Effect of Rhythmic Arm Movement on Soleus H-reflex Amplitudes in the Less and More Affected Legs After Stroke

By
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BSc. Physiotherapy, Shahid Beheshti University, Tehran, Iran, 1998

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Supervisory Committee

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Abstract

Rhythmic arm cycling suppresses the soleus H-reflex amplitude in stationary legs in neurologically intact (NI) participants. It has been suggested that interlimb pathways connecting cervical and lumbosacral spinal cord are responsible for modulating the reflex excitability. After stroke, stretch reflex and its electrical analogue the H-reflex become hyperactive. The purpose of this study was to examine the effect of arm cycling on the H-reflex amplitude in the stationary legs after stroke. It was hypothesized that rhythmic arm movement would suppress the H-reflex amplitudes in the legs after stroke. Sixteen stroke participants performed bilateral arm cycling at 1Hz and at the highest frequency possible they could maintain. Additionally, thirteen age-matched neurologically intact individuals participated as a control group. Tibial nerves were stimulated to evoke H-reflexes simultaneously in both legs. M-wave, H-reflex (M-H) recruitment curves (RC) were collected during arm cycling and with arms stationary. Four variables (i.e., M-H slope, H at threshold, H_{max} and 50% H_{max}) obtained from the ascending limb of the M-H RC were compared across conditions. Results showed that the general effects of arm cycling in suppressing H-reflex size are preserved after stroke. However, effects after stroke were limited in that arm cycling did not affect the whole recruitment curve similarly, as it does in the NI population. Overall the results suggest that incorporation of rhythmic arm movement in rehabilitation paradigms after stroke might be helpful in suppression of hyperactive reflexes in the legs and therefore assist in locomotion.

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Dedications

I would like to dedicate this thesis to my mom and dad who taught me how to follow my dreams.

Chapter 1: Introduction and Literature Review

Interlimb coordination between fore- and hindlimbs is a main feature of quadrupedal locomotion. In humans, production of coordinated locomotor tasks such as walking, running, and swimming needs some form of neural linkages between the cervical and lumbosacral networks (Wannier, Bastiaanse, Columbo, & Dietz, 2001; Zehr, 2005). The specific interaction between the arms and legs can be examined using indirect approaches such as the modulation of reflexes. Specifically, cutaneous and H-reflexes are task and phase modulated, which make them attractive tools to probe the function of the nervous system (Burke, 1999).

Most of the knowledge about control mechanism of human locomotion comes from studies in other animals especially the cat. Thus, in the first part of the literature review some findings about neural mechanisms of locomotor control in quadrupeds and humans will be discussed. In the next part, the role of interlimb reflexes in the coordinated movement will be described. Knowledge of the neural control of human locomotion helps our understanding of the function of the nervous system in health and provides information on mechanisms of motor impairments after injury to the nervous system, e.g., stroke. The last part of the review deals with the control of reflex function after neurotraumatic injury (e.g., after stroke).

Interlimb Coordination in Quadrupeds and Humans

Reduced animal studies

Studies by Brown in the early twentieth century suggested that there are clusters of neurons within the spinal cord that could generate the rhythm and pattern of locomotor movement. This was called the 'half-center' model as illustrated in Figure 1. In his experiments with cats, Brown (Brown, 1911; Brown, 1914) showed that after deafferentation and cutting the spinal cord, reciprocal activity could be seen in flexor and extensor muscles.

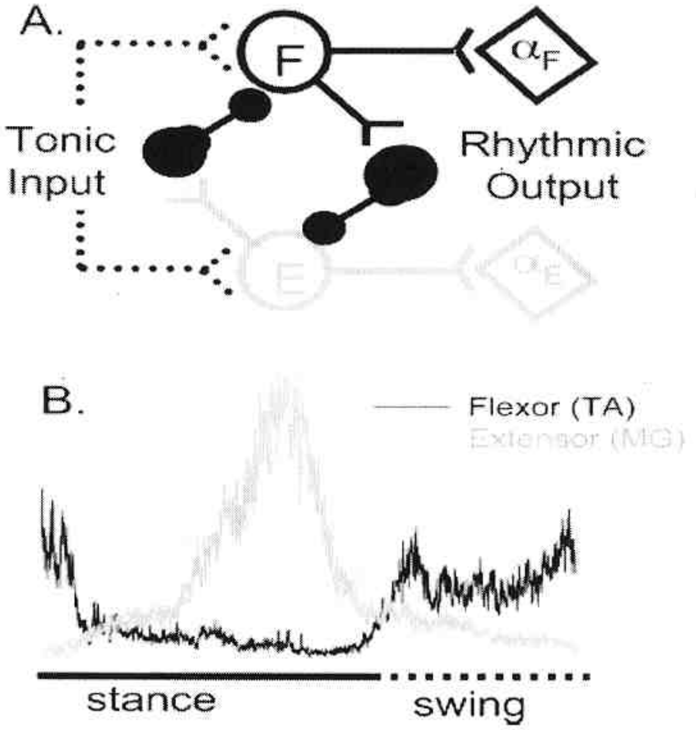

Figure1. A. Simplistic view of Brown's 'half-center' model. Inhibitory interneurons are filled in, whereas excitatory interneurons are left open. F= flexor half center; E= extensor half center. α_F = alphamotoneuron pool for flexors; $\alpha_{E=}$ alphamotoneuron pool for extensors. B. EMG activity of ankle flexor and extensor during human treadmill walking. TA= tibilalis anterior; MG= medial gastrocnemius. Solid line indicates stance and dashed line indicates swing phases of a step. Taken from (Zehr, 2005).

An extension of the half center model suggested that specialized neuronal organizations within the spinal cord (i.e., central pattern generators (CPGs)) can generate rhythm and shape the pattern of muscle activity during locomotion (Grillner & Wallen, 1985; Grillner, 1975; Grillner, 1981). It is also assumed that for both cats and humans, there is at least one CPG for each limb (Duysens & Van de Crommert, 1998).

The regulation of quadrupedal locomotion requires a close coordination between all four limbs. Coordination of the fore- and hindlimbs is well documented in quadrupedal locomotion (for review see (Kato, 1994)). A vast network of propriospinal neurons couple the CPGs of the cervical and lumbosacral regions in quadrupeds (Miller, Vanderburg, & Vandermeche, 1975; Viala & Vidal, 1978). Both ascending (Gernandt & Megirian, 1961) and descending (Skinner, Adams, & Remmel, 1980) pathways appear to assist in this coordination between cervical and lumbar enlargements of the spinal cord of quadrupeds. Usually, the short propriospinal neurons connect segments in proximity, however connections to distant segments do exist via long propriospinal neurons (Yezierski, Culberson, & Brown, 1980). Krutki, Grottel, and Mrowczynski (1998) found propriospinal neurons from C6 projecting to sacral segments with collaterals branching to lumbar segments (Krutki, Grottel, & Mrowczynski, 1998). In another study, the ascending projections from S2 segment to C6, the cerebellum, and the reticular formation were reported (Grottel, Krutki, & Mrowczynski, 1998). Dual and triple projections from most cells in these studies suggest the possibility that ascending and descending information can affect several motor centers controlling fore- or hindlimbs of the animal. Observation of quadrupedal locomotor control in neonatal rats suggested the dominant locomotor drive from the lumbar over cervical CPGs and was described as an "ascending caudorostral excitability gradient" (Juvin, Simmers, & Morin, 2005). This was previously suggested by Ballion and colleagues (Ballion, Morin, & Viala, 2001). Recently

Zaporozhets et al. (2006) suggested the cervical motor output is not a critical component, but may contribute to bipedal locomotion (Zaporozhets, Cowley, & Schmidt, 2006).

In summary, neural circuits (e.g. CPGs) lie within the spinal cord and are able to produce rhythm and pattern of locomotion independently of supraspinal and afferent input in quadrupeds. However, to produce a functional motor pattern, these centers require afferent feedback (Duysens, 1998; Duysens et al., 1998) and suprasinal input (Armstrong, 1988; Yakovenko, McCrea, Stecina, & Prochazka, 2005).

Human studies

In many respects, bipedal locomotion likely shares common spinal mechanisms with quadrupedal locomotion. Recent studies have challenged the traditional view of the spinal cord as the inflexible conduit for transformation of the commands from supraspinal structures (Wolpaw & Tennisen, 2001). Studies in patients with spinal cord injury showed that the spinal cord has the potential to generate rhythmic activity in a flexible manner (MacKay-Lyons, 2002; Harkema et al., 1997; Beres-Jones & Harkema, 2004; Dimitrijevic, Gerasimenko, & Pinter, 1998; Calancie et al., 1994). Partial body weight support treadmill walking ascribed CPG like mechanisms in lumbosacral spinal cord of human as a source of locomotor pattern for walking (Barbeau & Rossignol, 1994; Wernig, Muller, Nanassy, & Cagol, 1995). Limb coordination during human infant walking is more evidence of spinal control of locomotion (Yang et al., 2004; Thelen, Ulrich, & Niles, 1987), because the unmyelinated corticospinal tract restricts locomotor control to the spinal level.

A few studies have suggested propriospinal pathways coupling cervical and lumbosacral enlargements of the spinal cord in primates and humans (Skinner, Coulter, Adams, & Remmel, 1979; Nathan, Smith, & Deacon, 1996). In line with studies on other species, most of the propriospinal fibers connecting thoracic, lumbar, and sacral segments of the spinal cord in humans are short. However, there is suggestion of longer propriospinal projections that may link cervical and lumbosacral enlargements (Nathan et al., 1996).

The presence of these propriospinal connections coupling cervical and lumbosacral segments of the spinal cord is anatomical evidence that could underlie neural coupling between upper and lower limbs in human. It can be inferred that this coupling has a functional role in coordinating motor functions between the arms and legs, as suggested by a recent study (Balter & Zehr, 2007). Activity of the lower limbs when the arms are active suggests coupling of the limbs (Huang & Ferris, 2004). The facilitated neuromuscular recruitment of the lower limb muscles during a stepping task when the arms moved faster is further evidence for the coupling of the arms and legs (Kao & Ferris, 2005). It was then suggested by Ferris et al. (2006) to incorporate simultaneous arm and leg activity to take advantage of interlimb neural coupling for gait rehabilitation after neurotrauma (Ferris, Huang, & Kao, 2006). Visintin and Barabeu (1994) also showed that patients with incomplete spinal cord injury have greater gait symmetry and more normal EMG while walking on treadmill with body weigh support while arm swing was allowed than when arm swing was absent (Visintin & Barbeau, 1994). Wannier, Bastiaanse, Colombo, and Dietz (2001), have also shown that there is a frequency locked relationship of two pairs of limbs over a range of movement velocities (Wannier et al., 2001). Finally, recent work of Masanori et al. (2007) suggested a predominant lumbocervical influence of the legs on the arms during arm and leg cycling (Masanori et al., 2007), which is in line with animal studies (Zaporozhets et al., 2006).

In conclusion, coordination between arm and leg movement is quite robust across various types of locomotion, suggesting strong coupling between limbs in humans as occurs in quadrupeds.

Interlimb Pathways and Reflex Modulation

As discussed in the previous section, it is well documented that in nonprimate mammals the neural circuits within the spinal cord are able to produce a rhythmic pattern of locomotion independent of supraspinal and afferent input. There is also indirect evidence that interlimb coordination in quadrupeds is preserved in bipedal humans (Dietz, 2002). However, afferent and supraspinal inputs are needed to produce functional locomotion (Rossignol, 1996; Stein & Smith, 1997; Nielsen, 2003; Zehr & Duysens, 2004a; Rossignol, Dubuc, & Gossard, 2006).

It was first observed by Sherrington that the same sensory input did not necessarily generate the same output (Sherrington, 1900) as cited in (Brooke et al., 1997) and (Zehr et al., 2004a). He suggested that reflexes support and play roles in production and modulation of many kinds of movement (Sherrington, 1947). It was found later that these sensory inputs modify the behavior of various animals during many different behaviors, so the suggestion that reflexes are stereotyped is false. It can be inferred from the modulation of motor activity due to changes in peripheral feedback during movement that control of the reflex gain may rely on the output of the CPG network (Duysens et al., 1998; Van de Crommert, Mulder, & Duysens, 1998). Since both cutaneous and muscle reflexes work in collaboration with the central motor program (i.e. CPG), they can be used as a neural probe to the nervous system to access the central mechanisms of movement control (Burke, 1999).

It has been shown that cutaneous reflexes evoked in the lower limbs are task and phase modulated during human walking (Duysens, Tax, Trippel, & Dietz, 1993; Zehr & Stein, 1999; Tax, Van Wezel, & Dietz, 1995). It has also been shown recently that cutaneous reflexes are phase- and task-dependent during rhythmic movement of the arms (Zehr & Chua, 2000; Zehr & Kido, 2001; Zehr, Collins, Frigon, & Hoogenboom, 2003). These observations suggest that rhythmic arm movement is organized in a way similar to that of the legs.

Interlimb connections and their influences on reflex excitability in cats suggest spinal connecting pathways (Miller, Reitsma, & Meche, 1973; Miller & van der Meche, 1976). There is evidence in humans that movement of the arms affects cutaneous and H-reflexes in the legs and vice versa, as discussed below. Evidence for interlimb coupling during walking was observed by evoking cutaneous reflexes in both arm and leg muscles by stimulation at the hand and foot (Haridas & Zehr, 2003). A similar observation was also smade during combined arm and leg cycling (Sakamoto et al., 2006; Balter & Zehr, 2007).

Similar to the cutaneous reflexes, the stretch reflex and its electrical analogue the H-reflex have also been used as probes to discover the central mechanisms of movement control. The neural circuitry of the H-reflex is characterized by the monosynaptic projection of the group Ia afferents onto the homonymous motoneurons. However, these reflexes are not purely monosynaptic and have oligosynaptic contributions from Ia and group II afferents (Burke, Gandevia, & McKeon, 1984). Methodological considerations for elicitation of the H-reflex as well as limitations for interpreting data are of extreme importance and have been well discussed in several review papers (Tucker, Tuncer, & Turker, 2005; Zehr, 2002; Pierrot- Deseilligny & Burke, 2005; Misiaszek, 2003). Stretch and H-reflexes display task- and phase-dependent modulation patterns during locomotion (Capaday & Stein, 1986; Capaday & Stein, 1987; Duysens et al., 1995; Edamura, Yang, & Stein, 1991; Brooke et al., 1997; Schieppati, 1987; Zehr et al., 1999).

Interlimb connections have also been demonstrated during static tasks by stimulating nerves in the arms and record changes in the activity of leg muscles (Gassel & Ott, 1973; Kagamihara, Hayashi, Masakado, & Kouno, 2003; Zehr, Collins, & Chua, 2001). Calancie, Molano, and Broton (2002) reported changes in the EMG of the arm muscles by stimulating nerves in the legs of cervical spinal cord injured subjects (Calancie, Molano, & Broton, 2002).

Postural modification of the upper limbs also can be used to determine interlimb connections. Delwaide and colleagues (1977) showed the effect of arm position on the soleus H-reflex in the legs. They showed an increase in the amplitude of the soleus H-reflex in the right leg when the right shoulder was in flexion and inhibited when the left shoulder was held in the same flexed position (Delwaide, Figiel, & Richelle, 1977). There are only a few studies to date examining the effects of arm movement on H-reflexes in the legs. Passive movement of the elbow facilitated the H-reflex (Hiraoka & Nagata, 1999) and shoulder extension inhibited the soleus H-reflex (Hiraoka, 2001). Changes in excitability of H-reflexes in the upper limb with rhythmic oscillation of the foot have also been reported (Baldissera, Cavallari, & Leocani, 1998). They showed that the amplitude of the H-reflexes of flexor carpi radialis (FCR) increased with plantar flexion and was close to static values with dorsi flexion (Baldissera et al., 1998).

In an ongoing series of studies the effect of arm cycling on reflexes in the legs has been investigated (Frigon, Collins, & Zehr, 2004; Zehr, Hoogenboom, Frigon, & Collins, 2004b; Loadman & Zehr, 2006). Compared with values taken during no movement, arm cycling significantly suppressed the amplitude of soleus H-reflex in the legs as illustrated in Figure 2. This suppression was greater at shoulder flexion than at the extended position of the shoulder. These researchers also investigated the effect of somatosensory conditioning of the reflex pathway by stimulating sural and common peroneal (CP) nerves (Frigon et al., 2004). Sural nerve stimulation facilitated the H-reflex and CP nerve stimulation reduced the H-reflex amplitude. In another study by this group, stimulation of the superficial radial nerve had a facilitatory effect on the soleus H-reflex pathway in static position and cancelled the suppression induced by arm cycling in the pathway (Zehr et al., 2004b). These studies show that the H-reflex is not only conditioned by the arm movement but also the conditioned pathway is still sensitive to somatosensory conditioning from remote sources. They proposed presynaptic inhibition of Ia afferent as a possible mechanism for this modulation. They suggested that CPGs activated by arm cycling could change the presynaptic inhibition at the Ia afferent-alpha motoneuronal synapse and consequently suppress the H-reflex amplitude in the leg muscle (Frigon et al., 2004; Zehr et al., 2004b).

Recent data also show that leg cycling has a modulatory effect on the amplitude of FCR H-reflex on the forearm (Zehr, Klimstra, Johnson, & Carroll, 2007). All these studies investigated the movement-induced modulation of the remote sources on the H-reflex pathways and demonstrated the interaction between the arms and legs.

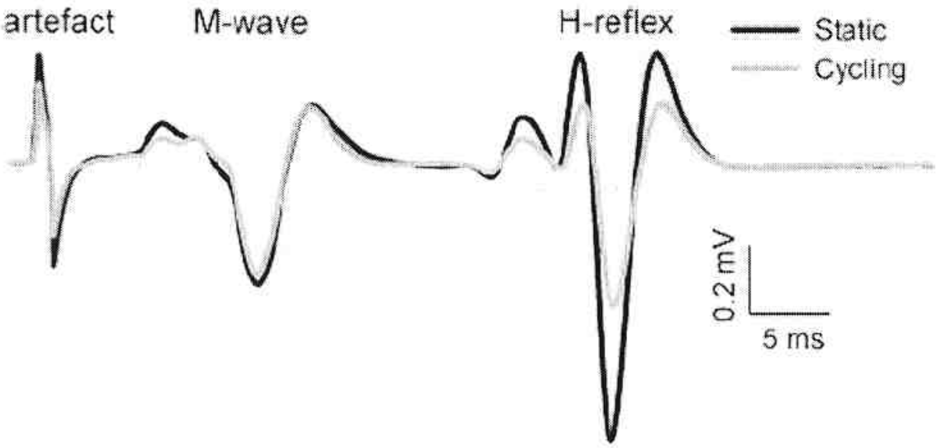

Figure 2. Soleus H-reflex amplitude suppressed with arm cycling (single subject). Average of 20 sweeps during static trials (black line) and during cycling trials (gray line) recorded. Stimulus artifacts, M-waves, and H-reflexes are indicated. Taken from (Frigon et al., 2004).

To further investigate what parameters of the arm cycling have the largest effects on soleus H-reflex amplitude, a recent study investigated the effects of: 1) rate of cycling; 2) range of motion of the arms (large or small arm crank length); 3) movement of ipsi (same side as the H-reflex), contra (opposite to the side of H-reflex recording) , and both arms; and, 4) phase of the arm in the movement cycle. Results from this study showed that the rate of cycling had the greatest suppressive effect on soleus H-reflex. The absence of phase-modulation in the H-reflex responses shows that a general signal of rhythmic arm movement mediates the suppression of the H-reflex in the soleus muscle (Loadman & Zehr, 2006). This study was done in an adult neurologically intact population with an age range of 22-42 years. As there is evidence for decrease in excitability of the spinal circuits due to aging (Kido, Tanaka, & Stein, 2004), it would be interesting to know if this modulation would be affected by the aging process.

In summary, these results suggest that postural modification, cutaneous nerve stimulation, and movement conditioning of the arms or legs can modulate H-reflexes elicited in the upper or lower limbs and support the hypothesis of interlimb connections as well as sensitivity of the reflex pathway to modulation.

Reflex Modulation after Neurotrauma

Many pathways control the excitability of the spinal reflexes and abnormality in any of those pathways could produce imbalances in spinal reflexes.

Hyperexcitability in H-reflex pathway

Similar to any other circuitry in the spinal cord, the H-reflex operates normally under the influence of supraspinal structures. It has been proposed that the imbalance between descending excitatory and inhibitory inputs from the descending tracts accounts for the hyperactivity in the reflex pathway (Pierrot-Deseilligny, 1990) that arises after neurotrauma.

Changes in transmission in the spinal pathway

After injury to the nervous system, specifically stroke, the H-reflex becomes hyperactive. Hyperexcitability of the monosynaptic reflex arc manifests itself as increase in H_{max}/M_{max} ratio. This measure is higher in the paretic side compared to the non-paretic side of the stroke patient (Faist, Mazevet, Dietz, & Pierrot-Deseilligny, 1994; Aymard et al., 2000). Also, the threshold of the H-reflex is decreased compared to that of the M-wave (Angel & Hofmann, 1963). Additionally, the H slope/M slope is higher in the paretic side than in normal subjects (Funase, Higashi, Yoshimura, Imanaka, & Nishihira, 1996; Higashi et al., 2001).

Among the spinal mechanisms influencing H-reflex pathway, only post activation depression (Aymard et al., 2000) was shown to contribute to H-reflex exaggeration after injury to the nervous system (i.e. stroke). Post activation depression is reduced after stroke, which would enhance synaptic efficacy of Ia-alpha motoneuron impulses and could contribute to reflex hyperexcitability (Aymard et al., 2000). Thus, other spinal mechanisms such as gamma hyperactivation (Hagbarth, Wallin, & Lofstedt, 1973); decreased recurrent inhibition (Katz, Meunier, & Pierrot-Deseilligny, 1988); and, decreased presynaptic inhibition (Faist et al., 1994; Aymard et al., 2000) seem not to have a role in reflex exaggeration after stroke.

Furthermore, assessing reflexes after neurotrauma showed that during movement, reflexes showed less modulation or even different patterns of modulation (Yang et al., 1991; Faist, Ertel, Berger, & Dietz, 1999). Unlike the neurologically impaired subjects, the neurologically intact subjects showed a modulated reflex pattern based on the phase of the movement (Yang & Whelan, 1993). One might attribute the results to an aging process as the study was conducted with adult stroke subjects. Interestingly, research with an age matched group revealed that the modulation of H-reflexes during walking is essentially the same at all ages. This suggests that the reflex pathways are relatively well preserved during the aging process (Chalmers & Knutzen, 2000; Kido et al., 2004).

Therefore, differential patterns of reflex modulation after injury to the nervous system might be due to changes in the sources that influence H-reflex pathway, (e.g. altered presynaptic inhibition).

The less modulated pattern of the reflexes has been shown in other spinal reflex pathways as well. As an example of a distorted reflex function, Zehr and colleagues (1998) studied cutaneous reflexes in response to stimulation to the superficial peroneal nerve in stroke subjects during treadmill walking (Zehr, Fujita, & Stein, 1998). Although cutaneous reflexes have a functional role in terms of kinematic changes (Prochazka, Sontag, & Wand, 1978; Forssberg, 1979; Zehr, Komiyama, & Stein, 1997), this corrective response was absent or very small in the stroke subjects compared to that observed in healthy individuals (Zehr et al., 1998). Because reflexes are less modulated as an effect of supraspinal lesion, one can infer that reflex pathways are not as sensitive to modulation as before the injury, and this could be one reason for the movement impairments.

It is important to note that although the behavior of the reflexes might seem normal on the non-paretic side after stroke, there is evidence of abnormal transmission in spinal pathways on the non-paretic side as well (Thilmann, Fellows, & Garms, 1990). The response of the soleus to stretch is increased on the paretic side, yet decreased on the non-paretic side (Thilmann, Burke, & Rymer, 1993) as cited in (Pierrot- Deseilligny et al., 2005). Additionally, reciprocal Ia inhibition from tibilais anterior to soleus is decreased in the non-paretic side (Crone, Johnsen, Biering-Sorensen, & Nielsen, 2003).

In summary, the H-reflex is a sensitive tool for movement studies examining phase and task modulation. It could also be used as a tool in researching for the interlimb connections or conditioning effects of nerve stimulation or movement. This study was designed as a follow up of the recent papers on the movement conditioning and interlimb connections to test the applicability of their results to the stroke population. The aim of this study was to investigate the availability of interlimb pathways after stroke. Mapping of these reflex changes may provide insight into the pathophysiological mechanism underlying disordered movement or spasticity.

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Chapter 2: Manuscript

Introduction

Interlimb coordination between fore- and hindlimbs is a main feature of quadrupedal locomotion (Kato, 1994). Neural pathways linking the fore- and hindlimbs have been well documented in quadrupeds (Miller, Van Der Burg, & Van Der Meche, 1975; Viala & Vidal, 1978). In humans, to produce coordinated locomotion, some form of linkages between arms and legs control networks similar to those observed in quadrupeds have been suggested (Dietz, 2002; Zehr & Duysens, 2004). The specific interlimb interaction could be examined using indirect methodology such as reflexes. Specifically, cutaneous and H-reflexes are task and phase modulated, which make them attractive tools to probe the function of the nervous system (Burke, 1999). Reflex modulation during locomotion provides insight into the connections between the neural centers regulating arm and leg movement (Balter & Zehr, 2007; Sakamoto et al., 2006; Haridas & Zehr, 2003). It is thought that the control of reflex gain during rhythmic movement may rely on output of central pattern generators (CPGs) that is activated during limb movement (Duysens & Van de Crommert, 1998).

Evidence for neural coupling between the arms and legs has also been explored using remote movement. Rhythmic arm cycling causes significant attenuation in excitability of the H-reflex pathway in the soleus muscle of the leg. The likely mechanism is modulation of Ia presynaptic inhibition by descending influences from arm CPG activity (Frigon, Collins, & Zehr, 2004). Indeed it was also suggested that this effect is indirect evidence of locomotor coupling between neural control of arm and leg movement (Frigon et al., 2004; Zehr, Hoogenboom, Frigon, & Collins, 2004b; Loadman & Zehr, 2006). It was later concluded that rhythmic arm movement causes suppression in the amplitude of soleus H-reflex that is generalized (Loadman & Zehr, 2006). The frequency of cycling seems to be the most important parameter contributing to the suppressive effect on soleus H-reflex amplitude (Loadman & Zehr, 2006). If conditioning of the H-reflex by arm cycling persists also after neurotrauma, it could be therapeutically incorporated in rehabilitation regimes to suppress hyperexcitable reflexes after stroke or spinal cord injury (Faist, Mazevet, Dietz, & Pierrot-Deseilligny, 1994; Aymard et al., 2000). Currently it is unknown if rhythmic arm movement can affect H-reflex excitability in leg muscles in the damaged nervous system arising after stroke. Therefore, the purpose of this study was to examine the effect of arm cycling on the H-reflex amplitude in the stationary legs after stroke. Because spinal pathway transmission undergoes some pathological changes even on the non-paretic side of the stroke (Thilmann, Fellows, & Garms, 1990), H-reflexes were recorded simultaneously from both legs of the stroke participants. Furthermore, as the excitability of the spinal pathways change as the result of aging (Kido, Tanaka, & Stein, 2004), there was an age-matched group of neurologically intact (NI) individuals who served as a control to the stroke participants. Since we previously suggested a spinal source for the suppressive effects of arm cycling (i.e. cervical CPG for arm cycling), we speculated that a portion of the arm cycling suppressing the soleus H-reflexes should be maintained after supraspinal lesion. We therefore hypothesized that the effect of arm cycling would be present also after stroke. However, since the intergrity of spinal reflex processing is significantly affected by descending supraspinal regulation of interneuronal excitability, we further predicted the arm cycling to have a much more limited effect in stroke as compared to the neurologically intact participants.

Methods

Participants

Sixteen adults with a history of a single stroke (see Table 1) and thirteen age-matched neurologically intact (NI) individuals (see Table 2) participated in this study. Inclusion criteria for stroke participants were that they 1) were a minimum of six months post stroke (chronic stroke); 2) were able to perform the arm cycling task (i.e. minimum required range of motion of 13° for the shoulder and 25° for the elbow (Hundza & Zehr, 2006)); and, 3) had sufficient cardiopulmonary status to perform the arm cycling task. For stroke and NI groups, any other health problem that limited participation in a moderate physical activity such as arm cycling was determined using a modified physical activity readiness questionnaire was used (see Appendix A). Written consent was obtained for the protocol that had been approved by the Human Research Ethics Board of the University of Victoria, and the study was conducted in accordance with the Declaration of Helsinki. Stroke participants were also asked to sign a form allowing access to their medical records, including imaging documents.

Clinical evaluation

The functional recovery stage of the stroke participants was assessed using the Brunnstrom 6 level assessment scale (Brunnstrom, 1970) (see Appendix B). Additionally, the Modified Ashworth Scale was used as a clinical measure of limb spasticity (see

Appendix C). A locomotor scale (adapted from (Wernig, Muller, Nanassy, & Cagol, 1995)) and a timed 10m walk were also used to quantify the functional mobility of the stroke participants.

Experimental Device

Rhythmic arm cycling was performed using a custom-made (Z. Kenwell, University of Alberta) hydraulic arm ergometer (described in (Zehr, Collins, Frigon, & Hoogenboom, 2003) which was positioned directly in front of the participants. Participants held the handles firmly but comfortably with pronated forearms. For those stroke participants who could not make a grip motion, a custom made wrist brace was used (see Figure 3). For this experiment, the arms were constrained to move together and were 180° out of phase with one another. The length of the arm crank was adjustable to accommodate the limited range of motion in a spastic arm.

Cycle Timing and Frequency of Cycling

An optical encoder on the ergometer provided information about crank arm position and cycling frequency (Zehr et al., 2003). Online feedback of cycling frequency was displayed on an oscilloscope (Hameg 20MHz, HM 205-3, Frankfurt/Main, Germany) allowing participants to match the required frequency. The recorded cycling frequency (Hz) was determined offline (custom-written software, Matlab, Nantick).

Table 1

Clinical Features of Stroke Participants

subject	sex	age	dom side†	hemi side	lesion location	Brunnstr-om UL/LL/ft‡	MAsh * UL/LL	M#	T●
1	M	70	R	L	No details	2 / 6 / 3	2 / 1	241	a
2	F	77	R	R	No details	3 / 7 / 7	1 / 0	49	a
3	M	51	R	R	Temporal	3 / 4 / 2	1^{+}/ 1	68	b
4	F	54	R	L	Temporoparietal	3 / 6 / 6	3 / 1	51	a
5	M	58	R	L	Parietal	6 / 4 / 5	1 / 1	91	a
6	M	58	R	L	Temporal	2 / 3 / 1	1 / 0	49	a
7	M	76	R	L	Internal Capsule	5 / 7 / 5	0 / 0	50	a
8	M	70	R	R	Parietal	2 / 4 / 2	3 / 2	105	b,c
9	M	89	R	R	Periventricular	7 / 7 /7	0 / 0	79	a
10	F	73	R	L	total MCA*	4 / 4 / 3	1 / 0	44	a
11	M	77	R	R	Temporofrontal	2 / 4 / 3	1^{+}/ 0	164	a
12	M	88	R	R	Lacunar infarct of the Internal Capsule	7 / 7 / 6	0 / 0	44	a
13	M	52	R	R	Frontoparietal	4 / 5 / 3	2 / 1^{+}	53	a
14	M	61	R	L	Temporoparietal	3 / 5 / 4	2 / 1	26	a
15	M	53	R	R	Internal Capsule, BG**, Parietal	4 / 5 / 4	2 / 1^{+}	28	a
16	M	76	R	L	Thalamic	7 / 6 / 7	0 / 1	23	b
Avg♦	3F 13M	67.6	16R	8R 8L					

†dominant side; ‡ UL= upper limb; LL= lower limb; ft= foot; MAsh=Modified Ashworth spasticity score for upper and lower limb; M#=months post stroke; T●= Treatment: a= none, b= Botox injection in the gastrocnemius or soleus area, c= muscle relaxant; MCA*= middle cerebral artery; BG**= Basal Ganglia; Avg* ♦=average of stroke data.

Experimental Protocol

The experimental set-up was very similar to previous H-reflex arm cycling experiments (Frigon et al., 2004; Zehr et al., 2004b; Loadman & Zehr, 2006). Participants sat in a custom adapted wheel chair which restricted unwanted movement of the trunk and legs.

Table 2
Features of Neurologically Intact Participants

subject	sex	age	dominant side
1	F	90	R
2	M	63	R
3	M	69	R
4	F	67	R
5	F	59	R
6	M	69	L
7	F	63	R
8	F	64	L
9	F	62	R
10	M	58	R
11	F	77	R
12	M	64	R
13	F	68	R
Average	8F 5M	67.1	11 R 2 L

Furthermore, both feet were placed securely on metallic blocks at neutral ankle position (approximately 90° dorsi flexion). The arm ergometer was placed directly in front of the participants.

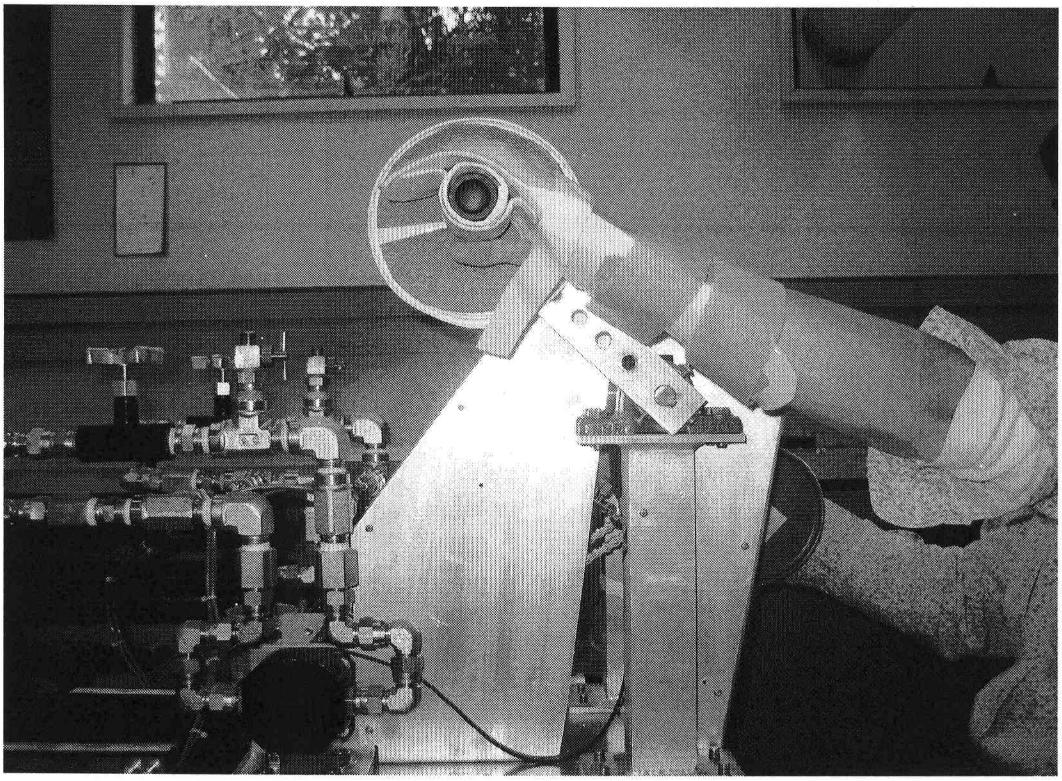

Figure 3. Brace used for the subjects who did not have grip power. The brace was custom designed to provide support for the wrist and allow for slight digital flexion. A tube designed opposite to the palmar surface of the brace was used to fit in the handle of the arm ergometer. The two cranks of the arm ergometer were moved together 180° out of phase.

For each experiment, participants performed two main tasks: static position and rhythmic arm cycling: 1 Hz; and the maximum frequency of cycling possible (high frequency). Static trials were obtained at the beginning of the experiment before collection of any movement trials and after completion of two movement trials. For static trials, participants held the handles bilaterally with the shoulder in flexion and the most extended elbow position for the less affected side of the stroke participants and the right arm of the NI group. Additionally, maximum voluntary isometric contraction (MVIC) was measured for plantar flexion (PF) and dorsi flexion (DF) separately. These measurements were taken for both sides and were used as another indicator for the comparison of the functional abilities between the two sides of the two participant groups.

Nerve Stimulation

Both tibial nerves were stimulated simultaneously (see section on simultaneous H-reflex elicitation) at the popliteal fossae using either 0.5 or 1 ms square wave pulses to evoke H-reflexes in the soleus muscles. In two of our participants for whom there was difficulty eliciting an H-reflex, a 2 ms pulse width was used. Under all circumstances, the pulse width used for eliciting H-reflex was consistent across all trials for a participant. Surface electrodes (NARCO BIO-SYSTEMS, INC. Houston, TX) in bipolar configuration with the electrode gel Spectra 360 (Parker Laboratories, INC. Orange, NJ) were used for nerve stimulation. In some cases, different placement of the electrodes was used. For example, one electrode was placed over the tibial nerve and the other was located over the patellar tendon. In either situation, a knee brace was used to hold the stimulating electrodes in place. Stimulation was delivered pseudo randomly between 3 to 5 seconds apart for all the trials. M-wave, H-reflex (M-H) recruitment curve (RC) consisting of 40 sweeps were collected for each trial. H-reflexes were elicited at the shoulder flexion and elbow extension for the less affected side of stroke and right side for the NI group. This position was chosen because previous studies determined significant effects of arm cycling on the reflex excitability in soleus muscle (Frigon et al., 2004;

Delwaide, Figiel, & Richelle, 1977). The two tibial nerves were stimulated using either a Grass S88 connected in series with an SIU5 isolator and two CCUI constant-current units (Grass Instrument, AstroMed) or two Digitimer DS7A (Digitimer Limited, UK) stimulators. Digitimer units were used in two scenarios: 1) if the Grass stimulator failed to elicit H-reflexes up to the H_{max} point (in other word, the ascending limb of the M-H RC), or, 2) if the Grass stimulator failed to get M_{max}. In the latter situation, the ascending limb of the RC was collected by the Grass stimulator while the M_{max} points were collected with a Digitimer to be used for normalization purposes. Current was measured using a mA-2000 Noncontact Millimeter (Bell Technologies, Orlando, FL) in all trials.

Simultaneous H-reflex elicitation

Because of the fact that reflex modulation is different for the less and more affected sides in the stroke subjects, in this study reflex modulation in both sides was investigated simultaneously. The bilateral simultaneous recording was advantageous in time and provided twice as much data as the single recording does. Due to the possible interaction of the reflex pathways in simultaneously evoked H- reflexes (Burke, Gandevia, & McKeon, 1983; Burke, Gandevia, & McKeon, 1984), the independence of the technique was determined before application. The independence of the simultaneously evoked H-reflexes was proposed by Mezzarane and Kohn (2002), however the study failed to demonstrate the detailed data (Mezzarane & Kohn, 2002). The independence of this technique was examined in our lab (Barzi, Klimstra, Javan, Dragert, & Zehr, 2006), and the sensitivity of this technique to the conditioning stimuli was also determined (Javan, Klimstra, Barzi, Dragert, & Zehr, 2006). This technique has also been used in cats (Manjarrez, Hernandez-Paxtian, & Kohn, 2005).

Electromyography (EMG)

EMG was recorded bilaterally using surface Ag-AgCl electrodes (Vermed, Bellows Falls, VT) in bipolar configuration from posterior deltoid (PD) and biceps brachii (BB) muscles from the arms and soleus (Sol), tibilais anterior (TA), and vastus lateralis (VL) muscles from the legs. EMG signals were amplified and band-pass filtered (P511 Grass Instruments, AstroMed). A gain of 500 was used for both Sol muscles and a gain of 5000 was used for the rest of the muscles. A 100-1000 Hz band-pass filter was used for both Sol muscles and a 100-300 Hz for the rest of the muscles. All the EMG signals were rectified except for the bilateral Sol.

Data Acquisition and Analysis

Data were sampled at a rate of 5000 Hz with a 12-bit A/D converter connected to a computer using a custom-written (Dr. T. Carroll, University of New South Whales, Sydney, Australia) LabView program (National Instruments, Austin, TX). For all trials, the sweep length was 90 ms with a 20 ms prestimulus window.

H-reflexes

Peak-to-peak amplitudes of M-waves and H-reflexes were determined off line (custom-written software, Matlab, Nantick) separately for each soleus muscle. To reduce inter-subject variability, M-waves and H-reflexes were normalized to the corresponding M_{max} values (average of three M_{max} values) collected from the RC for the same trial for each individual subject (Frigon, Carroll, Jones, Zehr, & Collins, 2007). The ascending limb of the RCs was fit using a general least squares model of a custom three-parameter sigmoid function (Zehr, Klimstra, Johnson, & Carroll, 2007) which was similar to one developed elsewhere (Carroll, Reik, & Carson, 2001). The function used for sigmoid fit was H(s):

$$H(s) = \frac{H_{\max}}{1 + e^{m(s50-s)}}$$

Where: H_{max} was the highest point in the curve (average of 3 largest H-reflexes), m was the slope, s50 is the M value at 50% of the H_{max} value, and H(s) is the H-reflex amplitude at a given M value. The slope was determined using the equation:

$$\frac{m(H_{\max})}{4}$$

In this study, similar to the previous study (Zehr & Stein, 1999), data from M-H curve was used. For each trial, the slope of the ascending limb at 50% of the H_{max} value was calculated as seen in figure 4. Later, the variables from the static curve were compared to those at the same M-wave values on the movement curves (Zehr & Klimstra, 2006). Thus, the same M-wave value which evoked a certain size H-reflex on the static RC, was used in the curve fit to the RCs of the movement trials and predicted H-reflex value obtained. Therefore, reflex variables from curve fitting are described as "@" the value from the static curves. Four variables were analyzed including: M-H slope; H@ threshold; H@ 50% H_{max} (H@ 50%); and, H@ 100% H_{max} (H@ 100%). This is similar in principle to the application of linear fits for the H-reflex analysis (Zehr et al., 1999; Funase, Imanaka, & Nishihira, 1994).

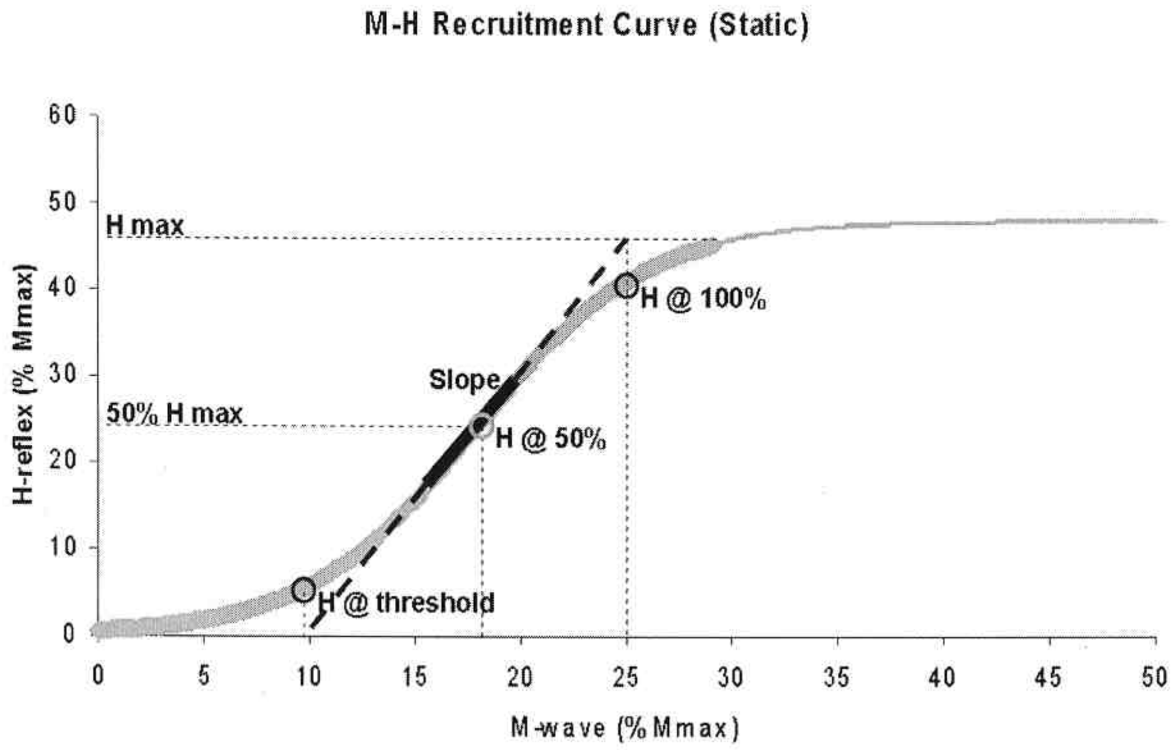

Figure 4. Sample curve fit to the ascending limb of the M-H recruitment curve in static position for a neurologically intact participant. H_{max} and 50% H_{max} was determined. A slope of the curve at 50% H_{max} was obtained. The slope line was extended to intersect with the H_{max} and H at zero lines. The M-wave values at the H_{max}, and H at 50%, and H at zero were determined. The H values for the corresponding M-wave values were obtained from the curve which demonstrated as H@ values (i.e., H@ threshold, H@ 50%, and H@ 100%).

EMG activity

The prestimulus EMG values (i.e. 20 ms prior to stimulation) were averaged and used as a measure of background muscle activity at the time of the nerve stimulation. These EMG values were then compared between static and movement trials.

Maximum voluntary isometric contraction recordings

For the maximum voluntary isometric contraction (MVIC) recordings, force values were collected via a load cell (Omegadyne Ltd. LC-101-105, range 0-226.7 kg) and amplified by a custom made high gain amplifier. Torque was then calculated by multiplying force with a moment arm of 0.15m (force was consistently applied with a moment arm length of 0.15m measured from the adjustable heel block to the centre of the load cell).

Statistics

Student's t-tests were performed on the variables obtained from the M-H curves to identify significant differences between static and movement trials for each side separately. Unpaired t-tests were also used to identify significant differences for frequency of cycling (between the two groups of participants) and MVIC values. Additionally, STATISTICA software (StatSoft, Tulsa, OK., USA) was used to perform one way repeated measures analysis of variance (ANOVA) on the background EMG and M_{max} values. Tukey's HSD *post hoc* tests were used to identify the significant main effects. Descriptive statistics included means ± standard error of mean (SEM). Statistical significance was set at $p < 0.05$.

Results

M_{max} *values*

M_{max} values for the four experimental trials (i.e. static begin, cycling 1 Hz, high frequency cycling, and static end), were compared separately for each side of the stroke and NI group. No significant differences were found for the M_{max} values between the trials for the less affected (LA) and more affected (MA) sides of the stroke and dominant side of the NI group. Significant main effect was found between the M_{max} values for the non-dominant side of the NI group. Tukey post hoc analysis found significant differences just between the static at the beginning and the high frequency trial with smaller M_{max} value for the high frequency trial ($p= 0.0376$).

Static trials

No significant differences were found between the H_{max}/M_{max} ratios across the two static trials for each group ($p> 0.05$). Therefore, the static begin and the static end trials were collapsed and used as a single static control as was done in another study (Loadman & Zehr, 2006).

The H_{max}/M_{max} ratios for the combined static trial of the stroke participants were 40.1 for the LA and 65.0 for the MA which was significantly larger for the MA side ($p= 0.003$). For the NI group, the H_{max}/M_{max} ratios for the combined static trial were 43.3 for the dominant and 43.1 for the non-dominant sides which were not significantly different ($p> 0.05$).

Rhythmic arm cycling movement trials

In movement trials, participants cycled at two different frequencies: 1Hz and the highest frequency that could be maintained. This meant that stroke participants (n=16) cycled at 0.96 Hz and (n=12) at 1.40 Hz. NI participants (n=13) cycled at 0.98 Hz and 1.46 Hz. The frequency of cycling was not significantly different between the stroke and NI groups and for both movement trials ($p> 0.05$).

The four variables (i.e. M-H slope; H@ threshold; H@ 50%; and, H@ 100%) obtained from the RC curves were calculated and compared across conditions. The comparisons were made between the values form the static curve and the equivalent ones form the movement trials as summarized below.

For the LA side of the stroke group, H@ threshold (p=0.04) and H@ 100% (p=0.02) were significantly smaller for the high frequency trial than for the static trial. The rest of the variables were not significantly different from the values obtained from the static trial (p> 0.05) (see Figure 5).

For the MA side, H@ 100% (p=0.005) was significantly suppressed for the 1Hz trial when compared to the static trial (see Figure 5). The rest of the variables from both 1Hz and high frequency movement trials were not significantly different from the values obtained from the static trial (p> 0.05).

For the dominant side of the NI group and for the cycling 1Hz, H@ threshold (p=0.03); H@ 50% (p=0.02); and, H@ 100% (p=0.008) were significantly smaller than the values from the static trial with the exception of the M-H slope (p> 0.05) (see Figure 6). For the high frequency cycling trial, all variables (i.e., M-H slope (p= 0.04); H@ threshold (p=0.04); H@ 50% (p= 0.001); and, H@ 100% (p=0.0002)) were affected by the arm movement and were significantly smaller for the fast cycling movement trial (see Figure 6).

For the non-dominant side and for cycling 1Hz, only H@ 100% was significantly smaller (p=0.03) than the values from the static trial (see Figure 6).

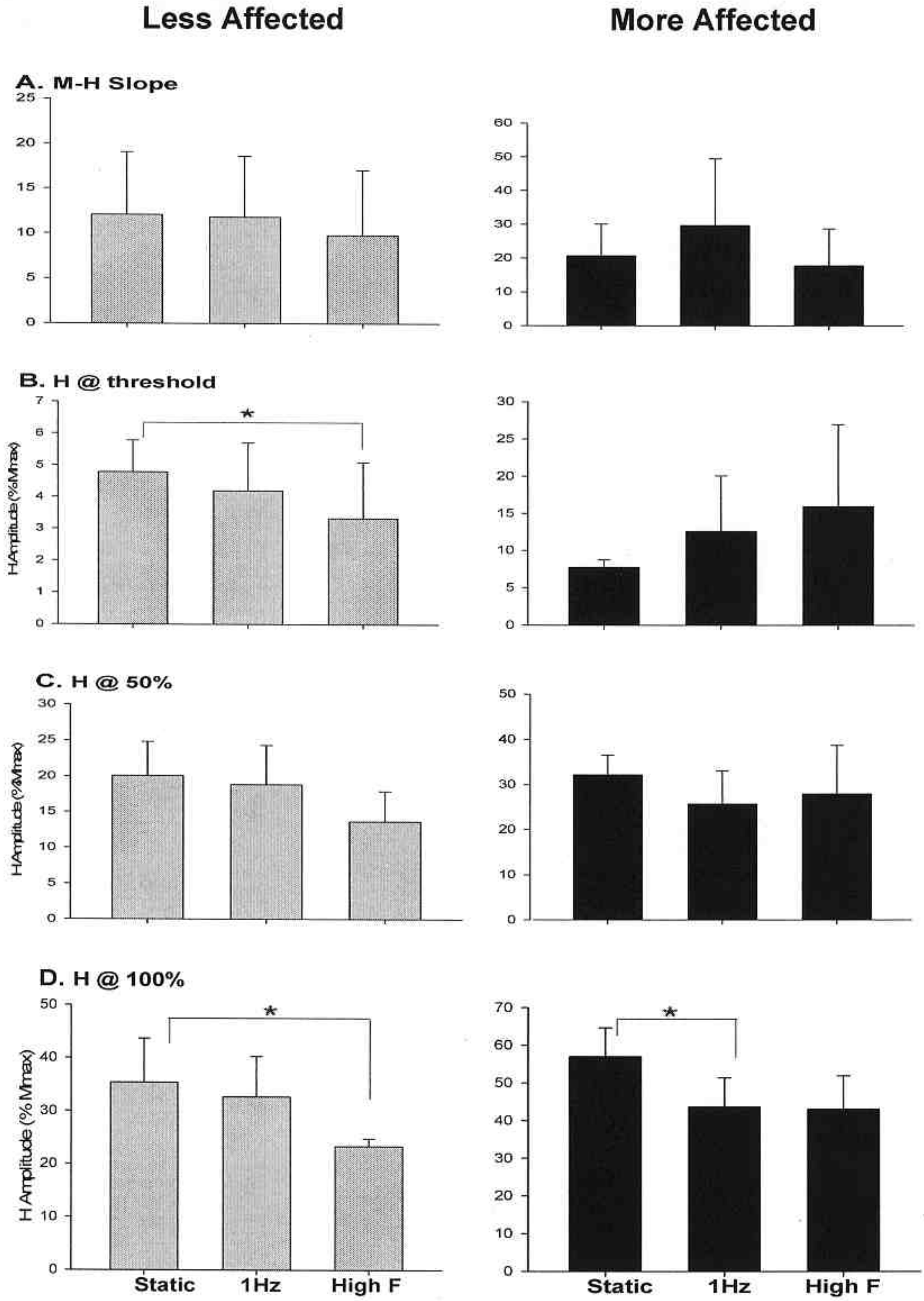

Figure 5. Comparison of the H-reflex parameters across conditions for the stroke participants. A. slope of the M-H curve; B. H@ threshold; C. H@50% H_{max}; and, D. H @100% H_{max}. For the less affected side, significant differences were found for the H@ threshold and H@ 100% H_{max} and between the static and high frequency trials. For the more affected side, significant differences was found for the H@ 100% H_{max} and between static and 1Hz trials.* Shows significant differences between conditions. Values are means ± SEM across all participants.

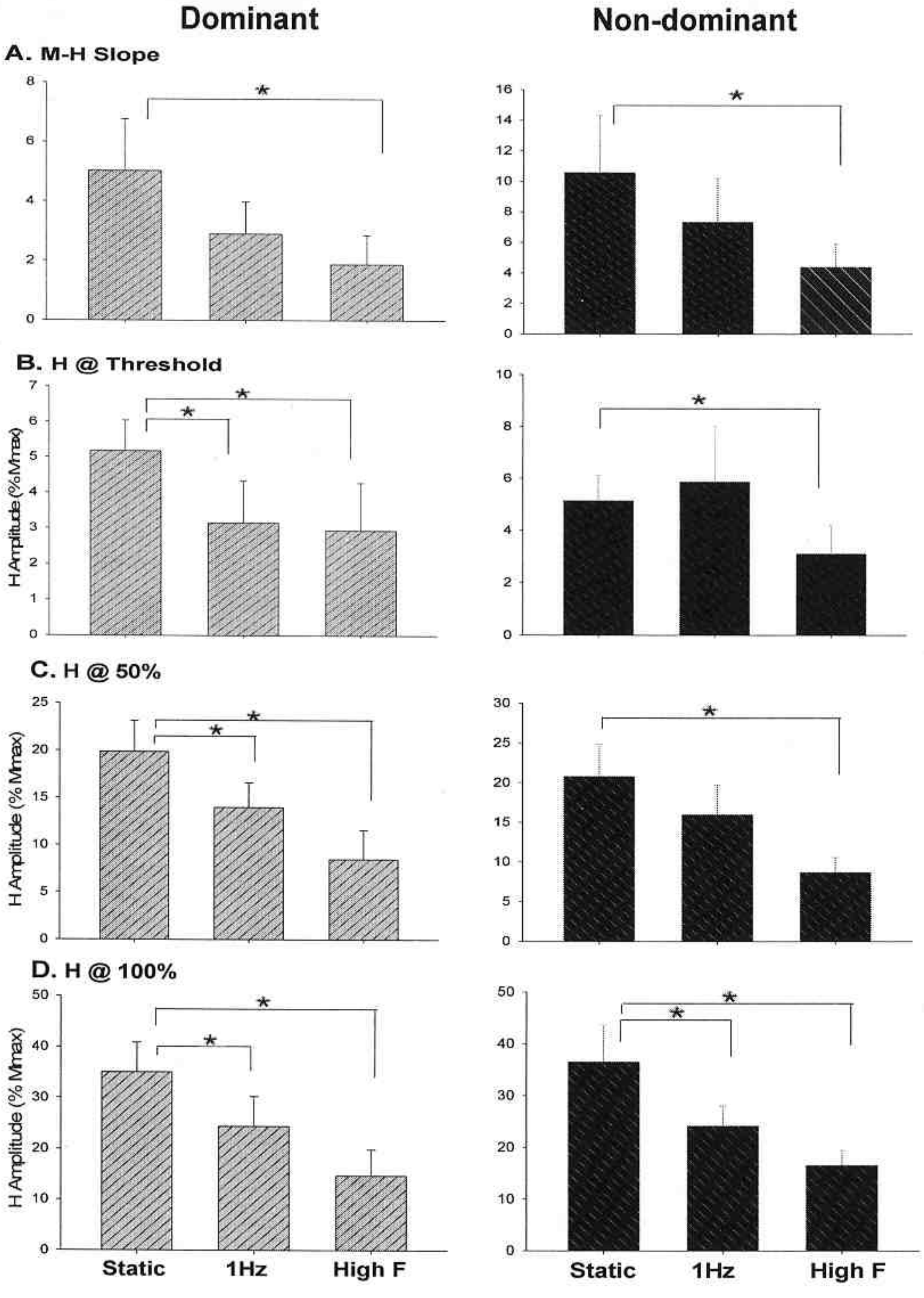

Figure 6. Comparison of the H-reflex parameters across conditions for the neurologically intact participants. A. slope of the M-H curve; B. H@ threshold; C. H@50% H_{max}; and, D. H @ 100% H_{max}. For the dominant side, significant differences were found in all the parameters except for the slope between static and cycling 1Hz. For the non-dominant side, significance was found in all the parameters except for the slope, H@ threshold and H @ 50% H_{max} and between static and 1Hz cycling. * Shows significant differences between the trials. Values are means ± SEM across all participants.

The rest of the variables were not significantly different from the static values ($p > 0.05$) (Figure 6). For the high frequency trial, all the variables (i.e., M-H slope ($p = 0.03$); H@ threshold ($p=0.01$); H@ 50% ($p = 0.001$); and, H@ 100% ($p=0.0007$)) were significantly smaller for the high frequency trial than the values obtained from static curve (see Figure 6).

EMG

For the LA side of the stroke group, there was a main effect for the EMG values for the three leg muscles. No significant differences were found for the EMG values of the three leg muscles between the static and 1Hz movement trials ($p>0.05$). Post hoc analysis showed that the EMG values were significantly higher in the high frequency trial than in the static trial (i.e. Sol ($p=0.008$); TA ($p=0.003$); and, VL ($p=0.004$)). For the MA side, there was a main effect for Sol EMG ($p=0.04$) between trials. No significant differences were found with Tukey post hoc analysis for Sol EMG across conditions ($p>0.05$). For TA and VL EMG, there was a main effect between trials. No significant differences were found between the static and 1Hz movement trial for both TA and VL EMG values ($p>0.05$). However, TA ($p=0.001$) and VL ($p=0.02$) EMG values were significantly higher for the high frequency trial than for the static trial.

For the dominant side of the NI participants, no significant differences were found for Sol EMG across trials ($p>0.05$). There was a main effect for TA and VL EMG values. No significant differences were found for the EMG values of the two muscles between the static and 1Hz trial ($p>0.05$), but EMG values were significantly higher (i.e. TA (p=0.0002) and VL (p=0.0004)) for the high frequency trial than for the static trial. For the non-dominant side, there was a main effect for both Sol and TA EMG values. The EMG of Sol and TA were not significantly different between static and 1Hz cycling trials (p>0.05), but were of higher values (i.e. Sol (p=0.0002) and TA (p=0.004)) for the high frequency trial than for the static trial. No significant differences were found between the three trials for VL EMG (p>0.05).

A more relevant index of the EMG effect on the H-reflex may be the relative ratio of muscular activity. Interestingly, when EMG ratios were compared across conditions, no significant differences were found for Sol/TA and Sol/VL ratios between the static and both movement trials (p>0.05) with the one exception for Sol/VL ratio and between the static and high frequency trial for the LA side of the stroke group (p=0.003) (see Tables 3 & 4).

Table 3
Soleus/Tibialis Anterior (Sol/TA) background EMG ratios. Values are means ± SEM across all participants.

Participants	Static	1 Hz	High Frequency
Stroke MA	2.08 ± 0.66	1.92 ± 0.78	1.53 ± 0.47
Stroke LA	2.12 ± 0.71	1.39 ± 0.56	0.86 ± 0.30
NI Dominant	1.57 ± 0.60	1.54 ± 0.61	0.81 ± 0.35
NI non-dominant	0.26 ± 0.60	0.30 ± 0.10	0.24 ± 0.60

MA: More affected; LA: less affected; NI: neurologically intact.

Table 4

Soleus/Vastus Lateralis (Sol/VL) background EMG ratios. Values are means ± SEM across all participants.

Participants	Static	1 Hz	High Frequency
Stroke MA	4.46 ± 1.12	3.92 ± 1.06	2.83 ± 0.52
Stroke LA	5.56 ± 1.27	4.61 ± 1.21	**2.47 ± 0.52***
NI Dominant	5.36 ± 1.39	3.67 ± 1.14	3.09 ± 1.27
NI non-dominant	1.16 ± 0.57	1.44 ± 0.60	1.75 ± 0.61

*MA: More affected; LA: less affected; NI: neurologically intact. * Significant differences between static and high frequency trials.*

For the two arm muscles (i.e. PD and BB), main effect were found for the EMG values across conditions for both stroke and NI groups. For both LA and MA sides of stroke, post hoc analysis showed significant bigger values for the high frequency trials than for the static values (i.e. LA PD (p=0.0002); LA BB (p=0.0002); and MA PD (p=0.0004); MA BB p=(0.0005)). For both dominant (D) and non-dominant (ND)sides of NI group, PD and BB EMG values were higher for both cycling 1Hz (i.e. D BB (p=0.04); ND PD (p=0.0005); and, ND BB (p=0.01)) and high frequency cycling (i.e. D PD (p=0.04); D BB (p=0.0001); ND PD (p=0.0005); and, ND BB (p=0.0002)) trials than during the static trial with one exception. Exception was found for the PD EMG of the dominant side which was not significantly different between the static and cycling 1Hz trials (p>0.05).

MVIC

For stroke participants, both PF and DF MVIC values were significantly larger for the LA side than the MA values (i.e. PF (p=0.03) and DF (p= 0.02)). For the NI participants, no significant differences were found for PF and DF values between the two sides (p>0.05) (see Figure 7).

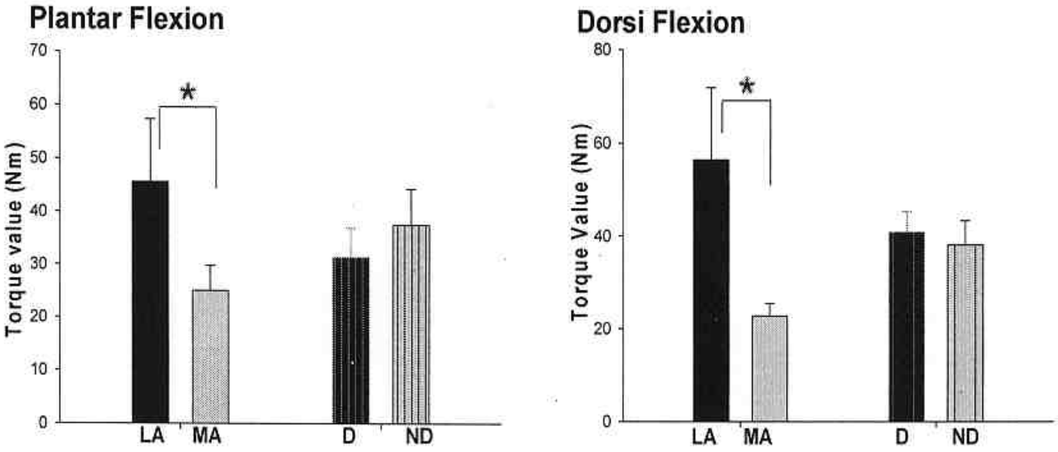

Figure 7. Maximum voluntary isometric contraction values for plantar and dorsi flexion. Comparison of the more affected (MA) and less affected (LA) sides in stroke participants and dominant (D) and non-dominant (ND) sides in the neurologically intact participants.* Significant differences between LA and MA sides of stroke participants. Values are means ± SEM across all participants.

Discussion

The main finding of this study was that there is partial preservation of the suppressive effect of arm cycling on soleus H-reflex amplitudes after stroke. Despite the exaggerated reflex amplitudes in the more affected side in static, the suppressive effect of arm cycling is still present in both legs after stroke. However, the suppression is weaker and not specified to all parts of the recruitment curve in contrast to the age-matched neurologically intact participants.

Methodological considerations

In this study, all M-waves and H-reflex values were normalized to the M_{max} value of the same condition to reduce inter-subject variability (Frigon et al., 2007; Zehr, 2002). M_{max} values were generally maintained across experiment with just one exception.

Participants did not maintain a low level contraction in soleus muscles bilaterally, which could lead to increase in variability in the results (Burke, Adams, & Skuse, 1989). However, we found the same results with the age-matched NI population, as was reported in previous studies which used a low level contraction in the soleus muscle (Loadman & Zehr, 2006; Frigon et al., 2004), thus this factor should not have had a significant effect on the differences between stroke and NI participants.

Also, the heteronymous sources such as reciprocal inhibition from the antagonistic muscles, such as TA (Crone, Hultborn, Jespersen, & Nielsen, 1987; Morita, Crone, Christenhuis, Petersen, & Nielsen, 2001; Petersen, Morita, & Nielsen, 1999) or the facilitation arising from knee extensor muscles such as VL (Pierrot- Deseilligny & Burke, 2005; Meunier, Pierrot-Deseilligny, & Simonetta, 1993) might affect H-reflex amplitudes. However, there were no significant differences in the relative EMG activity between the Sol/TA and Sol /VL pairs except for the Sol/VL on the less affected side of stroke participants (see section on EMG). In this condition, despite higher Sol and VL EMG amplitudes for the high frequency trial than during the control trial, H-reflex amplitude (H@ 100%) was significantly smaller. Therefore, it is unlikely that alteration in H-reflex amplitudes parameters during the high frequency trial arose due to changes in heteronymous muscle activity (Loadman & Zehr, 2006).

In summary, this study was well controlled and we are confident that none of the methodological considerations have a significant effect on the data.

Preservation of the effect of arm cycling on H-reflexes in leg muscles

The main finding of this study is that the general effect of arm cycling is still preserved after stroke. This suggests that interlimb pathways connecting the cervical and lumbosacral enlargements of the human spinal cord are still sensitive to movement-induced modulation after stroke.

Importantly, the details of the suppressive effect of arm cycling were different for stroke and age-matched NI population. Arm cycling had a suppressive effect on almost all the parameters of the curve for the NI group. However, effects for the stroke group were much more limited in that arm cycling did not affect the whole curve similarly as in NI population. It has been suggested that CPG-related activity during arm cycling (Zehr et al., 2004a) is responsible for changing the excitability of the H-reflex pathway in the leg muscle via changing the presynaptic inhibition (PSI) of Ia afferents (Frigon et al., 2004), and this mechanism could be reduced after stroke. Thus, it could be suggested that stroke may have weakened the regulation of PSI via effects on the PSI inhibitory interneurons which might be only weakly activated by the arm cycling. Additionally, the reduced effect of arm cycling might be due to the adaptive changes in the efficiency of the Ia- motoneuron synapse following the changes in the activation pattern of Ia terminal and motoneurons resulting from the motor impairments after stroke (Aymard et al., 2000). Moreover, each parameter investigated in this study (i.e. M-H slope; H@ threshold; H@ 50%; and, H@ 100%) provides slightly different information about the excitability of the H-reflex curve, therefore each responded differently to the movement conditioning. Specifically, the population of involved motor units is different for each point on the RC. Smaller lower threshold motor units are active at threshold and larger higher threshold units in combination with the smaller ones are active at the H_{max} point (Hennemann & Mendell, 1981), and middle range motor units are active for the 50% H_{max} (Crone et al., 1990; Meinck, 1980). Since the significant differences between static and movement trials were found for the H_{max} parameter in the stroke group, one might suggest that arm cycling specifically affected the larger motor units in the motorneuronal pool. Also, the fact that the arm movement is asymmetrical in stroke could reduce the effect on the reflex amplitude. However, the recent observation that unilateral arm cycling causes the same effect on the H-reflex amplitude as bilateral arm cycling would argue against that (Loadman & Zehr, 2006).

Despite the fact that we found significant suppressive effects of arm cycling on the amplitude of soleus H-reflexes, clearly much of the suppression that is present in neurologically intact participants is lost after stroke. The lesions due to the stroke could interrupt descending projections to spinal interneurons including the Ia PSI interneuron (Nielsen & Kogamihara, 1993; Nielsen & Petersen, 1994). Such changes in convergence onto these interneurons would lead to significant changes in excitability that may offset the effects induced by arm cycling. Additionally, descending input to any segmental commissural interneurons may also be altered after stroke which could affect any locomotor related activity patterns created by CPGs (Kiehn, 2006).

Within the stroke group, there was an increase in H_{max}/M_{max} ratio for the more affected side, which is well known in the literature (Faist et al., 1994). It may have been predicted this would blunt the suppression during cycling. Yet suppression was still observed. Surprisingly, the effect of arm cycling was also reduced for the less affected side when compared to the NI results. This finding demonstrates that abnormalities in transmission in spinal pathways might be found on the less affected side (Thilmann et al., 1990; Pierrot- Deseilligny, Bussel, & Morin, 1973; Thilmann, Fellows, & Ross, 1993), which might reflect damaged ipsilateral corticospinal projections and/or synaptic reorganization after stroke (Gandevia, 1993). Therefore, it is important to consider that the less affected side also undergoes pathological changes, so in reflex studies with stroke using the less affected side as a control for monitoring pathological reflexes must be avoided. The changes in the less affected side might also be evidence for the extensive plastic changes in the motor system in response to stroke which takes place not only on the affected side, but also on the contralateral side (Nudo, 2006; Mark, Taub, & Morris, 2006). These plastic changes occurring at different levels of the motor system might be an underlying mechanism for the adaptive behavior in the less affected side after stroke (Lamontagne, Richards, & Malouin, 2000). Therefore, changes observed in the less affected side might either be due to motor impairments to the contralateral side or be compensatory adaptation in response to the injury to preserve function.

Within the NI group, some slight differences were observed in response to the movement conditioning between the dominant and non-dominant sides. Asymmetries in the soleus H-reflex RCs in NI participants have been reported in the literature (Chandran, Maini, & Marya, 1988; Goode, Glenn, Manning, & Middleton, 1980; Nativ, Frank, & Allard, 1989; Tan, 1985). However, contradictory results have been reported with regard to the correlation of asymmetries in the RCs and the dominant side, in favor of the left side regardless of the handedness (Nativ et al., 1989), the non-dominant side (Tan, 1985), and asymmetry not related to handedness (Chandran et al., 1988). It has also been suggested that significant asymmetry is not related to the side dominance and could even switch in a few minutes (Mezzarane et al., 2002). Finding more significant results in the dominant side of the NI participants in response to arm cycling conditioning might be attributed to cortical laterality and possibly through selective activation of the motor pathways in the preferred side (Goode et al., 1980). Therefore, the conditioning effect of arm cycling may appear in a more restricted number of parameters and with less intensity in the neurophysiological measurement (i.e. H-reflex) in the non-dominant side. However, this study was not designed to specifically address this question and the data we have are too limited for discussion on the issue of laterality.

The observation that the older NI participants had the same results as earlier data in younger NI (Loadman & Zehr, 2006; Zehr et al., 2004b; Frigon et al., 2004) means that the differences are due to stroke and are not a product of aging. This is important because aging has been suggested to reduce excitability of the spinal reflexes (Kido et al., 2004) and could set a floor effect.

Translational implications for rehabilitation

Our results have functional implications for using arm movement strategies for rehabilitation of locomotion after stroke. The present demonstration that rhythmic arm movement has a general suppressive effect on the excitability of the soleus H-reflex pathway suggests a partially preserved interlimb linkage that could represent a part of the arm-leg coordination for walking (Frigon et al., 2004). Although the movement activity in this study does not directly translate to walking because the legs were not active at the same time, it provides insight into the underlying coupling between the arms and legs that could be operating during locomotion. The fact that arm movement could influence motoneuronal pools in the legs (Dietz, 2002; Huang & Ferris, 2004; Kao & Ferris, 2005; Kagamihara, Hayashi, Masakado, & Kouno, 2003; Haridas et al., 2003) shows it could assist in accessing neural circuitry responsible for walking or other locomotor tasks. Simultaneous activity of the arms and legs due to incorporation of the interlimb neural coupling has been suggested as an effective way for gait retraining after neurotrauma (Ferris, Huang, & Kao, 2006). Specific interactions between the arms and legs may be more accessible when the arms and legs are moving together (Balter & Zehr, 2007). Therefore, examination of the soleus H-reflex amplitudes during arm and leg cycling or walking in neurologically impaired population will be important to further refine effective rehabilitation strategies.

Lastly, stroke survivors typically have exaggerated reflex excitability (Faist et al., 1994; Aymard et al., 2000) which can interfere with their movements. Our research suggests that arm cycling could attenuate this high reflex excitability in the legs. Although suppression is small, it might be useful incorporating it in retraining paradigms to reduce hyperactive reflexes.

In conclusion, arm cycling can still access interlimb pathways after stroke and activate spinal control mechanisms of locomotion as described in NI population (Zehr, 2005). Additionally, this could help in attenuation of the exaggerated reflexes in the leg muscles after stroke. Therefore, incorporation of arm training as a part of rehabilitation programs after stroke, because of its suppressive effect on the hyperactive reflexes as well as its effect on activation of the rhythm generation centers, might lead to better functional outcomes in improving locomotion. This remains to be further examined in future research.

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Appendix A: Modified Physical Activity Readiness Questionnaire (modified PAR-Q)

Physical Activity Readiness Questionnaire (PAR-Q) is developed by Canadian Society for Exercise Physiology for people aged 15-69. If one plans to become more physically active, s/he starts by answering questions in the PAR-Q form. If the answer to one or more questions were yes or the person is older than 69, one needs to consult with her/his doctor in order to start the new exercise regimen. For more information check the following web address. http://www.csep.ca/forms.asp

In this study, we used a modified PAR-Q to test for general readiness for participation in a moderate physical activity such as arm cycling for all our participants.

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Modified Activity Screening Questionnaire (modified from the PAR-Q)

Name			Date
DOB	Age	Home Phone	Work Phone

Completion of this questionnaire helps us determine if the light exercise that you would perform in our experiments is a safe activity for you. Please read each question carefully and answer every question honestly:

Yes	No	1) Has a physician ever said you have a heart condition and you should only do physical activity recommended by a physician?
Yes	No	2) When you do physical activity, do you feel pain in your chest?
Yes	No	3) When you were not doing physical activity, have you had chest pain in the past month?
Yes	No	4) Do you ever lose consciousness or do you lose your balance because of dizziness?
Yes	No	5) Do you have a joint or bone problem that may be made worse by a change in your physical activity?
Yes	No	6) Is a physician currently prescribing medications for a heart condition?
Yes	No	7) Do you have any history of epilepsy or other seizures?
Yes	No	8) Do you have insulin dependent diabetes?
Yes	No	9) Are you 69 years of age or older?
Yes	No	10) Do you know of any other reason you should not perform light physical activity?

If you answered yes to any of the above questions, talk with your physician about your wish to participate in our experiments. We will provide for you a form that briefly explains the physical demands of the experiment. The form asks that your physician indicate if he or she feels there are any medical risks in your participation. We ask that you bring the signed form with you to the Rehabilitation Neuroscience Laboratory should you still wish to participate in our experiments.

Participant signature	Date

Appendix B: Brunnstrom motor assessment

Brunnstrom motor recovery stages were used to determine the severity of hemiparesis for the participants (Brunnstrom, 1970). Brunnstrom describe sequential stages of motor recovery after stroke. It has six stages of recovery judged by clinical observation of the participants and scores their ability to perform voluntary movement within and outside the flexor and extensor synergy pattern. Stage 1 is when no voluntary movement can be initiated. Stage 2 is basic limb synergy with minimal voluntary movement within synergy. Stage 3 is limited voluntary control of movement within synergy patterns. Stage 4 is when participants are able to produce some movement combination out side the path of synergy. Stage 5 is progression over stage 4 and basic limb synergies lose their dominance. Stage 6 is when participants are able to produce isolated joint movement. Stage 7 is normal coordination of movement performance.

Appendix C: Modified Ashworth Scale

As a clinical measure of spasticity, the Ashworth scale is the most widely used clinical scale for measuring spasticity (Ashworth, 1964). It records the resistance to passive movement across a relaxed joint on a scale of zero to four; the score of zero is when there is no increase in the tone and four is when the affected part is rigid in flexion or extension. The problem with this scale is clustering of most of the patients in the middle. A modified Ashworth scale attempts ton overcome this defect. It is a six digit scale from 0-1-1^+-2-3-4 with the same grading as the original Ashworth (Bohannon & Smith, 1987). The reliability of the modified Ashworth scale has been established in several studies (Gregson et al., 1999; Gregson et al., 2000). A recent systematic review of different spasticity scales, showed a high interrater reliability of the Modified Ashworth in the majority of circumstances (Platz, Eickhof, Nuyens, & Vuadens, 2005).