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All our science, measured against reality, is primitive and childlike—and yet it is the most precious thing we have.

--Albert Einstein

The human understanding is no dry light, but receives infusion from the will and affections; whence proceed sciences which may be called "sciences as one would". For what a man had rather were true he more readily believes. Therefore he rejects difficult things from impatience of research; sober things, because they narrow hope; the deeper things of nature, from superstition; the light of experience, from arrogance and pride; things not commonly believed, out of deference to the opinion of the vulgar. Numberless in short are the ways, and sometimes imperceptible, in which the affections color and infect the understanding.

--Francis Bacon

University of Alberta

A functional interpretation of electrically-evoked cutaneous reflexes during human walking

by

Elwood Paul Zehr, B.P.E., M.Sc. ©

A thesis submitted to the faculty of Graduate Studies and Research in partial fulfillment
of the requirements for the degree Doctor of Philosophy.

Division of Neuroscience

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Dedication

This thesis is dedicated to the memory of my late father, Elwood Eli Zehr, who showed that hard work and tenacity produce success.

Abstract

The extent to which peripheral reflexes function during human voluntary behaviour is unclear. This thesis focused upon the function of lower limb segmental reflexes in humans. The primary goal was to determine the function of cutaneous reflexes during walking. Additionally Hoffman (H-) reflexes during voluntary static activity were also studied. This thesis established appropriate methodology for the study of cutaneous reflex function and examined the contribution of cutaneous afferent input by electrically stimulating peripheral cutaneous nerves during walking. A technique which provided a global measure of reflex changes in muscle activation (electromyography, EMG) suitable for correlation to changes in leg mechanics was developed. This technique was found to be free of contamination from voluntary muscle activation, reliable and reproducible, and correlated with changes in muscle force changes in simple, single-joint static movements.

Reflexes to stimulation of nerves innervating different surfaces of the foot were studied during treadmill walking in neurologically intact (NI) subjects. The nerves studied were the superficial peroneal (SP, innervates the top of the foot), sural (lateral margin of foot), and tibial (plantar foot surface). After SP nerve simulation, the net response during swing was to flex the knee and reduce flexion at the ankle; a stumbling corrective response. Tibial nerve stimulation led to a withdrawing response at the stance to swing portion of the step cycle and a contacting response at the swing to stance transition. After sural nerve stimulation, the net response during early stance was to stabilize the orientation of the foot to preserve balance. During swing sural reflexes function to withdraw the stimulated foot from a contact point. In total, cutaneous reflexes

act to preserve balance and a stable locomotor pattern throughout the human step cycle. After stroke, cutaneous reflexes no longer perform their same function, and, at least after SP stimulation, there is more EMG suppression than that seen in NI subjects. In contrast to NI, the correlation between EMG effects and joint kinematics with SP stimulation is stronger during stance in stroke subjects.

Presynaptic inhibition of the soleus H-reflex induced by stimulation of the common peroneal nerve was shown to interact strongly with centrally-generated facilitation via the Jendrassik manouevre during tonic contraction. Thus, this is further evidence that peripherally generated inputs can strongly modulate central motor commands.

In total, the data contained in this thesis suggest that afferent input is used by the central nervous system to allow the expression of flexible and behaviourally relevant motor acts.

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I must thank first of all my wife, Lori, for following me to the frozen Arctic (or so it often seems!) on my scientific quest.

I must secondly acknowledge the support that my advisor, Dick Stein, provided during my doctoral training. I will always be grateful for the opportunity to pursue my own projects and to receive such excellent funding for presentation of my work at many prestigious conferences.

Also I would like to thank my Japanese colleagues, Dr. Tomoyoshi Komiyama and Dr. Kinya Fujita not just for their assistance with the experiments but also for their excellent companionship. Ii kenkyu o shimashita ne? Gambarimashita. Domo arigato gozaimashita.

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1. General Introduction[1]

"reflex: n. (physiol.) an automatic or involuntary response to a stimulus"

-New Webster's Dictionary and Thesaurus of the English Language (1992)

"A simple reflex is probably a purely abstract conception, because all parts of the nervous system are connected together and no part of it is probably ever capable of reaction without affecting and being affected by various other parts, and it is a system certainly never absolutely at rest. But the simple reflex is a convenient, if not a probable, fiction. Reflexes are of various degrees of complexity, and it is helpful in analyzing complex reflexes to separate from them reflex components which we may consider apart and therefore treat as though they were simple reflexes."

-Sir Charles S. Sherrington (1906)

The general concept of a reflex has been around for centuries; broadly speaking this concept encompassed some form of general motor response to sensory input. Both Fernel and Descartes made use of similar concepts, particularly in differentiating voluntary from so-called animal behaviour (cited in Brazier, 1959). It was not until 1748 that the first distinct reference to "reflex actions" was made by David Hartley (cited in Bastian, 1891). However, it was not until Georg Prochaska that the actual term reflex was more definitely described (cited in Bastian, 1891 and Shepherd, 1994). In 1784, Prochaska described the "...reflexion of sensorial into motor impressions..." which may

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[1] **A portion of this chapter will be published as "Neuro-mechanical function of reflexes during locomotion" authored by E. Paul Zehr and Richard B. Stein and appearing in *Biomechanics and Neural Control of Movement*, Edited by Jack Winters and Patrick Crago.**

take place "…either with consciousness or without…", thus making the first documented use of the word.

It may be argued that the term "reflex" was brought into common scientific usage by Sherrington (1906) and his exhaustive study of the nervous system. Since that time and until rather recently, the term had come to connote a stereotyped and distinct neural response, occurring largely at spinal level, evoked by a fixed, usually peripheral, stimulus. In the 20th century and previously, peripheral sensory inputs were shown to have powerful and sometimes stereotyped reflex effects in many animals (Sherrington 1906, 1939). These inputs modify the behaviour of various animals during many different behaviours (Rossignol 1996). An emerging concept over the past 25 years has been that, while the term reflex is a convenient one, the connotation that reflexes are stereotyped and immutable is patently false. It should be mentioned that the concept of a stereotyped response has persisted despite Sherrington's (1900) own experimental observations in spinalized preparations that reflexes certainly had some fixed components, but that the same input did not necessarily always generate the same output. Indeed, although he was addressing a somewhat different issue, Sherrington's own words highlighted at the beginning of this section address indirectly the fallacy of the simple, stereotyped reflex response. Perhaps Brooks (1986) has set down the most tenable definition of reflexes when he stated that they are "…best defined as responses evoked with great probability by particular stimuli". Rather than immutable, reflexes have been shown to be quite sensitive to *modulation*. However, the concept of the simple reflex persists as captured in the definition offered by Nicholls et al. (1992) "The simplest motor actions are reflexes, mediated by relatively straightforward circuitry in the spinal cord".

The usage of and reliance upon peripheral input in eliciting reflex responses in conjunction with central patterning has been documented for many behaviours, including walking, in mammals (particularly the quadrupedal cat; Grillner & Duboc 1988, Pearson 1993). However, the functions that reflexes might actually serve during such natural and purposive behaviours as walking has remained unclear. Further, it is only recently that the extent to which the bipedal human makes use of reflex responses generated by sensory input from peripheral receptors has been delineated in any detail. The *function* of reflexes in humans is only slowly becoming clearer.

Here the focus is to describe some of the reflex effects observed in human lower limb muscles subsequent to electrical stimulation of nerves at a level sufficient to activate muscle and cutaneous afferents. A goal is to describe the modulation of reflexes within and between given behaviours, which will be described as phase- and task-dependent reflex modulation, respectively. The main thrust of this review and this thesis is to elucidate the function of reflexes in humans and, as such, papers dealing with human experiments will be cited primarily and animal research supplemented where appropriate. Throughout this paper an attempt will be made to provide ample examples of the plasticity of reflex responses; i.e. reflex modulation will be shown to be behaviorally relevant and to have task-, phase-, and intensity dependence.

1.1 A note on methods

The majority of experiments mentioned make use of the two most common methods of investigating reflex function in humans: the Hoffmann (or H-) reflex and modulation curves of the rectified and averaged surface electromyogram (EMG). The H-reflex can provide information on presynaptic (to the motoneuron) modulation of reflexes (for review see Schiepatti 1987), while EMG modulation curves represent the integrated net neural response and are a direct measure of motor output. Accordingly, analysis of EMG modulation curves and H-reflexes can often reveal quite different aspects of reflex modulation and function and must be interpreted carefully.

1.2 Conditioning of cutaneous and H-reflexes while seated or lying down

The modulation of the SOL H-reflex by remote muscle contraction has been studied in various patient populations, but was first described in relation to stretch reflexes in the late 1800s (Jendrássik 1883). After some controversy early in this century (Sommer 1940), the SOL H-reflex was eventually shown to be potentiated by contraction of other muscles remote from the lower limb under study (Landau & Clare 1964). Since that time, many experiments have been repeated in both healthy and neurologically impaired subjects. Interestingly, some of these studies have shown that oral muscle activity has very powerful effects (Miyahara et al. 1996) on the H-reflex, an observation originally made by Jendrássik regarding the stretch reflex (Jendrássik 1883) but subsequently ignored. Experimentation has shown that the reflex facilitation is not due to changes in gamma outflow (Hagbarth 1975) or to post-synaptic facilitation (Dowman & Wolpaw 1988). The most likely remaining candidate is modulation of Ia presynaptic inhibition (PSI), but this remains to be conclusively demonstrated.

The effects of stimulating the common peroneal (CP) nerve on voluntary soleus (SOL) motor activity has been studied in both the normal and spastic human (Crone et al. 1991, Levin & Chapman 1987). CP stimulation has been shown to induce classical reciprocal inhibition in SOL motoneurones as measured by changes in the H-reflex (Tanaka 1974). Levin and Chapman (1987) found that CP nerve stimulation at 1.4 x motor threshold (MT) caused a reduction in the SOL H-reflex at short latency (40-90 ms) in neurologically intact subjects. A later facilitation was also observed, reaching a maximum between 170 and 190 ms post-stimulus. When these researchers stimulated the largely cutaneous superficial peroneal (SP) nerve (1.5 x perceptual threshold), only facilitation was observed in the SOL H-reflex. The spinal cord injured patients showed less H-reflex depression subsequent to CP stimulation and no effect or mild inhibition after SP stimulation. In a recent study, Iles (1996) has shown that cutaneous and corticospinal input can markedly alter the modulation of the SOL H-reflex induced by presynaptic inhibition via peripheral inputs. He showed that cutaneous afferents converge on spinal interneurones so as to reduce presynaptic inhibition and thus facilitate the H-reflex.

There exists a wealth of information on the effects of cutaneous nerve stimulation on lower leg musculature in intact subjects. Delwaide and collaborators (Delwaide et al. 1981, Delwaide & Crenna 1983) have shown that non-noxious sural stimulation induces marked periods of excitation in both SOL and TA muscles as measured by H-reflex modulation. However, more painful ipsilateral stimulation depresses SOL concomitant with facilitation of TA, as in the generation of a flexor reflex (Shahani & Young 1971). They also state that the response in the spastic patient is not as distinct. Others have shown cutaneous stimulation to induce triphasic response involving excitation, inhibition, and a later excitation (Gibbs et al. 1995, Jenner and Stephens 1982). Recently, Rossi et al. (1996) reported that non-nociceptive and nociceptive afferents from the medial plantar nerve (a distal branch of the posterior tibial nerve) of the foot share spinal pathways and converge on motoneurones of TA muscle in intact humans. They demonstrated that the level of descending activation of the motor pool can markedly influence which responses predominate, such that faster conducting (non-nociceptive) afferents can more easily elicit reflex discharge of the motor pool during contraction. Lastly, Kukulka (1994) showed that nonnoxious sural stimulation evokes very complex responses in human triceps surae motoneurones. The most common responses observed were a short latency (onset ~40 ms) inhibition (decrease in firing rate) and a longer latency (onset ~70 ms) excitation.

In the cat, a motor unit type specificity has been shown subsequent to sural stimulation, such that type I motor units are inhibited and type II excited (Burke 1981). Interestingly, this has also been reported for the TA muscle in human subjects (Nielsen & Kagamihara 1993).

To summarize, stimulation of muscular and cutaneous afferents in the sitting human subject induce complex excitatory and inhibitory effects on lower leg muscles. However, the exact extent to which these reflexes can be extrapolated to more functional activities such as standing and walking is not clear. The following sections will address these issues.

1.3 Reflex modulation during standing

As alluded to above, reflexes are very powerfully modulated in both the magnitude and sometimes the sign elicited during different tasks. Aniss et al. (1990) reported that stimulation of the posterior tibial and sural nerves at nonpainful levels produced changes in firing rates of muscle spindle endings both with and without alterations in SOL and TA motoneurone firing rates. This result was not shown when subjects were recumbent, even while producing active forces (Aniss et al. 1988, Gandevia et al. 1986), further providing evidence of task specific reflex effects. As well, Aniss et al. (1992) further investigated the effects of sural and posterior tibial stimulation on ongoing EMG of the SOL, TA, MG, and LG muscles. A short latency inhibition (onset ~45-50 ms) was observed in SOL after stimulation of both nerves. This effect was observed both while recumbent and during standing.

Capaday et al. (1990) found that stimulation of the CP nerve elicited a strong inhibition of SOL motor activity (as measured by the rectified and averaged EMG record) at a latency of ~60 ms. This inhibition was found at all levels of background EMG examined; there was no observed attenuation of the inhibition at higher activation levels and the responses persisted during standing and during walking.

Burke et al. (1991) examined in detail the task-dependent changes in the effect of cutaneous afferent input on several muscles of the human lower limb. Following sural stimulation, inhibition within 100 ms was recorded in TA, SOL, biceps femoris, and VL. There was no reflex effect when the muscles were not active. As well, the reflex effects in TA that occurred between 60 and 80 ms post-stimulus were different when examined while sitting, standing normally, or standing on an unstable base; the pattern (both excitation and inhibition) become more pronounced the more precarious the posture. These researchers were led to conclude that the reflex pattern within a given muscle as well as between other muscles is task dependent and that the responses may be quite plastic.

Also, Gibbs et al. (1995) showed that the triphasic (excitation-inhibition-excitation) effect that may occur subsequent to digital nerve stimulation at the toes while recumbent, persists as well during standing. However, their data indicate that supraspinal involvement modulates the cutaneous reflex such that a longer latency pathway is more active during voluntary (i.e. when seated) than during postural (i.e. standing) contraction. Rossi and Decchi (1994) found that noxious responses elicited in TA muscle by electrical stimulation of the plantar foot surface during standing were dependent upon the loading of the stimulated leg. Pain responses were observed to decrease as the stimulated leg bore a larger postural load. Rossi and Decchi (1994) suggested that this is indicative of functional modulation of segmental pathways so as to increase the loading capability of the leg with increased foot pressure and may play a role in the regulation of posture during stance by preserving balance (however, see below). Abbruzzese et al. (1996) also observed task-dependent modulation of reflexes after stimulation of afferents from the foot surface. They showed that low intensity electrical stimulaiton of the posterior tibial nerve at the ankle produced facilitation of SOL while prone, but inhibition during standing. If the foot were pressed against a firm surface while prone, a similar modulation as seen during standing could be observed. Abbruzzese et al. (1996)

suggested that afferent transmission from the foot and intrinsic foot muscles is modulated by cutaneous input to the foot sole.

With this task dependency in mind, we turn now to a discussion of reflexes during rhythmic movements.

1.4 Reflex modulation during rhythmic movement

In the preceding, evidence was presented that afferent input to the spinal cord delivered via the stimulation of muscular or cutaneous afferents can elicit prominent reflexes in various muscles of the human lower leg in a static condition. These effects to cutaneous inputs were shown to be somewhat variable, and were suggested to be task-dependent. Although not detailed above, task and phase dependent changes in the modulation of group I (muscular afferent) and cutaneous inputs has been shown during human locomotion (Belanger & Patla 1984, Crenna & Frigo 1984, 1987, Dietz 1987, Stein et al. 1991). Using the H-reflex technique, it has been shown that SOL H-reflex has its maximal amplitude during late stance phase (Capaday & Stein 1986) and is much larger during walking than during running in the same subject (Capaday & Stein 1987). Similarly, Dietz et al. (1990) showed that the quadriceps H-reflex reached its maximum during early stance phase and was also much smaller during swing. Recently, Faist et al. (1996) examined heteronymous Ia facilitation to SOL motoneurones induced by femoral nerve stimulation in addition to SOL H-reflex modulation during gait. They showed that both the heteronymous facilitation and H-reflex were modulated during walking and that the reflexes were smaller during walking than during sitting. It was suggested that the observed modulation is likely due to presynaptic inhibition of Ia excitation. Furthermore, there is evidence for task-modulation of the soleus H-reflex with different types of walking. Llewellyn et al. (1990) showed that the H-reflex was attenuated during narrow beam walking as compared to treadmill walking. It was suggested that the reflex gain should be lower in a task requiring greater stability where balance constraints are at a premium.

Another paradigm to study the influence of rhythmic activity on reflexes has been advocated by Brooke and colleagues (reviewed in Brooke et al. 1994, 1997). Brooke and McIlroy (1985) initially observed that controlled active pedaling movements in the human lower limb could lead to phasic modulation of evoked reflexes in the surface EMG of many leg muscles. Subsequently, the main objective of this work has been to try and elucidate the locus and mechanism of the modulation and the evidence is quite strong for modulation of presynaptic inhibition of peripheral afferents (see Brooke et al. 1997 and Stein 1995 for reviews). Both passive and active leg movements could induce a powerful modulation (Brooke et al. 1995), thus arguing for a peripheral locus. Further experiments have revealed that much of the source of the modulation likely lies in afferent input from muscle receptors in the upper leg (Misiaszek et al. 1995).

Also, Brown and Kukulka (1993) stimulated the tibial nerve at high intensity during stationary cycling and measured flexor reflex responses in TA and SOL muscles. They showed that, just as with the H-reflex, cutaneous reflexes are modulated throughout the cycle while pedaling on an ergometer. The pattern of the reflex was modulated in SOL, while both the onset latency and amplitude of the response were affected in TA muscle. Further, Andersen et al. (1995) noted that nociceptive cutaneous reflexes from the sural nerve showed a separation between reflex response and pain intensity during cyclic movements at the knee.

Duysens et al. (1993) showed that the amplitude of cutaneous reflexes is also modulated going from standing to running. Here, though, the reflex effect is larger during running than during standing. Also, complete reversals in the sign of a cutaneous reflex, originally documented in the cat (Forssberg et al. 1975), have been reported during human walking (Duysens et al. 1990, Duysens et al. 1992, DeSerres et al. 1995, van Wezel et al. 1997, Yang & Stein 1990; see Pearson 1995a and Duysens & Tax 1994 for reviews). In these instances, a middle latency (~50-90 ms) response in TA changes from excitation during swing to inhibition during stance. This reflex reversal has so far only been observed in muscles which display a two-burst pattern in the step cycle (i.e. TA and Biceps femoris), and only subsequent to stimulating nerves which are purely or mostly cutaneous (Stein 1991). It has thus been suggested, but not experimentally substantiated, that these changes in sign of a response reflect organization within the spinal cord in which reflex input during walking is functionally modulated so as to maximize compensatory reflex responses.

A reflex reversal in the group I disynaptic pathway (putative Ib) previously documented in the cat (Pearson & Collins 1993; for review see Pearson 1995a), has recently been observed in the human. Stephens and Yang (1996a) have shown that short latency inhibition of the homonymous (MG) and synergistic muscles (SOL) from group I afferents in MG muscle are absent during human walking. Interestingly, there was no difference in the reflex conditioning between sitting and standing at matched levels of muscle activation, indicating that rhythmic activation during locomotion may have been responsible for the modulation.

The effect of reflex conditioning via presynaptic inhibition has also been recently shown to be altered during walking. Capaday et al. (1995) measured the putative presynaptic inhibition on the SOL H-reflex induced by CP nerve stimulation during standing and during the stance phase of walking. Whereas prominent inhibition was noted during standing, virtually no effect was observed during walking.

In the majority of the studies described above, the focus has been to describe various phenomena involved in reflex function during various tasks and behaviours. However, the functional effect of reflex responses has only generally been implied from the neural responses; little or no description of movement kinematics or kinetics has been provided. The next section addresses those studies in which the function of reflexes during walking, one of the most common of purposive behaviours, have been examined in detail.

1.5 Reflex function during walking

As described above, many studies have often focused upon the details of the neural control signal sent to the involved muscles as measured by electromyography (EMG) (Rossignol 1996). Different afferent inputs have been studied to determine and evaluate their effects on walking. However, interpretation of the functional significance of these reflex responses has often been done in the absence of adequate mechanical data to corroborate the implied function based upon electroneurographic or EMG analysis (reviewed in Stein 1991). The need to understand and delineate the function of reflex control spans a range from determining which peripheral inputs are required to improve models and neural networks to determining which inputs might be useful in functionally altering abnormal reflex patterns in disease and after trauma in humans. This section will address the issue of reflex function by focusing upon those studies in cats and humans where mechanical and neural data have been collected together during locomotion and functional conclusions have been based upon both.

1.5.1 Stretch reflexes during walking

Reflex responses arising from muscular afferents, particularly the velocity-sensitive Group Ia afferents from the muscle spindles, have been studied in detail and the functional role investigated in many animal preparations in which walking can be elicited. Some time ago, it was shown that during selective peripheral nerve block of fusimotor axons EMG activity of the plantarflexor muscle group triceps surae was reduced by ~50% (Severin 1970). This indicates that muscle spindles (and therefore stretch reflexes) contribute significantly to muscle activation. However, the functional relevance (i.e. in terms of force production and consequent effects on limb mechanics) of the stretch reflex has remained enigmatic for quite some time (Stein et al. 1995). Akazawa et al. (1982) studied stretch reflexes during locomotion in the mesencephalic cat preparation and observed that stretch and H-reflexes were deeply modulated throughout the step cycle such that they were large during stance and small during swing phases. It was concluded that stretch reflexes assist in load compensation during gait, particularly during the extension or stance phase. Because of methodological difficulties stretch reflex responses have not been measured in intact, freely-walking animals. Further, until quite recently the magnitude of the reflex force produced by the stretch reflex was not quantified. Bennett et al. (1996) studied stretch reflex gain in the triceps surae muscle group in decerebrate and spinal cats during locomotor-like activities. A sample of their data is given in Figure 1-1. They observed that low frequency cyclic movements of the ankle during locomotion in the spinal cat produced up to 25% of the stretch-related force modulation.

In line with the observations of Akazawa et al. (1982) on the cat, Capaday and Stein (1986) observed that the soleus H-reflex was high during stance and low during swing phases in human gait. This indicated that this pathway should be capable of contributing functionally to force production during stance phase. Later, Yang et al. (1991a) used a pneumatic actuator to mechanically dorsiflex the foot and thus stretch soleus muscle during stance. Illustrated in Figure 1-2 is a sample of their data showing the stretch reflex response in Soleus and Tibialis Anterior (TA) muscles after the perturbation applied during early stance.

Figure 1-1 Reflex force responses with 5 Hz sinusoidal stretch of triceps surae muscle throughout the step cycle (from stance to swing, top to bottom) in the decerebrate cat. Dotted lines are force responses (intrinsic stiffness) with cut dorsal roots. Note the large stretch reflex force (solid lines) particularly during the first 4 phases of the step cycle. Adapted from Bennett et al. (1996).

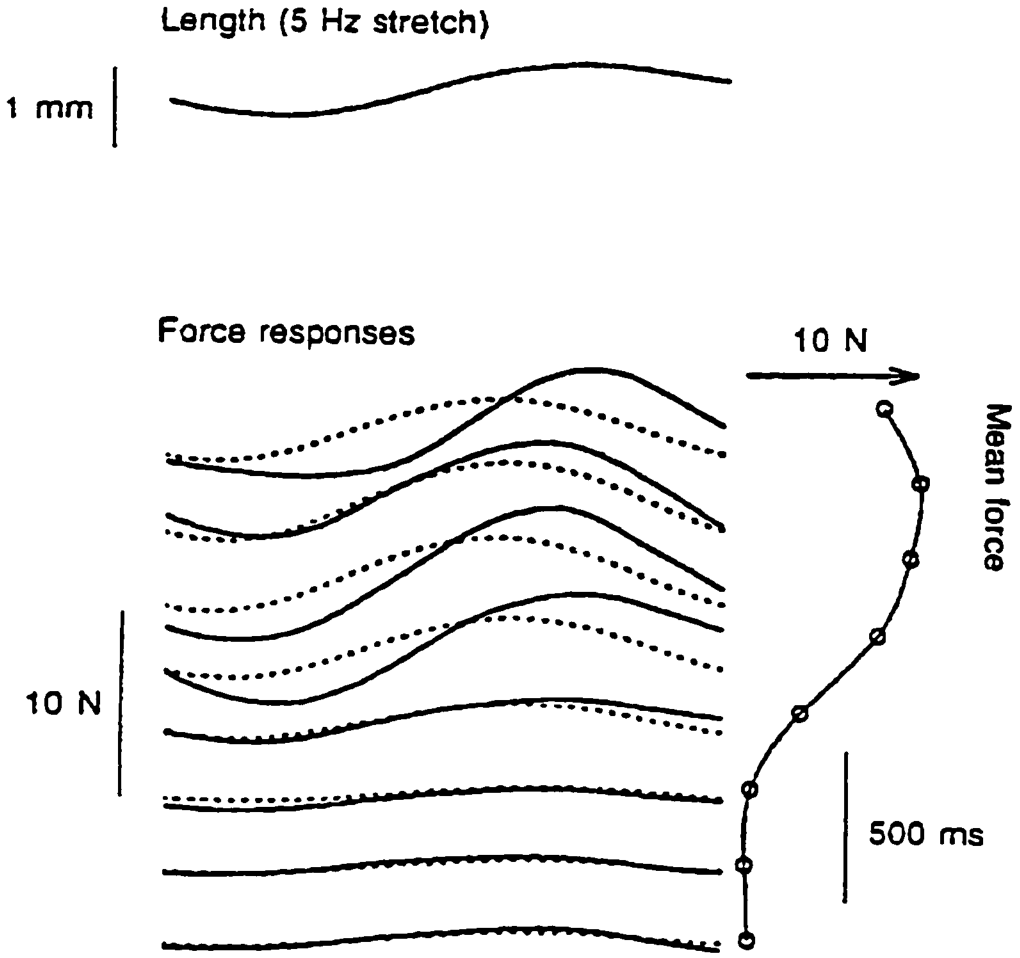
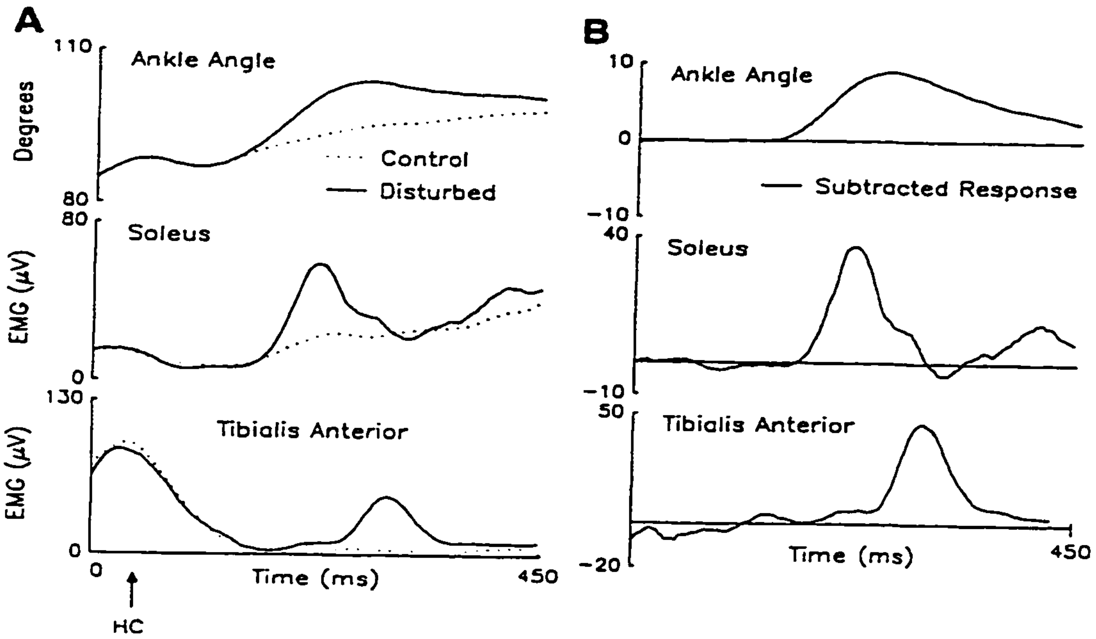


Figure 1-2 Stretch reflex EMG responses in Soleus muscle for one subject after mechanical dorsiflexion in stance phase during treadmill walking. Note the large Soleus EMG peak at short latency after ankle stretch. From Yang et al. (1991a).



They calculated that reflexes arising from a velocity-sensitive component (i.e., muscle spindle primaries) during stance might account for an estimated 30 to 60% of soleus activation. However, with this device it was not possible to quantify the force produced by the soleus stretch reflex throughout the step cycle. Anderson and Sinkjaer (1995) have recently made use of Bowden wire technology to construct an actuator capable of stretching the human ankle joint throughout all phases of the step cycle. This device has been used to study and compare short-latency stretch reflex modulation in soleus muscle during walking and responses obtained during standing (Sinkjaer et al. 1996a). They showed that the amplitude of the short-latency reflex had a maximum during stance, approached zero in the stance to swing transition, and reached a value of ~50% maximum during late swing. Additionally, a non-reflex component also peaked during stance. At increased walking speeds, the late swing phase stretch reflexes approximated the maximal stance phase values. Sinkjaer et al. (1996a) concluded, as did Yang et al. (1991a), that muscle afferent input contributes to a significant activation of the ankle extensors during stance. Unfortunately, though, it was not possible to partition out non-reflex and reflex torques in these experiments. As an estimate of the reflex forces that can be elicited, Stein and Kearney (1995) showed that stretch reflexes generated by random perturbations at the human ankle joint during isometric contraction could generate reflex torques larger than 20% of maximum voluntary contraction. Although not yet completely characterized, it nonetheless seems that the stretch reflex can contribute in a functionally meaningful way to force production during locomotion.

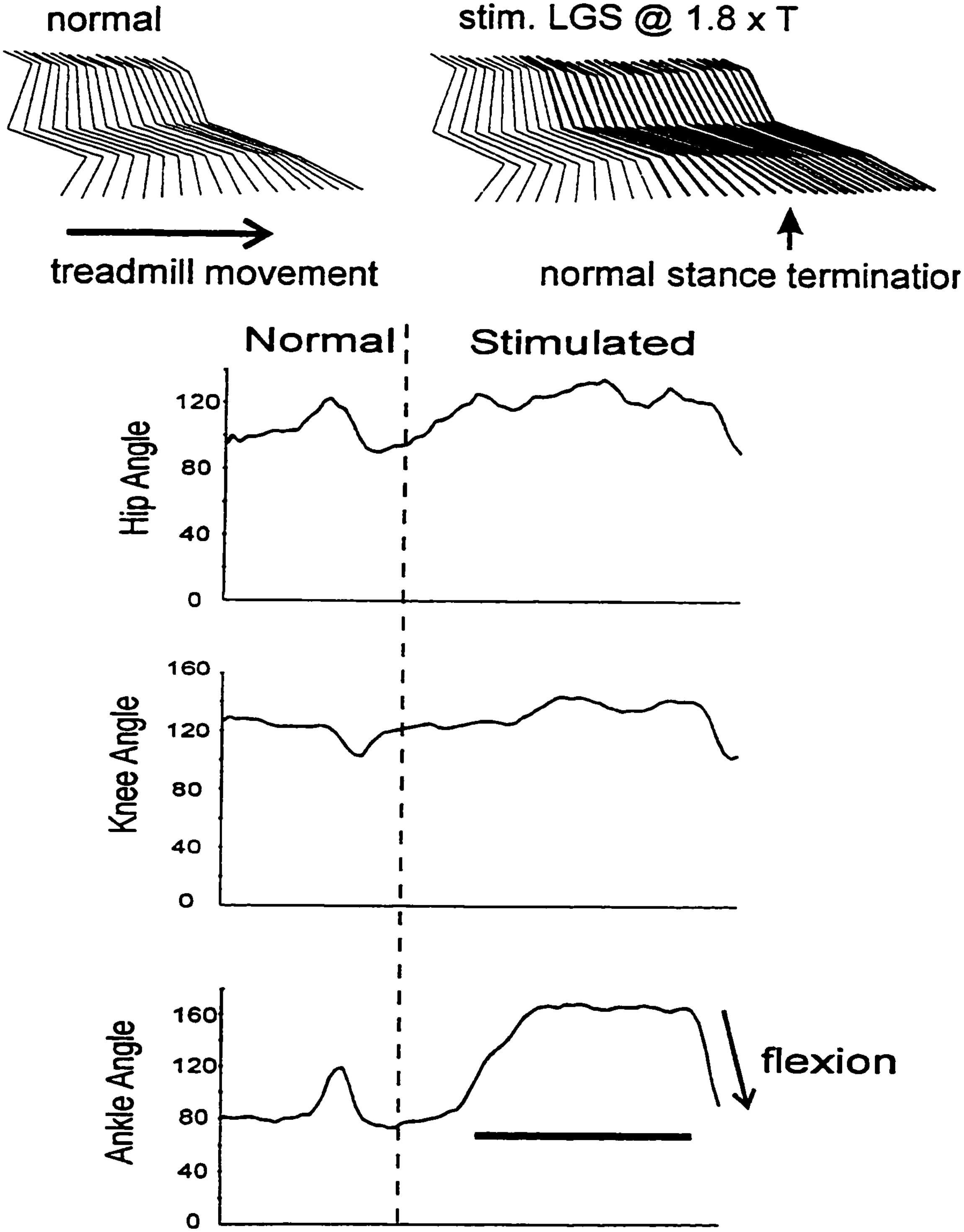
Studying dysfunctional motor control in pathological states may contribute to understanding normal function. For example, Yang et al. (1991b) showed that H-reflex modulation was impaired in spastic paretic subjects during treadmill walking and suggested that abnormal control of afferent input may contribute to the clonic behavior observed during gait in these subjects. Further, Sinkjaer et al. (1995) showed a similar dysfunctional reflex modulation in spastic multiple sclerosis patients. Recently, Sinkjaer et al. (1996b) have also shown impaired stretch reflex modulation during gait in these patients. However, in addition to the stretch reflex impairment, they concluded that non-reflex torque contributed substantially to the spasticity. Thus, impaired reflex input can cause severe dysfunction during human walking.

1.5.2 Load receptor reflexes and step cycle timing

Afferent input from group Ib afferents (Golgi tendon organs) has been shown to reverse from a disynaptic inhibition to a positive force feedback disynaptic and oligosynaptic excitation during locomotion in the decerebrate cat (Pearson & Collins 1993) and there is also now some evidence for this phenomenon in humans (Stephens & Yang 1996a). Recently, Pratt (1995) showed that positive force feedback elicited by activation of group Ib afferents generates strong reflexes in force and joint angles in the intact standing cat. These studies strongly suggest that extensor muscle group Ib afferent inputs contribute strongly to postural responses and stance phase weight support.

Proprioceptive inputs from muscle group I (in particular group Ib) afferents have been shown to be important in the regulation of the step cycle especially during phase transitions (Pearson 1995b). In the cat, load-sensitive afferents in the extensor muscles have been shown to modify the stepping rhythm. Whelan et al. (1995) showed that electrical stimulation of group I afferents in extensor nerves of the hindlimb significantly prolonged the stance phase in decerebrate cats walking on a treadmill. A sample of this data is given in Figure 1-3. The threshold for this effect (greater than 1.3 x the threshold for activation of the largest afferents) implicates the group Ib afferents. This strongly supports the assertion that the end of stance phase is signaled by a reduction of force in the extensor muscles (Duysens and Pearson 1980). Grillner and Rossignol (1978) suggested that another condition regulating step cycle timing is the signal from stretch-sensitive afferents in the flexor muscles which are activated at end stance (the hip flexors being stretched at this time). Hiebert et al. (1996) have recently shown that group I and group II afferents are crucial for forming the afferent signal for the termination of stance phase and the onset of swing in the cat.

Figure 1-3 **Top.** Stimulation of extensor (LGS) nerve during spontaneous stepping in a premamillary decerebrate cat prolongs stance phase of the step cycle. **Bottom.** Hip, knee, and ankle joint angle traces during normal step cycle (left) and during stimulation (right). Note that the stance phase is prolonged for the duration of stimulation (horizontal bar). Modified from Whelan et al. (1995).



There has been a dearth of information regarding the functional effects of load receptors in human subjects. Recently, however, Stephens and Yang (1996b) demonstrated that the addition or subtraction of additional load during human gait significantly increases extensor activity and prolongs stance phase duration. In comparison to the reduced cat preparations, though, the overall effect is smaller in human walking, perhaps reflecting intrinsic differences in the preparations studied. Taken together with the cat work described above, data of this type suggest that reflex activity can strongly modify and regulate step cycle timing in many preparations.

1.5.3 Cutaneous reflexes during walking

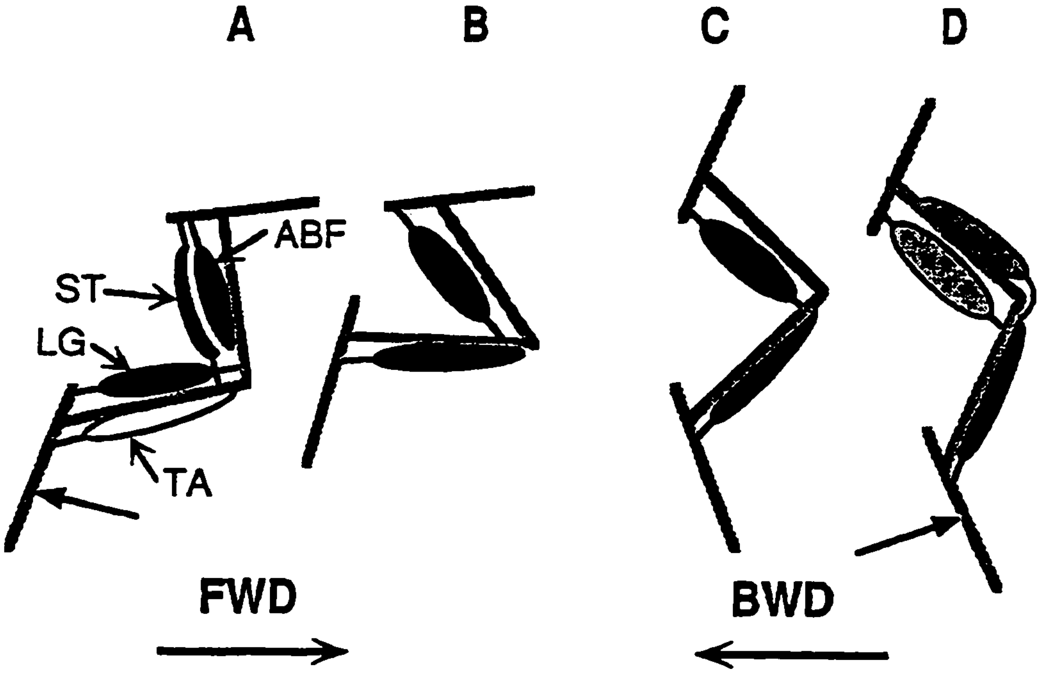
While effects on the locomotor rhythm had been observed earlier (Sherrington 1906, 1939), it was not until the work of Forssberg (1979) that a deliberate attempt to evaluate the functional role of cutaneous reflex responses by measuring both neural responses and kinematics was undertaken. These experiments involved both electrical and mechanical stimulation of the dorsal surface of the paw in the cat distal hindlimb during locomotion. A co-ordinated reflex forming a functionally-relevant "stumbling corrective response" was documented (Forssberg 1979). This response consisted of a sequential neural activation of the hindlimb musculature to allow the perturbed swing limb to continue past the encountered obstacle and maintain stability of ongoing locomotion. Similar responses were also observed by Wand et al. (1980) and Prochazka et al. (1978) who, in a series of experiments, systematically revealed that the origin of the corrective response lay in the cutaneous afferents arising from the paw dorsum. A similar neuro-mechanical linkage was demonstrated in the cat forelimb by Drew and Rossignol

(1987). More recently Buford and Smith (1993) showed that reflex responses elicited by mechanical and electrical stimulation during both forward and backward walking have relevant neuro-mechanical correlates. As is shown in Figure 1-4, a corrective response which was suitable for maintaining ongoing locomotion was elicited by dorsal surface stimulation during forward walking and by ventral stimulation during backward walking. In both instances the swing limb is moved over and by the mechanical or electrically-simulated perturbation.

From these results cutaneous afferents clearly have strong reflex responses which serve to functionally modify ongoing quadrupedal locomotion, particularly in the swing limb. What has remained unclear, though, is to what extent the results obtained in the experiments on the cat apply to the bipedal human in which balance and postural concerns are quite different.

As mentioned above (section 1.4 Reflex modulation during rhythmic movement), cutaneous reflexes, particularly those arising from stimulation of the sural nerve (innervating the lateral border of the foot) and the tibial nerve (innervating the plantar foot surface), have shown phase-dependent modulation of discrete reflex responses occurring at restricted latencies in human subjects (Yang & Stein 1990; for review see Duysens & Tax 1994). While many functional interpretations of the EMG responses in humans have been put forth, mechanical data to support these ideas has been lacking. Movement kinetics have never been quantified in these studies and limited kinematic data are available only in a few papers (e.g. Duysens et al. 1990, 1992; van Wezel et al. 1997). Further, only in Duysens et al. (1992) was a quantification between reflex EMG responses and changes in ankle joint trajectory conducted.

Figure 1-4 Schematic of responses to obstructions applied during swing phase for forward (FWD; dorsal surface stimulation) and backward (BWD; ventral surface stimulation) walking in cats. Note that coordinated muscle activation at knee and ankle lead to swing limb flexion over the obstacles. From Buford and Smith (1993).



A significant correlation was demonstrated between a phasic middle-latency excitatory response in tibialis anterior (TA; ankle dorsiflexor) muscle and increased ankle joint dorsiflexion. However the function of this biomechanical association has not been directly addressed. Further, the experiments in the cat described above, particularly the results of Buford and Smith (1993) would indicate that the issue of the local sign of cutaneous reflexes deserves further attention. That is, the anatomical location of the nerve seems crucial in determining the functional nature of any reflex responses.

Eng et al. (1994) studied strategies for recovering from a trip while subjects walked on a special obstacle walkway. It was shown that subjects used a lowering or an elevating strategy involving both ipsilateral and contralateral limbs and particularly the VL and BF muscles, dependent upon when obstacle was encountered in the swing phase. Some of their results at the ankle were similar to the electrical stimulation experiments described above and provide further evidence for the powerful effects of reflexes during swing phase. Further, Schillings et al. (1996) have recently performed experiments wherein mechanical perturbations were provided to elicit stumbling reactions in human subjects walking on a treadmill. During perturbations in early swing phase, Schillings et al. (1996) showed BF excitation and knee flexion as described above after SP n. electrical stimulation. These data indicated that during treadmill walking subjects can utilize similar strategies as during walking overground. Also, cutaneous reflexes do serve an important protective role in response to noxious stimuli at all phases of the step cycle (Bélanger & Patla 1984, 1987).

Finally, as with the monosynaptic H-reflex, polysynaptic cutaneous reflex modulation has also been shown to be impaired in spinal-cord injured patients. Jones and

Yang (1994) stimulated the tibial nerve during walking in these patients and found that, although some modulation did exist, the responses seemed to be predominantly excitatory. If the mechanical effects are also impaired to the same extent, this might account for much of the dysfunction. These issues require further research.

1.6 Thesis objectives

As described above, the main purpose of this thesis is to examine the function of reflexes during behaviour, particularly during walking. Accordingly the objectives of this thesis were:

1) to develop appropriate methodology for the evaluation of reflex function in the motor output as measured by surface EMG and in movement kinematics and kinetics;
2) to evaluate the task and phase modulation of reflexes arising from stimulation of muscle and cutaneous afferents in humans;
3) to evaluate the function of cutaneous reflexes during healthy and pathological human gait.

1.7 References

Abbruzzese, M., Rubino, V., and Schieppati, M. (1996). Task-dependent effects evoked by foot muscle afferents on leg muscle activity in humans. *EEG Clin. Neurophysiol.* 101:339-348.

Akazawa, K., Aldridge, J.W., Steeves, J.D., and Stein, R.B. (1982). Modulation of stretch reflexes during locomotion in the mesencephalic cat. *J. Physiol.* 329:553-567.

Andersen, O.K., Jensen, L.M., Brennum, J., and Arendt-Nielsen, L. (1995). Modulation of the human nociceptive reflex by cyclic movements. *Eur. J. Appl. Physiol.* 70:311-321.

Andersen, J.B., and Sinkjaer, T. (1995). An actuator system for investigating electrophysiological and biomechanical features around the human ankle joint during gait. *IEEE Trans. Rehab. Eng.* 3:299-306.

Aniss, A.M., Gandevia, S.C., and Burke, D. (1988). Reflex changes in muscle spindle discharge during a voluntary contraction. *J. Neurophysiol.* 59:908-921.

Aniss, A.M., Diener, H.-C., Hore, J., Burke, D. and Gandevia, S.C. (1990). Reflex activation of muscle spindles in human pretibial muscles during standing. *J. Neurophysiol.* 64(2):671-679.

Aniss, A.M., Gandevia, S.C., and Burke, D. (1992). Reflex responses in active muscles elicited by stimulation of low-threshold afferents from the human foot. *J. Neurophysiol.* 67(5):1375-1384.

Bastian, H.C. (1891). *The brain as an organ of mind.* New York, Appleton & Co.

Bélanger, M., and Patla, A.E. (1984). Corrective responses to perturbation applied during walking in humans. *Neurosci. Lett.* 49:291-295.

Bélanger, M. and Patla, A.E. (1987). Phase-dependent compensatory responses to perturbations applied during walking in humans. *J. Motor Behav.* 19:434-453.

Bennett, D.J., DeSerres, S.J., and Stein, R.B. (1996). Gain of the triceps surae stretch reflex in decerebrate and spinal cats during postural and locomotor activities. *J. Physiol.* 496:837-850.

Brazier, M.A.B. (1959). The historical development of neurophysiology. In. *Handbook of Physiology, Sec. 1, Neurophysiology, Vol. 1*, Field, J., Magoun, H.W., and Hall, V.E. (Eds), American Physiological Society, Washington D.C..

Brooke, J.D., and McIlroy, W.E. (1985). Locomotor limb synergism through short latency afferent links. *EEG Clin. Neurophysiol.* 60:39-45.

Brooke, J.D., Collins, D.F., and McIlroy, W.E. (1994). Human locomotor control, the Ia autogenic spinal pathway, and interlimb modulations. In: *Interlimb Coordination: Neural, Dynamical, and Cognitive Constraints,* edited by S.P. Swinnen, H. Heuer, J. Massion, and P. Casaer. San Diego, CA: Academic, p. 127-146.

Brooke, J.D., Cheng, J., Misiaszek, J.E., and Lafferty, K. (1995). Amplitude modulation of the soleus H reflex in the human during active and passive stepping movements. *J. Neurophysiol.* 73:102-111.

Brooke, J.D., Cheng, J., Collins, D.F., McIlroy, W.E., Misiaszek, J.E., and Staines, W.R. (1997). Sensori-sensory afferent conditioning with leg movement: gain control in spinal reflex and ascending paths. *Prog. Neurobiol.* 51:393-421.

Brooks, V.B. (1986). *The neural basis of motor control.* Oxford University Press, Oxford, p. 5.

Brown, D.A., and Kukulka,C.G. (1993). Human flexor reflex modulation during walking. *J. Neurophysiol.* 69:1212-1224.

Buford, J.A., and Smith, J.L. (1993). Adaptive control for backward quadrupedal walking. III. Stumbling corrective reactions and cutaneous reflex sensitivity. *J. Neurophysiol.* 70:1102-1114.

Burke, D., Dickson, H.G., and Skuse, N.F. (1991). Task-dependent changes in the responses to low-threshold cutaneous afferent volleys in the human lower limb. *J. Physiol.* 432:445-458.

Capaday, C., Cody, F.W.J. and Stein, R.B. (1990). Reciprocal inhibition of soleus motor output in humans during walking and voluntary tonic activity. *J. Neurophysiol.* 64(2):607-616.

Capaday, C. and Stein, R.B. (1986). Amplitude modulation of the soleus H-reflex in the human during walking and standing. *J. Neuroscience* 6(5):1308-1313.

Capaday, C. and Stein, R.B. (1987). Difference in the amplitude of the human soleus H reflex during walking and running. *J. Physiol.* 392:513-522.

Capaday, C., Lavoie, B.A., and Comeau, F. (1995). Differential effects of a flexor nerve input on the human soleus H-reflex during standing versus walking. *Can. J. Physiol. Pharmacol.* 73:436-449.

Crenna, P. and Frigo, C. (1984). Evidence of phase-dependent nociceptive reflexes during locomotion in man. *Exp. Neurol.* 85:336-345.

Crenna, P. and Frigo, C. (1987). Excitability of the soleus H-reflex arc during walking and stepping in man. *Exp. Brain Res.* 66:49-60.

Crone, C., Nielsen, J., Petersen, N., Ballegaard, M., and Hultborn, H.(1994). Disynaptic reciprocal inhibition of ankle extensors in spastic patients. *Brain* 117:1161-8.

Delwaide, P.J., Crenna, P. and Fleron, M.H. (1981). Cutaneous nerve stimulation and motoneuronal excitability: I, soleus and tibialis anterior excitability after ipsilateral and contralateral sural nerve stimulation. *J. Neurol. Neurosurg. Psychiat.* 44:699-707.

Delwaide, P.J. and Crenna, P. (1983). Exteroceptive influences on lower limb motoneurones in man: spinal and supraspinal contributions. In: *Motor control mechanisms in health and disease*, J. E. Desmedt (ed.), Raven Press, New York, pp707-807.

DeSerres, S.J., Yang, JF, and Patrick, S.K. (1995). Mechanism for reflex reversal during walking in human tibialis anterior motor units. *J. Physiol.* 488:249-258.

Dietz, V., Faist, M. and Pierrot-Deseilligny, E.(1990). Amplitude modulation of the quadriceps H-reflex in the human during the early stance phase of gait. *Exp. Brain Res* 79:221-224.

Dietz, V. (1987). Role of peripheral afferents and spinal reflexes in normal and impaired human locomotion. *Rev. Neurol. (Paris)* 143(4):241-254.

Dowman R, and Wolpaw J.R. (1988). Jendrássik maneuver facilitates soleus H-reflex without change in average soleus motoneurone pool membrane potential. *Exp. Neurol.* 101: 288-302.

Drew, T., and Rossignol, S. (1987). A kinematic and electromyographic study of cutaneous reflexes evoked from the forelimb of unrestrained walking cats. *J. Neurophysiol.* 57:1160-1184.

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

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

Duysens, J., Tax, A.A.M., Trippel, M. and Dietz, V. (1992). Phase-dependent reversal of reflexly induced movements during human gait. *Exp. Brain Res.* 90:404-414.

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

Duysens, J., and Tax, T.(1994). Interlimb reflexes during gait in cats and humans. In: *Interlimb Coordination: Neural, Dynamical, and Cognitive Constraints,* edited by S.P. Swinnen, H. Heuer, J. Massion, and P. Casaer. San Diego, CA: Academic, pp. 97-126.

Eng, J.J., Winter, D.A., and Patla, A.E. (1994). Strategies for recovery from a trip in early and late swing during human walking. *Exp. Brain Res.* 102:339-349.

Faist, M., Dietz, V., and Pierrot-Desielligny, E. (1996). Modulation, probably presynaptic in origin, of monosynaptic Ia excitation during human gait. *Exp. Brain Res.* 109:441-449.

Forssberg, H., Grillner, S., and Rossignol, S. (1975). Phase dependent reflex reversal during walking in chronic spinal cats. *Brain Res.* 85:103-107.

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

Gandevia, S.C., Miller, S., Aniss, A.M., and Burke, D. (1986). Reflex influences on muscle spindle activity in relaxed human leg muscles. *J. Neurophysiol.* 56:159-170.

Gibbs, J, P. Harrison, L.M., and Stephens, J.A. (1995). Cutaneomuscular reflexes recorded from the lower limb in man during different tasks. *J. Physiol.* 487(1):237-242.

Grillner, S., and Rossignol, S. (1978). On the initiation of the swing phase of locomotion in chronic spinal cats. *Brain Res.* 146:269-277, 1978.

Grillner, S. and Dubuc, R. (1988). Control of locomotion in vertebrates: spinal and supraspinal mechanisms. In: *Advances in neurology, Vol. 47: Functional recovery in neurological disease,* S.G. Waxman (ed.), Raven Press, New York, pp.425-453.

Hagbarth K-E, Wallin G, Burke D, Löfstedt L (1975) Effects of the Jendrássik manoeuvre on muscle spindle activity in man. *J. Neurol. Neurosurg. Psychiat.* 38: 1143-1153.

Hiebert, G.W., Whelan, P.J., Prochazka, A., and Pearson, K.G. (1996). Contribution of hindlimb flexor afferents to the timing of phase transitions in the cat step cycle. *J. Neurophysiol.* 75:1126-1137.

Iles, J.F. (1996). Evidence for cutaneous and corticospinal modulation of presynaptic inhibition of Ia afferents from the human lower limb. *J. Physiol.* 491(1):197-207.

Jendrássik E (1883) Beiträge zur Lehre von den Sehnenreflexen. *Deutsche Archiv für Klinische Medizin* 33: 177-199.

Jenner, J.R., and Stephens, J.A. (1982). Cutaneous reflex responses and their central nervous pathways studied in man. *J. Physiol.* 333:405-419.

Jones, C.A., and Yang, J.F. (1994). Reflex behavior during walking in incomplete spinal-cord injured subjects. *Exp. Neurol.* 128:239-248.

Kukulka, C.G. (1994). The reflex effects of nonnoxious sural nerve stimulation on human triceps surae motor neurons. *J. Neurophysiol.* 71(5):1897-1906.

Landau, W.M. and Clare, M.H. (1964) Fusimotor function Part IV. Reinforcement of the H reflex in normal subjects. *Arch. Neurol.* 10: 117-122.

Levin, M. and Chapman, C.E. (1987). Inhibitory and facilitatory effects from the peroneal nerve onto the soleus H-reflex in normal and spinal man. *EEG Clin. Neurophysiol.* 67:468-478.

Llewellyn, M., Yang, J.F. and Prochazka, A. (1990). Human H-reflexes are smaller in difficult beam walking than in normal treadmill walking. *Exp. Brain Res.* 83:22-28.

Misiaszek, J.E., Barclay, J.K., and Brooke, J.D. (1995). Inhibition of canine H reflexes during locomotor-like rotation about the knee arises from muscle mechanocreceptors in quadriceps. *J. Neurophysiol.* 73(6):2499-2506.

Miyahara, T., Hagiya, N., Ohyama, T., Nakamura, Y. (1996) Modulation of human soleus H reflex in association with voluntary clenching of the teeth. *J. Neurophysiol.* 76: 2033-2041.

Nicholls, J.G., Martin, A.R., and Wallace, B.G. (1992). *From neuron to brain (3rd Ed.).* Sinauer Associates, Inc., Mass.

Nielsen, J., and Kagamihara, Y. (1993). Differential projection of the sural nerve to early and late recruited human tibialis anterior motor units: change of recruitment gain. *Acta Physiol. Scand.* 147:385-401.

Pearson, K.G. (1993). Common principles of motor control in vertebrates and invertebrates. *Ann. Rev. Neurosci.* 16:265-97.

Pearson, K.G., and Collins, D.F. (1993). Reversal of the influence of group Ib afferents from plantaris on activity in medial gastrocnemius muscle during locomotor activity. *J. Neurophysiol.* 70:1009-1017, 1993.

Pearson, K.G. (1995a). Reflex reversal in the walking systems of mammals and arthropods. In: W.R. Ferrell and U. Proske (eds.) *Neural control of movement*, Plenum Press, New York, pp. 135-141.

Pearson, K.G. (1995b) Proprioceptive regulation of locomotion. In: *Current opinions in neurobiology* 5:786-791.

Pratt, C.A. (1995). Evidence of positive force feedback among hindlimb extensors in the intact standing cat. *J. Neurophysiol.* 73:2578-2583.

Prochazka, A., Sontag, K.-H., and Wand, P. (1978). Motor reactions to perturbations of gait: proprioceptive and somesthetic involvement. *Neurosci. Lett.* 7:35-39.

Rossi, A., and Decchi, B. (1994). Flexibility of lower limb reflex responses to painful cutaneous stimulation in standing humans: evidence of load-dependent modulation. *J. Physiol.* 481(2):521-532.

Rossi, A., Zalaffi, A., and Decchi, B. (1996). Interaction of nociceptive and non-nociceptive cutaneous afferents from the foot sole in common reflex pathways to tibialis anterior motoneurones in humans. *Brain Res.* 714:76-86.

Rossignol, S. Neural control of stereotypic limb movements. (1996). In: *Handbook of Physiology, Section 12. Exercise: regulation and integration of multiple systems,* Rowell, L.B. and J.T. Sheperd (eds.), American Physiological Society, pp.173-216.

Schieppati, M. (1987). The Hoffmann Reflex: a means of assessing spinal reflex excitability and its descending control in man. *Prog. Neurobiol.* 28:345-376.

Schillings, A.M., Van Wezel, B.M.H., and Duysens, J. (1996). Mechanically induced stumbling during human treadmill walking. *J. Neurosci. Meth.* 67:11-17.

Severin, F.V. (1970). The role of the gamma motor system in the activation of the extensor alpha motor neurones during controlled locomotion. *Biophysics* 15:1138-1144.

Shahani, B.T. and Young, R.R. (1971). Human flexor reflexes. *J. Neurol. Neurosurg. Psychiat.* 34:616-627.

Shepherd, G.M. (1994). *Neurobiology (3rd Ed.).* Oxford University Press, Oxford.

Sherrington, C.S. (1900). On the innervation of antagonistic muscles. Sixth note. *Proc. Royal Soc.* 66:66-67.

Sherrington, C.S. (1906). *The integrative action of the nervous system.* Oxford University Press, London.

Sherrington, C.S. (1939). *Selected writings of Sir Charles Sherrington*, A testimonial presented by the neurologists forming the guarantors of the journal Brain, D. Denny-Brown (ed.). Hamish Hamilton Medical Books, London.

Sinkjaer, T., Toft, E., and Hansen, H.J.(1995). H-reflex modulation during gait in multiple sclerosis patients with spasticity. *Acta Neurol. Scand.* 91:239-246.

Sinkjaer, T., Jacob, B.A., and Birgit, L. (1996a). Soleus stretch reflex modulation during gait in man. *J. Neurophysiol.*76:1112-1120.

Sinkjaer, T., Anderson, B.A., and Nielson J.F. (1996b). Impaired stretch reflex and joint torque modulation during spastic gait. *J. Neurol.* 243:566-74.

Sommer, J. (1940). Periphere Bahnung von Muskeleigenreflexen als Wesen des Jendrássikschen Phänomens. *Deutsche Zeitschrift fun Nervenheilkunde* 150: 249-262.

Stein, R.B. (1991). Reflex modulation during locomotion: functional significance. In: *Adaptability of human gait* A.E. Patla (ed.), Elsevier Science Publishers, pp.21-36.

Stein, R.B. (1995). Presynaptic inhibition in humans. *Prog. Neurobiol.* 47:533-544.

Stein, R.B., DeSerres, S.J., and Kearney, R.E. (1995). Modulation of stretch reflexes during behaviour. In: *Neural control of movment*, W.R. Ferrell and U. Proske (eds.), Plenum Press, New York, pp. 151-158.

Stein, R.B., Yang, J.F., Edamura, M. and Capaday, C. (1991). Reflex modulation during normal and pathological human locomotion. In: *Neurobiological basis of human locomotion* M. Shimamura, S. Grillner, and V.R. Edgerton (eds.), Japan Scientific Societies Press, Tokyo, pp. 335-346.

Stein, R.B., Yang, J.F., Belanger, M. and Pearson, K.G. (1993). Modification of reflexes in normal and abnormal movements. *Prog. Brain Res.* 97:189-196.

Stein, R.B., and Kearney, R.E. (1995). Nonlinear behavior of muscle reflexes at the human ankle joint. *J. Neurophysiol.* 73:65-72.

Stephens, M.J., and Yang, J.F. (1996a). Short latency, non-reciprocal group I inhibition is reduced during the stance phase of walking in humans. *Brain Res.* 743:24-31.

Stephens, M.J., and Yang, J.F. (1996b). The effects of load on the human step cycle. *Soc. Neurosci. Abs.* 22:1849.

Tanaka, R. (1974). Reciprocal Ia inhibition during voluntary movements in man. *Exp. Brain Res.* 21:529-540.

Van Wezel, B.M.H., Ottenhoff, F.A.M. & Duysens, J. (1997). Dynamic control of location-specific information in tactile cutaneous reflexes from the foot during human walking. *J. Neurosci.* 17:3804-3814.

Wand, P., Prochazka, A., and Sontag, K.-H. (1980). Neuromuscular responses to gait perturbations in freely moving cats. *Exp. Brain Res.* 38:109-114.

Whelan, P.J., Hiebert, G.H., and Pearson, K.G.(1995). Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res.* 103:20-30.

Yang, J.F. and Stein, R.B. (1990). Phase-dependent reflex reversal in human leg muscles during walking. *J. Neurophysiol.* 63(5):1109-1117.

Yang., J.F., Stein, R.B., and James, K.B.(1991a). Contribution of peripheral afferents to the activation of the soleus muscle during walking in humans. *Exp. Brain Res.* 87:679-687.

Yang., J.F., Fung, J., Edamura, M., Blunt, R., Stein, R.B., and Barbeau, H. (1991b). H-reflex modulation during walking in spastic paretic subjects. *Can. J. Neurol. Sci.* 18:44-452.

2. A method for the functional quantification of the reflex effect of human peripheral nerve stimulation[1]

2.1 Introduction

Complex patterns of EMG responses often consisting of alternating phases of inhibition and facilitation have been shown to occur after peripheral nerve stimulation in humans, with the most complicated observed after stimulation of primarily cutaneous nerves (Duysens and Tax, 1994; Jenner and Stephens, 1982). Within these patterns, data analysis has most often centered upon the peak amplitude of reflex responses occurring within or at a single discrete latency (Duysens et al., 1990; Yang and Stein, 1990). This analysis has revealed much about cutaneous reflexes at a restricted latency, information which is vitally important to the study of motor control mechanisms. However, as these reflex responses are generally at least biphasic, an examination of the functional consequence of the reflex effects of electrical nerve stimulation based upon analysis of phenomena occurring at a restricted latency is limited. As a result, this kind of limited EMG analysis often obviates comparison to movement biomechanics and thus functional evaluation of reflex responses.

However, simple and generalized methods for evaluating the overall reflex effect of nerve stimulation has not been used to analyze surface EMG data in this way, although methods have been suggested for nerve spike trains (e.g. CUSUM, Ellaway, 1977) and more complex statistical methods for surface EMG (Poliakov and Miles, 1992; van der

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[1] Portions of this chapter have been published in abstract form by E. Paul Zehr, Tomoyoshi Komiyama, and Richard B. Stein in *Soc. Neurosci. Abs. 21(1):681, 1995*, and by Tomoyoshi Komiyama, E. Paul Zehr,

Glas et al. 1995). We describe below the development and application of a simple technique, ACRE$_{150}$ (Average Cumulative Reflex EMG until 150 ms post-stimulation), for analyzing the overall reflex components in surface EMG recorded after nerve stimulation in humans. This index is thus intended to be used in the evaluation of the function of human reflex responses.

In this paper we address: 1) the basis of the technique, 2) the reflex origin of the measured ACRE$_{150}$ index, 3) the reproducibility of this technique during walking, and 4) the correlation between ACRE$_{150}$ and biomechanical parameters. A portion of these results has previously been reported in abstract form (Komiyama et al., 1995; Zehr et al., 1995a).

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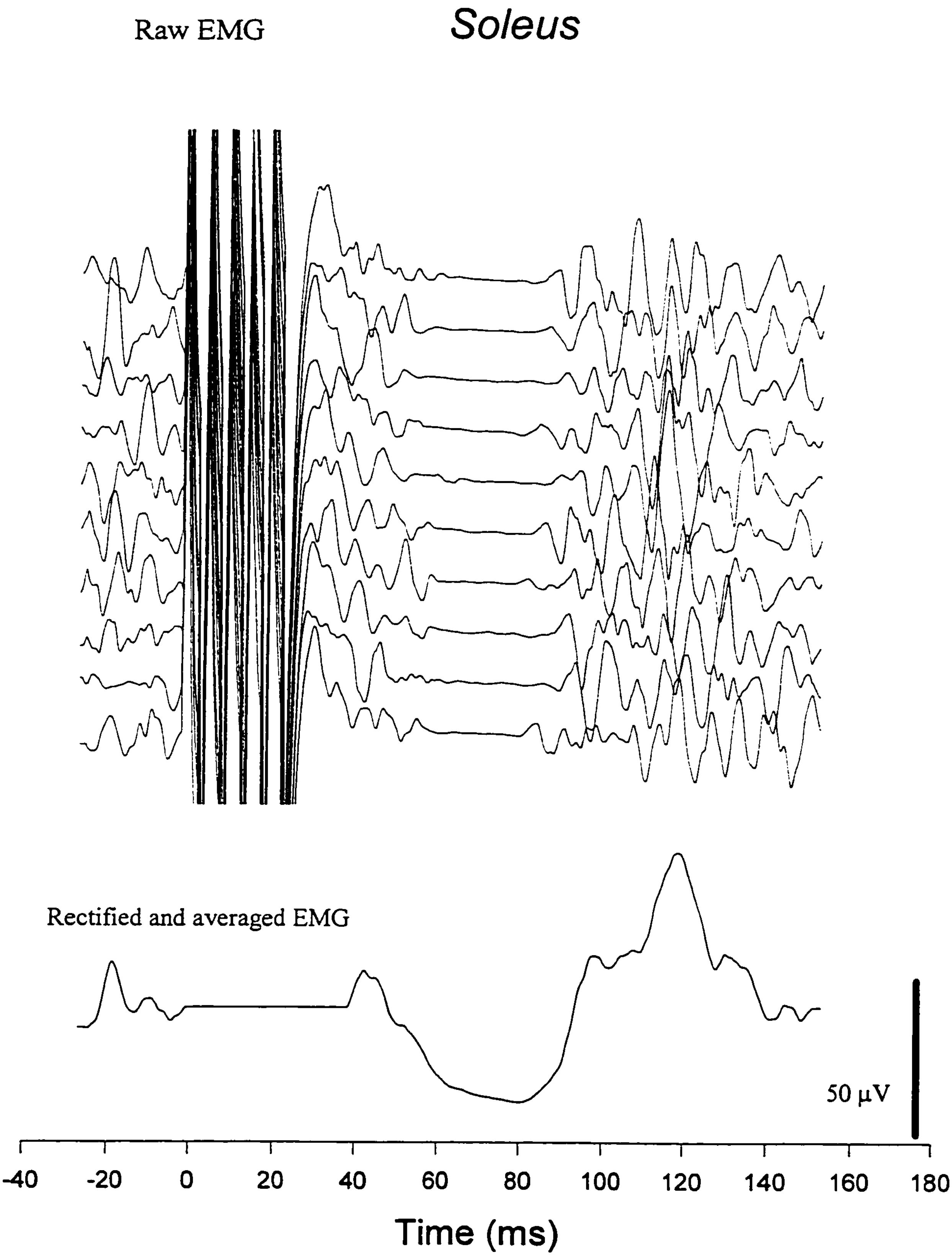
and Richard B. Stein in *EEG Clin. Neurophysiol. 97(4):S179, 1995.*

2.2 Materials and Methods

A total of 6 neurologically intact subjects participated in the experiments. These subjects comprised of 4 males and 2 females, ranging in age from 24-36 years. Subjects participated with informed, written consent and under the sanction of the University of Alberta Guidelines for Ethical experiments on humans.

As described above, phasic patterns of EMG activity can be observed after stimulation of particularly cutaneous peripheral nerve in human subjects. An example of this type of behaviour is shown in Figure 2-1, in which a raster plot of raw EMGs and the full-wave rectified EMG modulation curve (stimulus artifact removed) recorded after superficial peroneal (SP; innervates the foot dorsum) nerve are shown. The problem addressed in this paper is that of attempting to gauge the overall, integrated reflex effect

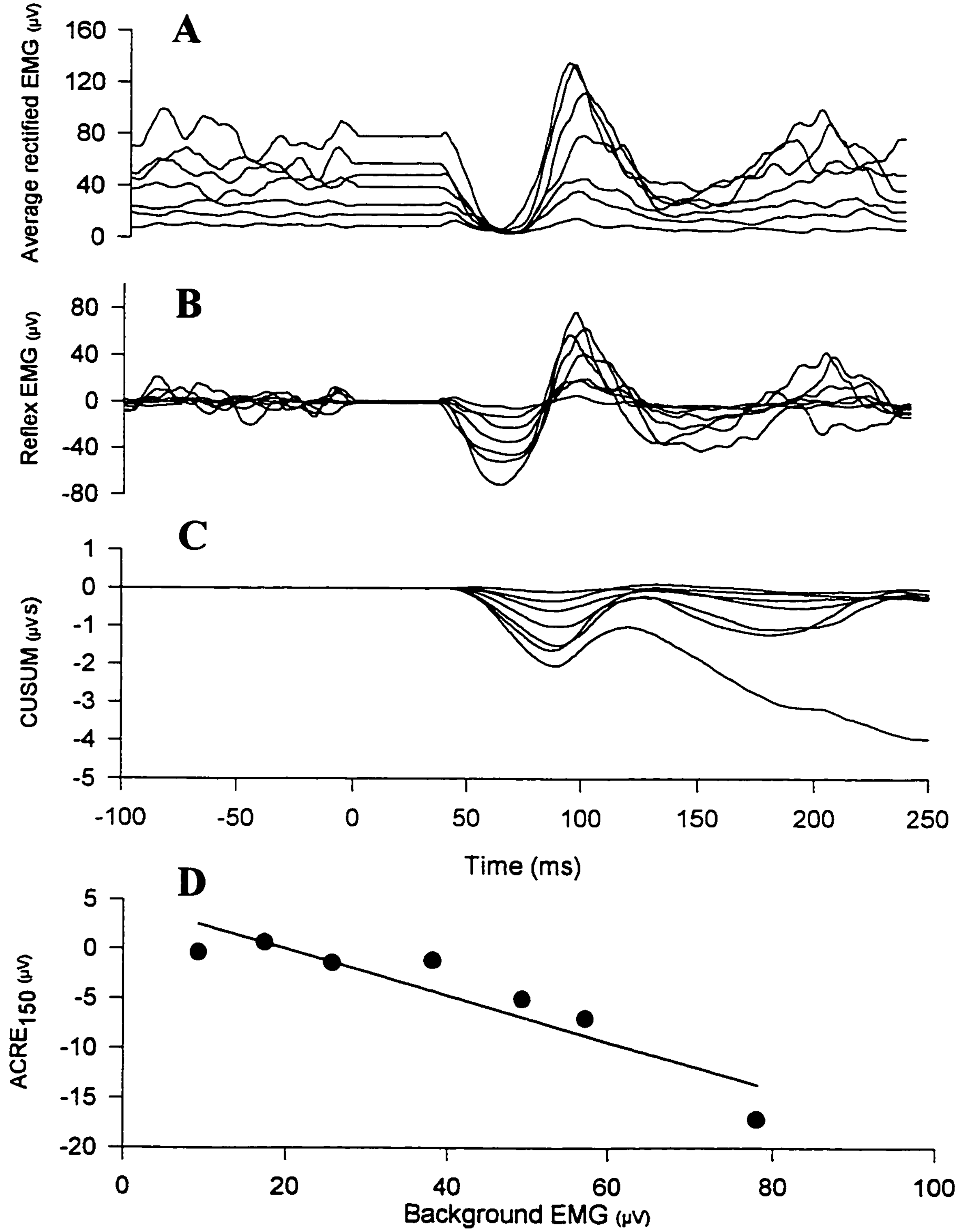
Figure 2-1 Raster plots of Sol raw and rectified and averaged EMG after SP n. stimulation during standing. The stimulus artifact has been suppressed in the averaged trace.



of stimulation based solely upon inspection of the phasic responses (that can be seen reaching their peaks at 80 and 120 ms in this example of SP n. stimulation).

Figure 2-2A provides an example of EMG modulation curves at various levels of SOL muscle activation after SP nerve stimulation. In order to evaluate the overall effect, a pre-stimulus EMG mean was calculated over a ~100 ms interval prior to nerve stimulation. This mean EMG level due to voluntary contraction was then subtracted from the entire length of the EMG trace, leaving a residual of mainly reflex EMG (Fig. 2-2B), an expansion of a similar technique to that commonly applied during phase-averaged analysis of EMG traces during walking (Yang and Stein, 1990). This residual was then cumulatively summed (integrated) from approximately 30 ms post-stimulus to 150 ms post-stimulus; i.e. for an approximately 120 ms interval (Fig. 2-2C). The summation did not begin until 30 ms because of prominent stimulus artifact (which has been suppressed in Figures 2-1, bottom trace, and 2-2). However, careful observation of the raw EMG records in separate experiments involving different stimulus train lengths, revealed that no reflex responses to cutaneous nerve stimulation could be expected to occur during this interval. The sum trace (similar to the CUSUM; see Ellaway, 1977) was then divided by the time interval of summation to provide an average EMG value (in μV) (see example in Fig.2-2D), which we have termed $ACRE_{150}$ (Average Cumulative Reflex EMG at 150 ms). Although not displayed in the following, this parameter can then be subjected to a normalization procedure (e.g. expressed relative to maximal EMG values occurring during maximal voluntary contraction (MVC) or during walking) to

Figure 2-2 The evolution of the ACRE_{150} technique. (A) Plotted are EMG modulation curves from SOL muscle activated at different levels (10-80 μV) of background contraction after SP nerve stimulation (5 pulses at 200 Hz). The stimulus artifact has been blocked out for clarity. (B) The background EMG levels have been subtracted from the traces shown in (A), so as to provide reflex responses only. (C) The reflex EMG is then cumulatively summed from the end-point of the stimulation artifact. (D) Dividing by the time interval of summation (from the end-point of artifact until 150 ms post-stimulation) provides the ACRE_{150} EMG index, shown here during standing.



facilitate comparison between subjects and across experiments. This technique was then tested in a variety of ways, as described below.

In separate experiments, bipolar stimulating electrode pairs were placed over the SP nerve on the ventral aspect of the foot immediately distal to the ankle joint, over the sural nerve (innervates lateral surface of the foot) immediately posterior to and at the level of the lateral malleolus, and over the distal tibial nerve (innervates plantar surface of the foot) distal and posterior to the medial malleolus. Nerve stimulation comprised of 3-7 pulses of 1.0 ms duration given at 200 Hz. Stimulation was applied in a pseudo-random fashion with minimum and maximum intervals of 0.9 and 1.8 s, respectively.

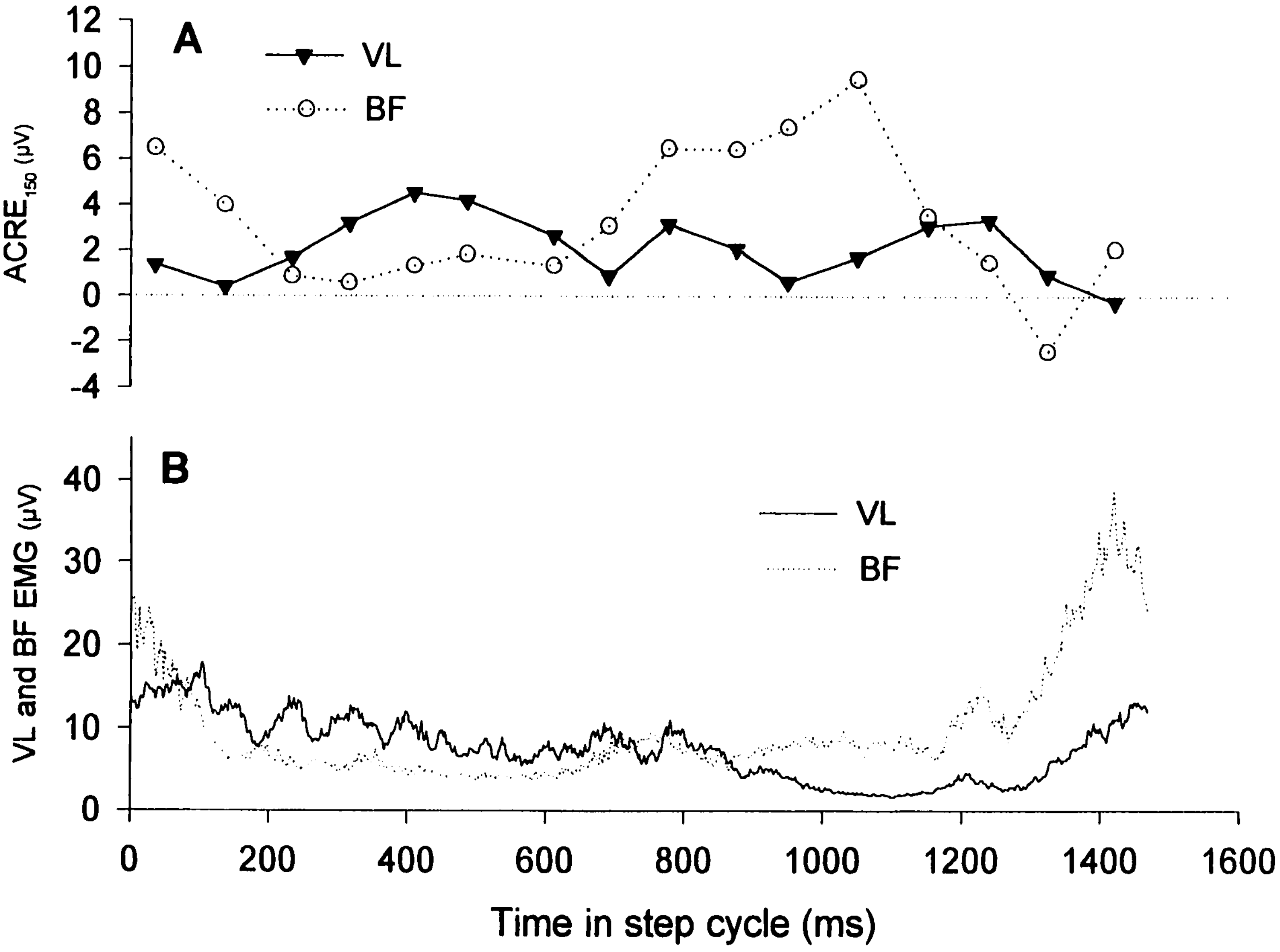
Surface EMG electrodes (Jason Electronics, Santa Monica CA) were placed over the bellies of the vastus lateralis (VL), biceps femoris (BF), soleus (SOL), lateral (LG) and medial (MG) gastrocnemii, and tibialis anterior (TA) muscles of the right leg. EMG signals were band passed and full wave rectified and input via a 16 bit A/D converter into a 486 microcomputer running AXOTAPE (AXON Instruments Inc.) data acquisition software and sampling at 1350 Hz. Full-wave rectified and averaged (n=20) EMG modulation curves were constructed in active muscles after nerve stimulation. Subjects performed MVC (sustainable for 5-10 s) of the target muscles (i.e. knee extension/flexion, and plantar/dorsiflexion) while monitoring EMG during standing. Thereafter subjects performed all contractions at graded selected percentages of these maximums.

In one set of experiments designed to determine the reflex origin of the technique, subjects were asked to perform 3 tasks: 1) hold a given EMG level during the entire stimulation run (HOLD), 2) attempt to voluntarily increase the EMG level immediately subsequent to stimulation (CONTRACT), and 3) attempt to voluntarily reduce the EMG level after stimulation (RELAX). In the latter two conditions, subjects were instructed to bring the EMG level back to the pre-stimulation level after their voluntary reactions. In these experiments EMG modulation curves of VL and SOL muscles were obtained after both SP and Sural nerve stimulation. ACRE values were then calculated at various latencies ranging from 100 to 220 ms post-stimulation. A 2-way repeated measures analysis of variance using Student Neumann-Keuls post hoc test was used to evaluate significant differences ($\alpha=0.05$) at 150 ms post-stimulation.

To determine the reproducibility of the $ACRE_{150}$ index in a behavioral context, values from two consecutive 4 km/h walking trials were correlated. Calculating the $ACRE_{150}$ during walking was quite similar to that described above for standing with a few differences. The step cycle was divided into 16 phases beginning at heel contact. EMG modulation curves after stimulation were constructed throughout the step cycle based on an n of 10 to 30 observations. Because the normal unstimulated background EMG level changes rhythmically throughout the human gait cycle, it was not appropriate to simply subtract a given undisturbed static background EMG level from the stimulated records as in the standing, controlled situation. Rather, to obtain the reflex EMG trace as described above during standing, the appropriate unstimulated EMG trace was subtracted in a phase-by-phase manner from each stimulated record. In Figure 2-3 $ACRE_{150}$ values for BF and VL muscles after SP n. stimulation during 2 km/h walking have been plotted (A) along with the undisturbed walking averages (B) without stimulation. It can be seen that the $ACRE_{150}$ index is modulated throughout the step cycle. To determine the reproducibility, $ACRE_{150}$ calculations were made for SOL, lateral (LG) and medial (MG) gastrocnemii muscles during repeated 4 km/h walking trials. Least means square linear regression was used to determine the trial-to-trial reproducibility.

As mentioned in the introduction, the primary motive for developing the $ACRE_{150}$ technique was to obtain a reliable index that would allow for an analysis of functional reflex effects of nerve stimulation during behaviours such as standing and walking. To illustrate this in a simple and controlled fashion, we attempted to evaluate the correlation between an observed change in $ACRE_{150}$ and force changes during standing. One subject stood on a specially constructed plantar flexion manipulandum wherein varying plantar flexion loads could be set. The subject wore a shoe in which calibrated force sensing resistors had been placed (Zehr et al., 1995b). The subject was asked to maintain a constant EMG level of the SOL muscle during which time the SP nerve was stimulated. The special manipulandum was used instead of normal standing because we wanted to get around the inertial effect of the body. By using the manipulandum set-up, changes in force production that might be associated with EMG changes could be determined without the damping influence of the whole body. Changes in force were determined along with the associated $ACRE_{150}$ values. Linear regression was then calculated on the relation between these two parameters.

Figure 2-3 An example of $ACRE_{150}$ calculated throughout the step cycle during 2 km/h walking with SP nerve stimulation. The calculations for VL and BF muscles are shown in (A) along the corresponding unstimulated background EMG levels (B).



2.3 Results

Figure 2-2D shows the $ACRE_{150}$ value, calculated as described in the Methods for different levels of voluntary contraction. A straight line has been fitted according to the standard least mean squares methods, which has the slope of -0.24 and an intercept of 4.8 µV. In this example, the $ACRE_{150}$ index increased with voluntary contraction level.

Results for the reaction time experiment are shown in Figure 2-4 for SOL (top) and VL (bottom) muscles. Values up until 160 ms post-stimulation are shown and were not significantly different ($p>0.05$) at this latency, thus illustrating that the quantity $ACRE_{150}$ is not affected by voluntary reaction and can be considered to be a measure of reflex responses.

The good trial-to-trial, within subject reproducibility of the method is shown for one subject in Figure 2-5. As shown in the Figure, there was significant correlation between $ACRE_{150}$ values from the two separate 4 km/h walking trials and 3 different muscles comprising the triceps surae. This figure shows that our method is reproducible and indicative of valid measurement of an underlying physiological phenomenon.

The strength of the association between our EMG index and measurable force change has been plotted in Figure 2-6. As can be seen in this figure, a reasonable and statistically significant ($r=0.57$, $p<0.03$) correlation was obtained between the $ACRE_{150}$ index and changes in plantarflexion force. This suggests that our method can be applied to evaluate the functional role of cutaneous reflexes in human behavior.

Figure 2-4 ACRE values for different activation strategies were not significantly different at 150 ms post-stimulation after SP nerve stimulation in both Soleus (top) and VL (bottom panel) muscles. Values are means, ± SEM for 6 subjects.

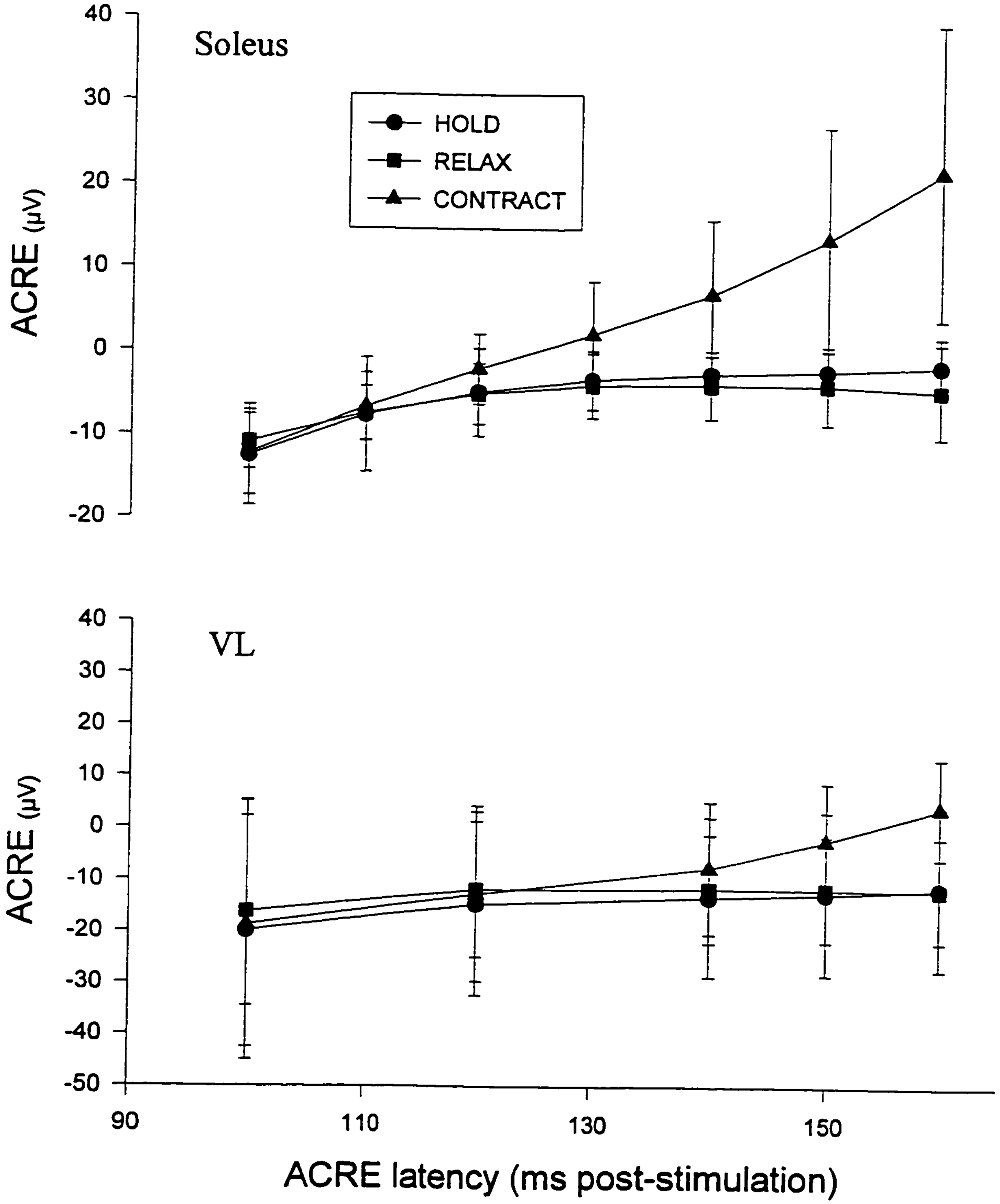


Figure 2-5 Reproducibility plot of ACRE$_{150}$ for SOL, LG, and MG muscles from 2 trials of 4 km/h walking during which SP nerve was stimulated. Linear regression lines (solid) have been plotted for each muscle. Pearson r values ($p<0.05$) were 0.56 for SOL, 0.65 for LG, and 0.94 for MG muscles for this sample subject.

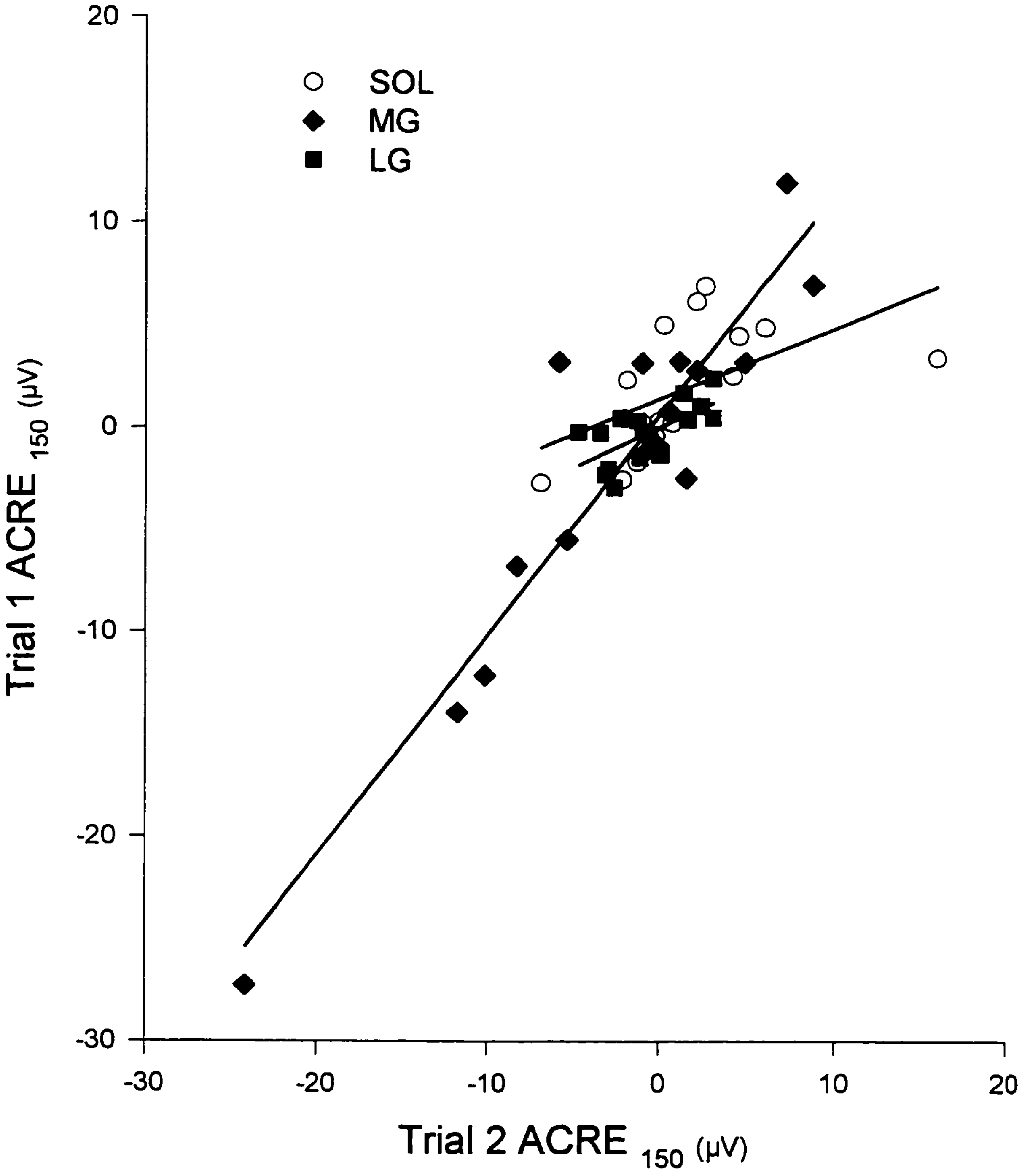
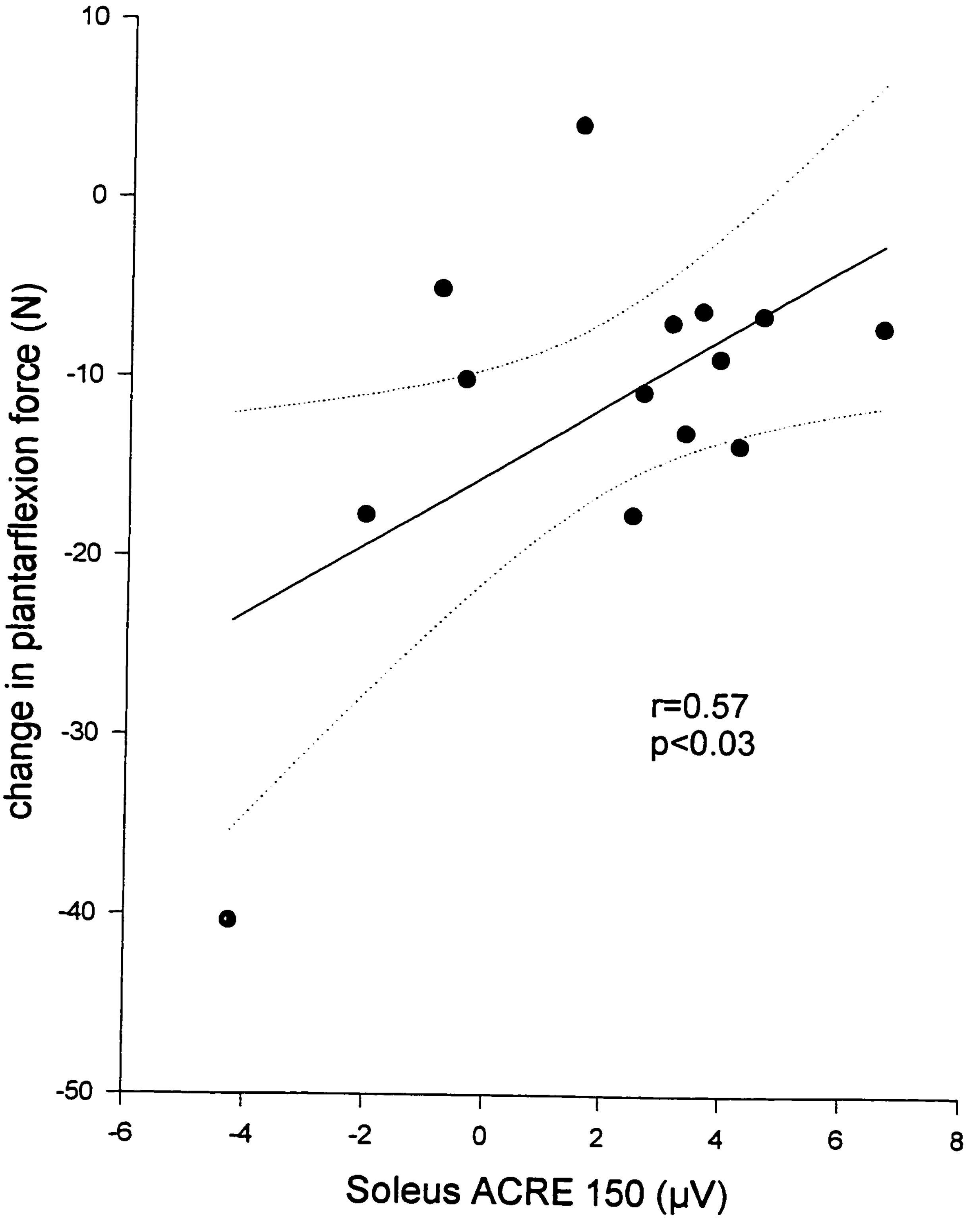


Figure 2-6 Correlation between $ACRE_{150}$ and force change during static plantarflexion. The significant linear regression (solid line; +/- 95% confidence interval, dashed line) indicates that there is an important correlation between the calculated EMG index and movement biomechanics.



2.4 Discussion

In this paper we have presented a simple method for analyzing and quantifying EMG modulation curves obtained in active muscle after stimulation of human peripheral nerve. While we have extensively used SP nerve as an example here, this method has also been successfully used in conjunction with tibial and sural nerves, as described in the Methods. The main advantage of using this method is that it allows for the quantification of the overall effect of nerve stimulation at reflex latencies in a functional context. A quantified electrophysiological index such as $ACRE_{150}$ provides the basis for comparison to biomechanical changes which may be seen after nerve stimulation; such changes being, as they are, the sum of the overall reflex effects. As many of the electrophysiological evaluations of reflex function in humans to date (Duysens et al., 1990; Yang and Stein, 1990; Duysens and Tax, 1994) have attempted to draw conclusions about the functional role played during walking based solely upon phasic changes at restricted latencies, the $ACRE_{150}$ index is indeed quite useful.

As mentioned in the Introduction, we suggested that for any new method to have utility, it must satisfy a number of criteria. Namely, it must truly measure reflex changes, be reproducible, and have a strong association to movement biomechanics. We discuss each of these factors in turn.

As was shown in Figure 2-4, our subjects were not able to significantly modify $ACRE_{150}$ values, either by deliberately contracting or relaxing the target muscles (SOL and VL), in a reaction-time task. This indicates that even if a given subject attempted to voluntarily alter the maintained EMG level upon detecting the stimulation pulses, such deliberate modulation, while affecting any calculation that might be done at longer latency, will have no significant effect on $ACRE_{150}$. Interestingly, Brodin et al. (1993) described somewhat longer reaction times when using EMG CUSUM records on recordings from oral muscle activity after mechanical tap and electrical lip shock. While not statistically significant, though, an examination of Figure 2-4, particularly the top panel illustrating SOL muscle, might suggest that the Contract condition seems to be diverging from Relax and Hold at ~130 ms. However, what must be mentioned rarely do subjects attempt to voluntarily modulate the maintained EMG in either the Contract or Relax fashion tested in this experiment. Therefore, based upon our statistical analysis and our anecdotal experience, we are confident that our method is a measure of the overall reflex response.

As with any method, reproducibility is extremely important. This is particularly important for the $ACRE_{150}$ index because it has application for evaluating subtle reflex changes that may occur between different tasks (e.g. standing vs. walking) and between different phases of the same task (e.g. different portions of the walking step cycle). As well, as there may be some variability in human reflex responses subsequent to nerve stimulation, errors in methodological reproducibility would compound with any physiological variability. To this end we examined the reproducibility of $ACRE_{150}$ values in various muscles during the behavioral (and therefore methodologically demanding) task of treadmill walking. As mentioned earlier, these $ACRE_{150}$ values were shown to be highly significantly correlated ($p<0.0001$, $r=0.85$). Thus we are satisfied that our new method is reproducible. Further, the fact that such a high correlation was shown during walking (a task in which some inherent step-to-step variability might be expected to occur) lends further credence to using this method to analyze functional reflex modulation during human gait.

Perhaps the most demanding criteria that we tested was demonstrating a correlation between our neurophysiological $ACRE_{150}$ technique and movement biomechanics. At the same time it is of great importance, as the very quantification of the overall neural responses is required to determine the functional role of the reflexes. This is, of course, vitally tied to biomechanics. However before testing the functional correlation during a dynamic task such as walking (where experiments are currently ongoing, see Zehr et al. 1996), where a lack of correlation may not necessarily indicate lack of causation, we needed a very basic test of the method itself. That is, we wanted to answer the question of whether there are measurable biomechanical changes when large $ACRE_{150}$ modulation is recorded. As well, to obviate the extrinsic influences that will prevail in a dynamic task (such as body sway and whole body inertia during walking), we used a mono-articular task that we could control (in this case the inertia of the foot is the only extrinsic parameter). As was shown in Figure 2-6, a statistically significant ($p<0.03$, $r=0.57$) correlation was demonstrated. Although the correlation is not particularly high, it should be noted that we correlated the EMG index from a single muscle, soleus, to the overall effect of all plantarflexor muscles. It remains to determine the functional correlation in a behavioral task such as walking (Zehr et al. 1996).

2.5 Conclusions

We have shown that our novel method can be reliably used to evaluate the functional reflex effect of human peripheral nerve stimulation. This method was shown to be correlated to biomechanical parameters and is broadly applicable to many nerves and muscles, providing a convenient index for comparison to movement biomechanics. Further, while this method was designed and discussed in terms of electromyographic measurement, it has potential application to other neurophysiological measures in which stimulus-triggered averages are made when superimposed upon a steady background, in which adequate pre-stimulus durations are available, and wherein evaluation of function is of primary importance.

2.6 References

Brodin, P., Miles, T.S., and Turker, K.S. (1993). Simple reaction-time responses to mechanical and electrical stimuli in human masseter muscle. *Archs oral Biols.* 38:221-226.

Capaday, C., Cody, F.W.J., and Stein, R.B. (1990) Reciprocal inhibition of soleus motor output in humans during walking and voluntary tonic activity. *J. Neurophysiol.* **64**(2), 607-616.

Duysens, J. and Tax, T. (1994) Interlimb reflexes during gait in cat and human. In: *Interlimb coordination: neural, dynamical, and cognitive constraints*, (Edited by Swinnen, S., Heuer, H., Massion, J., and Casaer, P.), pp.97-126. Academic Press Inc.

Duysens, J., Tax, A.A.M., Trippel, M., and Dietz, V. (1992) Phase-dependent reversal of reflexly induced movements during human gait. *Exp. Brain Res.* **90**, 404-414.

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

Ellaway, P.H (1977) An application of cumulative sum technique (cusum) to neurophysiology. *J. Physiol.* **265**,1-2P.

Jenner, J.R., and Stephens, J.A. (1982) Cutaneous reflex responses and their central nervous pathways studied in man. *J. Physiol.* **333**,405-419.

Komiyama, T., Zehr, E.P., and Stein, R.B. (1995) A novel method for evaluating the overall effect of nerve stimulation in humans. *EEG Clin. Neurophysiol.* **97**(4),S179.

Poliakov, A.V., and Miles, T.S. (1992) Quantitative analysis of reflex responses in the averaged surface electromyogram. *J. Neurosci. Methods* **43**,195-200.

van der Glas, H.W., Abbink, J.H., van der Bilt, A., and Cadden, S.W. (1995). Analysis of differences between conditioned and control reflex series in EMG recordings. *J. Neurosci. Methods* 58:117-125.

Yang, J.F., and Stein, R.B. (1990) Phase-dependent reflex reversal in human leg muscles during walking. *J. Neurophysiol.* **63**,1109-1117.

Zehr, E.P., Komiyama, T., and Stein, R.B. (1995a) Evaluating the overall electromyographic effect of cutaneous nerve stimulation in humans. *Soc. Neuroscience Abs.* **21**(1),681, #273.12.

Zehr, E.P., Stein, R.B., Komiyama, T., and Kenwell, Z. (1995b) Linearization of force sensing resistors (FSR's) for valid force measurement during gait. In *Proc.17th Ann. International Conf. IEEE Engineering in Medicine and Biology Society*, pp.300-301.

Zehr, E.P., T. Komiyama, and R. B Stein (1996) Functional reflex modulation by cutaneous nerve stimulation during human gait. *Can. J. Physiol. Pharm.*, in press.

3. Force measurement during human gait using shoe-mounted sensors: application to perturbation studies[1]

3.1 Introduction

The measurement of forces under the foot during human gait is a technically demanding enterprise. Further, the accurate measurement of force during locomotion has often been limited to single cumbersome trials over floor or treadmill-embedded force plates (Kram and Powell, 1989). As well, even when a treadmill-mounted force plate has been available the resulting data often must be subjected to complicated and time consuming decomposition analysis in order to determine the force profiles for each foot (Davis and Cavanaugh, 1993). Further, analysis of treadmill-mounted force plate data is often plagued by insensitivity to small changes in ankle moments that may occur after mechanically- or electrically-induced gait perturbations. As such, the availability of a technically simple and relatively inexpensive method of force measurement would be valuable for therapeutic and research interventions in human gait analysis.

While the linearization and calculation of center-of-pressure during gait with FSRs has previously been reported (Ferencz et al., 1993), they have not seen routine use in obtaining valid and calibrated force recordings. This is mostly due to two factors: 1) the intrinsic, highly non-linear properties of the sensors themselves, and 2) the difficulty in integrating the force of the load bearing surfaces of the human foot onto discrete insole-located measuring devices. The focus of this paper is to address these two

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[1] A portion of this chapter has been published by E. Paul Zehr, Richard B. Stein, Tomoyoshi Komiyama and Zoltan Kenwell in *Proc. 17th Ann. International Conf. IEEE Engineering in Medicine and Biology Society*, pp.300-301, 1995.

questions. A portion of the results has previously been published in abstract form (Zehr et al., 1995).

3.2 Materials and methods

All subjects who participated in this study did so with informed verbal consent.

3.2.1 Force sensing resistor (FSR) theory

FSRs consist of two layers of film substrate, one containing interdigitating conductive electrodes and the other a semiconductive polymer. As force is applied, there is increased shunting of the conductive layer resulting in a decline of FSR resistance. The conductance will saturate because the polymer is not infinitely compressible. A typical form for such a saturation is

1) $G=aF/(b+F)$

where G=conductance, F=force, a=the maximum conductance, and b=the force at which half the maximum conductance is reached. Using a standard operational amplifier circuit (Figure 3-1, inset) with the FSR in the input and a resistor R_f in the feedback loop will give an output voltage (V_o)

2) $V_o=V_iR_f/R=V_iR_faF/(b+F)$

where V_i is the input voltage, and R is the variable resistance of the FSR.

3.2.2 Response of FSR

Using the amplifier configuration described above, the voltage responses of the FSRs were obtained by statically loading (0 to 900 to 0 N) each FSR within a piston rod device. The voltage responses for the calibrations trials were fitted with eq. 3) using a nonlinear least squares fitting routine (MatLab, MathWorks Inc., Natick MA).

3) $V_o=[AF/(b+F)]+c$

where $A=V_iR_fa$, and c is a constant due to offset of the operational amplifier with no force input. The coefficients were then used to calibrate the FSR response values obtained during standing and treadmill walking.

3.2.3 Force and Center of Pressure during locomotion

In order to obtain the best voltage response, specialized force sensing elements were placed in a "sandwich" configuration. These elements consisted of a large semi-elliptical force collecting brass plate (6 x 5 cm diameter) with a small spacer (2 cm diameter) which was then affixed to a 3.5 cm diameter FSR. It was found that the best fixation between force collecting plate and FSR could be obtained by using a specially formulated adhesive (Sportsman's GOOP, Electic Products, Carson, CA). The FSR was then placed on top of thin (U-55 Rubberflex, Steenwyck, Red Deer, AB, Canada) insole material, on the bottom side of which were placed large semi-elliptical brass plates (6 x 5 cm diameter, as above). Three force sensing elements were placed under the major pressure points of the foot; approximately directly under the heel, at the medial metatarsal phalangeal joints, and immediately proximal to the lateral metatarsal-phalangeal joint. Subjects were asked to verify if the majority of body weight was indeed supported by the three force collecting plates. As well, subjects were asked to attempt to place the majority of their body weight upon each individual sensor while the maximal voltage response was checked. The location of each array was adjusted until these criteria were met.

3.2.4 Application during stationary stepping and treadmill walking

Two subjects performed stationary stepping on a Kistler force plate while the output from the insole was simultaneously recorded. These subjects performed a variety of tasks on the force plate, including single leg standing, slow and fast walking, and stationary stepping in place. In this way, a check on the performance and absolute validity of our sensor arrays could be obtained.

To evaluate the response of the FSRs during treadmill locomotion, one subject walked at 2 and 4 km/h on the treadmill. As well, to test the sensitivity of the force array to detect small perturbations, one subject performed static plantar flexion with various background force levels while the Common Peroneal n. (stimulation would cause dorsiflexion) was stimulated at 1.5 x motor threshold (3 pulses, 1 ms duration, 200 Hz) during standing. This subject also walked on the treadmill at 2 km/h during which time pseudo-random stimulation of the CP n. was applied, thus providing stimulated and undisturbed force records. The force response of each of the 3 sensor elements were then calibrated and linearly summed to obtain complete z-plane forces during walking. The step cycle was then divided into 16 phases and force changes for each phase were subtracted from the undisturbed forces to provide subtracted force records. Center of pressure was calculated based on a weighted triangular configuration of the three FSR sensor arrays.

3.3 Results and Discussion

3.3.1 Calibration of FSR array

We also evaluated the day-to-day reproducibility in the voltage output of the FSR arrays during the calibration runs. We were especially concerned as to whether the use of the special adhesive had potentially altered the voltage output of the FSRs, but Figure 3-1 shows that the reproducibility of the output was excellent. Although the response is still obviously not linear, as previously reported (Zehr et al., 1995), the hyperbolic fit shown in the figure can be seen to fit the data quite nicely, omitting the hysteresis.

3.3.2 Validity of FSR force estimation during standing and walking

The results of the stationary stepping trials for one subject are shown with the FSR summation and force plate (vertical ground reaction force; Fz) forces superimposed (Fig. 3-2A). In this example, the force profile obtained by the FSR arrays matches reasonably well the force record obtained from the stationary force plate, in both shape and absolute value.

Figure 3-2B shows the force profile obtained from a 70 kg subject walking on the treadmill at 2 and 4 km/h. As was shown with the stationary stepping, both the amplitude and the profile of the force records matches that which should be expected for a subject of this mass (see for example Winter, 1991).

Figure 3-1 FSR output day-to-day reproducibility averaged over 5 different experimental calibration trials. Mean data values (±SEM) are plotted along with the hyperbolic function used in force calculation. Inset is the standard amplifier circuit (see text).

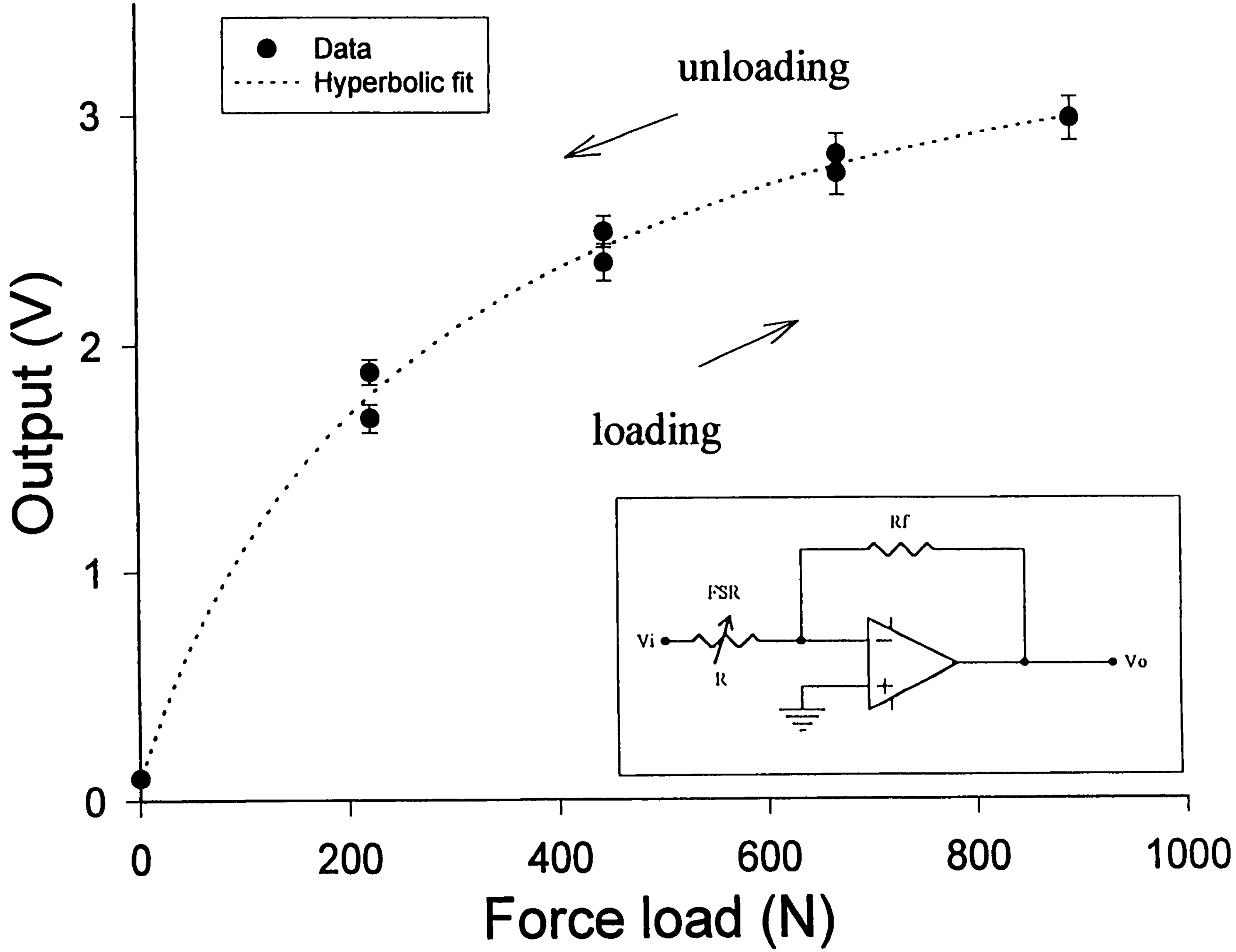
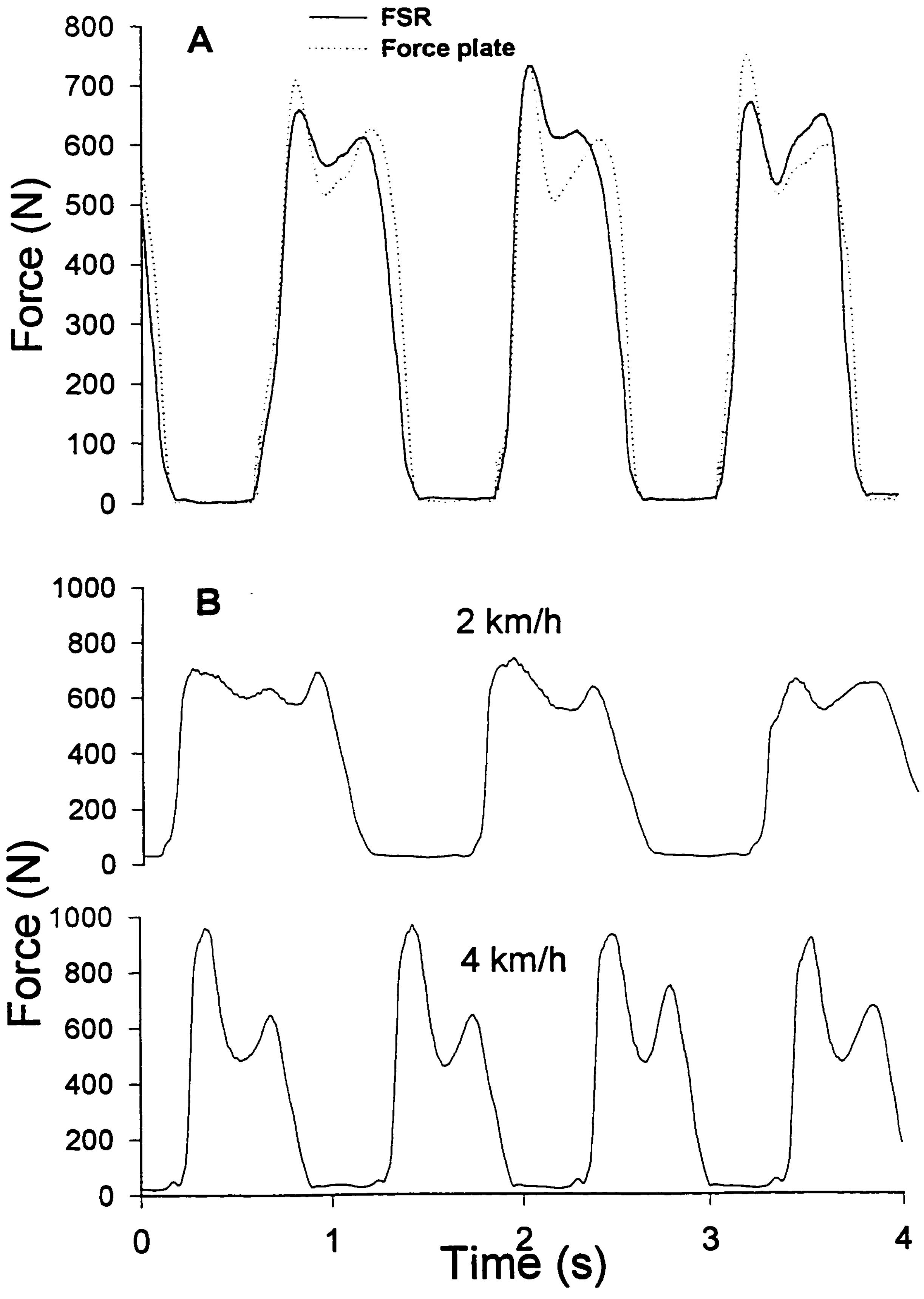


Figure 3-2 (A) Stationary stepping on a force plate with simultaneous recording of FSR summated output. (B) Summed FSR forces during treadmill walking at 2 and 4 km/h.



3.3.3 Application to reflex perturbation studies

To have practical application to reflex studies, the sensor arrays described in this paper must be sensitive enough to measure the small force changes that occur after reflex stimulation. To check this, we tested the sensitivity of the FSRs to small force perturbations that would occur directly after motor nerve stimulation. An example of this is shown in Fig. 3-3, in which the subject exerted a constant background plantar-flexion force while the CP nerve was stimulated and the force and center of pressure changes due to stimulation were recorded. This can be seen in the figure where the onset of the force deflection (due to the TA motor response) occurs around 50 ms and reaches a peak at approximately 150 ms post-stimulation. As well, an anticipated and clear backward shift of the center of pressure can be seen. It was also desirable to determine the sensitivity of the FSRs to small force perturbations during a functional task such as walking. Figure 3-4 (top) illustrates the undisturbed force profile during an 8 minute, 2 km/h walking trial. The subtracted force (i.e. the force change due to the CP n. stimulation) at 4 different phases of the step cycle is given at the bottom of the figure. As mentioned above, these traces were obtained by dividing the step cycle into 16 phases beginning at heel contact and averaging the undisturbed and stimulated force changes for each phase. Subtracting the stimulated from the undisturbed provides the subtracted force. As can be seen in this example, analyzing the data in this way shows that the CP n. stimulation has differing effects on plantar-flexion force depending upon when in the step-cycle the stimulation is delivered. That is, Figure 3-4 shows that during early stance (numbers 1 & 16 on the figure) there are large force changes, and during mid-stance (numbers 5 & 6) there are relatively small force changes. It should be emphasized at this point that acquiring phase-averaged data such as this on force recordings using a traditional floor embedded force-plate would have been nearly impossible, and certainly impractical. To obtain such data, 10-20 stimulated trials per phase of the step cycle would be used and 50-150 undisturbed step cycle averages would be used for subtraction. This means that a minimum of 210 steps across a force plate would have been necessary to accrue this data. As well, this estimation of trial numbers does not include those of missed trials and pre-steps.

Figure 3-3 Force and center of pressure changes after common peroneal n. stimulation during maintained plantar-flexion while standing. The vertical dashed line is stimulus onset.

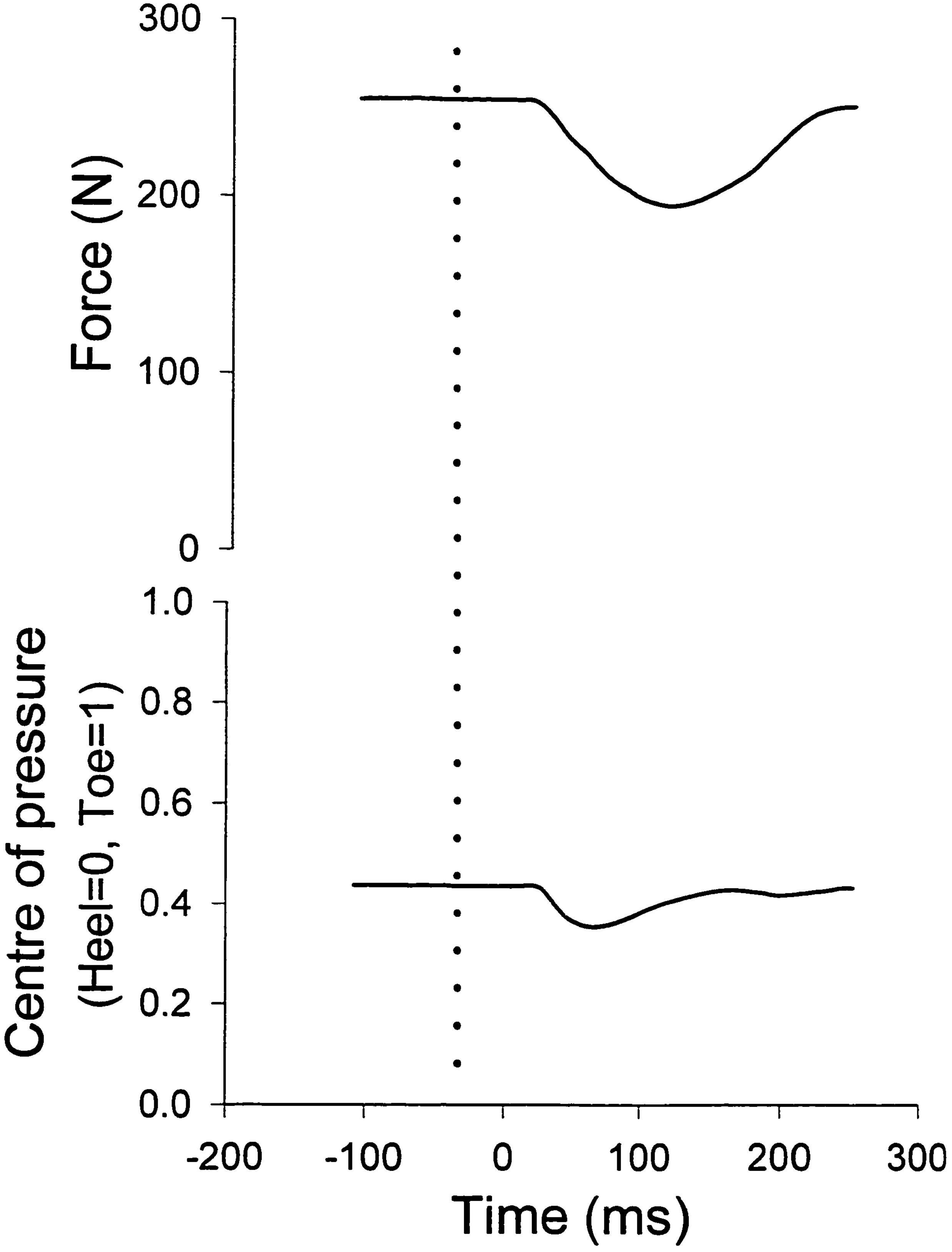
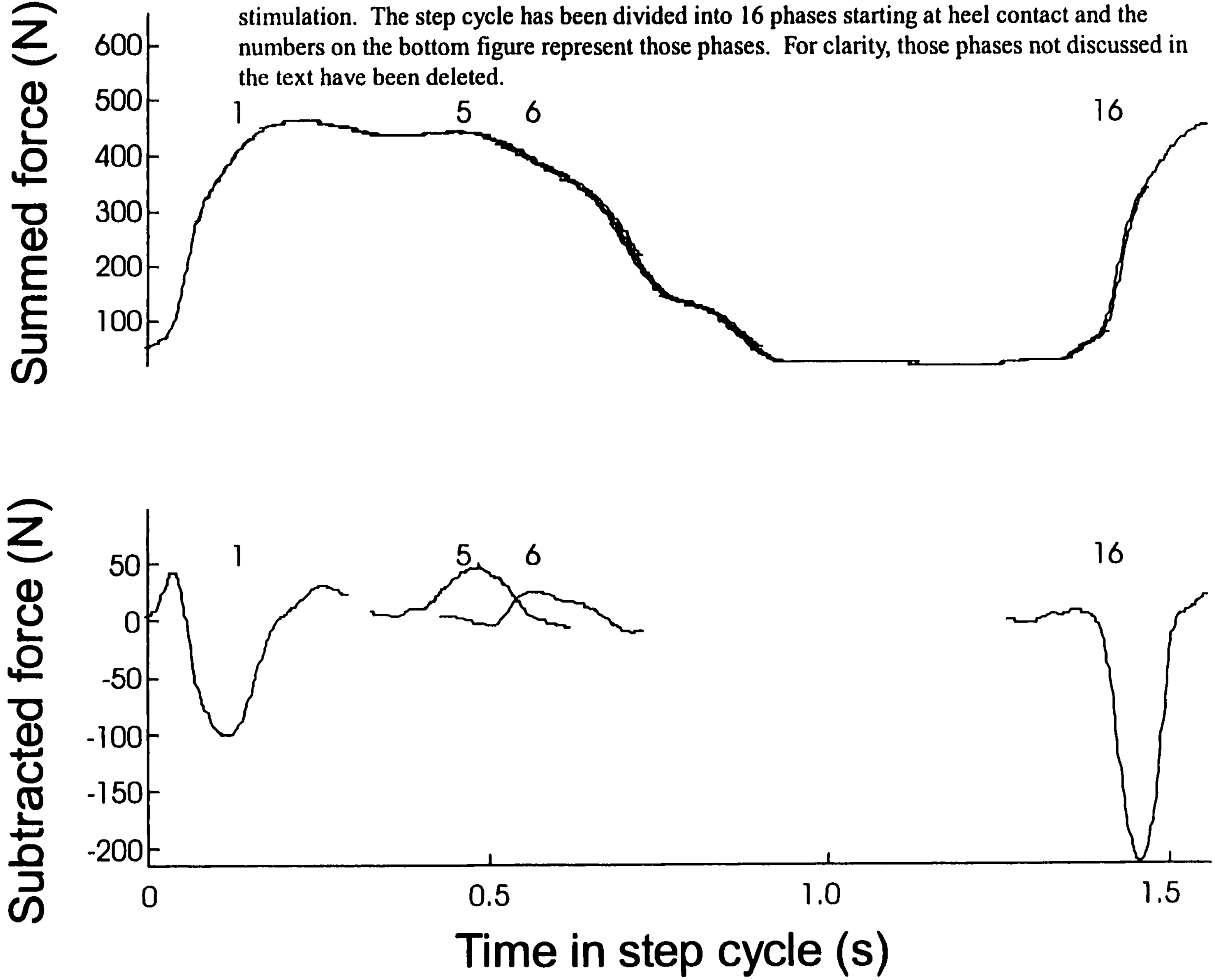


Figure 3-4 Force record during undisturbed 2 km/h walking (top) and subtracted force after CP n. stimulation. The step cycle has been divided into 16 phases starting at heel contact and the numbers on the bottom figure represent those phases. For clarity, those phases not discussed in the text have been deleted.



3.4 Technical considerations and conclusions

The main advantage of the FSRs is their low cost and simplicity of application. As we have shown, the inherent non-linearity can be readily fitted and corrected. Problems do remain, however, as is evident from the 'hysteresis' of Figure 3-1 (see Zehr et al., 1995, Fig.1; see also Smith and Hudson, 1994). The voltage during unloading is consistently higher than during loading. Also, the force on the foot is continuously distributed across its surface, rather than being limited to the 3 areas described in the Methods. This can cause some problems when individuals with large foot sizes are tested with these 3 sensor arrays, in that it becomes quite difficult to obtain valid absolute value forces. Further, if the 3 sensor arrays are not correctly placed, the force profile itself can be somewhat distorted. This is particularly the case for the metatarsal-phalangeal sensors, thus leading to an overemphasis of the heel sensor in the summated record. However, in our experience, even when the absolute force value may be less than expected based on body weight, if the force profile is correct, the summed record can easily be linearly scaled up to the appropriate values (see Winter, 1991).

Our initial work indicates that the FSR arrays as described in this paper can be used to accurately measure force under the human foot during walking. This method has the potential to find application in the study of normal and pathological locomotion as well as in rehabilitation programs that have a prerequisite of accurately determined gait kinetics. Currently, this method of using the FSRs is being applied to examining biomechanical changes associated with reflex modulation during locomotion.

3.5 References

Davis, B.L., and Cavanagh, P.R. (1993). Decomposition of superimposed ground reaction forces into left and right force profiles. *J. Biomech.* **26**(4/5):593-597.

Ferencz, D.C., Zhenxing, J., and Chizeck, H.J. (1993). Estimation of center-of-pressure during gait using an instrumented ankle-foot orthosis. *Proc. 15th Ann. International Conf. IEEE Engineering in Medicine and Biology Society,* pp.981-982.

Kram, R., and Powell, A.J. (1989). A treadmill-mounted force platform. *J. Appl. Physiol.* **67**(4):1692-1698.

Smith, B.P., and Hudson, W.B. (1994). The use of force sensing resistors for muscle force measurements, *CISA* 153-158.

Winter, D.A. (1991). *The biomechanics and motor control of human gait: normal, elderly and pathological (2nd Edition).* University of Waterloo Press, Waterloo.

Zehr, E.P., Stein, R.B., Komiyama, T., and Kenwell, Z. (1995). Linearization of force sensing resistors (FSR's) for valid force measurement during gait. *Proc. 17th Ann. International Conf. IEEE Engineering in Medicine and Biology Society,* pp.300-301.

4. Cutaneous reflexes during human gait: electromyographic and kinematic responses to electrical stimulation[1]

4.1 Introduction

Peripheral sensory inputs have long been known to have powerful and often stereotyped reflex effects in many animals (Sherrington 1906). Much of the initial work on cutaneous reflexes was conducted in cats with various levels of reduction from decerebrate to intact walking preparations (see Duysens & Tax 1994 and Rossignol 1996 for reviews). It was not until the work of Forssberg (1979), Prochazka et al. (1978), and Wand et al. (1980), though, that the functional role in terms of kinematic change was quantitatively assessed. These researchers found that cutaneous reflexes elicited in intact walking cats by electrical and mechanical perturbation of the dorsal surface of the distal hindlimb served to modify limb trajectory during swing such that stumbling was avoided; the "stumbling corrective reaction" (Forssberg 1979). Forssberg (1979) concluded that "...the reflex pattern and the induced corrective movements are adapted so that functionally meaningful movements are evoked in each phase of the step cycle". Later, Drew and Rossignol (1987) described functionally relevant cutaneous reflexes in the cat forelimb. These studies illustrate an association between EMG and kinematic data that suggest an important role of cutaneous receptors in modifying and correcting locomotor limb movement in the cat, particularly during swing.

The role of cutaneous reflexes is not so clear in the human. Electromyographic (EMG) responses have been measured in human leg muscles after non-noxious

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[1] A version of this chapter was published by E. Paul Zehr, Tomoyoshi Komiyama, and Richard B. Stein

stimulation of cutaneous nerves during walking. Such experiments have revealed that cutaneous reflexes are task-dependent (e.g. phasic locomotor vs. tonic maintained activity; Duysens et al. 1993; Kanda & Sato 1983; Lisin et al. 1973), intensity-dependent (e.g. noxious vs. non-noxious stimulation; Bélanger & Patla 1984; Crenna & Frigo 1984; Duysens et al. 1990), phase-dependent (e.g. swing vs. stance; DeSerres et al. 1995; Duysens et al. 1990, 1992; Yang & Stein 1990), and have contralateral as well as ipsilateral effects (Tax et al. 1995). However, with the exception of van Wezel et al. (1994), human studies have mainly examined reflex responses arising from stimulation of the distal tibial (plantar surface innervation) and sural (lateral border innervation) nerves. The reflex effects of stimulating the dorsal surface of the human foot (innervated by the primarily cutaneous superficial peroneal nerve), the same area as was thoroughly described by Forssberg and colleagues (Forssberg et al. 1975; Forssberg 1979) in the cat, have not been thoroughly studied.

Reflex changes in ankle (Duysens et al. 1990, 1992) and knee (Duysens et al. 1992) trajectory were reported after stimulation of sural (lateral foot surface innervation) nerve. Only Duysens et al. (1992) performed a brief analysis of the mechanical effect and found a significant correlation between tibialis anterior (TA) EMG and increased dorsiflexion after sural nerve stimulation during walking. Also, some changes in ankle angle were described after tibial nerve stimulation (Duysens et al. 1990). In the other studies mentioned above, functional conclusions were based only on observed changes in one or more EMG waves without kinematic confirmation.

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in the *Journal of Neurophysiology* 77:3310-3325, 1997.

The purpose of the present paper was, therefore, to test the hypothesis that reflex EMG responses elicited in leg muscles after non-noxious electrical stimulation of the other two main cutaneous nerves of the human foot, the SP and tibial, during treadmill walking have a functional mechanical effect. This approach is quite different from that employed by other researchers, who have mainly examined the pathways and modulation of cutaneous reflexes without a detailed examination of reflex function. The current hypothesis will be tested by correlating global reflex changes in the EMG activity with the kinematics and interpreting significant correlation in terms of possible functional roles, such as Forssberg's (1979) stumbling corrective responses. While electrical stimulation of a cutaneous nerve does not elicit exactly the same afferent volley as natural stimulation, we will argue that our results may mimic the responses to more natural perturbations. Portions of this work have previously been published in abstract form (Zehr et al., 1996a-c).

4.2 Methods

4.2.1 Subjects and general procedure

Six subjects (5 male and 1 female), aged 24-36 y, participated in the experiments with informed, written consent. Each subject participated in 2 separate experiments (one for each nerve studied), each lasting about 3 hours. Because there is often large inter-subject variation in the magnitude and nature of reflex responses after stimulation, the same subjects were involved in each experiment. Then, variation in reflex responses could be ascribed to functional differences between the nerves. All experiments were conducted under an approved protocol for human subjects at the University of Alberta. During each session, subjects walked on the treadmill at speeds of 2 and 4 km/h for approximately 7 to 10 minutes at each speed. These two speeds were selected to provide a range of amplitudes of responses. Since future experiments involving stroke patients (who walk much slower than neurologically intact subjects) are planned, data on 2 km/h walking was collected. Approximately 400-600 steps were collected for each speed (including stimulated and control unstimulated steps).

4.2.2 Nerve stimulation

The superficial peroneal (SP) and tibial nerves were stimulated using a GRASS SD9 (Grass Inst., Quincy Mass.) isolated constant voltage stimulator with trains of 3-6 pulses at 200 Hz with a pulse width of 1.0 ms. The electrodes for the SP nerve were placed on the anterior surface of the leg just near the crease of the ankle joint, while the tibial nerve was stimulated on the medial surface of the ankle posterior to the medial malleolus. The location of the electrodes were such that strong radiating parasthesias were reported by the subjects in the appropriate cutaneous receptive fields; foot dorsum and plantar surface for SP and tibial nerves, respectively. Flexible 1 cm disposable ELECTROTRACE (JASON, Huntington Beach, CA) Ag-AgCl surface EMG electrodes were used for cathodal stimulation. The threshold of stimulation in terms of the radiating threshold (x RT; defined as a clear radiating parasthesias in the cutaneous field appropriate for each nerve), were determined in all subjects. The perceptual threshold (PT), defined as the lowest stimulation that was just detectable by the subject, was also determined. PT likely represents local activation of cutaneous receptors lying immediately underneath the recording electrodes. In contrast, the RT likely represents electrical activation of fascicles in the underlying cutaneous nerve. In general we had less variability between subjects in setting this intensity when using measures of RT. Stimulation intensities were typically twice RT for each nerve. The intensity and number of pulses were varied somewhat in each experiment to obtain the strongest stimulation possible that was described as non-noxious by the subject and was subthreshold for evoking a flexion reflex (a generalized withdrawal of the limb by flexion at the ankle, knee, and hip) while standing. There were no changes in responses observed which could be attributed to any variation in stimulus parameters within the range used in the present experiments.

The stimulator was driven by a pseudo-random pulse generator with a minimal repeat time of 1.8 s and a maximum of 4 s. In this way we were able to collect many unstimulated steps between stimulated steps and no step had more than 1 stimulus.

Outputs from both the trigger pulse generator and the Grass stimulator were sent to a 12 bit A/D converter and then into a 486 66 MHz microcomputer running AXOTAPE (Axon Instruments) data acquisition software.

4.2.3 Electromyography

After light abrasion and cleansing of the skin with alcohol, disposable ELECTROTRACE (JASON, Huntington Beach, CA) Ag-AgCl surface EMG electrodes were applied in bipolar configuration longitudinal to the predicted path of the muscle fibers (~ 2 cm inter-electrode distance) over the soleus (SOL), lateral (LG) and medial gastrocnemii (MG), tibialis anterior (TA), vastus lateralis (VL), and biceps femoris (BF) muscles. SOL electrodes were placed distal to the termination of the gastrocnemius muscles, whereas MG and LG electrodes were placed over the medial and lateral heads of the gastrocnemius. TA electrodes were placed over the largest girth of the tibialis anterior muscle. For VL, the distal electrode was placed approximately 4-6 cm proximal to the lateral margin of the patella and for BF placement was over the muscle belly at approximately 1/3 of the distance from the knee to the hip. As the tibial nerve has a motor branch in the plantar nerve, we recorded motor responses of the intrinsic muscles by placing electrodes on the plantar foot surface and monitored these responses to evaluate stimulus stability throughout a walking trial. This check was not available for SP nerve. For SP nerve, though, the position of the stimulating electrodes was such that it typically produced some minor facilitation of the nearby extensor digitorum brevis muscle. We therefore monitored the EMG from this muscle to check that its stimulation remained constant throughout the cycle. Variation in stimulation across the step cycle was generally less than 10%. Ground electrodes were placed over electrically neutral tissue, such as the knee. EMG signals were pre-amplified and highpass filtered at100 Hz. Then they were full-wave rectified, thus yielding components down to DC, and lowpass filtered at 100 Hz. This filtering process provided a good linear envelope with little spread of the stimulus artifact (which could then be digitally removed off-line, see below). The processed output was then sent to a 12 bit A/D converter and then into a microcomputer running AXOTAPE (AXON Instruments) data acquisition software.

4.2.4 Kinematics and step-cycle timing

Angular position of knee and ankle were recorded with custom-made potentiometric electrogoniometers placed over the joint and secured with plastic tape and fabric straps. Signals obtained from custom-made force sensors located in the insole of the subject's shoe were used to establish step cycle parameters (e.g. heel contact, toe-off). This technique, based on force-sensing resistors (FSRs), has been previously described (Zehr et al., 1995a). Angle and force signals were pre-amplified at the subject (the subject wore a small pouch and belt to hold the amplifiers) and then sent directly to the AXOTAPE computer system.

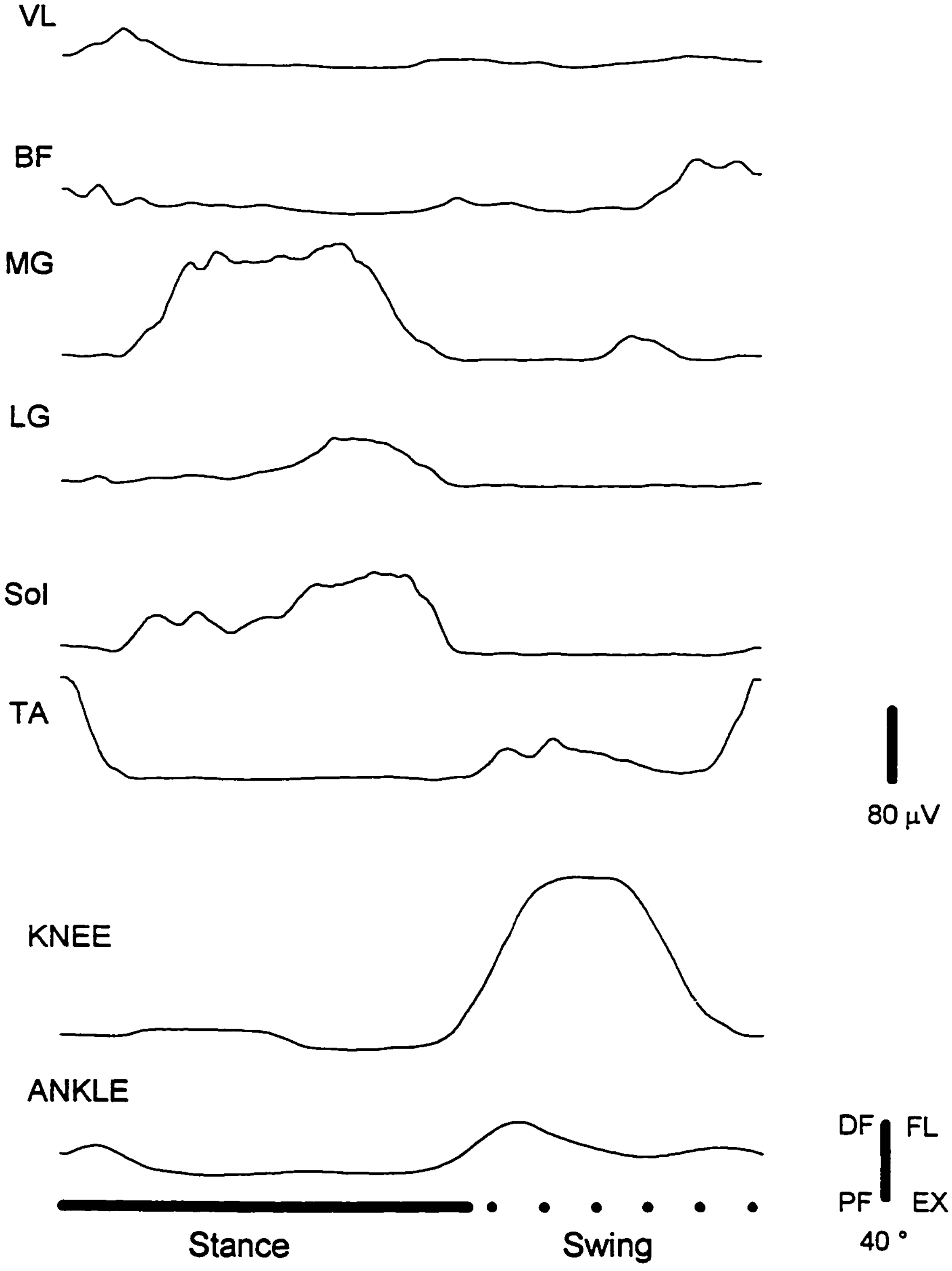
4.2.5 Data acquisition and analysis

The data were sampled continuously at 500 Hz and stored on hard disk for off-line analysis. Custom written software programs were used to separate the step cycle into 16 separate parts of the step cycle, beginning with heel contact. The stimuli occurred randomly throughout the step cycle. All responses to stimuli occurring in the same part of the step cycle were averaged together and aligned to stimulus delivery within that part of the step cycle. The values obtained for each of the 16 averages after stimulation were subtracted from the corresponding averages from unstimulated steps during the same trial (Fig. 4-1).

4.2.6 EMG analysis

To obtain smoother records, stimulus artifacts were digitally removed and then the EMGs were filtered with a 5-point digital moving average filter. The unstimulated control EMGs for each part of the step cycle were subtracted from the corresponding stimulated step cycle parts to yield subtracted evoked EMG traces. The evoked EMGs for each subject were analyzed for the net reflex effect using the Average Cumulative Reflex EMG after 150 ms ($ACRE_{150}$). This technique was employed because the major focus in this study was to evaluate the function of cutaneous reflexes. Hence it was

Figure 4-1 Averaged full-wave rectified and filtered EMG and kinematic data from one subject walking at 4 km/h. EMGs are from the following muscles: vastus lateralis (VL), biceps femoris (BF), medial and lateral gastrocnemii (MG and LG), soleus (Sol), and tibialis anterior (TA). Knee and ankle joint angles are also shown. Partitioning of the step cycle into stance and swing phases are is shown by the solid and dashed bars, respectively. EMG and angle calibrations are as indicated by the vertical lines. Ankle dorsiflexion (DF) and plantarflexion (PF), and knee flexion (FL) and extension (EX) are as indicated.



necessary to compare the net control signal (i.e. the net EMG reflex effect) to the net mechanical outcome (i.e. movement kinematics, see below). Further, previous studies on cutaneous reflexes (see Introduction) have focused mostly on an analysis of responses occurring at a given restricted range of latencies and with durations typically ~30 ms. If a facilitation for 30 ms were followed by an equal suppression for the next 30 ms, there would be no net effect and any transient would have its fundamental at about 16 Hz, which is above the physiological range. By measuring the net response over the entire reflex period of 150 ms, we can expect a realistic association with movement kinematics, which are the filtered output of the entire system. As previously described (see Zehr et al., 1995b, Komiyama et al., 1995), the $ACRE_{150}$ technique is a modified cumulative sum (CUSUM) based on the technique commonly employed to examine effects in post-stimulus time histograms (Ellaway 1978). In brief, the analysis program calculates the subtracted, residual reflex EMG traces and digitally removes the stimulus artifact. The post-stimulus data were then sequentially summed and any significant facilitation or suppression was identified as positive or negative deflections in the CUSUM record. The value obtained at 150 ms after stimulation was then divided by the time interval of integration to measure an overall reflex effect in microvolts (i.e., negative values indicate overall suppression and positive values overall facilitation). As we were interested in reflex effects, a 150 ms post-stimulus interval was chosen since it preceded any significant voluntary activation (see Zehr et al., 1995b). To reduce problems arising from individual differences or electrode placement, the $ACRE_{150}$ values for each subject were normalized to the peak EMG value (averaged over a 40 ms time window) occurring during the entire step cycle for each muscle at each walking speed and expressed as percentages.

4.2.7 Kinematic Analysis

Subtracted values for angular changes were obtained as described above. The maximum change occurring in these smoothed (n=5 point filtering) signals over an interval ranging from 140 to 220 ms post stimulation was calculated. This sliding latency has been used by others in similar studies (Duysens et al. 1992) and was chosen so as to truly reflect the delays between an EMG response and the peak mechanical change in moving muscles (see Stein et al. 1995). As with the EMG, these values were then normalized to the maximal values during the step cycle (e.g., maximum angular excursion occurring within the step cycle) and expressed as percentages.

4.2.8 Statistics

In all instances, analysis was conducted on averaged values of each subject from each part of the step cycle. Significant differences from zero for the net reflex effects were determined by calculation of t-ratios for each part of the step cycle. Statistics were calculated on the combined data from both walking speeds ((df=11). Linear least-means square regression analysis was used to evaluate kinematic correlation between EMG indices and changes in ankle and knee joint angle at each part of the step cycle. Descriptive statistics included means ±SEM and statistical significance was set at $p \leq 0.05$.

4.3 Results

4.3.1 SP nerve

Average rectified and integrated EMG and angle data are plotted in Figure 4-1 from an individual subject walking without stimulation. The typical pattern of EMG activities seen in the subjects is shown for the six knee and ankle muscles studied here, together with the changes in angle at the corresponding joints. The responses to stimulation of the SP nerve in each of 16 parts of the step cycle are shown for four muscles acting at the ankle in Fig. 4-2. The solid vertical line indicates those parts that fall in the stance phase and the dashed vertical line those that fall in the swing phase. Typically, the stance phase is parts 1-8 and the swing phase 10-15. The stance-to-swing transition occurs in part 9 and the swing-to-stance transition in part 16. The stimulus artifacts (representing the period of stimulation) have been removed for clarity, but the period is indicated by the horizontal dashed lines. The EMG without stimulation from Fig. 4-1 has been subtracted from each trace so that positive deflections represent facilitation and negative deflections represent suppression of EMG activity from the control values. Note that complex patterns of facilitation and suppression are often seen extending for more than 100 ms.

The overall response ($ACRE_{150}$ - see Methods) has been calculated for each subject walking at 2 and 4 km/h and averaged over the 6 subjects studied. The values are summarized in Fig. 4-3, together with the corresponding changes in ankle angle. Except for the suppression in MG (the asterisks represent values that are significant at $p< 0.05$) in

Figure 4-2 Subtracted EMGs of TA (top left), Sol (top right), LG (bottom left) and MG (bottom right) muscles after SP nerve stimulation for one representative subject. In all panels the stimulus artifact has been suppressed and replaced by a flat line, over top of which has been placed a thick dashed line. Each trace runs from 50 ms prior to stimulation to 250 ms after stimulation. The numbers on the far left indicate specific portions of the step cycle, while the vertical solid bar indicates stance and the dashed indicates swing phases.

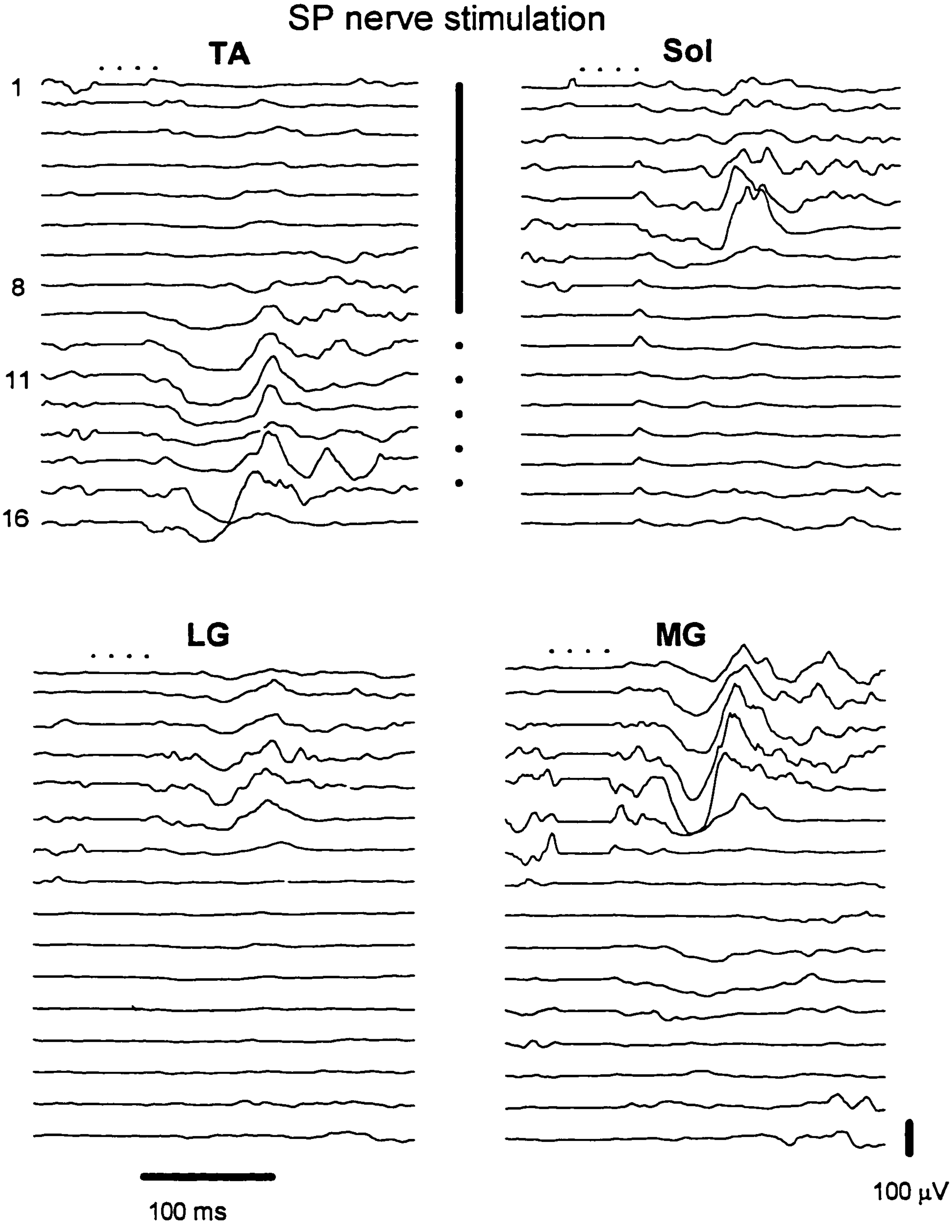
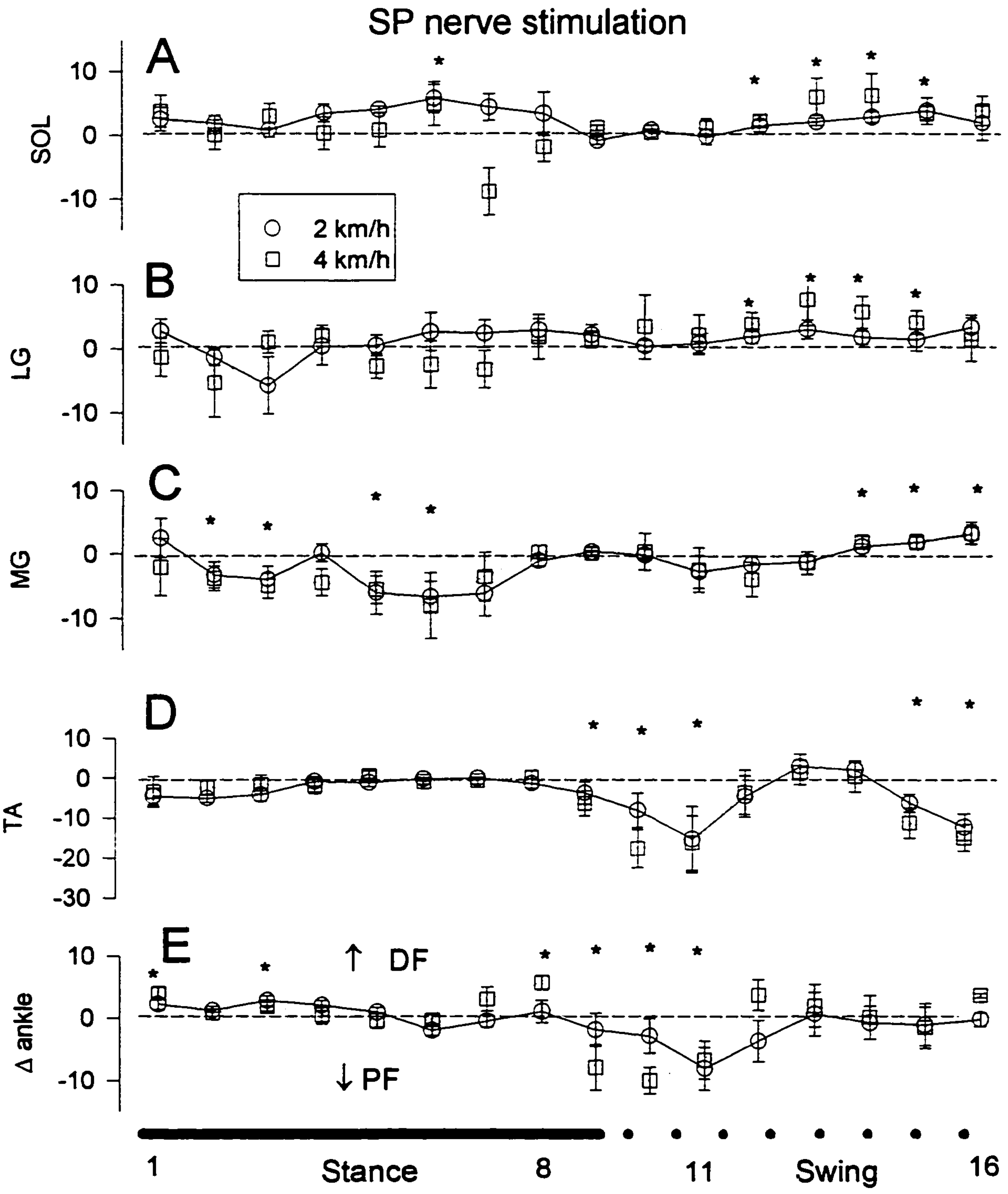


Figure 4-3 Grouped data (n=6; mean +/- SEM) for ACRE$_{150}$ values for SOL (A), LG (B), MG (C), and TA (D) muscles, along with stimulus-induced changes in ankle joint angle (E) throughout the step cycle after SP n. stimulation. Note that the ACRE$_{150}$ values are expressed as a percentage of the maximum EMG for each muscle during the step cycle and the angle changes as a percentage of the maximum excursion of the joint. Effects which are statistically different from zero at $p<0.05$ are indicated by *. The solid and dashed bars indicate stance and swing phases and specific portions of the step cycle are indicated by the labeled numbers. Dorsiflexion (DF) and PF are as indicated by the arrows.



some parts of the stance phase, there is little consistent effect of SP stimulation at this intensity on any of the muscles during the stance phase and little change in ankle angle. However, in the early part of swing phase stimulation produces about a 20% suppression of TA activity (all values are measured relative to the peak activity observed during the step cycle without stimulation) and this is correlated with a negative change in angle (a reduction in dorsiflexion, labeled as a change in the plantarflexion direction in Figure 4-3). A small but significant facilitation is observed in the triceps surae muscles (SOL, LG and MG), which should result in the generation of knee flexor/ankle plantarflexor torque in some later parts of the swing phase, but it is not enough to produce a change in ankle angle. This confirms the importance of measuring kinematic changes before attributing functional effects to changes in EMG.

Figure 4-4 shows data for the knee muscles (VL and BF) in one subject. In contrast to the ankle muscles, the responses are overwhelmingly facilitatory, particularly for BF. The average values for the six subjects are shown in Fig. 4-5, together with the changes in knee angle. As with the ankle, the changes during the stance phase are small, although a significant correlation in the knee flexor BF is associated with some knee flexion during several parts of the stance phase (5-7). Larger changes are observed during much of the swing phase in both muscles and this is again associated with significant knee flexion in several parts (12-16). An interesting point is that increased activity in both the knee extensor (VL) and the knee flexor (BF) is associated with knee flexion.

Figure 4-4 Sample data from one subject of subtracted EMG responses of BF (left), and VL (right) muscles throughout the step cycle. The same format has been used as in Fig. 4-2.

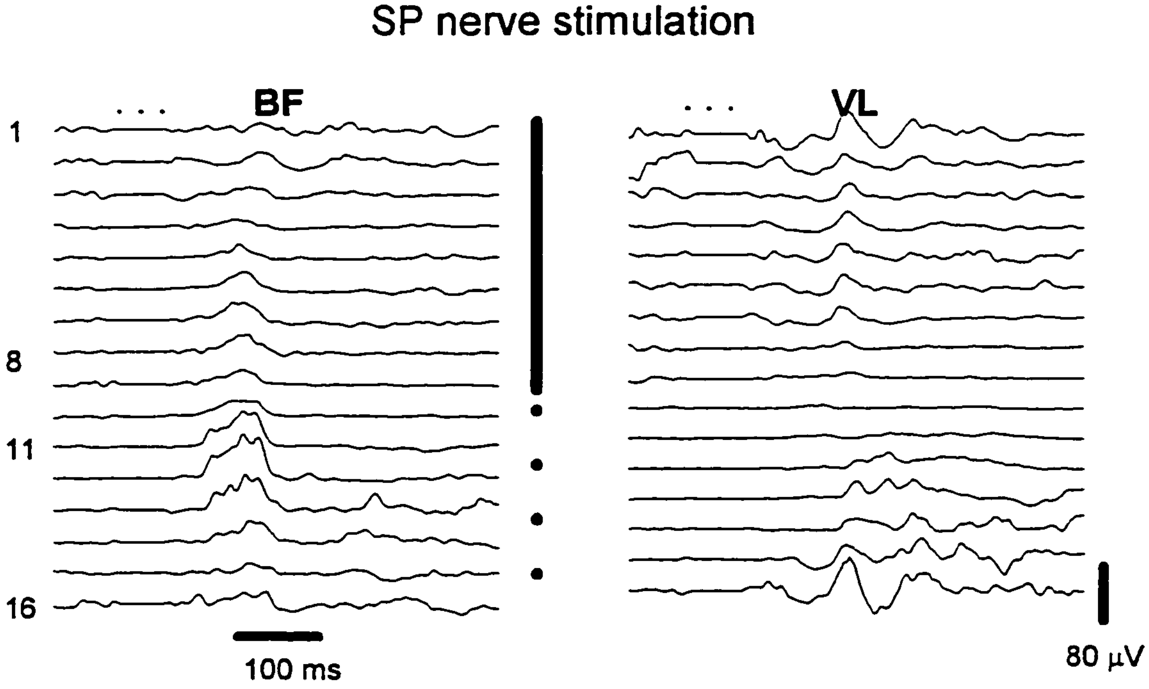
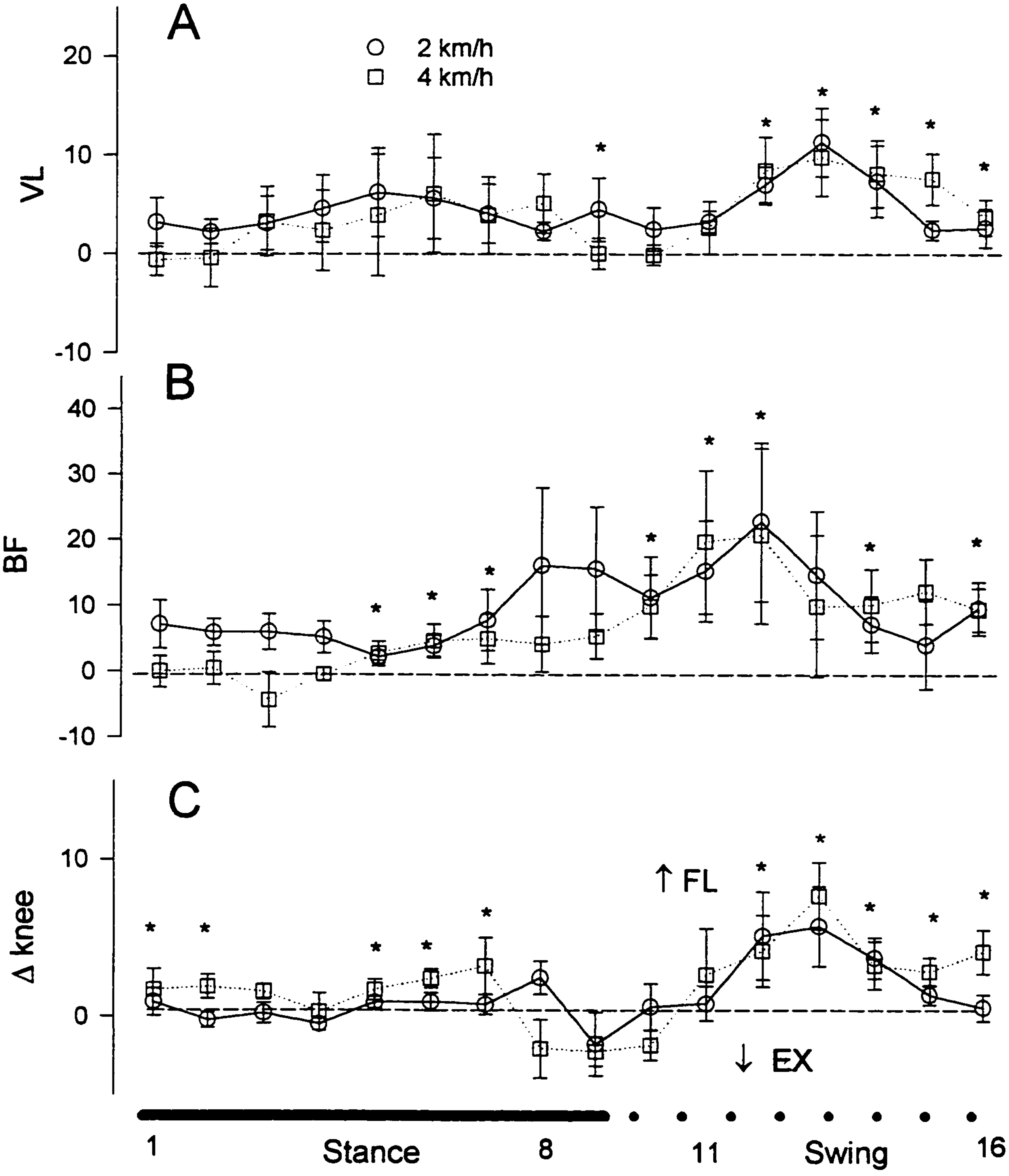


Figure 4-5 SP nerve grouped data for ACRE$_{150}$ values for VL (A) and BF (B) muscles, along with changes in knee angle (C) throughout the step cycle. The * indicate statistical significance at $p<0.05$. Knee flexion (FL) and extension (EX) are as indicated by the arrows. The ACRE$_{150}$ values are expressed as a percentage of the maximum EMG for each muscle during the step cycle and the angle changes as a percentage of the maximum excursion of the joint.



The increases in BF activity (about 20%) are larger than in VL activity (about 10%) so that the knee flexor action dominates. The coactivation of antagonist muscles will increase the stiffness of the knee joint.

A second method to analyze the changes is to run the correlations between EMG activity and angle change for each subject at both speeds in each part of the step cycle. All the data are plotted in Figure 4-6 and correlations up to R = 0.9 (part 11) are seen between TA EMG and ankle angle. The data for this particular correlation are shown in Figure 4-7 and the good fit is obvious for TA in comparison to the lack of a correlation in SOL. The relation of both knee muscles to knee flexion are also confirmed during the swing phase, although the small changes in BF during stance are not significant with this method. The correlations range up to R = 0.85 (in part 11) and again these data are plotted in Figure 4-7. Although there is actually a slightly higher correlation between VL activity and knee angle changes, the magnitude of the changes are much greater in the knee flexor BF (ranging up to 70%) which is associated with the resultant net flexion of the knee (15% of the maximum excursion during the step cycle).

Taken together the results of SP stimulation show three major points: 1) there is little effect on the EMG or kinematics during the stance phase; 2) stimulation results in a coordinated reduction in ankle dorsiflexion (seen as plantarflexion in the figures) and flexion of the knee during the swing phase of gait; 3) antagonistic knee muscles may be coactivated (at least in the representative muscles studied here).

Figure 4-6 Phase-by-phase linear regression analysis for correlations between TA and Sol $ACRE_{150}$ values and ankle angle (top) and BF and VL $ACRE_{150}$ values and knee angle (bottom) after SP n. stimulation. Significant r values are indicated by asterisks.

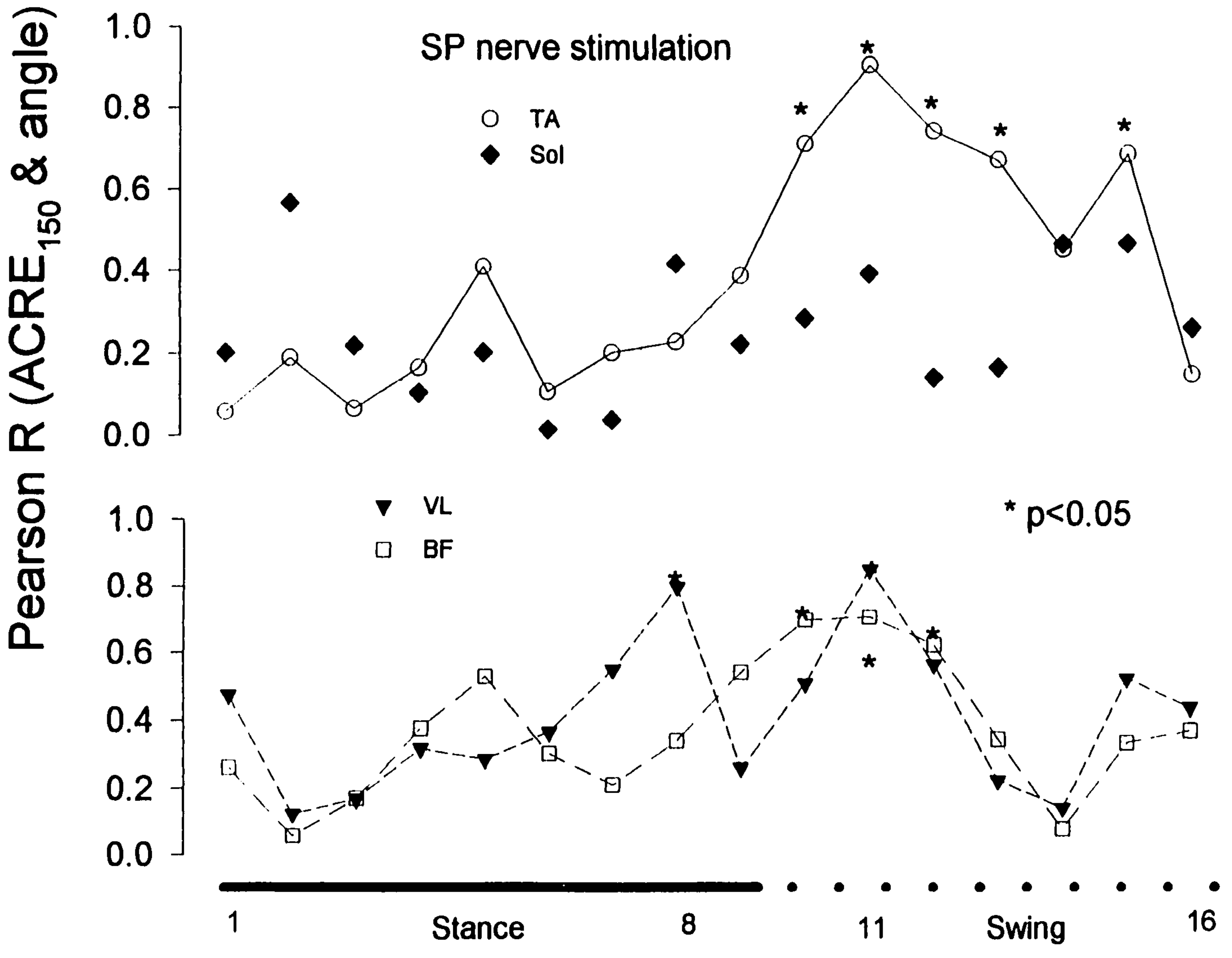
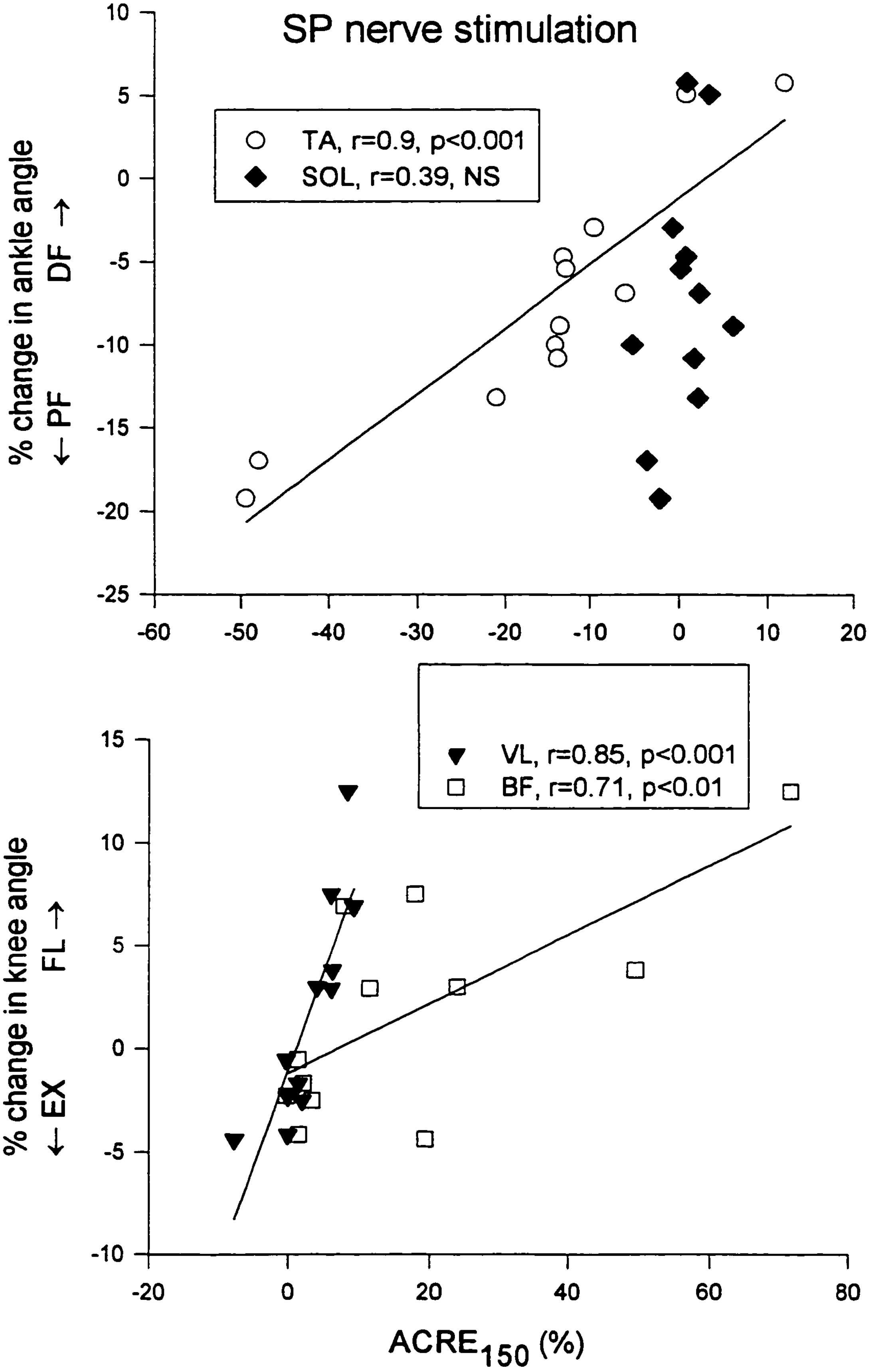


Figure 4-7 Grouped data for both 2 and 4 km/h walking from part 11 of the step cycle plotted for regression between TA, Sol and ankle angle (top), and BF, VL and knee angle (bottom). Note highly significant correlations between all muscles and angles except for SOL.



4.3.2 Tibial nerve

Figure 4-8 shows averaged data for tibial nerve stimulation for 6 subjects walking at 2 and 4 km/h. Tibial stimulation produced no substantial effects during the stance phase, except for a significant facilitation of TA muscle (*) at the transition between stance and swing, which is associated with a dorsiflexion of the ankle. This can also be seen in Figure 4-9 which shows Pearson R values of 0.70. Note that the increased TA activity occurs during much of swing phase with large values of R but that there is not a significant change in ankle angle (Fig. 4-8), presumably resulting from the increased activity in soleus which would counteract the TA effect.

The other significant ankle change in Figure 4-8 is a plantarflexion in parts 14 and 15 of the swing phase which is associated with an increased activity of the triceps surae (SOL, LG and MG) and small changes in the TA. Yang et al. (1990) and Duysens et al. (1990) found an actual reversal of TA activity with tibial nerve stimulation producing suppression at a middle latency response, but this can be more than balanced by the early and later facilitation in some subjects. Thus, it is important to use an overall measure such as the $ACRE_{150}$. There is a significant R value of 0.63 at part 14 of the cycle (Figure 4-9). Whereas there was generally good agreement in data obtained in different subjects (e.g. see error bars in all grouped data figures), there was variability in the responses at this part of the step cycle after tibial nerve stimulation. In some subjects there was a net suppression and in others a net facilitation in TA and the angle changes varied accordingly (Fig. 4-10). The predominant movement is plantar flexion, associated with the increase in triceps surae muscles. Thus, tibial nerve stimulation does produce a functional reversal with dorsiflexion during the transition from stance to swing and a plantar flexion during late swing.

The results at the knee are shown in Figure 4-11. Again, the predominant effect is facilitation, particularly during the swing phase and this is associated with a flexion of the knee during this phase. However, looking at the Pearson R values in Figure 4-9, there is only 1 significant correlation. Thus, much of the flexion of the knee must be coming from other sources, such as being secondary to flexion at the hip.

Figure 4-8 Tibial nerve grouped data for ACRE$_{150}$ values for SOL (A), LG (B), MG (C), and TA (D) muscles, along with stimulus-induced changes in ankle joint angle (E) throughout the step cycle during 2 and 4 km/h walking. Same format as in Fig. 4-5. Statistically significant net responses at $p<0.05$ are indicated by *.

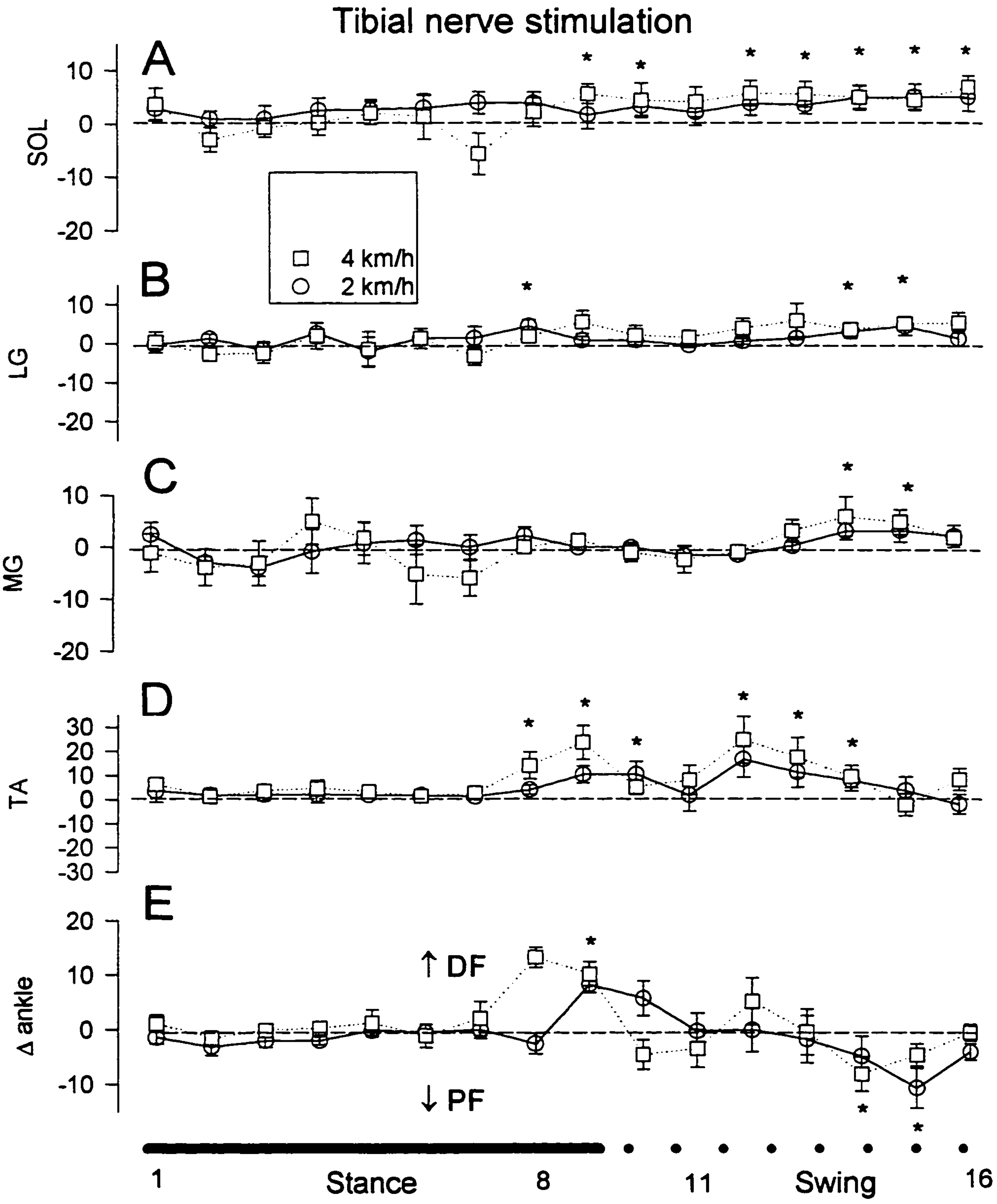


Figure 4-9 Phase-by-phase linear regression analysis for correlation between TA and SOL $ACRE_{150}$ values and ankle angle (top) and BF and VL $ACRE_{150}$ values and knee angle (bottom) after tibial nerve stimulation. Significant r values are indicated by asterisks.

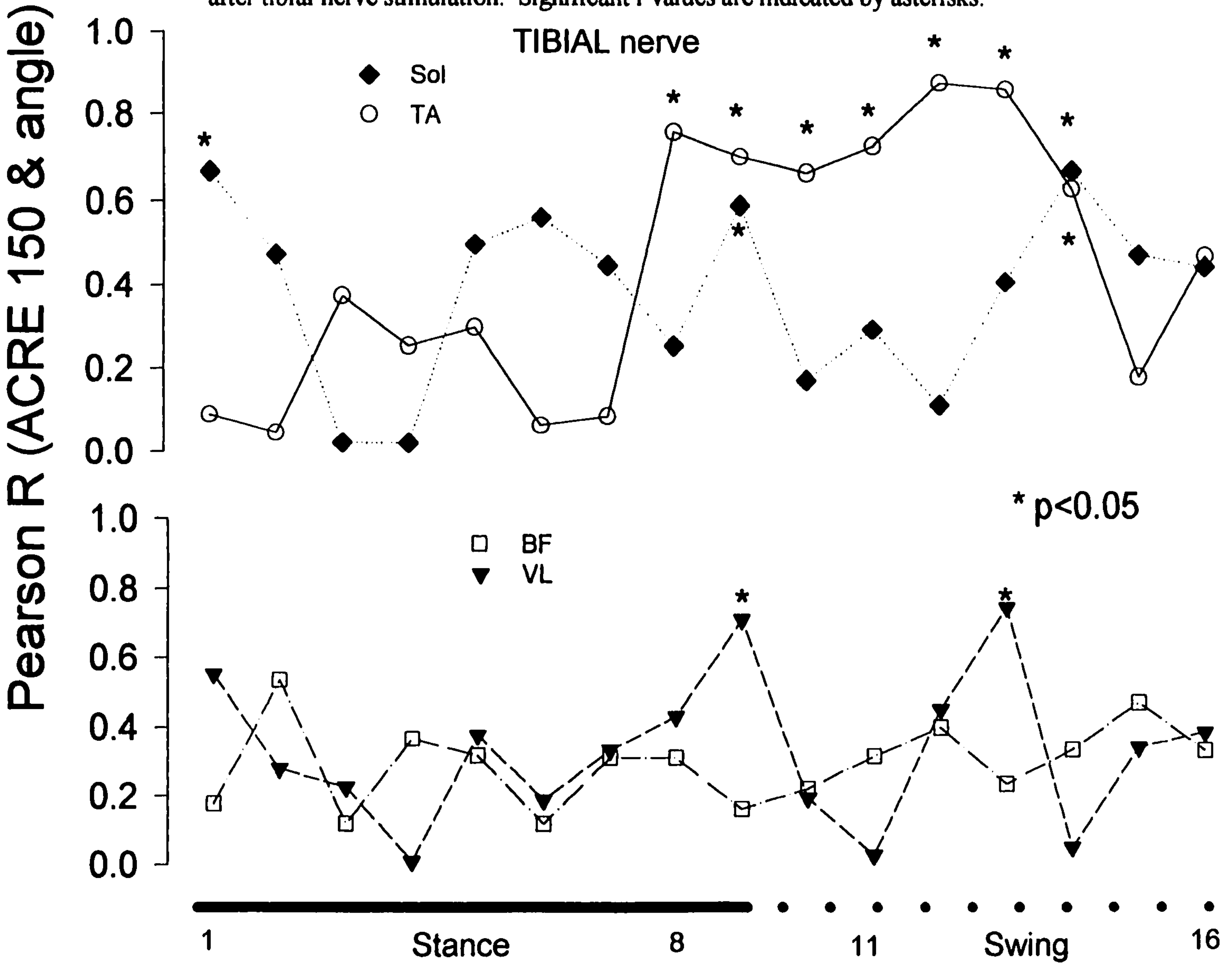


Figure 4-10 Subject data points for both 2 and 4 km/h walking plotted for regression between TA and SOL and ankle angle (top) and BF and VL muscles and knee angle (bottom), after tibial nerve stimulation. In the top panel, TA responses at the stance to swing transition (part 9) are plotted as filled circles and those in swing (part 14) as open circles. Significant regression statistics are given in the legend and are represented by regression lines on the plots. Note the reversal in the net mechanical effect at the ankle joint between parts 9 (net DF) and 14 (net PF) after tibial nerve stimulation and that the activity of the knee extensor VL is correlated with knee flexion. See text for further details.

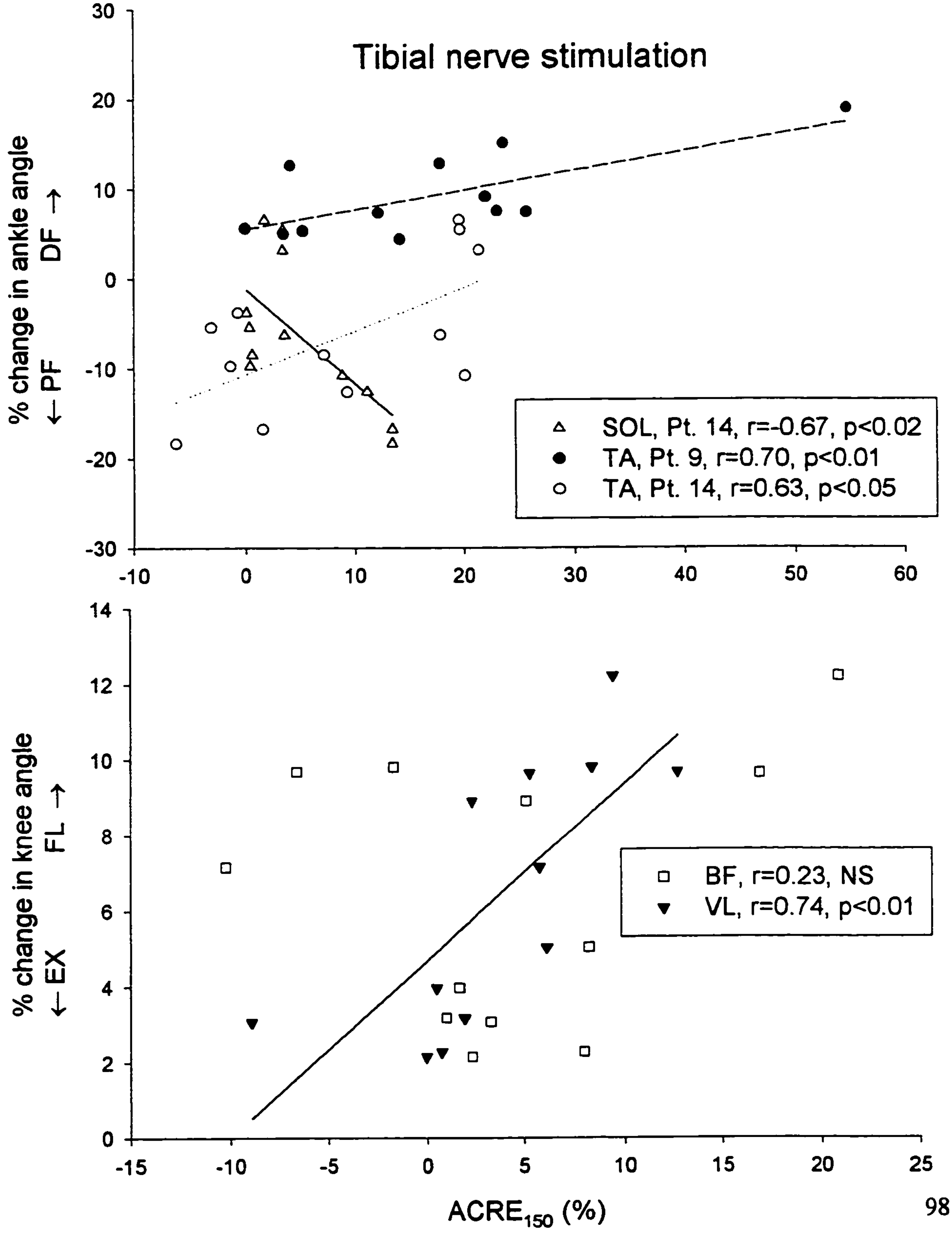
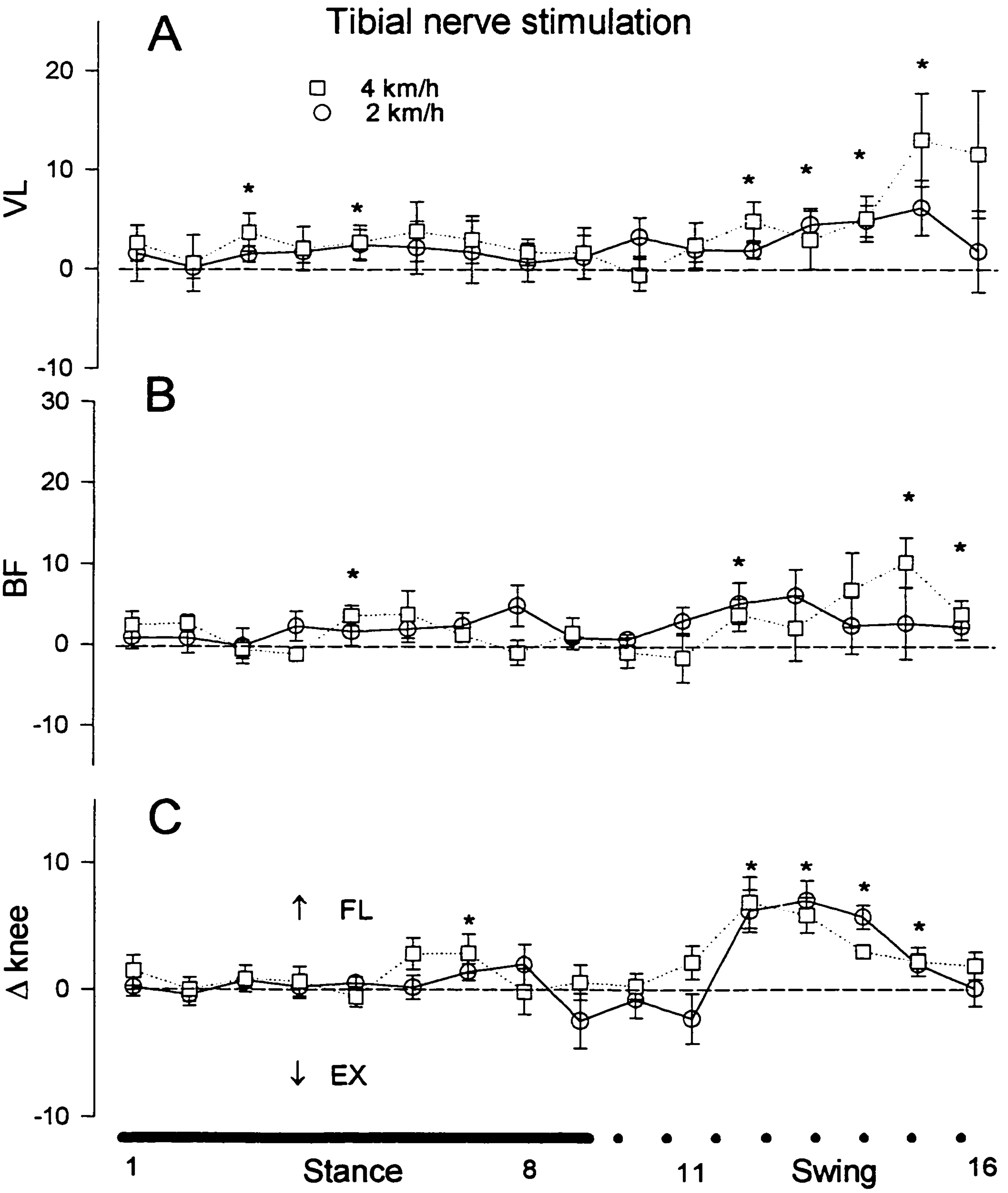


Figure 4-11 Tibial nerve grouped data (n=6 subjects; mean +/- SEM) for ACRE$_{150}$ values for VL (A) and BF (B) muscles, along with stimulus-induced changes in knee angle (C) throughout the step cycle during 4 km/h walking. Same format as in Fig. 4-5.



4.4 Discussion

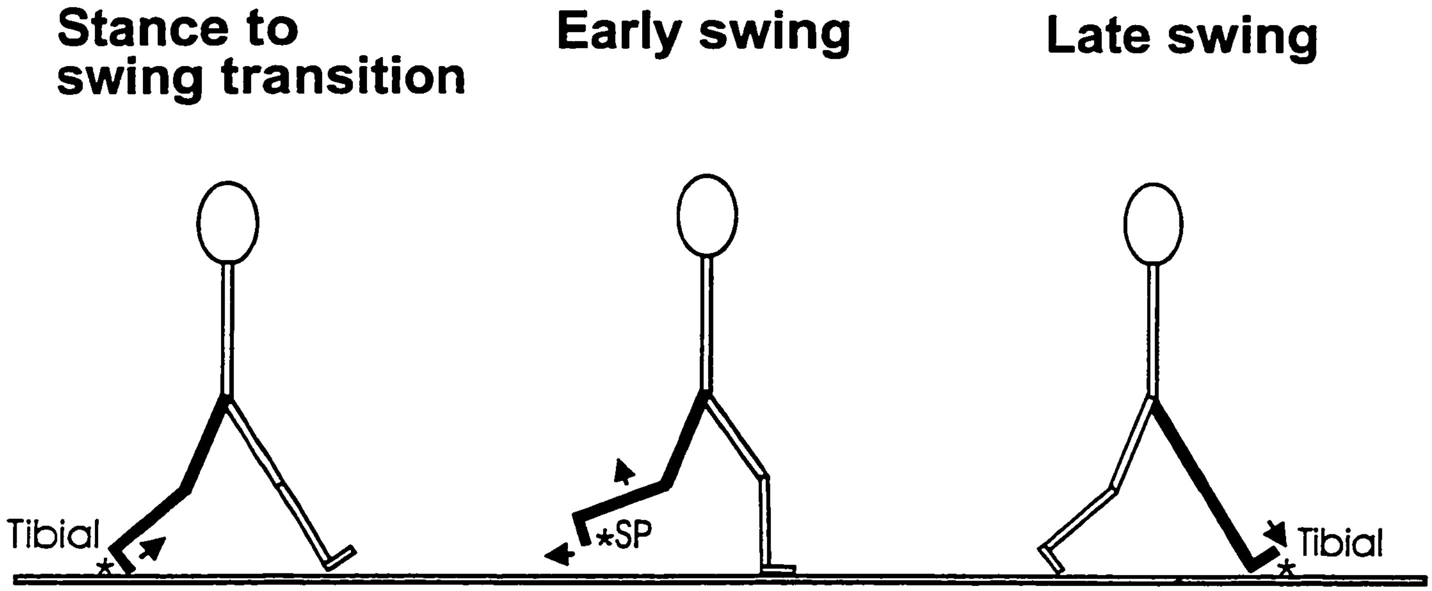
In this paper, we have shown that volleys in cutaneous pathways to leg muscles from electrical stimulation of two major lower leg cutaneous nerves during human gait can elicit EMG and kinematic responses. The third, the sural nerve, has previously been studied in some detail by Duysens et al. (1992). Here, the overall responses were generally larger during the swing phase and transitional phases than during stance. Further we have shown a significant correlation between the net EMG and mechanical measures of stimulus-induced changes in ankle and knee joint angle trajectory after stimulation of each nerve. Below, we argue for the functional relevance of the observed responses and discuss the relative contribution of cutaneous input during the various phases of human gait.

4.4.1 Are the responses functional?

4.4.1.1 SP nerve results

As was mentioned in the introduction, Forssberg (1979) spoke of a "stumbling corrective response" in the feline preparation as one in which a given stimulus elicited robust reflex EMG responses which had mechanical effects permitting undisturbed locomotor progression. This response was essentially increased knee, hip and ankle flexion, a pattern quite suited to the more stable nature of quadrupedal locomotion. This response allowed the animal to continue movement of the swing limb with little overall disturbance to the act of walking. Our observed responses to electrical stimulation of SP nerve in human subjects showed some similarities and some differences. The only way for the innervation area of SP nerve (foot dorsum) to be strongly activated during walking, particularly during swing, would be for contact with some form of impediment. In our experiments stimulation of this nerve elicited a radiating parasthesias that resembled to some extent banging the foot on an obstacle. The sensation is not pain, but rather pressure and tingling. If one were to catch the foot on an obstacle during early swing phase, the responses observed here would allow for smooth leg movement as shown schematically in Figure 4-12 (center). A suppression of normal TA muscle activity would allow for passive plantar flexion (a reduction in dorsiflexion, as mentioned previously) which we observed to be functionally concomitant with slight knee flexion , to lift the limb over the obstacle. In contrast, if normal muscle activation and swing leg kinematics were maintained, movement would be blocked and a fall could result. Thus, this is a stumbling corrective response to electrical stimulation in humans. A difference between this result and that described by Forssberg (1979) is that, while in the cat knee

Figure 4-12 Schematic diagram of the functional effects of cutaneous reflexes from tibial nerve at the stance to swing transition (far left) and late swing (far right) and from SP nerve during mid-swing (center panel). Note that only after SP n. stimulation is there a linkage between knee and ankle joint mechanics. * indicates general cutaneous field activated by the electrical stimulation for each nerve.



and ankle flexion result, we observed knee flexion and reduced dorsiflexion in our human subjects. It is postulated that this occurs as a result of inherent differences in balance control and stability that exist in quadrupeds and bipeds. Therefore, while the general quality of the response may be similar across species, the details at crucial joints (i.e., the ankle joint) may be different.

While it is difficult to compare our results arising from electrical stimulation to naturally occurring stumbling, Schillings et al. 1996) have recently described stumbling reactions to obstacles encountered during human treadmill locomotion. They describe kinematic changes that, while of larger amplitude, are quite similar to our electrically-stimulated responses. They demonstrated increased plantarflexion and knee flexion responses in concert with enhanced BF activity. Eng et al. (1994) described various corrective responses to actual physical obstacles during swing and their data, while time-shifted somewhat from the present data (e.g. TA suppression is noted in a late swing lowering response in Eng et al.), seem qualitatively quite similar. These findings corroborate our assertion that electrically “simulated” perturbations may elicit functionally relevant reflexes in the swing leg during human walking.

The question remains, though, as to why the knee extensor VL undergoes a net facilitation at the same time the functionally relevant net BF facilitation is occurring? The increased activity across the knee joint may serve to increase the stiffness of the knee joint in case the distal modification at the ankle is unsuccessful. If the reduction in resistance to ankle joint dorsiflexion is not enough to allow smooth swing across the obstacle, stumbling and tripping could occur. If so, increased loading of knee extensors in the swing leg will ensue. The nervous system may be anticipating this possible outcome and the increased activation of the knee extensors along with the knee flexors would provide a finer control of knee joint trajectory and a larger safety margin in case of a stronger perturbation. Also, the increased knee joint stiffness along with reduced ankle joint stiffness may force the perturbation to be accommodated at the distal limb segment. Thus the perturbation will have a smaller destabilizing effect on the whole swing leg. Interestingly, while they did not report data on the VL muscle specifically, Schillings et al. (1996) have reported enhanced rectus femoris (a knee extensor synergist of VL, but also a hip flexor) activation in their mechanical stumbling paradigm. Also, in the cat, Drew and Rossignol (1987) reported coactivation of forelimb flexors and extensors after superficial radial nerve stimulation. They suggested that their results might be interpreted in terms of control over the inertia of the distal segment. This may also play a role in the present experiments. Here coactivation was seen in the more proximal muscles, controlling the larger inertia of the proximal and distal leg segments, and not in the distal muscles (i.e. SOL, LG, MG, and TA), controlling the smaller inertia of the most distal segment. However, it must also be noted that we measured one knee extensor (VL) and one hip extensor/knee flexor (BF) out of the many muscles which cross the knee in the anterior and posterior compartments. Therefore, while we believe the current explanation to be plausible, caution must be exercised in extending the results too far, particularly as regards potential differences between electrical and more natural stimulation.

4.4.1.2 Tibial nerve responses

We observed significant kinematic correlation between the net effect in TA muscle and ankle joint trajectory during the stance to swing transition and throughout swing (see Figure 4-9, top panel) after tibial nerve stimulation. However, the kinematic association switched from being one in which significantly ($p<0.05$) increased ankle joint dorsiflexion was observed (part 9 in Figure 4-8E) to one in which increased plantarflexion was noted (late swing, parts 14 & 15). This is similar to the kinematic changes reported in some subjects by Duysens et al. (1990) after tibial nerve stimulation. However, in that study a correlational analysis such as plotted in Figure 4-10 between EMG index and angle change, was not conducted. The reversal in kinematic correlation can be clearly seen in Figure 4-10 (top panel) in which responses from stance transition (part 9, filled circles) all lie above zero (increased ankle joint dorsiflexion) while those from late swing (part 14, open circles) are mainly below zero and thus represent increased ankle joint plantarflexion. We interpret the effects observed during the stance to swing transition (Fig. 4-13, left stick figure) as follows. During this phase the normal pattern of tactile input to the foot sole should be reduced (as in the cat, Popovic et al. 1993), not increased as our stimulation would emulate, in preparation for swing phase. The linkage between increased TA activation and increased ankle dorsiflexion should lift the foot off the ground to avoid scuffing of the foot and potential tripping when swing phase begins. We also observed increased plantarflexion during late swing (right part of Fig. 4-12). At this time, input to the sole of the foot would also indicate ground contact. However, the functionally relevant response might not be to increase dorsiflexion as observed earlier in the step cycle. Rather, ground contact is expected and weight is being transferred toward this limb. Therefore our observed plantarflexion may be interpreted in terms of a form of placing reaction in order to get the foot firmly on the ground once foot contact is sensed, again to accept weight and prevent tripping.

The correlations were less numerous and sizeable between reflex effects and knee joint trajectory after tibial nerve stimulation, so functional responses at the knee may not be as prominent after non-noxious stimulation of this nerve. As pointed out earlier, some of the kinematic changes may be secondary to movements at other joints, such as the hip. Patla and Prentice (1995) indicated that voluntary, visually-cued corrections to obstacles during human gait may act by altering the hip moment. Therefore, changes measured at the ankle and knee might be more passive processes, within which suppression (e.g. SP effects on TA muscle as described above) may be as important as facilitation of normal locomotor activity. This is an issue worthy of further study.

4.4.2 Why are there smaller kinematic effects during stance and larger effects during swing?

During locomotion in cats the afferent volley in SP nerve has two bursts of activity, one when the paw hits the ground and a second when the paw is lifted from the ground (Popovic et al. 1993). However, there is continuing activity during the stance phase as the skin surface is stretched or wrinkled as the ankle extends or flexes. Afferent activity is low during swing phase at a time when the receptive field is in an opportune location for detecting foot contact with external obstacles. Unexpected inputs relevant to the control of locomotion during this phase could have a more marked effect on the progress of locomotion, as demonstrated here. Alternatively, such inputs could be gated out either by a central oscillator (Duysens et al. 1995) or perhaps a peripheral modulation making use of interposed interneurons or presynaptic inhibition, as has been demonstrated for the monosynaptic H-reflex (Stein 1995). The cutaneous nerves can provide cognitive information during stance about pressure on the foot and the ground surface that would be involved in the planning of subsequent steps, but which is beyond our reflex time scale. In contrast, obstacles encountered during swing need rapid, reflex responses to maintain secure, stable walking, and the responses observed here may be important for this reflex function. Lastly, it must also be pointed out that during stance the foot is planted firmly on the ground and one might expect less movement than when the limb is free to move during swing.

In conclusion, we have documented that electrical stimulation of the tibial, and SP nerves, which have distinct and anatomically opposed cutaneous innervation areas, elicit prominent net EMG and kinematic reflex effects. We have also argued for a simple functional interpretation (Figure 4-12) in terms of integrated responses whereby cutaneous reflexes can functionally stabilize human gait. For example, contrast the plantarflexor response and mechanical correlation seen after early swing SP nerve stimulation (Figure 4-3E) with the dorsiflexion response seen after tibial nerve stimulation (see Figure 4-8E). Interestingly, these results are quite similar to those reported by Buford and Smith (1993) when they applied mechanical and electrical perturbations to the ventral and dorsal foot surfaces during forward and backward walking in the cat. They found antagonistic EMG and mechanical reflex responses which were specific to the forward or backward walking pattern and anatomical location of the cutaneous receptive field and that were functionally relevant to allow continued gait. We agree with a functional role of these cutaneous reflex responses to prevent stumbling and tripping during critical transitional and swing phases of human gait.

4.5 References

Bélanger, M., and Patla, A.E. Corrective responses to perturbation applied during walking in humans. *Neurosci. Lett.* 49:291-295, 1984.

Buford, J.A., and Smith, J.L. Adaptive control for backward quadrupedal walking. III. Stumbling corrective reactions and cutaneous reflex sensitivity. *J. Neurophysiol.* 70:1102-1114, 1993.

Crenna, P. and Frigo, C. Evidence of phase-dependent nociceptive reflexes during locomotion in man. *Exp. Neurol.* 85:336-345, 1984.

DeSerres, S.J., Yang, JF, and Patrick, S.K. Mechanism for reflex reversal during walking in human tibialis anterior motor units. *J. Physiol.* 488:249-258, 1995.

Drew, T., and Rossignol, S. A kinematic and electromyographic study of cutaneous reflexes evoked from the forelimb of unrestrained walking cats. *J. Neurophysiol.* 57:1160-1184, 1987.

Duysens, J., Tax, A.A.M., Nawijn, S., Berger, W., Prokop, T., and Altenmuller, E. Gating of sensation and evoked potentials following foot stimulation during human gait. *Exp. Brain Res.* 105:423-431, 1995.

Duysens, J., and Tax, A.A.M. Interlimb reflexes during gait in cats and humans. In: *Interlimb Coordination: Neural, Dynamical, and Cognitive Constraints,* edited by S.P. Swinnen, H. Heuer, J. Massion, and P. Casaer. San Diego, CA: Academic, 1994, p. 97-126.

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

Duysens, J., Tax, A.A.M., Trippel, M. and Dietz, V. Phase-dependent reversal of reflexly induced movements during human gait. *Exp. Brain Res.* 90:404-414, 1992.

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

Ellaway, P.H. Cumulative sum technique and its application to the analysis of peristimulus time histograms. *EEG & Clin. Neurophysiol.* 45:302-04, 1978.

Eng, J.J., Winter, D.A., and Patla, A.E. Strategies for recovery from a trip in early and late swing during human walking. *Exp. Brain Res.* 102:339-349, 1994.

Forssberg, H., Grillner, S., and Rossignol, S. Phase dependent reflex reversal during walking in chronic spinal cats. *Brain Res.* 85:103-107, 1975.

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

Kanda, K., and Sato, H. Reflex responses of human thigh muscles to non-noxious sural stimulation during stepping. *Brain Res.* 288:378-380, 1983.

Lisin, V.V., Frankstein, S.I., and Rechtmann, M.B. The influence of locomotion on flexor reflex of the hind limb in cat and man. *Exp. Neurol.* 38:180-183, 1973.

Komiyama, T., Zehr, E.P., and Stein, R.B. A novel method for evaluating the overall effect of nerve stimulation in humans. *EEG Clin. Neurophysiol.* 97,S179, 1995.

Patla, A.E., and Prentice, S.D. The role of active forces and intersegmental dynamics in the control of limb trajectory over obstacles during locomotion in humans. *Exp. Brain Res.* 106:499-504, 1995.

Popovic, D., Stein, R.B., Jovanovic, K., Dai, R., Kostov, A., and Armstrong, W.W. Sensory nerve recording for closed-loop control to restore motor functions. *IEEE Trans. Biomed. Eng.* 40:1024-1031, 1993.

Prochazka, A., Sontag, K.-H., and Wand, P. Motor reactions to perturbations of gait: proprioceptive and somesthetic involvement. *Neurosci. Lett.* 7:35-39, 1978.

Rossignol, S. Neural control of stereotypic limb movements. In: *Handbook of Physiology, Section 12. Exercise: regulation and integration of multiple systems,* Rowell, L.B. and J.T. Sheperd (eds.), American Physiological Society, 1996, pp.173-216.

Schillings, A.M., Van Wezel, B.M.H., and Duysens, J. Mechanically induced stumbling during human treadmill walking. *J. Neurosci. Methods* 67:11-17, 1996.

Sherrington, C.S. *The integrative action of the nervous system.* Oxford University Press, London, 1906.

Stein, R.B. Presynaptic inhibition in humans. *Prog. Neurobiol.* 47:533-544, 1995.

Stein, R.B., Hunter, W., Lafontaine, S.R., and Jones, L.A. Analysis of short-latency reflexes in human elbow flexor muscles. *J. Neurophysiol.* 73:1900-1911, 1995.

Tax, A.A.M., Van Wezel, B.M.H., and Dietz, V. Bipedal reflex coordination to tactile stimulation of the sural nerve during human running. *J. Neurophysiol.* 73:1947-1964, 1995.

Van Wezel, B.M.H., Ottenhoff, F.A.M., and Duysens, J. Reflex responses to low-intensity stimulation of the sural, tibial, and peroneal nerves during human walking. *Soc. Neuroscience Abs.* **20**:1582, 1994.

Wand, P., Prochazka, A., and Sontag, K.-H. Neuromuscular responses to gait perturbations in freely moving cats. *Exp. Brain Res.* 38:109-114, 1980.

Yang, J.F. and Stein, R.B. Phase-dependent reflex reversal in human leg muscles during walking. *J. Neurophysiol.* 63:1109-1117, 1990.

Zehr, E.P., Stein, R.B., Komiyama, T., and Kenwell, Z. Linearization of force sensing resistors (FSR's) for force measurement during gait. *Proc. 17th Ann. International Conf. IEEE Engineering in Medicine and Biology Society*, 1995a, pp.300-301.

Zehr, E.P., Komiyama, T., and Stein, R.B. Evaluating the overall electromyographic effect of cutaneous nerve stimulation in humans. *Soc. Neuroscience Abs.* **21**:681, 1995b.

Zehr, E.P., Komiyama, T., and Stein, R.B. Functional reflex modulation by cutaneous nerve stimulation during human gait. *Can. J. Physiol. Pharmacol.* 74:Axxxviii, 1996a.

Zehr, E.P., Komiyama, T., and Stein, R.B. Cutaneous reflexes in leg muscles after electrical stimulation of the dorsal surface of the foot functionally modify human walking. Proceedings of *Biomechanics and Neural Control of Movement IX: Neuro-mechanical control, interaction between neural circuits and biomechanics*, June 1-6, 1996b, pp. 117-118.

Zehr, E.P., Komiyama, T., and Stein, R.B. Functional antagonism of cutaneous reflexes in the human tibialis anterior (TA) muscle during walking. Proceedings of *Canadian Society for Biomechanics 9th Biennial Meeting*, pp. 170-171, 1996c.

5. Reflexes from the superficial peroneal nerve during walking in stroke subjects[1]

5.1 Introduction

Investigations of reflexes after spinal cord injury or CNS insult often reveal hyperactive and generally excitatory responses (Stein et al. 1993). Reflexes arising from muscle afferents have been studied in spinal cord injured subjects during slow walking. Yang et al. (1991) showed that the phasic H-reflex modulation observed in neurologically intact subjects was impaired in spastic paretic subjects and that the reflex was greatly enhanced. These responses seemed to be related to the degree of motor impairment in a given patient. Likewise, Sinkjaer et al. (1995) found the SOL H-reflex to be modulated only by the level of background muscle activation and not by phasic locomotor activity in spastic multiple sclerosis subjects, indicating a deficient central modulatory mechanism. Sinkjaer et al. (1996) recently showed that modulation of stretch reflexes and ankle joint torque is also deficient in these subjects. They demonstrated that the reflex impairment, as well as alterations in intrinsic stiffness of the ankle joint contribute to the locomotor deficit. El-Abd and Ibrahim (1994) studied cerebral somatosensory evoked potentials (SEPs) elicited by stimulation of the motor nerve to SOL during gait in stroke subjects with spastic hemiplegia. They documented a deficiency in modulation of the SEPs on the affected side of most of their subjects.

Cutaneous reflexes are also affected by CNS insult. Jones and Yang (1994) studied cutaneous reflexes arising from stimulation of the tibial nerve in spinal cord

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[1] A version of this chapter will be published by E. Paul Zehr, Kinya Fujita and Richard B. Stein, in the

injured patients and found an altered pattern of reflex modulation to that seen in uninjured subjects (Yang & Stein 1990; Zehr et al. 1997a). The patients showed very little inhibitory modulation and instead excitation predominated throughout the step cycle in TA muscle. In SOL, there were some inhibitory responses during stance, but facilitation predominated during swing phase. Interestingly, Fung and Barbeau (1994) stimulated the medial plantar nerve (a mixed nerve and distal branch of the tibial nerve) in spastic paretic spinal cord injured subjects during walking. They observed that this cutaneomuscular stimulation could modulate the excitability of SOL H-reflex to a level which could be similar to NI subjects (see Stein et al. 1993). To the best of our knowledge, cutaneous reflexes from other nerves have not been studied during gait in other patient groups.

The function of cutaneous reflexes during walking in humans has been uncertain. Recently, we showed that reflexes arising from the superficial peroneal nerve (SP), which innervates the dorsal surface of the foot, and the tibial nerve, which innervates the plantar foot surface, elicit functional EMG and kinematic responses during treadmill walking (Zehr et al. 1997a). Electrical stimulation of the SP nerve during early swing was shown previously to give rise to a stumble correction in which TA muscle was suppressed and BF muscle facilitated (van Wezel et al. 1997, Zehr et al. 1997a). These neural responses gave rise to kinematic changes in which ankle dorsiflexion and knee extension were reduced, such as would be predicted in a stumble avoidance of an encountered object (Zehr et al. 1997a). These responses to electrical stimulation seemed similar to the stumble correction observed in cats after both electrical and mechanical stimulation

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(Forssberg 1979) and after perturbing humans during treadmill walking (Schillings et al. 1996). However, the extent to which this stumbling corrective response may be maintained in pathological gait is not known.

The purpose of the present study was to evaluate the reflex responses to SP nerve stimulation in subjects who had had a stroke. The function of observed reflexes in the EMG were tested by correlation with kinematic changes in knee or ankle joints, conducted previously in neurologically intact subjects (Zehr et al. 1997a). Portions of these results have been presented briefly in abstract form (Zehr et al. 1997b).

5.2 Methods

5.2.1 Subjects and experimental protocol

Eleven NI subjects (9 males and 2 females), aged 26-56 y, and eight stroke subjects (7 males and 1 female), aged 49-78 y, participated in the experiments with informed, written consent. The average age was 62 (median=59.5) in the stroke and 37.7 (median=33) in the NI group. All patients had some extent of foot drop and many had some minor level of spasticity (approximately 1 on the modified Ashworth scale). Two of the stroke subjects occasionally demonstrated periods of clonic activity in the lower limb musculature and 5 stroke subjects regularly used a cane for overground walking. The stroke subjects were 3-48 months post-injury and were studied on the more affected side. All experiments were conducted under an approved protocol for human subjects at the University of Alberta. During each session, subjects walked on the treadmill at self-selected and comfortable speeds for periods of approximately 7 to 10 minutes at each speed. For the stroke subjects, the walking speeds were in the range of 0.71 to 1.6 km/h (median=1.2 km/h) and for the NI subjects 1.5 to 3.5 km/h (median=2 km/h). The majority of the stroke subjects held the treadmill handrail for support throughout a walking trial. Approximately 400-600 steps were collected for each speed (including stimulated and control unstimulated steps). A more detailed description of the experimental protocol and data analysis has been published elsewhere (Zehr et al. 1997a).

5.2.2 Nerve stimulation

The superficial peroneal (SP) nerve was stimulated using either a GRASS SD9 (Grass Inst., Quincy Mass.) isolated constant voltage stimulator or a custom-built constant current stimulator with trains of 5 pulses at 200 Hz with a pulse width of 1.0 ms. No differences in responses were observed with either type of stimulation. The electrodes for the SP nerve were placed on the front of the leg just near the ankle joint, such that stimulation produced a strong radiating parasthesia over the foot dorsum. Flexible 1 cm disposable Ag-AgCL surface EMG electrodes (ELECTROTRACE, Jason, Huntington Beach, CA) were used for cathodal stimulation. The threshold of stimulation in terms of the perceptual threshold (PT), defined as the lowest stimulation that was just detectable by the subject, and the radiating threshold (RT; defined as a clear radiating parasthesia), were determined in all subjects. Stimulation intensities were typically twice RT. The stimulator was driven by a pseudo-random pulse generator with a minimal repeat time equal to the step cycle time and a maximum that was approximately twice the step cycle time for each subject; thus a stimulus arrived approximately once every 3 steps. Accordingly, we collected many unstimulated steps and no step had more than 1 stimulus. Outputs from both the trigger pulse generator and the stimulator were sent to a 12 bit A/D converter and then into a 486 66 MHz microcomputer running AXOTAPE (Axon Instruments) data acquisition software.

5.2.3 Electromyography

The skin was lightly abraded and cleansed with alcohol and disposable ELECTROTRACE (JASON, Huntington Beach, CA) Ag-AgCL surface EMG electrodes were applied in bipolar configuration longitudinal to the predicted path of the muscle fibers (~ 2 cm inter-electrode distance) over the soleus (SOL), medial gastrocnemius (MG), tibialis anterior (TA), vastus lateralis (VL), and biceps femoris (BF) muscles. SOL electrodes were placed distal to the termination of the gastrocnemius muscles, whereas MG electrodes were placed over the medial head of the gastrocnemius. TA electrodes were placed over the largest girth of the tibialis anterior muscle. For VL, the distal electrode was placed approximately 4-6 cm proximal to the lateral margin of the patella and for BF placement was over the muscle belly at approximately 1/3 of the distance from the knee to the hip. The position of the stimulating electrodes was such that it typically produced some minor facilitation of the nearby extensor digitorum brevis muscle. We therefore monitored the peak to peak EMG of the M-wave from this muscle to check that its stimulation remained relatively constant throughout the cycle. Variation in stimulation across the step cycle was generally less than 10%. Ground electrodes for the EMG were placed over electrically neutral tissue, such as the knee, and EMG signals were pre-amplified and highpass filtered at100 Hz. Then they were full-wave rectified, thus yielding components down to DC, and lowpass filtered at 100 Hz. This filtering process provided a good linear envelope with little spread of the stimulus artifact (which could then be digitally removed off-line, see below) and is one which we have previously employed (Zehr et al. 1997a). The processed output was sent to a 12 bit A/D converter and then into a microcomputer sampling at 500 Hz.

5.2.4 Kinematics and step-cycle timing

Angular position of knee and ankle were recorded with custom-made potentiometric electrogoniometers placed over the joint and secured with plastic tape and fabric straps. Signals obtained from custom-made force sensors located in the insole of the subject's shoe were used to establish step cycle parameters (e.g. heel contact, toe-off). The electrogoniometers and force sensors could resolve angular changes greater than 1° and forces greater than 5 N, respectively. Angle and force signals were pre-amplified (the subject wore a small pouch and belt to hold the amplifiers) and then sent directly to the AXOTAPE computer system.

5.2.5 Data acquisition and analysis

The data were sampled continuously and stored on hard disk for off-line analysis. Custom written software programs were used to separate the step cycle into 16 separate parts, beginning with heel contact. The stimuli occurred randomly throughout the step cycle. All responses to stimuli occurring in the same part of the step cycle were averaged (n=~10-20 in each part) together and aligned to stimulus delivery within that part of the step cycle. The values obtained for each of the 16 averages after stimulation were subtracted from the corresponding averages from unstimulated steps during the same trial.

5.2.6 Background step cycle EMG profiles

To compare phasic levels and timing of muscle activation during walking between the NI and stroke subjects, unstimulated, control EMG profiles were obtained throughout the entire step cycle and a mean value was obtained for each part of the step cycle for each subject. These values were normalized to the maximum activation level occurring in the step cycle, thus yielding an EMG activation profile ranging from a minimum activation to a maximum of 1 for each subject. These values were then averaged across each part of the step cycle for each group of subjects. Significant differences between groups in these values would indicate a different muscle activation profile during gait which is independent of absolute activation level (which may vary widely across subjects and between groups).

5.2.7 Net reflex EMG analysis

Stimulus artifacts were digitally removed and then the EMGs were filtered with a 5-point digital moving average filter. The unstimulated control EMGs for each part of the step cycle were subtracted from the corresponding stimulated step cycle parts to yield subtracted evoked EMG traces. The evoked EMGs for each subject were analyzed for the net reflex effect using the **A**verage **C**umulative **R**eflex **E**MG after **150** ms (ACRE_{150}) (Zehr et al. 1995). This technique was employed because it provides a useful quantification of the net EMG reflex effect and provides an index for correlation to kinematic changes (Zehr et al. 1997a). Briefly, the analysis program calculated the subtracted, residual reflex EMG traces and digitally removed the stimulus artifact. The post-stimulus data were then sequentially summed and any significant facilitation or suppression was identified as positive or negative deflections in the EMG record. The value obtained at 150 ms after stimulation was then divided by the time interval of integration to measure an overall reflex effect (i.e., negative values indicate overall suppression and positive values overall facilitation). As we were interested in reflex effects, a 150 ms post-stimulus interval was chosen since it preceded any significant voluntary activation in lower leg muscles (see Zehr et al. 1995). The $ACRE_{150}$ values for each subject were normalized to the peak EMG value (averaged over a 40 ms time window) occurring during the entire step cycle for each muscle and expressed as percentages.

5.2.8 Kinematic Analysis

Subtracted values for angular changes were used for analysis. The maximum change observed in these smoothed (n=5 point filtering) signals over an interval ranging from 140 to 220 ms post stimulation was calculated. We have used this sliding latency previously (Zehr et al. 1997a), which was chosen to reflect the delays between an EMG response and the peak mechanical change in moving muscles. As described for the EMG, these values were then normalized to the maximal values during the step cycle (e.g., maximum range of motion occurring within the step cycle) and expressed as percentages.

5.2.9 Statistics

In all instances, analysis was conducted on averaged values for each subject from each part of the step cycle. Significant differences from zero for the net reflex effects were determined by calculation of t-ratios for each part of the step cycle and differences between groups of subjects were determined with t-tests. Linear least-means square regression analysis was used to evaluate correlation between EMG indices and changes in ankle and knee joint angle at each part of the step cycle. Descriptive statistics included means ±SEM and statistical significance was set at $p \leq 0.05$. When available, datasets from different walking speeds for a given subject were pooled in the analysis. In this way, 13 data sets were analyzed for each group yielding 12 degrees of freedom for statistical analysis. For the NI subjects, 6 data sets at 2 km/h walking were included from our previous publication (Zehr et al. 1997a).

5.3 Results

5.3.1 Locomotor cycle duration and EMG profiles

Although the two subject groups walked at different speeds, the relative timing of the step cycle was not different. Stance accounted for 66.2±1.6 % of the step cycle duration in stroke and 64.2±1.6 % in NI subjects (NS).

Average values of the mean normalized EMG profiles for each part of the step cycle and for all 5 muscles studied in both groups of subjects have been plotted in Figure 5-1. NI subjects are represented by the filled and stroke subjects by the open symbols. At the bottom of the figure, the solid horizontal line indicates those parts of the step cycle that fall in the stance phase and the dashed line those that fall in the swing phase. Typically, the stance phase was parts 1-8 and the swing phase 10-15. The transitional portions of the step cycle, in which only part of the foot is in contact with the ground, occurred in part 9 (stance-to-swing) and part 16 (swing-to-stance). There were few differences in the relative activation of SOL and no differences when the maximum absolute values were compared (45.6 vs. 39.0 μV for stroke and NI, respectively). Relative MG muscle activation was significantly greater at the transition from the end of swing to the beginning of stance (* indicate significant differences in Fig. 5-1) in stroke compared to NI subjects, but stroke subjects had reduced maximal MG activation (27.5 vs. 84.9 μV, $p<0.01$).

Most importantly because it relates directly to the foot drop in the stroke subjects, the TA muscle activation profile during swing was quite different between stroke and NI subjects. Whereas NI subjects had peak TA activation at end swing (part 15) or the swing to stance transition (part 16), stroke subjects showed peak activation in early to mid swing and the end swing burst was significantly reduced. The absolute values of TA EMG were also lower ($p<0.05$) in stroke subjects during late stance and swing. However, while reduced as compared to NI subjects (29.6 vs. 41.6 μV), the maximal activation level in TA was not significantly different between the 2 groups across the step cycle. In the upper leg muscles VL and BF, stroke subjects generally had highest muscle activation during stance and lowest muscle activation during swing in contrast to NI subjects. The absolute activation levels were lower in both VL (21.9 vs. 41.2 μV) and BF

Figure 5-1 EMG activation profiles throughout the step cycle for stroke (open symbols) and NI subjects (filled symbols). Values are normalized to the peak muscle activation recorded during the step cycle for each subject. Data points represent means and SEM and * indicate differences between subject groups at $p<0.05$.

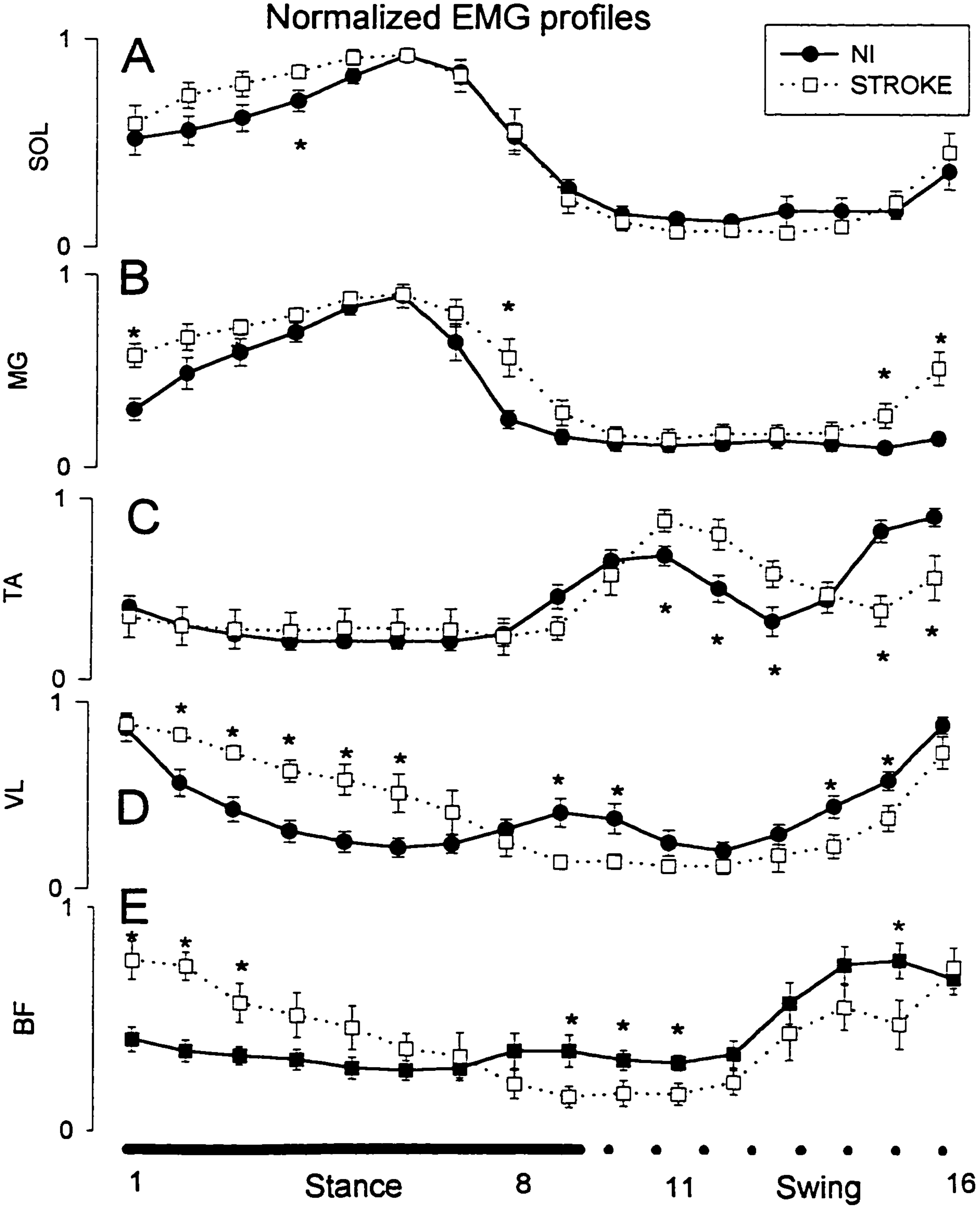
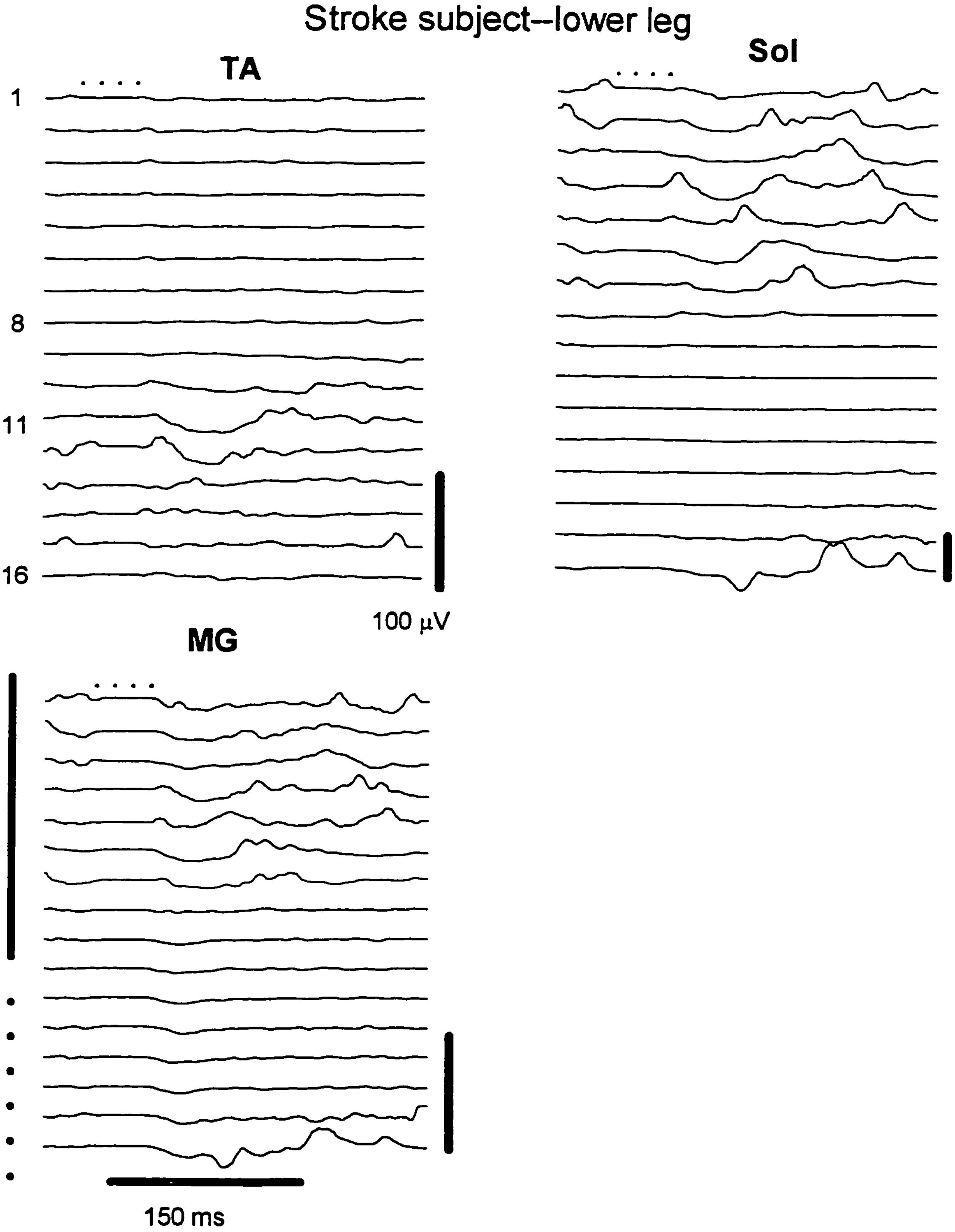


Figure 5-2 Subtracted EMGs of TA (top left), SOL (top right), and MG (bottom left) muscles of a representative stroke subject (aged 56 y) after SP nerve stimulation. The stimulus artifact has been suppressed in all traces and replaced with a flat line, atop which has been placed a dashed line. Each trace has 50 ms prior to and 250 ms after stimulation. The numbers at the far left indicate specific portions of the step cycle while the long horizontal solid and dashed bar indicates approximate duration of stance and swing portions of the step cycle.



(24.3 vs. 32.4 μV) muscles in stroke subjects as compared to NI, but these differences were not significant.

5.3.2 Lower leg responses

The responses (after subtraction of the background EMG) to SP nerve stimulation in each of the 16 parts of the step cycle for TA, SOL, and MG muscles of one representative stroke subject (aged 56 y) have been plotted in Figure 5-2. In this and all such figures, the solid vertical line indicates approximately the portions of the step cycle which fall in stance and the dashed line those in swing. The horizontal dashed lines at the top of each muscle indicates approximately the stimulation period; the stimulation artifacts have been removed for clarity in all figures.. The solid calibration bar at the bottom right of each muscle indicates 100 μV. In Figure 5-3, the same format has been used to display data from one age-matched NI subject (55 y). Note the complex pattern of responses especially at longer latency (~135 ms post-stimulation) seen in the NI (particularly in MG) as compared to the stroke subject.

The overall response to stimulation ($ACRE_{150}$ - see Methods) has been calculated for each subject and mean values for both groups of subjects are plotted in Figure 5-4. Stroke subjects showed large suppressive responses throughout stance (Figure 5-4, top panel) and no significant responses during swing in SOL muscle. In contrast, NI subjects had little net response except for some minor, but statistically significant (the asterisks represent values that are significant at $p< 0.05$) facilitation during late swing (parts 13-15, Fig. 5-4 A) in SOL. Both groups of subjects had significant suppressive responses in

Figure 5-3 Subtracted EMGs of lower leg muscles in a sample NI subject (aged 55 y) after SP nerve stimulation. Format is the same as Figure 5-2.

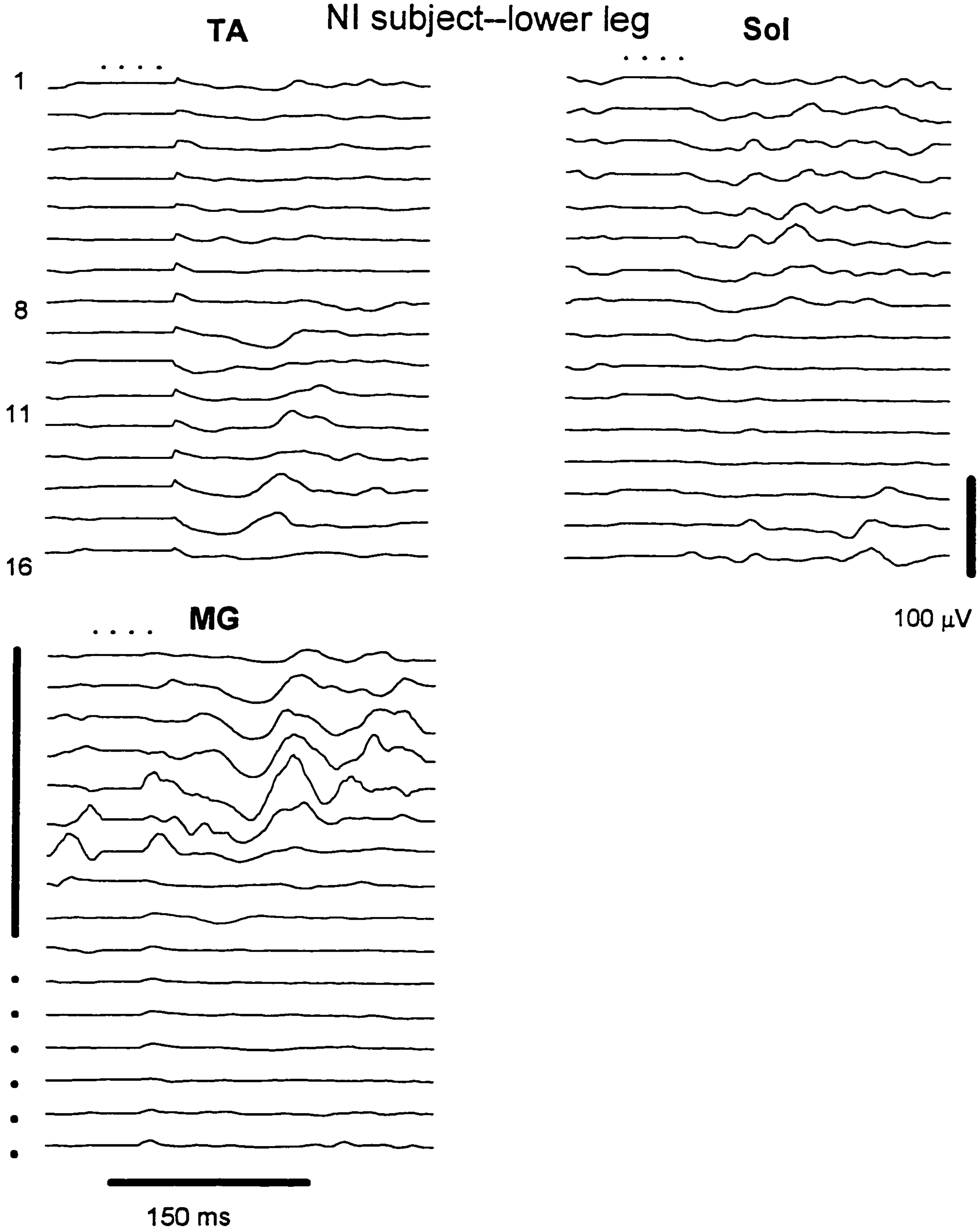
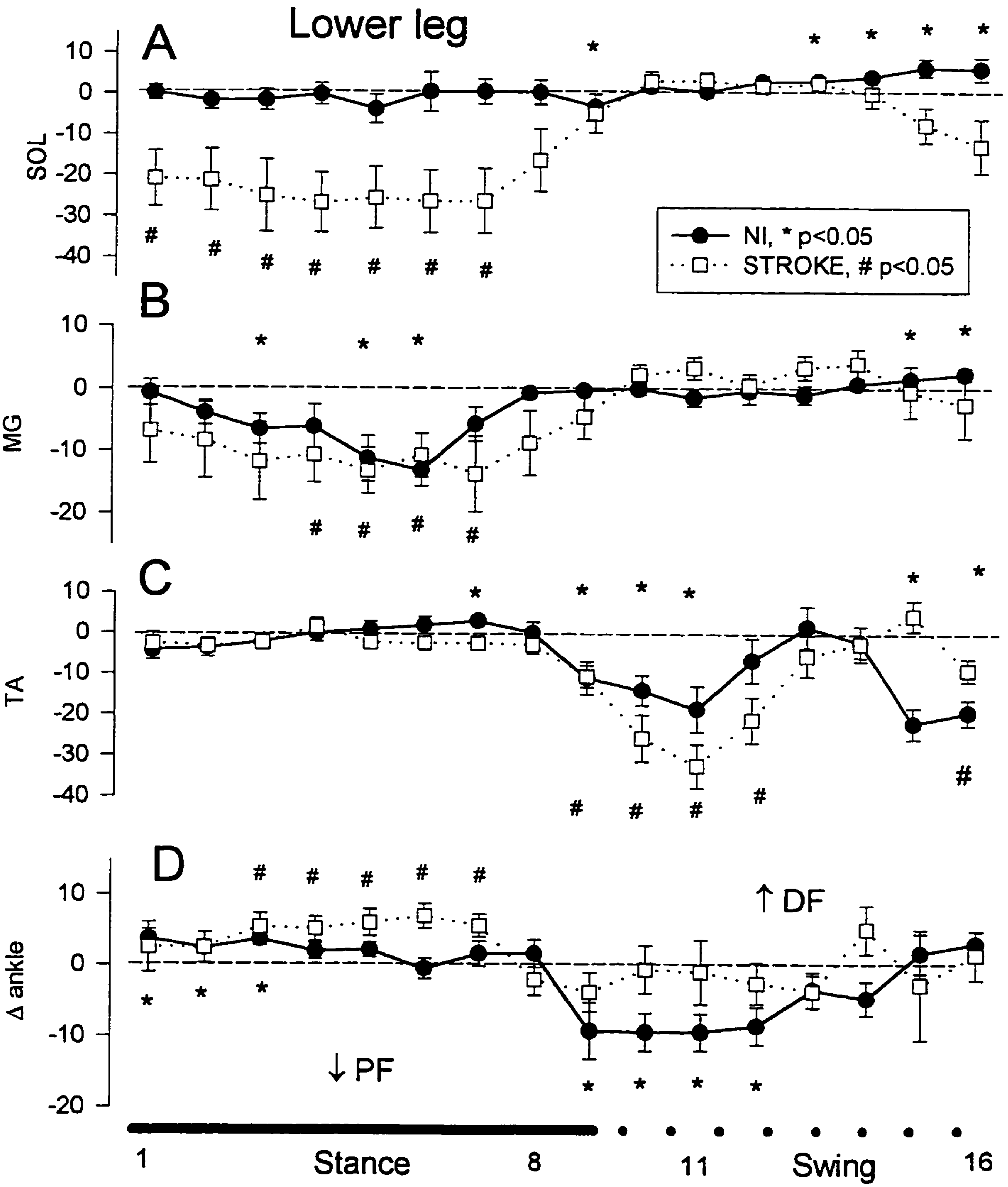


Figure 5-4 Averaged values for $ACRE_{150}$ (as percentages of the maximum locomotor EMG) for lower leg muscles and ankle angle changes in both groups. Statistically significant effects are as indicated by * (NI, filled symbols) and # (Stroke subjects, open symbols) at $p<0.05$. DF: dorsiflexion, PF: plantarflexion.



MG muscle during mid to late stance and NI subjects also showed some facilitation at end swing. The responses in MG muscle were significantly correlated to angle changes during stance in both groups (r=0.63 and 0.55 for NI and stroke subjects, respectively)

In TA muscle, stroke and control subjects showed large and significant suppression in the early part of swing phase (parts 10 & 11 in Fig. 5-4C). In the stroke subjects stimulation produced about a 30% suppression of TA activity in early swing, though a smaller than normal response in late swing (all values are measured relative to the peak activity observed during the step cycle without stimulation). Along with the effects in EMG, both groups also had associated changes in ankle joint angle due to stimulation (Fig. 5-4D). The stroke subjects showed significantly increased ankle dorsiflexion throughout stance (labeled as a change in the plantarflexion (PF) direction in Fig. 5-4D), whereas NI subjects showed only some minor increase in ankle dorsiflexion during early stance. The major response in NI subjects was a reduction in ankle dorsiflexion during the stance to swing transition and early to mid swing (parts 10 to 12), which was much less prominent in stroke subjects. TA suppression was correlated with the reduced ankle dorsiflexion in only one part (early swing, r=0.62) of the step cycle for the stroke but in one third of the step cycle for NI subjects (r=0.60 to 0.75). Plotted in Figure 5-5 (top) are the correlations between ankle angle and TA effect for early swing for stroke (part 11; open symbols) and NI subjects (part 10; filled symbols). Data from late swing (part 14) are plotted at the bottom of Figure 5-5. Note that only NI subjects show significant correlation at this part of the step cycle.

Figure 5-5 Data from the lower leg of NI and stroke subjects for normalized ACRE$_{150}$ and kinematic changes during swing. Data for early swing are plotted at top (open and filled symbols represent stroke and NI subjects, respectively). Plotted at figure bottom is late swing. Significant regression is indicated by the solid (NI) and dashed (Stroke) lines. Note that correlation between TA effect and ankle angle was seen only in NI subjects during late swing.

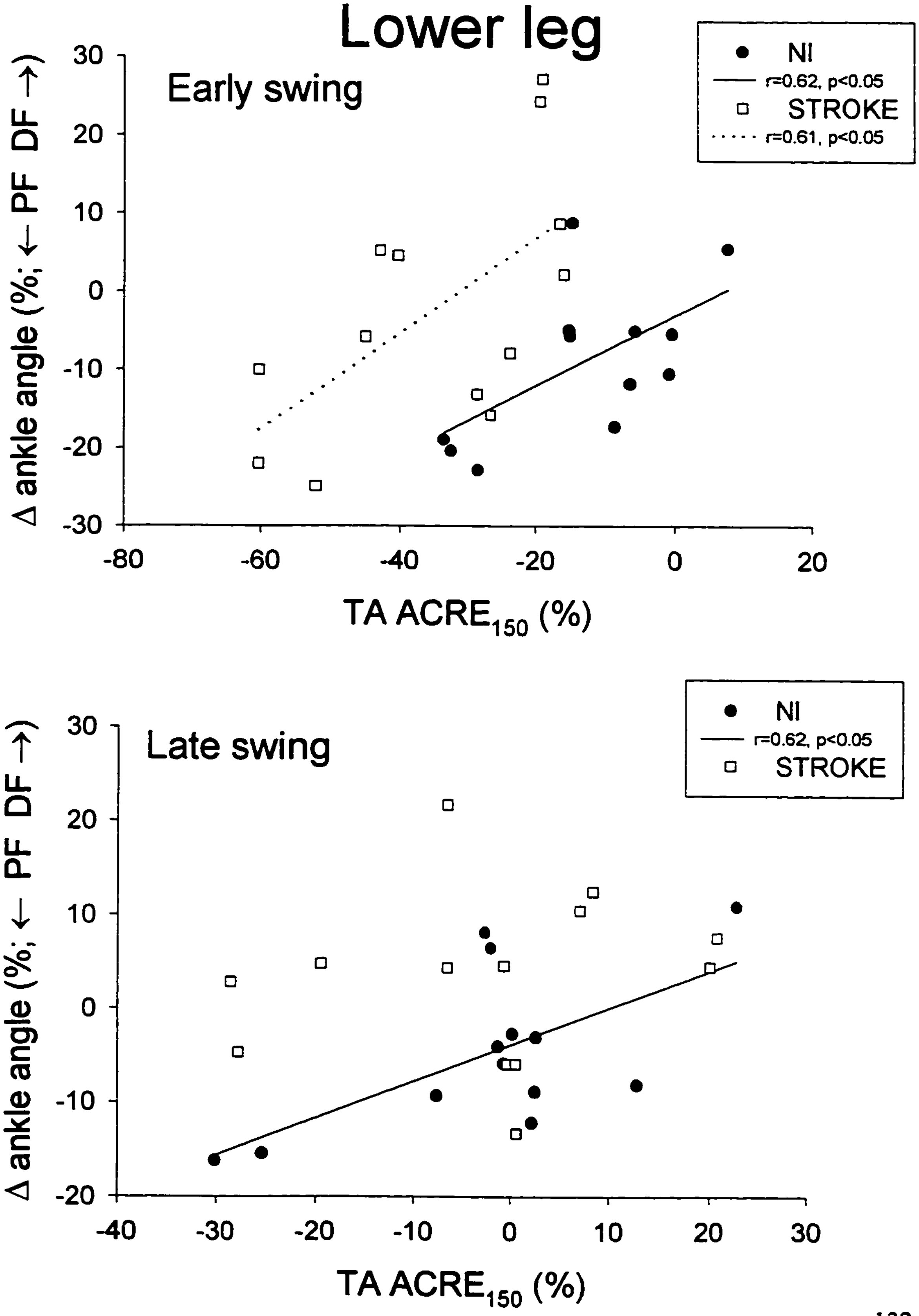


Figure 5-6 Sample data from representative stroke subject EMG responses in BF (left) and VL (right) muscles. Same subject and format as in Fig. 5-2.

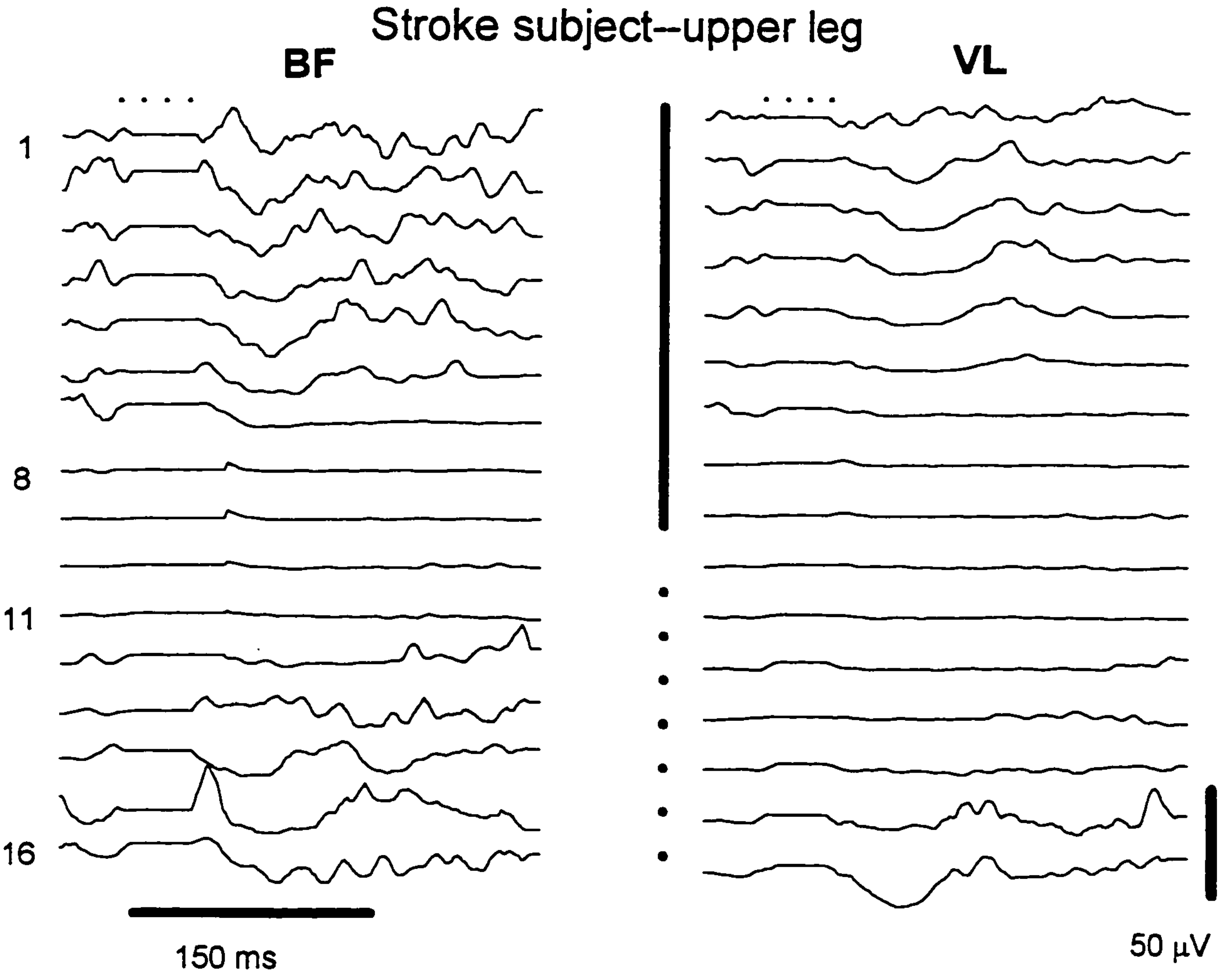
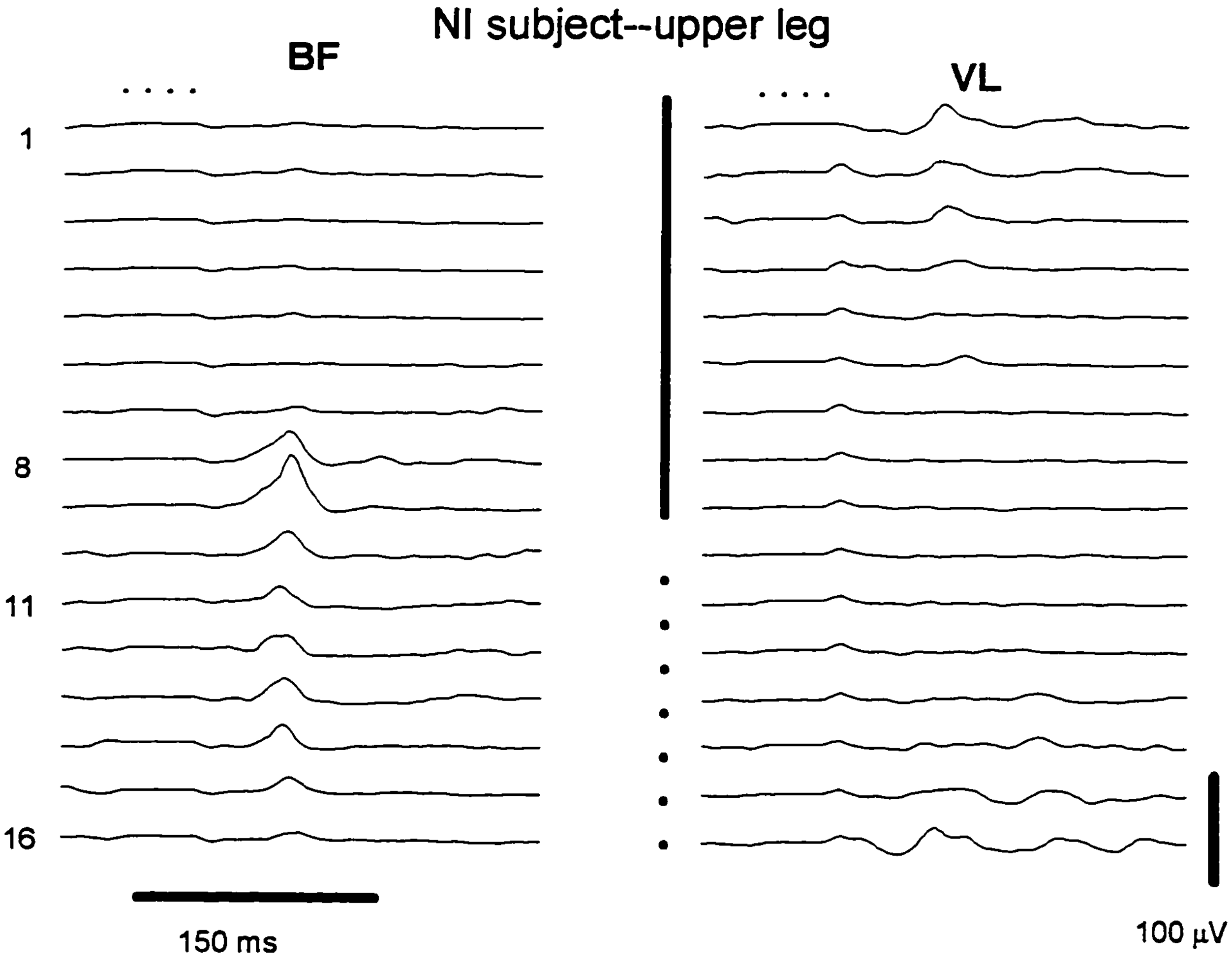


Figure 5-7 Sample data from representative NI subject EMG responses in BF (left) and VL (right) muscles. Same subject and format as in Fig. 5-3.



5.3.3 Upper leg responses

Figures 5-6 and 5-7 show data from the upper leg of the same stroke and age-matched NI subjects as presented in Figures 5-2 and 5-3. Note that the stroke subject has a predominant net suppressive response in both muscles which is in clear contrast to the facilitation seen in the NI subject.

Mean values for VL and BF muscles and changes in knee angle have been plotted for both groups of subjects in Figure 5-8. As with the lower leg extensor muscles SOL and MG, VL muscle was significantly suppressed in the stroke subjects during most of stance (parts 1-6) and at late swing and the swing to stance transition (parts 15 & 16, Fig. 5-8A). In contrast, VL muscle was significantly facilitated throughout stance (parts 2,4,6, & 8, Fig. 5-8A) and mid to late swing (parts 12, 14, & 15) in the NI subjects. With regard to BF muscle, stroke subjects had significant facilitation only at the stance to swing transition (part 9, Fig. 5-8B) and during early swing (parts 10-12), whereas NI subjects showed significant facilitation throughout the step cycle, reaching a peak at the stance to swing transition. In concert with the suppression in VL muscle during early and mid-stance, knee extension was reduced during stance (parts 4, 6 & 7, Figure 5-8C) in the stroke subjects. Knee extension was also reduced in NI subjects in concert with BF facilitation, but the prominent effect in these subjects was increased flexion during swing.

Figure 5-8 Averaged values for ACRE$_{150}$ (as percentages of the maximum locomotor EMG) for upper leg muscles and knee angle changes in both groups. Format is the same as Figure 5-2. FL: knee flexion, EX: knee extension.

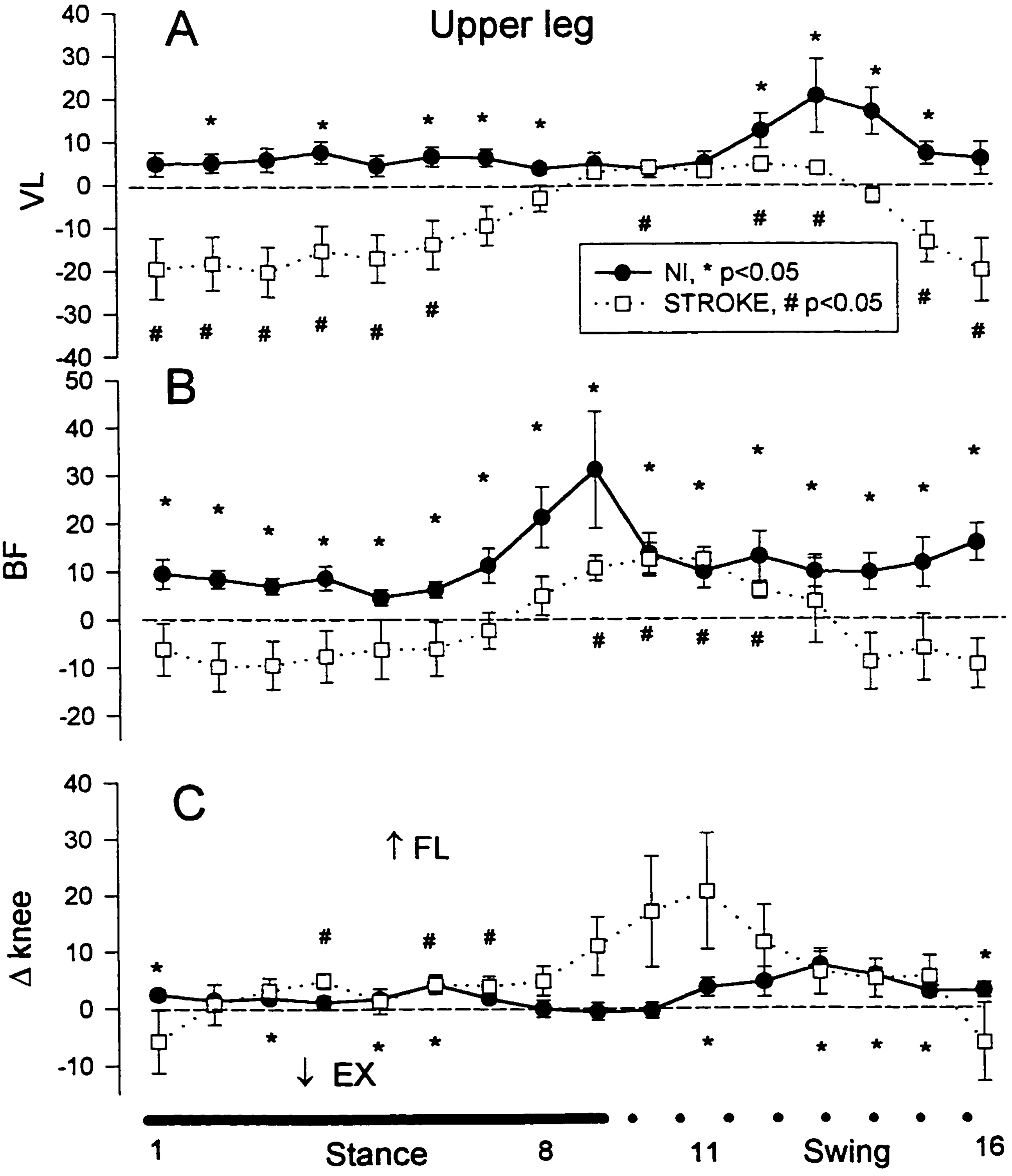
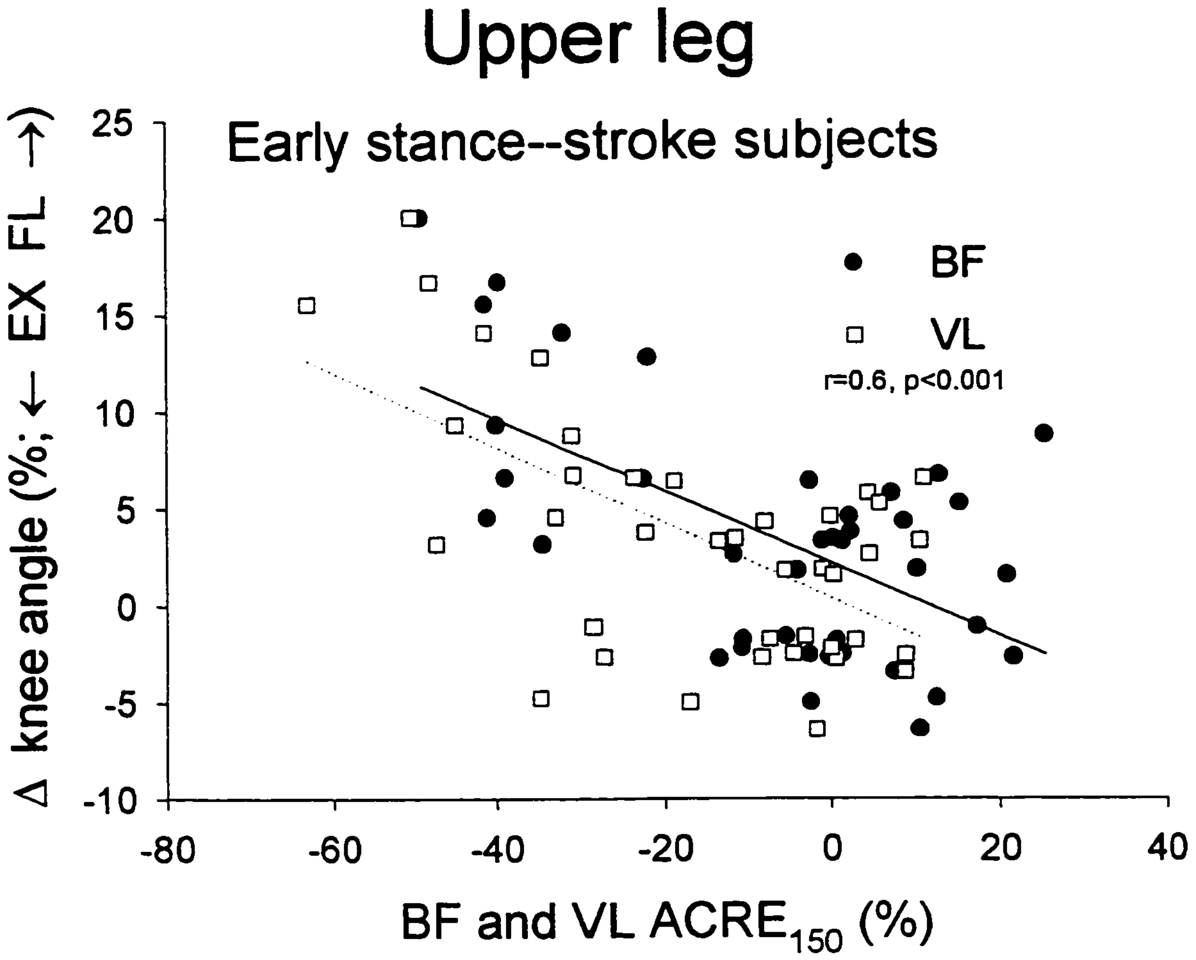


Figure 5-9 Correlation between BF and VL and knee angle for stroke subjects during early stance. Open and filled symbols represent BF and VL muscles, respectively. Significant regression lines are as plotted by the solid and dotted lines. Note that this correlation was not a prominent feature in the NI subjects. Format is the same as Figure 5-5.



In the stroke subjects, there was significant correlation between reflexes in both BF and VL muscles and knee angle changes during stance (data from several parts of stance are plotted in Figure 5-9; largest $r=0.85$ and 0.86 for BF and VL, respectively), but this was essentially absent in the NI subjects. NI subjects had significantly increased knee flexion during late swing which was correlated to the net effect in BF muscle ($r=0.66$, $p<0.05$).

5.4 Discussion

Taken together the responses in the stroke subjects show some similarity to the NI subjects during swing, and are similar to those reported by us previously (Zehr et al. 1997a). However, the stroke subjects show several interesting differences. Firstly, the stroke subjects showed suppression during stance in all extensor muscles studied (SOL, MG, & VL), which were associated with and correlated to changes in knee and ankle kinematics. Secondly, during swing they showed a similar suppression of TA muscle as in the NI subjects, yet the angular changes were much smaller and significant correlation between the kinematic and EMG indices occurred at only one portion of the step cycle. Thirdly, stroke subjects, had significant correlation between knee joint changes and upper leg reflexes during stance, unlike the NI subjects.

5.4.1 Do stroke subjects have a stumble-like correction to foot dorsum stimulation?

Previously we described significant correlation between TA and BF reflex effects and ankle and knee joint angle after SP nerve electrical stimulation in young, neurologically intact subjects (Zehr et al. 1997a). We suggested that these responses represented a portion of a stumble correction to activation of the cutaneous field overlying the foot dorsum. That is, if the foot dorsum were contacted during swing a reduction of ankle dorsiflexion and knee extension would occur to prevent stumbling, which was replicated here in our expanded sample of NI subjects and is corroborated by recent results from van Wezel et al. (1997). It should be noted that contact with an actual object would result in the activation of other receptors and reflexes, most notably the stretch reflex, in addition to cutaneous reflexes. After SP nerve electrical stimulation, the stroke subjects showed similar TA suppressive responses (early and late swing, Fig. 5-2C) and BF facilitation (early swing, Fig. 5-4B) to NI subjects. However, significant mechanical changes did not occur simultaneously at the ankle (Fig. 5-4D) and knee (Fig. 5-8C) in the stroke subjects, except for a few parts during swing (see correlation in Figure 5-5). Hence, only a portion of the previously described stumble corrective response to cutaneous electrical stimulation (van Wezel et al. 1997, Zehr et al. 1997a) persists after stroke. This is reflected in the weaker correlation between EMG indices and kinematics during swing.

Why do stroke subjects not also have kinematic changes as large as NI subjects associated with the EMG effects? One explanation lies in a potential confounding effect of walking speed, which was significantly different in the two groups. The EMG reflex effects have a fixed duration and delay regardless of movement speed. Using TA and ankle angle as examples, a net suppression of ongoing locomotor activity might have a lesser effect at a slower rather than a faster walking speed. Our NI subjects found it unnatural and very difficult to walk at the slower speeds typically found in stroke subjects. The best we could do was to have them walk at speeds ranging from 1.5 to 4 km/h and extrapolate to the slower speeds found in stroke subjects. The same correlations were observed in the NI subjects regardless of speed. Hence, the differences between NI and stroke subjects in the expression of the stumble correction is not likely to be due to differences in walking speed between the two groups.

Another explanation might be the age differences in the subject groups. However an examination of the data of 2 age-matched subjects as was shown for the lower leg (Figures 5-2 & 5-3) and upper leg (Figs. 5-6 & 5-7) reflexes reveals this to be unlikely. The patterns observed in the older NI subject are quite similar to that seen in the young NI subject (aged 26 y) shown in Zehr et al. (1997a; Figure 4-2, lower leg, Figure 4-4, upper leg). On balance, we are confident that the differences seen between the NI and stroke subjects are due to the pathological changes arising from the stroke.

A more probable explanation may arise from the mechanical properties of the muscles and joint stiffness of the stroke subjects. Any correlation between EMG and kinematics will be affected by the inherent passive stiffness of the joint. If the passive stiffness is quite low, a large EMG reflex would be more highly correlated to a large kinematic change and vice versa. Sinkjaer and Magnussen (1994) showed that the passive stiffness in ankle plantarflexors was increased in hemiparetic subjects compared to healthy controls during isometric contraction. Recently, Sinkjaer et al. (1996) showed that passive stiffness was also significantly higher during locomotion in spastic multiple sclerosis subjects. Although we have not performed this analysis on our stroke subjects, the intrinsic and passive stiffness at the knee and ankle joint may well explain the lack of a kinematic stumble correction despite the neural responses in the stroke subjects.

5.4.2 Stroke subjects show prominent effects during stance

As described in the Results, the stroke subjects showed significant suppressive responses in all 3 extensor muscles studied (SOL, MG, & VL). These responses were associated with (see Figs. 5-4D and 5-8C) reductions in plantarflexion and knee extension. Changes in the upper leg were significantly correlated to both VL and BF and knee responses (see Figure 5-9). These results are in contrast to the NI subjects in whom SOL was relatively unaffected and VL was in fact facilitated rather than suppressed during stance. It is difficult to argue for a functional role of these observed responses in stroke subjects during stance. It may indicate impaired reflex function during stance. The generalized suppression of extensor activity at a time when the ipsilateral limb is being loaded could be dangerous to the patient and lead to limb collapse and a fall. Just why the stimulation leads to such profound EMG and mechanical effects during stance (in contrast to the results in NI subjects) is not clear at present, but may be important in rehabilitation of these patients (see below).

5.4.3 Cutaneous reflex modulation after stroke

Interestingly, although we previously showed a difference in triceps surae responses to SP stimulation (MG suppressed, lateral gastrocnemius and SOL relatively unaffected) during stance (Zehr et al. 1997a), this was not found in the stroke subjects where suppression predominated in all extensor muscles during stance. Jones and Yang (1994) noted that tibial nerve cutaneous stimulation also caused suppressive responses in SOL during stance in spinal cord injured subjects, contrary to the modulation observed during gait in NI subjects. Further, while we showed profound suppression of TA during swing after SP stimulation, Jones and Yang (1994) reported generally excitatory responses with no reflex reversal or modulation during swing. This is in contrast to NI subjects, where there is a reflex reversal from TA facilitation during early swing to suppression at end swing (Yang & Stein 1990) with kinematic correlates (Duysens et al. 1992, Zehr et al. 1997a).

If neurological impairment and spasticity from supraspinal lesions acts through a decreased descending control over interneuronal circuits within the spinal cord (Delwaide & Olivier, 1987), it's not surprising that cutaneous modulation is also impaired or abnormal in stroke subjects. DeSerres et al. (1995) suggested that the reflex reversal and modulation seen in TA muscle after tibial nerve stimulation most probably results from the control of parallel excitatory and inhibitory pathways to TA motor units. This type of modulation has been described in the cat by Degtyarenko et al. (1996), who suggested that segmental interneurons (whose excitability would be partially regulated by supraspinal input) play a dominant role.

Interestingly, Nielsen et al. (1997) recently showed that there may be a transcortical pathway from cutaneous afferents to TA motoneurons. They suggested that longer latency reflexes in TA evoked by sural and SP nerve stimulation are partly mediated by a transcortical connection. While we did not make an extensive study of the latencies of the responses here (see Methods), in Figures 5-2 and 5-6 the longer latency (and generally facilitatory) responses are smaller in the stroke versus the NI subjects. This could lead to the large, net suppressive responses observed in the present paper. This interpretation is also consistent with previous studies showing reduced polysynaptic components in the stretch reflexes of spastic hemiparetic subjects subjected to treadmill acceleration during stance (Berger et al. 1984, 1988).

5.4.4 Implications for rehabilitation

The significant suppressive responses elicited in lower leg EMG after SP nerve stimulation may be used to modulate exaggerated reflexes such as those arising from spasticity (such as suggested by Fung & Barbeau, 1994 for stimulation of the plantar foot surface and H-reflex modulation). Stimulation of the SP nerve during swing might reduce excessive stretch reflexes that impair normal dorsiflexion in spastic gait. However, two points must be kept in mind. Firstly, the stimulation of SP nerve could conceivably contribute to foot drop by suppression of residual TA activity during early swing, although foot drop was not noted in the kinematics of the studied stroke subjects.

Secondly, stimulation during stance had such large effects that consistent mechanical changes were observed in the stroke subjects in contrast to the NI subjects reported here and previously (Zehr et al. 1997a). However, too much stimulation might compromise stability during stance, as mentioned above. It may be possible to phasically induce reflex changes when needed (see Fung & Barbeau 1994) to counter excessive excitation of TA (Jones & Yang 1994) or to prevent clonus at the beginning of stance (Yang et al. 1991).

In summary, stroke subjects appear to retain the neural component (as measured in the EMG) while the mechanical linkage in the stumble corrective response is weakened. Stroke subjects also have strong responses during stance in the extensor muscles which are mirrored in leg kinematics. These responses may have possible therapeutic applications but might result in unwanted destabilization of balance and posture. Therapeutic application in these or more compromised subject populations will require further study.

5.5 References

Berger, W., Horstmann, G., and Dietz, V. Tension development and muscle activation in the leg during gait in spastic hemiparesis: independence of muscle hypertonia and exaggerated stretch reflexes. *J. Neurol. Neurosurg. Psychiat.* 47:1029-1033, 1984.

Berger, W., Horstmann, G., and Dietz, V. Spastic paresis: impaired spinal reflexes and intact motor programs. *J. Neurol. Neurosurg. Psychiat.* 51:568-571, 1988.

Degtyarenko, A.M., Simon, E.S., and Burke, R.E. Differential modulation of disynaptic cutaneous inhibition and excitation in ankle flexor motoneurons during fictive locomotion. *J. Neurophysiol.* 76:2972-2985, 1996.

Delwaide, P.J. and Olivier, E. Pathophysiological aspects of spasticity in man. In: *Motor Disturbances I*, Benecke, R., B. Conrad, and C.D. Marsden (eds.), Academic Press Ltd., pp153-167, 1987.

DeSerres, S.J., Yang, J.F., and Patrick, K. Mechanism for reflex reversal during walking in human tibialis anterior muscle revealed by single motor unit recording. *J. Physiol.* 488:249-258, 1995.

Duysens, J., Tax, A.A.M., Trippel, M., and Dietz, V. Phase-dependent reversal of reflexly induced movements during human gait. *Exp. Brain Res.* 90:404-414, 1992.

El-Abd, M.A.R., and Ibrahim, K.I. Impaired afferent control in patients with spastic hemiplegia at different recovery stages: contribution to gait disorder. *Arch. Phys. Med. Rehabil.* 75:312-17, 1994.

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

Fung, J., and Barbeau, H. Effects of conditioning cutaneomuscular stimulation on the soleus H-reflex in normal and spastic paretic subjects during walking and standing. *J. Neurophysiol.* 72:2090-2104, 1994.

Jones, C.A. and Yang, J.F. Reflex behavior during walking in incomplete spinal-cord-injured subjects. *Exp. Neurol.* 128:239-248, 1994.

Nielsen, J., Petersen, N., and Fedirchuk, B. Evidence suggesting a transcortical pathway from cutaneous foot afferents to tibialis anterior motoneurones in man. *J. Physiol.* 501(2):473-484, 1997.

Schillings, A.M., Van Wezel, B.M.H., and Duysens, J. Mechanically induced stumbling during human treadmill walking. *J. Neurosci. Methods* 67:11-17, 1996.

Sinkjaer, T., and Magnussen, I. Passive, intrinsic and reflex-mediated stiffness in the ankle extensors of hemiparetic patients. *Brain* 117:355-363, 1994.

Sinkjaer, T., Toft, E., Hansen, H.J. H-reflex modulation during gait in multiple sclerosis patients with spasticity. *Acta Neurol. Scand.* 91:239-246, 1995.

Sinkjaer, T., Anderson, J.B., Nielsen, J.F. Impaired stretch reflex and joint torque modulation during spastic gait. *J. Neurol.* 243:566-74, 1996.

Stein, R.B., Yang, J.F., Bélanger, M., and Pearson, K.G. Modification of reflexes in normal and abnormal movements. In: *Progress in Brain Research*, Vol. 97, edited by J.H.J. Allum, D.J. Allum-Mecklenburg, F.P. Harris, and R. Probst, 1993, pp. 189-196.

van Wezel, B.M.H., Ottenhoff, F.A.M., and Duysens, J. Dynamic control of location-specific information in tactile cutaneous reflexes from the foot during human walking. *J. Neuroscience* 17(10):3804-3814, 1997.

Yang, J.F. and Stein, R.B. Phase-dependent reflex reversal in human leg muscles during walking. *J. Neurophysiol.* 63:1109-1117, 1990.

Yang, J.F., Fung, J., Edamura, M., Blunt, R., Stein, R.B., and Barbeau, H. H-reflex modulation during walking in spastic paretic subjects. *Can. J. Neurol. Sci.* 18:443-452, 1991.

Zehr, E.P., Komiyama, T., and Stein, R.B. Evaluating the overall electromyographic effect of cutaneous nerve stimulation in humans. *Soc. Neuroscience Abs.* **21**:681, 1995.

Zehr, E.P., Komiyama, T., and Stein, R.B. Cutaneous reflexes during human gait: electromyographic and kinematic responses to electrical stimulation. *J. Neurophysiol.* 77:3311-3325, 1997a.

Zehr, E.P., Fujita, K., and Stein, R.B. Cutaneous reflexes from the foot dorsum are maintained in stroke patients. *Proceedings of the International Society of Biomechanics IX biennial meeting, Tokyo, Japan,* 1997b.

6. Function of sural nerve reflexes during human walking[1]

6.1 Introduction

Non-noxious electrical stimulation of cutaneous nerves during human locomotion produces reflexes that are task-dependent (e.g. phasic locomotor vs. tonic maintained activity; Lisin, Frankstein, & Rechtmann 1973; Kanda & Sato 1983; Duysens, Tax, Trippel, & Dietz 1993), intensity-dependent (e.g. noxious vs. non-noxious stimulation; Bélanger & Patla 1984; Crenna & Frigo 1984; Duysens, Trippel, Horstmann, & Dietz 1990), and phase-dependent (e.g. swing vs. stance; Yang & Stein 1990; Duysens et al. 1990; Duysens, Tax, Trippel, & Dietz 1992; DeSerres, Yang, & Patrick 1995; Zehr, Komiyama, & Stein 1997). Additionally, cutaneous reflexes have contralateral as well as ipsilateral effects (Tax, van Wezel, & Dietz 1995; van Wezel, Ottenhoff, & Duysens 1997). Local sign is also important, as revealed by experiments in which nerves with different cutaneous fields have been studied (Zehr et al. 1997; van Wezel et al. 1997). The majority of the experiments have concerned the sural nerve, which innervates the lateral margin of the foot, although the tibial nerve, which innervates the plantar foot surface, has also been studied (Yang & Stein 1990; Duysens et al., 1990, 1992; Zehr et al., 1997; van Wezel et al. 1997). Recently, reflexes from the superficial peroneal nerve (SP; innervates the foot dorsum) have been examined (Zehr et al., 1997; van Wezel et al. 1997).

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[1] A version of this chapter will be published by E. Paul Zehr, Richard B. Stein, and Tomoyoshi Komiyama in the *Journal of Physiology*.

Most of the human experiments have relied solely upon information obtained from electromyography (EMG) to delineate reflex function; rarely have measurements of movement kinematics been included in human studies examining cutaneous reflexes after electrical stimulation. Thus, evaluating the function of cutaneous reflexes during human walking has been difficult. We previously described kinematic and EMG responses to superficial peroneal and tibial nerve stimulation and incorporated these into a simple framework in which cutaneous reflexes function to stabilize gait in the face of perturbation (Zehr et al. 1997). Alterations in ankle and knee flexion and extension at reflex latencies were reported after stimulation of sural nerve by Duysens et al. (1992). Van Wezel et al. (1997) also reported kinematic changes in the saggital plane associated with sural nerve stimulation. However, these results from the sural nerve, unlike those from SP and tibial nerve stimulation, have been difficult to interpret in a functional framework.

From experiments in the cat, Nichols (1994) suggested that the anatomical linkage and lines of force generated by a muscle or muscle group participating in cutaneous or other reflexes may determine reflex function. He also suggested that reflexes may play a powerful role in responses outside of the saggital plane (such as inversion-eversion at the ankle). To date only limited data on ankle and knee flexion and extension and none on inversion-eversion are available for cutaneous reflexes during human gait. Therefore the function of sural nerve reflexes during gait remains uncertain.

The purpose of the present paper was, therefore, to test the functional effect of non-noxious electrical stimulation of the sural nerve during treadmill walking. This was done by examining net reflex changes in the EMG activity and in the kinematics about the hip (flexion-extension), knee (flexion-extension), and ankle (flexion-extension and inversion-eversion). We interpreted these reflexes in terms of possible functional roles, such as Forssberg's (1979) stumbling corrective responses in the cat. Portions of this work have previously been published in abstract form (Zehr, Komiyama, & Stein 1996).

6.2 Methods

6.2.1 Subjects and general procedure

Twelve subjects (10 male and 2 female), aged 24-55 y, participated in the experiments with informed, written consent and according to the Declaration of Helsinki. All experiments were conducted under an approved protocol for human subjects at the University of Alberta. During each session, subjects walked on the treadmill at speeds of 2 and 4 km/h for approximately 7 to 10 minutes at each speed. Approximately 400-600 steps were collected for each speed (including stimulated and control unstimulated steps). Two stimulation intensities were employed (six subjects participated in each condition) and the data collected varied between the two conditions (see details below).

6.2.2 Nerve stimulation

The sural nerve was stimulated using either a GRASS SD9 (Grass Inst., Quincy Mass.) isolated constant voltage stimulator or a custom-designed constant current stimulator with trains of 5 pulses at 200 Hz with a pulse width of 1.0 ms. The sural nerve was stimulated on the lateral surface of the ankle, just posterior to the lateral malleolus. At this location subjects reported strong radiating parasthesia in the cutaneous receptive field of the sural nerve, i.e., at the lateral margin of the foot and towards the heel. Flexible 1 cm disposable ELECTROTRACE (JASON, Huntington Beach, CA) Ag-AgCL surface EMG electrodes were used for cathodal stimulation. The threshold of stimulation in terms of the radiating threshold (x RT; defined as a clear radiating parasthesia in the cutaneous field), was determined in all subjects. The perceptual threshold (PT), defined as the lowest stimulation that was just detectable by the subject, was also determined. The PT probably represents local activation of cutaneous receptors lying immediately underneath the recording electrodes, whereas the RT represents electrical activation of fascicles in the underlying cutaneous nerve. Two stimulus intensities were used, a medium and a high intensity and six subjects were tested at each intensity. The medium stimulation intensities were on average 1.9 x RT and the high intensity 2.3 x RT. These corresponded to between 2.5 and 3.6 x PT. For the high intensity, the intensity was varied somewhat for each subject to obtain the strongest stimulation possible that was described as non-noxious by the subject and was subthreshold for evoking a flexion reflex (a generalized withdrawal of the limb by flexion at the ankle, knee, and hip) while standing. In our most recent publication (Zehr et al. 1997) we were able to use small motor responses to ascertain that the stimulation intensity was constant throughout the step cycle; this check is unavailable for the sural nerve. However our stimulus delivery is quite similar to methodology previously described (see Yang & Stein 1990; Duysens et al. 1995) and variation in stimulus intensity throughout the step cycle probably played a very small role in results observed here.

The stimulator was driven by a pseudo-random pulse generator with a minimal repeat time approximately equal to the step cycle duration and a maximum that was twice this. In general this procedure resulted in a stimulus delivered once in a 3- 4 second period. We were thus able to collect many unstimulated steps between stimulated steps and no step had more than 1 stimulus train. Outputs from both the trigger pulse generator and the Grass stimulator were sent to a 12 bit A/D converter and then into a 486 66 MHz microcomputer running AXOSCOPE (Axon Instruments) data acquisition software.

6.2.3 Electromyography

After light abrasion and cleansing of the skin with alcohol, disposable ELECTROTRACE (JASON, Huntington Beach, CA) Ag-AgCl surface EMG electrodes were applied in bipolar configuration longitudinal to the predicted path of the muscle fibers (~ 2 cm inter-electrode distance) over the soleus (SOL), lateral (LG) and medial gastrocnemii (MG), tibialis anterior (TA), vastus lateralis (VL), and biceps femoris (BF) muscles. SOL electrodes were placed distal to the termination of the gastrocnemius muscles, whereas MG and LG electrodes were placed over the medial and lateral heads of the gastrocnemius, respectively. TA electrodes were placed over the largest girth of the tibialis anterior muscle. For VL, the distal electrode was placed approximately 4-6 cm proximal to the lateral margin of the patella and for BF placement was over the muscle belly at approximately 1/3 of the distance from the knee to the hip. Ground electrodes were placed over electrically neutral tissue. EMG signals were pre-amplified, highpass filtered (100 Hz), full-wave rectified (thus yielding components down to DC), and then lowpass filtered (100 Hz). The processed output was sent to a 12 bit A/D converter and then to a microcomputer running AXOSCOPE (AXON Instruments) data acquisition software.

6.2.4 Kinematics and step-cycle kinetics

Data on movement kinematics (ankle and knee joint angle) and dynamics (vertical ground reaction force measured under the ipsilateral, or stimulated, foot) were recorded. Angular position of the leg were recorded with custom-made potentiometric electrogoniometers as well as bi-axial goniometers (Penny + Giles Biometrics Ltd, Cwemfellinfach, Gwent, U.K.) placed over the joint and secured with plastic tape and fabric straps. For the ankle joint, the bi-axial goniometers were placed with the distal end on the heel of the subject's shoe and the proximal end fixed to the lower leg along the midline. Signals obtained from custom-made force sensors located in the insole of the subject's shoe were used to establish step cycle parameters (e.g., heel contact, toe-off). This technique, based on force-sensing resistors (FSRs), has been previously described (Zehr, Komiyama, Stein, & Kenwell 1995a). Angle and force signals were pre-amplified at the subject (the subject wore a small pouch and belt to hold the amplifiers) and then sent directly to the AXOSCOPE/computer interface.

6.2.5 Data acquisition and analysis

The data were sampled continuously at 500 Hz and stored on hard disk for off-line analysis. Custom written software programs were used to separate the step cycle into 16 equal parts, beginning with heel contact. The stimuli occurred randomly throughout the step cycle. All responses to stimuli occurring in the same part of the step cycle were averaged together and aligned to stimulus delivery within that part of the step cycle. The averages of unstimulated steps were subtracted from the corresponding values obtained for each of the 16 parts of the step cycle after stimulation.

6.2.6 EMG analysis

Stimulus artifacts were digitally removed and then the EMGs were filtered with an equally-weighted 5-point digital moving average filter. The evoked EMGs for each subject were analyzed for the net reflex effect using the Average Cumulative Reflex EMG up to **150** ms ($ACRE_{150}$; see Zehr et al. 1997). Using the subtracted EMGs, the post-stimulus data were integrated and any significant facilitation or suppression was identified as a positive or negative deflection. The value obtained at 150 ms after stimulation was then divided by the time of integration to measure a net reflex (i.e., negative values indicate overall suppression and positive values overall facilitation). A 150 ms post-stimulus interval was chosen since it preceded any significant voluntary activation (see Zehr, Komiyama, & Stein 1995b; Komiyama, Zehr, & Stein, 1995). To facilitate comparison between subjects, the $ACRE_{150}$ values for each subject were normalized to the peak EMG value (averaged over a 40 ms time window) occurring during the step cycle for each muscle at each walking speed and expressed as percentages.

6.2.7 Kinematic Analysis

Subtracted values for angular changes were obtained as described above. The maximum change observed in these smoothed (n=5 point filtering) signals over an interval of 140 to 220 ms post stimulation was calculated. This window has been previously employed by us (Zehr et al. 1997) and was chosen to take into account the delays between an EMG response and the peak mechanical change in moving muscles (see Stein et al. 1995). As with the EMG, these values were then normalized to the maximal range of motion recorded for each subject during the step cycle and expressed as percentages.

6.2.8 Statistics

In all instances, analysis was conducted on averaged values of each subject from each part of the step cycle. Significant differences from zero for the net reflex effects were determined by calculation of t-ratios for each part of the step cycle. Statistics were calculated on the combined data from both walking speeds yielding 11 degrees of freedom. Linear least-means square regression analysis was used to evaluate correlation between EMG indices and changes in ankle and knee joint angle at each part of the step cycle. Descriptive statistics included means ± standard error of the mean and statistical significance was set at $p \leq 0.05$.

6.3 Results

6.3.1 High Intensity Stimulation

6.3.1.1 Lower leg responses

High intensity sural nerve stimulation produced significant suppression of the LG and MG during the middle parts of the stance phase (see Figure 6-1 B & C), but no significant effect on SOL (Figure 6-1 A; in all such figures filled symbols indicate significant differences at $p<0.05$) during stance. At this time in the step cycle there were some small changes in plantarflexion force (Fig.6-1 D) which were related to MG and LG suppression. As well, a significant reduction in ankle PF (seen as a change in the DF direction in Fig. 6-1 F) occurred during mid swing. These changes in the gastrocnemii muscles were correlated to the kinematic changes. Regression data from mid-stance (part 5) has been plotted in Figure 6-2 (top panel) for MG muscle and ankle flexion/extension. Further, there were some periods of significant facilitation throughout swing for the triceps surae. However, the prominent feature was the LG and MG suppression and associated mechanical change during stance.

TA muscle showed only small net effects on average (see Fig. 6-1 E) during most of the step cycle. However, during swing the Pearson r values were quite high and significant correlation between TA and ankle movement was observed. Regression data from swing (part 12) during 4 km/h walking have been plotted in Figure 6-2 (see bottom panel). The reason for the high value for the correlation despite the small mean value was that some subjects showed net facilitation and others net suppression and the angle changes followed these effects closely. With this intersubject variability (see error bars),

Figure 6-1 Percent change in lower leg responses after high intensity (2.3 x RT) sural nerve stimulation averaged across all subjects. Values are means ± SEM. Filled symbols indicate values significantly different from no effect (dashed line) at $p<0.05$. SOL, soleus; LG, lateral gastrocnemius; MG, medial gastrocnemius; TA, tibialis anterior; PF, plantarflexion; DF, dorsiflexion; ankle f-e, ankle flexion-extension. The solid and dashed lines indicate stance and swing, respectively. Numbers indicate portions of the step cycle.

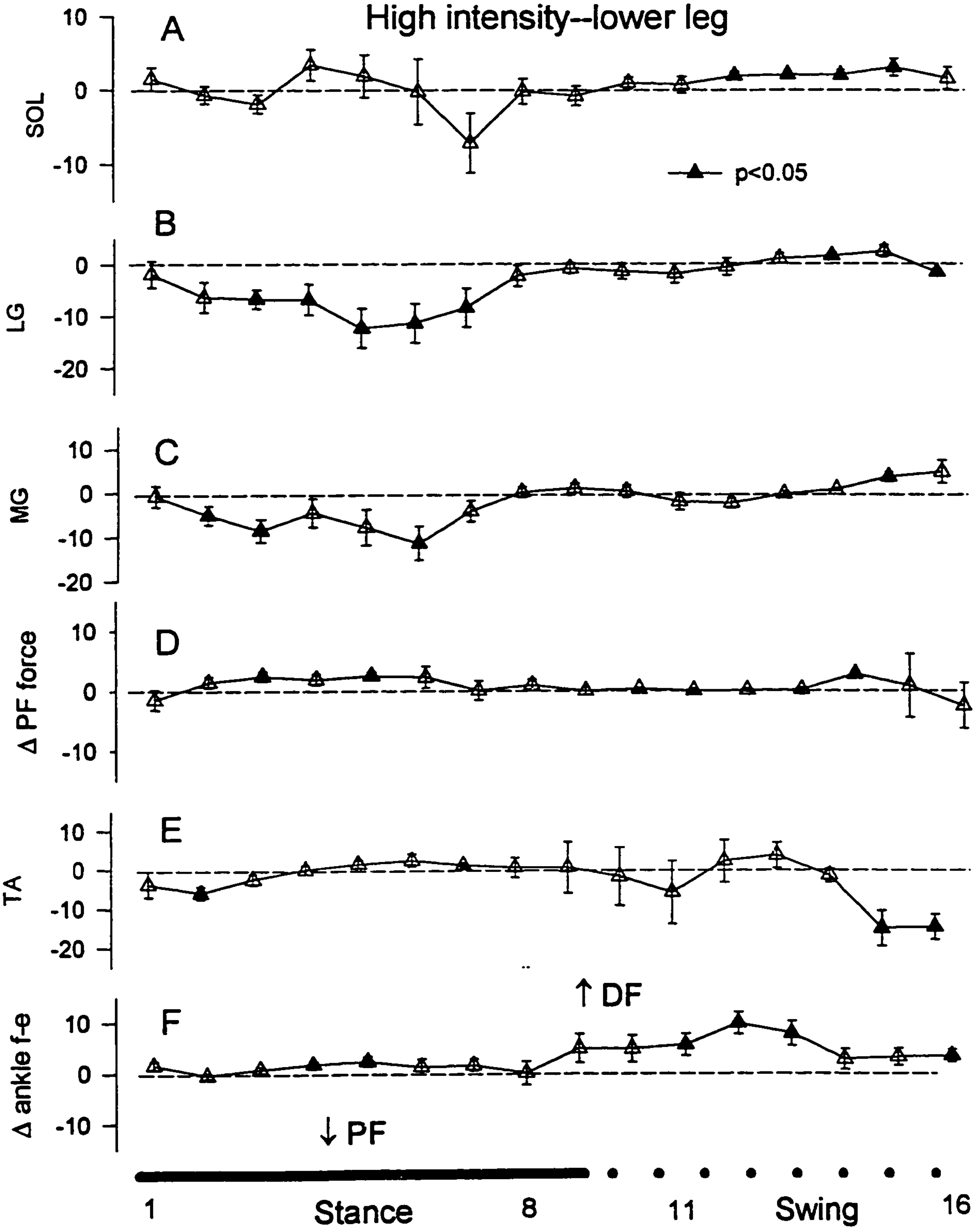
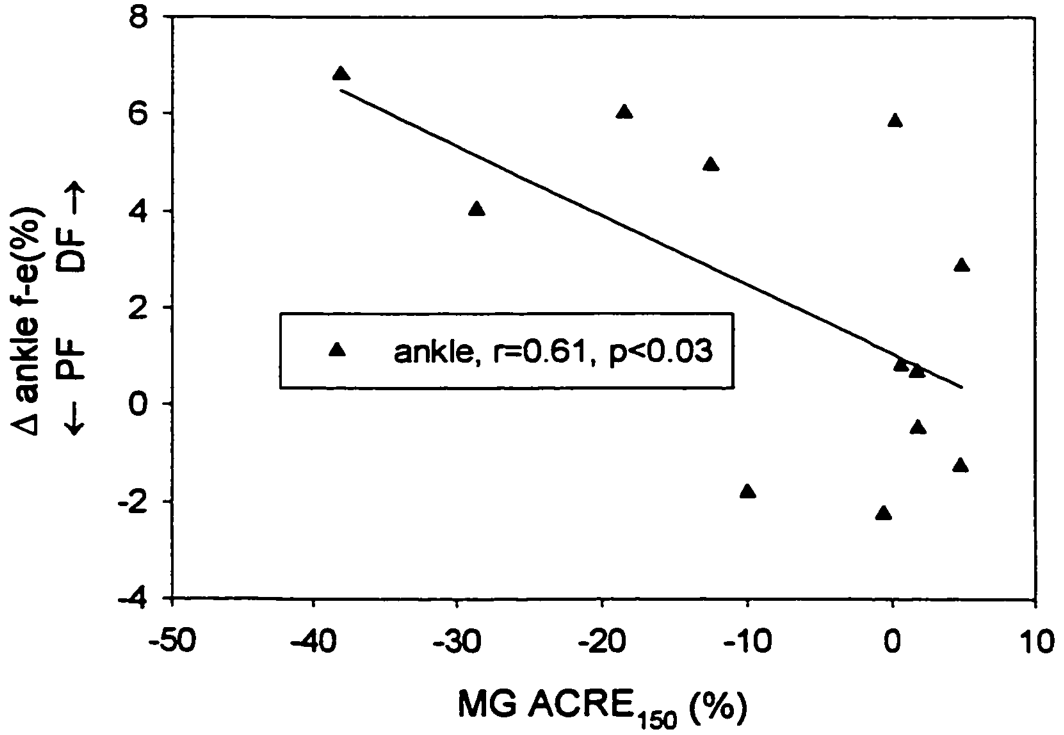


Figure 6-2 Regression plots between MG (top) and TA (bottom) and ankle kinematics and dynamics after high intensity stimulation for all subjects. MG data is from mid-stance (part 5) and TA is from mid-swing (part 12). Significant regression is as indicated by the solid lines.

High intensity--lower leg during stance



Lower leg--swing

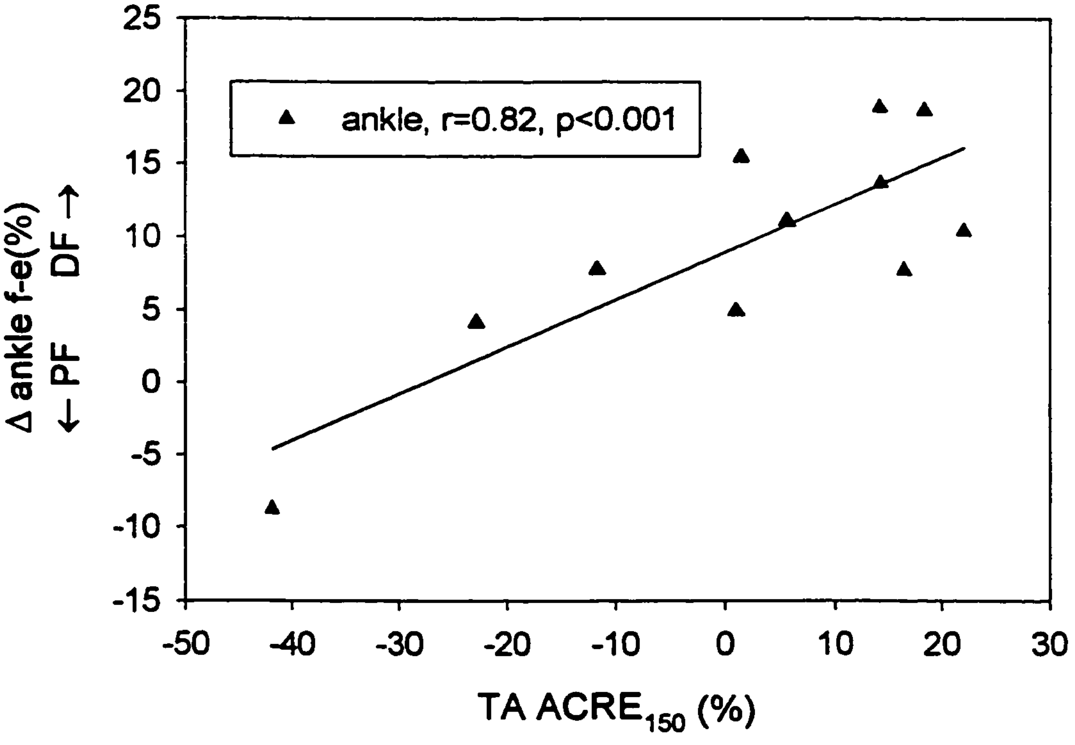
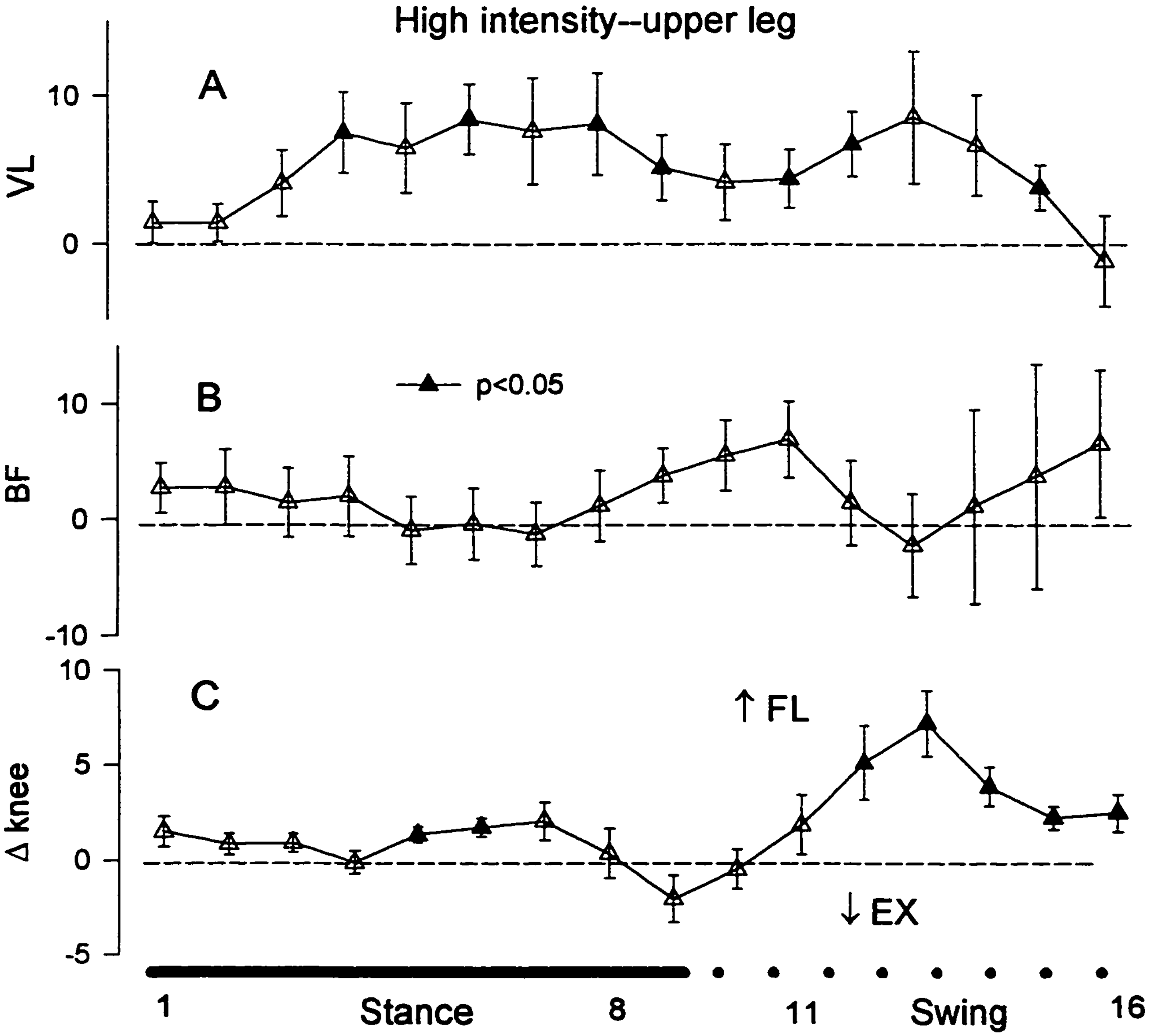


Figure 6-3 Average data from the upper leg after high intensity stimulation for all subjects. Values are means ± SEM. Filled symbols indicate values significantly different from no effect (dashed line) at $p<0.05$. VL, vastus lateralis; BF, biceps femoris; FL, knee flexion; EX, knee extension. The solid and dashed lines indicate stance and swing, respectively. Numbers indicate portions of the step cycle.



the average effects were not significantly different from zero. The reason for the variability is unknown, but the receptive field of the sural nerve is on the lateral border of the foot. Thus, movements in other planes such as inversion or eversion may be more important, but such angular changes were not measured at this intensity (see below). Additionally, other muscles, such as peroneous longus, may have contributed to the reflex but were not recorded here.

6.3.1.2 Upper leg responses

Significant flexion of the knee with sural nerve stimulation was seen particularly during mid to late swing (Figure 6-3 C). This was associated with increased VL activity which would be expected to extend the knee (Fig. 6-3A). However, while the responses were generally facilitatory, no significant effect was observed in BF (see Fig. 6-3B). Thus, more flexion was associated with higher VL activity, so this activity appears to be braking flexion that is produced elsewhere (e.g., secondarily to hip flexion). However, the correlation Pearson r values were generally not significant between either VL or BF and knee angle after high intensity stimulation.

Figure 6-4 Grouped lower leg data after medium intensity (1.9 x RT) sural nerve stimulation. Format is the same as Figure 6-1. EV, ankle eversion; IN, ankle inversion.

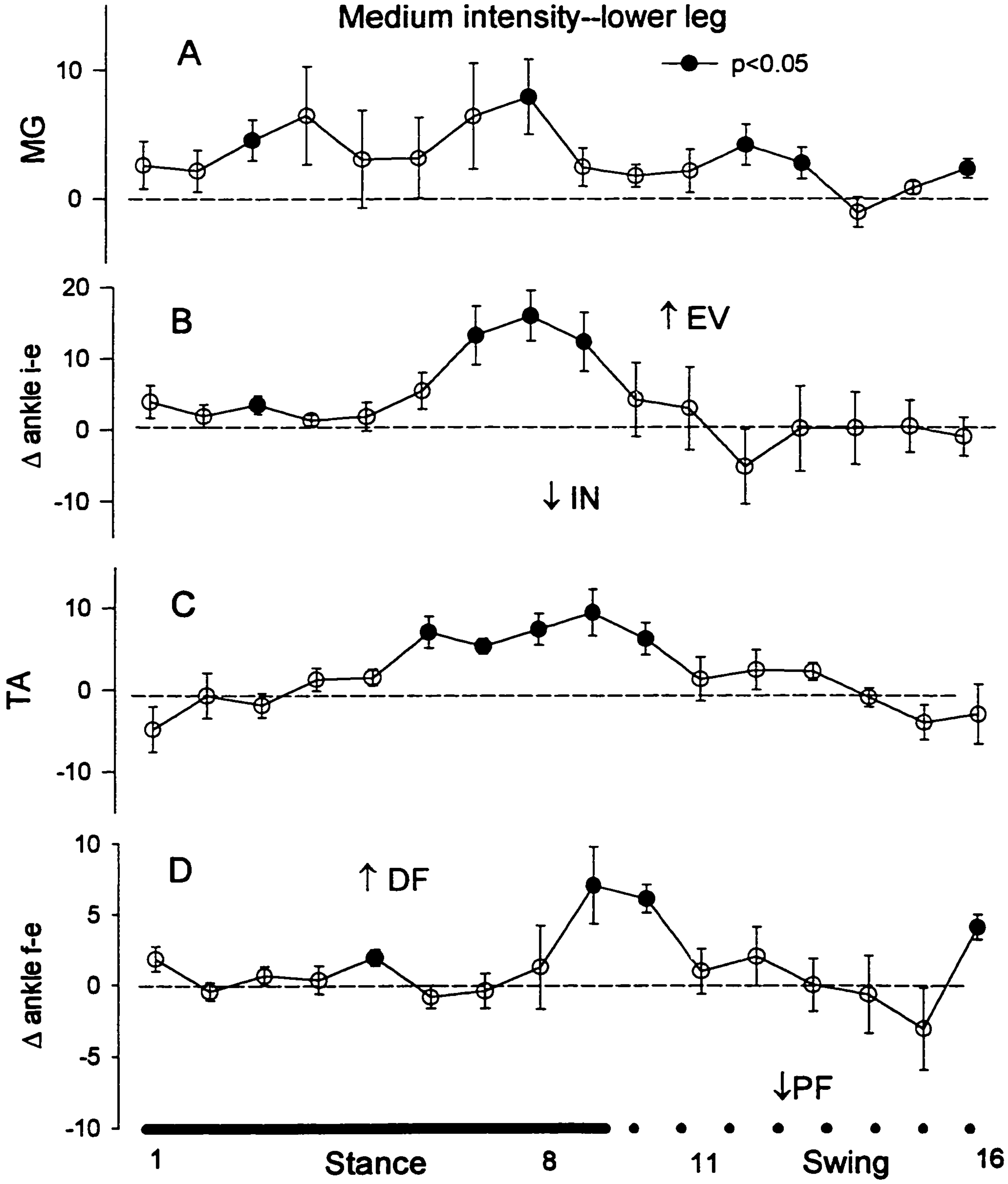
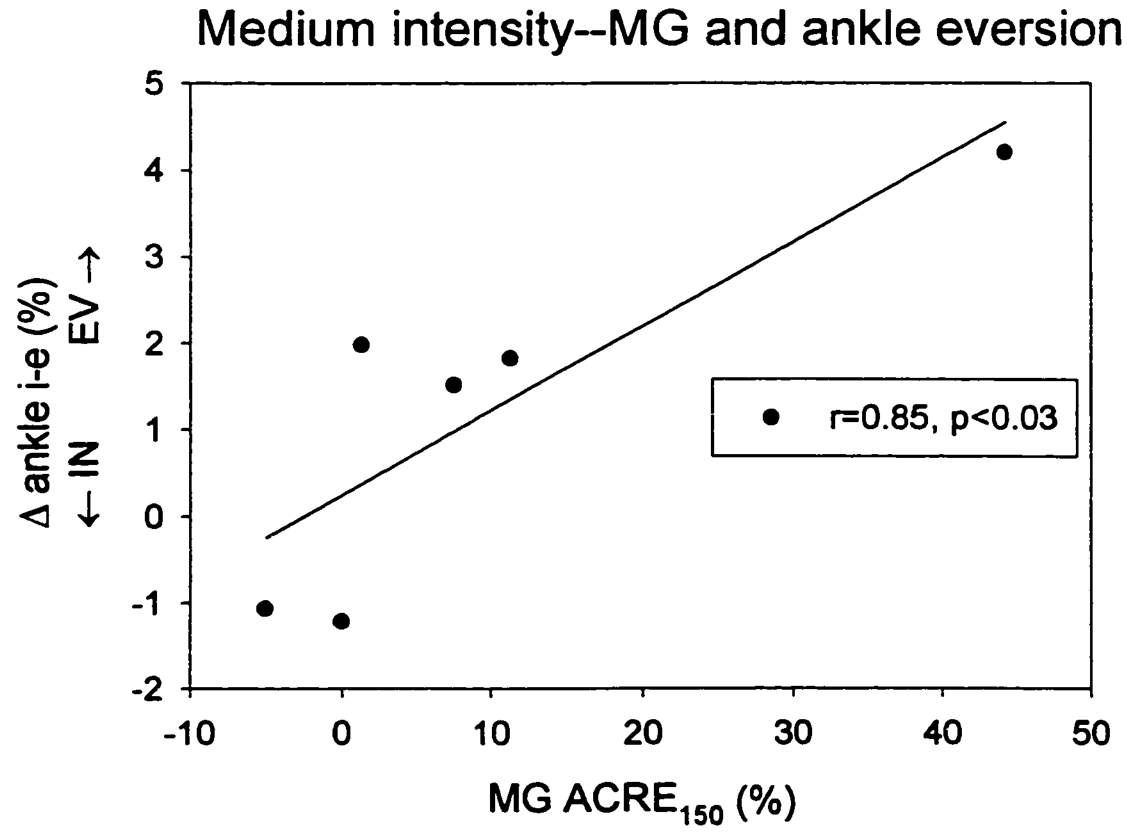
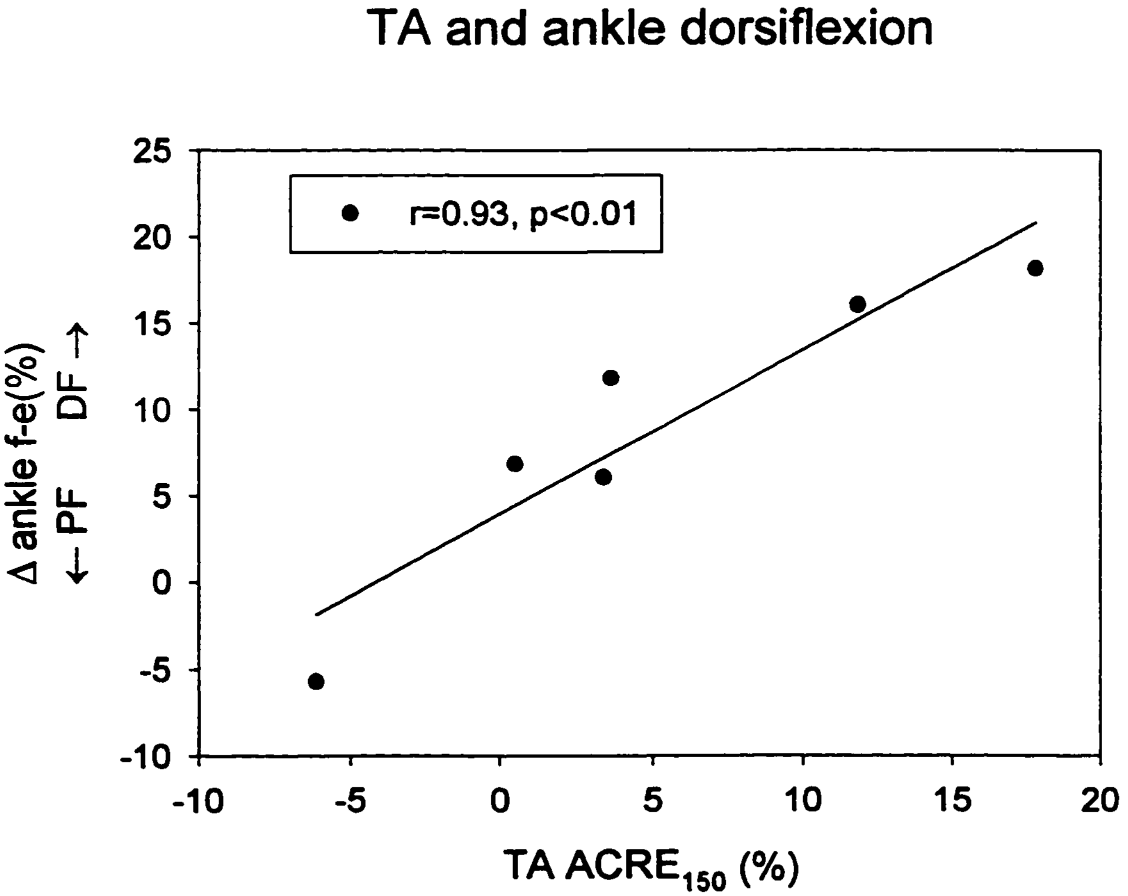


Figure 6-5 Regression plots for MG and ankle eversion (top) and TA and ankle dorsiflexion (bottom) during stance after medium intensity stimulation. Data for MG are from mid-stance (part 4) and for TA from late stance (part 9).


Medium intensity--MG and ankle eversion


TA and ankle dorsiflexion

6.3.2 Medium Intensity Stimulation

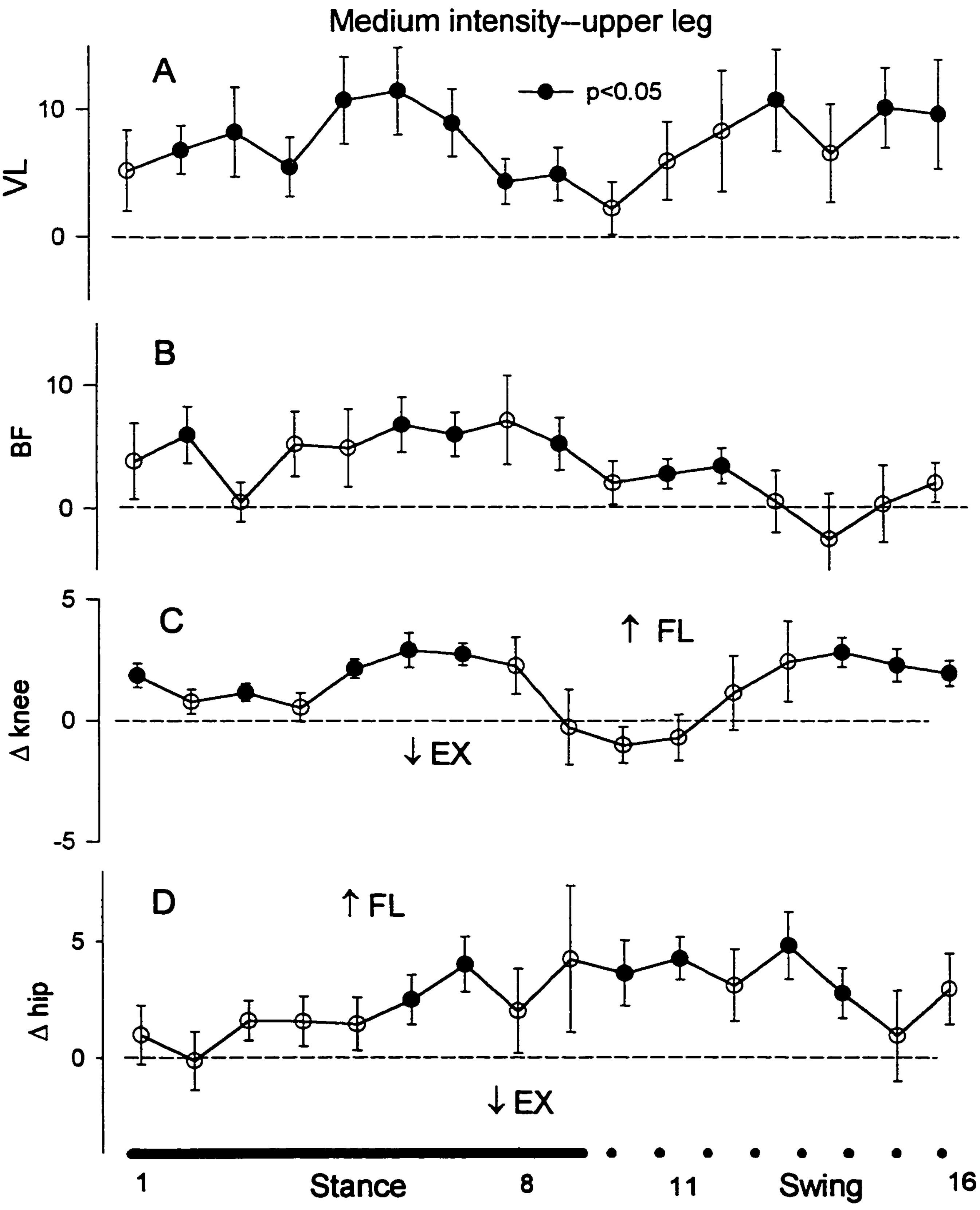
6.3.2.1 Lower leg responses

Both MG and TA muscles showed significant facilitatory responses to sural stimulation; the largest effects were observed during mid to late stance (see Figure 6-4 A & C). MG muscle also had some significant facilitation during swing phase. These results should be contrasted with those from high intensity stimulation in which suppression of MG was the prominent feature. Associated with these EMG changes were significant increases in ankle eversion (Fig. 6-4 B) and dorsiflexion (Fig. 6-4 D), again during late stance and at the stance to swing transition. Regressions plotted in Figure 6-5 (top panel) are mid stance (part 4) data for MG and ankle inversion-eversion at 2 km/h and plotted at figure bottom is data from late stance (part 9) for TA and ankle flexion-extension at 4 km/h.

6.3.2.2 Upper leg responses

Medium intensity sural stimulation produced significant facilitation in VL and BF muscles throughout the step cycle, particularly during stance (see Figure 6-6 A & B). For VL, these responses are quite similar to those observed after high intensity stimulation (see above and Figure 6-3, top panel). However, significant facilitation was observed in BF which was absent after high intensity stimulation. This facilitation in BF was associated with and correlated (highest r=0.92 and 0.97, respectively) to knee flexion (Fig. 6-6 C) and hip extension (Fig. 6-6 D). VL was also correlated (r=0.79) to knee flexion during swing. These anomolous results would require coactivation with other hip muscles that we did not record from and could arise from mechanical linkage secondary to movement at the hip joint.

Figure 6-6 Grouped upper leg data after medium intensity sural stimulation. Format is similar to Figure 6-3.



6.4 Discussion

In this study we have shown significant effects of sural nerve stimulation on many muscles in both the upper and lower leg during treadmill walking. Changes in kinematics were associated with and correlated to the EMG responses at both high and medium intensity stimulation. New findings include: 1) the correlation between reflex facilitation of MG and ankle eversion during stance, 2) the association of BF facilitation with knee and hip flexion, and 3) the widespread facilitation of VL responses throughout the step cycle.

6.4.1 Comparison with the literature

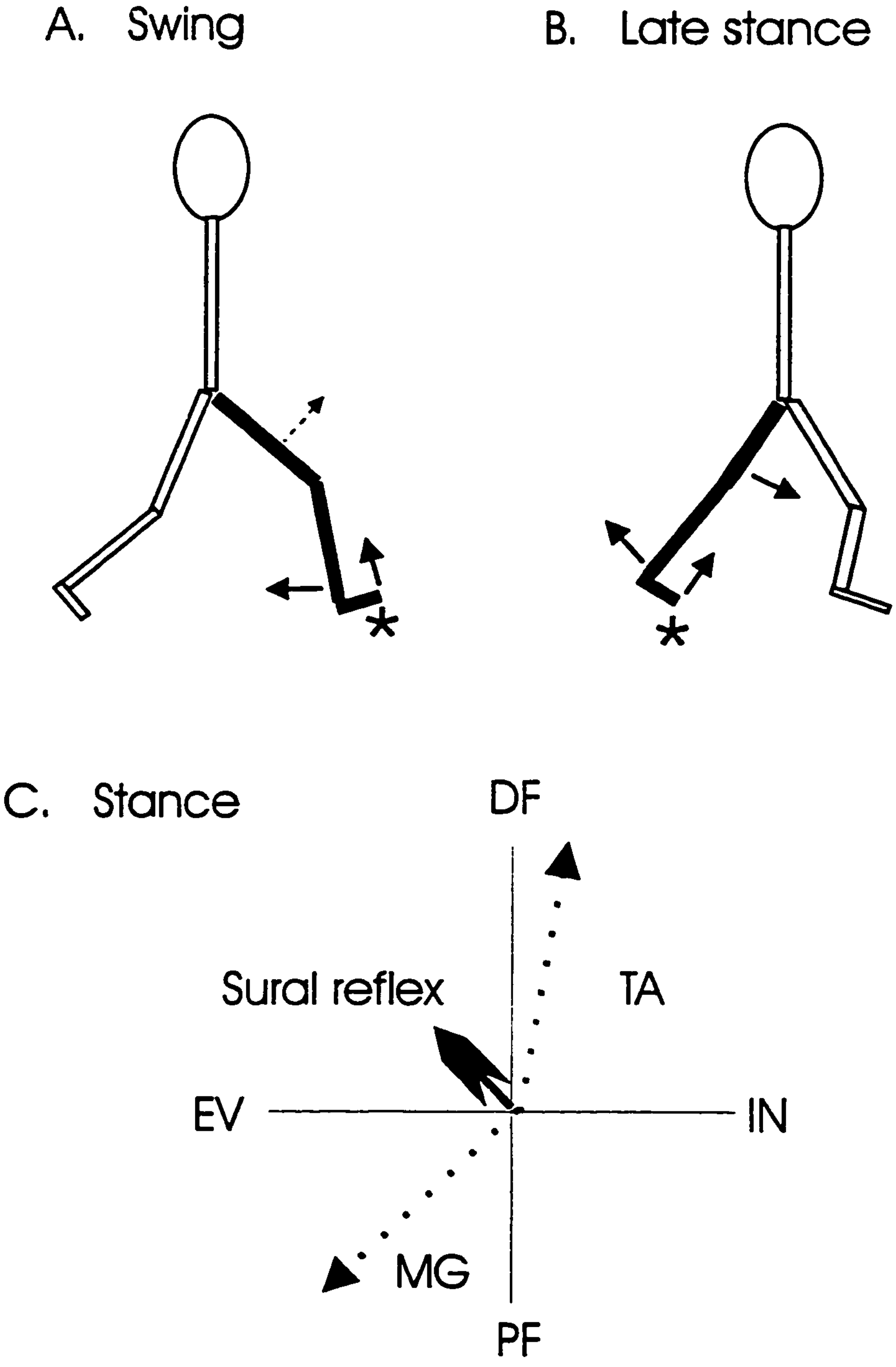
As well as the novel findings, we confirmed and extended previous studies that investigated sural nerve reflexes during gait. Ankle joint changes mirrored the trends described previously (Duysens et al. 1992; van Wezel et al. 1997). In this paper we also observed a differential response to high intensity sural nerve stimulation within the triceps surae. This was previously observed after superficial peroneal nerve (SP) stimulation (Zehr et al. 1997) and a separation within the gastrocnemii after sural stimulation has been described by Duysens, van Wezel, Prokop, and Berger (1996). Also the general facilitation of BF muscles has been observed previously, most recently by van Wezel et al. (1997). With regard to upper leg kinematics, Duysens et al. (1992) also reported knee flexion, and a reversal to extension at end swing, after both high and low intensity sural nerve stimulation. We observed a predominant knee flexion response after both high and medium intensity stimulation. In another study of upper leg responses, Tax et al. (1995) studied 3 different stimulus intensities and found BF facilitation to be a robust feature. However, knee kinematics were not reported in that study.

One difference is that we did not observe the phenomenon of "reflex reversal" as distinctly here as in other papers. This is most likely due to the fact that our EMG method, $ACRE_{150}$ (see Methods), is by its nature less sensitive to small fluctuations at a discrete latency (i.e. the middle latency P2 response; see Duysens & Tax 1994) which do seem to be amenable to phasic reversals. Our methodology is well suited for investigating reflex function and providing a useful index for comparison to kinematics. However, we did observe that TA muscle which has often shown such reversals (see Yang & Stein 1990) from facilitatory responses during stance to suppressive during swing, showed net suppressive responses at end swing and either facilitation or no significant net effect during stance at both stimulus intensities (see Figs. 6-1E and 6-4C). Thus, our results are mainly similar to previously published reports, but need integration into a functional framework for sural nerve reflexes during human gait.

6.4.2 Reflex function during swing phase

The responses during swing are the most straightforward to interpret, particularly those reflexes generated by high intensity stimulation. Stimulation resulted in increased dorsiflexion at the ankle and flexion at the knee. There was a very tight correlation between the TA and ankle DF and VL and knee flexion. Activation of the sural nerve cutaneous field would occur during swing if an obstacle was encountered or if the foot prematurely touched the ground and the lateral foot margin were compressed. If this were to occur, then the most efficient and and stable response would be to increase ankle

Figure 6-7 Schematic illustration indicating proposed functional roles of sural reflexes during gait. A, swing phase in which knee flexion and ankle DF predominate; B, late stance in which hip and knee flexion as well as ankle DF are key features, and; C, net effect of lower leg responses during stance (large arrowhead), wherein MG and TA responses act in concert to evert (EV) and DF the foot. The putative contributions of MG to PF and EV and TA to DF and inversion (IN) are shown by the dotted lines. dorsiflex the foot to accommodate uneven terrain. The * indicates activation of the sural nerve cutaneous field.



DF and flex the knee slightly to avoid the obstacle and clear the ground. Hip flexion was also observed at medium intensity. Thus, ground clearance and obstacle avoidance would both be achieved, as observed here in the upper and lower leg responses (see schematic diagram in Figure 6-7 A). The angular trajectory of the swing limb is changed to avoid the obstacle.

The VL response (i.e. increased activation) may seem somewhat puzzling as it occurred in concert with increased knee flexion. Although the simplest explanation for knee flexion would have been increased BF activation, this facilitation was not significant here. However, flexion at a more proximal joint (i.e. the hip) would cause flexion at the knee as well. Thus, the VL response can serve to control and prevent excessive knee flexion. As described after SP nerve stimulation (Zehr et al. 1997), activation of VL during swing may also serve as a "fail safe" if the ankle response fails to overcome the perturbation. Then, stumbling and increased loading of the swing limb could occur and VL activation, by increasing knee stiffness, would help reduce the likelihood of limb collapse and a consequent fall.

6.4.3 Reflex function during stance phase

The function of the reflexes during stance is somewhat more complex. Nichols (1994) advocated an anatomical approach to understand reflex function in the cat. In particular, he suggested that the lines of force generated by the muscles as prime movers and as synergists be closely examined. Parsons (1894) initially made the observation that the MG muscle fibres pass obliquely outwards and over the Achilles tendon and that the tendon itself twists around to insert on the lateral margin of the calcaneous. In this way the outer part of the tendon is largely formed by MG while LG and SOL make up the inner part. Indeed, this was found to be a common feature in many mammalian species examined (Parsons 1894). Thus, in addition to causing plantarflexion, MG will also evert the foot. Ankle eversion during stance did occur here and was correlated to MG facilitation after medium intensity stimulation. In contrast, TA was facilitated at this time which would produce DF and inversion. The resultant vector of these and other muscles not recorded could be flexion and eversion, as schematically illustrated in Figure 6-7 C. Recall that the sural innervation area could be strongly activated by contact or pressure on the lateral foot surface and near the heel. This would produce ankle extension (PF) and inversion, which, in principle, would be balanced by the resultant effect of TA and MG. The diagram of Fig. 6-7C is merely for illustrative purposes and would have to be tested by measuring the force vectors of each of the major ankle muscles. Interestingly, it has recently been suggested that MG can contribute significantly to isometric torque production in the sagittal plane after medial perturbation at the knee joint (Buchanan & Lloyd 1997). This could, in an unrestrained subject, generate eversion at the ankle.

Excitatory responses in the upper leg in BF and VL muscles and flexion at the knee and hip also occurred during stance (refer again to Fig. 6-7 B). The net effect of these reflexes would be to increase stiffness at the knee while still allowing for the perturbation at the foot (i.e. foot lift/inversion) to be associated with knee flexion. The addition of hip flexion would also assist by lowering the centre of body mass and the net effect is accommodation in the stance limb to the encountered perturbation. Further, the BF activation with hip flexion could serve the same purpose as described above for VL and knee flexion; excessive hip movement (as could be caused by sudden loading) would be countered by BF activation. Although the BF effects were not significant during high intensity stimulation, the knee joint kinematics were quite similar to those observed after medium intensity stimulation. Lastly, if the BF responses during stance (Figure 6-6 B) contribute to exorotation of the femur (see Tax et al. 1995) then it is conceivable that this might generate a torque at the foot that could cause eversion, as recorded here (Figure 6-4 B). However, rotation of the femur was not directly recorded and awaits further study.

6.4.4 Effect of stimulus intensity

The subtle differences between high and medium intensity stimulation likely result from the application of two slightly different strategies. With high intensity stimulation the feeling of tingling or pressure on the foot margin is quite strong. The responses in the lower leg are therefore suppressive and allow for accommodation at the proximal segments (i.e. knee and hip flexion) with some dorsiflexion but no excitatory MG response. During swing, the foot withdraws from the encountered object to continue on through to heel contact. However, with medium intensity stimulation, the reflexes function to stabilize gait during stance and play a more minor role during swing.

To summarize, our data on the sural nerve indicate that non-noxious reflexes function to stabilize human gait, both during stance and swing, so that unimpeded locomotion can continue. The effect of a perturbation will be minimized by accommodation of the limb to uneven terrain during stance and avoidance of an obstacle during swing. In this way, the results extend our previous interpretation of SP and tibial nerve reflexes during gait in a logical way (Zehr et al. 1997). In addition, the present results describe functional responses during stance as well as swing. Gradually, the roles of cutaneous reflexes are emerging. Further work is still needed in relation to contralateral responses, more natural stimulation (i.e., contact with real objects), and pathological gait.

6.5 References

Bélanger, M. & Patla, A.E. (1984). Corrective responses to perturbation applied during walking in humans. *Neuroscience Letters* **49,** 291-295.

Buchanan, T.S. & Lloyd, D.G. (1997). Muscle activation at the human knee during isometric flexion-extension and varus-valgus loads. *Journal of Orthopaedic Research* **15**: 11-17.

Crenna, P. & Frigo, C. (1984). Evidence of phase-dependent nociceptive reflexes during locomotion in man. *Experimental Neurology* **85,**336-345.

DeSerres, S.J., Yang, J.F. & Patrick, S.K. (1995). Mechanism for reflex reversal during walking in human tibialis anterior motor units. *Journal of Physiology* **488,** 249-258.

Duysens, J., Trippel, M., Horstmann, G.A. & Dietz, V. (1990). Gating and reversal of reflexes in ankle muscles during human walking. *Experimental Brain Research* **82,** 351-358.

Duysens, J., Tax, A.A.M., Trippel, M. & Dietz, V. (1992). Phase-dependent reversal of reflexly induced movements during human gait. *Experimental Brain Research* **90,** 404-414.

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

Duysens, J. & Tax, T. (1994). Interlimb reflexes during gait in cats and humans. In: *Interlimb Coordination: Neural, Dynamical, and Cognitive Constraints*, eds. S.P. Swinnen, Heuer, H., Massion, J., & Casaer, P., pp 97-126. Academic, San Diego, CA.

Duysens, J., Tax, A.A.M., Nawijn, S., Berger, W., Prokop, T. & Altenmuller, E. (1995). Gating of sensation and evoked potentials following foot stimulation during human gait. *Experimental Brain Research* **105**, 423-431.

Duysens, J., van Wezel, B.M.H., Prokop, T., & Berger, W. (1996). Medial gastrocnemius is more activated than lateral gastrocnemius in sural nerve induced reflexes during human gait. *Brain Research* **727**, 230-232.

Forssberg, H. (1979). Stumbling corrective reaction: a phase-dependent compensatory reaction during locomotion. *Journal of Neurophysiology* **42**, 936-953.

Kanda, K. & Sato, H. (1983). Reflex responses of human thigh muscles to non-noxious sural stimulation during stepping. *Brain Research* **288**, 378-380.

Komiyama, T., Zehr, E.P. & Stein, R.B. (1995). A novel method for evaluating the overall effect of nerve stimulation in humans. *Electroencephalography and Clinical Neurophysiology* **97**,S179.

Lisin, V.V., Frankstein, S.I. & Rechtmann, M.B. (1973). The influence of locomotion on flexor reflex of the hind limb in cat and man. *Experimental Neurology* **38**,180-183.

Nichols, T.R. (1994). A biomechanical perspective on spinal mechanisms of coordinated muscular action: an architecture principle. *Acta Anatomica* **151**, 1-13.

Parsons, F.G. (1894). On the morphology of the tendo-achillis. *Journal of Anatomy and Physiology* **28**, 414-418.

Stein, R.B., Hunter, W., Lafontaine, S.R. & Jones, L.A. (1995). Analysis of short-latency reflexes in human elbow flexor muscles. *Journal of Neurophysiology* **73**,1900-1911.

Tax, A.A.M., Van Wezel, B.M.H. & Dietz, V.(1995). Bipedal reflex coordination to tactile stimulation of the sural nerve during human running. *Journal of Neurophysiology* **73**,1947-1964.

Van Wezel, B.M.H., Ottenhoff, F.A.M. & Duysens, J. (1997). Dynamic control of location-specific information in tactile cutaneous reflexes from the foot during human walking. *Journal of Neuroscience* **17**, 3804-3814.

Yang, J.F. and Stein, R.B. (1990). Phase-dependent reflex reversal in human leg muscles during walking. *Journal of Neurophysiology* **63**,1109-1117.

Zehr, E.P., Stein, R.B., Komiyama, T. & Kenwell, Z.(1995a). Linearization of force sensing resistors (FSR's) for force measurement during gait. *Proc. 17th Ann. International Conf. IEEE Engineering in Medicine and Biology Society*, pp.300-301.

Zehr, E.P., Komiyama, T. & Stein, R.B. (1995b). Evaluating the overall electromyographic effect of cutaneous nerve stimulation in humans. *Society for Neuroscience Abstracts* **21**,681.

Zehr, E.P., Komiyama, T. & Stein, R.B. (1996). Functional antagonism of cutaneous reflexes in the human tibialis anterior (TA) muscle during walking. Proceedings of *Canadian Society for Biomechanics 9th Biennial Meeting*, pp. 170-171.

Zehr, E.P., Komiyama, T. & Stein, R.B. (1997). Cutaneous reflexes during human gait: electromyographic and kinematic responses to electrical stimulation. *Journal of Neurophysiology* 77:3311-3325.

7. Interaction of the Jendrássik manoeuvre and segmental presynaptic inhibition on the soleus H-reflex[1]

7.1 Introduction

In the late 19th century, Ernst Jendrássik demonstrated that the contraction of muscles in the human upper body (particularly the forearm and jaw muscles) could markedly potentiate tendon jerks (phasic stretch reflexes) in the lower limbs (Jendrássik 1883). The potentiation of stretch reflexes by remote muscle contraction has subsequently become known as the Jendrássik manoeuvre (JM). Since its initial description, JM has been used in clinical neurological practice as a means of potentiating the tendon jerk in neurologically impaired patients. Later, JM potentiation of the electrical analogue of the stretch reflex, the Hoffman (H-) reflex, was tested by Sommer (1940) and found to be lacking. However, Landau and Clare (1964) showed that potentiation was evident if small H-reflexes (which more closely resembled stretch reflex responses) were studied.

For some time the locus of JM facilitation of the H-reflex was thought to be related directly to muscle spindles and presumably gamma or fusimotor drive (Landau and Clare, 1964). However, in a study in which both tendon and H-reflexes were compared in the same subjects, Bussel et al. (1978) found both to be facilitated by JM. This facilitation was observed in the absence of Ia feedback as it persisted during ischemic block. These researchers suggested that JM facilitation is not dominated by the

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[1] **A version of this chapter has been submitted by E. Paul Zehr and Richard B. Stein for publication in *Experimental Brain Research*.**

gamma loop. Also, microneurographic recordings in human subjects (Hagbarth et al.1975) have shown no change in spindle activity as measured by traffic in the Ia axons during JM.

Another suggested mechanism was a direct post-synaptic facilitation of motoneurones (MNs). As the experiments had been performed in quiescent muscle in which sub-threshold levels of MN depolarization could vary widely, this seemed a plausible explanation. Dowman and Wolpaw (1988) tested this hypothesis by conducting JM experiments at rest and during two levels of voluntary plantarflexion (PF). They showed quite clearly that JM facilitation persisted even during steady voluntary PF, thus weakening the argument for a post-synaptic locus. They suggested that the main candidate for JM modulation may be the reduction of presynaptic inhibition (PSI) of Ia afferents.

Mizuno et al. (1971) suggested that inhibition of the soleus H-reflex at condition-test (C-T) intervals of >10 ms of the antagonist muscle nerve (common peroneal, CP) was due to changes in presynaptic inhibition. Capaday et al. (1995) stimulated CP with a single 1 ms pulse at a level equivalent to 1.5 times the motor threshold (x MT) during PF. They observed a significant suppression of H-reflex size at C-T intervals of 100 to 120 ms. The significance of this result is that the inhibition was observed with little or no effect in the full-wave rectified and averaged EMG of soleus. Accordingly, they postulated that the H-reflex modulation was presynaptic. Recently, Iles (1996) described H-reflex modulation due to PSI by CP stimulation at a C-T of 100 ms. In Iles' experiments stimuli were below MT and most of the data were collected in quiescent muscles.

The purpose of the present study was to help clarify the mechanism of JM by evaluating H-reflex facilitation in the presence of the JM alone and when combined with a stimulus that causes an increase in segmental presynaptic inhibition (CP at 1.5 x MT and a C-T of 100 ms). We tested whether JM acts by blocking segmental PSI to facilitate the H-reflex. This work has been presented briefly in abstract form (Zehr and Stein, 1996).

7.2 Methods

7.2.1 Subjects and protocol

Eleven (9 males, 2 females) neurologically intact subjects, aged 23-45 years, participated in the experiments with ethical approval from the University of Alberta and gave informed consent according to the Declaration of Helsinki. Subjects sat with the knee flexed and the ankle dorsiflexed. The ipsilateral foot was fastened firmly to an immobile metal plate. Reflexes were elicited while subjects were at rest or were performing a mild plantarflexion (PF; ~10% maximum voluntary contraction, MVC). The H-reflex was elicited without (test) and with conditioning. With the fixation of the leg there was negligible movement at the ankle or knee during the PF contraction or during reflex stimulation (see below). Muscle contraction due to the conditioning nerve stimulation did not cause measurable ankle movement.

7.2.2 Electromyography (EMG) and nerve stimulation

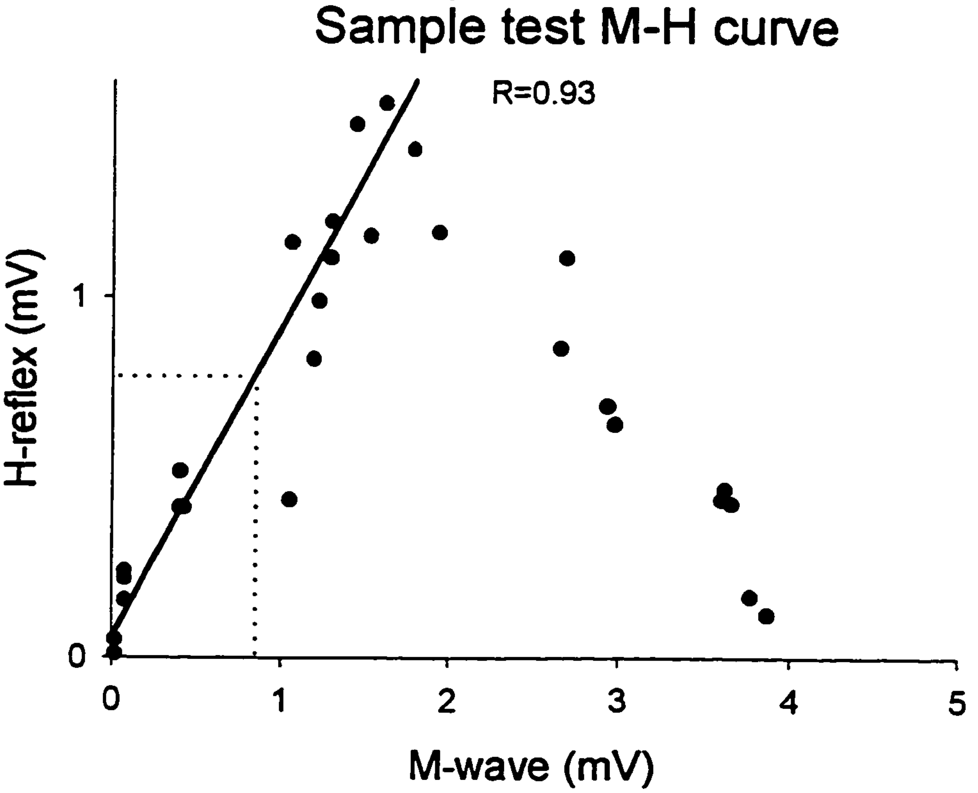
Flexible surface EMG electrodes (Electrotrace, Jason Electronics, Huntington Beach, CA, USA) were placed longitudinally (~2 cm inter-electrode spacing) over the soleus and tibialis anterior (TA) muscles in a bipolar configuration. TA electrodes were placed over the approximate motor point, near the largest muscle bulk, while soleus electrodes were placed distal to the gastrocnemius muscle in a belly and tendon arrangement.

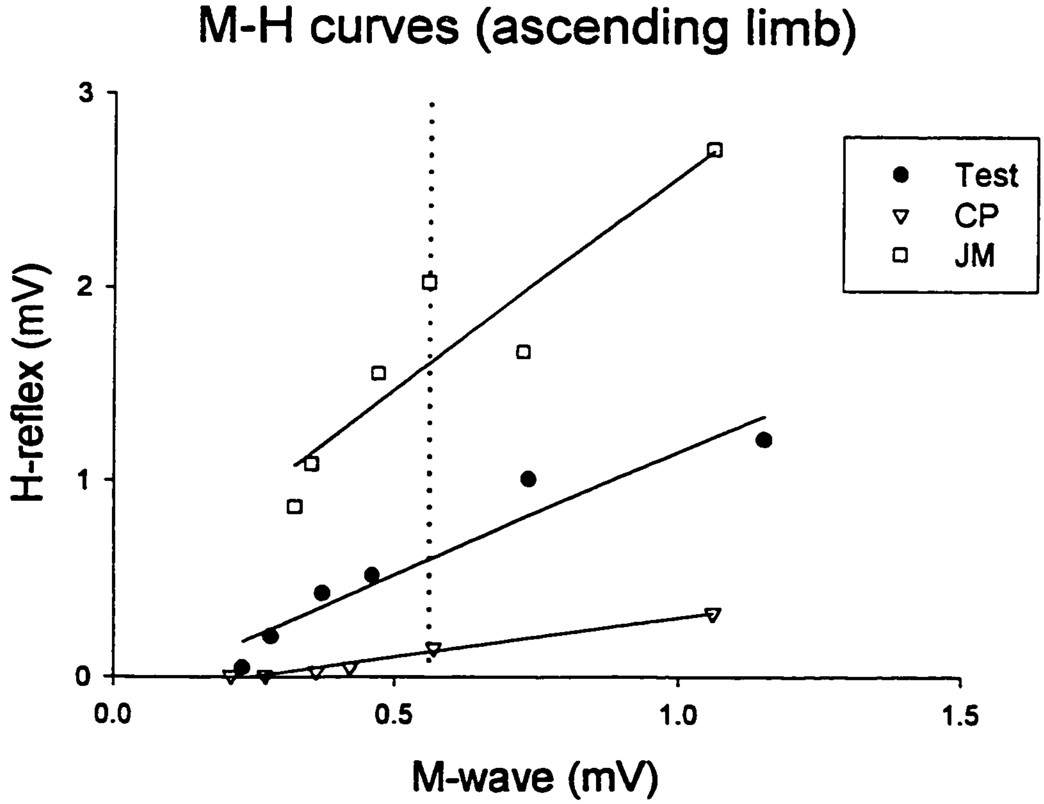
7.2.3 H-reflex stimulation

The H-reflex was elicited by electrically stimulating the tibial nerve with the active electrode in the popliteal fossa with a 1 ms pulse provided by a Grass SD9 isolated stimulator (Grass Inst., Quincy Mass., USA). Reflexes were elicited pseudo-randomly with an interval of 1.5 to 3 seconds and data were sampled by a 486 microcomputer running AXOTAPE software (Axon Instruments). The indifferent electrode was placed over the patella. EMG responses representing direct motor stimulation (M-wave) and the H-wave were created by increasing the stimulus amplitude in step changes up to the H-reflex plateau region. Generally, three M-H pairs were collected at each of 10 stimulus amplitudes, which ranged from H-reflexes at the M threshold up to beyond where the reflexes were maximum (H_{max}). These M-H curves were collected for the test and the conditioning series (see below). M- and H-wave sizes were measured by taking the maximum peak to peak amplitude of the raw soleus EMG signal within a manually set time window.

Later, the M-H pairs for each condition were rank-ordered according to M-wave size and averaged (n=3). Least mean square linear regression lines were fit to the ascending limb of each curve (e.g. from the liminal H-reflex size to H_{max}; see Figure 7-1 top and bottom). The M-wave for 50% of the test H_{max} was used as the M-wave in the regression equations for all other conditioned series to calculate a stable reflex size in each condition for each subject. 50% H_{max} was selected because it most closely adhered to the reflex size used in prior experiments and because this size reflex is sensitive to both facilitation and inhibition.

Figure 7-1 Top. Sample M-H curve for one subject during a test (unconditioned H-reflex) run. The regression line has been fitted to the ascending limb of the curve from the initial H-reflex to Hmax (see text for details), and the dotted lines indicate the M-wave at 50% Hmax. Bottom. Sample M-H curves for another subject during test (filled circles), CP conditioning (open triangles), and JM (open squares) runs. The M-wave at 50% Hmax for the test condition is shown by the vertical dashed line and was then used in all subsequent regression calculations for conditioned reflex series in this subject (see text).





This more complex procedure was used because it compensates for any small changes in M-wave that accompany plantarflexion and CP stimulation. Sample M-H curves for test, CP, and JM conditions are plotted in Figure 7-1 (bottom, ascending limb) and the selected M-wave is shown by the dashed vertical line.

7.2.3.1 Reflex facilitation

The classical Jendrássik manouevre was used to facilitate the H-reflex. On an auditory cue, subjects clenched their teeth and pulled on their interlocked and clenched fists. As previous work by others (Kawamura and Watanabe 1975; Delwaide and Toulouse, 1980; Péréon et al. 1995) found that JM facilitation reaches a peak near 300 ms after JM onset, the conditioned reflex was elicited at 300 ms.

7.2.3.2 Reflex inhibition

Stimulation of the antagonist motor nerve (CP) was used to inhibit the H-reflex. The CP was stimulated at a level equivalent to 1.5 times the threshold for eliciting an M-wave in the TA muscle (MT) with a 1 ms pulse provided by another Grass SD9 isolated stimulator (Grass Instruments, Quincy Mass., USA). As described in the Introduction, several other investigators (Capaday et al. 1995; Iles 1996) have suggested that H-reflex suppression induced by applying CP stimulation in a condition-test (C-T) paradigm is due to presynaptic inhibition at a latency of 100 ms. Accordingly, we used a C-T interval of 100 ms in this study.

7.2.3.3 Combined stimulation

To measure interaction between the JM facilitation and CP inhibition, both conditioning stimuli were applied simultaneously. In this part of the experiment, the CP stimulator was triggered 200 ms after the tone onset so that the maximal PSI was timed to interact with the maximal Jendrássik facilitation.

7.2.4 Statistics

Repeated measures analysis of variance (ANOVA) was used to evaluate significant differences between conditions. In those cases where the data failed a normality test, Friedman's repeated measures ANOVA on ranks was used. Student-Neumann-Keuls post-hoc procedure was used to evaluate significant main effects. Student's t-ratios were calculated to evaluate whether conditions were significantly different from 1. Student's t-test or the Wilcoxon signed-rank test was used when paired data were compared. Descriptive statistics included means ± standard error of the mean (SEM). Statistical significance was set at $p<0.05$.

7.3 Results

7.3.1 JM facilitation of the H-reflex

A sample record from one subject is shown in Figure 7-2 (top) in which a clear facilitation can be observed during JM in a contraction trial. The JM increased H-reflex size in most (6 of 8 at rest, and 8 of 11 during contraction) subjects. On average, the facilitation was significant ($p<0.05$) only during contraction and not at rest, in large part due to large inter-subject variability. Grouped data for all subjects during rest and contraction are shown at the top of Figure 7-3.

Epochs of rectified and averaged EMG prior to and from 270-300 ms after tone onset were analyzed for all trials during contraction. There was no significant change in baseline EMG between the epochs prior to and during JM.

Figure 7-2 Sample average (n=20) M- and H-waves for one subject showing the effect of JM (top panel), CP (middle panel), and combined JM & CP (bottom panel) conditioning stimulation versus test reflex size during soleus contraction. The sharp spike at the beginning of each trace represents the stimulus artifact.

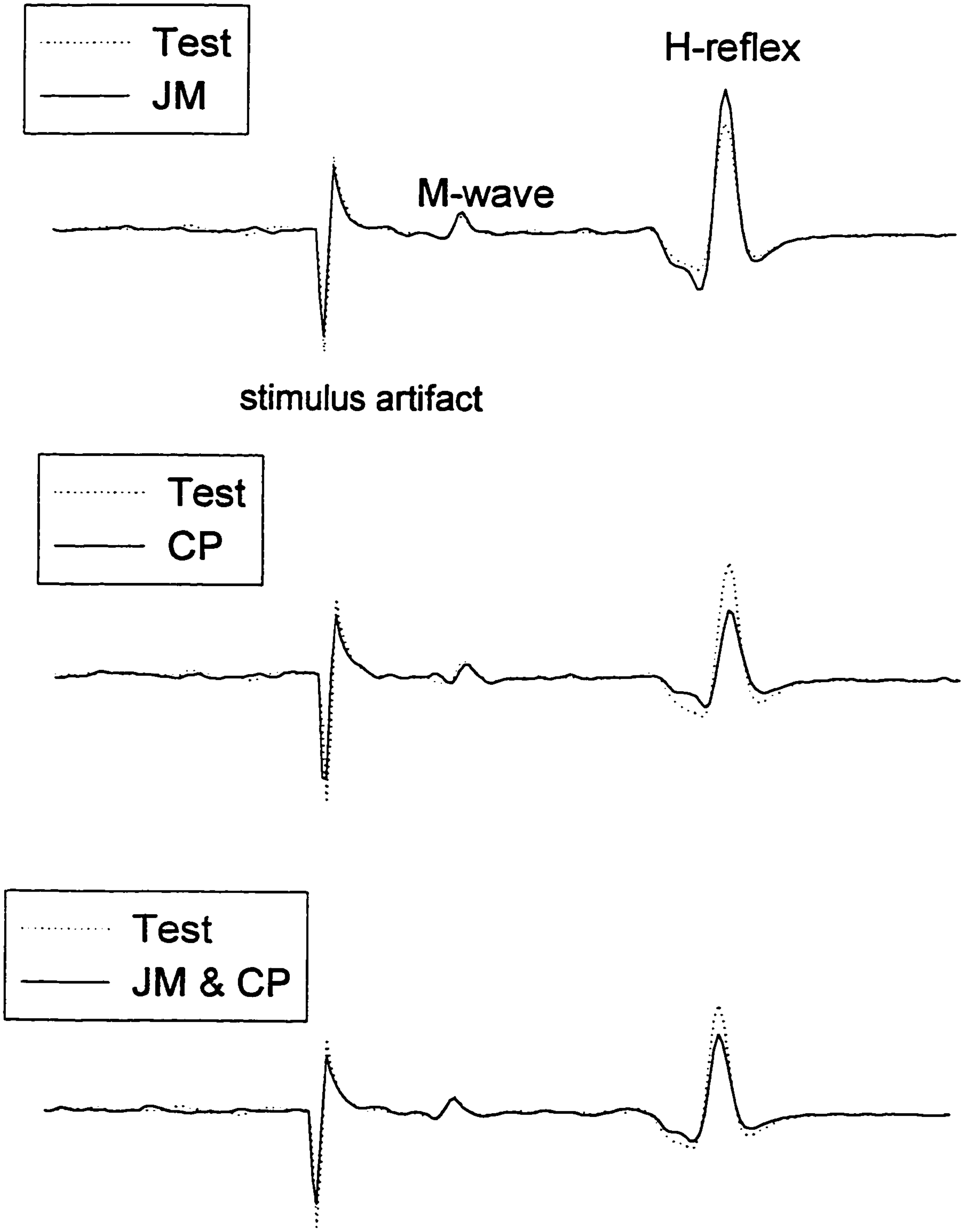
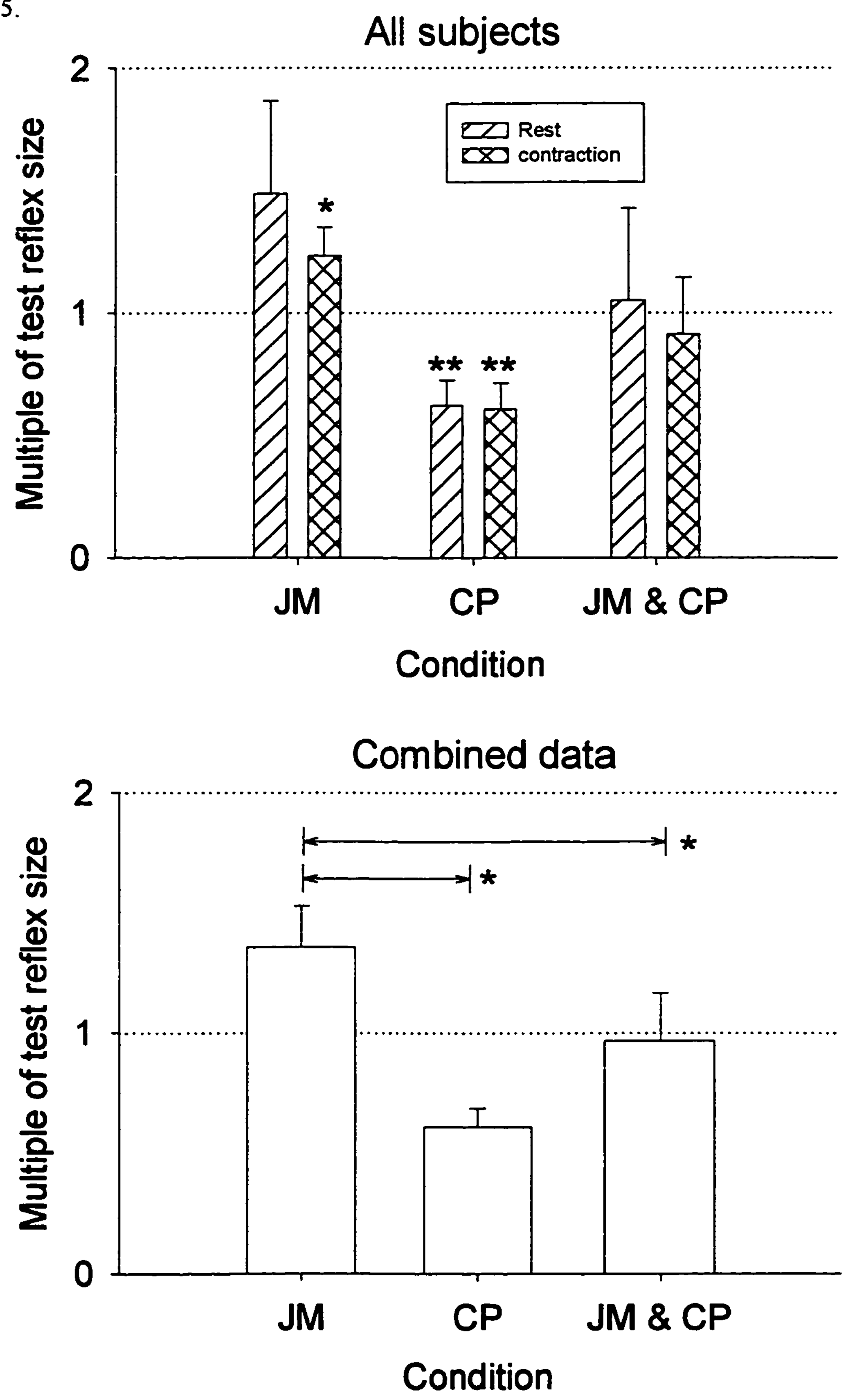


Figure 7-3 Top. Data for the 3 conditioning series (JM, CP, and JM & CP) for all subjects. Values at rest are represented by the hatched and during contraction by the cross-hatched bars. * and ** indicate different from 1 at $p<0.05$ and $p<0.01$, respectively. Bottom. Combined data for the 3 conditioning series (JM, CP, and JM & CP. All values are multiples of test reflex size and are presented as means ±SEM. * indicates conditions which are significantly different at $p<0.05$.



7.3.2 CP inhibition of the H-reflex

Figure 7-2 (middle panel) shows an example of CP conditioning for a single subject during contraction. As can be seen clearly in this subject, CP could profoundly inhibit the H-reflex. CP stimulation significantly ($p<0.01$) inhibited the H-reflex on average, as plotted in Figure 7-3 (top) for all subjects during rest and contraction. Seven of 8 subjects showed inhibition at rest and 10 of 11 during contraction. CP values were also significantly smaller than those from the JM condition.

As mentioned above, an important factor to consider is the post-synaptic effect of the CP conditioning on the motoneurones; membrane potential must remain constant during the stimulation if the inhibition is to be considered presynaptic. To evaluate this we examined the rectified EMG before CP stimulation and also over a 30 ms window starting at 100 ms post-stimulation. The rectified and filtered EMG was steady before the stimulus, but showed a decrease at 40-60 ms which is due to the well-known disynaptic inhibition from CP nerve to triceps surae motoneurones (Capaday et al. 1990). After this period the EMG was relatively constant near its pre-stimulation value. When values across all subjects were evaluated, no significant modulation of the surface EMG was found and by implication no change in the trajectory of the membrane potential of soleus motoneurones; the H-reflex modulation was therefore deemed to be presynaptic.

7.3.3 Combined JM and CP stimulation

Reference to Figure 7-3 (top) reveals that applying JM and CP together (JM & CP) had no significant effect on H-reflex size on average at rest or during contraction.

In fact, there was no significant effect of contraction on any of the reflex conditions. As a result, the data were combined to increase statistical and predictive power. The combined data are shown at the bottom of Figure 7-3. The data for JM were significantly ($p<0.05$) greater than for either CP or CP & JM conditions. CP conditioning was not significantly different from JM & CP. Therefore, JM facilitation does not block CP inhibition. Additionally, to more clearly test for JM and CP interaction, an analysis in which only subjects who showed both JM facilitation and CP suppression was conducted. Results from this analysis corroborated the results described above on all subjects.

7.4 Discussion

This study confirms previous work in demonstrating: 1) significant suppression of the soleus H-reflex after CP conditioning at a long latency and 2) significant facilitation of the H-reflex after JM. This is the first study of the interaction of these two effects and methodological considerations will be discussed briefly. We will then consider the mechanisms of the interaction between CP stimulation and the JM and finally the functional implications.

7.4.1 Methodological considerations

Since the degree of modulation is sensitive to the size of the H-reflex , Crone et al. (1990) suggested that the reflex size should be adjusted to a common value for each condition. This method is not practical for studying the interaction of two inputs, and various combinations of the two could all produce the same reflex size. Instead, we used an intermediate reflex size that was sensitive to both facilitation and suppression (Figure 7-3, top). Since we fit the ascending limb of the M-H curve, the values of the M-wave could be matched precisely between conditions and we could examine the effect of choosing different values for the M-wave. Irrespective of the value of the M-wave selected, the results are qualitatively similar.

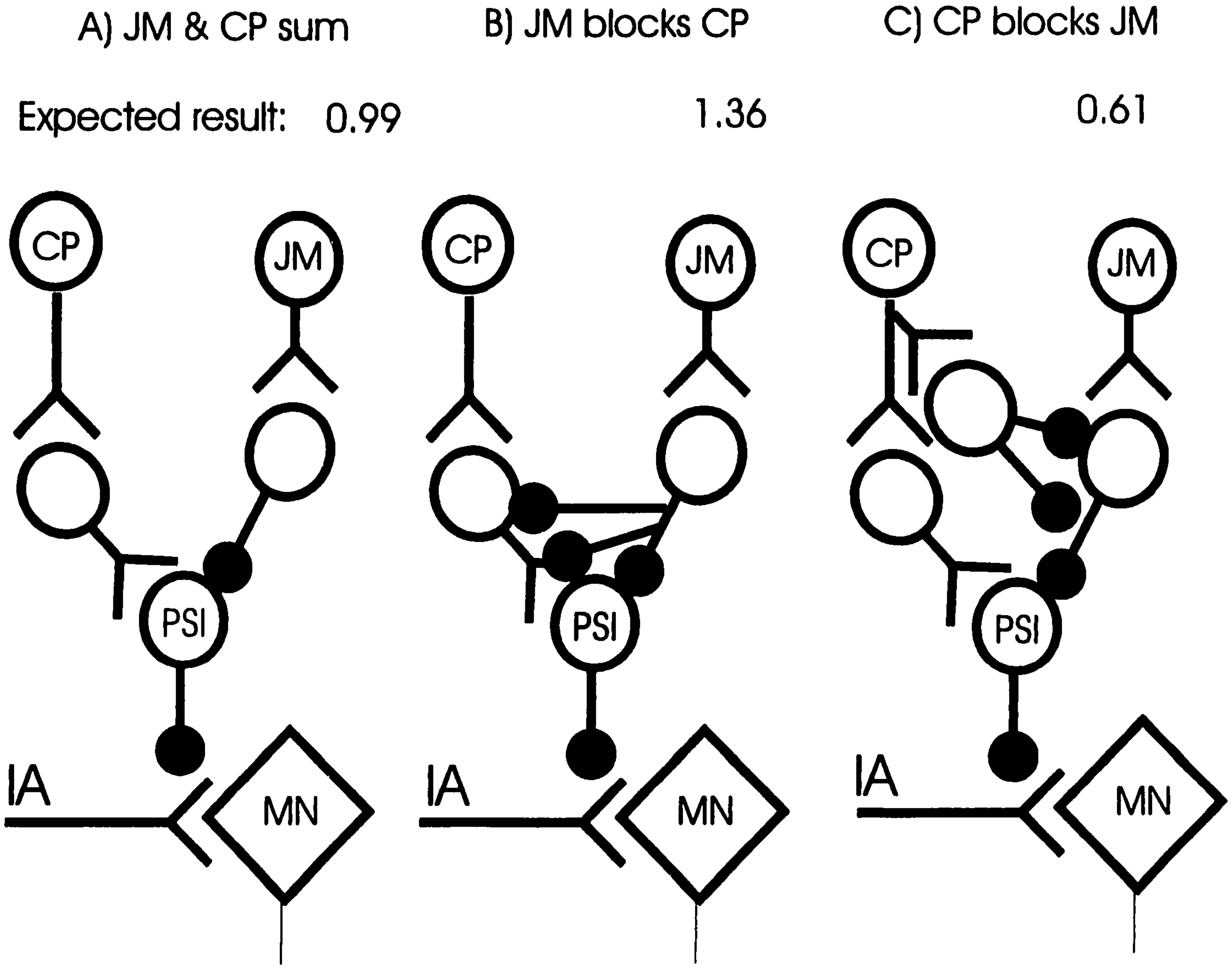
7.4.2 The effects produced by CP stimulation and the Jendrassik manoevre are presynaptic

The modulation of the soleus H-reflex at a latency of 100 ms occurred without a concomitant change in the rectified EMG during a steady contraction. As mentioned in the Introduction this is good evidence for the effects to be presynaptic (Stein, 1995). The results also agree with previous reports (Iles, 1996; Capaday et al., 1995). Iles (1996) used a conditioning stimulation that was at or below MT whereas Capaday et al. (1995) used predominantly 1.5x MT. We used a stimulus of 1.5 MT because it produced a clearer inhibition, presumably because more afferents were activated. A stimulus above motor threshold could have other effects, since it will produce a contraction of the dorsiflexor muscles that are innervated by the CP nerve. The contraction of the dorsiflexors could stretch the soleus muscle and produce excitation from stretch receptors in the muscle, as first suggested by Mizuno et al. (1971). More recently, Hultborn et al. (1996) showed that a profound depression of the monosynaptic Ia pathway can occur following a passive stretch of the homonymous muscle. They termed this phenomenon post-activation depression and argued that it was separate from the classical presynaptic inhibition. To minimize these effects we restricted movement about the ankle joint as much as possible. Furthermore, if the soleus stretch receptors were activated by stretch, we would have expected an initially increased EMG, due to their strong monosynaptic connections. No such excitation was seen in either Capaday et al. (1995) or our study, so we are confident that the CP modulation is presynaptic to the soleus motoneurons.

As discussed in the Introduction various possible mechanisms have been suggested for the action of the JM, but the pathway is still not known. Segmental reflexes are facilitated after transcranial magnetic stimulation (Péréon et al., 1995), so corticospinal inputs could be important. Vestibulospinal and bulbar reticulospinal input may also be involved, because of the strong effect that clenching the teeth has on the H-reflex (Miyahara et al., 1996). At one time fusimotor effects were considered likely, but have largely been ruled out by direct recordings from muscle afferents in human subjects (Hagbarth et al., 1975).

In the only other study to investigate JM reinforcement in active muscles, Dowman and Wolpaw (1988) found no significant change in the rectified surface EMG at either of two background soleus EMG levels, which agrees with the present results. Thus, the data are consistent with both JM facilitation and CP inhibition of the soleus H-reflex acting presynaptically.

Figure 7-4 Simple models for interaction between Jendrássik manouevre (JM) and CP nerve conditioning on the Soleus H-reflex. A) JM and CP sum linearly on presynaptic interneurones; B) JM blocks CP; C) CP blocks JM. CP afferents and JM input are shown along with excitatory and inhibitory interneurones, including the Ia presynaptic inhibitory interneurone (PSI). Expected results of combined stimulation based upon experimentally-derived individual values are given below the caption for each model.



7.4.3 Mechanisms for the interaction of JM facilitation and CP inhibition

Conceptually, the simplest scheme for the interaction of the two effects is on a common presynaptic interneurone (Fig. 7-4A). Both pathways are polysynaptic, but only a single, extra interneurone is shown for simplicity. The JM increased the H-reflex by 36% and the CP stimulation decreased it by 39%. If the two effects summed linearly, they would be expected to nearly cancel. Experimentally, the value of 0.97 was very close to the prediction. Fig. 7-4B shows another possibility in which the JM also blocked the pathway from the CP nerve presynaptically and/or postsynaptically. Then, CP stimulation would have little or no effect and the expected value would be close to the 36% increase seen with JM stimulation alone. Our experiments rule out this possibility. Yet another possibility (Fig. 7-4C) is that the CP stimulation blocks the JM, so a value close to the 39% reduction with CP stimulation would be predicted. With the sample size and the variability between subjects, this possibility can not be ruled out statistically. However, it is less likely since descending pathways such as the cortico-motoneuronal connection are not susceptible to inputs that produce PSI in humans (Nielsen and Petersen, 1994; Iles and Pisini, 1992). A partial, rather than a complete blockage, could be considered as well as a number of more complex interactions, but the data do not permit us to decide. For simplicity as a working hypothesis, we favor the schema shown in Fig. 7-4A. Granit et al (1966) showed that excitatory and inhibitory synaptic inputs could sum linearly to change the firing rate of motoneurones post-synaptically. The schema of Fig. 7-4A would echo Granit's idea on presynaptic interactions in the human.

7.4.4 Functional and clinical relevance

Hultborn et al. (1987) suggested that Ia PSI is reduced at the onset of a focused muscle contraction. This would permit more afferent input for reflex and voluntary control of the movement. Furthermore, reflexes are modulated during different phases of a movement and between different tasks (Stein and Capaday, 1988), presumably to optimize control. Having some degree of convergence of inputs from descending (JM) and segmental (CP) inputs would allow the degree of PSI to be finely tuned. Humans often perform tasks involving coordinated and synchronous use of both upper and lower limbs (e.g., weight lifting, rowing). Linkage between descending and segmental mechanisms could allow feedback from the limbs to modulate the descending commands and precisely regulate the motor task (see Rudomin 1990 for a discussion of PSI interactions in the cat).

Since JM and CP modulation act with some degree of convergence, this experimental paradigm may also have some clinical utility as a probe of the integrity of the nervous system. A reduction in presynaptic inhibition of the soleus H-reflex occurs after spinal cord injury and is implicated in reflex dysfunction (briefly reviewed in Stein, 1995). The reduction may be due to loss of tonic descending inputs to segmental inhibitory interneurones. As CP stimulation activates these interneurones and JM converges onto this pathway, their combination could be useful as a probe for the state and integrity of spinal pathways and control mechanisms after injury or a stroke.

7.5 References

Bussel B, Morin C, Pierrot-Deseilligny E (1978) Mechanism of monosynaptic reflex reinforcement during Jendrássik manoeuvre in man. J Neurol Neurosurg Psychiat 41: 40-44.

Capaday C, Cody FWJ, Stein RB (1990) Reciprocal inhibition of soleus motor output in humans during walking and voluntary tonic activity. JNeurophysiol 64: 607-616.

Capaday C, Lavoie BA, Comeau F (1995) Differential effects of a flexor nerve input on the human soleus H-reflex during standing versus walking. Can J Physiol Pharmacol 73: 436-449.

Delwaide PJ, Toulouse P (1980) Jendrássik maneuver vs controlled contractions conditioning the excitability of Soleus monosynaptic reflexes. Arch Phys Med Rehabil 61: 505-510.

Dowman R, Wolpaw JR (1988) Jendrássik maneuver facilitates soleus H-reflex without change in average soleus motoneurone pool membrane potential. Exp Neurol 101: 288-302.

El-Tohamy A, Sedgwick EM (1983) Spinal inhibition in man: depression of the soleus H reflex by stimulation of the nerve to the antagonist muscle. J Physiol 337: 497-508.

Granit,R, Kernell,D, Lamarre,Y. (1966) Algebraical summation in synaptic activation of motoneurones during within the 'primary range' to injected currents. J Physiol 187: 379-399.

Hagbarth K-E, Wallin G, Burke D, Löfstedt L (1975) Effects of the Jendrássik manoeuvre on muscle spindle activity in man. J Neurol Neurosurg Psychiat 38: 1143-1153.

Hayes KC, Allatt RD, Wolfe DL, Kasai T, Hsieh J (1992) Reinforcement of subliminal flexion reflexes by transcranial magnetic stimulation of motor cortex in subjects with spinal cord injury. EEG Clin Neurophysiol 85:102-109.

Hultborn H, Meunier S, Morin C, Pierrot-Deseilligny E (1987) Changes in presynaptic inhibition of Ia fibres at the onset of a voluntary contraction in man. J Physiol 389: 757-772.

Hultborn, H., Illert, M., Nielsen, J., Paul, A., Ballegaard, M., Wiese H. (1996). On the mechanism of the post-activation depression of the H-reflex in human subjects. Exp. Br. Res. 108:450-62.

Iles JF (1996) Evidence for cutaneous and corticospinal modulation of presynaptic inhibition of Ia afferents from the human lower limb. J Physiol 491: 197-207.

Iles JF, Pisini JV (1992) Cortical modulation of transmission in spinal reflex pathways in man. J Physiol 455: 425-466.

Jendrássik E (1883) Beiträge zur Lehre von den Sehnenreflexen. Deutsche Archiv f ür Klinische Medizin 33: 177-199.

Kawamura T, Watanabe S (1975) Timing as a prominent factor of the Jendrássik manouevre on the H reflex. J Neurol Neurosurg Psychiat 38: 508-516.

Landau WM, Clare MH (1964) Fusimotor function Part IV. Reinforcement of the H reflex in normal subjects. Arch Neurol 10: 117-122.

Miyahara T, Hagiya N, Ohyama T, Nakamura Y (1996) Modulation of human soleus H reflex in association with voluntary clenching of the teeth. J Neurophysiol 76: 2033-2041.

Mizuno Y, Tanaka R, Yanagisawa N (1971) Reciprocal group I inhibition on triceps surae motoneurons in man. J Neurophysiol 34: 1010-1017.

Nielsen J, Petersen N (1994) Is presynaptic inhibition distributed to corticospinal fibres in man? J Physiol 477:47-58.

Péréon Y, Genet R, Guihéneuc P (1995) Facilitation of motor evoked potentials: timing of Jendrássik maneuver effects. Muscle Nerve 18: 1427-1432.

Rudomin, P (1990). Presynaptic control of synaptic effectiveness of muscle spindle and tendon organ afferents in the mammalian spinal cord. In: The Segmental Motor System, Binder, M.D., and Mendell, L.M. (Eds.), Oxford University Press, New York, New York, pp. 349-380.

Sommer J (1940) Periphere Bahnung von Muskeleigenreflexen als Wesen des Jendrássikschen Phänomens. Deutsche Zeitschrift fun Nervenheilkunde 150: 249-262.

Stein RB (1995) Presynaptic inhibition in humans. Prog Neurobiol 47: 533-544.

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

Zehr EP, Stein RB (1996) The Jendrássik manoeuvre does not affect presynaptic inhibition of the H-reflex. Soc Neurosci Abs 22:1, 422.

8. General discussion

The main objective of this thesis was to evaluate the function of lower limb segmental reflexes in humans. Within this the primary focus was on the function of cutaneous reflexes during human gait. This section summarizes the main findings of this thesis and integrates them into a framework encompassing reflex function during gait and voluntary movement.

8.1 Reflex function during human gait

As mentioned, the function of reflexes during human gait has been uncertain. This has especially been the case with cutaneous reflexes. Within this thesis experiments were conducted in which different cutaneous nerves in the human lower leg were electrically stimulated at non-noxious intensities during treadmill walking. Reflex EMG responses from the upper and lower leg muscles were measured and changes in joint kinematics were also recorded along with the neural responses. To provide a quantified EMG index with which to compare to the kinematic data, an EMG technique which represents the net reflex effect of stimulation was employed. Thus, in evaluating reflex function, it was possible to directly compare the net neural command (i.e. the net reflex response) to the net mechanical outcome (i.e. kinematics). Further, in order to contribute functionally, reflexes should have not only association with mechanical change but also the association should be one in which the response modifies the gait pattern in a behaviourally relevant way.

As mentioned in the Chapter 1, it was not until the work of Yang and Stein (1990) and Duysens et al. (1990) that a systematic analysis of non-noxious cutaneous reflexes was conducted during human walking. Previously, most experiments involving cutaneous stimulation during human walking involved painful stimulation (Belanger & Patla 1987, Crenna & Frigo 1984). Yang and Stein (1990), based on their analysis of tibial nerve (and some sural nerve) reflexes and reflex reversals, tentatively concluded that cutaneous reflexes likely are important in 1) withdrawal responses to stimuli, and then 2) responses which would preserve balance during the step cycle. Later, Duysens et al. (1992) published another paper on the reversal of movements induced by sural nerve stimulation during the human step cycle. However, contrary to the conclusions on the potential functional role of cutaneous reflexes during human gait (e.g. Forssberg's (1979) stumbling corrective response), Duysens et al. (1992) concluded that cutaneous reflexes do "not correspond directly to corrections for stumbling following mechanical perturbations during the step cycle" but are related more to the opening and closing of reflex pathways by a central pattern generator for locomotion. In this thesis it has been documented that all 3 cutaneous nerves studied have functional effects throughout the step cycle. Interestingly, van Wezel et al. (1997) have recently published a paper which addressed reflex responses from these same 3 nerves. Although their mechanical data were lacking, their EMG responses and interpretation were similar to the data and conclusions provided in this thesis.

The functions of reflexes during human walking are described in the following 4 sub-sections which break the step cycle into swing, swing to stance, stance, and stance to swing portions. The results from this thesis have been integrated with those from other papers to provide a general overview of reflex function during these different parts of the human step cycle gait.

8.1.1 Swing phase

All 3 nerves studied showed functional effects during swing or the swing to stance transition (see below). As described in Chapter 4, SP nerve reflexes were reminiscent of Forssberg's (1979) stumbling corrective response in which the swing limb passes by the imposed obstacle to maintain a relatively unperturbed step cycle. Further, as was shown in Chapter 6, responses to sural nerve stimulation during swing resulted in a withdrawal of the foot from the stimulus point. While the specifics of the correction are different in the two cases (an example of local sign: i.e. DF after sural and PF after SP nerve stimulation), the net result is to avoid a destabilizing stumble. Thus during swing cutaneous reflexes act to preserve balance in the step cycle in a stumble corrective response (see Figure 8-1, top). As described in Chapter 5, this stumble corrective response is markedly reduced after stroke such that only portions of the neural response are observed and the mechanical effect is negligible. There are no comparable studies of the function of muscle reflexes during swing (i.e. mechanical data are lacking) and these are thus absent from the figure.

8.1.2 Swing to stance transition

The careful placing of the foot when moving from swing to stance during walking is a very dynamic and important part of the step cycle; incorrect foot placement could lead to tripping or falling. It is not surprising that Yang & Stein (1990) observed reflex reversals from a response earlier in the step cycle to this crucial portion after tibial nerve stimulation. Reflexes from tibial nerve stimulation (see Chapter 4) here were shown to be quite important in a reaction which involved the appropriate placing of the swing limb when a sensation of ground contact was evoked. Accordingly and as shown in Figure 8-1 (right), cutaneous reflexes are important in placing reactions during the swing to stance portion of the step cycle.

8.1.3 Stance phase

In Chapter 6, it was shown that reflexes in TA and MG muscles from activation of the sural nerve caused a mechanical eversion and dorsiflexion of the ipsilateral foot. This response would act to stabilize the foot if there were pressure activation on the lateral foot border caused by uneven terrain in early stance. This could also potentially assist in preventing an ankle sprain which might result if excessive inversion occurred. It must be mentioned, though, that these responses to severe inversion would occur in concert with reflexes arising from muscle afferents in the peroneal muscles (e.g. the "dynamic defence reaction" Konradsen et al 1997). In conclusion, cutaneous reflexes act to stabilize gait during the stance phase and this is shown schematically at the bottom of Figure 8-1. Additionally, in this figure muscle reflexes are indicated as functioning in body weight support and propulsion, a conclusion reached from papers discussed in the introduction (e.g. Sinkjaer et al. 1996; Stephens & Yang 1996a, Yang et al. 1991).

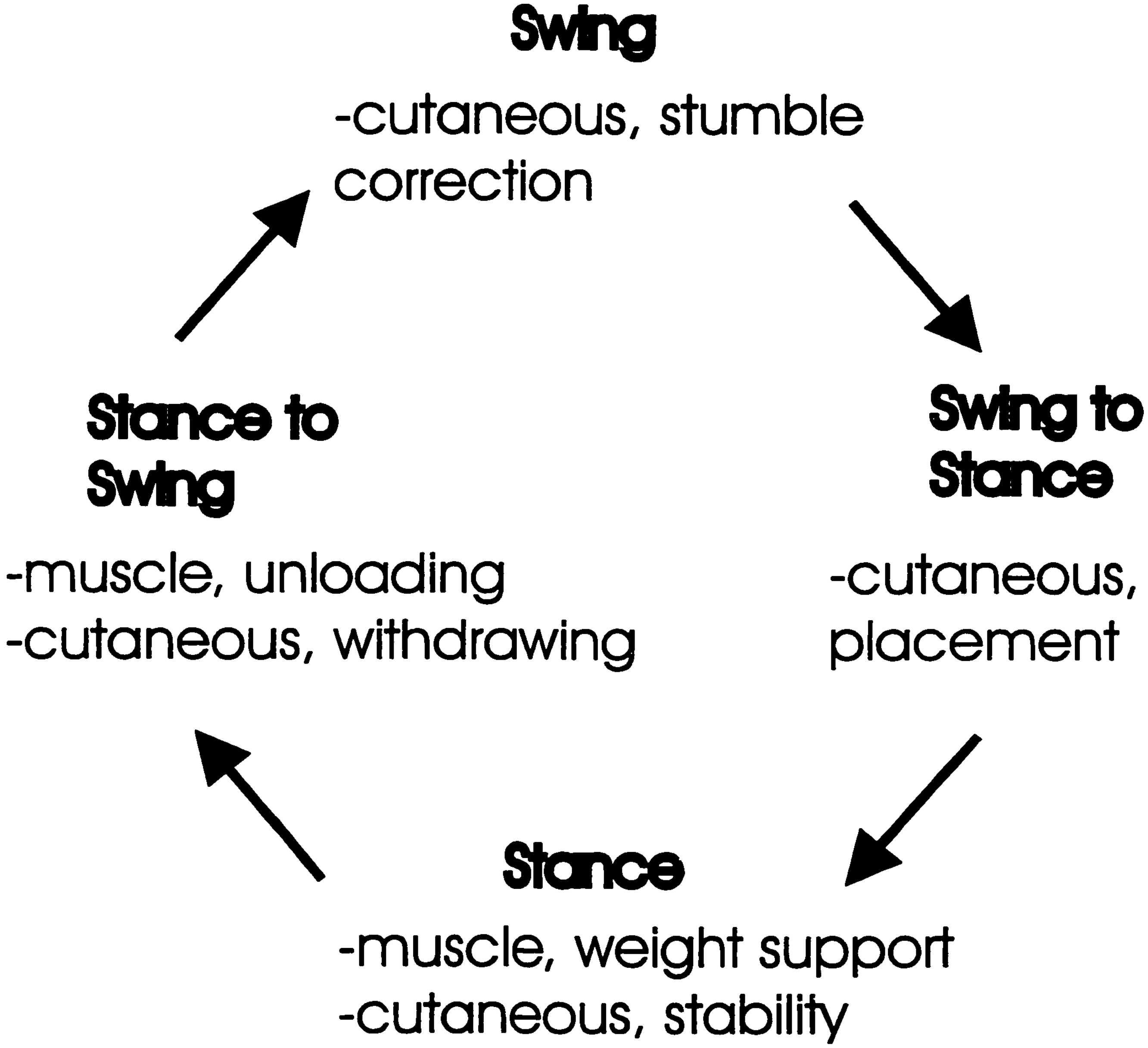
8.1.4 Stance to swing transition

In this part of the step cycle, there is a shift of weight support from the ipsilateral and formerly stance limb to the contralateral limb and therefore loading and sensation of loading on the ipsilateral limb is expected to be reduced. However, if, as indicated in

Chapters 4 and 6, the tibial or sural nerves (both of which have innervation areas which cover some aspect of the foot sole) are stimulated (thus indicating unexpected ground contact) the limb is withdrawn from the ground, primarily through actions primarily at the ankle, but also at the knee and hip. Thus cutaneous reflexes function in withdrawal reactions in this part of the step cycle, such that balance and cadence are maintained (see Fig. 8-1, left). As with the muscle reflexes for stance, the available data indicate that muscle reflexes signal unloading and help trigger the swing phase. While this data is rather tenuous in humans (Stephens & Yang 1996b), data from the cat indicate that this is quite powerful (see Hiebert et al. 1996, Whelan et al. 1995).

In summary, cutaneous reflexes function to preserve balance and ensure a stable walking pattern throughout the step cycle. They act in concert with muscle afferent reflexes and have their most robust effects during swing and the transitional portions of the step cycle where feedback from muscle afferents is not expected to be as large as during stance. As was described in Chapter 5, cutaneous reflexes are still seen prominently in the neural control signal (where they are generally suppressive) while the mechanical effect is blunted (e.g. no stumble correction during swing) or actually destabilizing (e.g. large suppressive responses in extensor muscles during stance). Hence, after injury to the central nervous system, reflexes may no longer function to preserve balance during the step cycle. However the pathological reflexes may have some value in mitigating other deficiencies (e.g. spasticity).

Figure 8-1 Schematic illustration of putative reflex function during various portions of the step cycle. Cutaneous reflexes were as deduced by the present experiments and muscle reflexes from the literature.



8.2 Lower limb reflex function

In Chapter 7, it was shown that JM facilitation of the H-reflex was markedly affected by IA PSI arising from activation of group I afferents in the CP nerve. The JM facilitation is central in origin as well as a sort of voluntary movement (in that the remote muscle contraction is a voluntary contraction). This is an example of a segmental reflex input (CP stimulation) modulating the specifics of a voluntary movement. The example given in Chapter 7 was one in which lifting a heavy object while standing (in which balance would be important and feedback from TA group I afferents would be large). Thus feedback from the periphery modulates the movement outcome in a way that appropriately sculpts the movement. This can be seen as quite similar to the modulation of the locomotor rhythm observed after cutaneous nerve stimulation. Cutaneous input modulated the central command (or central pattern) such that the behaviour was appropriate for the environment (e.g. the presence of obstacles contacting the swing limb). When the results of this thesis are taken together with the other available studies (see Chapter 1), it can be seen that the appropriate movement evolves as an interaction between a central command(s) and peripheral feedback.

In conclusion, the data presented in this thesis support the view that segmental reflexes act to support and modify human motor commands. In this way the afferent input generated by contact with the environment or due to the movement itself can appropriately modify the net motor output such that the desired behavioural outcome is achieved.

8.3 Future directions

The understanding of reflex function has been progressing, particularly with regard to the mechanical function of reflexes during human walking. However, while the understanding of the neuro-mechanical effects of cutaneous reflexes during gait has progressed, more complex mechanical effects need to be investigated. For example, do cutaneous reflexes affect rotation of the femur, as has been suggested on the basis of neural data alone (Tax et al. 1995)? How do cutaneous and muscular afferent reflexes interact to affect gait mechanics? While it is clear that peripheral inputs generate bilateral responses, do reflexes have powerful contralateral functions? To what extent is neuro-mechanical reflex linkage altered after trauma or during disease? How can this effectively be applied to gait rehabilitation and retraining? Answering these questions remains a challenge for future studies.

8.4 References

Bélanger, M. and Patla, A.E. (1987). Phase-dependent compensatory responses to perturbations applied during walking in humans. *J. Motor Behav.* 19:434-453.

Brooke, J.D., Cheng, J., Collins, D.F., McIlroy, W.E., Misiaszek, J.E., and Staines, W.R. (1997). Sensori-sensory afferent conditioning with leg movement: gain control in spinal reflex and ascending paths. *Prog. Neurobiol.* 51:393-421.

Crenna, P. and Frigo, C. (1984). Evidence of phase-dependent nociceptive reflexes during locomotion in man. *Exp. Neurol.* 85:336-345.

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

Duysens, J., Tax, A.A.M., Trippel, M. and Dietz, V. (1992). Phase-dependent reversal of reflexly induced movements during human gait. *Exp. Brain Res.* 90:404-414.

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

Hiebert, G.W., Whelan, P.J., Prochazka, A., and Pearson, K.G. (1996). Contribution of hindlimb flexor afferents to the timing of phase transitions in the cat step cycle. *J. Neurophysiol.* 75:1126-1137.

Konradsen, L., Voigt, M., and Hojsgaard, C. (1997). Ankle inversion injuries: the role of the dynamic defense mechanism. *Amer. J. Sports Med.* 25(1):54-58.

Sinkjaer, T., Jacob, B.A., and Birgit, L. (1996). Soleus stretch reflex modulation during gait in man. *J. Neurophysiol.*76:1112-1120.

Stephens, M.J., and Yang, J.F. (1996a). Short latency, non-reciprocal group I inhibition is reduced during the stance phase of walking in humans. *Brain Res.* 743:24-31.

Stephens, M.J., and Yang, J.F. (1996b). The effects of load on the human step cycle. *Soc. Neurosci. Abs.* 22:1849.

Tax, A.A.M., Van Wezel, B.M.H., and Dietz, V. (1995). Bipedal reflex coordination to tactile stimulation of the sural nerve during human running. *J. Neurophysiol.* 73:1947-1964.

Van Wezel, B.M.H., Ottenhoff, F.A.M. & Duysens, J. (1997). Dynamic control of location-specific information in tactile cutaneous reflexes from the foot during human walking. *J. Neurosci.* 17:3804-3814.

Whelan, P.J., Hiebert, G.H., and Pearson, K.G.(1995). Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res.* 103:20-30.

Yang, J.F. and Stein, R.B. (1990). Phase-dependent reflex reversal in human leg muscles during walking. *J. Neurophysiol.* 63(5):1109-1117.

Yang., J.F., Stein, R.B., and James, K.B.(1991a). Contribution of peripheral afferents to the activation of the soleus muscle during walking in humans. *Exp. Brain Res.* 87:679-687.

IMAGE EVALUATION
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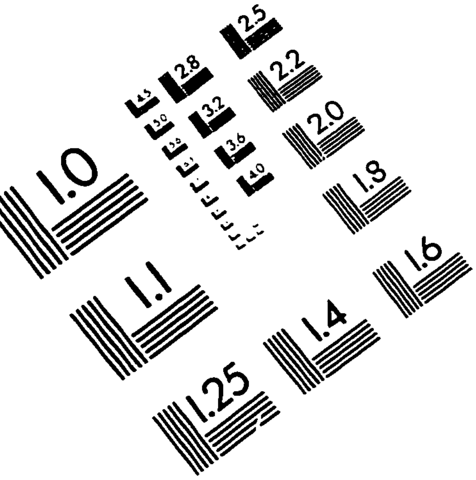

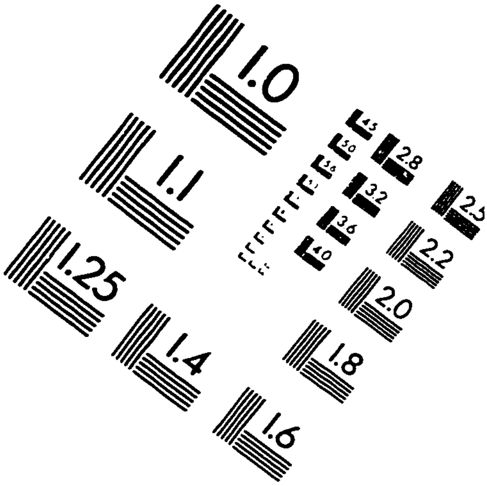

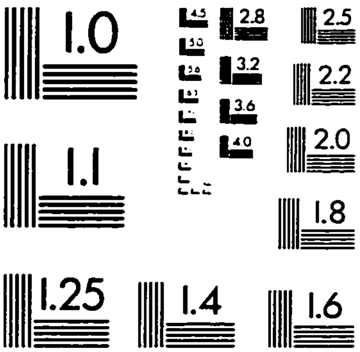

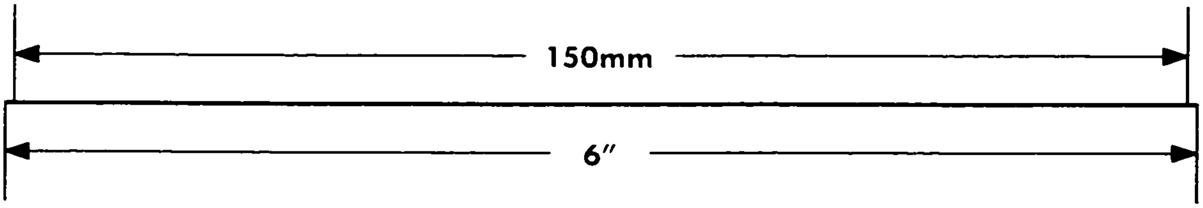

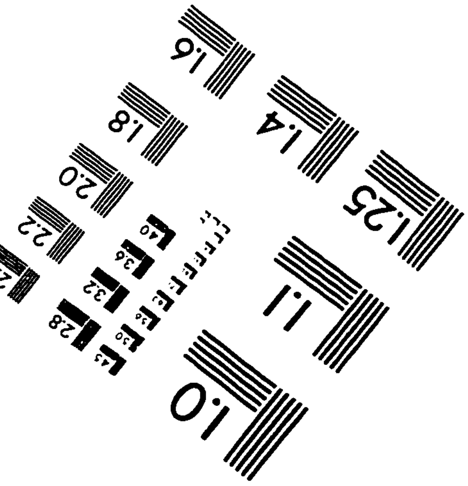

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