NEURAL COUPLING BETWEEN UPPER AND LOWER LIMBS DURING RECUMBENT STEPPING

by

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“A determined soul will do more with a rusty monkey wrench
than a loafer will accomplish with all the tools in a machine shop.”
-Robert Hughes

To my Mom, Dad, brother, and friends

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Without the support of my family, academic family, and friends, this dissertation would not exist. To help put into context how significant their support has been, it is important to know that during my graduate career, I had to learn to manage my mental illness, major episodic and dysthymic depression. It was not until recently, that I came to realize how disabling a mental illness can be. When my depression was at its worst, it was difficult to concentrate and doing anything seemed to require a great deal of effort and energy. Those years were not very productive. But, with support, encouragement, and patience of my friends and family, several therapy appointments, and a combination of medications, I have learned to manage my depression. Now, I can actually be who I want to be and achieve what I and others believe I can achieve. I am incredibly thankful for everyone’s unwavering support and encouragement but a few individuals deserve special thanks.

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CHAPTER 1

INTRODUCTION

In this thesis, I asked a simple question, “Can using the arms help recruit muscles in the legs?” I proposed that incorporating upper limb effort with lower limb stepping movements may increase and improve lower limb muscle activation patterns. I based this general hypothesis on a simple observation that humans naturally coordinate and swing their arms in concert with their legs during walking. This observation suggested a likely coupling of upper limb neural networks with lower limb neural networks during rhythmic tasks (Wannier, Bastiaanse et al. 2001; Dietz 2002; Zehr and Duysens 2004). If combining upper limb effort with lower limb rhythmic exercise indeed improved lower limb muscle recruitment, then incorporating upper limb movements to therapies for lower limb motor rehabilitation could improve therapy efficacy. Patients could use their arms to assist their legs. Self-assisted therapy would enable patients to be in control of the timing and amount of assistance provided. Potential benefits of self-assisted therapies are decreased clinical labor, more frequent training sessions, and implementation within the comforts of the patients’ homes. Development of new devices and strategies to augment current rehabilitation therapies will greatly decrease the cost and increase the effectiveness of gait rehabilitation after spinal cord injury (Reinkensmeyer, Lum et al. 2002).

Background

Spinal Cord Injury in Humans

There are approximately 250,000 Americans who live with a spinal cord injury (NSCISC 2008). Each year, approximately 12,000 new individuals will suffer a spinal cord injury, at an average age of 38 years (Jackson, Dijkers et al. 2004; NSCISC 2008). The leading cause of spinal cord injury is motor vehicle accidents, followed by falls, violence, and disease (Jackson, Dijkers et al. 2004; NSCISC 2008). Advancements in medical treatment have increased the likelihood of surviving an acute spinal cord injury. Short term mortality rates due to spinal cord injury have decreased approximately 40%, but longer term mortality rates, post 2 years of injury, have not changed significantly (Strauss, Devivo et al. 2006). This suggests a need for more research that addresses long term care and treatment. The self-perceived life satisfaction of spinal cord injured individuals seems to be related to participation in life activities such as having a job and being married (Charlifue, Lammertse et al. 2004; Meade, Lewis et al. 2004; Whiteneck, Meade et al. 2004). Environmental factors, including physical, policy, and societal barriers, also strongly influences life satisfaction (Whiteneck, Meade et al. 2004).

Individuals with spinal cord injury have impaired motor and sensory function. The level of the injury is based on the location of the injury within the vertebral column. The specific neurologic injury level is the lowest point on the spinal cord that has impaired function. Cervical level injuries affect the upper limb, lower limb, chest, and abdominal muscles and afferents. Thoracic injuries have preserved upper limb functionality but impaired functionality of the chest, abdominals, and lower limbs. Lumbar and sacral injuries only affect the motor and sensory function of the lower limbs. Spinal cord injuries are also classified as either complete or incomplete. Individuals with complete injuries have no motor or sensory function below the level of injury. They cannot voluntarily move or feel sensations in parts of the body innervated by nerves below the injury level. Individuals with incomplete injuries have some functionality below the level of the injury. They may be able to voluntarily activate some muscles and/or feel different sensations in impaired body parts. Spinal cord injuries are also often graded according to the American Spinal Injury Association (ASIA) Impairment Scale. ASIA scores range from A to E, with A being the most severely impaired and E being normal. An ASIA score of A indicates a complete injury while scores of B, C, and D are incomplete. ASIA C individuals have some motor function but cannot overcome gravity while ASIA D individuals have sufficient muscle strength to overcome gravity.

Rehabilitation Therapies

Successful neurorehabilitation relies on three main principles: 1) practice, 2) specificity, and 3) effort (Ferris, Sawicki et al. 2005). When learning or relearning a motor skill, practice typically leads to improved performance. It is also important to practice the specific task to be learned. This specificity principle implies that to relearn to walk, a person must practice walking. If a person cannot walk, then s/he should choose a task that s/he can practice that is as similar to walking as possible. Lastly, successful rehabilitation requires effort. Greater effort or voluntary drive has been shown to improve performance and promote neural reorganization (Lotze, Braun et al. 2003; Kaelin-Lang, Sawaki et al. 2005). These rehabilitation principles contribute to promote activity dependent plasticity (Wolpaw and Tennissen 2001).

An effective gait rehabilitation technique is locomotor training. Manual locmotor training (Dietz, Colombo et al. 1995; Wernig, Muller et al. 1995; Wernig, Nanassy et al. 1999; Behrman and Harkema 2000) and mechanized locomotor training (Hesse and Uhlenbrock 2000; Colombo, Wirz et al. 2001; Werner, Von Frankenberg et al. 2002) have been shown to greatly improve walking ability in individuals with spinal cord injury These body-weight supported treadmill training methods involve therapists or mechanized devices that move the subject’s legs through the stepping motion. The subject also wears a harness during training that provides body weight support as needed. It is generally accepted that sensory stimulation contributes greatly to improved walking ability after injury. The stepping motion of locomotor training activates residual pathways and results in modification of existing pathways and/or generation of new pathways (de Leon, Roy et al. 2001). Even though locomotor training can improve walking ability, it is not accessible to the majority of the spinal cord injured population. Only a handful of clinics in the United States currently offer manually assisted or mechanized locomotor training.

Coordination of Upper and Lower Limbs

Humans naturally coordinate upper and lower limb movements during rhythmic tasks. When humans walk, the right arm swings in-phase with the left leg, and likewise, the left arm swings in-phase with the right leg. Despite its pendular nature, arm swing still involves some muscle activation, particularly to drive the arm backwards into shoulder extension (Ballesteros, Buchthal et al. 1965). Even in other rhythmic tasks such as swimming and crawling, humans tend to coordinate the limbs to move in integer ratio relationships (i.e. 1:1, 2:1, 3:1, 4:1) (Wannier, Bastiaanse et al. 2001). Because the swimming arm motion is not pendular-like, it requires more active neural control compared with walking. Thus, it seems that the human nervous system actively seeks to maintain interlimb coordination. Even though the exact neural mechanisms responsible for coordination of upper and lower limbs during rhythmic tasks are not known, it is likely that there are connections between the upper and lower limb locomotor neural networks (Dietz 2002; Zehr, Hundza et al. 2009).

Recumbent Stepping

Recumbent stepping is a type of low impact, rhythmic exercise. The exercise motion is a hybrid of recumbent cycling and stair stepping (Figure 1.1C). The manufacturer of the recumbent stepper (NuStep Inc., Ann Arbor, MI) has had increases in units produced and sold with each subsequent year.

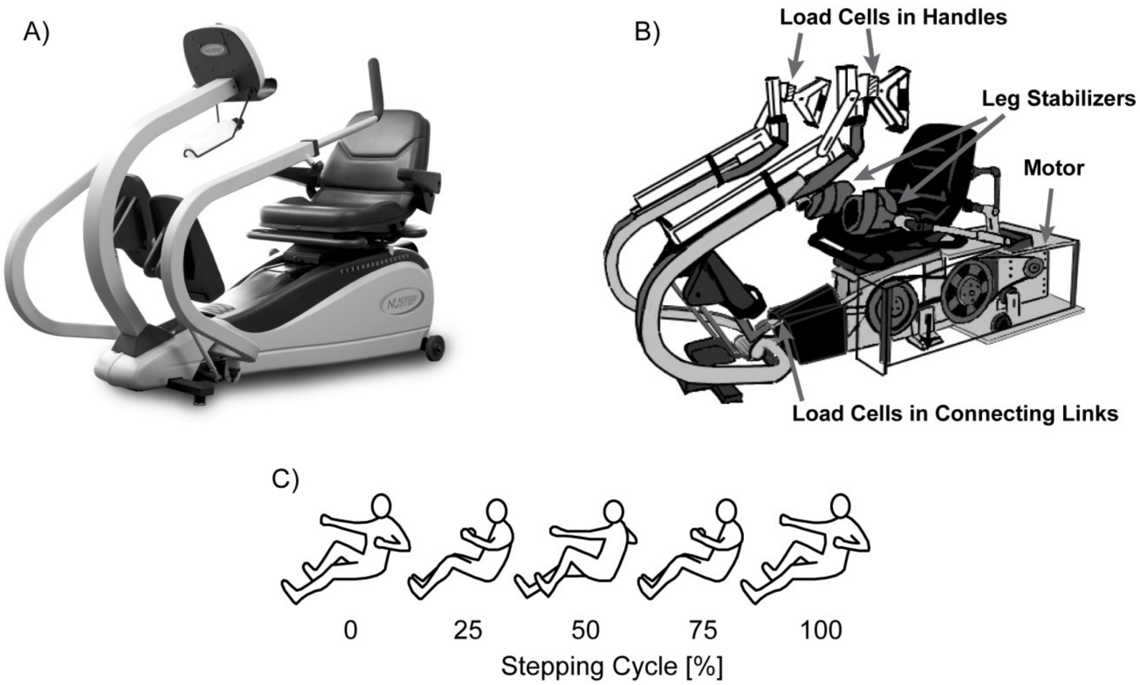

Figure 1.1 A) NuStep TRS 4000 recumbent stepper. B) Michigan's Human Neuromechanics Laboratory Modified NuStep System. Load cells in the handles and connecting links for measuring subject effort. A computer controlled motor provides real-time assistance or resistance. C) Schematic of the stepping motion.

The recumbent stepping exercise device has handles and pedals that are mechanically linked such that users can exercise using just their legs, just their arms, or both their arms and legs (Figure 1.1A). For an individual who is unable to drive the stepping motion using just his/her legs, he/she can use his/her arms to assist the legs with the stepping motion. Additionally, the phase relationships of the limb movements during recumbent stepping match the phase relationships of the limbs during walking. When a person walks, the left arm swings forward as he/she steps forward with his/her right leg. Similarly, the right arm swings forward when a person steps forward with his/her left leg. The contralateral limb pairs (right arm and left leg; left arm and right leg) move in-phase. Because the two legs alternate and are out-of-phase with each other, the two arms also alternate and are out-of-phase with each other. These same interlimb phase relationships also occur during recumbent stepping. While recumbent stepping is not exactly like walking, recumbent stepping and walking do share similar neural control networks (Stoloff, Zehr et al. 2007). Thus, recumbent stepping can be considered to be “simplified walking.”

Dissertation Outline

This dissertation provides results from experimental studies on humans exercising using different combinations of arm and leg efforts on a recumbent stepping device and from computer simulations that investigated potential neural mechanisms of upper to lower limb excitatory neural coupling. The recumbent stepper had mechanically coupled handles and pedals which provided a convenient method to determine if adding upper limb effort improved and/or increased lower limb muscle activation patterns during a rhythmic locomotor-like task. Below are the individual parts of this dissertation:

- A technical note that describes the modifications made to the recumbent stepper to implement computer-controlled resistance and force sensors (Figure 1.1B). (Chapter 2)
- In Study 1, neurologically intact individuals performed recumbent stepping with different grades of upper limb effort (at easy, medium, and hard resistances) and with passive lower limbs. The main finding of this study

indicated that greater upper limb effort resulted in increased rhythmic muscle activation in the passive lower limb muscles. This suggested that there is excitatory neural coupling between the upper limbs and lower limbs in neurologically intact humans. (Chapter 3)

- Study 2 was an extension of the previous results and sought to determine more details on interlimb neural coupling in neurologically intact individuals. The main findings of this study were that neural coupling was bidirectional, more ipsilaterally coupled than contralaterally coupled, and had limited excitatory effects. (Chapter 4)
- Study 3 tested whether neural coupling between the upper and lower limbs could further enhance muscle activation in individuals with incomplete spinal cord injuries. The primary results of this study indicated that maximal effort of the upper limbs did not increase active lower limb muscle recruitment in spinal cord injured individuals. (Chapter 5)
- Study 4 used computer simulations to investigate potential neural mechanisms that may explain the empirical results of upper and lower limb excitatory neural coupling. (Chapter 6)
- Conclusions about neural coupling between upper and lower limbs based on the results of this dissertation. Study limitations and future work are also discussed. (Chapter 7)

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CHAPTER 2

DESIGN AND PERFORMANCE OF A COMPUTER-CONTROLLED RECUMBENT STEPPER

We modified a commercially available recumbent stepper, the NuStep (TRS 4000 NuStep Inc, Ann Arbor, MI), to have computer-controlled resistance and load measuring capabilities.

Hardware

NuStep Recumbent Stepper

The NuStep recumbent stepper is an exercise machine that is a hybrid of a recumbent bicycle and a stair stepper (Figure 2.1A). It has handles and pedals that allow users to exercise using just their lower limbs, just their upper limbs, or a combination of upper and lower limbs. It also has a large bucket seat that allows users to be seated while performing a stepping task. The bucket seat also swivels for easier transfers from wheelchairs or other assistive devices. The position of the seat relative to the pedals is adjustable to accommodate users with different leg lengths. The handles are also adjustable to maximize user comfort. The recumbent stepper has 10 resistance levels that are based on an eddy current disk brake mechanism.

There were several benefits and advantages of using a recumbent stepper. First, recumbent stepping can be considered “simplified” walking. During recumbent stepping the limbs move in phase as they do during walking. When a person walks, the right upper limb and left lower limb move in-phase and likewise, the left upper limb and right lower limb move in-phase. On the recumbent stepper, the right handle and left pedal are part of a single rigid body and thus, move together. Similarly, the left handle and right pedal are part of a single rigid body and they also move together. Furthermore, the right handle-left pedal unit is connected such that it moves anti-phase with the left handle-right pedal unit. This out-of-phase relationship between the two upper limbs and between the two lower limbs is also a feature of walking. Additionally, recumbent stepping and walking has been shown to share neural networks based on principle components analysis of the muscle activation patterns (Stoloff RH, et al., 2007). Another benefit of the recumbent stepper was that the mechanical coupling of the handles and pedals provided an easy way for the arms to assist the legs with the stepping motion. Lastly, the recumbent position reduced the need for users to actively balance themselves and allowed those with impaired balance such as individuals with spinal cord injury to be able to exercise.

To implement force sensing capabilities and computer-controlled resistance, hardware modifications to the recumbent stepper included mounting load cells in custom redesigned handles, mounting load cells within the handle-pedal unit connecting links, and adding a motor with a two stage belt drive (Figure 2.1 B). Customized parts for mounting the load cells and attaching the motor were designed and drawn using computer-aided-design software (SolidWorks 2003, SolidWorks Corporation, Concord, Massachusetts). A two stage belt drive transmitted power from the motor attached behind the stepper to the pivot disk axis (Figure 2.2) which connected to the handle-pedal units. The motor rotated both clockwise and counterclockwise to drive the stepping motion forward and backward. Because the device has one degree of freedom, only one position sensor was needed. We used the encoder within the motor to measure angular displacement.

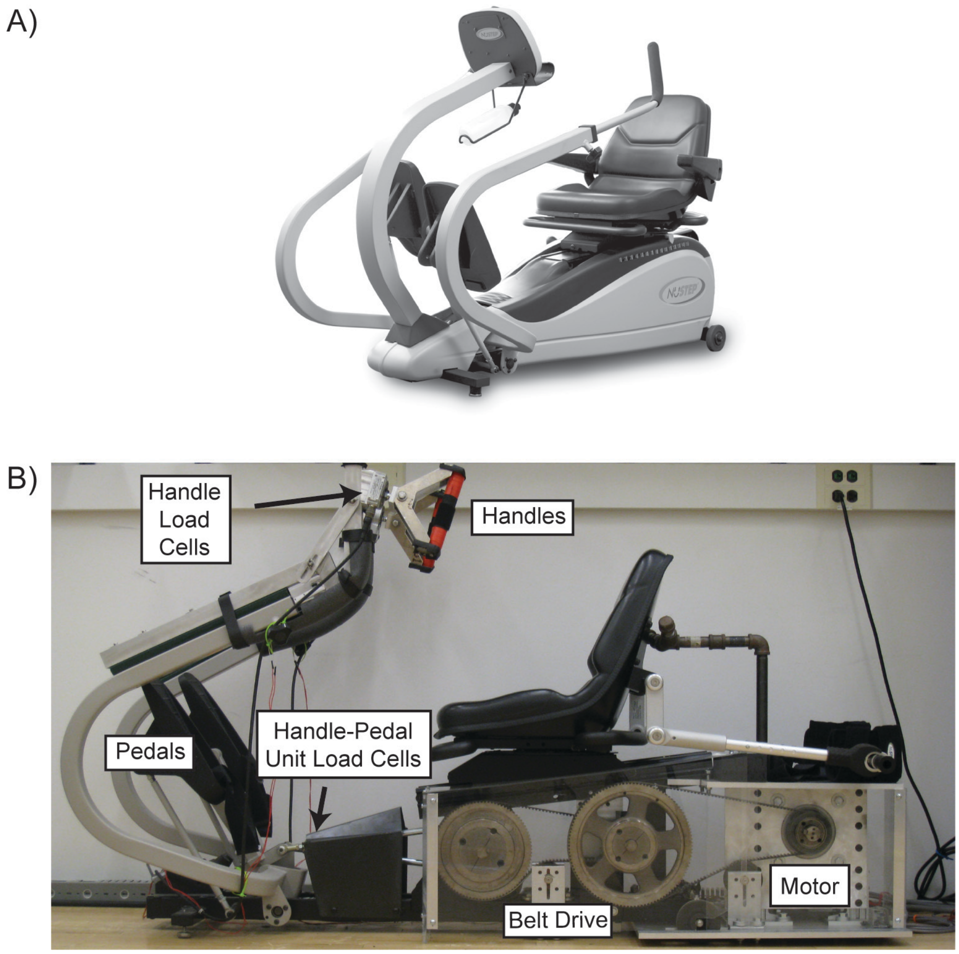

Figure 2.1 A) Recumbent stepper (TRS 4000, NuStep, Inc. Ann Arbor, MI). B) Computer controlled recumbent stepper system.

Servo Motor

A Kollmorgen Goldline XT Servo Motor MT706C1-R1C1 (Kollmorgen, Radford, Virginia) and a SERVOSTAR 600 Amplifier were used to provide resistance or assistance during the stepping motion. This motor has a continuous torque capacity of 48 Nm, a peak torque of 86.5 Nm, rated horsepower of 7.8 HP, and a rated speed of 1300 rpm. The motor weighed 36 kg. A command signal from the amplifier controlled the motor's torque, speed, or position depending on the operation mode of the motor and amplifier system.

Encoder

The system had only one position sensor, the encoder within the motor. The encoder had a resolution of 4096 ticks per revolution.

Belt Drive

A two stage belt drive was used to amplify the motor torque. The system torque design specification was ~800 Nm at the handle-pedal axis of rotation. This torque corresponded to a 2000 N force applied by the foot, approximately twice the body weight of a 100 Kg person. To reuse the axles on the original recumbent stepper, there was a spatial constraint of a fixed center distance of 0.337 m and maximum sprocket diameter of 0.36 m (Figure 2.2). Based on these constraints, a two stage belt drive with gear ratios of 2.81 and 3.29 was implemented. We paired these gears with the most powerful rated synchronous belts available, polyurethane belts with kevlar tensile member cords (PolyChain GT2, Gates Corporation, Denver, CO). Two idler pulleys tensioned each belt.

With this belt drive system, the maximum torque capability of the system was ~1000 Nm about the handle-pedal axis of rotation.

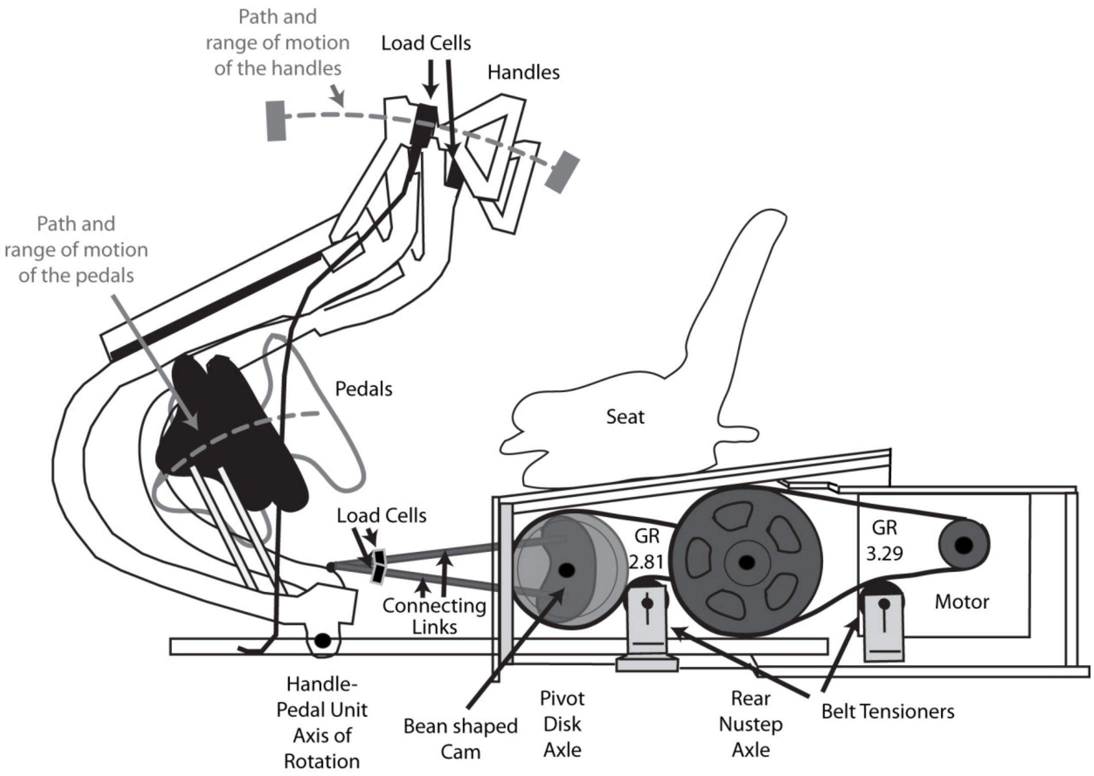

Figure 2.2 Detailed schematic of the computer controlled resistance recumbent stepper components. Grey dashed lines indicate the paths of the handles and pedals during stepping. GR: Gear ratio.

Load Cells Mounted in the Handles

Two Strainsert FL1U(C)-2SGKT universal flat load cells with a 1000 lb capacity (Strainsert, West Conshohocken, Pennsylvania) were mounted in customized adjustable handles to measure directly the forces applied by the hands that contributed to the stepping motion. The load cells measured both compression and tension. The handles travel along an arc with a radius of approximately 1 m (Figure 2.2). Because the length of the handles can be adjusted to accommodate users with different arm lengths, the radius from the center of the load cell to the axis of rotation ranged from 0.89 m to 1.04 m.

Handle forces were isolated along a single axis such that only forces tangent to the handle arc path were measured.

Load Cells Mounted in the Connecting Links

Two Omegadyne LC202-3K miniature universal load cells (Omegadyne, Sunbury, OH) were mounted in the connecting link of each handle-pedal unit to measure the total force each contralateral hand-foot pair produced. The load cells measured both compression and tension.

Overall Force Measurement System

The sum of the handle and pedal torques equaled the handle-pedal unit torque (Figure 2.3). The connecting link attachments at each end of the rod were pin joints which meant the moment arm was not constant throughout the stepping motion. We used a 2-dimensional motion simulation software (Working Model 2D, Design Simulation Technologies, Inc., Canton, MI) to determine the moment arm relationships of the connecting links about the handle-pedal (HP) axis and the pivot-disk (PD) axis (Figure 2.2). The moment arm relationships (in meters) of the connecting links (CL) were

$$r_{HP,left\ CL} = r_{HP,right\ CL} = -0.000003\theta_{PD}^2 + 0.0001\theta_{PD} + 0.1383 \quad \text{(Eq. 2.1)}$$

$$r_{PD,left\ CL} = -0.000008\theta_{PD}^2 - 0.0001\theta_{PD} + 0.0633 \quad \text{(Eq. 2.2)}$$

$$r_{PD,right\ CL} = -0.000008\theta_{PD}^2 + 0.0001\theta_{PD} + 0.0633 \quad \text{(Eq. 2.3)}$$

where θ_{PD} is the angular position about the pivot disk axis.

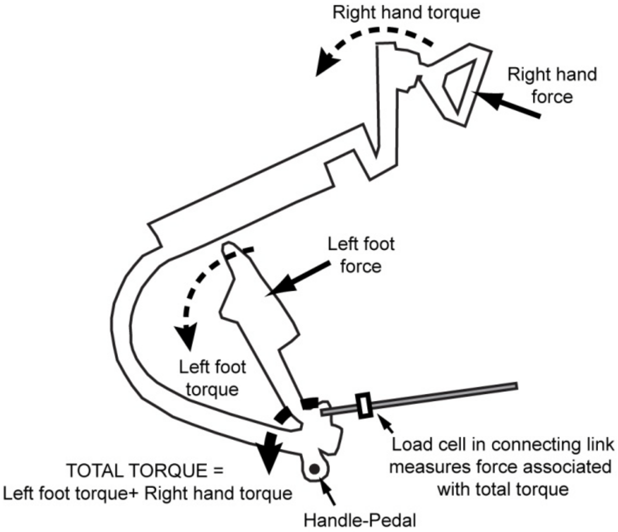

Figure 2.3 Schematic of the sum of the moments about the handle-pedal unit axis of rotation for the force measurement system.

Software

The primary objective of the computer-controlled recumbent stepper was to maintain a constant stepping position profile. Subjects could then exert maximal effort while stepping at a constant frequency. Because all subjects stepped at the same frequency, we could then compare muscle activation without the confounding factor of variable stepping frequency.

RT-Lab and Simulink

RT-LAB 6.2 Solo (Opal-RT Technologies, Quebec, Canada) software was used to perform real-time signal processing. There was a single host computer with a Windows operating system and a single target computer with a QNX operating system. Custom programs were created using Simulink (The Mathworks, Inc., Natick, MA) on the host computer and then compiled into a C based program on the target computer. The target computer was fully devoted to running only real-time processes when the program was running. The host computer with the Windows operating system provided users with a user-friendly interface to control model parameters or view real-time data. The two computers communicated through an Ethernet cable. A Sensoray 626 data acquisition board communicated hardware analog input signals to the real-time running target computer and motor command signals to the motor amplifier.

Control Design

A proportional-integral-derivative (PID) controller was designed to minimize error between a desired stepping angular profile and measured angular data from the encoder. The advantage of designing a custom PID controller in RT-LAB rather than using the motor software's position or analog speed controller was better ability to tune the control parameters and improved performance. Initial attempts to use the motor's software position controllers resulted in choppy movements. For the custom controller, we estimated the system's plant to be

$$P = \frac{1}{s(ms+b)} \qquad \text{(Eq. 2.4)}$$

with m = 15e-6 and b = 5e-6. We used the control system toolbox features of MATLAB to design several PD controllers and then tested each controller on the recumbent stepping system. To improve performance, we added an integral term for better disturbance rejection. The best initial position for a smooth start to the stepping motion was with the handles and pedals balanced in the middle of the stepping range of motion. We implemented the controller that produced the smoothest stepping motion for a target stepping frequency of 75 BPM, our desired stepping frequency.

Custom Operation Modes

The customized control program developed for the recumbent stepper had two primary modes: a) a stepping mode that followed a specified sinusoidal position profile and b) a static mode that resisted movement from an initial starting position. Additionally, the program could collect force and position measurements without the motor enabled.

<u>Stepping mode:</u> The controller generated the appropriate motor torque command signal to maintain the desired stepping position profile. The starting position of the stepper was set to be in the middle of the stepping range of motion. To ensure a smooth start up, the amplitude of the stepping position sine wave was gradually increased until full range of motion was reached, approximately 10 seconds after starting the program. The controller could operate at a range of stepping frequencies from 30-150 BPM. For experiments in this dissertation, the desired stepping position profile was a sine wave with a frequency of 0.625 Hz to provide a stepping frequency of 75 BPM. This stepping frequency corresponds approximately to an average normal walking speed of 1.2 m/s. If the subject exerted forces that would result in a stepping frequency faster than the desired 75 BPM, the motor would output a greater torque to maintain the desired stepping profile. Thus, subjects encounter greater resistance when they stepped with greater effort.

Static mode: The controller generated the appropriate motor torque command signal to resist any movement. A reference signal of zero was inputted to the controller. The static position was set to the initial position of the system when the controller was activated. Thus, any position of the devices handles and pedals could be held statically.

Safety Features

There were several safety measures implemented to ensure subject safety. The primary safety feature was an emergency stop based on a magnetic reed switch. Whenever the two magnetic halves of the switch were separated, the motor was disabled. This type of switch functions like the safety stops often found on treadmills. The experimenter had easy access to one of these emergency switches on the computer cart while the subject had two available switches on the handles. There were also rubber stoppers in the recumbent stepper that limited the maximum range of motion the handles and pedals could travel. Because the seat was adjustable, we could choose a seat position such that the user's knees were always flexed and prevent any possible occurrence of the knee being fully extended in a locked out position. Foam padding protected subjects from any edges that the subject might accidently hit. A plastic case around the belt drive also shielded subjects and equipment from the moving sprockets. Additionally, if the motor were to drive the stepper faster than a predetermined velocity limit, the control program would output a motor command signal of zero volts corresponding to zero torque until the program was reset.

There were also saturation limits implemented within the control program to prevent the motor command signal from exceeding the motor's maximal output.

System Performance

Validation of Force Measurement System

The force measurement system adequately measured the forces applied at the hands and feet. We validated the system using an analog force measuring scale to apply known forces to the handles and pedals while the system was static. The left handle load cell measured forces of 62, 134, and 207 N when a pushing force of 45, 134, and 223 N (10, 30, 50 lbs), respectively, was applied (Figure 2.4A). The right connecting link which measured the total force of the left handle and right pedal also captured left handle forces. These forces scaled by a factor of 6.7, which was similar to the ratio of the handle moment arm to the connecting link moment arm, ~7.0. The right handle and left connecting link load cells did not measure significant forces in this loading condition. Using the sum of the moments, we calculated right foot forces of 200, 326, and 445 N when foot forces of 223, 356, and 490 N (50, 80, 110 lbs) were applied, respectively (Figure 2.4B). The applied pedal force dominated the force measured in the right connecting link. The left handle and left connecting link load cells did not measure significant forces. Lastly, when we applied a 90 N (20 lb) force on the right handle and a 223 N (50 lb) force on the left pedal, the right handle-left pedal connecting link measured both the handle and pedal forces (Figure 2.5).

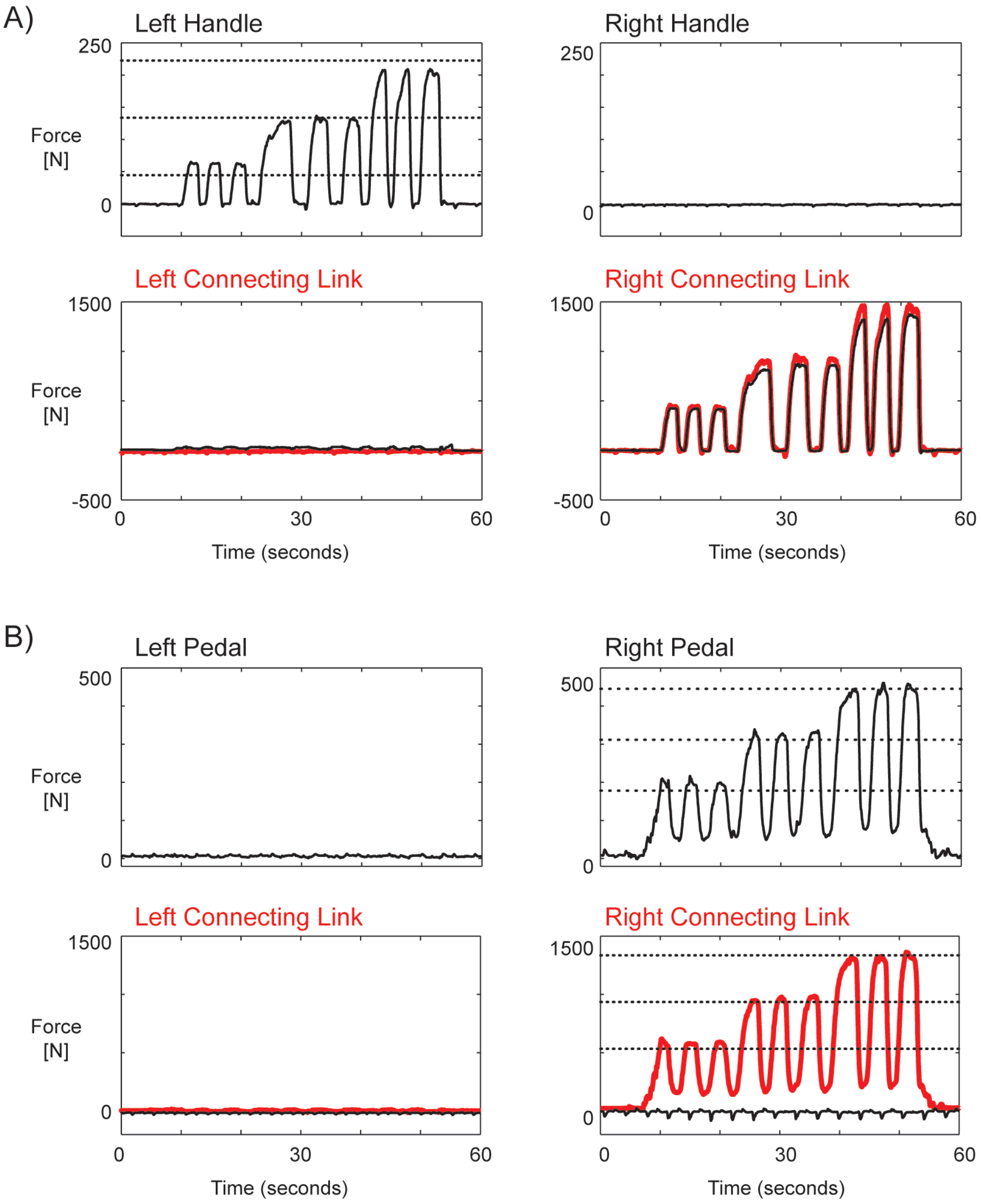

Figure 2.4 A) Example validation of handle load cells. Forces of 45, 134, and 223 N were applied to the only the left handle. The right connecting link load cell measured (in red) the scaled handle force accurately (black). B) Example validation of pedal force calculation (black). Forces of 223, 356, and 490 N were applied to the only the right pedal. Dotted lines are the known applied forces.

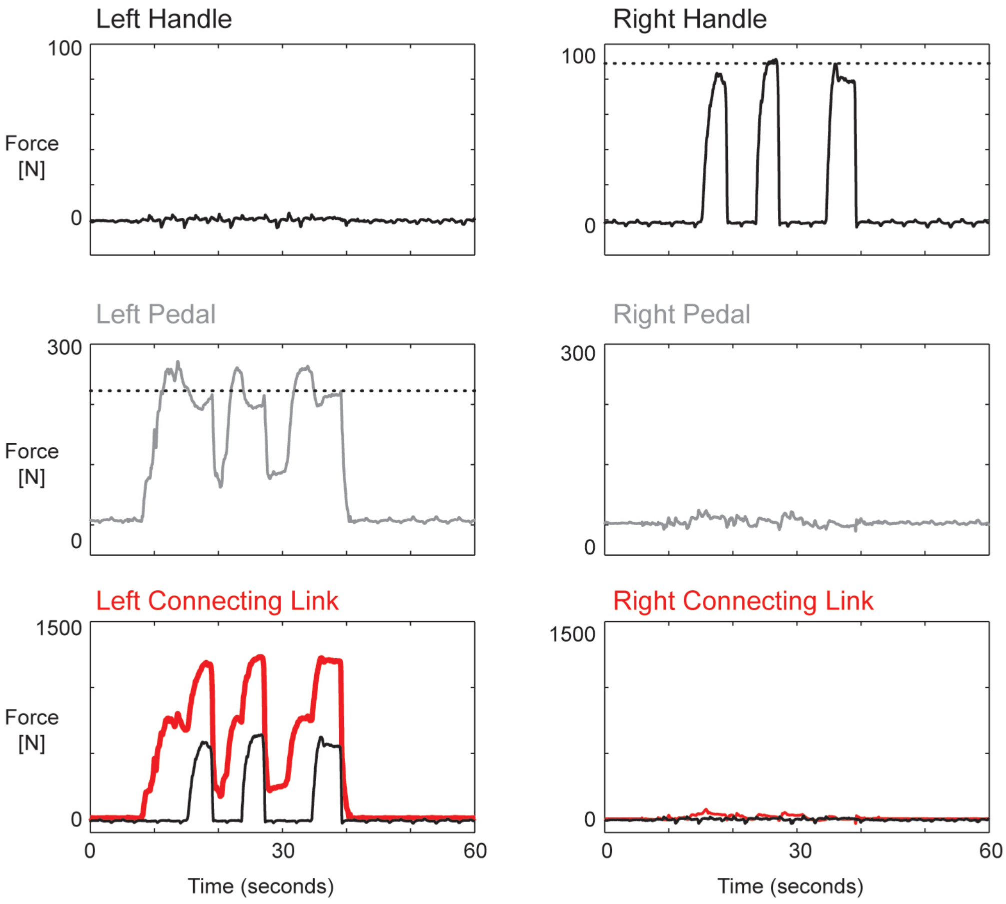

Figure 2.5 Validation of summation of torques were accurately measured by the system's load cells in a static case. In the left connecting link figure, red is the measured force of the connecting link. Black is the scaled right handle force. The left pedal force calculated from the difference between the left connecting link and right handle torques is in grey. Dotted lines equal known applied forces of 90 N for the handle and 223 N for the left pedal.

Stepping Mode

The system was able to produce appropriate torques to maintain a smooth constant stepping motion when users drove the stepping motion (Figure 2.6). The largest position errors occurred when subjects exerted maximal effort using their arms and legs. The average peak error was 10 ± 3 % (mean ± standard deviation) of the stepping range of motion and the average error over the stepping cycle was 5.7 ± 1.7%. Even though the errors increased with greater subject effort, the actual stepping frequency was within < 1% of the target stepping frequency. The system could drive the stepping motion at a range of frequencies (Figure 2.7). For stepping frequencies of 30, 60, 75, 90, and 120 BPM, the root mean squared position error increased from 0.375, 0.59, 0.723, 0.836, to 1.170 percent of the range of motion, respectively.

Static mode

The system was able to produce appropriate torques to maintain a static position (Figure 2.8). Ten healthy individuals applied maximal effort forces with the system in static mode. The mean position error was -0.26% of the stepping range of motion. The group averaged maximum mean left handle force, right handle force, left pedal force, and right pedal force for a 500 millisecond duration were 274, 302, 1252, 1493 N, respectively.

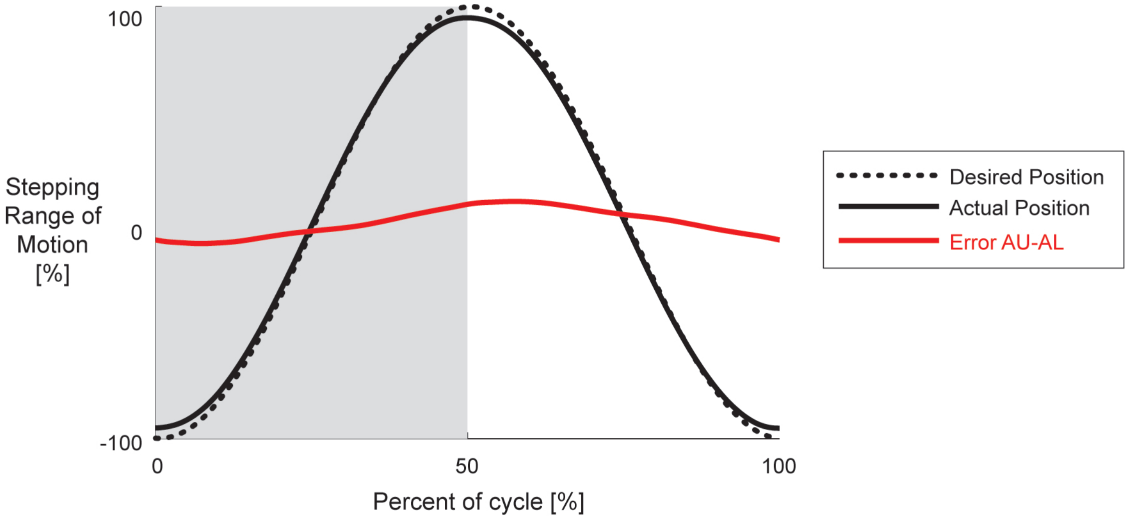

Figure 2.6 Stepping mode performance. Average position error during a maximal effort arms and legs stepping condition (AU-AL) for 16 neurologically intact subjects.

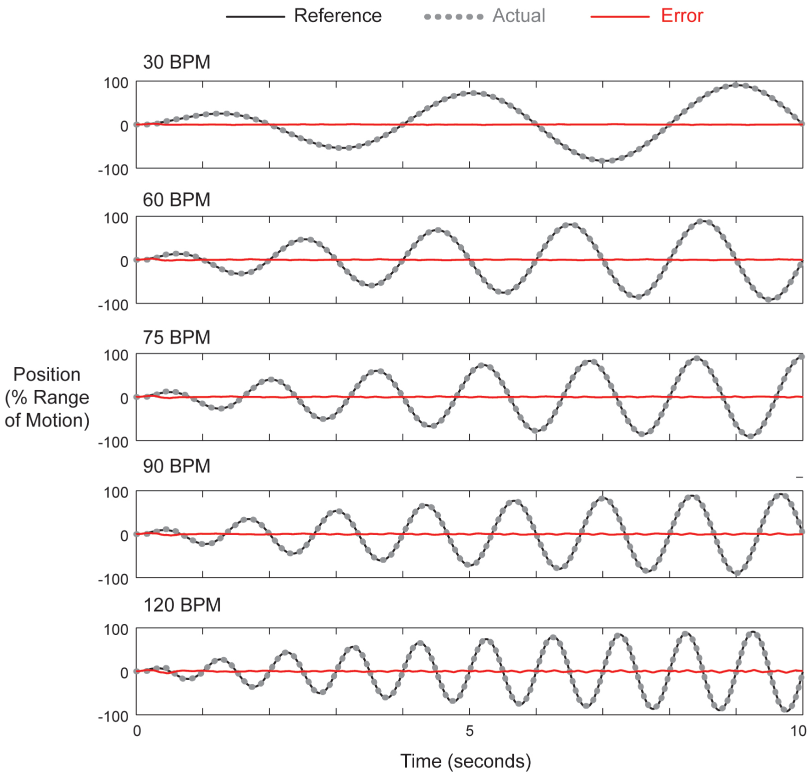

Figure 2.7 Position data for motor driven stepping at 30, 60, 75, 90, and 120 BPM. The error was small, < 1.2% of the range of motion.

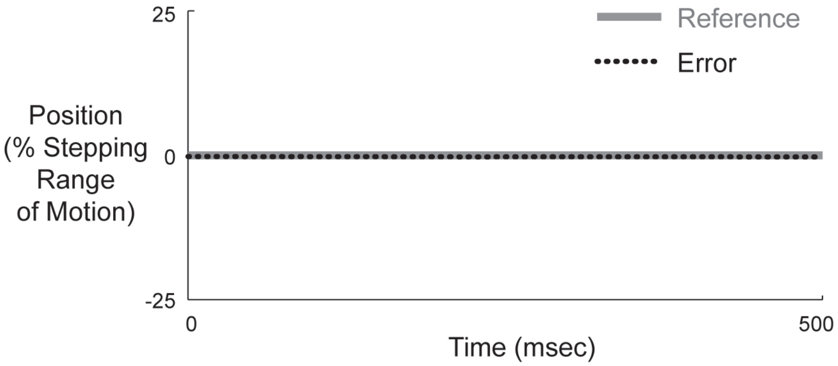

Figure 2.8 Static mode performance.

References

Stoloff RH, Zehr EP and Ferris DP. Recumbent stepping has similar but simpler neural control compared to walking. Exp Brain Res 2007; 178: 427-438

CHAPTER 3

NEURAL COUPLING BETWEEN UPPER AND LOWER LIMBS DURING RECUMBENT STEPPING IN NEUROLOGICALLY INTACT INDIVIDUALS

Abstract

During gait rehabilitation, therapists or robotic devices often supply physical assistance to a patient’s lower limbs to aid stepping. The expensive equipment and intensive manual labor required for these therapies limit their availability to patients. One alternative solution is to design devices where patients could use their upper limbs to provide physical assistance to their lower limbs (i.e. self-assistance). To explore potential neural effects of coupling upper and lower limbs, we investigated neuromuscular recruitment during self-driven and externally-driven lower limb motion. Healthy subjects exercised on a recumbent stepper using different combinations of upper and lower limb exertions. The recumbent stepper mechanically coupled the upper and lower limbs, allowing users to drive the stepping motion with upper and/or lower limbs. We instructed subjects to step with: 1) active upper and lower limbs at an easy resistance level (Active Arms & Legs); 2) active upper limbs and relaxed lower limbs at easy, medium, and hard resistance levels (Self-Driven); and 3) relaxed upper and lower limbs while another person drove the stepping motion

(Externally-Driven). We recorded surface electromyography (EMG) from six lower limb muscles. Self-Driven EMG amplitudes were always higher than Externally-Driven EMG amplitudes (ANOVA $p < 0.05$). As resistance and upper limb exertion increased, Self-Driven EMG amplitudes also increased. EMG bursts during Self-Driven and Active Arms & Legs stepping occurred at similar times. These results indicate that active upper limb movement increases neuromuscular activation of the lower limbs during cyclic stepping motions. Neurologically impaired humans that actively engage their upper limbs during gait rehabilitation may increase neuromuscular activation and enhance activity-dependent plasticity.

Introduction

The most promising gait rehabilitation therapy currently available for individuals that have experienced stroke or spinal cord injury is manually-assisted locomotor training (Barbeau, Norman et al. 1998; Wernig, Nanassy et al. 1999; Harkema 2001). This therapy uses a harness to help support the body weight of patients and manual assistance to help patients practice stepping on a treadmill. Multiple therapists supply manual assistance to the patients' lower limbs, promoting normal stepping kinematics. The task-specific motor practice improves gait control and functional ability. More recently, a number of research groups have developed and begun testing robotic devices for providing physical assistance during locomotor training (Hesse and Uhlenbrock 2000; Colombo, Wirz et al. 2001; Reinkensmeyer, Lum et al. 2002).

A drawback to both manually-assisted and robotic locomotor training is that patients may allow the external assistance to do most of the mechanical work, becoming less active during training. For motor learning and recovery to occur, the patient must provide sufficient effort to promote activity-dependent plasticity (Muir and Steeves 1997; Wolpaw and Tennissen 2001). It is obvious that to maximize activity-dependent plasticity, the patient must be as active as possible during his/her therapy. Encouraging patients to be active during therapy increases neuromuscular recruitment and should therefore accelerate motor recovery. Ideally, the amount and timing of physical assistance should complement the subject's exertion, assisting the motion but not dominating it. Physical therapy methods that rely on external-assistance may cause patients to fight the assistance or become less active. Both situations are undesirable.

One way to minimize inappropriately-timed assistance and/or increase patient activity is to put the patient in control of the physical assistance. This would encourage patients to be more active and allow them to practice stepping without the need for constant therapist intervention. During gait rehabilitation, patients could use their upper limbs to assist their lower limbs.

Self-assistance (i.e. using upper limbs to assist lower limbs) could potentially be beneficial during gait rehabilitation due to inherent interlimb neural coupling (Dietz 2002; Zehr and Duysens In Press). There are neural connections in the spinal cords of cats that coordinate muscle activation between the forelimbs and hindlimbs (Miller, Reitsma et al. 1973; Miller, Van Der Burg et al. 1975). Although similar functional connections in humans have not been irrefutably proven, humans do adopt phase-locked coordination patterns between their upper and lower limbs during many locomotor tasks such as walking, creeping, and swimming (Wannier, Bastiaanse et al. 2001). Humans also demonstrate neural coupling in reflex responses between upper and lower limbs during walking (Dietz, Fouad et al. 2001; Haridas and Zehr 2003; Zehr, Collins et al. 2003; Frigon, Collins et al. 2004). Lastly, anecdotal evidence suggests that reciprocal arm swing can help to initiate lower limb muscle activation during stepping in subjects with incomplete spinal cord injury (Behrman and Harkema 2000). These observations support the premise that upper limb neuromuscular activation may affect lower limb neuromuscular activation during cyclic stepping movements.

The purpose of this study was to determine if evidence of neural coupling between the upper limbs and lower limbs exists in healthy subjects during a simplified stepping task. To constrain movement kinematics, we studied subjects as they exercised on a recumbent stepper that mechanically coupled upper and lower limb motion. We compared muscle activation during self-driven and externally-driven stepping motions. Self-driven refers to an individual using only his/her upper limbs to drive his/her relaxed lower limbs through the stepping motion. Externally-driven refers to a separate individual driving the subject’s relaxed upper and lower limbs through the stepping motion. We hypothesized that self-driven stepping motion will result in greater lower limb muscle activity compared to externally-driven stepping motion. We based this hypothesis on evidence that the upper and lower limbs of humans appear to be neurally coupled during locomotor movements (Behrman and Harkema 2000; Dietz, Fouad et al. 2001; Wannier, Bastiaanse et al. 2001; Dietz 2002; Haridas and Zehr 2003; Zehr, Collins et al. 2003; Frigon, Collins et al. 2004; Zehr and Duysens In Press).

Methods

Subjects

Twenty-four healthy subjects (14 male and 10 female; age range 19-29 years) participated in this study. The University of Michigan Medical School Institutional Review Board granted approval for this project and all subjects gave informed written consent.

Recumbent Stepper

The NuStep recumbent stepper (TRS 4000, NuStep, Inc. Ann Arbor, MI) is a commercially available exercise machine that is a hybrid between a recumbent bicycle and a stair stepper. It has two handles and two pedals that are all coupled to one another, allowing users to exercise with upper and/or lower limbs (Figure 3.1). The right handle and left foot pedal move together, as does the left handle and right foot pedal. The contralateral handle-pedal pairs are 180° out of phase with each other so that when the right upper limb and left lower limb are fully extended, the left upper limb and right lower limb are fully flexed. This mechanical coupling results in a simplified one-degree of freedom stepping motion that preserves normal walking interlimb phase relationships. The recumbent stepper also has ten unitless levels of resistance, created via an eddy current disk brake. A mechanical lever allows the user to move an array of magnets closer and farther from the spinning conductive disk, thus increasing or decreasing, respectively, the resistive forces.

Figure 3.1 NuStep TRS 4000 recumbent stepper (NuStep Inc., Ann Arbor, MI).

General Procedure

Subjects adjusted the stepper’s handle and seat positions so that their knees did not reach full knee extension. Velcro straps secured the subject’s feet to the stepper’s pedals and the subject’s torso to the stepper’s seat. A digital metronome set to a frequency of 1.25 Hz (75 beats per minute) helped subjects maintain a constant stepping frequency. We recorded electromyography (EMG) from six muscles on each lower limb (Konigsberg Instruments, Inc., Pasadena, CA). We measured the pedal force for each foot during stepping using single-axis compression load cells (LCWD-1000, Omegadyne, Inc., Sunbury, OH). We also measured joint angles using electrogoniometers (Biometrics, Ltd., Ladysmith, VA). All subjects were given time to practice stepping using each combination of upper and lower limb exertions. For each trial, we collected data for ten seconds after subjects verbally confirmed that they were comfortable with the test condition. We recorded two trials for each test condition and randomized trial order for each subject to minimize potential learning effects. Subjects also rested for approximately twenty seconds between trials and had the option to rest longer.

Experimental Design

We conducted two separate experiments. In the first experiment, the upper and lower limb motions were mechanically coupled as dictated by the stepper's design. In the second experiment, we used two recumbent steppers to test a similar protocol but with the upper and lower limb kinetics decoupled. In this second experiment, we placed one recumbent stepper behind another and modified the front stepper with long handle extensions (Figure 3.2). This allowed subjects to drive the front stepper with their upper limbs while sitting in the back stepper. Decoupling the upper and lower limb kinetics in this manner prevented subjects from pushing with their lower limbs to lessen the work performed by the upper limbs.

<u>Experiment 1:</u> Subjects (n=20) stepped using four different combinations of upper and lower limb exertions. We classified these exertions as "active" and "passive" in reference to the subject's conscious intent. There was one condition where subjects stepped using both their upper and lower limbs (**Active Arms &**

Legs). This condition provided us with information about the normal timing of lower limb muscle activation during active recumbent stepping. There were three conditions where subjects attempted to totally relax their lower limbs (i.e. passive lower limbs). For the simplest passive condition, subjects rested their hands on their laps as another person drove their lower limbs through the stepping motion (**Externally-Driven**). For a second passive condition, subjects' hands and feet were fixed to the handles and pedals using Velcro mitts and straps, respectively, as another person drove their relaxed upper and lower limbs through the stepping motion (**Externally-Driven Arms & Legs**). We tested this condition to determine if passive movement of the upper limbs made a difference in the results. For the last passive condition, subjects actively used their arms to drive their relaxed lower limbs through the stepping motion (**Self-Driven)**.

We examined three levels of resistance for the Self-Driven passive condition: easy, medium, and hard. These resistance levels were determined prior to testing for each subject. Each subject's hard resistance level corresponded to the maximum resistance that he/she could maintain using just his/her arms moving at the designated frequency for at least 20 seconds. The medium resistance level corresponded to ~60% of the subject's hard resistance level. The easy resistance level was the lowest resistance setting on the recumbent stepper. Because the level of resistance was not important for the externally-driven conditions, the resistance was set at easy for all externally-driven trials.

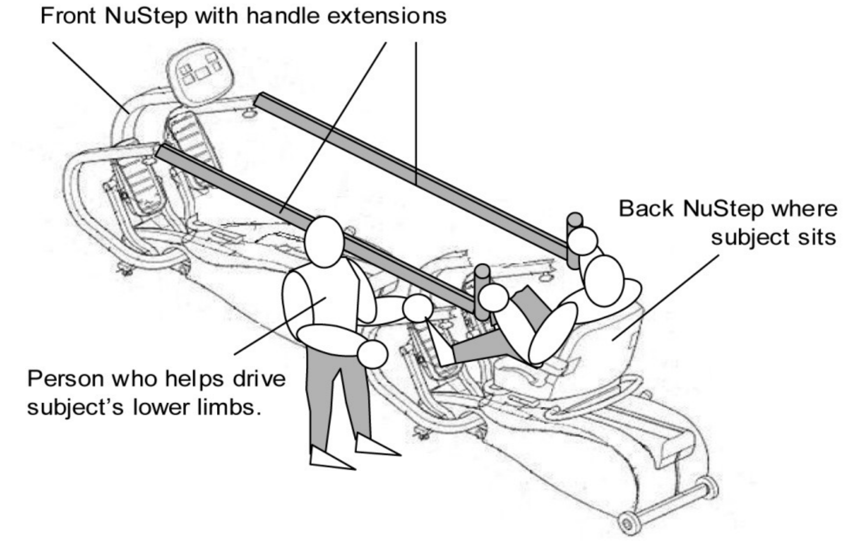

Figure 3.2 Schematic of the kinetically decoupled setup used in experiment 2. Subjects used the handle extensions to drive the front NuStep. Because subjects were instructed to relax their lower limbs, another person had to drive the subject's lower limbs through the stepping motion. In this setup, subjects could not use their lower limbs to ease the upper limb task (i.e. cheat). Modified from (Hildebrandt, Sutton et al. 2003).

Experiment 2: The main difference between this experiment and the first experiment was that a second recumbent stepper was used to decouple the kinetics of the pedals and handles (Figure 3.2). We tested four healthy male subjects under three conditions: 1) Externally-Driven, 2) Upper Limb Exertion (easy), and 3) Upper Limb Exertion (hard). In the Externally-Driven condition, subjects were instructed to attempt to totally relax their upper and lower limbs, as other people drove the subject's upper and lower limbs through the range of motion at the designated frequency. In the Upper Limb Exertion conditions, subjects were instructed to actively use their upper limbs to drive the front stepper at the designated frequency while relaxing their lower limbs as another person drove their legs through the motion. We instructed the person driving the subject's lower limbs to match the subject's upper limb movement. For the Upper

Limb Exertion conditions, we examined two resistance levels, easy and hard. These resistance levels were determined prior to testing for each subject. Each subject's hard resistance level corresponded to the maximum resistance that he/she could step at using just his/her arms while maintaining the designated frequency for at least 20 seconds.

Data Acquisition and Analysis

In the first experiment, we collected electromyography (EMG), joint angle (hip, knee, and ankle), and pedal force data during each trial. In the second experiment, we collected EMG and joint angle (knee and elbow) data during each trial. For both experiments, a personal computer sampled each data channel at 1000 Hz via an analog to digital board.

Electromyography. For experiments 1 and 2, we measured muscle activity from six muscles on each lower limb (vastus lateralis, VL; vastus medialis, VM; medial hamstrings, MH; medial gastrocnemius, MG; tibialis anterior, TA; soleus, SO muscles) using surface electrodes (Konigsberg Instruments, Inc., Pasadena, CA). For each electrode site, we shaved and cleaned the area with alcohol. We then placed EMG surface electrodes (diameter 1.1 cm, inter-electrode distance 3.5 cm) in the middle of the muscle belly, along its long axis. For the soleus, however, we placed the electrodes over the lateral distal third of the muscle belly rather than the center to avoid potential cross-talk from the gastrocnemius. We then visually examined each EMG signal for noise and cross-talk (Winter, Fuglevand et al. 1994). We placed tape over all electrodes and covered the subject's lower limbs with elastic stockings to minimize mechanical artifacts.

To compare muscle activation across conditions, we calculated the averaged normalized root-mean-square (RMS) EMG amplitude for each condition and muscle for flexion and extension phases. We processed EMG with a fourth order high-pass Butterworth filter with zero phase shift (cut off frequency of 20 Hz) and then full wave rectified the signals. For each phase, condition, muscle, and subject, we averaged RMS amplitudes for six step cycles. We then normalized the averaged RMS amplitudes to the maximum RMS amplitude calculated for each muscle across conditions for each subject to reduce intersubject variability (Yang and Winter 1984). To compare EMG timing across conditions, we used cross-correlation analysis to calculate R-values and lag times.

<u>Joint Angles</u>. For experiment 1, we measured joint angles of the hip, knee, and ankle on both lower limbs using twin-axis electrogoniometers (Biometrics, Ltd., Ladysmith, VA), placed along the sagittal plane. For experiment 2, we measured knee joint angles on both lower limbs and elbow joint angles on both upper limbs using twin-axis electrogoniometers (Biometrics, Ltd., Ladysmith, VA), placed along the sagittal plane. Electrogoniometers were zeroed as subjects stood in a neutral position. From these data, we identified the beginning and end of step cycles. We also used goniometer data to define flexion and extension phases.

<u>Pedal Forces</u>. For experiment 1, we measured the pedal force for each foot during stepping using a set of three compression load cells (LCWD-1000, Omegadyne, Inc., Sunbury, OH). These load cells were coplanar, positioned in a

tripod formation between two custom shaped aluminum plates for each foot. The summation of the three load cells for each foot provided a measure of the force between the foot and pedal. Before each data collection, we calibrated each load cell within the aluminum plates with known weights. We summed the three load cell measurements for each foot plate and then filtered the data with a fourth order low-pass Butterworth filter with zero phase shift (cut off frequency of 6 Hz). We calculated the mean forces during lower limb flexion and extension for six step cycles per condition. We then normalized the forces to the maximum mean force across conditions for each subject. Lastly, we averaged the forces across all the subjects for the flexion and extension phases. We were only able to collect pedal forces on ten subjects.

Statistical Analyses

For each experiment, we used a repeated measures analysis of variance (ANOVA) to determine if there were significant differences across conditions. For the ANOVA analyses of EMG in the six muscles, we set $p < 0.0083$ for the significance level (Bonferroni correction). When the ANOVA indicated a significant difference, we used a Tukey Honestly Significant Difference (THSD) post-hoc test to determine which conditions were significantly different ($p < 0.05$).

Results

Experiment 1: One NuStep with Upper and Lower Limb Kinetics Coupled

Self-Driven stepping motion resulted in greater lower limb muscle activation compared to Externally-Driven stepping motion. Externally-Driven

EMG raw data showed little EMG activity for all six muscles while distinctive rhythmic EMG bursts were visible in Self-Driven (hard) EMG raw data (Figure 3.3). Group averaged EMG profiles indicated that lower limb muscle activation for the Self-Driven (hard) condition had similar patterns compared to the Active Arms & Legs condition (Figure 3.4). Onset of the EMG bursts during Self-Driven (hard) and Active Arms & Legs conditions occurred at nearly the same time in the step cycle. Lag times at maximum correlation between Self-Driven (hard) and Active Arms & Legs were close to zero (Table 3.1). This confirmed that Self-Driven (hard) and Active Arms & Legs EMG bursts had similar timing. Cross-correlation results comparing Self-Driven (medium) and Self-Driven (easy) to Active Arms & Legs also showed similar timing in muscle activation (not shown).

For all six muscles during both flexion and extension, the normalized EMG amplitudes for the three Self-Driven conditions were greater than the amplitudes for the Externally-Driven and Externally-Driven Arms & Legs conditions (Figure 3.5). Across all six muscles, Self-Driven EMG amplitudes for the flexion phase were approximately 35, 42, and 55% for easy, medium, and hard resistances, respectively. In contrast, Externally-Driven and Externally-Driven Arms & Legs conditions had EMG amplitudes of 30% across all six muscles. Similarly, Self-Driven EMG amplitudes averaged for all six muscles for the extension phase were 38, 46, and 55% for easy, medium, and hard resistances, respectively. Externally-Driven and Externally-Driven Arms & Legs conditions had EMG amplitudes of 32% and 31%, respectively, averaged for all six muscles. Statistical analyses indicated for both flexion and extension phases, that Self-

Driven (hard) and Active Arms & Legs were significantly different (THSD, $p < 0.05$) from Externally-Driven and Externally-Driven Arms & Legs conditions for a majority of the muscles (Figure 3.5).

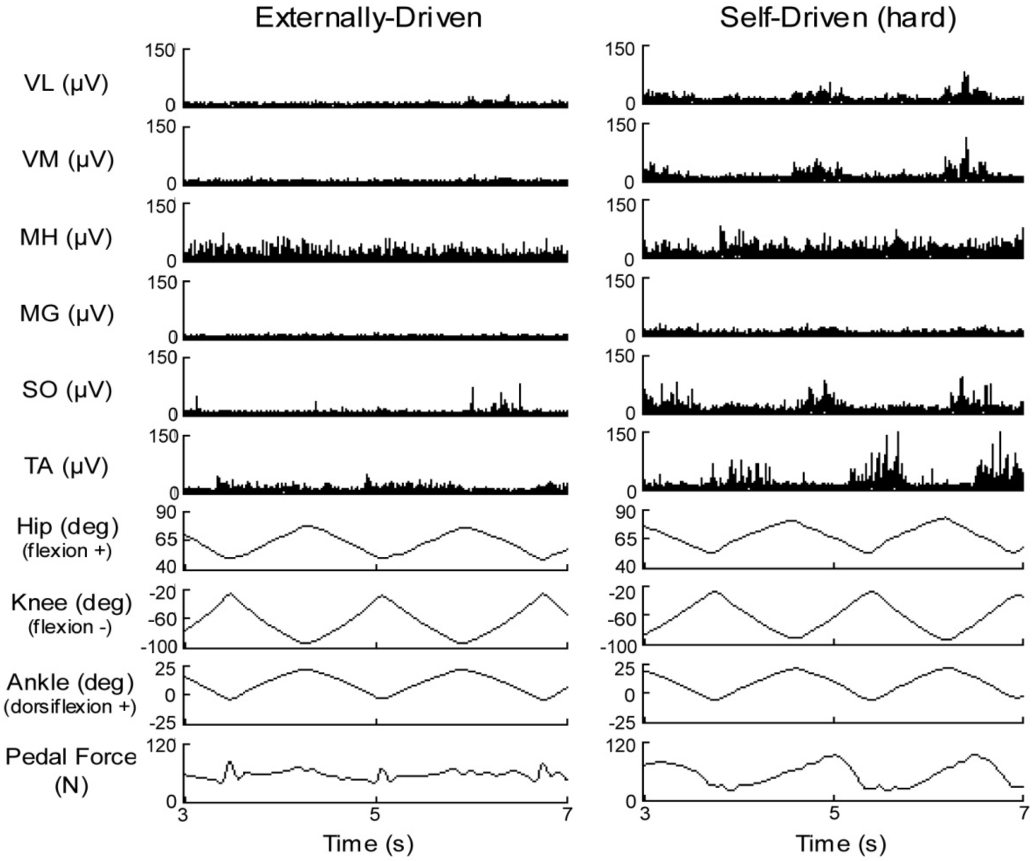

Figure 3.3 Single subject raw EMG, joint angle, and pedal force data for Externally-Driven and Self-Driven (hard) conditions. Self-Driven (hard) EMG has distinct bursts and greater muscle activity compared to Externally-Driven EMG, which has little activity. Joint profiles for the hip, knee, and ankle show that all three joints have a triangular pattern and reach their range of motion endpoints simultaneously.

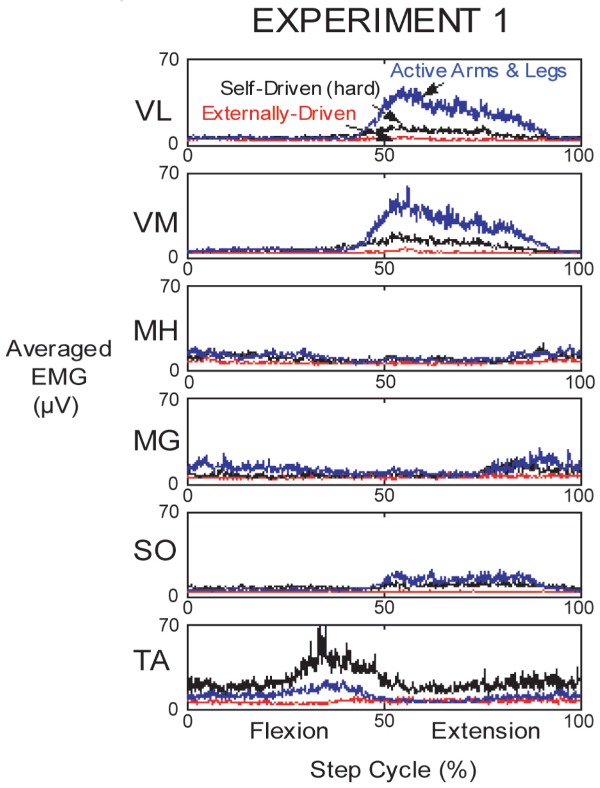

Figure 3.4 Group averaged EMG bursts for Active Arms & Legs, Self-Driven (hard), and Externally-Driven. The timing of the Self-Driven (hard) passive leg EMG patterns is similar to the timing of the active leg EMG patterns in the Active Arms & Legs condition (see Table 1 for more analysis).

Table 1. Self-Driven (hard) vs. Active Arms & Legs EMG Cross-correlation Analysis

Muscle	R	Lag time (% cycle)
VL	0.84 (± 0.10)	-1 (± 11)
VM	0.84 (± 0.09)	-3 (± 14)
MH	0.89 (± 0.06)	4 (± 12)
MG	0.90 (± 0.06)	1 (± 5)
SO	0.90 (± 0.06)	-2 (± 13)
TA	0.88 (± 0.10)	2 (± 14)

Table 3.1 Values are mean (± SD). A positive lag time indicates that Self-Driven (hard) follows Active Arms & Legs. A negative lag time means that Self-Driven (hard) begins before Active Arms & Legs. Mean lag times for all muscles are less than 4% of a step cycle from zero, indicating that Self-Driven (hard) and Active Arms & Legs have similar timing.

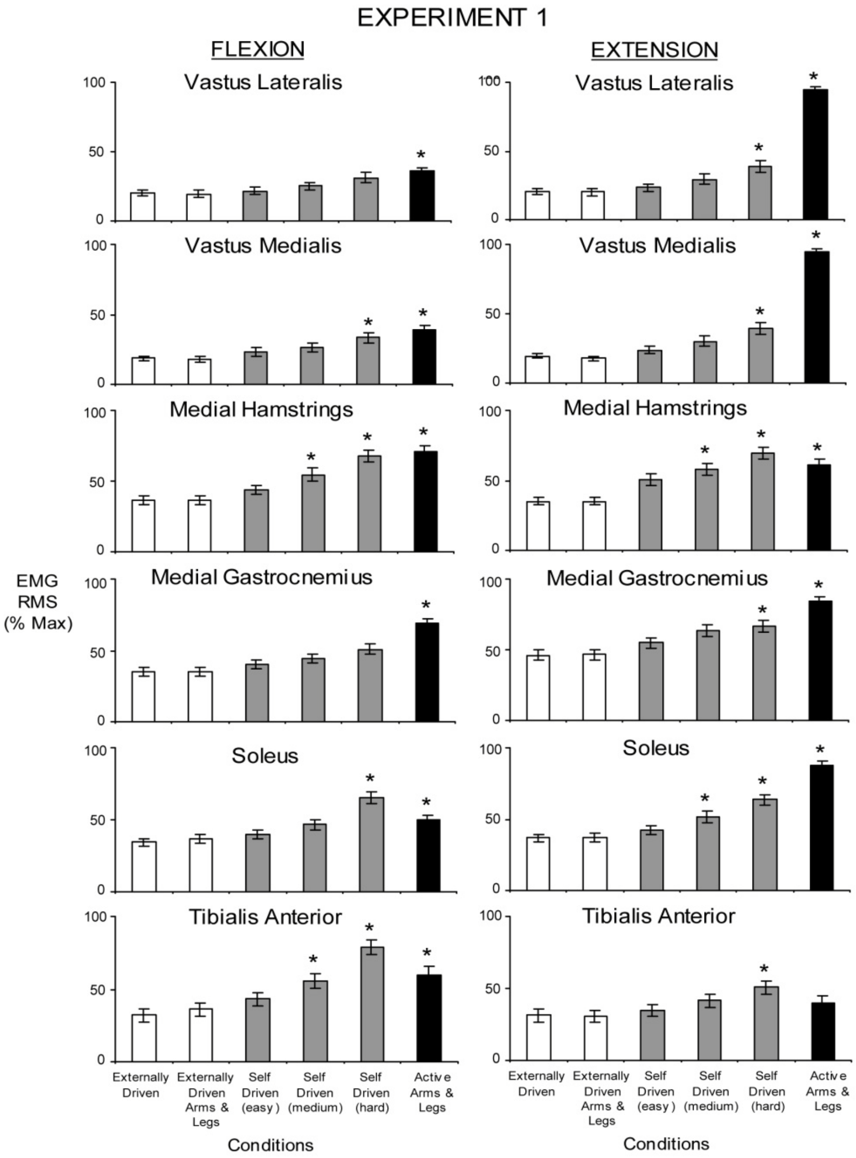

Figure 3.5 Averaged normalized root-mean-square EMG with standard error bars for all subjects for flexion and extension phases. White columns represent externally-driven conditions while gray columns indicate self-driven conditions. Black columns correspond to the active condition. Columns marked with an asterisk (*) indicate that the marked column is significantly different from the Externally-Driven condition on the far left (THSD, $p < 0.05$). For both flexion and extension, Active Arms & Legs and Self-Driven (hard) RMS EMG amplitudes were significantly different from both Externally-Driven conditions for a majority of the muscles (THSD, $p < 0.05$). Externally-Driven and Externally-Driven Arms & Legs RMS EMG amplitudes were not significantly different for any of the six muscles in either phase (THSD, $p > 0.05$).

During Self-Driven stepping, greater upper limb exertion led to greater lower limb muscle activation. Self-Driven (easy), Self-Driven (medium), and Self-Driven (hard) EMG amplitudes increased in a step-wise manner (Figure 3.5). Self-Driven (medium) was not significantly different from Self-Driven (easy) for any of the muscles (THSD, $p > 0.05$). Self-Driven (hard) was significantly different from Self-Driven (easy) for the medial hamstrings, soleus, and tibialis anterior muscles during flexion and for the vastus lateralis, vastus medialis, medial hamstrings, soleus, and tibialis anterior during extension (THSD, $p < 0.05$). Self-Driven (hard) was significantly different from Self-Driven (medium) for the tibialis anterior and soleus muscles, during flexion (THSD, $p < 0.05$).

Pedal force profiles were similar for Self-Driven and Active Arms & Legs stepping (Figure 3.6A). Both conditions had higher peak forces during the extension phase than during the flexion phase, and the two conditions demonstrated similar timing of force increase during the start of the extension phase. In contrast, the Externally-Driven pedal force profile had a different pattern (Figure 3.6A). Overall, the Externally-Driven condition had lower peak forces during the extension phase than during the flexion phase. There was a slight rise in pedal force at the end of extension and the beginning of flexion to decelerate the lower limb. Self-Driven mean flexion pedal forces were 45, 42, and 40% for easy, medium, and hard resistances, respectively (Figure 3.6B). Externally-Driven mean flexion pedal forces were 50% for both conditions (Externally-Driven, Externally-Driven Arms & Legs). For the extension phase, Self-Driven mean pedal forces were 39, 44, and 53% for easy, medium, and hard

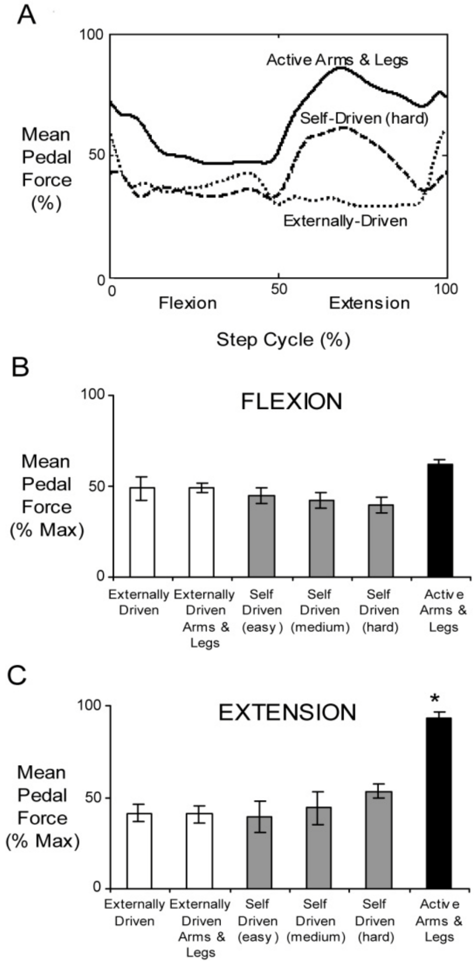

Figure 3.6 A) Mean low-pass filtered (fc = 6 Hz) pedal forces for Active Arms & Legs, Self-Driven (hard), and Externally-Driven conditions. Timing was similar for Self-Driven (hard) and Active Arms & Legs filtered force profiles. The Externally-Driven filtered force profile, however, has a different pattern. B) Averaged normalized mean pedal force for flexion phase. White columns represent externally-driven conditions while gray columns indicate self-driven conditions. Black columns correspond to the active condition. There was no significant difference (THSD, $p > 0.05$) between Externally-Driven and any Self-Driven condition or the Active Arms & Legs condition. However, Self-Driven (medium) and Self-Driven (hard) were both significantly different from Active Arms & Legs. Mean flexion force for Active Arms & Legs stepping was 53 N. C) Averaged normalized mean pedal force for extension phase. The Active Arms & Legs extension force, marked with an asterisk, was the only condition significantly different from Externally-Driven extension force (THSD, $p < 0.05$). There were no significant differences between the three Self-Driven and two Externally-Driven conditions. Mean extension force for Active Arms & Legs stepping was 75 N.

conditions, respectively (Figure 3.6C). Both Externally-Driven and Externally-Driven Arms & Legs mean extension pedal forces were 41%. Self-Driven and

Externally-Driven mean pedal forces were not significantly different from each other for either phase (THSD, $p > 0.05$). Active Arms & Legs mean extension force, 93%, was significantly different from Externally-Driven mean extension force (THSD, $p < 0.05$).

Joint angle data indicated that ranges of motion for the hip, knee, and ankle were similar for each subject across all conditions. Hip, knee, and ankle profiles during recumbent stepping were regular and synchronized, having a triangular pattern (Figure 3.3). The average hip angle excursion for all subjects was 73° to 43° of hip flexion (for all three joints, 0° was standing posture). The average knee angle excursion was 75° to 23° of knee flexion. The average ankle angle excursion was 19° of dorsiflexion to -3° of plantarflexion. There was no significant difference in range of motion between conditions (ANOVA, $p > 0.05$).

Experiment 2: Two NuSteps with Upper and Lower Limb Kinetics Decoupled

Upper Limb Exertion conditions resulted in greater lower limb muscle activation compared to the Externally-Driven condition (Figure 3.7 & Figure 3.8). Group averaged EMG showed that the coupled and decoupled protocols resulted in similar EMG patterns (Figure 3.7). Externally-Driven EMG profiles were fairly constant with no distinct bursts in any of the muscles. Upper Limb Exertion (hard) EMG profiles had distinct EMG bursts for the vastus lateralis, vastus medialis, and tibialis anterior muscles. Both Upper Limb Exertion conditions had greater normalized EMG RMS amplitudes compared to the Externally-Driven condition for both flexion and extension phases (Figure 3.8). Statistical analyses indicated that Upper Limb Exertion (hard) was significantly different (THSD, $p < 0.05$) from

Externally-Driven for a majority of the muscles during both flexion and extension phases.

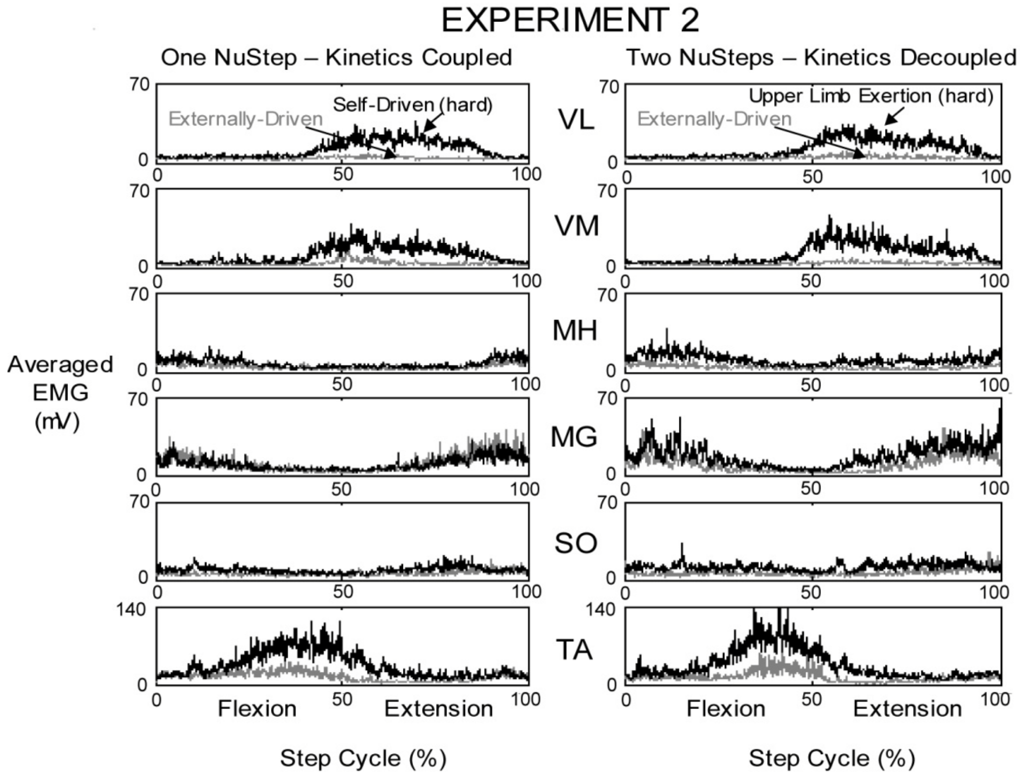

Figure 3.7 Group averaged EMG bursts for Self-Driven (hard) and Externally-Driven in the kinetically coupled setup and Upper Limb Exertion (hard) and Externally-Driven in the kinetically decoupled setup. Both Self-Driven (hard) and Upper Limb Exertion (hard) conditions had greater EMG activity than the Externally-Driven conditions.

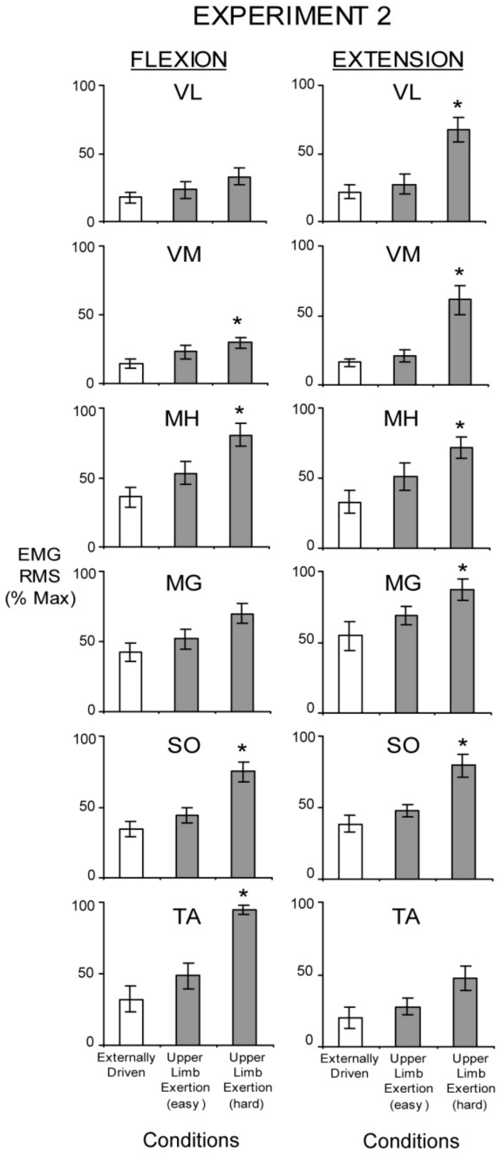

Figure 3.8 Averaged normalized root-mean-square EMG with standard error bars for all subjects in the kinetically decoupled setup with two NuSteps for flexion and extension phases. Columns marked with an asterisk (*) indicate that the marked column is significantly different from the Externally-Driven condition on the far left (THSD, $p < 0.05$). Upper Limb Exertion (hard) RMS EMG amplitudes were significantly different from Externally-Driven condition for a majority of the muscles in either phase (THSD, $p < 0.05$).

Discussion

Our main finding is that rhythmic upper limb activity increases lower limb neuromuscular recruitment when healthy subjects attempt to relax their lower limbs. In experiment 1, Self-Driven conditions had greater EMG amplitudes compared to Externally-Driven and Externally-Driven Arms & Legs conditions. In experiment 2, Upper Limb Exertion conditions had greater EMG amplitudes compared to the Externally-Driven condition. Thus, upper limb activity resulted in greater lower limb muscle activity regardless of whether upper limb and lower limb kinetics were coupled or decoupled. An important aspect of this finding was that lower limb muscle activation during the Self-Driven conditions was dependent on upper limb effort. As resistance level increased for the upper limbs, EMG amplitudes for the lower limb muscles also increased.

At all resistance levels, the timing of the Self-Driven EMG bursts in the lower limbs was similar to the timing of active stepping EMG bursts. Muscles were primarily active during the concentric phase of the stepping motion. For the vastus lateralis, vastus medialis, and soleus, this was the extension phase. For the tibialis anterior, this was the flexion phase. The biarticular medial hamstrings and medial gastrocnemius showed some activation during both flexion and extension phases. The concentric timing of the uniarticular muscles indicates that the increased muscle activation during Self-Driven stepping was probably not a result of stretch reflexes. If the stretch reflexes had caused the muscle activation, the EMG bursts would have occurred during and/or slightly after the muscles were stretched in their eccentric phase.

One potential neural mechanism responsible for lower limb muscle activation during Self-Driven stepping is spinal connections in locomotor neural networks. Humans have spinal connections coordinating left and right lower limbs during stepping (Ferris, Gordon et al. 2004) in a manner similar to cats (Duysens and Pearson 1980). Cats also have spinal connections between cervical and lumbar locomotor networks coordinating forelimb and hindlimb muscle activation patterns (Sherrington 1910; Miller, Van Der Burg et al. 1975; Kato, Murakami et al. 1984). Indirect evidence indicates that humans also coordinate upper limb and lower limb movements during locomotion through spinal connections, reviewed in (Dietz 2002; Zehr and Duysens In Press). Humans demonstrate natural frequency locking between upper limb movement and lower limb movement during walking, crawling, and swimming (Wannier, Bastiaanse et al. 2001). Mechanical and electrical perturbations to the lower limbs result in short latency reflex responses in the upper limbs during walking, but not during standing or sitting (Dietz, Fouad et al. 2001; Haridas and Zehr 2003). Furthermore, near-infrared spectroscopic topography reveals that there is little brain activation in presumed arm areas of primary sensorimotor cortex during human walking (Miyai, Tanabe et al. 2001). In contrast, active arm swinging during standing activated cortical areas not activated during gait (lateral and rostral parts of primary sensorimotor cortex) (Miyai, Tanabe et al. 2001). These findings point to humans having similar spinal interlimb connections as cats and other quadruped vertebrates.

A second potential neural mechanism that could explain our findings is neural cross-talk above the spinal cord level. When humans perform muscle contractions greater than a certain force threshold, unintended muscle activity frequently occurs in other contralateral and ipsilateral muscles (Cernacek 1961;

Dimitrijevic, McKay et al. 1992; Gandevia, Macefield et al. 1993; Armatas, Summers et al. 1994; Zijdewind and Kernell 2001; Aranyi and Rosler 2002). When the unintended muscle activity occurs in contralateral homologous muscles, it has traditionally been referred to as mirror movements or contralateral irradiation. Several observations suggest a cortical origin of the unintended activation, potentially related to a decrease in inhibition along the corpus callosum (Mayston, Harrison et al. 1999; Shinohara, Keenan et al. 2003). Other studies have found evidence for a different type of neural cross-talk that occurs when humans perform rhythmic upper limb movements combined with rhythmic ipsilateral lower limb movements (Baldissera, Cavallari et al. 1982; Kelso and Jeka 1992; Carson, Goodman et al. 1995; Swinnen, Dounskaia et al. 1995), reviewed in (Swinnen 2002). These studies indicate that the nervous system has a natural tendency to prefer in-phase movements of ipsilateral limbs rather than out-of-phase movements.

These observations of supraspinal neural cross-talk do not appear to be relevant to our findings however. The lower limb muscle activation during Self-Driven stepping had a timing pattern similar to active stepping (ipsilaterally out-of-phase). Thus, the unintended lower limb muscle activity did not occur at the same time as ipsilateral upper limb muscle activity. Both of the neural cross-talk forms identified above would be associated with concurrent activation of upper limb and lower limb muscles. Based on the timing of the lower limb muscle activity, it seems likely that the neural signal responsible for activating lower limb motor neurons was filtered through neural networks responsible for active stepping.

The tibialis anterior demonstrated the greatest EMG amplitudes of all the muscles during Self-Driven conditions. The mean tibialis anterior EMG during Self-Driven (hard) was even higher than during the active stepping condition. It is possible that the subjects' strong intent to inhibit lower limb muscle activation may have decreased inhibition onto tibialis anterior motor neurons via reciprocal inhibition from the plantarflexors (Crone, Hultborn et al. 1987; Crone and Nielsen 1994; Petersen, Christensen et al. 1998; Petersen, Morita et al. 1999). This is only speculation, however, and future electrophysiological studies would yield more insight.

A limitation of this study was the necessity to rely on subjects' intent to not use their lower limbs during the Self-Driven conditions. Subjects did not have prior knowledge of the study purpose or hypothesis. We instructed all subjects to completely relax their lower limbs prior to each trial collection. Subjects verbally confirmed that they understood the instructions and did not intentionally use their lower limbs to push the pedals. They may have been tempted to cheat if fatigued, but our protocol limited that possibility because of the short data collection periods and frequent rest breaks. On average, there was also approximately twenty seconds of rest between each fifteen-second trial. All trials were randomized, reducing the probability that subjects would have to work actively for extended periods of time. Furthermore, we analyzed step cycles from the middle of the data collection period, when subjects were most likely not fatigued. Most importantly, the results from experiment 2 indicate that increased lower limb recruitment still occurs with upper limb exertion even when pedals and handles have been kinetically decoupled. Cheating in experiment 2 could not decrease the work performed by the upper limbs. We conclude that any muscle activity during Self-Driven conditions was indeed unintentional.

Regardless of mechanism, the apparent neural coupling between upper limbs and lower limbs during cyclic stepping movements could be useful during rehabilitation. We only tested subjects using one exercise device (i.e. a recumbent stepper), but it seems feasible that the neural coupling effect would also occur during other types of rhythmic upper and lower limb movements (e.g. upper & lower limb cycling). If neurologically impaired subjects demonstrate similar neural coupling, repetitive upper & lower limb motor tasks may help improve muscle coordination compared to lower limb motor tasks alone. The specificity of learning hypothesis (Schmidt and Lee 1999) implies that the upper & lower limb motor task should be as close to possible to normal walking to provide the greatest functional benefit for overground locomotion. However, locomotor neural networks appear to be active during other cyclic lower limb motor tasks such as cycling (Brooke, Cheng et al. 1997; Ting, Raasch et al. 1998; Raasch and Zajac 1999; Ting, Kautz et al. 1999; Ting, Kautz et al. 2000). A recent study on spinally transected rats compared the effects of manually assisted treadmill stepping and mechanically assisted cycling (Bose, Li et al. 2004). The study found that cycling produced similar or better recovery of locomotor function than treadmill stepping (Bose, Li et al. 2004). In addition, Werner and colleagues (Werner, Von Frankenberg et al. 2002) have demonstrated that upright use of an elliptical-type trainer produces improvements in overground walking ability comparable to improvement with manually assisted treadmill stepping. These findings indicate that rhythmic stepping tasks are likely to contribute to gait rehabilitation even if they do not follow exactly the same movement dynamics as walking.

When comparing recumbent stepping to walking, there are some obvious differences between the dynamics of the two motor tasks. First, the hip joint does not hyperextend at the end of the extension phase during recumbent stepping like it does during walking. Second, the bottom of the foot is continually in contact with the pedal during lower limb flexion while recumbent stepping, unlike lower limb flexion while walking. Third, the ankle and knee joints only flex and extend once during a complete cycle in recumbent stepping but flex and extend twice during each cycle in walking. Fourth, recumbent stepping uses a reclined posture instead of the vertical posture characteristic to walking. These four differences between recumbent stepping and walking clearly produce discrepancies in sensory feedback. In particular, the lack of hip flexor muscle stretch at the end of lower limb extension and the presence of cutaneous pressure during lower limb flexion are potentially critical to gait rehabilitation (Sherrington 1910; Grillner and Rossignol 1978; Muir and Steeves 1995; Wernig, Muller et al. 1995; Muir and Steeves 1997; Bouyer and Rossignol 2003; Dietz and Harkema 2004; Ferris, Gordon et al. 2004; Rossignol, Bouyer et al. 2004). Future research would be needed to determine how critical these discrepancies would be on neurorehabilitation.

There are some benefits to recumbent stepping that partially offset limitations in task specificity and make it appealing as an alternative and/or supplemental gait rehabilitation therapy. Self-assisted recumbent stepping offers a way to give patients control over the amount and timing of physical assistance as they practice stepping. Currently, locomotor training for gait rehabilitation relies on external-assistance from therapists or robots to induce stepping in neurologically impaired patients (Barbeau, Norman et al. 1998; Wernig, Nanassy et al. 1999; Hesse and Uhlenbrock 2000; Colombo, Wirz et al. 2001; Harkema 2001; Reinkensmeyer, Lum et al. 2002). Self-assisted gait rehabilitation devices eliminate these expensive manual labor costs. Additionally, self-assisted devices may provide more appropriately timed and scaled physical assistance for stepping. Another advantage of recumbent steppers or other future self-assisted gait rehabilitation devices is that they offer neurologically impaired individuals a means to practice stepping at home. Because individuals could practice whenever they choose, they could complete more training sessions compared to therapies that are only available at clinics. Performing a stepping task that is only ‘50% similar to walking’ daily may be more beneficial to gait rehabilitation than performing a stepping task that is ‘95% similar to walking’ once a week. More generally, it appears that self-assisted stepping devices of some design may be able to capitalize on neural coupling between the upper and lower limbs during rhythmic locomotor-like tasks.

Acknowledgments

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CHAPTER 4

UPPER AND LOWER LIMB MUSCLE ACTIVATION IS BIDIRECTIONALLY AND IPSILATERALLY COUPLED

Abstract

Purpose: There are neural connections between the upper and lower limbs of humans that enable muscle activation in one limb pair (upper or lower) to modulate muscle activation in the other limb pair (lower or upper, respectively). The aims of this study were to extend previous findings regarding submaximal exercise to maximal effort exercise and determine if there is an ipsilateral or contralateral bias to the neural coupling during a rhythmic locomotor-like task.

Methods: We measured upper and lower limb muscle activity, joint kinematics, and limb forces in neurologically intact subjects (n = 16) as they performed recumbent stepping using different combinations of upper and lower limb efforts.

Results: We found increased muscle activation in passive lower limbs during active upper limb effort compared to passive upper limb effort. Likewise, increased muscle activation in passive upper limbs occurred during active lower limb effort compared to passive lower limb effort, suggesting a bidirectional effect. Maximal muscle activation in the active lower limbs was not different between conditions with active upper limb effort and conditions with passive upper limb movement. Similarly, maximal muscle activation in the active upper limbs was not different between conditions with active lower limb effort and conditions with passive lower limb movement. Further comparisons revealed that neural coupling was primarily from active upper limb muscles to passive ipsilateral lower limb muscles.

Conclusion: These findings indicate that interlimb neural coupling affects muscle recruitment during maximal effort upper and lower limb rhythmic exercise and provide insight into the architecture of the neural coupling.

Introduction

Humans naturally couple limb movements. It is easier to move two limbs in the same direction rather than in opposite directions or when using homologous muscles rather than non-homologous muscles (Baldissera, Cavallari et al. 1982; Swinnen 2002; Meesen, Wenderoth et al. 2006). Humans also choose coordination patterns that maintain an integral frequency ratio between the upper limbs and lower limbs during rhythmic whole-body tasks like walking, swimming, and crawling (Wannier, Bastiaanse et al. 2001). Muscle activation patterns (Ballesteros, Buchthal et al. 1965; Dimitrijevic, McKay et al. 1992; Jakobi and Chilibeck 2001) and reflex responses (Dietz, Fouad et al. 2001; Cerri, Borroni et al. 2003; Balter and Zehr 2007) during multi-joint and/or multi-limb tasks suggest that the coupled limb movements have a neural component. For example, during walking humans use shoulder muscles to help drive backward arm swing in-phase with the backward swing of the contralateral leg. When the arms are bound to restrict arm swing, there is still muscle activation in the shoulder muscles (Ballesteros, Buchthal et al. 1965). A likely candidate for facilitating coordinated interlimb movements in humans is propriospinal connections between upper limb neural networks and lower limb neural networks (Dietz 2002; Zehr and Duysens 2004).

Studies have shown that adding upper limb movement or effort concurrently with lower limb movement during rhythmic tasks may improve lower limb muscle recruitment. We previously demonstrated that increased upper limb muscle activity resulted in greater muscle activation in passively moving legs of neurologically intact subjects performing recumbent stepping (Huang and Ferris 2004; Kao and Ferris 2005). Kawashima and colleagues similarly examined the effects of resting, passive, and active arm swing on passive lower limb muscle activation during a reciprocal leg swinging task. They found that passive arm swing improved muscle activation patterns in passively moved lower limbs compared to a resting arms condition in incomplete spinal cord injured individuals (Kawashima, Nozaki et al. 2008). These two studies demonstrate that upper limb activation or afferent feedback can increase or improve lower limb muscle activation.

When examining muscle recruitment during multi-limb tasks, another neurally mediated interlimb effect is the so-called bilateral deficit (Howard and Enoka 1991). A bilateral deficit occurs when the force output of two bilateral limbs performing a task simultaneously is less than the sum of the force output of each single limb performing the same task. Deficits in muscle activation often parallel the deficits in force production (Ohtsuki 1983; Vandervoort, Sale et al.

1984) and suggest that the bilateral deficit may represent a limitation in neuromuscular activation (Jakobi and Chilibeck 2001). Bilateral deficits occur in both the upper and lower body during isometric tasks (Ohtsuki 1983; Secher, Rube et al. 1988; Schantz, Moritani et al. 1989; Koh, Grabiner et al. 1993; Oda and Moritani 1994). Dynamic and/or multi- joint lower limb movements also typically produce bilateral deficits (Vandervoort, Sale et al. 1984; Weir, Housh et al. 1995; Simon and Ferris 2008). Despite the common use of simultaneous upper and lower limb tasks for exercise (such as using elliptical trainers), no study has examined how maximum muscle activation is affected by simultaneous upper and lower limb rhythmic exercise compared to just upper or lower limb exercise.

The general purpose of this study was to examine the effect of maximal voluntary upper limb muscle activation on lower limb muscle activation during a rhythmic task in neurologically intact humans. A secondary general purpose was to examine the same effect, but in the reverse direction (the effect of maximal voluntary lower limb muscle activation on upper limb muscle activation). We wanted to answer several specific questions. First, does maximal voluntary effort in the upper (or lower) limbs lead to increased muscle recruitment of passive lower (or upper) limbs during rhythmic movement? This question seeks to understand whether interlimb neural coupling can increase muscle recruitment of passively moving limbs. We hypothesized that active effort in the upper (or lower) limbs will increase muscle activation in passive lower (or upper) limbs. Second, does simultaneous upper and lower limb maximal effort produce more or less lower (or upper) limb muscle activation compared to only lower (or upper) limb maximal effort. This second question seeks to understand whether interlimb neural coupling can increase muscle recruitment during maximal effort. We hypothesized that simultaneous upper and lower limb maximal effort would produce greater lower limb muscle activation compared to only lower limb maximal effort. Third, does single upper (or lower) limb maximal effort produce more or less muscle activation in the ipsilateral or contralateral lower (or upper) limb? This third question seeks to understand whether interlimb neural coupling is more ipsilateral or contralateral in nature. We hypothesized that single limb effort would produce more muscle activation in the in-phase contralateral limb. To examine these questions, we studied subjects performing recumbent stepping similar to our previous works (Huang and Ferris 2004; Kao and Ferris 2005), but modified the stepping device to allow maximal effort at a constant stepping frequency (Figure 4.1A).

Methods

Subjects

Sixteen healthy female subjects (age range 18-29 yrs) participated in this study. We could only test subjects who did not exceed an upper limit of the stepper's power output. Subjects provided informed written consent, and the University of Michigan Medical School Institutional Review Board approved the protocol and consent form. The study complied with the Declaration of Helsinki.

Computer-controlled Recumbent Stepper

We have modified a commercially available recumbent stepper (TRS 4000, NuStep Inc., Ann Arbor, MI) to have computer-controlled real-time resistance and force measuring capabilities (Figure 4.1A). We use RT Lab Solo software (Opal-RT, Montréal, Québec, Canada) to customize control of the servomotor (Kollmorgen, Radford, VA) that powers the recumbent stepper. We use the position sensor in the servomotor to measure the kinematics of the recumbent stepper. The stepper has one degree of freedom and thus needs just one position sensor to describe its kinematics.

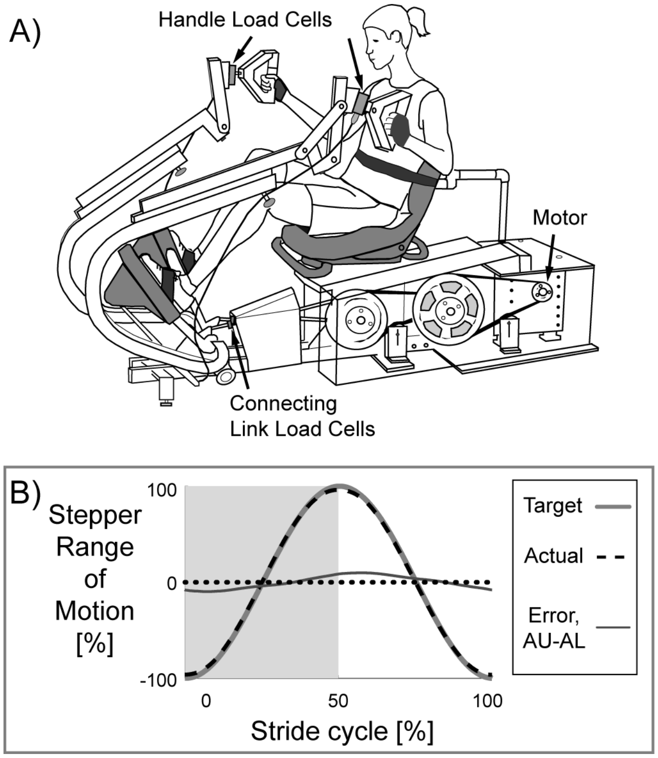

Figure 4.1 A) Recumbent stepping machine with real-time computer-controlled resistance and force and position sensors (modified TRS 4000, NuStep Inc, Ann Arbor, MI). The handles and seat are adjustable. Velcro gloves, foot straps, and a torso belt help minimize unwanted movement. B) The machine provides smooth consistent stepping regardless of subject effort through a custom designed position control of a prescribed sine wave stepping profile. The group mean profile for the actual stepper position (black dashed line) closely follows the target sine wave (thick dark grey line). The thin grey line is the maximum error which occurred during the Active Upper & Active Lower condition. Dotted line is zero.

For this study, we programmed the recumbent stepper to follow a prescribed sine-wave position profile (Figure 4.1B) to produce smooth consistent stepping at a set frequency (75 BPM, equivalent to the stepping frequency of walking at 1.25 m/s). The harder the subjects pushed or pulled, the more resistance they encountered to maintain a constant stepping frequency and minimize error. The largest errors occurred in the Active Upper & Active Lower condition, reaching an average peak error of 10 ± 3 % (mean ± standard deviation) of the stepper range of motion and an average error of 5.7 ± 1.7% across the cycle. Some design limitations made it difficult to further reduce the error, but all data collected were within < 1% of the target stepping frequency. To measure the force each arm contributed to the stepping motion, we mounted a single axis load cell (Strainsert, West Conshohocken, PA) in each handle. We also mounted a single axis load cell (LCWD-1000, Omegadyne, Sunbury, OH) in the connecting link of each handle-pedal unit to measure the total force each contralateral upper-lower limb pair supplied to the stepping kinetics. We found that the sum of the handle and pedal torques equaled the handle-pedal unit torque. Based on this, we could determine the force contribution of each lower limb to the stepping motion.

Protocol

Subjects performed recumbent stepping using different combinations of upper (U) and lower (L) limb effort, being either active (A) or passive (P). Active effort was always with maximal effort, and passive effort was with minimal effort or as relaxed as possible. Subjects could choose any combination of pushing and pulling to drive the stepping motion, unless specifically told to just push or just pull (for the single limb conditions).

We used Velcro gloves to attach the hands to the handles, and foot straps to attach the feet to the pedals during passive conditions. This adaptation allowed subjects to be as passive as possible because they did not have to actively hold the handles or keep their feet on the pedals throughout the stepping motion. A torso strap minimized torso movement during stepping. The seat position was set so that the subject's knees were near full extension but could not lock out. The position of each handle was adjusted for subject comfort (Figure 4.1A). For each condition, we collected fifteen seconds of data, approximately six to eight complete stride cycles. The order of the conditions was pseudo-randomized for each subject. There was an average of one minute of rest between conditions.

Question 1: Does Maximal Effort in the Upper (or Lower) Limbs Increase Muscle Activation in Passive Lower (or Upper) Limbs?

To answer our first question, we compared lower limb muscle activation between Passive Upper & Passive Lower [PU-PL] and Active Upper & Passive Lower [AU-PL] to determine if maximum voluntary effort in the upper limbs leads to greater muscle activation in the passive lower limbs. We also looked at the reverse direction and compared Passive Upper & Active Lower [PU-AL] to Passive Upper & Passive Lower [PU-PL] to determine if maximum voluntary effort in the lower limbs leads to greater muscle activation in the passive upper limbs.

Question 2: Does Simultaneous Upper and Lower Limb Maximal Effort Increase Lower (or Upper) Limb Muscle Activation Compared to Only Lower (or Upper) Limb Maximal Effort?

To answer our second question, we compared lower limb muscle activation between Active Upper & Active Lower [AU-AL] and Passive Upper & Active Lower [PU-AL] conditions. We also compared upper limb muscle activation between Active Upper & Active Lower [AU-AL] and Active Upper & Passive Lower [AU-PL] conditions. These comparisons will determine if simultaneous upper and lower limb maximal effort produces more or less muscle activation compared to only lower (or upper) limb maximal effort.

Question 3: Does Single Limb Maximal Effort Increase Muscle Activation in the Ipsilateral or Contralateral Limb?

To answer our third question, we examined the effect of single upper limb effort on muscle activation of passive lower limbs to determine if there was more muscle activation in the ipsilateral or contralateral passive lower limb. We tested conditions of just left upper limb effort, Active Left Upper & Passive Lower and just right upper limb effort, Active Right Upper & Passive Lower. For these conditions, subjects were instructed to push and pull using just their left (or right) upper limb, while the right (or left) upper limb was as passive as possible. We also tested conditions instructing subjects to just pull with a single upper limb, Active Left Upper Pulling & Passive Lower and Active Right Upper Pulling & Passive Lower. Similarly, we tested conditions instructing subjects to just push with a single upper limb, Active Left Upper Pushing & Passive Lower and Active Right Upper Pushing & Passive Lower. By focusing active effort of a single upper limb to just pulling (or pushing), we could potentially observe how specific upper limb muscle groups affect passive lower limb muscle activation. During these conditions, the device drove the stepping motion for the portion of the stride when the subject was instructed to be passive until reaching the portion of the stride when the subject was instructed to push (or pull) with the specified single upper limb. To examine bidirectionality, we also tested a Passive Upper & Active Left Lower and a Passive Upper & Active Right Lower condition to examine whether any ipsilateral or contralateral coupling also occurred in the lower to upper direction.

Data Acquisition and Analysis

Two computer systems sampled all of the data signals at 1,000 Hz. We used a common data signal sampled in both systems to synchronize the data offline.

Electromyography (EMG)

We measured muscle activity from sixteen muscles, four muscles on each limb, using a surface electromyography system with an EMG bandwidth of 20-450 Hz (Delsys, Boston, MA). On each lower limb, we measured muscle activity from the vastus medialis (VM), medial hamstrings (MH), tibialis anterior (TA), and soleus (SO). On each upper limb, we measured muscle activity from the anterior deltoid (AD), posterior deltoid (PD), biceps brachii (BB), and triceps brachii (TB). We cleaned each electrode site with rubbing alcohol, placed the electrode sensor over the muscle belly along the long axis, and then secured the electrode with tape. To further minimize mechanical artifact, we wrapped excess loose electrode wires to the limbs with elastic foam wrap. We processed the EMG data with a second order high-pass Butterworth filter (cutoff frequency 20 Hz) with zero phase lag to attenuate low frequency components such as mechanical artifact. We then full wave rectified the EMG data signals.

Joint Angles

We measured joint angles of the ankles, knees, and hips on both legs and the elbows of both arms using twin-axis electrogoniometers placed along the sagittal plane (Biometrics Ltd, Ladysmith, VA). The electrogoniometers were zeroed with the limbs in the anatomically neutral position. We processed the joint angle data with a second order low-pass Butterworth filter (cutoff frequency 6 Hz) with zero phase lag.

Kinetics

We calculated the forces each hand and foot contributed to the stepping motion via single axis load cells (Figure 4.1A). We measured the force exerted by each hand through a load cell mounted in the handle and the total force exerted by each contralateral hand-foot pair through a load cell mounted in a connecting link on the machine. We filtered this force data using a second order low-pass Butterworth filter (cutoff frequency 6 Hz) with zero phase lag. Using the measured forces and moment arm relationships, we calculated the torques associated with each handle and handle-pedal unit. To determine the pedal torque, we subtracted the handle torque from the handle-pedal unit torque. We then divided the pedal torques by the pedal moment arm to find the pedal forces.

Calculation of Mean Profiles

To compare EMG patterns between conditions, we calculated group EMG mean profiles over a stride cycle for each condition. The beginning and end of each stride corresponded with the left lower limb and right upper limb at full extension as indicated from the position data. We first calculated an intra-subject EMG mean profile for a stride cycle per condition. We then calculated a group EMG mean profile for each condition by averaging all of the intra-subject EMG mean profiles for that condition. We used the same procedure for the joint angle and force mean profiles.

Calculation of EMG Root-Mean-Square (RMS)

To compare EMG amplitudes across conditions, we calculated a group averaged (n=16) normalized EMG root-mean-square (RMS) for each muscle and condition. The data for left and right muscles were analyzed independently. For each muscle, we calculated EMG RMS during the half of the stride when the muscle was concentrically contracting. We calculated an intra-subject average EMG RMS for each muscle per condition. We then normalized the lower limb EMG RMS amplitudes for each muscle (left VM, MH, SO and TA; right VM, MH, SO and TA) to the intra-subject average EMG RMS for the Passive Upper & Active Lower condition. Likewise, we normalized upper limb EMG RMS amplitudes for each muscle (left AD, PD, BB and TB; right AD, PD, BB and TB) to intra-subject average EMG RMS for the Active Upper & Passive Lower condition. We then averaged the intra-subject EMG RMS values to calculate the group EMG RMS value for each muscle per condition.

Statistical Analysis

For each question, we used a repeated measures analysis of variance (rmANOVA) to determine if there were significant differences between conditions for each lower (or upper) limb muscle. For example, for question 1, we performed the rmANOVA looking at only the passive lower limb muscles for the Passive Upper & Passive Lower and Active Upper & Passive Lower conditions. If the rmANOVA showed a significant difference among conditions, we used a Tukey's honestly significant difference (THSD) post hoc test to determine which condition(s) were significantly different ($P < 0.05$). For the single limb conditions, we used a Chi-Squared test of association ($P < 0.05$) to determine if there was a significant difference in the number of muscles that had significant increases in EMG RMS with ipsilateral versus contralateral limb effort.

Results

Question 1: Does Maximal Effort in the Upper (or Lower) Limbs Increase Muscle Activation in Passive Lower (or Upper) Limbs?

Active upper limb effort resulted in increased muscle activation of the passive lower limbs. In a representative single subject, the Passive Upper & Passive Lower condition had minimal muscle activation in the passive lower limbs while the Active Upper & Passive Lower condition had greater amplitudes and more distinct bursts in the passive lower limb muscle activation (Figure 4.2A, black vs. grey respectively). When looking at the group average of all the subjects, the data showed the same effects as in the representative single subject data (Figure 4.2B). The Active Upper & Passive Lower condition had significantly greater muscle activity than the Passive Upper & Passive Lower condition for the bilateral vastus medialis, medial hamstrings, tibialis anterior, and soleus (Figure 4.2C, * over grey bars, THSD $P < 0.05$). The knee joint angle data were similar for the two conditions, Passive Upper & Passive Lower and Active Upper & Passive Lower (Figure 4.2A &B). The handle and pedal forces indicated that subjects performed the stepping conditions as instructed, with the handle forces being significantly different and the pedal forces being similarly minimal. The small pushing pedal forces indicated the pedal pushing against the subject's passive foot (Figure 4.2A & B).

Similarly, lower limb muscle activation resulted in increased muscle activation of passive upper limb muscles. Representative single subject data and group mean profiles showed burst-like muscle activity in the passive upper limbs during the Passive Upper & Active Lower condition compared to the minimal muscle activity during the Passive Upper & Passive Lower condition (Figure 4.3A & B, grey vs. black lines). Passive Upper & Active Lower EMG RMS amplitudes were significantly greater than Passive Upper & Passive Lower EMG RMS amplitudes for the bilateral posterior deltoid, biceps brachii, and triceps brachii muscles (Figure 4.3C * over grey bars, THSD $P < 0.05$). The elbow joint angle, handle force, and pedal force data again indicated that subjects performed the stepping conditions as instructed (Figure 4.3A & B) as the handle forces were similar while the pedal forces were different.

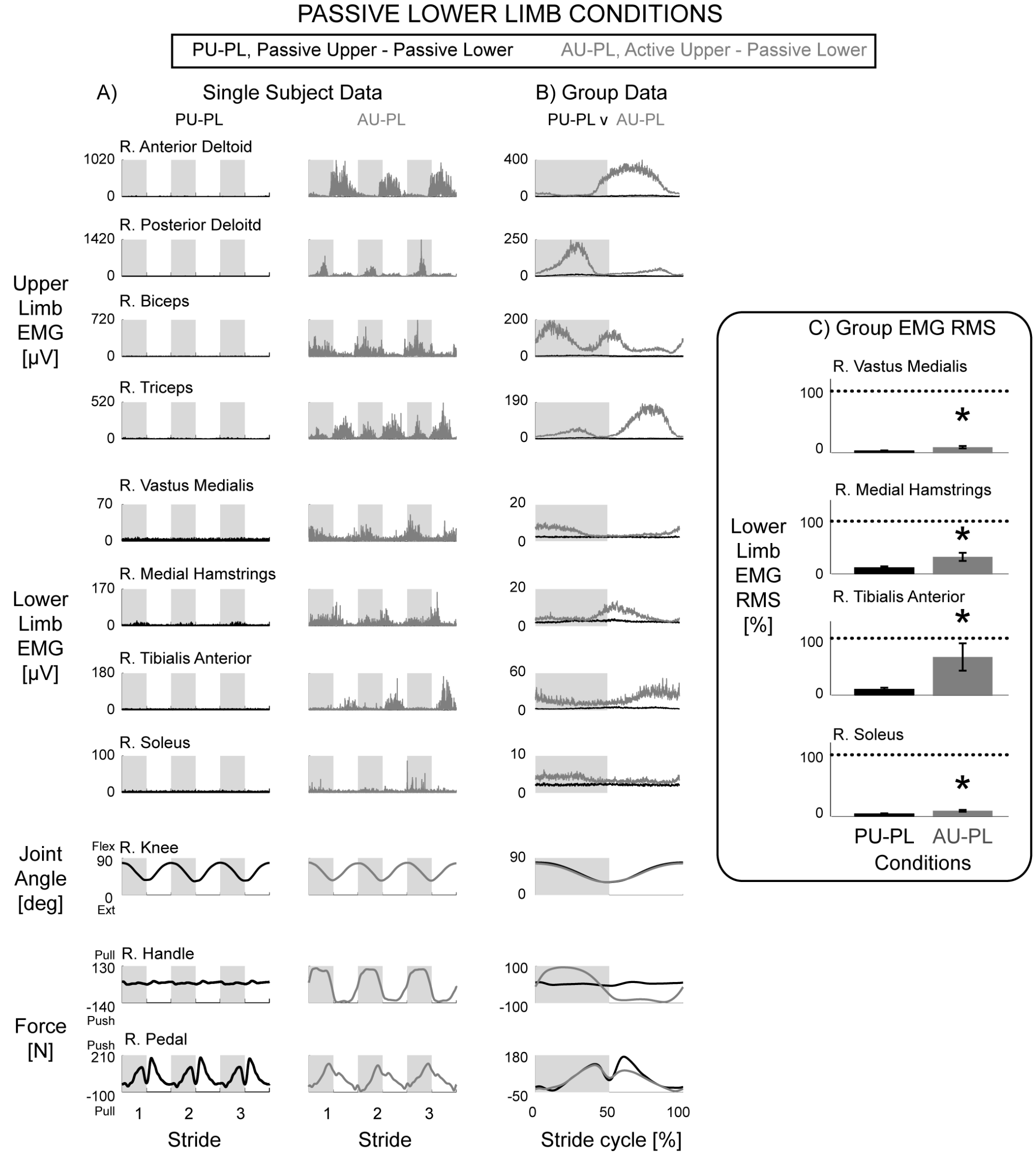

Figure 4.2 Data from the right limbs for the passive lower limb conditions, Passive Upper & Passive Lower (black) and Active Upper & Passive Lower (grey). Representative single subject data (A) and group EMG mean profiles (B) show minimal EMG activity in the Passive Upper & Passive Lower condition while the Active Upper & Passive Lower condition had rhythmic bursts of EMG. Group EMG RMS amplitudes with standard error bars (C) for Active Upper & Passive Lower were significantly greater than Passive Upper & Passive Lower for the vastus medialis, medial hamstrings, tibialis anterior, and soleus muscles (* significantly different, AU-PL > PU-PL, THSD *P* < 0.05). Dotted line equals 100%. Note different y-axes between A and B. The knee joint angle profiles and passive pedal forces were similar between the two conditions. Handle forces during the Active Upper & Passive Lower condition had a clear increase in pulling force during the upper limb flexing (and lower limb extending) phase and pushing force during the upper limb extending (and lower limb flexing) phase.

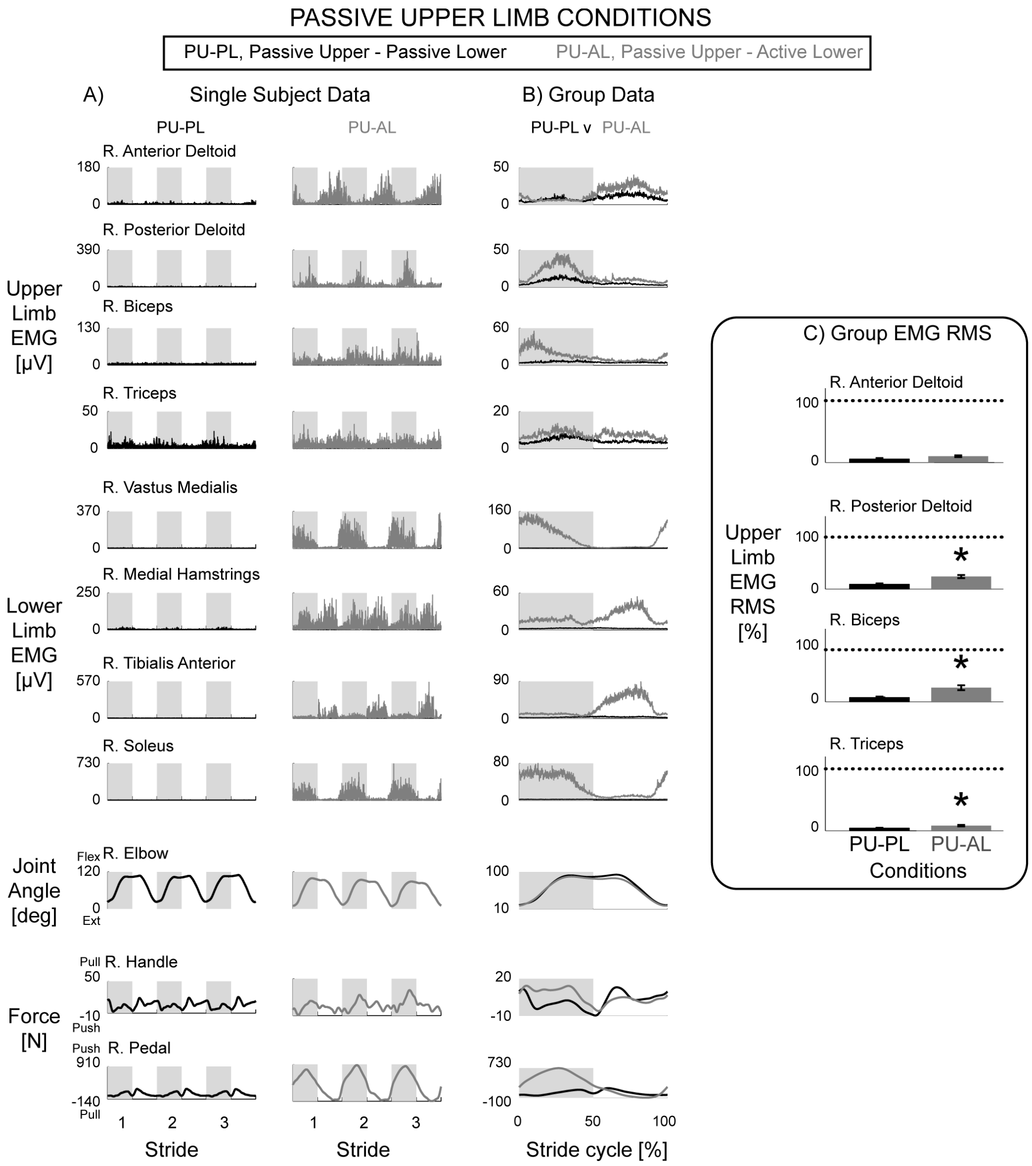

Figure 4.3 Data from the right limbs for the passive upper limb conditions, Passive Upper & Passive Lower (black) and Passive Upper & Active Lower (grey). Representative single subject data (A) and group EMG mean profiles (B) showed a rhythmic burst-like pattern in passive upper limbs during the Passive Upper & Active Lower condition compared to the Passive Upper & Passive Lower condition. Group EMG RMS amplitudes with standard error bars (C) for Passive Upper & Active Lower were significantly greater than Passive Upper & Passive Lower for the posterior deltoid, biceps, and triceps but not the anterior deltoid (* significantly different, PU-AL > PU-PL, THSD $P < 0.05$). Dotted line equals 100%. Note different y-axes between A and B. The elbow joint angle profiles and passive handle forces were similar between the two conditions. The pedal force profiles for Passive Upper & Active Lower showed a large increase in lower limb pushing force during the lower limb extending phase of the stride cycle.

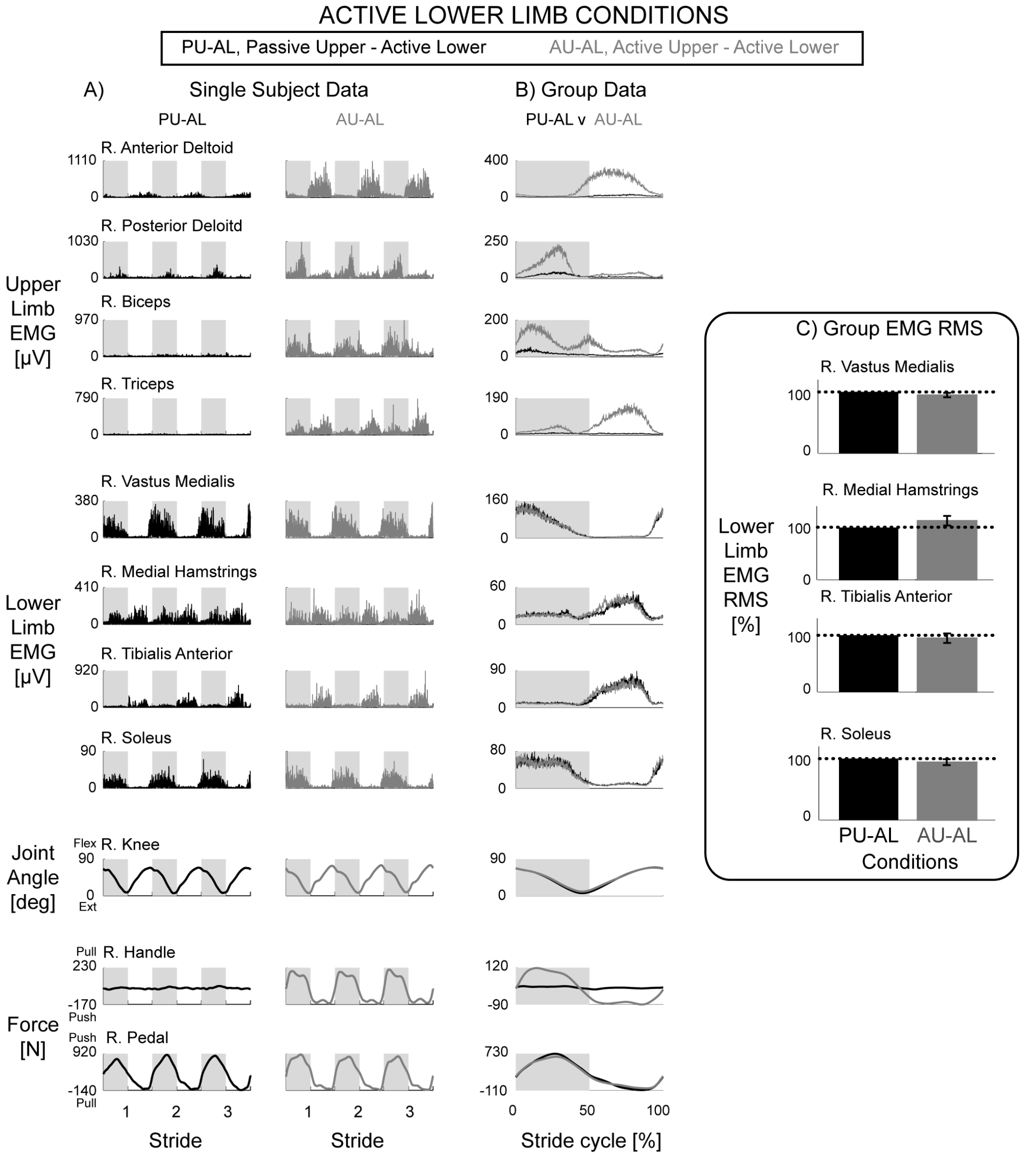

Figure 4.4 Data from the right limbs for active lower limb conditions, Passive Upper & Active Lower (black) and Active Upper & Active Lower (grey). Representative single subject data (A) and group EMG mean profiles (B) showed no observable differences in active lower limb muscle activity during Passive Upper & Active Lower and Active Upper & Active Lower conditions. Group EMG RMS amplitudes with standard error bars (C) were not significantly different between Passive Upper & Active Lower and Active Upper & Active Lower (rmANOVA $P > 0.05$). Dotted line equals 100%. Note different y-axes between A and B. The knee joint angle profiles and active lower limb forces were similar between the two conditions (Fig. 4A & 4B). There were large increases in lower limb pushing force during the lower limb extending phase of the stride cycle. The handle forces were minimal during the Passive Upper & Active Lower condition and had increases in pulling and pushing forces during the Active Upper & Active Lower condition (Fig. 4A & 4B).

Question 2: Does Simultaneous Upper and Lower Limb Maximal Effort Increase Lower (or Upper) Limb Muscle Activation Compared to Only Lower (or Upper) Limb Maximal Effort?

During simultaneous upper and lower limb maximal effort, there was no difference in muscle activation amplitudes compared to only upper limb maximal effort or only lower limb maximal effort. Representative single subject data and group EMG mean profiles showed that muscle activation in the active lower limbs for the Passive Upper & Active Lower and Active Upper & Active Lower conditions were similar in amplitude and shape (Figure 4.4A & B, black vs. grey respectively). There were no significant differences in lower limb EMG RMS between the Passive Upper & Active Lower and Active Upper & Active Lower conditions (Figure 4.4C, rmANOVA $P > 0.05$). Similarly, there were no significant differences in upper limb EMG RMS between Active Upper & Passive Lower and Active Upper & Active Lower (rmANOVA $P > 0.05$). The knee joint angle, handle force, and pedal force data indicated that subjects performed the stepping conditions as instructed (Figure 4.4A & B).

Question 3: Does Single Limb Maximal Effort Increase Muscle Activation in the Ipsilateral or Contralateral Limb?

Single upper limb active effort resulted in increased muscle activation in the passive ipsilateral lower limb compared to the contralateral lower limb. Representative single subject data (Figure 4.5, black) and group EMG mean profiles (Figure 4.6A, black) for the Active Left Upper & Passive Lower condition showed clear rhythmic burst activity in the ipsilateral vastus medialis, ipsilateral tibialis anterior, ipsilateral soleus, and contralateral medial hamstrings. When focused on just pulling during the Active Left Upper Pulling & Passive Lower condition, the EMG data had clear rhythmic burst activity in the ipsilateral vastus medialis, ipsilateral soleus, and contralateral medial hamstrings (Figure 4.5 &Figure 4.6A, light grey). When focused on just pushing during the Active Left Upper Pushing & Passive Lower condition, the EMG data had clear rhythmic burst activity in the ipsilateral tibialis anterior (Figure 4.5 & Figure 4.6A, dark grey). The knee joint angle, handle force, and pedal force data indicated that subjects performed the stepping conditions as instructed (Figure 4.5 & Figure 4.6A).

The EMG RMS amplitudes of the ipsilateral vastus medialis, medial hamstrings, tibialis anterior, and soleus muscles were greater during the Active Left Upper & Passive Lower condition compared to Passive Upper & Passive Lower (Fig 6B* Left Push & Pull column, THSD $P < 0.05$). The left medial hamstrings and tibialis anterior EMG RMS were also significantly greater during the contralateral Active Right Upper & Passive Lower condition compared to the Passive Upper & Passive Lower amplitudes (Fig 6B* Right Push & Pull column, THSD $P < 0.05$). In the Pull Only instructions, Active Left Upper Pulling & Passive Lower resulted in significantly greater EMG RMS amplitudes in the ipsilateral vastus medialis and soleus compared to Passive Upper & Passive Lower (Figure 4.6B* Left Pull Only column, THSD $P < 0.05$). The left medial hamstrings had significantly greater EMG RMS during the contralateral Active Right Upper Pulling & Passive Lower condition compared to Passive Upper & Passive Lower

(Figure 4.6B * Right Pull Only column, THSD $P < 0.05$). In the Push Only instructions, the Active Left Upper Pushing & Passive Lower condition resulted in

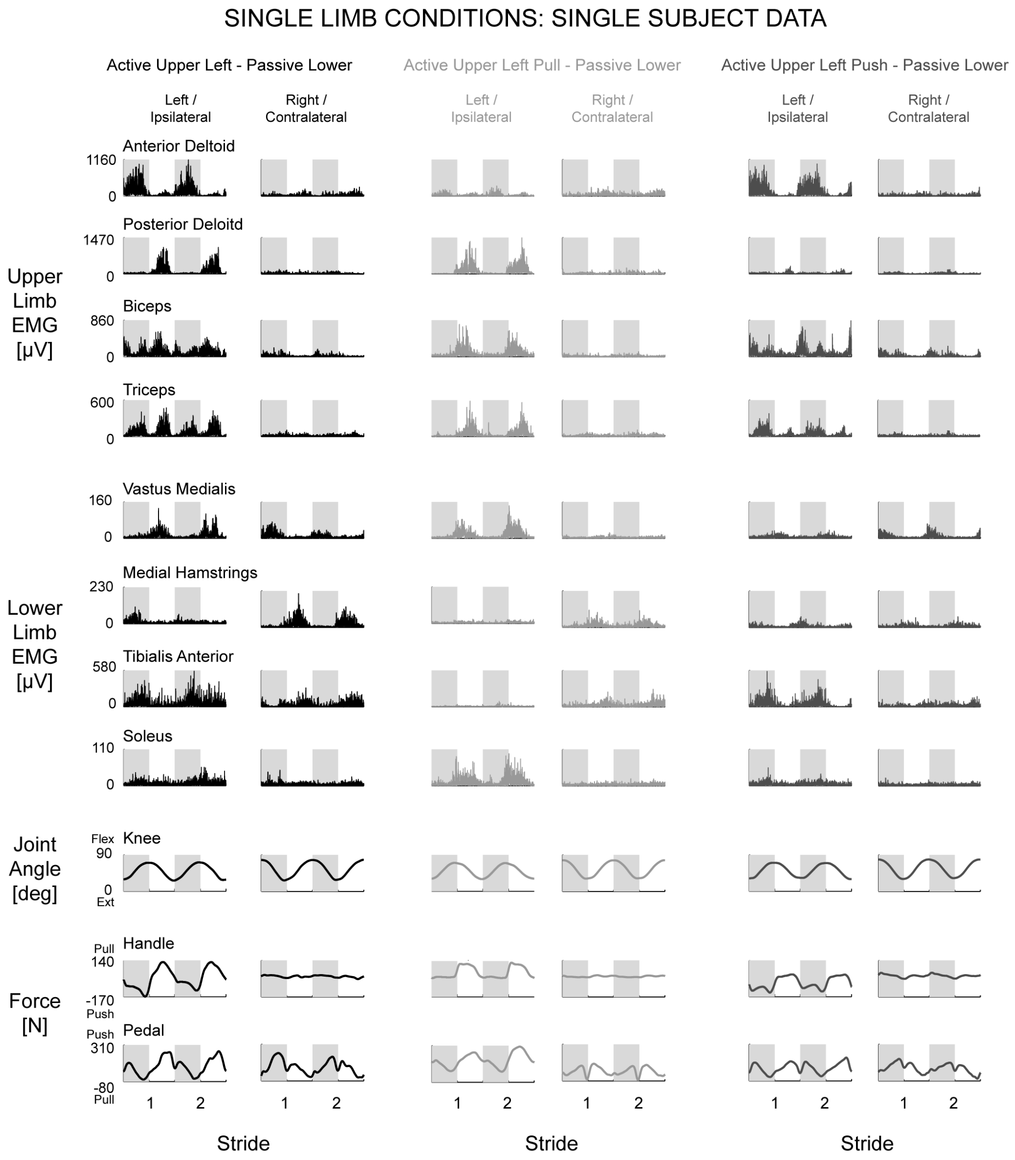

Figure 4.5 Representative single subject data from single left upper limb conditions, Active Left Upper & Passive Lower (black), Active Left Upper Pulling & Passive Lower (light grey), and Active Left Upper Pushing & Passive Lower (dark grey). Overall, more muscle activation occurred in the passive ipsilateral lower limb muscles compared to the passive contralateral lower limb muscles, except for the contralateral medial hamstrings. Same y-axes for each row.

significantly greater EMG RMS amplitudes in the ipsilateral tibialis anterior and medial hamstrings compared to the Passive Upper & Passive Lower condition (Figure 4.6B * Left Push Only column, THSD P < 0.05).

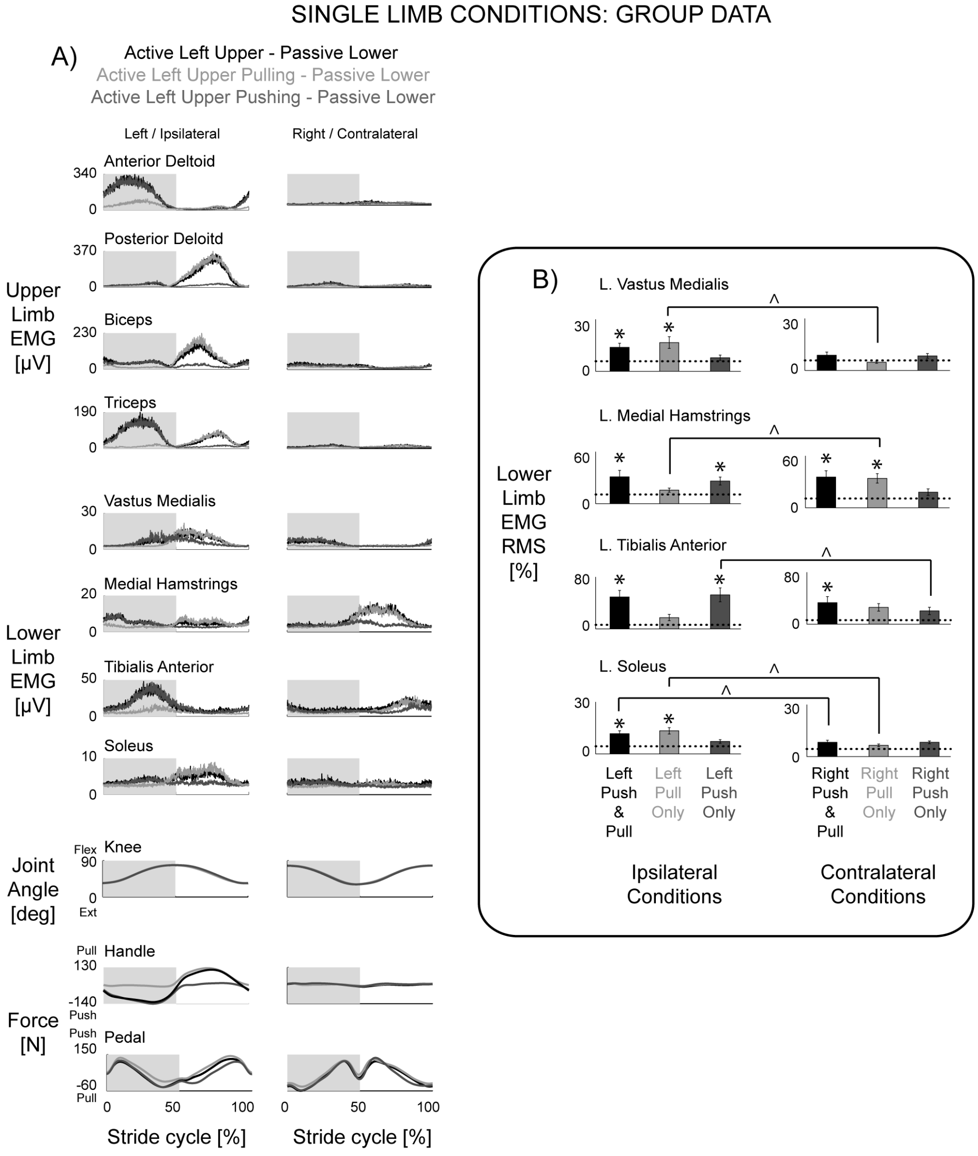

Figure 4.6 A) Group data for single left upper limb conditions, Active Left Upper & Passive Lower (black), Active Left Upper Pulling & Passive Lower (light grey), and Active Left Upper Pushing & Passive Lower (dark grey). The dotted line is Passive Upper & Passive Lower. Except for the contralateral medial hamstrings, group EMG mean profiles showed more burst-like patterns in passive ipsilateral lower limb muscles with single upper limb effort. The passive pedal force profiles for all three conditions were minimal. There was a large pulling handle force during the upper limb flexing (and lower limb extending) phase for Active Left Upper Pulling & Passive

Lower and a large pushing handle force during the upper limb extending (and lower limb flexing) phase for Active Left Upper Pushing & Passive Lower. B) Group EMG RMS amplitudes with standard error bars indicate ipsilateral coupling of muscle activation with single upper limb effort (* significantly different from Passive Upper & Passive Lower, ^ significantly different between left and right upper limb conditions).

Comparing left versus right single limb conditions, left upper limb effort resulted in significantly greater EMG RMS in the left vastus medialis and soleus during Pull Only instructions compared to right upper limb effort (Figure 4.6B ^ Pull Only columns, THSD $P < 0.05$). Right upper limb effort resulted in significantly greater EMG RMS in the left medial hamstrings during the Pull Only instructions compared to left upper limb effort (Figure 4.6B ^ Pull Only columns, THSD $P < 0.05$).

Left upper limb effort corresponded to greater EMG RMS in the left tibialis anterior during Push Only instructions compared to right upper limb effort (Figure 4.6B ^ Push Only columns, THSD $P < 0.05$). Left soleus EMG RMS amplitudes were significantly greater during the Left Push & Pull condition compared to the Right Push & Pull condition (Figure 4.6B ^ Push & Pull columns, THSD $P < 0.05$). Right upper limb effort conditions also showed more ipsilateral coupling with passive right lower limb muscle activation (not shown). A Chi-squared test revealed a significant association of ipsilateral upper limb effort with a greater number of significant increases in passive lower limb EMG RMS amplitudes compared to contralateral upper limb effort ($P < 0.05$). This ipsilateral coupling was also evident in the lower to upper direction. Passive upper limb muscle activation patterns and EMG RMS amplitudes showed more significant increases with ipsilateral single lower limb effort conditions (Chi-squared test $P < 0.05$).

Discussion

We found three novel features of interlimb coupling on muscle activation during rhythmic movement in neurologically intact individuals in this study. Our first finding was a bidirectional coupling of muscle activation between upper and lower limbs. Maximum voluntary effort in the upper limbs increased passive muscle activation in the lower limbs. Likewise, maximum voluntary effort in the lower limbs increased passive muscle activation in the upper limbs. Our second finding was that interlimb neural coupling did not increase or decrease the total muscle recruitment possible during maximally activated lower (or upper) limbs. When subjects exerted simultaneous maximum upper and lower limb effort, there was neither facilitation nor inhibition of muscle activation compared to exclusively upper limb effort or exclusively lower limb effort. Our third finding was an ipsilateral coupling of muscle activation between upper and lower limbs. Maximum voluntary effort in a single upper limb increased muscle activation more in the ipsilateral lower limb than the contralateral limb. This ipsilateral effect was also bidirectional. Single lower limb active effort also resulted in greater muscle activation in the ipsilateral passive upper limb (not shown). These results provide a more thorough understanding of the features and limitations of interlimb coupling of muscle activation between upper limbs and lower limbs.

The general result that active effort in one limb pair resulted in increased muscle activation in passive muscles in the other limb pair was robust. It was consistent with our previous studies (Huang and Ferris 2004; Kao and Ferris 2005), held for single upper limb active effort conditions (Figs. 5 & 6), and was bidirectional (i.e. upper to lower, Figure 4.2, and lower to upper, Figure 4.3). This bidirectional effect agrees with studies examining the role of arm movement on cutaneous reflexes in the legs and the role of leg movement on reflexes in the arms (Haridas and Zehr 2003; Zehr and Haridas 2003; Balter and Zehr 2007). The increases in passive muscle activation with active effort in another limb(s) were small but significant. This agrees with an arm-leg cycling study that demonstrated a nontrivial subtle effect of arm cycling on lower limb reflexes even in the presence of the more dominant effect of leg cycling on lower limb reflexes (Balter and Zehr 2007).

The single limb conditions revealed a surprising ipsilateral, rather than contralateral, coupling of muscle activation. The ipsilateral coupling was evident in both directions, upper to lower (Figure 4.5 & Figure 4.6) and lower to upper. This ipsilateral coupling is interesting because one might suspect contralateral coupling between the upper and lower limbs. Reflex studies suggest that contralateral upper to lower limb coupling may be more prevalent during rhythmic movements compared to ipsilateral upper to lower limb coupling, though the relative strengths are uncertain in humans (Zehr and Duysens 2004; Zehr 2005). The nervous system also naturally prefers in-phase movements (isodirectional) of ipsilateral limbs rather than anti-phase movements (Baldissera, Cavallari et al. 1982; Swinnen 2002). This suggests that there would be a preference for contralateral coupling during recumbent stepping because the contralateral upper limb moves in-phase with the lower limb while the ipsilateral upper limb moves anti-phase with the lower limb. Despite the anti-phase movements of the ipsilateral limbs, we found a greater increase in muscle activation in the passive ipsilateral lower (or upper) limb during single active upper (or lower) limb effort (Figs. 5 & 6). The preference for ipsilateral coupling of wrist and ankle flexion has been attributed to coupled corticospinal drive rather than afferent signals associated with limb movements (Baldissera, Borroni et al. 2002; Cerri, Borroni et al. 2003). Based on reflex studies, we might expect to see a preference for contralateral coupling if spinal mechanisms are dominant. Our results suggest that supraspinal drive may be more dominant compared to spinal mechanisms during a maximal effort rhythmic upper and lower limb task.

It is likely that a combination of neural mechanisms contribute to our observations of increases in passive muscle activation. One possible contributor is spinal connections between upper limb neural networks and lower limb neural networks (Dietz 2002; Zehr and Duysens 2004). These spinal connections allow information about muscle activation in one limb to modulate interlimb reflexes, coordination, and muscle activation of other limbs in both neurologically intact individuals and individuals with spinal cord injury (Dietz, Colombo et al. 1995; Harkema, Hurley et al. 1997; Dietz, Fouad et al. 2001; Wannier, Bastiaanse et al. 2001; Haridas and Zehr 2003; Ferris, Gordon et al. 2004; Balter and Zehr 2007; Kawashima, Nozaki et al. 2008). Another possible contributor is sensory feedback from one or more moving limbs that modulates neural activity in another limb (Collins, McIlroy et al. 1993). Stretch reflexes, however, do not appear to contribute to our results because the timing and shape of the increased muscle activation during the passive limb conditions were similar to the timing and shape of the active limb conditions (Huang and Ferris 2004). Because recumbent stepping has been shown to have similar neural control to walking (Stoloff, Zehr et al. 2007; Zehr, Balter et al. 2007), locomotor commands from central pattern generators and/or supraspinal centers and the propriospinal pathways that modulate locomotor commands are also possible neural mechanisms for our findings. Another possible contributor is descending supraspinal drive that results in “cross talk” and unintended muscle activation (Baldissera, Cavallari et al. 1982; Dimitrijevic, McKay et al. 1992). Postural adjustments may also have a role in our observation of increased passive muscle activation; however, we stabilized the torso as much as possible using a torso strap. We previously tested torso stabilization with multiple straps but still observed increases in passive muscle activation. Regardless, anticipated postural demands required to stabilize the body during the maximal effort tasks cannot be excluded as a possible contributor. Future studies would need to use more extensive electrophysiological measurements to further delineate the possible pathways involved.

An important result of this study was that adding simultaneous maximal upper limb effort with maximal lower limb effort did not enhance lower limb muscle activation in neurologically intact subjects. The presumed spinal connections that contributed to increased passive muscle activation were not a significant factor when lower limbs were maximally activated. During the simultaneous upper and lower limb condition, most subjects were able to attain but not exceed the muscle activation levels of the only upper limbs or only lower limbs conditions (Figure 4.4). The mean force results (not shown) paralleled our EMG RMS results showing that simultaneous upper and lower limb effort did not produce a significant decrease in handle or pedal forces compared to the conditions with only upper limb or only lower limb effort. This agrees with a previous study that showed no difference between unilateral and bilateral force production in a static task for an upper limb and contralateral lower limb pair (Howard and Enoka 1991). These results suggest that a phenomenon like a bilateral deficit does not occur during a simultaneous maximum effort upper and lower limb rhythmic task of non-homonymous muscles. Our active lower limb results (Figure 4.4) also compliment an arm and leg cycling study that demonstrated no significant differences in lower limb EMG during a combined arm and leg cycling task to only leg cycling (Balter and Zehr 2007). This also suggests that humans are able to generate maximum voluntary muscle activation and force production during rhythmic tasks whether using both upper and lower limbs, only upper limbs, or only lower limbs.

A limitation of this study was the subject’s ability and motivation to perform the task as instructed. Because the device was always moving, there was no incentive to do any work during passive conditions. There was no reason to “cheat” and use the passive limbs to aid the active limbs. On the other hand, because the device was always moving, the only motivation for full effort was to comply with the instructions given. When subjects used maximal effort, the resistance increased to maintain the specified stepping frequency and the subject had to do more work. For our experiment, we only provided subjects with verbal encouragement to use maximal effort or stay relaxed during the data collections. We chose not to provide some form of biofeedback such as a display showing handle and pedal forces generated during the collection. Giving subjects biofeedback could allow subjects to voluntarily negate any underlying natural neural coupling between the upper and lower limbs through increased supraspinal activity.

Another limitation with this experiment was that we did not examine what happens at submaximal effort. There is still the possibility that upper limb exertion can increase muscle activation in lower limbs during submaximal exercise despite our results at maximal efforts. Transcranial magnetic stimulation could be used to determine if there is an excitatory interlimb coupling during submaximal muscle activation that results in less supraspinal descending neural drive to the lower limbs with upper limb exertion (Zehr, Klimstra et al. 2007). Understanding the role of upper limb effort on lower limb muscle activation at submaximal efforts has potential rehabilitation implications. This is of interest because therapeutic exercise and activities of daily living are often performed at submaximal levels. Perhaps incorporating active effort from unimpaired limbs may increase or improve muscle activation patterns in impaired limbs during whole body rhythmic tasks such as walking.

We conducted this study to answer questions about the effect of interlimb neural coupling on muscle activation. We found that maximum voluntary effort in the upper (or lower) limbs did increase muscle recruitment during passive rhythmic movement of the lower (or upper) limbs. Single limb effort conditions revealed a stronger ipsilateral coupling of muscle activation compared to contralateral coupling. We also found that simultaneous maximum upper and lower limb effort produced neither more nor less muscle activation compared to exclusively upper limb effort or exclusively lower limb effort in the active limbs. These results showed that active effort in one limb(s) can influence muscle activation in other unintended passive limbs during a rhythmic locomotor-like task in neurologically intact individuals. However, the presumed excitatory neural coupling did not enhance maximum activation. There are several factors that may contribute to this ipsilateral facilitatory neural coupling, including interlimb spinal neural connections that provide pathways for muscle activation from one limb(s) to contribute to muscle recruitment in another limb. These results support the existence of neural connections between the upper limbs and lower limbs and demonstrate that muscle activation in one limb(s) increases muscle activation in another limb(s) during a whole body rhythmic task. Further studies examining the role of upper limb effort on lower limb muscle activation patterns will provide more insight into the potential of integrating upper limb effort during lower limb rehabilitation.

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Cord Research Foundation. The results of the present study do not constitute endorsement by American College of Sports Medicine.

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CHAPTER 5

UPPER LIMB EFFORT DOES NOT INCREASE MAXIMAL VOLUNTARY MUSCLE ACTIVATION IN INDIVIDUALS WITH INCOMPLETE SPINAL CORD INJURY

Abstract

Objective: To determine the effect of upper limb effort on maximal lower limb muscle activation in individuals with incomplete spinal cord injury.

Methods: Fifteen individuals with incomplete spinal cord injury performed recumbent stepping using different combinations of upper and lower limb efforts.

Results: There was no significant difference in active lower limb electromyography amplitudes regardless of whether the upper limbs were resting or exerting maximal effort. Upper limb effort increased passive lower limb muscle activation and likewise, lower limb effort increased passive upper limb muscle activation.

Conclusions: Upper limb effort did not increase lower limb muscle activation during active lower limb effort in individuals with incomplete spinal cord injury during recumbent stepping. This suggests that individuals with incomplete spinal cord injury cannot recruit additional lower limb motor units using maximal volitional effort of their upper limbs.

Significance: Understanding how upper limb effort and movement influences lower limb muscle activation patterns in incomplete spinal cord injury patients has implications for prescribing therapies for lower limb rehabilitation.

Introduction

Upper limb muscle activation can increase muscle activity in the passive lower limbs during a rhythmic motor task (Ferris DP, et al., 2006). In previous studies, we examined neurologically intact subjects performing recumbent stepping on an exercise device that coupled motion of the upper and lower limbs. We found that increasing upper limb muscle activation through greater resistance (Huang HJ and Ferris DP, 2004) or higher movement frequency (Kao PC and Ferris DP, 2005) resulted in greater lower limb muscle electromyography amplitudes in passively moving legs. The most likely explanation for the observed lower limb muscle recruitment with active upper limb exertion is an excitatory connection between upper limb motor neurons and lower limb motor neurons involving the neural networks controlling locomotion (Ferris DP, et al., 2006).

Clinically, it has been suggested that active upper limb movement during gait training can be beneficial for rehabilitation (Behrman and Harkema 2000). When subjects with incomplete spinal cord injury freely swing their arms, their lower limb muscle activity looks more symmetric and has greater rhythmic bursts (Visintin M and Barbeau H, 1994). Kawashima and colleagues recently showed that individuals with incomplete spinal cord injury using an upright exercise device had improved muscle activation in passively moved lower limbs with passive arm swing compared to a stationary arm condition (Kawashima N, et al., 2008). These studies support the idea that reciprocal upper limb movement can enhance lower limb muscle activation patterns and promote activity-dependent neural plasticity during gait rehabilitation (Ferris DP, et al., 2006).

An unanswered question is whether active upper limb exertion provides a means to increase lower limb muscle recruitment over what could be achieved without active upper limb exertion. Therapeutic interventions after incomplete spinal cord injury often focus on increasing volitional muscle activation through strength training and exercise. Both muscle hypertrophy and enhanced neural drive contribute to the increased muscle strength that accompanies resistance training. If active upper limb exertion allows individuals with incomplete spinal cord injury to increase maximal recruitment of lower limb muscles during resistance training, then it could be helpful to include simultaneous upper and lower limb maximal exercise in their rehabilitation.

The purpose of this study was to determine the effect of upper limb effort on maximal lower limb muscle activation in individuals with incomplete spinal cord injury. Previous work (Huang HJ and Ferris DP, 2004; Kao PC and Ferris DP, 2005; Kawashima N, et al., 2008) has focused on passive lower limb muscle activation rather than active lower limb muscle activation, but active lower limb effort is more characteristic of exercise during rehabilitation. Gaining a more thorough understanding of how upper limb effort influences lower limb muscle activation during active voluntary effort is important for incorporating combined upper and lower limb exercise into neurological rehabilitation practices (Ferris DP, et al., 2006).

Subject	Age	Gender	ASIA Level*	Injury Level	Post Injury (yrs)	Injury Etiology	Est. WISCI †
A	51	F	D	C3	7	Epidural Abcess	13
B	62	M	D	C3	5	Cervical Stenosis	19
C	64	M	D	C4	4	Trauma	15
D	40	M	D	C6	5	Trauma	9
E	42	M	D	C6	28	Trauma	18
F	61	M	D	C7	42	Trauma	13
G	41	F	C	T5	28	Transverse Myelitis	15
H	78	M	E	T7	8	Sarcoma	20
I	47	F	D	T9	8	Transverse Myelitis	13
J	57	F	C	T11	4	Trauma	18
K	53	F	C	T11	6	Dermoid Cyst	12
L	30	M	C	L1	3	Trauma	9
M	46	M	C	L3	4	Surgical Complications	18
N	41	F	C	L3	20	Trauma	9
O	23	M	D	L3	3	Trauma	20

* ASIA = American Spinal Injury Association Impairment Scale. A = complete. E = normal.

† Est. WISCI = Estimated Walking Index of Spinal Cord Injury based on observation and subject self-reported walking ability. 0 = unable to walk with assistance. 20 = unassisted walking.

Table 5.1 Subject information. Data for each subject showing age, injury level, and walking ability.

Methods

Subjects

Fifteen individuals with incomplete spinal cord injury participated in this study after providing written informed consent. There were six subjects with a cervical injury, five with a thoracic injury, and four with a lumbar injury (Table 5.1). All subjects were at least 12 months post-injury and free of any conditions that would limit their ability to exercise safely. Subjects had to be able to perform the recumbent stepping task with just their upper limbs to participate in the study. All subjects were screened and approved for participation by a physician from the

Physical Medicine and Rehabilitation Department at the University of Michigan. The University of Michigan Medical School Institutional Review Board approved the protocol and consent form in accord with the Declaration of Helsinki.

Computer-controlled Recumbent Stepper

We have taken a commercially available recumbent stepper (TRS 4000, NuStep Inc., Ann Arbor, MI) and modified it to have computer-controlled real-time resistance (Figure 5.1A) (Huang HJ and Ferris DP, In Press). We also instrumented the recumbent stepper with load cells to measure handle and pedal forces. For this study, the stepper followed a prescribed sine-wave position profile with a stepping frequency of 75 beats per minute (equivalent to the stepping frequency of walking at ~1.25 m/s). If subjects were unable to step at the desired frequency, then the stepper drove the stepping motion. If subjects were strong enough to drive the stepping motion faster than the desired stepping frequency, the motor generated a torque to oppose the subject’s effort. This allowed the stepper to have a fixed position profile and to maintain the desired stepping frequency.

Experimental Set Up

We adjusted the stepper to make the range of the stepping motion as comfortable as possible for each subject. The seat position was set so that the knees were near full extension but could not lock out. For some more hyper-reflexive subjects, we had to set the seat so that their legs were more flexed for

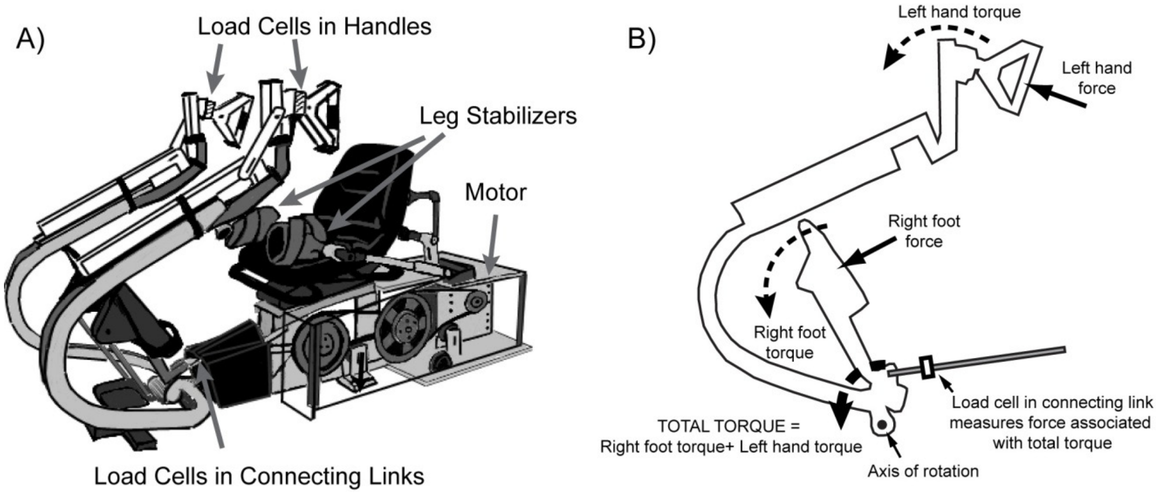


Figure 5.1 A) Recumbent stepping machine with real-time computer-controlled resistance and force and position sensors (modified TRS 4000, NuStep Inc, Ann Arbor, MI). The handles and seat are adjustable. Velcro gloves, foot straps, and a torso belt help minimize unwanted movement. Leg stabilizers also help prevent excessive medial-lateral movement. B) Schematic of the forces and torques for one handle-pedal unit on the recumbent stepper.

safety reasons. If needed, we used leg stabilizers to prevent the subject’s legs from abducting and potentially colliding with the moving handles. We aligned each foot to be centered within the pedal. As the pedal was only 5.5 inches wide, it prevented subjects from rotating their feet medially or laterally. We used a torso strap to minimize torso movement during stepping. We also used Velcro gloves to attach the hands to the handles and used foot straps to attach the feet to the pedals during passive conditions. This allowed subjects to be as passive as possible because they did not have to actively hold the handles or keep their feet on the pedals throughout the stepping motion.

Protocol

Subjects performed recumbent stepping using different combinations of upper (U) and lower (L) limb effort. For active effort, we instructed subjects to use maximal effort. For passive effort, we instructed subjects to relax as much as possible. We tested three active lower limb conditions: a) Resting Upper & Active Lower [RU-AL], b) Passive Upper & Active Lower [PU-AL], c) Active Upper & Active Lower [AU-AL]. For the resting upper limb condition, we had subjects cross their arms and rest them on his/her lap. These active lower limb conditions examined whether different upper limb states altered active lower limb muscle electromyography amplitudes. We also tested two passive lower limb conditions, d) Passive Upper & Passive Lower [PU-PL], and e) Active Upper & Passive Lower [AU-PL], to determine how upper limb effort influences passive lower limb muscle activation in individuals with incomplete spinal cord injury.

We collected two sets of data, with each set consisting of five trials for each of the five conditions. Conditions were randomized for each subject. Before each trial, we verbally described the combination of arm and leg effort to the subject. Subjects were instructed to relax and use the first fifteen seconds to get used to the stepping frequency as the stepper slowly ramped up to full range of motion. Then on a verbal cue, we instructed subjects to perform the stepping condition with maximal effort for approximately fifteen seconds. This yielded six to eight strides of data. Throughout the trial, we gave the subject verbal cues and encouragement. Subjects were also given an opportunity to practice the condition prior to testing at their discretion. The average length of rest between trials was one minute.

Data Acquisition

We collected data signals using two computer systems at a sampling rate of 1000 Hz. One computer was used to collect electromyography, load cell, and joint angle data signals. The other computer ran the real-time software program and sampled data signals related to the recumbent stepper hardware. We used a common data signal sampled in both systems to synchronize the data offline.

Electromyography (EMG)

We measured surface electromyography (Delsys, Boston, MA) from sixteen muscles, four muscles on each limb. On each lower limb, we measured muscle activity from the vastus medialis (VM), medial hamstrings (MH), tibialis anterior (TA), and soleus (SO). On each upper limb, we measured muscle activity from the anterior deltoid (AD), posterior deltoid (PD), biceps brachii (BB), and lateral head of the triceps brachii (TB). We shaved each electrode site and cleaned them with rubbing alcohol. We then placed the electrode sensor over the muscle belly along the long axis, secured the electrode with tape, and wrapped excess loose electrode wires to the limbs with elastic foam wrap. We processed the EMG data with a second order high-pass Butterworth filter with zero lag (cutoff frequency of 20 Hz) to attenuate low frequency components such as mechanical artifact. We then full wave rectified the EMG data signals and applied a low-pass Butterworth filter with zero lag (cutoff frequency of 499 Hz).

Joint Angles

We measured bilateral joint angles of the ankles, knees, hips, and elbows using twin-axis electrogoniometers placed along the sagittal plane (Biometrics Ltd, Ladysmith, VA). Electrogoniometers were zeroed with the limbs in the anatomically neutral position. Joint angle data were processed with a second order low-pass Butterworth filter with zero lag (cutoff frequency of 6 Hz). Because of equipment malfunctions, we were not able to obtain a full set of joint angle data for several subjects.

Kinetics

We calculated the forces each hand and foot contributed to the stepping motion via single axis load cells (Figure 5.1). Because the handle and contralateral pedal were part of a single rigid body, the torques generated by a force from the hand and a force from the contralateral foot summed and yielded a net torque for the handle-pedal unit (Figure 5.1B). We measured directly the force exerted by each hand through a load cell mounted in the handle. We also measured the force associated with the net torque for each handle-pedal unit through a load cell mounted in a connecting link between the handle-pedal unit and a cam. Using the measured forces and moment arm relationships, we calculated the torques associated with each handle and handle-pedal unit. We subtracted the handle torque from the handle-pedal unit torque to determine the pedal torque of that contralateral hand-foot pair. We then divided the pedal torques by the pedal moment arm to find the pedal forces. We filtered measured force data using a second order low-pass Butterworth filter with zero lag (cutoff frequency of 6 Hz).

Data Analysis

For all subjects, we analyzed the data from the second set. The subjects with incomplete spinal cord injury were more consistent during the second set.

Calculation of Mean Profiles

To compare EMG patterns between conditions, we calculated group normalized EMG mean profiles over a stride cycle for each condition. The beginning and end of each stride corresponded with the left lower limb and right upper limb at full extension as indicated from the position data (Figure 5.2A). We first calculated an intra-subject EMG mean profile for a stride cycle per condition. We then normalized the intra-subject EMG mean profiles to the maximum value among all conditions. We then calculated a group normalized EMG mean profile for each condition by averaging all of the intra-subject normalized EMG mean profiles for that condition. We used the same general procedure, but without normalization, for the joint angle and force mean profiles.

Calculation of EMG Amplitudes

To compare EMG amplitudes across conditions, we calculated a group averaged normalized root-mean-square (RMS) EMG for each muscle and condition. For each muscle, we only calculated RMS EMG during the half of the stride when the muscle was concentrically contracting. For example, for the right vastus medialis, we calculated the RMS EMG during the first half of the stride cycle when the knee was extending (Figure 5.2, grey blocks). We calculated each muscle's RMS EMG for the concentric half of the cycle for each subject-condition data set. We calculated an intra-subject average RMS EMG for each muscle per condition. We then normalized the intra-subject RMS EMG amplitudes for each muscle (left and right vastus medialis, medial hamstrings, soleus, tibialis anterior, anterior deltoid, posterior deltoid, biceps brachii, and triceps brachii) to the maximum intra-subject average RMS EMG amplitude across all conditions. We excluded any subject's data that did not have at least a 10% difference between Passive Upper & Passive Lower and Passive Upper & Active Lower conditions for lower limb RMS EMG and between Passive Upper & Passive Lower and Active Upper & Passive Lower conditions for upper limb RMS EMG. We then averaged across subjects to calculate the group averaged normalized RMS EMG amplitude for each muscle per condition.

Statistical Analysis

We used a repeated measures analysis of variance (rmANOVA) to determine if there were significant differences in lower limb muscle activation among active lower limb conditions. We also ran another rmANOVA to determine if there were significant differences in lower (or upper) limb muscle activation among passive lower (or upper) limb conditions. If the rmANOVA showed a significant difference among conditions, we used a Tukey's honestly significant difference (THSD) post hoc test to determine which conditions were significantly different ($P < 0.05$).

Results

Adding upper limb effort did not enhance lower limb muscle activation during active lower limb effort in subjects with incomplete spinal cord injuries. The group mean joint angle profiles were consistent among the different conditions for the bilateral hip, knee, ankle, and elbow joints (Figure 5.2B). In a representative single subject, the muscle activation patterns for the active lower limbs for the Resting Upper & Active Lower, Passive Upper & Active Lower, and Active Upper & Active Lower conditions were similar in amplitude and had a rhythmic burst like pattern, particularly for the vastus medialis, tibialis anterior, and soleus muscles (Figure 5.3). In this particular subject, the medial hamstrings muscle activity was not rhythmic, but the muscle activation shape and amplitude were similar among the three conditions. The upper limb muscle patterns corresponded to the different upper limb states of resting, passive, and active. There was minimal upper limb EMG during the resting upper limb condition, small amplitudes of EMG during the passive upper limb condition, and greater burst-like EMG during the active upper limb condition. The active knee joint angle and pedal forces were similar across the three active lower limb conditions. The handle forces indicated that subjects correctly followed directions for each condition. Only the Active Upper & Active Lower handle forces had a distinct pushing and pulling handle force while the Resting Upper & Active Lower and Passive Upper and Active Lower conditions had minimal handle forces (Figure 5.3). Looking at the group average EMG data for all the subjects (Figure 5.4), the

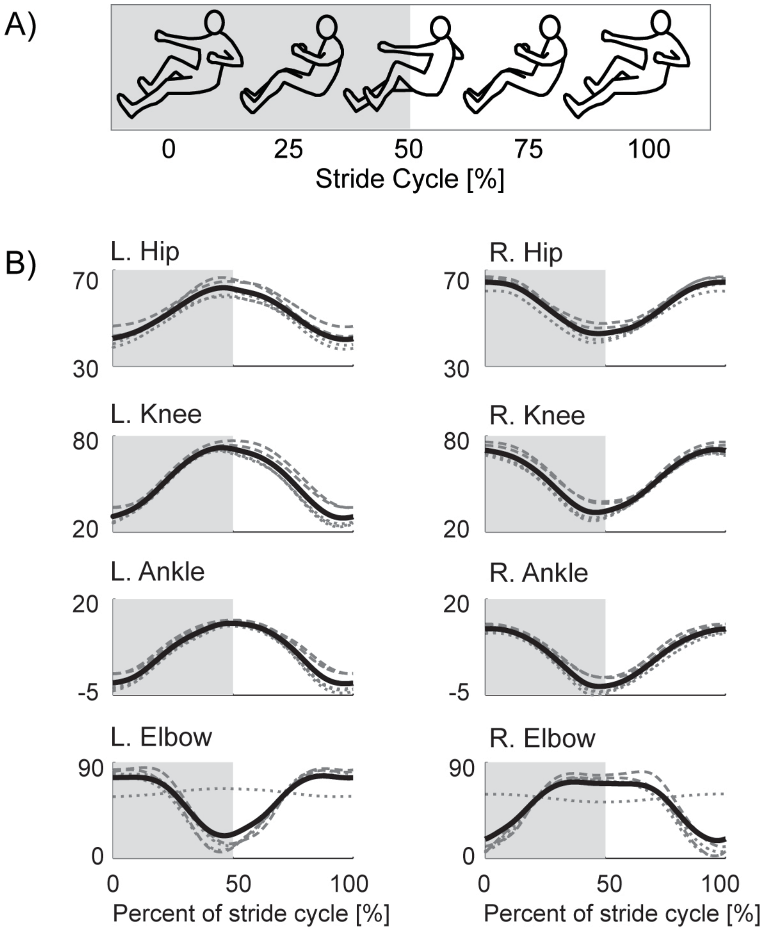


Figure 5.2 A) Schematic of recumbent stepping motion. At 0% of the stride cycle, the left lower limb and right upper limb are at full extension. From 0% to 50% of the stride cycle, the left lower limb and right upper limb are flexing while the right lower limb and left upper limb are extending. At 50% of the stride cycle, the right lower limb and left upper limb are at full extension. From 50% to 100% of the stride cycle, the right lower limb and left upper limb are flexing while the left lower limb and right upper limb are extending. B) Group mean joint angle profiles for the bilateral hip, knee, ankle, and elbow during one stepping cycle. Black solid line: average for all conditions. Dotted grey lines: active lower limb conditions, Resting Upper & Active Lower, Passive Upper & Active Lower, and Active Upper & Active Lower. Dashed grey lines: passive lower limb conditions, Passive Upper & Passive Lower and Active Upper & Passive Lower.

data showed the same effects as the representative single subject data. There were no observable differences in the left and right lower limb muscle activation patterns among any of the active lower conditions despite varying levels of upper limb effort. The group EMG mean profiles for the active left and right lower limb

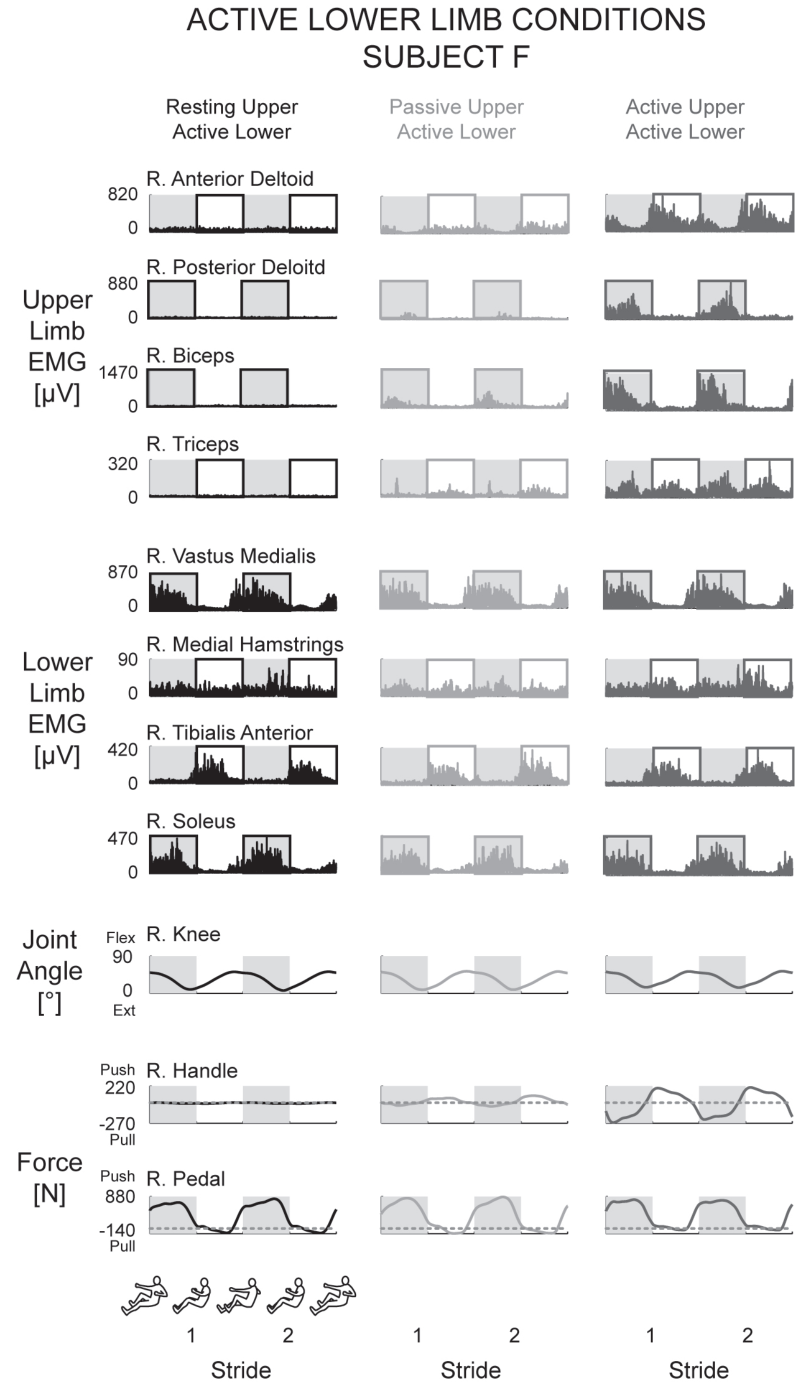


Figure 5.3 Right limb data from a single representative subject for the active lower limb conditions, Resting Upper & Active Lower (black), Passive Upper & Active Lower (light grey), Active Upper & Active Lower (dark grey). There was no observable difference in active lower limb muscle activation patterns regardless of the activity in the upper limbs. There was minimal upper limb muscle activation during the resting and passive conditions and increased burst-like activity during the active condition. Boxed halves indicate concentric half of the cycle. The knee joint angle profiles and active pedal forces were similar between the conditions. The Resting Upper & Active Lower and Passive Upper & Active Lower handle forces were minimal while the Active Upper & Active Lower handle forces had a large pushing and pulling force. Dashed lines in the force data is zero force.

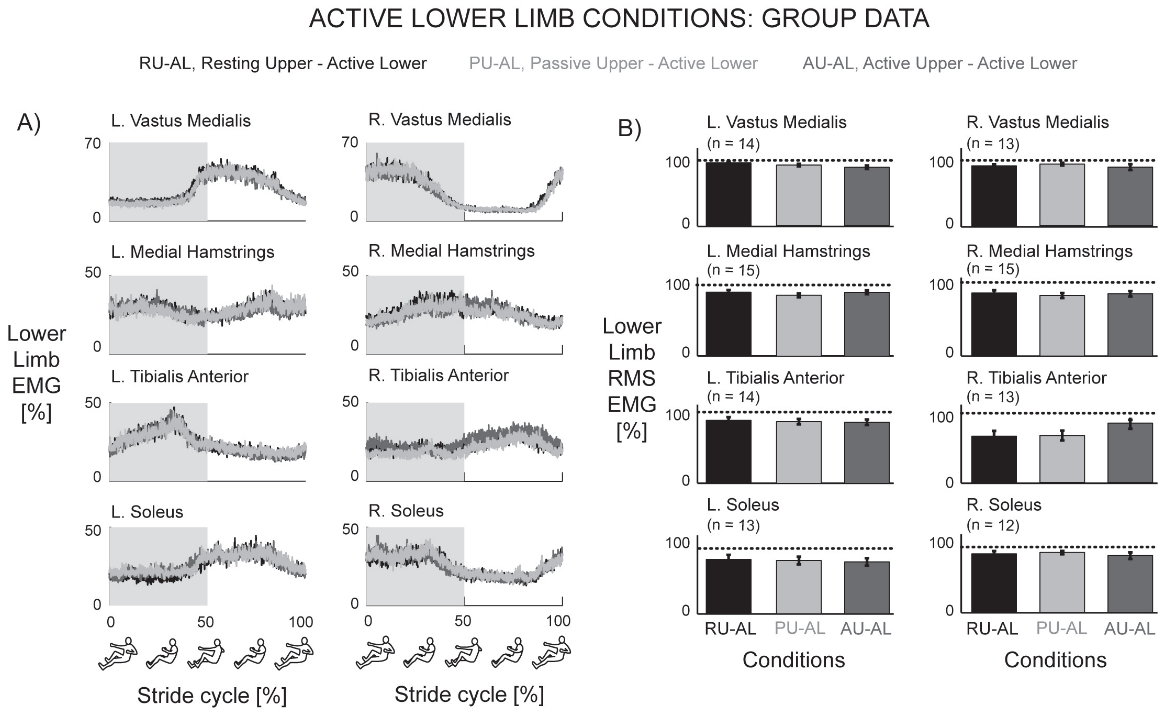
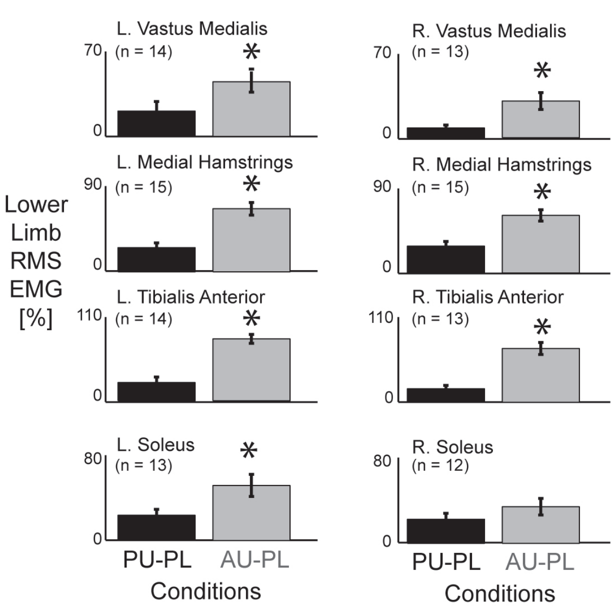


Figure 5.4 Left and right limb group data for the active lower limb conditions, Resting Upper & Active Lower (black), Passive Upper & Active Lower (light grey), Active Upper & Active Lower (dark grey). A) Group normalized EMG mean profiles showed no observable difference in active lower limb muscle activation patterns regardless of the activity in the upper limbs. B) Group normalized RMS EMG amplitudes with standard error bars for the active lower limb conditions. There were no significant differences among the three conditions (rmANOVA *P* > 0.05).

muscles all overlapped one another (Figure 5.4A). The group averaged RMS EMG amplitudes for the lower limb muscles also indicated no significant differences among active lower limb conditions (Figure 5.4B, rmANOVA P > 0.05). Statistical powers for the active lower limb conditions for the left and right vastus medialis, medial hamstring, tibialis anterior, and soleus muscles were 0.541, 0.130, 0.165, 0.081, 0.068, 0.380, 0.064, and 0.098, respectively. For the passive lower limb conditions, the statistical powers were 0.514, 0.829, 0.997, 0.980, 1.000, 0.999, 0.623, and 0.218 for the left and right vastus medialis, medial hamstring, tibialis anterior, and soleus muscles, respectively. Group mean


A) PASSIVE LOWER

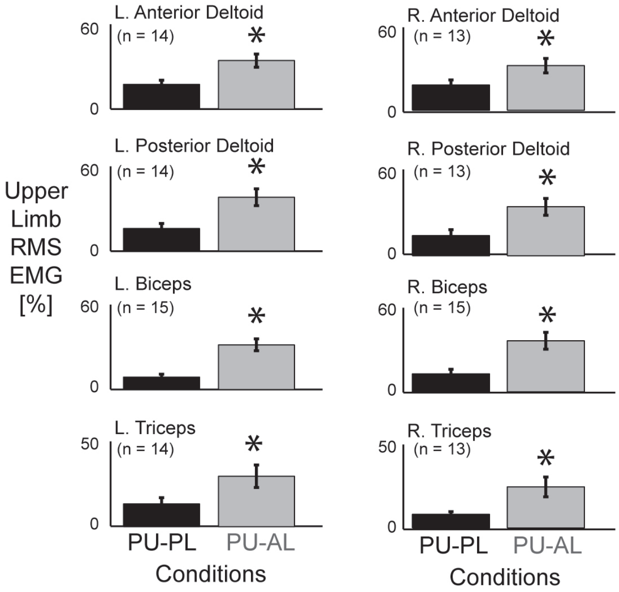

B) PASSIVE UPPER

Figure 5.5 A) Normalized RMS EMG group data for the left and right lower limb for the passive lower limb conditions, Passive Upper & Passive Lower (PU-PL, black) and Active Upper & Passive Lower (AU-PL, grey). The RMS EMG for the bilateral vastus medialis, bilateral medial hamstrings, bilateral tibialis anterior, and left soleus muscles during the Active Upper & Passive Lower condition were significantly greater compared to the Passive Upper & Passive Lower condition (* THSD $P < 0.05$). B) Normalized RMS EMG group data for the left and right upper limb for the passive upper limb conditions, Passive Upper & Passive Lower (PU-PL, black) and Passive Upper & Active Lower (PU-AL, grey). The RMS EMG amplitudes for the bilateral anterior deltoid, bilateral posterior deltoid, bilateral biceps brachii, and bilateral triceps brachii muscles during the Passive Upper & Active Lower condition were significantly greater compared to the Passive Upper & Passive Lower condition (* THSD $P < 0.05$).

force profiles for the active lower limb conditions had similar shapes and amplitudes for the pedal forces while the handle forces reflected the different levels of upper limb effort, resting, passive, and active (Figure 5.6A). There were also no significant differences among the mean handle and pedal forces for the active lower limb conditions (Figure 5.6B, rmANOVA $P > 0.05$)

Active upper limb effort resulted in greater passive lower limb muscle activation. Single subject data and group mean EMG profiles showed greater burst-like muscle activation in the passive lower limbs when coupled with active upper limb effort. Group RMS EMG data indicated that for the passive lower limbs, Active Upper & Passive Lower RMS EMG amplitudes were significantly greater than Passive Upper & Passive Lower RMS EMG amplitudes for the bilateral vastus medialis, bilateral medial hamstring, bilateral tibialis anterior, and left soleus muscles (Figure 5.5A*, THSD $P < 0.05$). Similarly, active lower limb effort resulted in greater passive upper limb muscle activation. Single subject data and group mean EMG profiles showed greater burst-like muscle activation in the passive upper limbs when coupled with active lower limb effort. The group RMS EMG amplitudes of the passive upper limb muscles were significantly greater during the Passive Upper & Active Lower condition compared to the Passive Upper & Passive Lower for the bilateral anterior deltoid, posterior deltoid, biceps brachii, and triceps brachii (Figure 5.5B*, THSD $P < 0.05$). Passive lower limb pedal forces were small compared to active lower limb conditions. The mean force of the right pedal during the first half stepping cycle for the Active Upper &

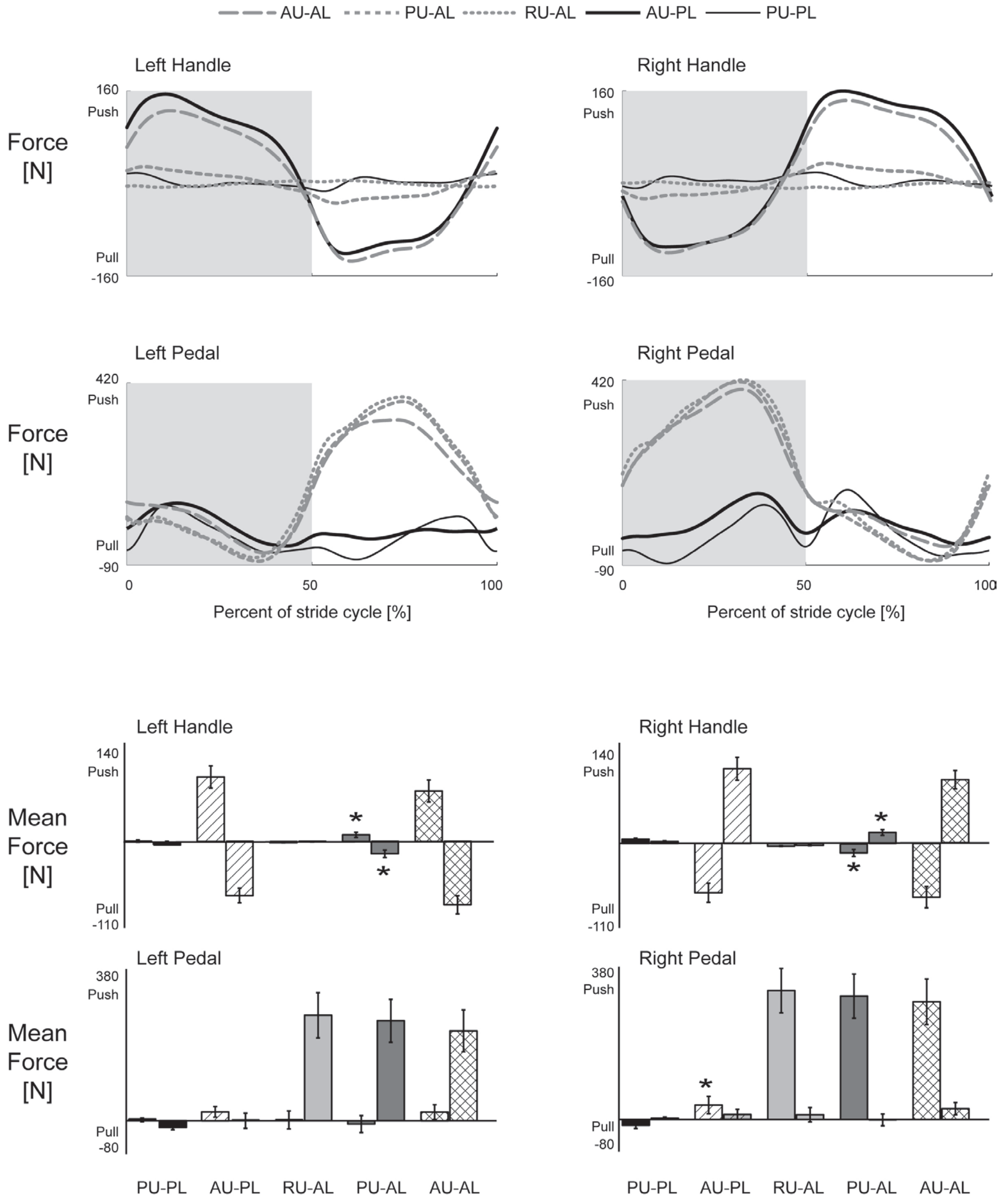


Figure 5.6 A) Group mean force profiles for the left and right handles and pedals. The force profiles match the levels of effort required for each of the conditions. Handle forces only had substantial pushing and pulling phases for the active upper limb effort conditions. Pedal forces only had substantial pushing phases for the active lower limb effort conditions. B) Mean forces for each half of the stepping cycle for the left and right handles and pedals. For each condition, the bar on the left is the mean force for the first half of the stepping cycle and the bar on the right is for the second half of the stepping cycle. *Significantly different from the Passive Upper & Passive Lower condition during the same half of the stepping cycle. PU-PL, Passive Upper & Passive Lower. AU-PL, Active Upper & Passive Lower. RU-AL, Resting Upper & Active Lower. PU-AL, Passive Upper & Active Lower. AU-AL, Active Upper & Passive Lower.

Passive Lower condition was significantly greater than the Passive Upper & Passive Lower condition (Figure 5.6B*, THSD $P < 0.05$).

Discussion

Our main finding was that upper limb effort did not increase muscle activation during active lower limb effort in individuals with incomplete spinal cord injury during recumbent stepping. During active lower limb conditions, subjects generated similar lower limb EMG amplitudes regardless of whether the upper limbs were resting, passive, or exerting maximal effort. The mean forces mirrored the RMS EMG data for the knee and ankle musculature, suggesting that hip musculature EMG would not have shown substantially different findings from the ankle and knee EMG. If hip muscles had a different muscle activation pattern compared to the ankle and knee muscles then the force data would have shown different changes in pedal forces by condition (Figure 5.6). The finding that active lower limb muscle activation was indifferent to upper limb passive or active effort was contrary to our hypothesis. This result suggests that individuals with incomplete spinal cord injury are not able to recruit additional lower limb motor units during maximal volitional effort by actively using their upper limbs. This result is also similar to our results on neurologically intact individuals who showed no significant change in maximal lower limb muscle activation despite the effort level of the upper limbs (Huang HJ and Ferris DP, In Press). We expected that we might find different results for individuals with incomplete spinal cord injury compared to neurologically intact individuals because the spinal cord injury patients had a lower capacity to maximally recruit their lower limb motor neurons.

We did find that upper limb effort increased muscle activation in the passive lower limbs and lower limb effort increased muscle activation in the passive upper limbs. These results on individuals with incomplete spinal cord injury were similar to our previous results on neurologically intact individuals (Huang HJ and Ferris DP, 2004; Huang HJ and Ferris DP, In Press; Kao PC and Ferris DP, 2005). These results differ somewhat from Kawashima and colleagues recent work (Kawashima N, et al., 2008). They found no significant differences in lower limb EMG amplitudes between passive and active arm swing conditions for stepping movements in a standing frame glider. In contrast, we found a significant increase in passive lower limb muscle activation amplitude when coupled with active upper limbs compared to passive upper limbs (Figure 5.5). The differences between the two studies may be a result of differences between the two tasks, reciprocal leg swing versus recumbent stepping. In the standing frame glider, there was no knee flexion during the rhythmic motion unlike in recumbent stepping. Another difference in movement kinematics between the two devices was that the standing frame glider had hip motion more similar to the hip excursions seen during locomotion. As hip afferents have been found to play an important role in the neural control of walking in humans (Dietz V, et al., 2002), this could be an important difference between the two movement tasks.

The increase in muscle activation of passive limbs when coupled with maximal effort in the other limb pair is likely a result of the convergence of multiple neural drives. Spinal interneurons could relay increased locomotor output in the networks of the upper limb pair to the networks of the lower limb pair and vice versa (Dietz V, 2002; Zehr EP and Duysens J, 2004). Furthermore, even though reflexes in one limb are often suppressed with movements of the other limbs (Collins DF, et al., 1993; Frigon A, et al., 2004; Knikou M, 2007), reflex facilitation from other sensory feedback pathways such as cutaneous stimulation can prevail (Zehr EP, et al., 2004; Zehr EP, et al., 2007a). Decreased inhibition to the passive limbs from supraspinal centers or spinal interneurons could also allow the emergence of a rhythmic motor pattern. Additionally, an excitatory locomotor drive from the mesencephalic locomotor region in the brain could lead to increased recruitment of passive limb motor neurons (Shik ML, et al., 1966). Descending supraspinal drive from regions other than the mesencephalic locomotor region could also produce unintended muscle activation, possibly through general motor neuron excitation (Cernacek J, 1961; Dimitrijevic MR, et al., 1992; Shinohara M, et al., 2003; Zijdewind I, et al., 2006). Clearly, there are multiple neural drives which could contribute to our results. Future studies using other neural techniques (transcranial magnetic stimulation, electrophysiological reflex testing, etc.) may provide greater insight about specific mechanisms.

Our findings suggest that the maximal recruitment of lower limb motor neurons in individuals with incomplete spinal cord injury has a neural limit despite the convergence of multiple neural drives. The lack of a change in muscle activation when subjects simultaneously use their upper and lower limbs at maximal effort compared to only using their lower limbs at maximal effort suggests that individuals with incomplete spinal cord injury did not gain any additional recruitment from using their upper limbs with maximal lower limb stepping. Despite the convergence of neural drives from spinal neural networks and supraspinal centers, muscle activation associated with maximal effort was not enhanced. It is also possible that suppressive effects such as a bilateral deficit masked facilitatory effects. A bilateral deficit occurs when the combined output force or output muscle activation during a simultaneous multi-limb exertion is less than the sum of the individual limb's forces or muscle activation amplitudes. The exact mechanisms responsible for the bilateral deficit are not known, but it is thought to be neurally mediated (Howard JD and Enoka RM, 1991). There are several proposed neural mechanisms for bilateral deficit including spinally based neural inhibition (Khodiguian N, et al., 2003), interhemispheric inhibition (Oda S, 1997), and decreased input to the primary motor cortex (Post M, et al., 2007). Bilateral deficits are often observed in tasks using homologous muscles during isometric and isokinetic contractions in the upper limbs (Oda S and Moritani T, 1994; Ohtsuki T, 1983) and in the lower limbs (Khodiguian N, et al., 2003; Simon AM and Ferris DP, 2008; Vandervoort AA, et al., 1984). Because our task combined maximal effort of not just two limbs, but all four limbs, it is possible that a bilateral deficit or a quadrupedal deficit was present but unobserved due to enhancement from interlimb neural coupling. This will also require additional techniques to determine.

Grouping subjects by injury level produced similar results and led to the same conclusions, indicating that the results of this study were robust. When we grouped subjects into cervical, thoracic, or lumbar groups, we observed increased passive limb muscle activation with maximal effort for the other limb pair in all three groups. We also performed statistical analysis on the grouped data which revealed nearly identical results compared to all of the subjects grouped together. The cervical group (n = 6) showed a significant increase in passive lower limb muscle activation for the bilateral vastus medialis, medial hamstrings, and tibialis anterior muscles with maximal upper limb effort (THSD $P < 0.05$). Likewise, the thoracic group (n= 5) had significant increases in the left vastus medialis, bilateral medial hamstrings, and bilateral tibialis anterior muscles (THSD $P < 0.05$). The lumbar group (n = 4) only reached significance for the bilateral medial hamstrings and the right tibialis anterior (THSD $P < 0.05$). Because we found similar trends and results regardless of how subjects were grouped, we feel confident that analyzing all subjects together was appropriate.

Normalization procedure used and cycle portion analyzed also did not affect the results. For this study, we used a non-zero variance normalization procedure for the RMS EMG data. We also analyzed the data using a zero-variance normalization condition similar to our normalization procedure in our study of neurologically intact subjects (Huang HJ and Ferris DP, In Press). For that procedure, we normalized lower (or upper) limb RMS EMG amplitudes to the Passive Upper & Active Lower (or Active Upper & Passive Lower) condition such that the Passive Upper & Active Lower (or Active Upper & Passive Lower) condition had zero variance. Regardless of normalization, passive lower (or upper) limb muscle activation significantly increased with maximal upper (or lower) limb effort. Lastly, we also analyzed RMS EMG with respect to the eccentric half of the stride cycle and the full cycle. The results had the same trends and led to the same conclusions regardless of the portion of the cycle used in the RMS EMG calculation.

A limitation of this study was that we had to rely on the subjects' confirmation of their effort for each stepping condition. During the Passive Upper & Passive Lower condition, the motor moved with the subject, promoting subject passivity because the subject did not need to do any work. During maximal effort conditions however, the device was still moving but would increase its resistance to maintain a constant stepping frequency if the subject's maximal effort was strong enough to drive the stepping motion faster than the specified stepping frequency (75 BPM). This means that the harder subjects worked, the more resistance they encountered. The only motivation for the subject to exert maximal effort was to comply with the instructions given. We provided verbal encouragement, but did not provide any other forms of feedback. Providing feedback such as a display of the subject's force production would alter the task and involve more voluntary and supraspinal processes. Another limitation was that we did not examine any submaximal levels of recumbent stepping. Based on our previous work, we chose to have subjects use maximum effort to produce the greatest change in passive limb motor neuron recruitment (Huang HJ and Ferris

DP, 2004; Kao PC and Ferris DP, 2005). Submaximal levels of effort, however, correspond better to daily tasks and customary therapeutic exercise.

Based on the results in this study, studies on neurologically intact individuals (Huang HJ and Ferris DP, 2004; Huang HJ and Ferris DP, In Press; Kao PC and Ferris DP, 2005) and clinical observations (Behrman AL and Harkema SJ, 2000; Visintin M and Barbeau H, 1994), it is likely that upper limb effort would result in an increase in submaximal effort lower limb muscle activation. Therefore, an experiment examining submaximal active upper and lower limb exercise combined with other neural techniques such as transcranial magnetic stimulation might provide valuable insight. Zehr and colleagues used transcranial magnetic stimulation to show that rhythmic arm movement (Carroll TJ, et al., 2006) decreased cortiospinal excitability of a forearm muscle compared to tonic voluntary contraction. In a similar experiment, they demonstrated that rhythmic leg cycling increased corticospinal excitability of a forearm muscle compared to a static position. Likewise, we could determine if adding upper limb effort to lower limb stepping decreases supraspinal descending neural drive compared to just lower limb stepping. This would support the idea that upper limb effort aids lower limb muscle recruitment along a convergent pathway from descending supraspinal drives (Ferris DP, et al., 2006).

We found that upper limb effort did not increase lower limb muscle activation when subjects with incomplete spinal cord injury were already using their lower limbs maximally during rhythmic exercise. Upper limb effort did increase lower limb muscle activation when the subject’s lower limbs were passive. Likewise, lower limb effort increased upper limb muscle activation when the subject’s upper limbs were passive. Combined with our previous work, individuals with incomplete spinal cord injury behaved similarly to neurologically intact individuals performing a similar stepping protocol and maximal effort (Huang HJ and Ferris DP, In Press). These findings suggest that despite presumed interlimb neural connections (Dietz V, 2002; Zehr EP and Duysens J, 2004), any excitatory influence from the interlimb neural connections does not add on to the maximal motor recruitment. There is a neural limit on muscle activation in actively moving lower limbs during rhythmic whole body exercise. Even though these results do not indicate that maximal upper limb effort increases muscle activation in active lower limbs, they do not rule out the possibility that at submaximal levels, upper limb effort may improve lower limb muscle activation. Understanding how upper limb effort and movement influences lower limb muscle activation patterns has implications for designing exercise therapies for lower limb rehabilitation. If adding upper limb effort increases lower limb muscle activation and improves muscle activation patterns at submaximal levels, then incorporating upper limb effort in lower limb rehabilitation may help patients regain lower limb functionality more quickly (Ferris DP, et al., 2006).

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CHAPTER 6

COMPUTER SIMULATIONS OF NEURAL MECHANISMS EXPLAINING UPPER AND LOWER LIMB EXCITATORY NEURAL COUPLING

Abstract

When humans perform rhythmic upper and lower limb locomotor-like movements, there is an excitatory effect of upper limb exertion on lower limb muscle recruitment. To investigate potential neural mechanisms for this behavioral observation, we developed computer simulations modeling interlimb neural pathways among central pattern generators and supraspinal inputs. We used Matsuoka oscillators for the central pattern generators and tested hypotheses about how neural coupling dynamics affects motor output. Our base model had a descending tonic signal that acted only on the upper limb oscillators, inhibitory sensory feedback to the upper and lower limb oscillators, and bilateral inhibitory connections. We hypothesized that enhancement of muscle recruitment from interlimb spinal mechanisms was not sufficient to explain muscle enhancement levels observed in experimental data. When we increased the strength of excitatory ipsilateral gains in our model, the lower limb oscillators produced greater amplitudes of rhythmic flexor and extensor bursts but the pattern deteriorated above a 15% enhancement of lower limb muscle recruitment. This percentage of enhancement was not sufficient to explain our

previous experimental results. Alternative models with supraspinal pathways acting on the central pattern generators or on motor neuron groups had greater flexibility in producing higher limb muscle recruitment amplitudes. Based on these simulations, we suggest that supraspinal mechanisms are the more likely explanation for excitatory neural coupling between upper and lower limbs during rhythmic locomotor-like movements.

Introduction

Central pattern generators (CPGs) are spinal neural networks that produce rhythmic motor commands. For vertebrate locomotion, they are theorized to consist of two half-centers with reciprocal inhibition (Brown 1914). When one half-center is active, the other half is inhibited, producing alternating rhythmic bursts. Key features of central pattern generators are that they can produce rhythmic outputs without rhythmic inputs and they can entrain their rhythmic outputs to sensory feedback. Experimental data on both animals and in humans support the idea that central pattern generators exist. A spinalized cat can be taught to walk after repeated step training (Lovely, Gregor et al. 1986; de Leon, Hodgson et al. 1998). In humans, individuals with clinically complete spinal cord injuries can produce rhythmic lower limb motor patterns with appropriate sensory feedback (Dietz, Colombo et al. 1995; Ferris, Gordon et al. 2004).

Central pattern generators can be modeled with nonlinear mathematical equations that produce an oscillatory output. Several modeling studies have examined the role of inter-oscillator connections on synchronization and coordination of oscillator outputs (Ijspeert 2008). In these studies, the frequency and phasing of the oscillators are of primary interest. Other studies have used artificial neural oscillators to control a dynamic system such as a robot (Williamson 2003; Pelc, Daley et al. 2008) or a computer simulated mechanical system (Taga 1995).

We are interested in understanding the role of inter-oscillator connections on oscillator output because it may provide greater insight about interlimb neural coupling observed in humans. Experiments on humans have shown that upper limb movement and muscle recruitment can alter lower limb muscle activation (Zehr and Duysens 2004; Zehr 2005; Zehr, Hundza et al. 2009). Specifically, greater upper limb effort increases muscle activation of passive lower limbs in neurologically intact individuals and individuals with incomplete spinal cord injuries during a rhythmic upper and lower limb movement task (Huang and Ferris 2004; Kao and Ferris 2005; Huang and Ferris In Press). Conversely, active lower limb effort also increases passive upper limb muscle activation (Huang and Ferris In Press). Other research has shown that upper limb movement alone can alter lower limb muscle activation patterns in individuals with incomplete spinal cord injuries during a standing reciprocal leg swing task (Kawashima, Nozaki et al. 2008). Additionally, clinical observations suggest that reciprocal arm swing increases and improves muscle activation in individuals with spinal cord injuries (Visintin and Barbeau 1994; Behrman and Harkema 2000). The neural mechanisms responsible for these interlimb excitatory effects are difficult to determine in humans.

One approach for investigating the neural mechanisms involved in the experimental observations is to model the neural pathways. The purpose of this computer simulation study was to test potential neural mechanisms that may explain excitatory interlimb coupling in humans. We hypothesized that interlimb spinal pathways could not account for the levels of muscle recruitment enhancement revealed in our previous experimental studies (Huang and Ferris In Press). Believing in the principle that the simplest model that can explain an observed behavior provides key insight into the dynamics (Alexander 1995), we aimed to create the simplest model possible that still faithfully reproduced the most important behavioral observations from our previous studies. We used a Matsuoka oscillator to model the central pattern generator for each limb. We then interconnected the four Matsuoka oscillators to test the effects of different combinations of inhibitory and/or excitatory interlimb pathways. We also added supraspinal descending pathways to test the effects of potential supraspinal inputs to the motor neurons and central pattern generators.

Methods

Matsuoka Oscillators

We modeled each limb's central pattern generator using a Matsuoka oscillator (Figure 6.1) with the following governing equations:

$$\tau_1 \dot{x}_{\mathrm{i\_Flex}} = k_i - x_{\mathrm{i\_Flex}} - \beta v_{\mathrm{i\_Flex}} - \eta \left[x_{\mathrm{i\_Ext}}\right]^+ - \sum_{\mathrm{j=1}}^{\mathrm{n}} h_j \left[g_j\right]^+ \qquad \text{(Eq. 6.1)}$$

$$\tau_2 \dot{v}_{\mathrm{i\_Flex}} = -v_{\mathrm{i\_Flex}} + \left[x_{\mathrm{i\_Flex}}\right]^+ \qquad \text{(Eq. 6.2)}$$

$$\tau_1 \dot{x}_{\mathrm{i\_Ext}} = k_i - x_{\mathrm{i\_Ext}} - \beta v_{\mathrm{i\_Ext}} - \eta \left[x_{\mathrm{i\_Flex}}\right]^+ - \sum_{\mathrm{j=1}}^{\mathrm{n}} h_j \left[g_j\right]^- \qquad \text{(Eq. 6.3)}$$

$$\tau_2 \dot{v}_{\mathrm{i\_Ext}} = -v_{\mathrm{i\_Ext}} + \left[x_{\mathrm{i\_Ext}}\right]^+ \quad \text{(Eq. 6.4)}$$

$$y_{\mathrm{i\_Flex}} = \left[x_{\mathrm{i\_Flex}}\right]^+ \quad \text{(Eq. 6.5)}$$

$$y_{\mathrm{i\_Ext}} = \left[x_{\mathrm{i\_Ext}}\right]^+ \quad \text{(Eq. 6.6)}$$

Each flexor (Flex) and extensor (Ext) neuron has a firing rate, x_{i} and an adaptation state, v_{i} where $i =$ RU (Right Upper Limb), LU (Left Upper Limb), RL (Right Lower Limb), and LL (Left Lower Limb). The output of the flexor or extensor neuron is $y_{\mathrm{i\_Flex}}$ or $y_{\mathrm{i\_Ext}}$ and is equal to $[x_{\mathrm{i}}]^+$ the positive part of the flexor or extensor neuron firing rate x_{i}, respectively. Similarly, $\left[g_{\mathrm{j}}\right]^+$ is the positive part of the external input and $\left[g_{\mathrm{j}}\right]^-$ is the negative part of the external input. Each external input has as associated gain, h_j. These gains can be negative for inhibitory feedback or positive for excitatory feedback (Williams and DeWeerth 2007). Inhibitory sensory feedback appears to more faithfully reproduce biological systems. The constant k_i is the tonic descending signal. The β constant modulates the strength of self-inhibition and the η constant modulates the strength of reciprocal inhibition between the flexor and extensor neurons. τ_1 and τ_2 are time constants that affect the shape and intrinsic frequency of the oscillator.

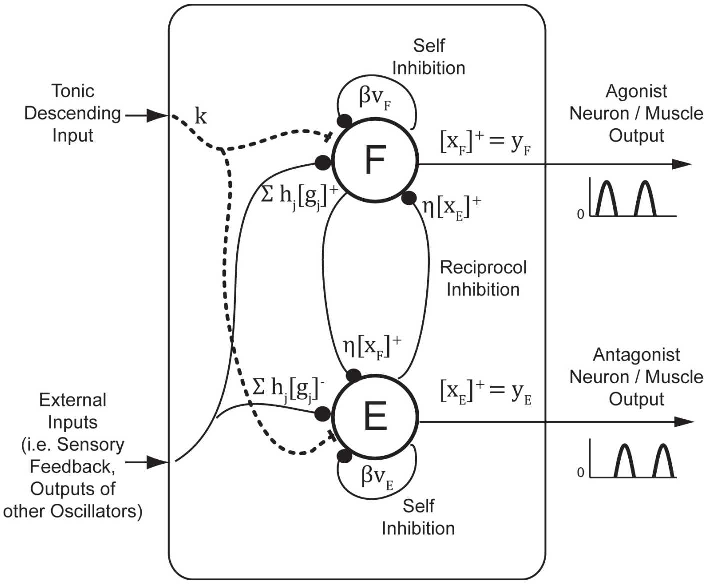

Figure 6.1 Schematic of a Matsuoka artificial neural oscillator.

For our model, we set $\beta = 2.5$, $\eta = 2.5$, $\tau_1 = 0.35$, and $\tau_2 = 0.7$ according to previously developed guidelines (Williamson 1998). We set τ_1 and τ_2 to provide an endogenous oscillator frequency of 0.32 Hz, which is slower than normal walking step frequencies. We also used a sine wave with a frequency of 0.625 Hz and amplitude of 1 as our sensory feedback signal. This frequency matched the stepping frequencies we used in our recumbent stepping experimental studies (Huang and Ferris 2004; Huang and Ferris In Press).

Excitatory Ipsilateral Pathways

Experimental studies suggest that there is interlimb neural coupling (Dietz 2002; Zehr and Duysens 2004). If the primary mechanisms of interlimb neural coupling are spinal connections among the locomotor networks, then a model interconnecting Matsuoka oscillators would be the best match. Our base model had a tonic descending input to just the upper limb oscillators, inhibitory sensory feedback to both the upper and lower oscillators, and inhibitory bilateral connections (Table 6.1). We then varied the strength of the ipsilateral excitatory pathways that connected flexors to extensors and extensors to flexors. We crossed the excitatory ipsilateral connections to act from flexor to extensor and extensor to flexor based on our previous study that showed a preference for ipsilateral neural coupling of flexors and extensors (Huang and Ferris In Press). The ipsilateral connections were also symmetrical and had the same excitatory strength in the upper to lower direction and the lower to upper direction.

Base Model Parameters	
Descending tonic input, k	20
Inhibitory sensory feedback gain, upper limbs	10
Inhibitory sensory feedback gain, lower limbs	1
Bilateral inhibitory gain	0.1

Table 6.1 Parameter values for the base model. We chose these parameters because they produced alternating rhythmic bursts of the flexors and extensors at the desired frequency of 0.625 Hz. The lower limb sensory feedback gain had to be significantly less than the upper limb sensory feedback gain because the lower limb oscillators had excitatory inputs of lower amplitudes. A relatively small bilateral inhibitory gain was used because only low gains (< 0.2) for bilateral inhibition produced the desired rhythmic outputs.

Supraspinal Pathways

Supraspinal pathways are also a potential neural mechanism that may explain increases in muscle recruitment in one limb with activity in another limb. Motor overflow or motor irradiation occurs when muscles activated with high levels of effort also activate unintended muscles (Mills and Quintana 1985; Shinohara, Keenan et al. 2003). Based on this behavior, one possibility is that at high levels of excitation, part of the tonic descending drive to the upper limb locomotor networks also excites the lower limb locomotor networks. To model this, we modified our base model to have inhibitory ipsilateral connections with a gain of 0.1, in addition to the tonic descending input to just the upper limb oscillators, inhibitory sensory feedback, and inhibitory bilateral connections. We then varied the ratio of the descending tonic drive to the lower limb oscillators relative to the upper limb oscillators, from 0 to 100%.

Another possibility is a supraspinal pathway that acts on motor neurons, rather than to the locomotor networks, to produce a general excitation. To model this, we added motor neurons to our base model with inhibitory ipsilateral connections. We simplified the motor neurons to be summation centers. The full strength of the supraspinal signal acted on the upper limb motor neurons and a percentage of the supraspinal signal overflowed to act on the lower limb motor neurons. We used a sinusoidal supraspinal input instead of a tonic input. This sinusoidal signal could represent an internal model of the motor pattern within the brain (Wolpert and Kawato 1998).

Simulation and Analysis

We built the model in MATLAB/Simulink software program and performed each simulation using the Runge-Kutta method with a time step of 0.01 seconds. We obtained 60 seconds of data for each parameter set. We considered muscle recruitment to be the oscillator output or the sum of the oscillator output plus the supraspinal contribution directly to the motor neuron. To determine muscle recruitment amplitudes, we used the average peak values of the outputs once they reached steady state. We also calculated a ratio of the lower limb muscle recruitment amplitude to the upper limb muscle recruitment amplitude. We only calculated this ratio for muscle recruitment patterns with alternating rhythmic bursts of extensors and flexors. We identified the maximum ratio of lower to upper limb muscle recruitment to be the maximum possible enhancement predicted by the model. We compared the model's prediction for muscle enhancement to the percentage of lower (and upper) limb muscle enhancement from our experimental data on neurologically intact individuals (Huang and Ferris In Press). For the lower limbs, muscle enhancement was the root-mean-square electromyography amplitude of the lower limb muscles during an upper limb only exertion condition. For the upper limbs, muscle enhancement was the root-mean-square electromyography amplitude of the upper limb muscles during a lower limb only exertion condition.

Results

All models produced rhythmic alternating bursts of flexors and extensors in the upper and lower limbs (Figure 6.2 and 6.4). These muscle recruitment patterns were entrained to the sensory feedback frequency, 0.625 Hz. Additionally, the alternation of flexor and extensor muscle recruitment bursts for the left upper and right lower limbs were in-phase. Likewise, the flexor and extensor bursts of the right upper and left lower limbs were also in-phase with each other. The left upper and right lower muscle recruitment patterns were out-of-phase with the right upper and left lower limb muscle recruitment patterns.

The model with excitatory ipsilateral pathways showed that increases in the gain of the excitatory ipsilateral pathways produced greater lower limb muscle recruitment amplitudes without a descending tonic signal to the lower limb oscillators (Figure 6.2). The amplitudes of the upper limb muscle recruitment bursts did not change (Figure 6.2). The ratio of lower to upper limb muscle recruitment revealed a linear increase with greater excitatory ipsilateral gains, but only a small range of gains produced rhythmic alternation of flexors and extensors (Figure 6.3). The maximum muscle enhancement predicted from the excitatory ipsilateral pathways model was 15% (Figure 6.3).

Models with supraspinal pathways to either the motor neurons (Figure 6.4B) or the central pattern generators (Figure 6.4C) also produced rhythmic alternating flexor and extensor muscle recruitment patterns in the lower limbs. Increasing the percentage of the supraspinal signal that acted onto the lower limb oscillators resulted in greater lower limb muscle recruitment amplitudes. The increases in lower limb muscle recruitment amplitudes could reach up to 100% of the upper limb muscle recruitment amplitudes without losing its rhythmic pattern (Figure 6.5).

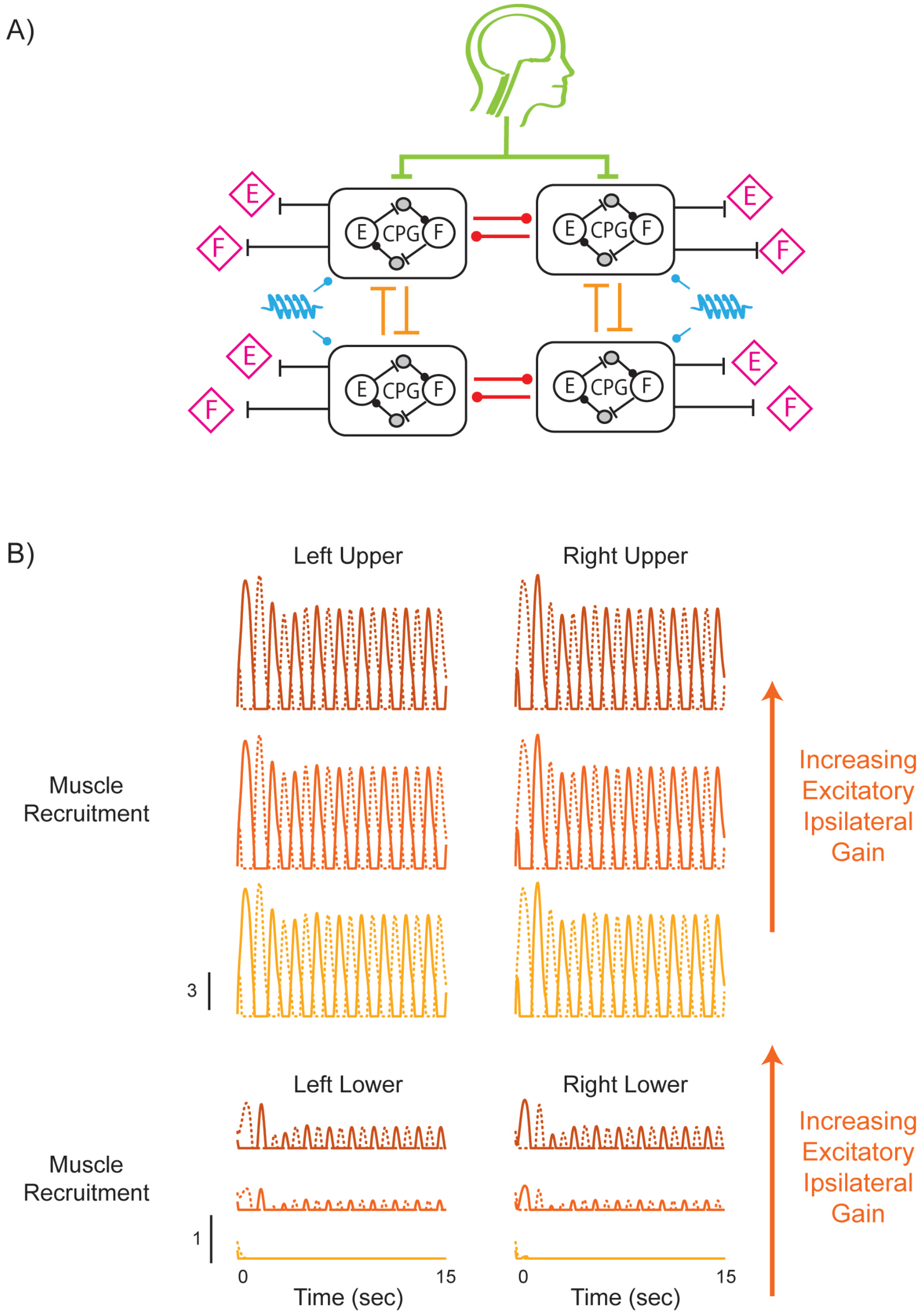

Figure 6.2 Schematic of excitatory ipsilateral pathways model (A) and muscle recruitment patterns with increasing excitatory ipsilateral gains (B). A) Four central pattern generators (CPGs), one for each limb, were interconnected to have bilateral inhibition (red) and ipsilateral excitation (orange). The central pattern generators also received inhibitory sensory feedback (blue). Diamonds (pink) are the motor neuron groups for the flexors (F) and extensors (E). A supraspinal descending tonic signal (green) only acted on the upper limb central pattern generators. Short lines are excitatory and filled circles are inhibitory. B) With increasing excitatory ipsilateral gains, upper limb muscle recruitment amplitudes did not change while lower limb muscle recruitment amplitudes increased. Solid lines are extensors and dotted lines are flexors. Muscle recruitment amplitude scales are the black vertical lines. Note differences in upper and lower muscle recruitment scales.

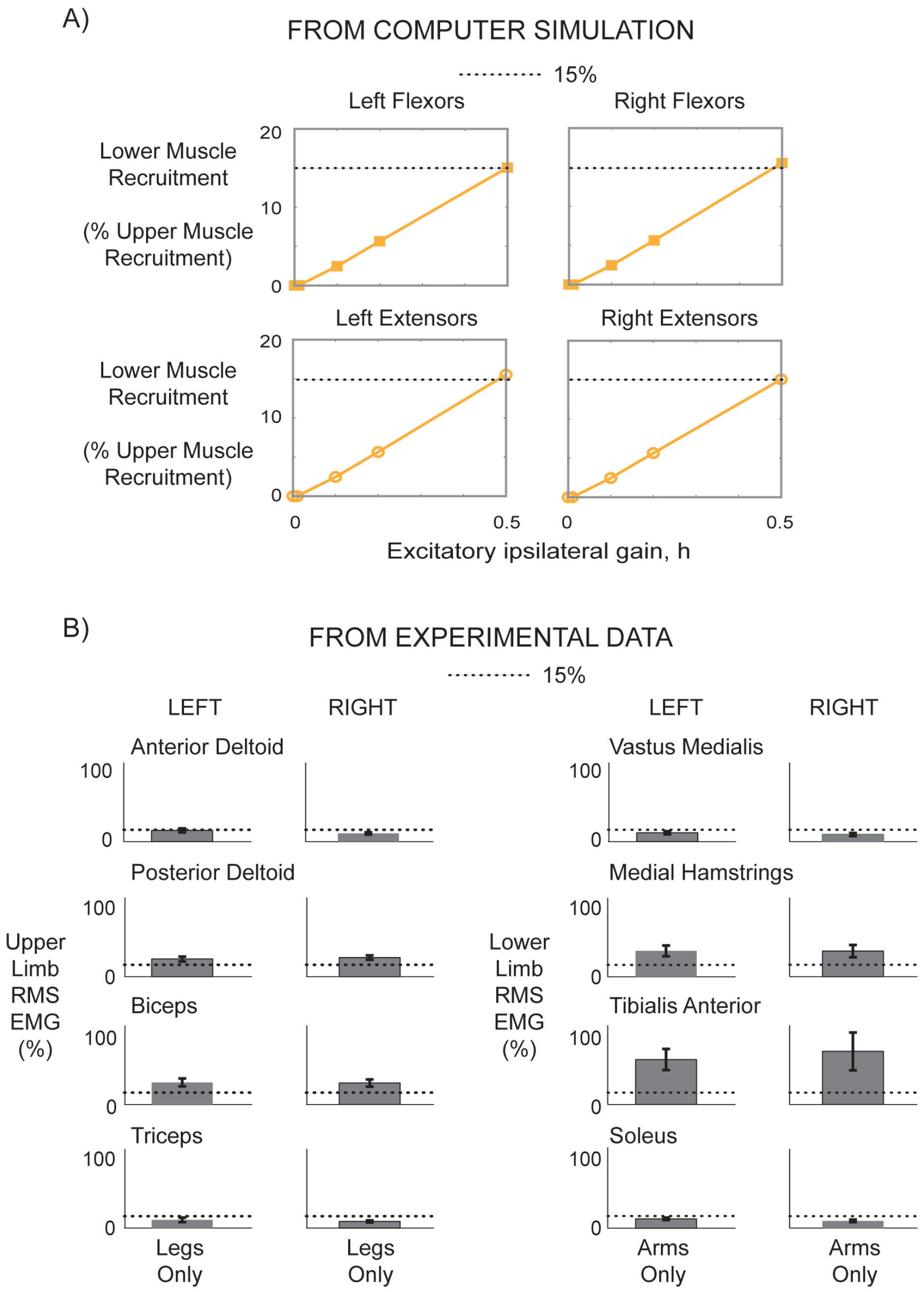

Figure 6.3 A) Ratio of lower to upper limb muscle recruitment from the computer simulation of excitatory ipsilateral connections. Greater excitatory ipsilateral gains resulted in greater ratios of lower to upper limb muscle recruitment, but reached a maximum of 15%, dotted lines. At excitatory ipsilateral gains above 0.5, the muscle recruitment pattern did not have symmetric alternating flexor and extensor activity. B) Ratio of muscle enhancement from experimental data. Dotted line is 15%, based on the prediction from the computer simulation. The left and right posterior deltoids and biceps in the upper limbs and the left and right medial hamstrings and tibialis anteriors in the lower limbs had root-mean-square (RMS) electromyography (EMG) amplitudes greater than 15%.

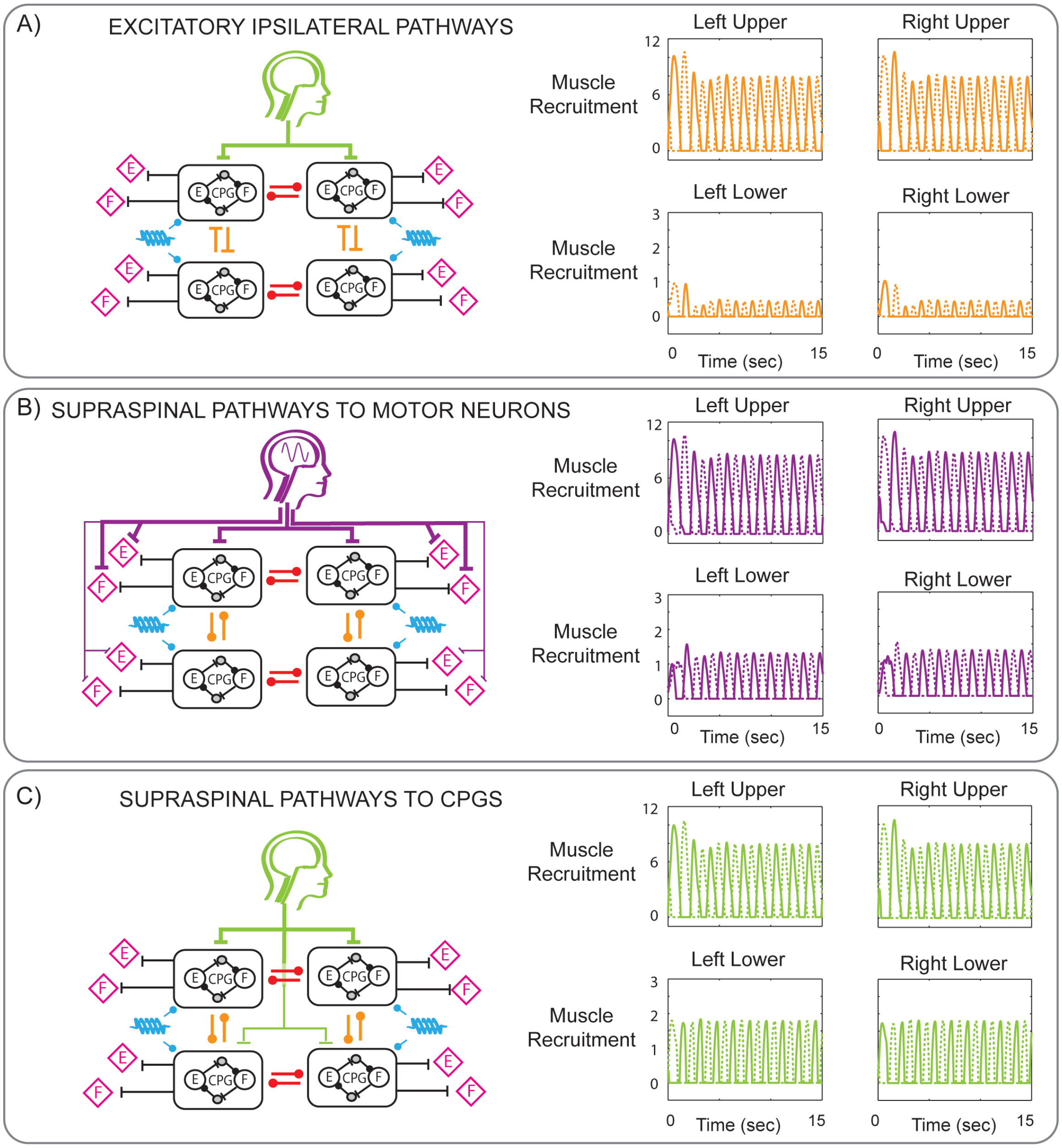

Figure 6.4 Schematics and muscle recruitment patterns for three potential mechanisms that may contribute to excitatory neural coupling between upper and lower limbs. In all schematics, short lines are excitatory and filled circles are inhibitory. A) Excitatory ipsilateral pathways (orange). B) Supraspinal pathways (purple) that act on the flexor (F) and extensor (E) motor neuron groups (pink diamonds). Full strength of the supraspinal signal stimulates the upper limb motor neuron groups while a fraction of the supraspinal signal stimulates the lower limb motor neuron groups. We proposed that the supraspinal signal was rhythmic and represented an internal model of the rhythmic task. C) Supraspinal pathways (green) that act on the central pattern generators. Full strength of the supraspinal signal stimulates the upper limb central pattern generators while a fraction of the supraspinal signal stimulates the lower limb central pattern generators. Solid lines are extensors and dotted lines are flexors. Note differences in upper and lower muscle recruitment scales.

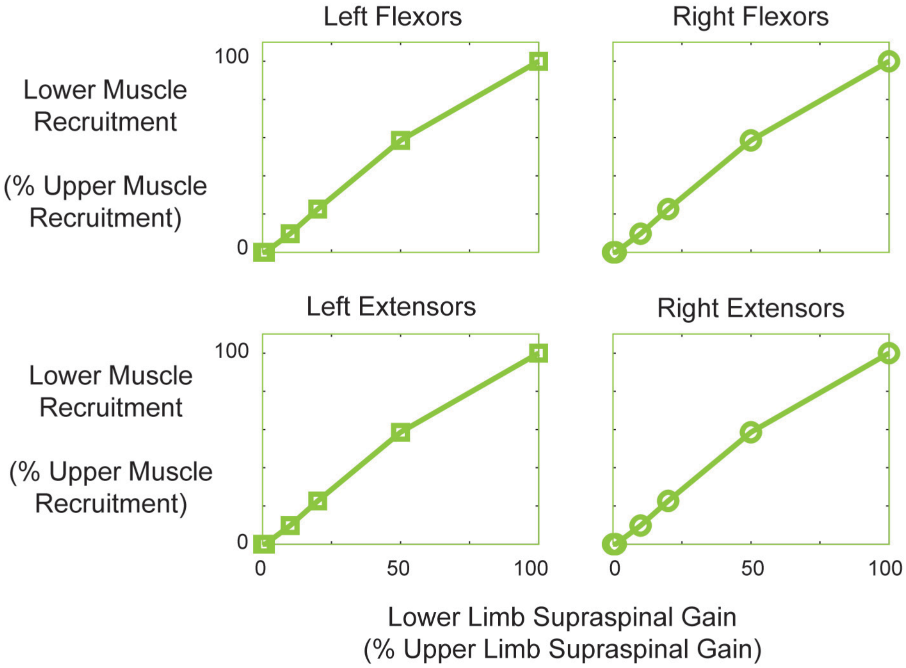

Figure 6.5 Ratios of lower to upper limb muscle recruitment from the computer simulation of supraspinal pathways that act on the central pattern generators. Increases in the percentage of the supraspinal signal to the lower limb central pattern generators resulted in greater amplitudes of the lower limb flexors and extensors, up to 100%.

Discussion

Our computer simulations showed that excitatory ipsilateral pathways produced limited enhancement of muscle recruitment amplitudes while supraspinal pathways were not limited and could produce muscle recruitment amplitudes up to 100%. If the descending tonic signal only acted on the upper limb oscillators, excitatory ipsilateral pathways could only produce rhythmic lower limb muscle activity up to 15% of the upper limb muscle recruitment amplitudes. At greater excitatory ipsilateral gains, the lower limb flexors and extensors no longer produced rhythmic alternating bursts. Our experimental data, however, indicated that muscle enhancement of unintended muscles could exceed 15%.

Thus, this suggested that excitatory ipsilateral pathways alone were insufficient to explain muscle enhancement of unintended muscles. Supraspinal pathways that act on either the central pattern generators or motor neuron groups could produce lower limb muscle recruitment amplitudes levels greater than 15% and up to 100% of the upper limb muscle recruitment amplitudes. We interpreted these results as support for a supraspinal mechanism being the more likely explanation for excitatory neural coupling of upper and lower limbs.

Interlimb pathways that connect the upper and lower limb locomotor networks facilitate interlimb coordination and are one potential mechanism that may partially explain our experimental results. Propriospinal interneurons couple the cervicothoracic to the lumbosacral segments to help coordinate movements of hindlimbs and forelimbs in cats (Miller, Van Der Burg et al. 1975; English, Tigges et al. 1985) and in humans (Nathan, Smith et al. 1996). However, it is not clear if these pathways are excitatory or inhibitory, or if they modulate to improve efficacy of the motor patterns for particular movements. A study of decerebrate cats walking on a transversely split treadmill revealed that the hindlimbs adapted to changes in forelimb stepping speed; however, the forelimbs did not adapt to changes in hindlimb stepping speed (Akay, McVea et al. 2006). They suggested that there are excitatory ipsilateral ascending pathways and inhibitory ipsilateral descending pathways between the flexors of the hindlimb and forelimb locomotor networks (Akay, McVea et al. 2006). In a neonatal rat spinal cord preparation, pharmacological activation of the hindlimb locomotor neural networks could drive the forelimb locomotor neural networks, but not in the reverse direction (Juvin, Simmers et al. 2005). They proposed that caudorostral excitatory pathways help coordinate forelimb and hindlimb movements (Juvin, Simmers et al. 2005). These asymmetrical behaviors observed in the animal studies suggest asymmetrical connections between the forelimb and hindlimb locomotor neural networks. Our previous experimental data revealed a symmetrical behavior, and thus, we believe that in humans, the connections between upper and lower limb are symmetrical.

Supraspinal pathways alone or in combination with excitatory interlimb pathways can sufficiently explain our experimental results. We based our supraspinal models on motor overflow or motor irradiation, which refers to unintended extraneous muscle activity. The unintended muscle activity from motor overflow can also lead to involuntary movements, or mirror movements (Armatas, Summers et al. 1994). Motor overflow tends to parallel the level of effort. High levels of effort or more complex tasks produce greater amounts of unintended muscle activation (Mayston, Harrison et al. 1999; Zijdewind and Kernell 2001; Aranyi and Rosler 2002). Our experimental data also demonstrated a graded effect, where greater levels of effort resulted in greater increases in passive muscle activity (Huang and Ferris 2004). Most motor overflow studies focus on just the upper limbs or just the hands (Addamo, Farrow et al. 2007). The effect extends beyond just between the arms or hands and can manifest among all four limbs, similar to our experimental observations (Panin, Lindenauer et al. 1961; Mills and Quintana 1985). Proposed theories to explain motor overflow are supraspinal in origin and suggest coincidental cortical activation and/or activity in the corticospinal projections of unintended muscles (Addamo, Farrow et al. 2007).

Other potential configurations could have been analyzed. One possible alternative configuration we considered was excitatory contralateral connections from flexors to flexors and extensors to extensors (i.e. uncrossed). A contralateral connective scheme seems to be more intuitive based on the contralateral limbs' phase relationships during walking and a human preference for in-phase movements (Swinnen 2002). We created a model using this uncrossed contralateral configuration and found that this configuration resulted in the same muscle recruitment patterns as a configuration with excitatory ipsilateral pathways that crossed, going from flexor to extensor and extensor to flexor. The ipsilateral crossed flexor and extensor pathways agree with our previous experimental data showing that neural coupling was ipsilaterally biased between flexors and extensors. Upper limb pulling was coupled to ipsilateral vastus medialis and soleus muscle activation, while upper limb pushing activated the tibialis anterior (Huang and Ferris In Press).

Another possible alternative configuration was to have excitatory ipsilateral connections from upper to lower limb oscillators and inhibitory ipsilateral connections from lower to upper limb oscillators. This configuration would be more similar to the proposed asymmetrical lumbocervical connections in cats (Akay, McVea et al. 2006) and rats (Juvin, Simmers et al. 2005). Our model did show that excitatory upper to lower and inhibitory lower to upper ipsilateral connections produced greater increases in lower limb muscle recruitment amplitudes compared to excitatory ipsilateral connections in both directions. This asymmetrical configuration, however, seems unlikely because our experimental results were symmetrical. High levels of upper limb effort enhanced unintended lower limb muscle activity and also, high levels of lower limb effort enhanced unintended upper limb muscle activity in neurologically intact individuals (Huang and Ferris In Press) and individuals with incomplete spinal cord injury. The asymmetrical configuration of excitatory upper to lower and inhibitory lower to upper ipsilateral connections would have to switch to an inhibitory upper to lower and excitatory lower to upper ipsilateral connective scheme to explain our symmetrical results.

There were also multiple combinations of parameter sets that could have been analyzed. We chose not to test a variety of combinations of bilateral, ipsilateral, and contralateral gains. Specific combinations of bilateral, ipsilateral, and contralateral gains may produce better quantitative results to match our experimental more precisely. However, those specific parameter combinations would probably not alter the relative relationships or ratios of lower to upper limb muscle recruitment.

We also considered creating more complex models, in particular using the Hodgkin Huxley model for the motor neurons. The Hodgkin Huxley model is a set of non-linear equations that describes the initiation and propagation of an action potential in a neuron (Hodgkin and Huxley 1952). Increases in spike or burst frequency of the Hodgkin Huxley model would signify greater muscle recruitment. This analysis would have been more complicated and may not have provided much more insight. Thus, we chose to keep the models as simple as possible to identify the characteristics of the model that were necessary and sufficient to explain the behavioral results (Alexander 1995).

We used simple computer simulations to model interlimb spinal pathways and supraspinal pathways to test whether these potential neural mechanisms could explain excitatory coupling of muscle recruitment between upper and lower limbs. Our computer simulation results indicated that excitatory ipsilateral pathways alone could only produce enhancement of muscle activity up to 15% before the rhythmic pattern deteriorated. This amount of enhancement was not sufficient to explain experimental data with levels of enhancement greater than 15%. Supraspinal pathways that acted on either the central pattern generators or motor neurons could produce enhancement levels greater than 15%. These results suggest that supraspinal pathways are a likely explanation of excitatory neural coupling between upper and lower limbs during rhythmic movements. Future studies could examine corticospinal excitability during submaximal arm and leg rhythmic tasks to determine if supraspinal drive is indeed a primary neural mechanism for excitatory neural coupling between upper and lower limbs.

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CHAPTER 7

CONCLUSIONS

The overall goals of this dissertation were to 1) modify a recumbent stepping exercise device to have computer-controlled resistance and to measure forces applied during stepping, 2) investigate principles of neural coupling between upper and lower limbs during recumbent stepping in neurologically intact individuals, 3) investigate neural coupling in individuals with incomplete spinal cord injury, and 4) use computer simulations to identify potential specific neural mechanisms that explain the empirical neural coupling results.

I successfully built a computer controlled recumbent stepper with force measuring capabilities. The system had a dynamic constant stepping profile mode and a static mode. The motorized stepper could drive the stepping motion at multiple frequencies ranging from 30 BPM to 150 BPM. For the stepping mode during maximal effort conditions, the maximal average error over the stepping cycle was 5.7 ± 1.7% of the stepping range of motion. For the static mode, the average position error was -0.26% of the stepping range of motion.

The main findings of the recumbent stepping studies were that upper limb effort increased passive lower limb muscle activation. This result was robust and observed in multiple experiments and in both neurologically intact individuals and individuals with incomplete spinal cord injury. Neural coupling between upper and lower limbs in neurologically intact individuals was bidirectional and biased towards ipsilateral neural coupling compared to contralateral neural coupling. The excitatory effects of upper and lower limb neural coupling were also limited and did not enhance maximal voluntary muscle activation. Interestingly, individuals with spinal cord injury also did not demonstrate enhanced active lower limb muscle activation with maximal upper limb effort. We had hypothesized that spinal cord injured individuals who had a lower capacity to recruit motor neurons would show an enhancement of active lower limb muscle recruitment with active upper limb effort. Individuals with incomplete spinal cord injuries, like neurologically intact individuals, also had increased passive lower limb muscle activation with maximal upper limb effort.

The computer simulations demonstrated that excitatory ipsilateral pathways alone could not sufficiently explain the experimental results. Excitatory ipsilateral connections only produced enhancement of muscle activity up to 15% which was less than the amount of enhancement observed in the experimental data. Supraspinal pathways that acted on either the central pattern generators or motor neurons could produce enhancement levels greater than 15% according to the models. Thus, the simulations suggest that supraspinal pathways are the more likely primary neural mechanism of excitatory neural coupling between upper and lower limbs during rhythmic movements.

Overall, my findings increase our understanding of excitatory neural coupling between upper and lower limbs. Even though upper limb effort did not enhance maximal voluntary muscle recruitment, this does not necessarily imply that simultaneous upper and lower limb exercise would not be beneficial for rehabilitation. The excitatory neural coupling between the upper and lower limbs may be masked by suppressive effects like a bilateral deficit and/or inhibitory spinal pathways. The findings of this thesis provide important information for the design of gait rehabilitation exercise therapies after neurological injury.

Recommendations for Future Work

Improvements to the Computer-controlled Recumbent Stepper

The current design of the computer-controlled recumbent stepper could be improved with an updated controller, a drive system with less backlash, reduced inertia, and load cells to directly measure forces applied by the feet. For our control design, we estimated the system to be a second order linear system with mass and damping. The recumbent stepper, however, had nonlinear dynamics. Nonlinear control techniques would likely improve stepper performance. The current belt drive system had backlash, lost motion due to clearance between components or slack when the system reversed direction. Because the system had one degree of freedom, a single actuator should be sufficient. We used a single motor that had to reverse directions and rotate clockwise and counter clockwise to move the handles and pedals back and forth. Spatial and financial constraints limited our drive system options. The implemented belt drive sprockets also added nontrivial inertia that probably contributed to the backlash. An improved drive system with less backlash and inertia would improve the computer-controlled recumbent stepper's performance. Another possible improvement would be to use one or two actuators that acted directly on the handle-pedal units. The two actuators option would likely require a complicated control to maintain the proper phasing between the two handle-pedal units. Lastly, better foot force measurements could be obtain with additional load cells to measure directly the forces applied by the foot. Calculating the pedal forces using the sum of the moments works well in a static case. In the dynamic case, if the system was truly isokinetic, then the angular acceleration would be zero. Our system is not isokinetic, however, and there is an inertial term to consider during dynamic stepping. Because we were interested primarily in relative changes of forces among the conditions, we were satisfied with the force measurement. Nevertheless, additional pedal load cells would improve the foot force measurements in the dynamic stepping mode.

Experiments Using More Sophisticated Neural Techniques

My experimental protocol and results were not sufficient to determine specific neural mechanisms of neural coupling. The original intent of my project, however, was to determine if upper limb effort could increase and/or improve lower limb muscle activation for gait rehabilitation. It became clear that understanding the neural mechanisms for excitatory interlimb neural coupling was important for designing effective rehabilitation therapies.

Experiments using more sophisticated neural techniques such as transcranial magnetic stimulation could be used to determine the specific neural mechanisms for neural coupling between upper and lower limbs in humans.

Transcranial magnetic stimulation is a non-invasive technique for stimulating superficial areas of the brain. This method can be used to excite or inhibit corticospinal excitability. One possible experiment would be to apply inhibitory transcranial magnetic stimulation to the part of the brain associated with lower limb movement during an upper and lower limb task. If supraspinal drive is a major contributor to excitatory neural coupling between upper and lower limbs, then lower limb muscle activation should be less during an active arm and leg task with inhibitory transcranial magnetic stimulation compared to without transcranial magnetic stimulation. Testing individuals with other motor impairments such as stroke or a complete spinal cord injury may also provide greater information about neural mechanisms. If supraspinal drive is the primary mechanism, individuals with complete thoracic level spinal cord injuries will probably not produce increased lower limb muscle activation with upper limb effort.

Additionally, submaximal effort experiments in individuals with incomplete spinal cord injury might also provide additional insight about the benefits of interlimb neural coupling for rehabilitation. I would hypothesize that upper limb effort or movement would increase submaximal lower limb muscle activation. Knowing if upper limb effort does indeed result in greater lower limb muscle recruitment at submaximal efforts would provide further support for simultaneous upper and lower limb exercise therapies. This has clinical relevance because most therapies are performed at submaximal effort.