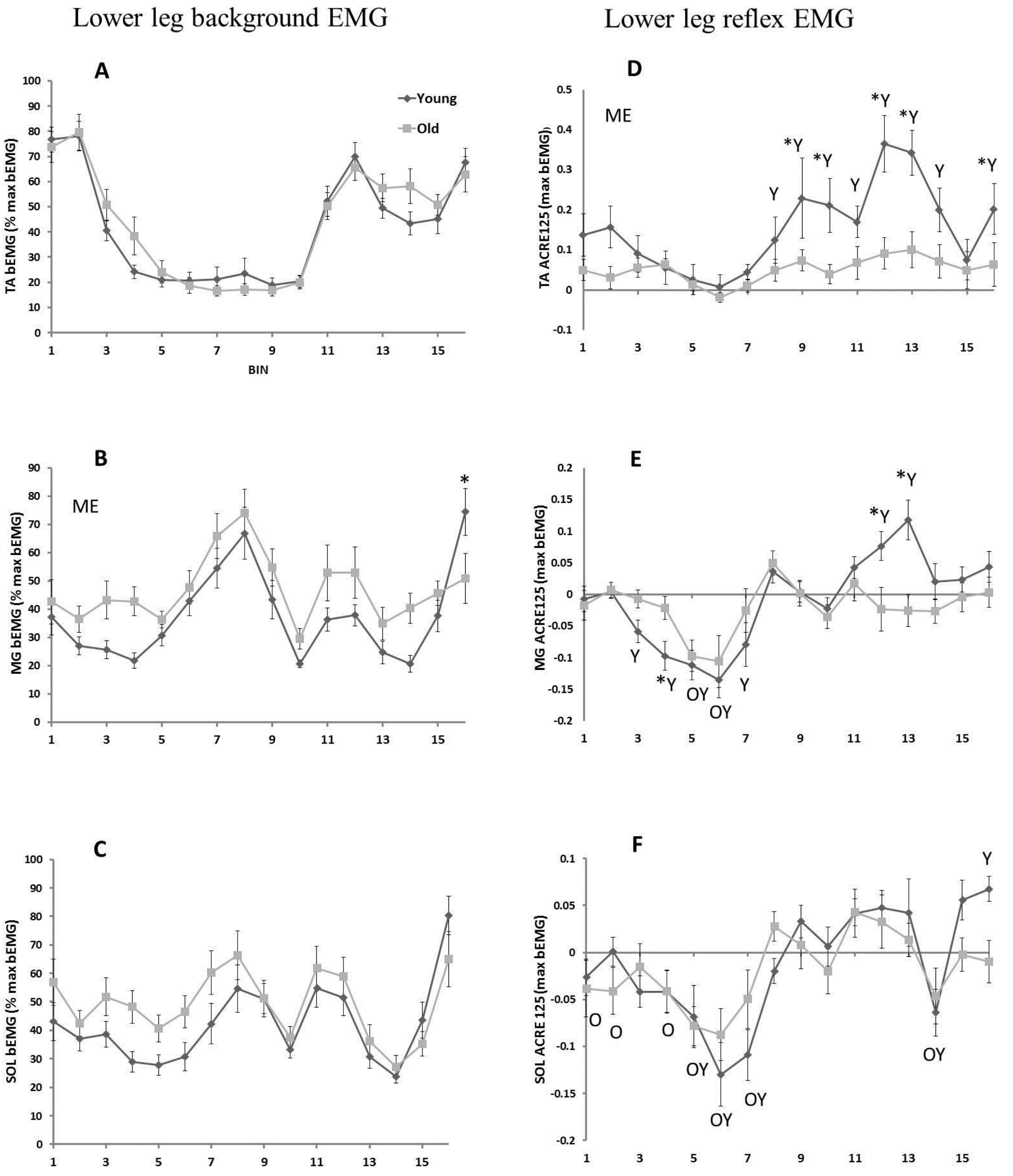


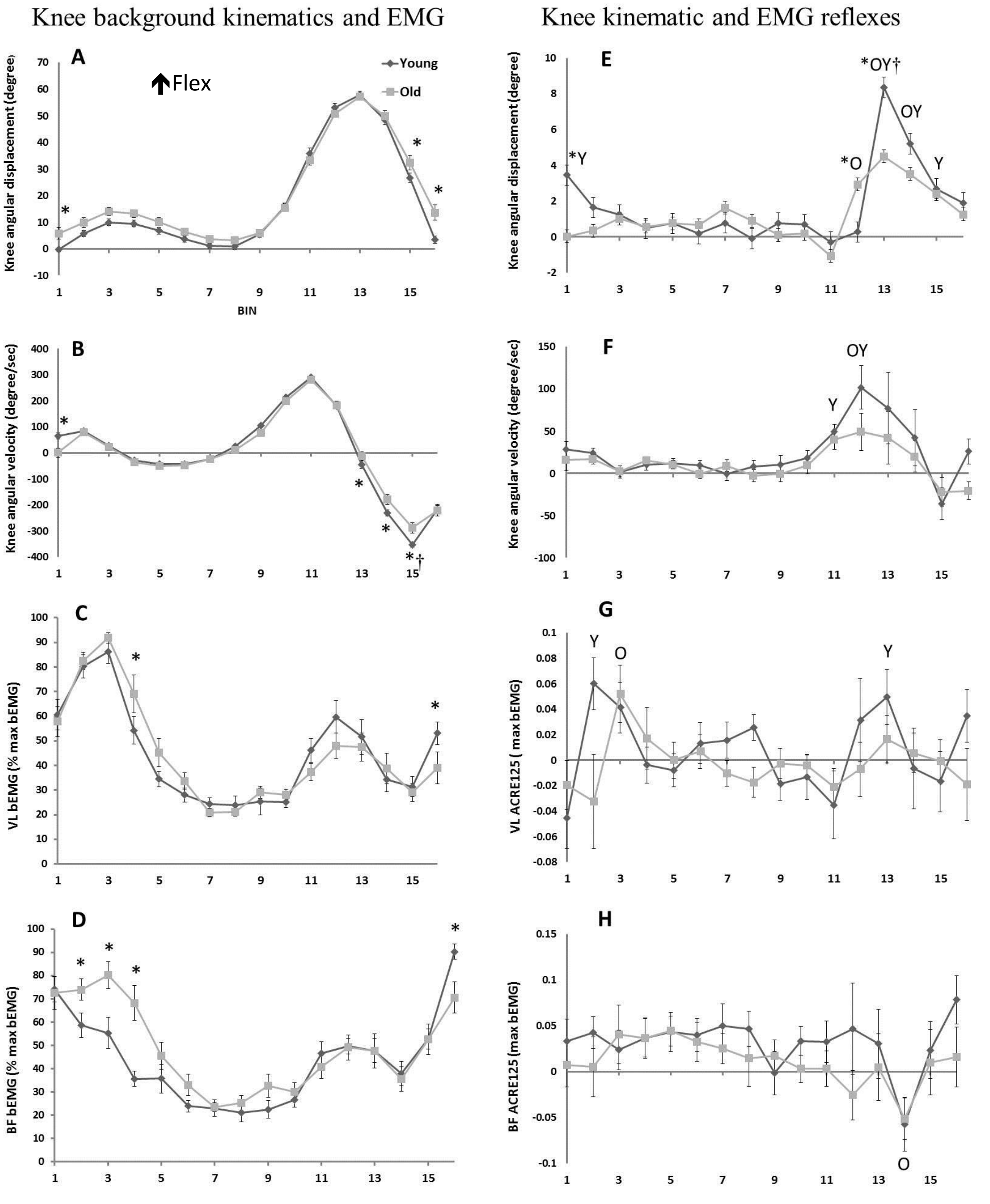
Figure 6 (A-F). Group data for background EMG (A-C) and ACRE$_{125}$ values (D-F) for TA, SOL and MG throughout the step cycle for old (grey) and young (black). Background EMG and ACRE$_{125}$ values are expressed as a percentage of the maximum; background EMG during the step cycle. * shows significant group differences, O and Y indicates a response significantly different from zero in the Old and the Young respectively. ME indicates a significant main-effect for age across the gait cycle. † represents significant difference in peak values. Bins 1-9 represent stance, 10-16 swing phase of gait cycle.

Knee kinematic and EMG responses

Average kinematic and EMG group responses to stimulation for the knee are shown in Figure 7(E-H), with single subject kinematic comparisons shown in Figure 8C. There was no main effect for age for these measures nor was there a significant interaction for knee angular velocity; however, a significant interaction was seen in knee angular displacement (F(15,360)=1.94, p=0.019). The OLD had a significantly greater knee flexion at bin 12 compared to the YOUNG, but displayed significantly less knee flexion displacement in mid-swing (bin 13) and heel strike (bin 1).

Both groups showed a significant knee flexion displacement response from zero (bin 6) in swing. There was a significant flexion displacement response in the OLD in early to middle swing (bins 12-14); while for the YOUNG flexion displacement response was present in late swing (bins 13-15) and at heel strike (bin 1). Both groups also showed a significant reflex in knee angular velocity toward flexion during swing (bin 11-13 for the YOUNG and bin 12 for the OLD).

There was no significant main effect for age or interaction between groups in the EMG reflexes in VL and BF. Reflexes in VL were significantly different from zero (bin 5) in the YOUNG during stance (bin 2) and swing (bin 13), while for the OLD, a significant reflex was seen during bin 3 of stance. Reflexes in BF were not significantly different from zero (bin 9) in the YOUNG. In the OLD a significant reflex was seen during swing (bin 14) from zero (bin 2).


Knee background kinematics and EMG

Knee kinematic and EMG reflexes

Figure 7 (A-H) Group data for background kinematics (A,B), and background EMG (C,D) as well as changes in kinematics in response to stimulation (E,F) and ACRE$_{125}$ values (G,H) for movements and muscles acting at the knee throughout the step cycle for OLD (grey) and YOUNG (black). Background EMG and ACRE125 values are expressed as a percentage of the maximum; background EMG during the step cycle. * shows significant group differences , O and Y indicates a response significantly different from zero in the Old and the Young respectively, † represents significant difference in peak values. Bins 1-9 represent stance, 10-16 swing phase of gait cycle. Flex=knee flexion.

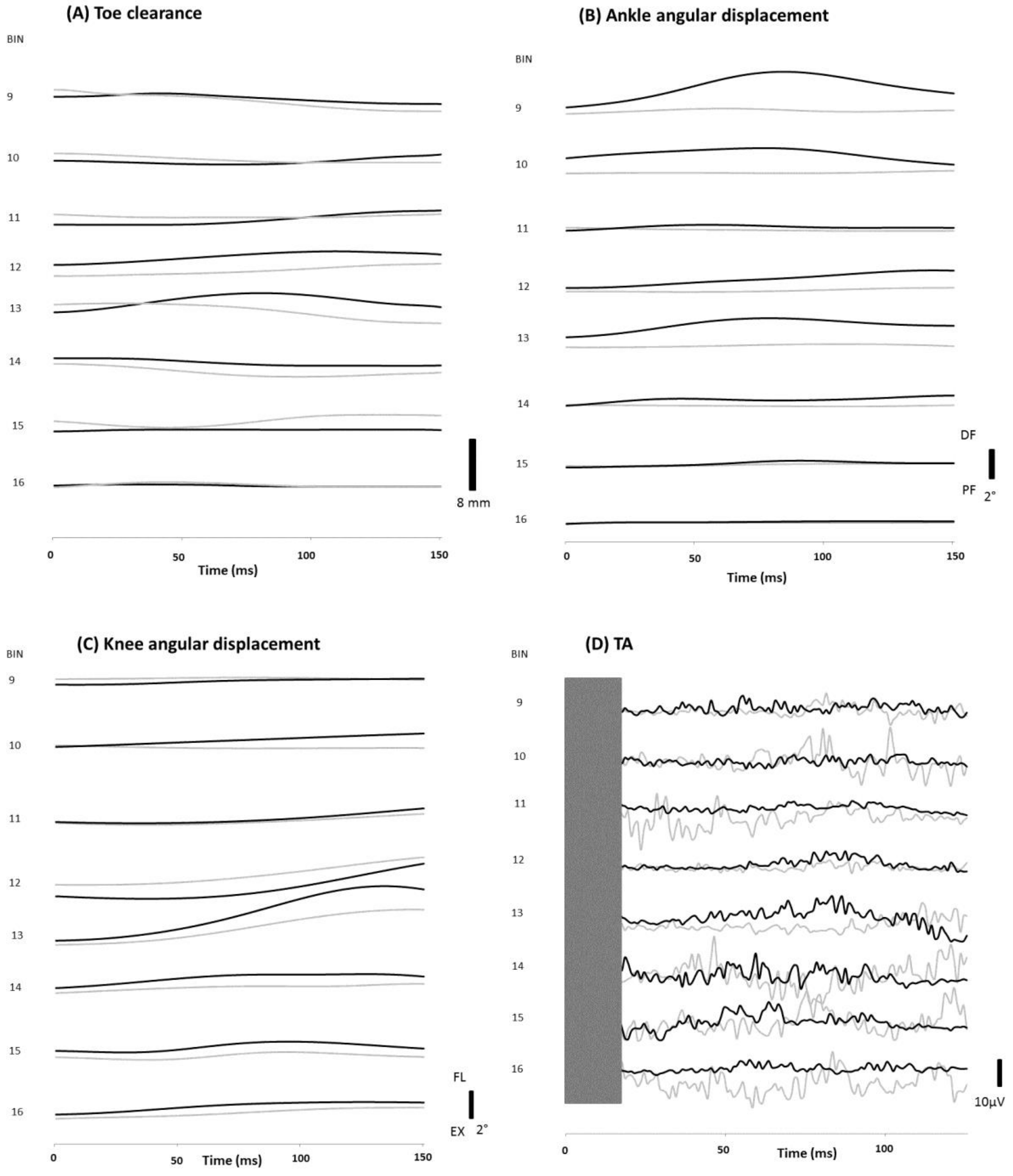


Figure 8 (A-D). Representative single subject responses for toe clearance (A), ankle angular displacement (B), knee angular displacement (C) and EMG for TA (D) during swing phase (bins 10-16) of the gait cycle with the YOUNG indicated with solid black and OLD with gray. Angular displacement is reported in degrees and angular velocity in degrees per second. EMG traces are reported as percentage of peak background EMG across the step cycle. DF= dorsiflexion, PF= plantarflexion, FL= flexion, EX= extension. Stimulation artifact is replaced with a grey box in (D).

2.4 Discussion

This is the first study to compare and contrast kinematic and EMG reflexes to non-noxious, electrically-evoked stimulation to the sole of the foot between OLD and YOUNG during walking. Further this is the first study to explicitly measure toe clearance responses following stimulation to the sole of the foot. The main finding of this work was the significant erosion of the stumble reactions in the OLD compared to the YOUNG. While there were significant stumble reactions in the OLD at similar bins with similar signs as the YOUNG, the erosion of these responses was evident as either a significant reduction in amplitude or a sign reversal in toe clearance, ankle and knee joint displacement and ankle velocity as well as ankle muscle activity. These degraded responses were superimposed on altered kinematics observed during unstimulated walking in the OLD compared to the YOUNG. This combination of degraded reflexes and altered unstimulated kinematics resulted in significantly reduced toe clearance in the OLD and could suggest that these older adults are in the prodromal stage of fall risk.

Mid-Swing – Reflex erosion and altered unstimulated walking

Encountering an object or the ground with the foot during swing phase can be destabilizing to dynamic postural control during gait and result in falls (Berg et al., 1997). Therefore, reduced toe clearance and the resultant increased potential impact of the swing leg with obstacles or the ground, could contribute to increased fall risk (Lai et al., 2012). In the present study there was significantly reduced amplitude in toe clearance with stimulation in the OLD during mid-swing (bin 12). This reduced response was superimposed on the significantly decreased toe clearance also observed in OLD during unstimulated walking (bins 11-12). Despite the absence of falls in the last year for the sample of OLD in the current study, the additive effect of altered reflexes and reduced background toe clearance could increase the risk of tripping in these healthy OLD compared to the YOUNG. It should be noted that this lower toe clearance response occurred at peak toe clearance where the foot is furthest from the ground. However, this degraded reflex could represent a decreased ability to modify toe clearance in response to an obstacle during mid-swing.

The reduced toe clearance in the OLD compared to the YOUNG in both unstimulated and stimulated walking could result from a combination of altered kinematic responses throughout the kinematic chain in the lower limb bilaterally. Though this study recorded from ipsilateral knee and ankle joints, we acknowledge that toe clearance could be affected by altered reflexes at the ipsilateral hip joint as well as the contralateral limb. In the present study, significantly reduced dorsiflexion ankle displacement response seen in the OLD during mid-swing (bin 12) as compared to the YOUNG is consistent with the lower toe clearance response (bin 12) observed in the OLD. This decreased ankle dorsiflexion amplitude could be due to increased joint stiffness in passive joint structures limiting the kinematic expression of a reflex (Vandervoort et al., 1992) or altered EMG reflexes.

It is interesting that in the OLD during swing (bins 11-12) in unstimulated walking the toe was closer to the ground given that the OLD held their ankle joint in increased dorsiflexion (i.e. less plantarflexion) throughout swing (bin 11-13). This suggests the involvement of other joints other than the ipsilateral ankle and knee. The dorsiflexed position of the ankle in the OLD in unstimulated walking could have limited the expression of the dorsiflexion response as the OLD are closer to end range dorsiflexion relative to the YOUNG. Moreover, during unstimulated walking the OLD had reduced ankle dorsiflexion velocity during mid-swing which could have contributed to the decreased dorsiflexion displacement response due to decreased ongoing limb angular momentum. Similarly, Zehr and colleagues (1997) found that following electrical stimulation of nerve innervating the sole of the foot, there was an increased ankle dorsiflexion response to remove the foot from the stimulus. However, this response was dissimilar to the current results in that it was only noticed during stance to swing transition without any overt reflexes during mid-swing. The excitatory reflex in TA and MG seen in the current study in the YOUNG during mid-swing (bin 12-13) was absent in the OLD. This finding supports the decreased dorsiflexion displacement observed in the OLD during mid-swing (bin 12). Further, the excitatory reflex seen in the YOUNG in both MG and TA would result in a co-activation of muscles acting at the ankle joint as seen by Zehr and colleagues (1997). This co-activation response is missing in the OLD.

Similar to Zehr et al. (1997), we found that in the YOUNG, stimulation to the sole of the foot evoked a significant knee flexion response during mid-swing. Our comparisons between the YOUNG and OLD showed that the contributions of knee flexion responses to the obstacle avoidance strategy was impaired in the OLD as evidenced by the significantly reduced overall knee flexion response peak amplitude at mid-swing (bin 13) compared to the YOUNG. The present results are similar to the reduced but non-significant knee flexion response observed in older adults when a mechanical perturbation was applied to the foot during swing (Schillings et al., 2005). The inability to detect a significant flexion response may be related to the limited sensitivity of the kinematic measurement tool employed, smaller relative proportion of the cutaneous field stimulated, as well as the lower phase resolution of the gait cycle for analysis (Schillings et al., 2005; Domingo et al., 2013).

The stumble reactions in the YOUNG as well as the erosion of these responses in the OLD were specifically sculpted based on the anatomical location of the stimulus. Stimulation to the sole of the foot evoked knee flexion and ankle dorsiflexion in the YOUNG in mid swing, while stimulation to the top of the foot evoked an obstacle avoidance response comprising plantarflexion and knee flexion in mid swing (Zehr et al., 1997; Brodie et al., submitted). Our earlier study found these mid swing responses at both the ankle and knee reduced in the older adults compared to the young contributing to decreased toe clearance seen throughout swing (Brodie et al., submitted).

Interestingly, in spite of an overall decreased knee flexion response in the OLD compared to the YOUNG, the OLD initiated the knee flexion response earlier in the gait cycle than the YOUNG. This resulted in a significant knee flexion reflex in the OLD at bin 12 that was not present in the YOUNG. Given that during unstimulated walking the knee position (i.e. displacement) is nearly identical between the groups, the greater knee flexion responses in bin 12 would likely result in the knee being more flexed at this point in swing phase in the OLD than the YOUNG. Thus, the lower toe clearance response seen in the OLD at bin 12 is most likely not contributed to by altered ankle responses or unstimulated kinematics at the knee.

Terminal Stance -Reflex erosion and altered unstimulated stepping

During terminal stance (bin 9), there was a reflex reversal in toe clearance between the age groups. The reflex in the OLD brought their toe closer to the ground by 4.3mm, while in the YOUNG the reflex moved the toe upwards away from the ground/stimulus by 3.2mm. Therefore there was a 0.75 of a cm difference in the toe clearance response between the groups. Concurrently, the YOUNG had significant dorsiflexion responses in bins 8-10 which explains the upward toe elevation response in the YOUNG. In the OLD the responses are less straightforward because the direction of the toe responses towards the ground is concurrent with significant ankle dorsiflexion at bin 9, although this dorsiflexion is significantly less in amplitude than the YOUNG. The movement of the toe closer to the ground is likely related to the OLD having a dorsiflexion response that promotes weighting whereas in the YOUNG the dorsiflexion response contributes to toe elevation as the lower limb continues to progress forward during terminal stance. Since the toe marker is placed on the head of the fifth metatarsal, ankle inversion could cause the 5th toe to move closer to the ground in the OLD. This would explain this toe movement in light of the fact that the foot is already on the ground prior to the stimulus as indicated by the unstimulated walking toe height data.

During unstimulated stepping, the OLD demonstrated greater dorsiflexion (or reduced plantarflexion) at the stance to swing transition and initial swing (bin 10) than the YOUNG. Our results of reduced plantarflexion at stance to swing transition in the OLD corroborate findings from earlier studies (Begg & Sparrow, 2006; Arnold et al., 2014; Brodie et al., submitted). This reduced plantarflexion through swing (bins 11-13) is likely related to age-related strength and power loss in plantar flexors resulting in reduced push-off force at stance to swing transition in OLD (Winter et al., 1990; Christ et al., 1992; Judge et al., 1996). Of note, this reduced plantarflexion at stance to swing transition in the OLD was not supported by muscle activity; there was significantly higher overall activity in MG in the OLD as reflected by a main effect for age.

Late swing to heel strike- Altered unstimulated stepping

During late swing and heel strike in unstimulated stepping, knee kinematics shows significantly reduced knee extension angular displacement (bin1, 15-16) and slower angular velocity (bin 1, 13-15) in the OLD. This is similar to Begg and Sparrow (2006) who showed that the OLD favored a flexed-knee gait during weight acceptance. This limited knee extension can be attributed to physiological strength loss in quadriceps with age (Young, Stokes & Crowe, 1984) or osteoarthritis-related quadriceps weakness (Omori et al., 2013). Background muscle activity in VL complements these findings where the OLD had significantly lower activity during terminal swing (bin 16) than YOUNG. Further, reduced BF activity in terminal swing (bin 16) in unstimulated walking in the OLD suggests a reduction in co-contraction at terminal swing in preparation for heel strike. Further there was higher overall activity in MG during stance, perhaps contributing to a "tentative" gait often seen in older adults characterized by knee flexion in stance phase and decreased excursion at the ankle joint in swing (Nigg & Skleryk, 1988).

Clinical implications

The significantly reduced kinematic and EMG reflexes to tibial nerve stimulation in OLD suggest that their functional capacity to respond to perturbations during walking is eroded; however this erosion is subclinical given that these older adults have no history of falls. Further these reduced reflexes were superimposed on altered kinematics seen during stimulated walking in the OLD compared to the YOUNG. Together these changes in neural control, that are part of the normal aging process, potentially place these older adults in the prodromal phase for fall risk. While the current study does not isolate the locus of impairment in the nervous system, previous research has found reduced sensitivity of sensory receptors of the foot (Maki et al., 1999; Perry et al., 2006), reduced amplitudes in stretch reflexes (Burke & Kamen, 1996) and longer latencies in electrical and mechanical responses in older adults (Schilling & colleagues, 2005; Bernard & Seidler, 2012). Thus the study of the integrity of stumble corrective reflexes adds to a basic understanding of age-related changes in neuromechanical control of gait. Further, by using reflexes as early biomarkers of fall risk, this methodology has potential application for early diagnosis of fall risk and a means to evaluate the efficacy of fall prevention rehabilitation interventions for the older population. This work supports the development and implementation of fall prevention interventions that can enhance reflex control such as footwear insoles that stimulate cutaneous mechanoreceptors of the foot (Maki et. al., 1999).

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