Neural Mechanisms for Bilateral Force Asymmetry During Supine Lower Limb Extensions in Neurologically Intact Individuals and Individuals with Post-Stroke Hemiparesis

by

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You can do anything.

Edward Bartkowicz

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This dissertation is dedicated

to my loving husband, Nick.

Acknowledgments

My five years at Michigan have been filled with great friends and colleagues, great science, and plenty of happy hours. Although I don't have enough paper in this dissertation to thank the vast number of people that have shaped my time at Michigan, I would like to call attention to those who I am exceptionally appreciative of.

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List of Abbreviations

Abbreviations

COP	Center of Pressure
EMG	Electromyography
GM	Gluteus Maximus
MH	Medial Hamstrings
MVC	Maximum Voluntary Contraction
RMS	Root Mean Squared
SBR	Symmetry-Based Resistance
THSD	Tukey-Kramer Honestly Significant Difference
VL	Vastus Lateralis
VM	Vastus Medialis

Abstract

When individuals with post-stroke hemiparesis train with upper or lower extremity robotic devices, they increase muscle recruitment and strength specific to the joints exercised. Although current robotic devices address muscle weakness in individuals post-stroke, they do not address patients' impaired force scaling abilities. In this dissertation I examined foot forces produced during lower limb extensions and designed and tested the use of a novel control mode (symmetry-based resistance) for improving individuals' force-scaling abilities. With symmetry-based resistance, exercise resistance increases with increasing lower limb force asymmetry. Subjects who train with symmetry-based resistance perform the least work when they produce symmetric forces. In the first and second experiments, I investigated foot reaction forces in neurologically intact and post-stroke individuals. When both subject populations were asked to produce equal isometric forces in their lower limbs, they generated less force in their weaker limb even though they believed their forces were equal. Normalizing force by each limbs' bilateral maximum voluntary contraction force revealed no significant differences between limbs. These results suggest that individuals relied primarily on sense of effort, rather than proprioceptive feedback, for gauging isometric lower limb force production. Results suggest that sense of effort is also major factor determining force production during isotonic, or

dynamic, movements in subjects post-stroke. In the third experiment, I demonstrated that neurologically intact individuals can successfully use the robotic device with symmetry-based resistance to improve their force scaling abilities and increase lower limb force symmetry from ~46% to ~50% (where 50% indicates perfect symmetry). In the final experiment, individuals with post-stroke hemiparesis were able to improve their lower limb symmetry from an initial average value of ~29% to ~36% during exercise with symmetry-based resistance. Improvements in lower limb symmetry, however, were not maintained during the one day training session when the controller was turned off. Subjects who trained for four weeks showed a trend towards retention of improved symmetry as initial lower limb symmetry values were improved from Day 1 to Day 4. Overall these studies provide information about the neural mechanisms for lower limb force generation and suggest an innovative controller for stroke rehabilitation.

Chapter 1

Introduction

Motivation

Stroke is the leading cause of long-term disability in the United States with 5.8 million stroke survivors alive today and over 600,000 new cases emerging each year (Rosamond et al. 2008). Over 50% of these post-stroke individuals experience moderate to severe impairments that require special care or placement in a long-term nursing facility. This neurological injury puts a large strain on the US economy. Forecasts for 2008 place expenses over $65.5 billion in both direct healthcare costs and indirect costs due to lost productivity (Rosamond et al. 2008). Although there are current therapies for stroke rehabilitation, such as audio and visual biofeedback that work towards improved balance and mobility, studies have shown only small changes in function when compared to no feedback controls (Geiger et al. 2001). As a result, there exists a strong desire to develop new rehabilitation techniques that have the potential to improve individuals' functional ability while reducing training times.

A common deficit in stroke survivors is hemiparesis, weakness on one half of the body. This strength deficit has origins in both muscle and neural systems (Bertrand et al. 2004; Horstman et al. 2008) and leads to decrements in functional ability and mobility (Teixeira-Salmela et al. 1999; Weiss et al. 2000). The goals of this dissertation were to better understand physiological principles governing lower limb strength asymmetry in neurologically intact and post-stroke subjects, and to develop and test the learning effects of a robotic exercise machine for rehabilitation of lower limb strength asymmetries in stroke patients. Results from these tests on individuals with post-stroke hemiparesis will advance the field of rehabilitation robotics and rehabilitation therapies.

Background

Motor impairments due to stroke often translate to functional disabilities and decreased mobility. Stroke patients have an impaired ability to recruit affected muscles contralateral to their lesion. If these muscles remain unused, patients most likely experience a stiffening of the affected joints that is caused by muscle atrophy and muscle fiber shortening. Patients' muscles also may become spastic, reducing their passive range of motion. All these impairments result in hemiparesis, reducing individuals' ability to perform bilateral tasks (Bertrand et al. 2004). Weakness in the lower extremities affects performance during standing, walking, climbing stairs, and standing from a sitting position (De Quervain et al. 1996; Teixeira-Salmela et al. 1999; Weiss et al. 2000).

Stroke-induced hemiparesis affects patients' ability to approximate force production in their limbs. During submaximal upper extremity matching tasks, stroke subjects consistently overestimate forces produced in the paretic limb, even though maximum voluntary force trials reveal that they have the ability to produce forces of equal magnitude (Bertrand et al. 2004; Mercier et al. 2004). This limb force asymmetry has been replicated for neurologically-intact subjects with one upper limb in a state of muscle fatigue (Carson et al. 2002). Individuals base muscle activation on sense of effort, rather than sense of force (Gandevia and McCloskey 1977b). For neurologically intact subjects, sense of effort scales with an individual's maximum force ability for the involved muscles (Carson et al. 2002). Since a stroke subject has reduced maximum force ability in the paretic limb, basing muscle recruitment on proportion of maximum force ability will result in less force in the paretic limb. Previous research lacks information on stroke subjects' lower limb force matching capabilities and whether or not this sense of effort scaling translates to the paretic and non-paretic lower limb muscles of stroke subjects.

Strength training is one rehabilitation strategy that counteracts muscle weakness and limb force asymmetry. Strength training regimens continue two to three days per week and include lower extremity resistance training, circuit training and aerobic exercises (Teixeira-Salmela et al. 1999; Weiss et al. 2000; Gordon et al. 2004a). This strategy leads to increased motor recruitment of both the paretic and non-paretic limbs without increasing spasticity (Badics et al. 2002). Increasing muscle strength in stroke patients can increase functional abilities such as sit-to-stand performance, gait speed, and dynamic balance (Mercier et al. 1999; Weiss et al. 2000; Monger et al. 2002). Typical strength training therapies, however, do not address improving patients' impaired force scaling abilities.

Constraint-induced movement therapy is another rehabilitation strategy that can reduce motor impairments of the paretic limb (Taub et al. 1999). During therapy mass practice of the paretic limb of a post-stroke individual can be achieved by constraining the non-paretic upper limb for 90% of the waking hours. Constraining the non-paretic limb forces patients to rely only on their paretic limb for training tasks and activities of daily living. This type of therapy focuses on overcoming the learned disuse phenomenon. Decreased use of the paretic limb results in further disuse because patients become more skilled using just their non-paretic limb and become less skilled at using their paretic limb. Results from trials testing constraint-induced movement therapy vs. a time-matched exercise program found greater improvements for constraint-induced therapy in motor performance, quality of movements, and functional use of the paretic limb (Taub and Morris 2001; Wu et al. 2007; Lin et al. 2008).

A recent trend in rehabilitation science is to automate training techniques with robotic devices with the intent of improving the efficacy of therapy. Many robotic devices have emerged with the ability to mimic therapists' movements during task-specific repetitive exercise (Hesse et al. 2003; Reinkensmeyer et al. 2004). Stroke patients have shown the ability to adapt to novel force fields when training with these devices (Reinkensmeyer et al. 2004; Patton et al. 2006). For the upper extremity, subjects training on the MIT-MANUS or MIME robot have shown improvements of increased strength of the exercised joints (Lum et al. 2002; Fasoli et al. 2003). There is initial evidence showing that stroke subjects' motor improvements are increased when the robots are operated in an erroramplification mode rather than an error-reducing mode (Patton et al. 2006). Much attention on lower extremity robotics is focused on gait training. The mechanized gait trainer and the LOKOMAT were developed to lessen the physical exertion of therapists during manual assisted treadmill training (Colombo et al. 2000; Werner et al. 2002). Chronic stroke subjects who undergo six weeks of gait training on the mechanized gait trainer produced similar functional outcomes compared to subjects who only underwent manual assisted gait training. The majority of these devices use controllers that program a desired kinematic trajectory. Robotic devices such as these are promising although to date, the results are very joint specific (Hesse et al. 2001; Lum et al. 2002; Krebs et al. 2005).

Other types of rehabilitation used in clinics to improve patients' performance are audio and visual biofeedback. Therapists have used audio and/or visual feedback about patients' muscle activation or limb forces to attempt to improve limb force symmetry. Post-stroke individuals provided with visual force feedback while standing and performing upper limb tasks improve stance symmetry and decrease sway compared to subjects receiving similar therapy without feedback (Sackley and Lincoln 1997; Wong et al. 1997). Sit-to-stand training with audio feedback of paretic lower limb loading shows increased improvement toward symmetric body weight distributions over no feedback controls (Engardt et al. 1993). Although these results show improvements after training with feedback, they occur over relatively long training periods. Training sessions range between 45 to 60 minutes a day, 3 to 5 days a week, for 4 to 6 weeks (Engardt et al. 1993; Bourbonnais et al. 2002). An alternative type of therapy that reduces training time could speed patients' motor recovery and decrease therapy costs.

There is a need for a new rehabilitation strategy that has the potential to take into account three specific points. The new technique should focus on post-stroke individuals' lower limb function and mobility. It should address these patients decreased strength on their paretic lower limb. Finally, it should also focus on improving stroke subjects' impaired force scaling abilities in their lower limbs. While addressing these points, the new rehabilitation strategy should provide feedback in such a way that training times can be decreased.

This dissertation outlines a new control paradigm for robotic devices that uses a novel control strategy, symmetry-based resistance, as a means of lower limb stroke rehabilitation. Symmetry-based resistance alters the resistance as a means of informing subjects of their performance. We have applied our new control strategy to a robotic exercise device where subjects perform lower limb extensions. The exercise device, shown in Figure 1.1, was modified and built at the University of Michigan Human Neuromechanics Laboratory. Subjects lie on a sled and place their feet on a vertical force plate. A motor controls resistance in real-time through a rack and pinion mechanism. The subjects' goal is to perform bilateral lower limb extensions as symmetrically as possible (i.e. pushing equally with both the right and left feet). While exercising, subjects receive symmetry-based resistance where a real-time controller increases resistance as subjects' performance declines, or as their lower limb forces become asymmetric. Therefore if they perform extensions with perfect symmetry, resistance will be set

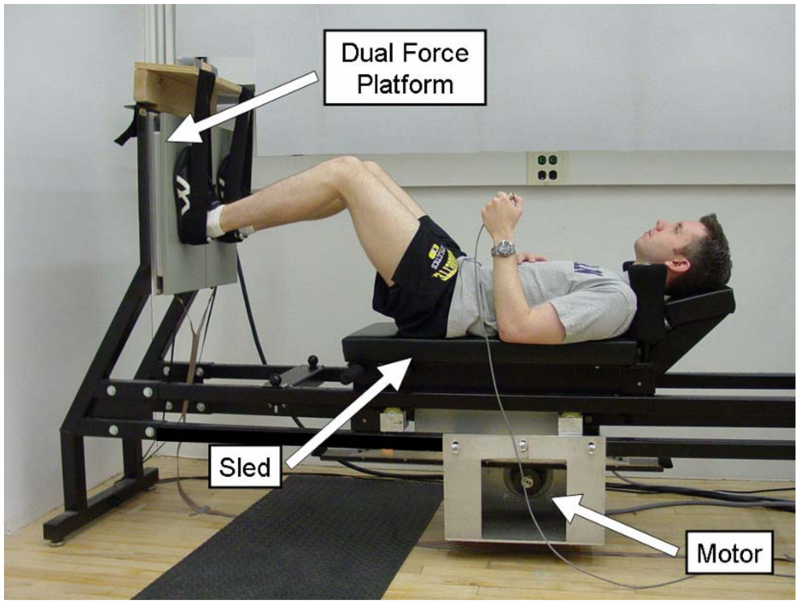

Figure 1.1 Robotic machine for lower limb exercise. A force platform measured lower limb forces while a computer controlled motor controlled resistance.

to a baseline value and subjects will perform minimal total work. The more asymmetric their lower limb forces become, the higher the resistance will be, causing subjects to perform more work while completing the same task.

Exercise with symmetry-based resistance may improve the rate of motor learning compared to just strength training alone. Motor neuron activation and muscle forces are encoded at the spinal cord level (Bosco and Poppele 2001a; Bizzi et al. 2002), resulting in a shorter proprioceptive feedback loop for symmetry-based resistance compared to the higher cognitive processing required for audio/visual biofeedback. Symmetry-based resistance training also has the potential to counteract the learned disuse phenomenon. During symmetry-based training, subjects perform minimal mechanical work when they generate equal forces with their two limbs. Although the task at first requires more effort, recruitment of the paretic limb should require less effort as use of this limb increases. This type of training could be considered within the same continuum occupied by constraint-induced movement therapy. The difference between constraint-induced movement therapy and symmetry-based resistance training is the amount of non-paretic limb involvement. Many lower limb tasks in activities of daily living involve both legs. Symmetry-based resistance training involves both lower limbs and takes advantage of the ability of the patient to compare descending motor commands as a means to recalibrate their effort to force relationship.

Dissertation Outline

This dissertation contains seven chapters and includes experimental analyses pertaining to lower limb force production sense and the learning effects of exercise with symmetry-based resistance. Chapter 2 is a technical note discussing hardware and software components of the robotic exercise machine with symmetry-based resistance. In Chapter 3 I use a contralateral limb matching task to investigate how neurologically intact subjects gauge foot reaction forces and whether these individuals mainly rely on their sense of effort (i.e. feedforward signal of the descending motor command) or sense of force (i.e. feedback signal of the ascending sensory information). Results from this chapter indicate that neurologically intact subjects rely primarily on their sense of effort to gauge lower limb isometric force production. Chapter 4 builds upon the results of Chapter 3 and examines how individuals with post-stroke hemiparesis gauge both isometric (static) and isotonic (dynamic) foot reaction forces. Results from Chapter 4 show that stroke subjects do have impaired force scaling abilities and, like neurologically intact subjects, mainly rely on their sense of effort to gauge both static and dynamic force production. In Chapter 5 serves as a preliminary trial to test the robotic exercise machine with symmetry-based resistance with neurologically intact subjects. I present data illustrating that when these subjects train with symmetry-based resistance they are able to alter their lower limb force production towards a target symmetry or asymmetry. In Chapter 6 I discuss a preliminary trial of symmetry-based resistance training with post-stroke individuals. In this study, exercise with symmetry-based resistance is used as a means to recalibrate their sense of effort. Results from this chapter show that during training subjects are able to significantly improve their lower limb symmetry. During one day of training these improvements were not maintained when the controller was turned off. Subjects who trained for four weeks showed a trend towards improved lower limb symmetry retention from the first training session to the fourth training session. Chapter 7 includes a general discussion of the main accomplishments of this dissertation, experimental limitations, and recommendations for future work.

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Chapter 2

Design and Implementation of a Lower Limb Robotic Exercise Machine with Symmetry-Based Resistance

Hardware

The core piece of equipment used to implement this device was a plyometric exercise machine called the Plyo-Sled (LifeStyle Sports, Dunkirk, New York) (Figure 2.1A). This machine was a high performance glide system in which users could perform calf raises, squats, and jumping movements against the resistance of elastic bands in order to strengthen muscles and develop leg power. The sled rested on low friction rollers for ease of movement throughout exercise. To perform lower limb extensions, subjects were supine on the sled and placed their feet on the vertical footplate.

We choose this leg press exercise machine for several reasons. This machine allowed for lower limb extensions with the body positioned in the horizontal plane. Subjects did not have to completely stabilize their upper body, as the sled provided the majority of this support. Consequently, subjects could devote most of their attention to sensing what it feels like to produce more symmetric forces rather than focusing their attention on stabilizing their upper body. Performing extensions in the horizontal plane also allows weaker subjects to exercise at resistance levels lower than body weight. Another advantage to this exercise machine was that it could be easily retrofitted with a motor to provide programmable resistance.

(A)

(B)

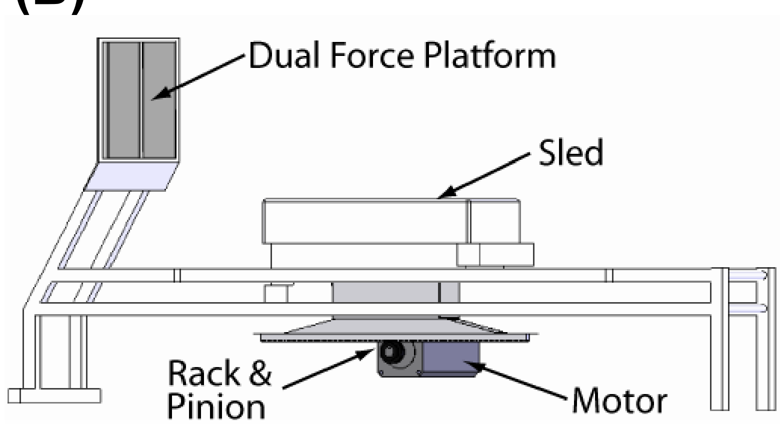


Figure 2.1. Robotic device design. (A) Plyo-Sled exercise machine manufactured by Lifestyle Sports. The device could be used for horizontal lower limb extensions. (B) SolidWorks computer renderings of the robotic device. Design additions shown in grey include a motor, rack and pinion, and dual force platform.

Design modifications necessary to integrate computer-controlled resistance into the Plyo-Sled exercise machine included a motor, rack and pinion, and dual force platform (Figure 2.1B). The attachment of these additions was drawn up using the computer-aided-design tool SolidWorks 2003 (SolidWorks Corporation, Concord, Massachusetts). The motor was attached to the Plyo-Sled platform to provide programmable resistance to the sled through a rack and pinion transmission. A horizontal rack affixed to the sled was driven by a pinion on the motor to transform rotational motion of the motor to linear motion of the sled. A dual force platform attached to the vertical footplate captured individual foot forces during movement. These components are below.

Rack and Pinion

The mechanism consisted of a helical rack and gear (SRH2-1000R and SH3-60R, respectively, Quality Transmission Components, Garden City Park, New York). Both the gear and the rack had a helical angle of 15º. The helical gear had a radius of 4.14 cm, resulting in 26 cm linear motion for one revolution of the gear. This linkage system decreased the amount of backlash in the system as well as decreased the cogging of the motor felt by the subject on the sled.

Servo Motor

The motor that provided resistance to the sled is a Kollmorgen Goldline XT Servo Motor MT706C1-R1C1 (Kollmorgen, Radford, Virginia) matched with a SERVOSTAR 600 Amplifier. This motor was selected because it could provide a continuous torque of 48 Nm. The motor inertia was 0.0126 kgm^2 and had a weight of 36 kg. The rated speed of the motor was 1300 rpm. The motor was controlled by a DC current command signal output from the motor amplifier. Through combination of the available motor torque and the gear ratio, a maximum of 1200 N (continuous force) could be applied to the sled.

Force Platform

A dual force platform (Model Dual Accu-Gait, AMTI, Watertown, MA) mounted vertically on the footplate of the exercise machine captured individual foot forces during movement. Each individual platform had a vertical capacity of 2669 N (600 lbs). Analog force data was sampled at 1000 Hz.

Software

The robotic exercise machine was designed for increased proprioceptive feedback through use of symmetry-based resistance. Feedback in this mode included person-in-the-loop, where the subject perceived increases and decreases in resistance and adjusted their foot forces accordingly (Figure 2.2). As the subject performed bilateral lower limb extensions, his/her individual foot forces were recorded from the dual force platform. The analog data was sent to a data acquisition board (Model Sensoray 626, Sensoray Co. Inc., Tigard, Oregon) within a real-time processor. Computer software used force data to generate and output a motor command voltage signal. This signal was sent to the motor drive, converted to a current command signal, and output through the motor as torque.

The software components involved are discussed in detail below.

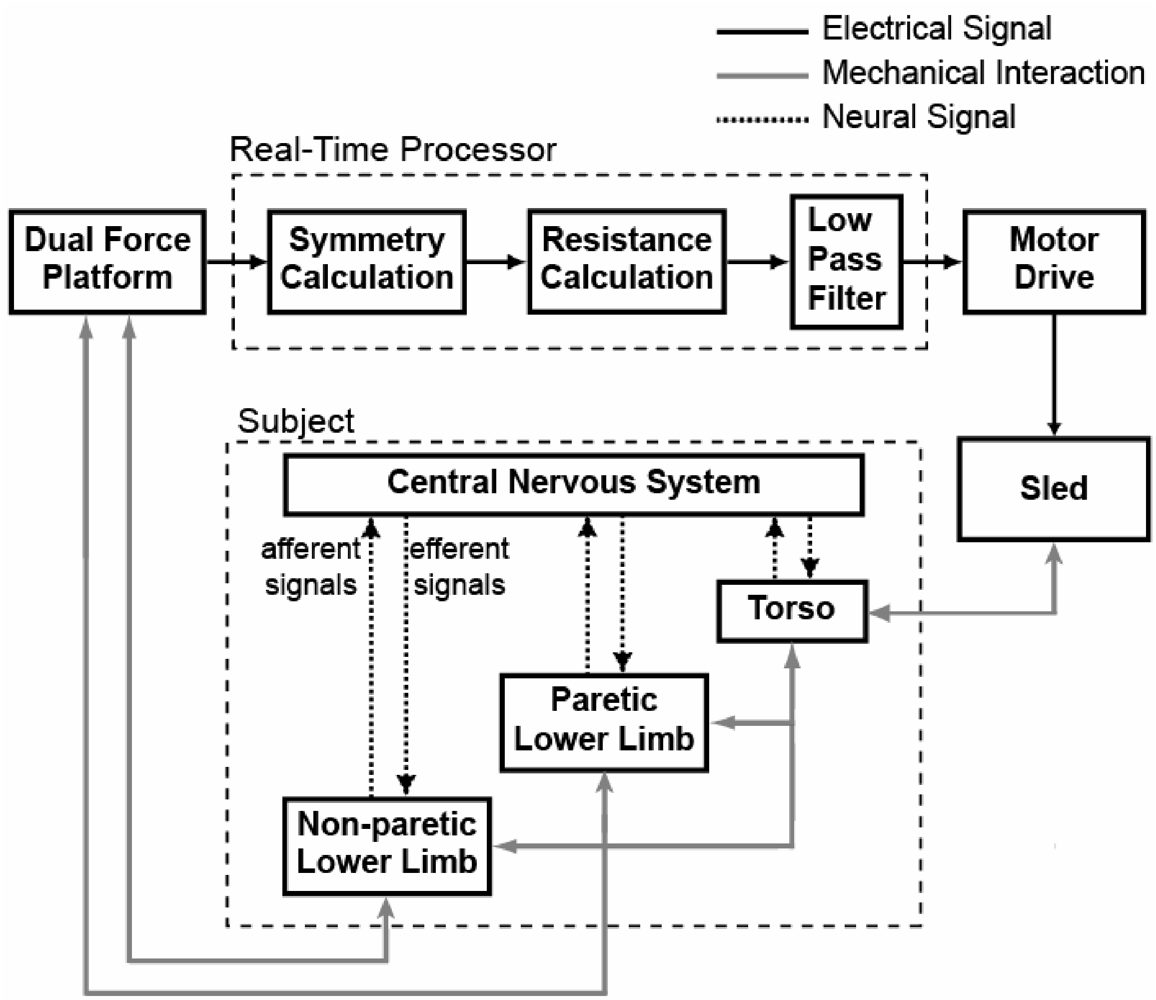


Figure 2.2. Information flow diagram. A force platform recorded individual foot forces during bilateral lower limb extensions and sent data to a real-time processor. The real-time processor calculated lower limb symmetry and motor resistance based on individual foot force data. The motor command signal was low-pass filtered (LPF) and output to the motor drive. In real-time the motor drive commanded the motor in to produce the appropriate torque and acted on the sled.

RT-Lab and Simulink

Real-time signal processing was performed through a software package, RT-LAB 6.2 Solo (Opal-RT Technologies, Quebec, Canada). RT-LAB 6.2 Solo was a single host, single target software-only version of RT-LAB that was designed for real-time control applications running custom Simulink models (The Mathworks, Inc., Natick, MA). The software calculated motor resistance or velocity by automatically compiling these models into a C based programming language. The compiled code was then run under real-time QNX on the target machine. Real-time control and visualization of several model parameters was available through the RT-LAB user interface.

The robotic device was controlled by one of three different custom modes: isokinetic, isotonic, or symmetry-based resistance.

<u>Isokinetic Mode:</u> In isokinetic mode, the computer controlled resistance so that movement velocity was held constant over the entire lower limb extension movement. If a subject pushed hard and therefore the sled moved faster, the controller increased resistance to maintain the reference velocity. If a subject pushed too little and therefore the sled moved slower, the controller decreased resistance to maintain the reference velocity. During operation of this mode, subjects received visual feedback of movement timing (i.e. when to start and stop pushing).

Isokinetic model parameter inputs included the movement velocity and extension time. Movement velocity was converted to a voltage command, $V_{Velocity}$, according to Equation 2.1. Extension time was calculated using to the linear distance the sled traveled during one extension for each subject, as shown in Equation 2.2.

$$V_{\text{Velocity}} = (\text{Desired Velocity in cm/s}) \times \frac{1\,\text{rev}}{26\,\text{cm}} \times \frac{60\,\text{sec}}{1\,\text{min}} \times \frac{10\,\text{volts}}{1000\,\text{rpm}} \quad (2.1)$$

$$T_{\text{Extension}} = \frac{\text{Desired Linear Distance in cm}}{V_{\text{Velocity}}} \quad (2.2)$$

Movement velocity and extension time created the square pulse voltage command (Figure 2.3) sent to the motor drive. A positive control signal represented an extension movement and a negative control signal represented a flexion movement. Movement occurred upon a trigger by the experimenter. Setting the voltage command signal to zero volts, or a velocity of zero, locked the position of the sled.

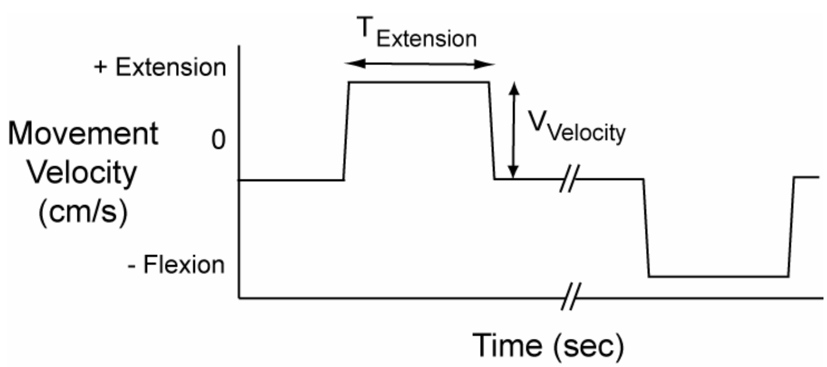


Figure 2.3. Isokinetic mode control signal. V_{Velocity} represents movement velocity and $T_{\text{Extension}}$ indicates the time needed to reach full extension (or flexion) at a given velocity. Positive command signal represents extension movement and negative signal represents flexion. Extension (or flexion) command signals are generated upon a trigger by the experimenter. A signal of zero represents the static condition (i.e. no movement).

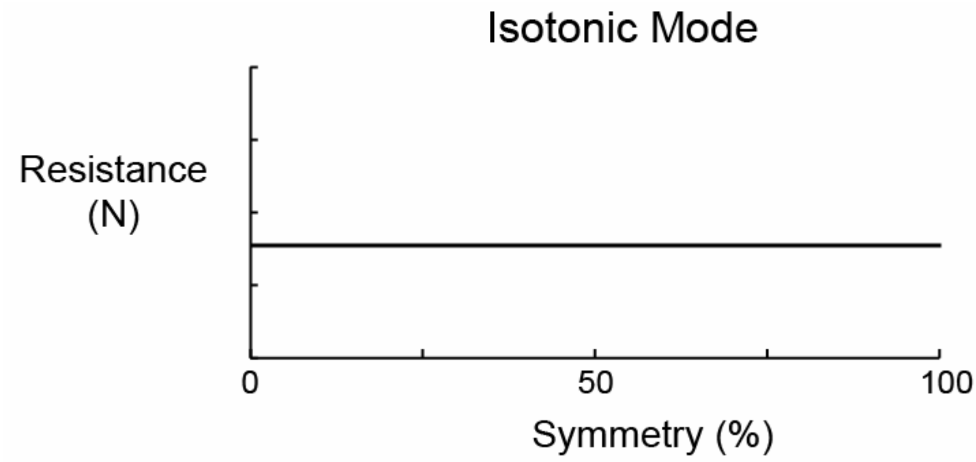


Figure 2.4. Isotonic mode: Lower limb symmetry vs. resistance. In isotonic mode, resistance, R, was constant and independent of lower limb symmetry values.

Isotonic Mode: Isotonic mode allowed subjects to practice lower limb extensions similar to an exercise machine that makes use of weights. In isotonic mode, the only parameter input was the level of constant resistance, R. The resistance level remained constant between repetitions but could increase or decrease between sets or as required by experimental protocol (Figure 2.4).

The equation necessary to transform desired resistance to the command voltage signal required by the motor amplifier was generated experimentally. While a subject was on the robotic device, an experimenter increased the command voltage signal, $V_{Resistance}$, at intervals of 0.2 volts and recorded the output resistance, R, as force data from the force platform. From these data, a plot of command voltage vs. resistance was generated (Figure 2.5A) and a linear regression was performed to define their relationship (Equation 2.3, R^2 = 0.9991).

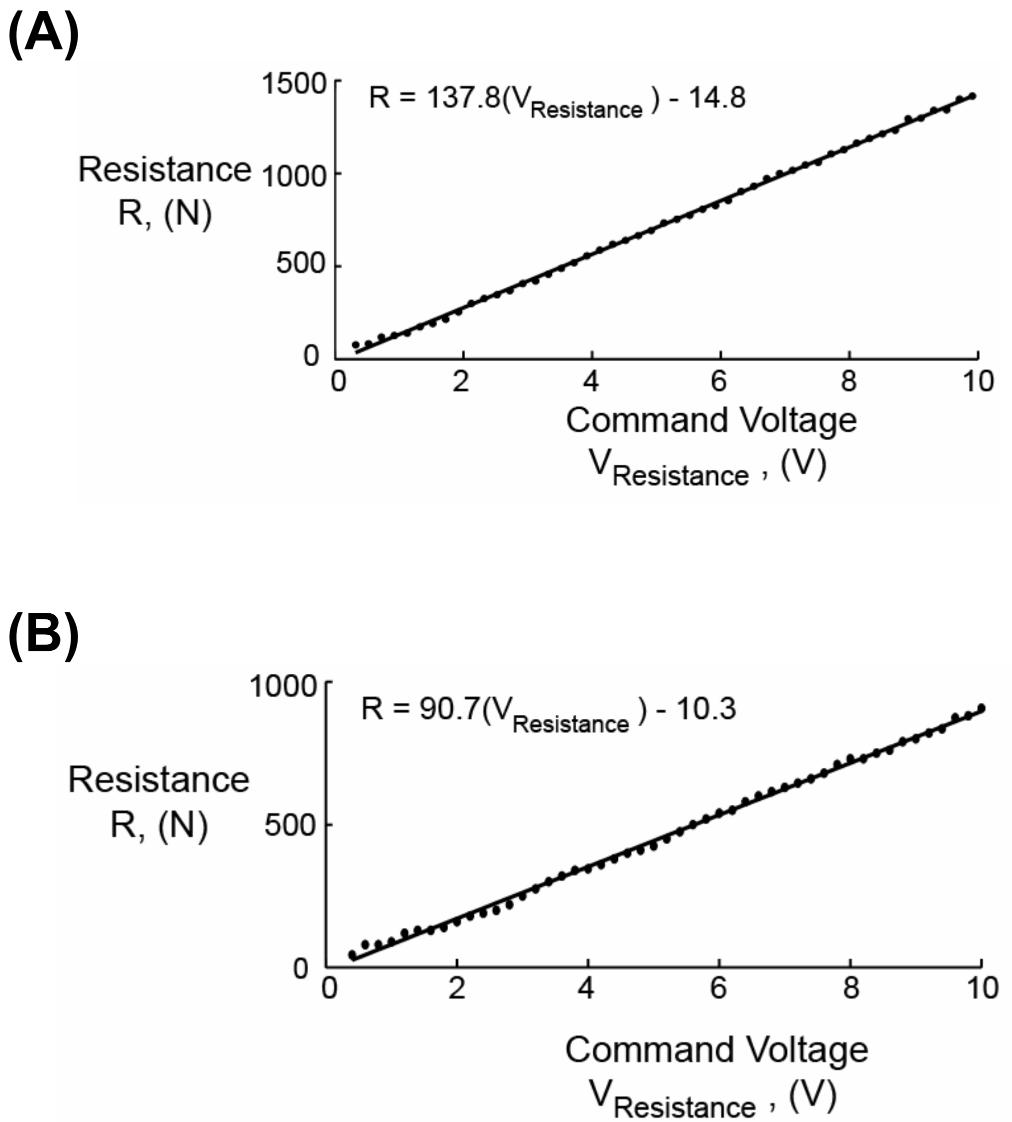


Figure 2.5. Command voltage vs. resistance in Analog Torque mode. Plots were generated under experimental conditions with a subject on the robotic device. Black dots represent individual data points and line represents linear regression trend line. (A) Without limiting motor output, a maximum command voltage of 10.0 volts resulted in a maximum resistance of 1363 N and a resolution of 0.0073 V/N (Linear regression, R^2 = 0.9991). (B) Limiting the motor output by one-third resulted in a maximum resistance of 897 N for 10.0 volt input and an increased resolution of 0.0111 V/N (Linear regression, R^2 = 0.9978).

$$R = 137.8\ \text{N/V} \times V_{\text{Resistance}} - 14.8\ \text{N} \tag{2.3}$$

A maximum command voltage of 10.0 volts resulted in a maximum resistance of 1363 N.

For studies involving individuals with post-stroke hemiparesis, less total resistance was necessary. Therefore, the maximum resistance was limited by one-third in the motor drive software. The resulting command voltage vs. resistance relationship was generated (Figure 2.5B) and a linear regression was performed to define their relationship (Equation 2.4, R^2 = 0.9978).

$$R = 90.7\ \text{N/V} \times V_{\text{Resistance}} - 10.3\ \text{N} \tag{2.4}$$

A maximum command voltage of 10.0 volts now resulted in a maximum resistance of 897 N. Reducing the maximum resistance increased the resolution of the robotic device from 0.0073 V/N to 0.0111 V/N.

<u>Symmetry-Based Resistance Mode:</u> In symmetry-based resistance mode, the controller varied resistance in real-time. The resistance was proportional to the amount of asymmetry in the subject's foot forces thereby providing immediate information about force symmetry in the subject's lower limbs. Resistance was set to a minimum, or baseline, when equal forces were generated between the limbs. Resistance increased to saturation as forces became asymmetric. Subjects could perform extensions with minimal total work if they generated equal forces at their left and right feet.

Symmetry-based resistance parameter inputs included the instantaneous foot forces recorded from the force plate (F_{Paretic} and $F_{\text{Non-paretic}}$), baseline and saturation resistances (B and S, respectively), and the initial root mean squared symmetry (SYM_{RMS}) measured for each subject while performing extensions against a constant resistance (isotonic mode).

The control algorithm determined resistance levels in real-time based on individual's instantaneous lower limb symmetry. Instantaneous lower limb symmetry (SYM_i) was calculated in real-time by dividing the paretic limb foot force by the sum of the paretic limb and non-paretic limb foot forces (Equation 2.5). The resulting signal ranged from 0 to 100 with 50% representing perfect symmetry in lower limb forces.

$$Sym_i = \frac{F_{Paretic}}{F_{Paretic} + F_{Non\text{-}paretic}} \times 100\% \tag{2.5}$$

The controller gain (K) and resistance (R), were calculated according to the following equations:

$$K = \frac{S - B}{\sqrt{0.32\pi}} \tag{2.6}$$

$$R = -K \times exp\left[-\frac{4.5 \times (50 - Sym_i)^2}{(50 - Sym_{RMS})^2} \right] + S \tag{2.7}$$

After the real-time controller calculated resistance the signal was passed through a 2nd order low pass Butterworth filter with a cutoff frequency of 1 Hz (Figure 2.2). The resistance signal was then converted to a command voltage signal $V_{Resistance}$, according to Equation 2.4. The command signal was then sent to the motor drive and converted to physical resistance. The overall result of Equations 2.7 was resistance followed the shape of the standard normal distribution curve reflected over the horizontal axis (Figure 2.6). Resistance was lowest with perfect lower limb force symmetry and increased as lower limb forces become asymmetric.

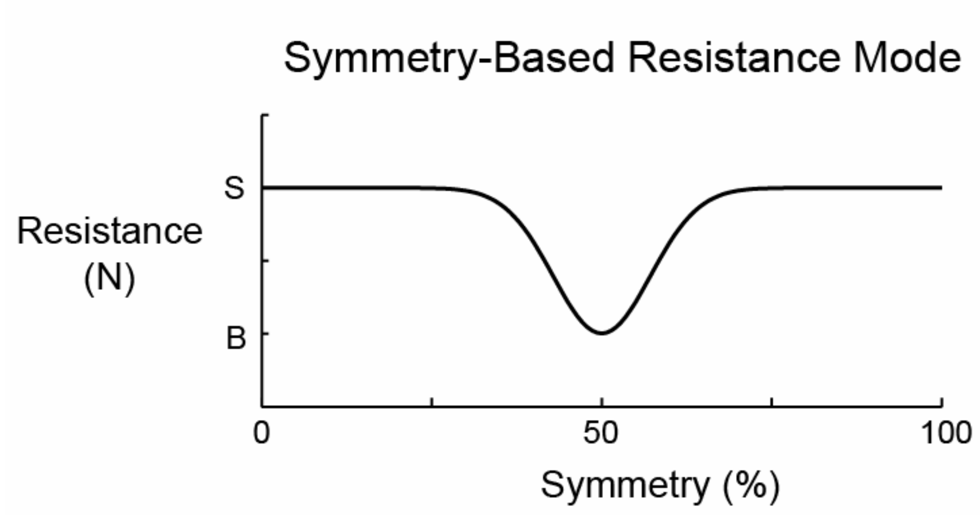


Figure 2.6. Symmetry-based resistance mode: lower limb symmetry vs. resistance. In symmetry-based resistance mode, resistance, R, was set to a minimum baseline value, B, when foot forces were equal (i.e. symmetry value of 50%). As foot forces became more asymmetric, the motor resistance increased until saturation, S. The shape of the resistance curve was defined by Equation 2.7.

Motor Drive

The motor amplifier utilized a closed loop servo system configuration. Within the motor drive software, there were six options to control the motor. Two of these, Analog Speed and Analog Torque, were utilized for operation of the robotic device. These modes monitored either motor velocity or torque in a closed loop.

<u>Analog Speed:</u> When Analog Speed was selected as the feedback system, the servo amplifier compared the reference motor velocity (input as a voltage signal originating from RT-Lab) with the measured velocity. Measured velocity was calculated from position information collected from the optical

encoder. The encoder has a resolution of 4096 ticks per revolution. The servo amplifier then made the adjustments as needed and generated a new current signal to bring the motor closer to the commanded velocity. This option was selected when running the robotic device in isokinetic mode.

Analog Position: When Analog Torque was selected as the feedback system, the servo amplifier compared the reference motor torque (input as a voltage signal originating from RT-Lab) with the measured torque. This torque loop was called the current loop since the amplitude of the electrical current was directly proportional to torque. The servo amplifier then made adjustments as needed and generated a new current signal to bring the motor closer to the commanded torque. This option was selected when running the robotic device in either isotonic or symmetry-based resistance mode.

Safety Measures

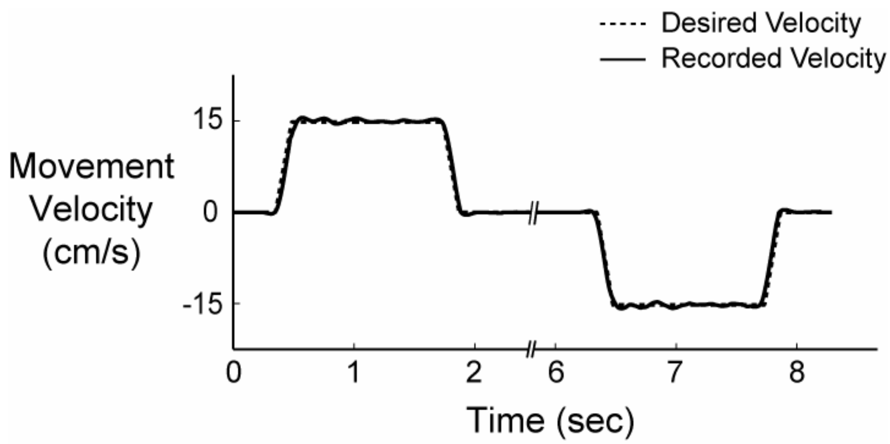
Three separate safety measures were designed into the system to ensure subject safety at all times. First, computer software limited motor command voltage and therefore limited device resistance. The limit was dependent upon individual subject strength. The motor command voltage limit was coded into Simulink software using a saturation icon placed directly prior to outputting the voltage command. As the calculated motor resistance command increased, it saturated at the voltage limit. Second, mechanical stops were included in the hardware setup of the device. These safety stops were adjusted to the range of motion of individual subjects and ensured that the sled could not physically exceed set limits. Finally, both the researcher and the subject had an emergency stop button within their reach at all times throughout the experiment. Activation of one or both of these buttons triggered the motor to stall. During this stall, the motor produced no torque output and the sled position was locked. The motor remained in this state until a manual reset button was pushed.

Device Performance

Isokinetic Mode

To verify performance in isokinetic mode, we quantified the average percent error between the desired and recorded sled velocities and recorded the maximum force generated by a subject during a bilateral lower limb extension that the device could resist without slipping. A test subject was instructed to push as hard as they could during the extension phase and relax during the flexion phase. The sled velocity ($V_{Velocity}$) was set to 15 cm/s and the extension time ($T_{Extension}$) was set to 1.5 seconds. Comparing the desired and recorded sled velocities across time showed small deviations during movement initiation and termination as well as damped oscillations during constant velocity movement (Figure 2.7A). The difference between these two signals resulted in an average percent error of 4.5% ± 9.2% (mean +/ s.d.) and a peak error of 7.9%. The peak force recorded from a male subject while performing a bilateral lower limb extension at maximal effort was 2310 N (Figure 2.7B). During this trial, the motor was able to resist the torque generated by the subject without slipping or stalling.

(A)



(B)

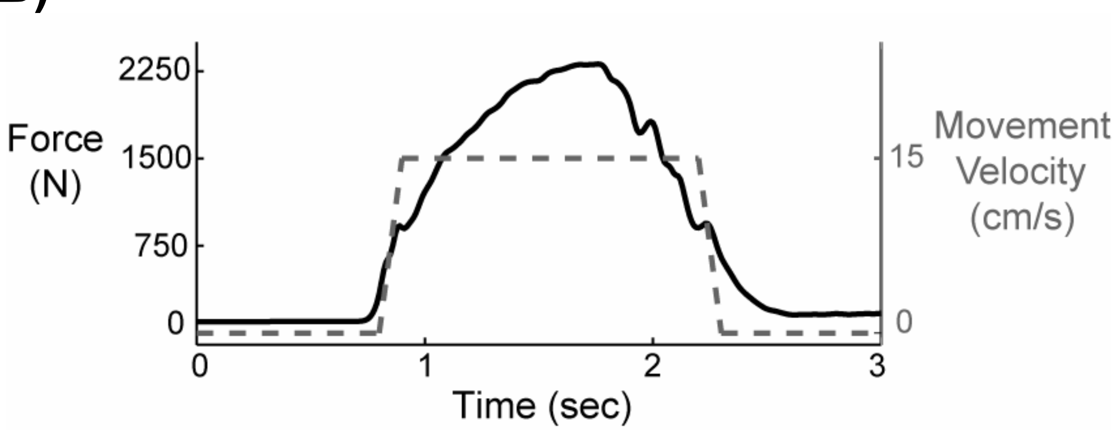


Figure 2.7. Isokinetic mode performance. (A) Plot represents the desired (dashed line) and recorded (solid line) movement velocity of the sled throughout time in isokinetic mode. Recorded movement velocity was generated as the derivative of position data from the motor encoder. A positive commanded velocity indicated extension and a negative velocity indicated flexion. Percent error between the desired and recorded movement velocities was 4.5% ± 9.2% (mean ± std). (B) Force (solid black) and movement velocity (dashed grey) vs. time during a bilateral maximum voluntary contraction trial in isokinetic mode. The subject was instructed to only produce maximum forces during the extension phase (shown) and relax during the flexion phase (not shown). The healthy subject was able to generate a peak force of 2310 N.

Although this peak force does not represent the maximum value the motor can resist, it was the highest force a subject was able to generate in isokinetic mode.

Isotonic Mode

In isotonic mode, we quantified the average percent error between the desired and recorded resistance across varying levels of symmetry. A test subject on the exercise machine was instructed to first generate force solely on her left lower limb and then shift the production of force to her right lower limb. Throughout this trial, as force production was shifted between limbs, the level of symmetry varied from 0% (left lower limb producing 100% of the force) to 50% (equal force production between the lower limbs) to 100% (right lower limb producing 100% of the force). The resistance (R) was set to a constant 715 N.

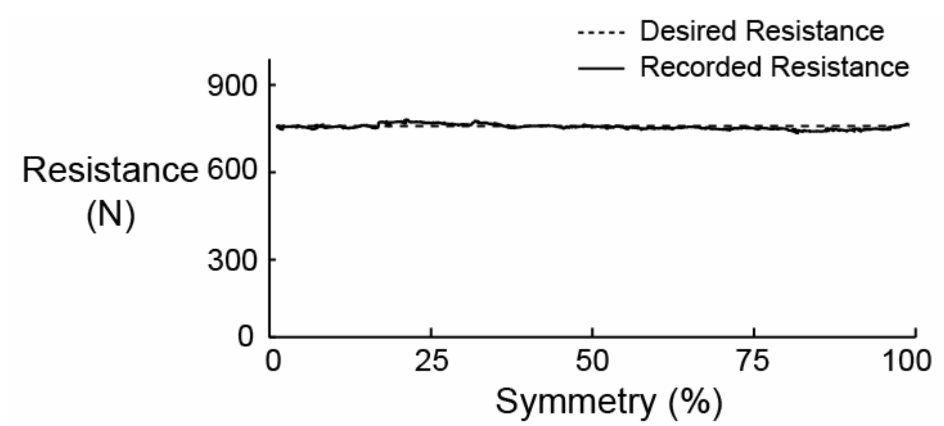


Figure 2.8. Isotonic mode performance. Plot represents desired (dashed line) and recorded (solid line) resistances vs. percent symmetry in isotonic mode. Resistance did not significantly vary with percent symmetry.

The recorded data (Figure 2.8) demonstrates that resistance remained fairly constant throughout the trial with only minor fluxuations. The difference between the desired motor resistance and the recorded motor resistance resulted in an average percent error of 0.43% ± 1.7%.

Symmetry-Based Resistance Mode

In symmetry-based resistance mode, we quantified the average percent error between the desired and recorded resistance across varying levels of symmetry. Similar to the testing of the isotonic mode, a test subject on the machine was instructed to first generate force soley on her left lower limb and then shift the production of force to her right lower limb. The baseline resistance (B) the relationship of desired and recorded resistance as a function of lower limb

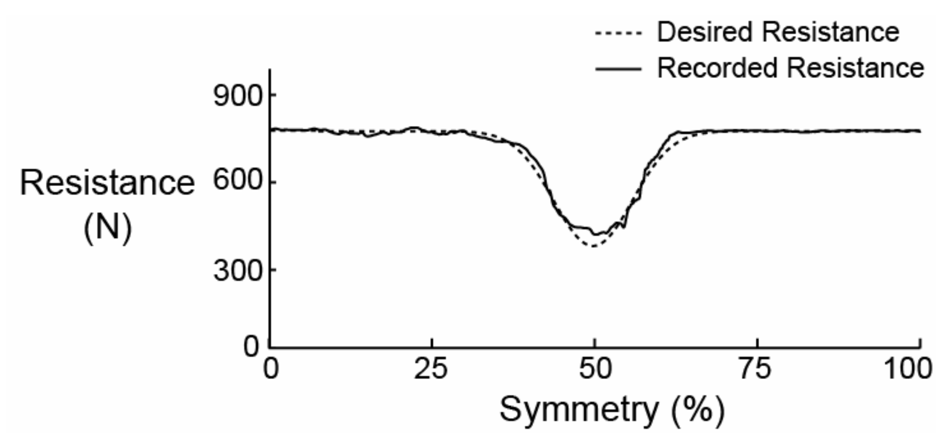


Figure 2.9. Symmetry-based resistance mode performance. Plot represents desired (dashed line) and recorded (solid line) resistances vs. percent symmetry in symmetry-based resistance mode. Resistance was at a minimum when individual foot forces were equal (i.e. 50% symmetry value) and increased to saturation as forces became more asymmetric.

was set to 345 N and the saturation resistance (S) to 715 N. Figure 2.9 shows symmetry. Both desired and recorded resistances were at a minimum baseline value when lower limb forces were equal (i.e. 50% symmetry) and increased with increasing lower limb force asymmetry. The difference between the desired resistance and the recorded resistance resulted in an average percent error of 2.7% ± 2.6% and a peak error of 11.6%.

Chapter 3

Lower Limb Force Production and Bilateral Force Asymmetries Are Based on Sense of Effort

Abstract

Previous research suggests that individuals use a sense of effort, more than proprioceptive feedback, to gauge force production in their upper limbs. We have adopted an isometric force matching task to determine if force asymmetry between lower limbs during bilateral force production results from a neural mechanism related to sense of effort. We hypothesized that subjects attempting to produce equal foot reaction forces would generate equal percentages of their bilateral maximum voluntary strength rather than equal absolute forces. Ten subjects performed isometric lower limb extensions on an exercise machine. Subjects attempted to match forces in their lower limbs at three different submaximal levels (20, 40, and 60% of their weaker limb peak force during bilateral maximum voluntary contraction). Subjects received visual feedback of only the target and stronger limb force. Results showed that subjects consistently produced less force in their weaker limb during all force matching levels when normalized to their unilateral maximum voluntary contraction force (ANOVAs 20% $P = 0.0473$, 40% $P = 0.0012$, 60% $P = 0.0007$). As predicted by our hypothesis, normalizing force magnitudes by bilateral maximum voluntary

contraction forces revealed no significant differences between limbs at all force levels (ANOVA P = 0.8490). Regardless of whether humans produce maximal or submaximal forces, limb force asymmetry appears to be related to neural factors rather than differences in mechanical capabilities between the limbs. Our findings have implications for bilateral asymmetries during movement in healthy and neurologically impaired populations.

Introduction

Humans can control force production in their limbs via two main mechanisms. Muscle force sensation generated centrally from feedforward neural signals is generally termed sense of effort. It originates from an individual's perception of the descending motor command (McCloskey et al. 1974; Jones 1995; Proske 2006). This neural information has also been described as corollary discharge (Sperry 1950). An alternative mechanism generated peripherally from feedback neural signals (ascending sensory information) is generally termed sense of force or tension (Roland and Ladegaard-Pedersen 1977). The peripheral receptors, such as Golgi tendon organs and cutaneous receptors, can provide information about muscle tension and pressure in order to gauge the sense of force. Studies eliciting the tonic vibration reflex have provided evidence that the sense of force can operate in isolation without a sense of effort (McCloskey et al. 1974). Many studies have examined various upper limb motor tasks in an attempt to clarify when and how humans use these two mechanisms for activating their muscles.

Isometric force production is a simple motor task that has been previously used to examine how individuals estimate limb forces. In one variation, subjects first produce a target isometric force level in one of their two limbs (the reference limb), usually with visual force feedback. They are then asked to match the same force in the contralateral limb (the matching limb) without force feedback. Studies on healthy subjects have found that humans are able to match absolute forces between upper limbs fairly well (Carson et al. 2002). If the force capabilities of one limb are altered through unilateral fatigue of either the elbow extensors (Carson et al. 2002) or the elbow flexors (Jones and Hunter 1983; Proske et al. 2004), individuals produce less force in that limb during isometric force matching. Regardless of which limb (fatigued or unfatigued) was the reference limb, errors are consistently in this direction of the fatigued limb generating less force (Weerakkody et al. 2003; Proske et al. 2004). Carson et. al. (2002) demonstrated that the end forces produced by each upper limb were equal percentages of each limb’s maximum voluntary strength rather than equal absolute force levels. These studies suggest that humans use a sense of effort originating from a corollary discharge of the motor command to the muscles (Sperry 1950; McCloskey et al. 1974; Gandevia and McCloskey 1977b), rather than absolute reliance on proprioceptive feedback, to gauge force production. Because the task of producing equal forces is prevalent in the upper limbs (i.e. holding a box or tray), researchers have focused their attention on the way individuals estimate force production in their upper limbs.

Symmetric lower limb forces are also necessary for many activities of daily living such as quiet standing, sitting and rising from a chair, or lifting a box from the floor to a shelf. In healthy individuals, a force asymmetry exists between limbs during a two-legged vertical jump (Bobbert et al. 2006; Newton et al. 2006). The bilateral asymmetry in vertical jumps is present even when there are no lower extremity anthropometric differences between limbs (Lawson et al. 2006). The prevalence of this asymmetry in healthy bilateral force production of the lower limbs in tasks other than the vertical jump is not reported in the literature. Several studies define the existence of a lower limb bilateral deficit, or a reduction in maximal voluntary strength during bilateral contractions compared with unilateral contractions, during bilateral tasks such as extensions at the knee and leg extensions (Schantz et al. 1989; Taniguchi 1997; Janzen et al. 2006). These studies do not report individual limb forces during bilateral trials. Comparing the individual limb forces between combinations of unilateral, bilateral, maximal and submaximal trials will provide insight into whether the resulting force asymmetries are more related to sense of effort or sense of force.

We have adopted the isometric force matching task used by Carson et al. (2002) to study normal force asymmetry in the lower limbs of humans. The goal of this study was to determine if force asymmetry during bilateral force production results from a neural mechanism related to sense of effort. We hypothesized that subjects attempting to produce equal foot forces would generate equal percentages of their bilateral maximum voluntary strength rather than equal absolute limb forces. If true, this could provide critical insight into the neural origins of lower limb force asymmetry during movement.

Methods

Subjects

Twelve neurologically intact subjects (seven males and five females; age: 25 ± 3.0 years, mean ± S.D.M.) gave written informed consent and participated in this study. The Institutional Review Board for Human Subject Research at the University of Michigan Medical School approved the protocol.

Experimental design

Subjects performed isometric lower limb extensions on a leg press exercise machine (Figure 3.1). Subjects reclined on the exercise machine and placed their feet on a vertical dual force platform (Model Dual Accu-Gait, AMTI, Watertown, MA, USA) and their shoulders firmly braced. The device was locked with a mechanical stop such that each subjects' lower limbs were positioned in the middle of the range of motion used for a full lower limb extension (i.e. half-way between the sled position of 90° knee flexion and full knee extension). Subjects' feet were positioned hip width apart on the force platform and stabilized with foot straps to minimize movement during the experiment. For all trials, the subjects' lower limbs remained in the same posture (i.e. both feet are in the foot straps during unilateral as well as bilateral conditions). Therefore, regardless of the condition, all the data were collected with the same body position, same joint

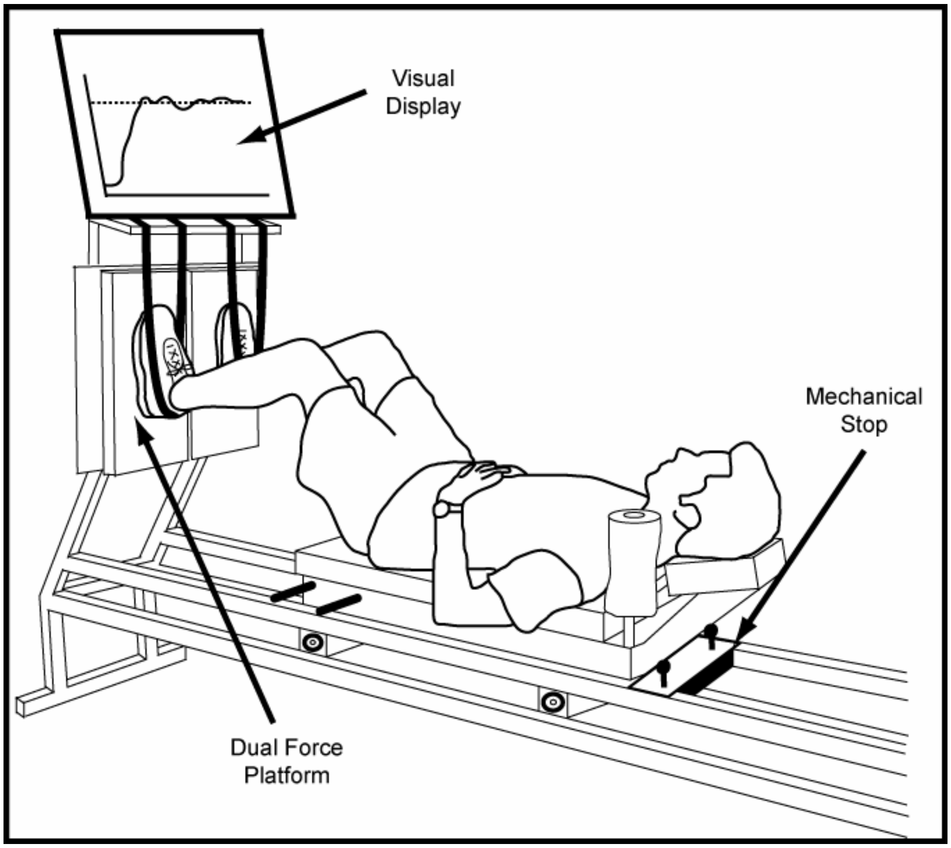


Figure 3.1. Leg press exercise machine for isometric contractions. A dual force platform measured individual lower limb forces. A mechanical stop prevented movement and allowed for isometric lower limb extensions. For the force matching conditions, subjects received visual feedback of the target force (dashed line) and the force produced by the stronger limb (black line).

angles, and same muscle lengths.

All subjects performed a pre-test consisting of three bilateral isometric maximum voluntary contraction (MVC) trials. We verbally encouraged subjects to push as hard as they could with both feet and allowed them to rest two to three minutes between trials. Subjects were excluded from the study if there was less than 10% difference between the maximum forces recorded at their left and right feet during each trial (2 of 12 subjects, both males). This criterion was chosen because the purpose of the study was to determine if discrepancy between limbs during bilateral voluntary contractions could be explained by sense of effort. Ten subjects (five male, five female) possessed a greater than 10% force discrepancy in bilateral foot forces and completed the remainder of the study.

After completing the initial screening of MVC trials, we placed electromyography (EMG) electrodes on non-excluded subjects. Approximately 15 minutes later, subjects returned to the leg press machine for testing. We assessed subjects' isometric strength with three trials each of bilateral, left limb, and right limb MVCs. The order of the nine trials was randomized. We verbally encouraged subjects to push as hard as possible with either one foot or both feet throughout each five second collection. During unilateral trials, subjects' resting limb remained in the same position as during bilateral trials (i.e. foot in the footstrap against the vertical force platform). Subjects rested two to three minutes between each MVC trial. When all nine trials were completed, we analyzed data from the bilateral MVC condition to identify the stronger limb. We determined the stronger limb as the limb that produced the higher peak force during the bilateral MVC condition.

After another ten minute rest period, we assessed subjects' ability to match forces in their lower limbs with nine trials of force matching tasks. Subjects exerted a force equal to 20, 40, and 60% of the peak force from the weaker limb during the bilateral MVC condition. Subjects received visual feedback of the target force level and the amount of force applied by the stronger limb throughout each trial. When subjects reached the target force level in the stronger limb, we instructed them to begin applying force with the weaker limb. No feedback was given to indicate the force applied by the weaker limb. We instructed subjects to verbally signal to the experimenter once they believed they had matched forces in both limbs. Upon this verbal cue, subjects held the isometric contractions for three seconds and then were told to relax. Subjects performed three trials at each of the three force levels in a randomized order with two to three minutes rest between each trial. Subjects were not told the study's purpose or which limb produced more force during the bilateral MVC condition. We instructed subjects using the identifiers "right limb" and "left limb" rather than "stronger limb" and "weaker limb" as described above.

Data acquisition and analysis

We recorded individual foot forces at 1,000 Hz from the dual force platform mounted to the vertical footplate (Figure 3.1). Each limb's MVC, both unilateral and bilateral, were determined as the maximum force measured within the three trials of each condition (Jones and Hunter 1983; Proske et al. 2004). For the three different levels of force matching, we calculated the average force applied by each limb for three seconds after the verbal cue was signaled. We normalized foot forces to each limbs' unilateral MVC force. In other words, the force recorded during each condition was divided by the force recorded during that limbs' unilateral MVC force. This analysis can provide insight into whether or not the lower limb force asymmetry might be due to musculoskeletal differences (e.g. a fundamental difference in muscle strength between limbs). In a separate analysis, we normalized force to each limbs' bilateral MVC force to detect any bilateral facilitation or deficit in the subjects.

We recorded surface electromyography (EMG) at 1,000 Hz (Delsys Inc., Boston, MA, USA) from four lower limb muscles on each limb (vastus lateralis: VL, vastus medialis: VM, medial hamstrings: MH, and gluteus maximus: GM) using bipolar surface electrodes. To examine changes in EMG amplitude between trials, we calculated root mean squared (RMS) EMG values for each subject during a one second period in the middle of each trial (Tracy and Enoka 2006). EMG data were high pass filtered (second-order Butterworth filter, cutoff frequency 20 Hz) and rectified before RMS EMG values were computed. For each muscle, RMS EMG values were normalized to the highest RMS EMG value recorded during any of the unilateral MVC trials.

From the unilateral and bilateral MVC force values, we calculated a bilateral index for each subject using Equation 3.1 (Koh et al. 1993; Taniguchi 1998; McLean et al. 2006):

$$BI\ (\%) = 100\left(\frac{Left\ Bilateral + Right\ Bilateral}{Left\ Unilateral\ +\ Right\ Unilateral}\right) - 100 \qquad (3.1)$$

where left and right bilateral indicate the respective MVC forces during the isometric bilateral MVC condition, and left and right unilateral indicate the respective MVC forces during the unilateral MVC condition for each limb. A bilateral index less than zero indicated that the total bilateral force was less than the sum of the unilateral forces (i.e. bilateral deficit), whereas a bilateral index of greater than zero indicated that the total bilateral force was greater than the sum of the unilateral forces (i.e. bilateral facilitation).

For MVC trials, we used a repeated measures two-way ANOVA (limb by condition) to test for differences between peak force measured during the bilateral and unilateral MVC conditions, as well for interaction effects (JMP IN software, SAS Institute, Inc., Cary, NC, USA). For submaximal force matching trials, we used separate repeated measures two-way ANOVAs (limb by force level) to test for differences in force normalized to unilateral MVC, force normalized to bilateral MVC, and RMS EMG, as well as interaction effects. When interaction effects were significant, we ran separate ANOVAs on each limb, condition, and force level. When ANOVAs indicated significance ($P < 0.05$), we used Tukey-Kramer Honestly Significant Difference (THSD) post hoc tests to determine differences between limbs and force levels ($P < 0.05$). Post hoc power analyses were carried out where appropriate.

Results

MVC trials showed significant differences in foot reaction force magnitude between limbs and conditions (ANOVA $P < 0.0001$, limbs $P = 0.0043$, conditions $P < 0.0001$) (Table 3.1; Figure 3.2). There was also a significant interaction effect between limbs and conditions (ANOVA $P = 0.0394$). During the bilateral MVC condition, subjects produced an average peak force of 1143 N ± 130 N (mean ± S.E.M.) in the stronger limb and 904 N ± 111 N in the weaker limb. Peak forces produced in the weaker limb were significantly lower than in the stronger limb (separate ANOVA $P < 0.0001$). A difference in peak forces between limbs for the bilateral MVC condition was expected because this was the criteria for selection

Table 3.1. Summary of main and interaction effects of repeated measures ANOVA of peak force recorded during unilateral and bilateral MVC trials.

	df	F	P
Two-way ANOVA (Limb by Condition)			
Effect of Limb	(1,27)	9.73	0.0043
Effect of Condition	(1,27)	164.39	< 0.0001
Limb * Condition	(1,27)	4.69	0.0394
Separate ANOVAs			
Effect of Limb			
Unilateral MVC	(1,9)	0.84	0.3832
Bilateral MVC	(1,9)	72.98	< 0.0001
Effect of Condition			
Weaker Limb	(1,9)	97.37	< 0.0001
Stronger Limb	(1,9)	43.81	< 0.0001

Limb: weaker/stronger, condition: unilateral/bilateral MVC, *df* = degrees of freedom

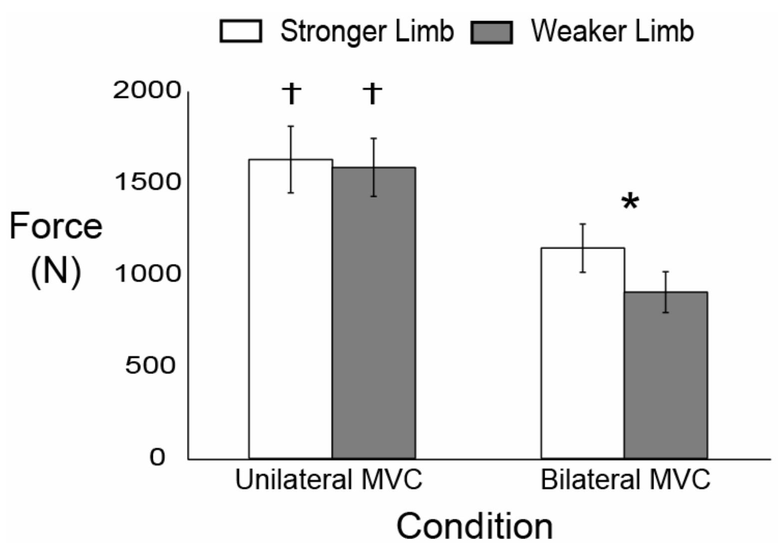


Figure 3.2. Average peak force during bilateral and unilateral MVC conditions. White columns represent average peak forces recorded in the stronger limb and grey columns represent average peak forces recorded in the weaker limb. The stronger limb produced significantly more force than the weaker limb during the bilateral MVC condition (ANOVA *: $P < 0.0001$). Forces during the unilateral MVC conditions were significantly higher than the bilateral MVC condition for each limb (ANOVA †: $P < 0.0001$). Error bars are the standard error of the mean.

into the study. Peak force averages produced during the unilateral MVC trials of 1625 N ± 180 N and 1582 N ± 157 N, respectively for the stronger and weaker limb, showed no significant differences (separate ANOVA P = 0.3832). All subjects demonstrated less peak force during the bilateral MVC condition when compared to the unilateral MVC condition for each limb (separate ANOVA P < 0.0001). These data resulted in a bilateral index of -35.3 ± 7.1%, indicating a bilateral deficit.

Example data from one subject attempting to produce equal forces in her lower limbs show the general trend for all subjects during the submaximal force matching task (Figure 3.3). During this trial the target force equaled 60% of the

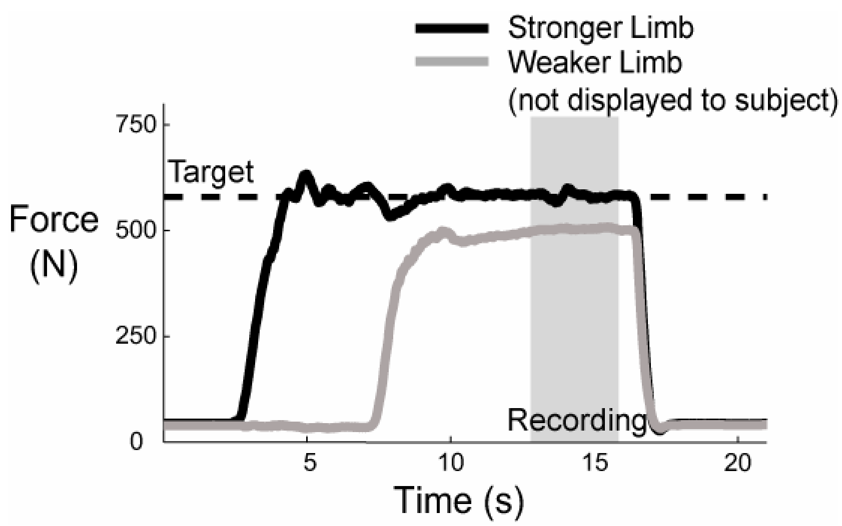


Figure 3.3. Example plot of foot forces vs. time during a 60% force matching trial for one subject. The dashed line represents force level target. The black trace represents stronger limb force and the grey trace represents weaker limb force. Weaker limb force profiles were not displayed to subjects at any time. Grey shading indicates the period over which data was recorded and analyzed. The start of recording was determined by a verbal cue from the subject

indicating that they believed the forces in both limbs were equal.
maximum force recorded on the weaker limb during the bilateral MVC condition.

The subject was able to match the force of her stronger limb to the target force with visual feedback but was not able to accurately produce equal forces between limbs. The subject produced significantly less force in her weaker limb. When normalizing average force magnitude by unilateral MVC force, there were significant differences between limbs and force level (ANOVA $P < 0.0001$, limbs $P < 0.0001$, force level $P < 0.0001$). There was also a significant interaction effect between limbs and force level (ANOVA $P = 0.0059$). When normalizing average

Table 3.2. Summary of main and interaction effects of repeated measures ANOVA of normalized average force during three submaximal force matching conditions.

		Force as % Unilateral MVC		Force as % Bilateral MVC	
	df	**F**	**P**	**F**	**P**
Two-way ANOVA (Limb by Force Level)					
Effect of Limb	(1,45)	35.04	< 0.0001	0.037	0.8490
Effect of Force Level	(2,45)	214.71	< 0.0001	476.33	< 0.0001
Limb * Force Level	(2,45)	5.78	0.0059	1.53	0.2263
Separate ANOVA					
Effect of Limb					
20% Force Level	(1,9)	5.27	0.0473		
40% Force Level	(1,9)	21.58	0.0012		
60% Force Level	(1,9)	25.65	0.0007		

Limb: weaker/stronger, force level: 20/40/60% force matching level, *df* = degrees of freedom force magnitude by unilateral MVC force, subjects consistently produced less force in their weaker limb at all force levels (separate ANOVAs 20% *P* = 0.0473, 40% *P* = 0.0012, 60% *P* = 0.0007) (Table 3.2; Figure 3.4A). When normalizing average force magnitude by bilateral MVC force, there were significant

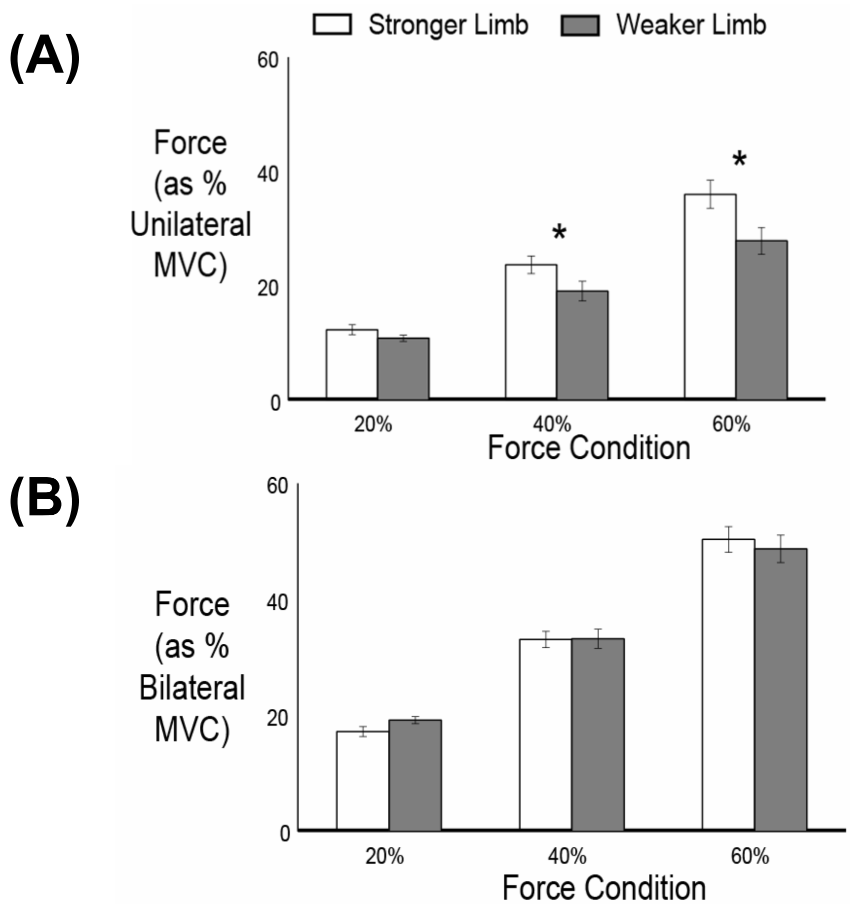


Figure 3.4. Average forces for all subjects during all force matching levels. Target forces were equal to 20%, 40%, and 60% of the weaker limb peak force during the bilateral MVC condition. White columns represent forces recorded in the stronger limb and grey columns represent forces recorded in the weaker limb. A) Forces normalized to unilateral MVC for each limb show significant differences between limbs (ANOVAs *: 20% *P* = 0.0473, 40% *P* = 0.0012, 60% *P* = 0.0007). B) Forces normalized to bilateral MVC shows no differences between limbs (ANOVA *P* = 0.8490). Error bars are standard error of the mean.

differences between force levels but not between limbs at any of the three force levels (ANOVA $P < 0.0001$, force levels $P < 0.0001$, limbs $P = 0.8490$). There was no significant interaction effect when average force magnitude was normalized to bilateral MVC force ($P = 0.2263$) (Figure 3.4B).

Lower limb EMG analysis during MVC trials revealed significant differences in normalized RMS EMG between conditions and limbs for vastus medialis (ANOVA $P < 0.0001$, conditions $P < 0.0001$, limbs $P = 0.0455$) (Table 3.3). EMG analysis showed significant differences between conditions but not limbs for vastus lateralis (ANOVA $P = 0.0013$, conditions $P < 0.0001$, limbs $P = 0.2468$), medial hamstrings (ANOVA $P < 0.0001$, conditions $P < 0.0001$, limbs $P = 0.1649$), and gluteus maximus (ANOVA $P < 0.0001$, conditions $P < 0.0001$, limbs $P = 0.1129$) (Figure 3.5). There was a significant interaction effect for vastus medialis ($P = 0.0269$) and gluteus maximus ($P = 0.0251$) but not for vastus lateralis ($P = 0.1136$) or medial hamstrings ($P = 0.3166$). Comparing muscle activation of the stronger limb between the unilateral and bilateral MVC conditions showed significantly lower normalized RMS EMG in the bilateral condition for vastus lateralis (THSD $P < 0.05$), vastus medialis (separate ANOVA $P = 0.0135$), and medial hamstrings (THSD $P < 0.05$). Comparing muscle activation of the weaker limb during the unilateral MVC condition to the bilateral MVC condition showed significantly lower normalized RMS EMG in the bilateral condition for vastus lateralis (THSD $P < 0.05$), vastus medialis (separate ANOVA $P < 0.0001$) medial hamstrings (THSD $\mathrm{P} < 0.05$), and gluteus maximus (separate ANOVA $\mathrm{P} < 0.0001$). When comparing RMS EMG of the stronger leg

Table 3.3. Summary of main effects and interaction effects of repeated measures ANOVA of RMS EMG during unilateral and bilateral MVC trials.

		VL		VM		MH		GM	
	df	F	P	F	P	F	P	F	P
Two-way ANOVA (Limb by Condition)									
Effect of Limb	(1,27)	1.4	0.2468	4.40	0.0455	2.04	0.1649	2.69	0.1129
Effect of Condition	(1,27)	34.59	< 0.0001	49.71	< 0.0001	42.56	< 0.0001	34.57	< 0.0001
Limb * Condition	(1,27)	2.67	0.1136	5.48	0.0269	1.04	0.3166	5.62	0.0251
Separate ANOVAs									
Effect of Limb									
Unilateral MVC	(1,9)			0.047	0.8332			1.66	0.2296
Bilateral MVC	(1,9)			10.13	0.0111			3.68	0.0874
Effect of Condition									
Weaker Limb	(1,9)			54.19	< 0.0001			444.82	< 0.0001
Stronger Limb	(1,9)			9.37	0.0135			4.48	0.0636

limb: weaker/stronger, condition: unilateral/bilateral MVC, *df* = degrees of freedom, VL: vastus lateralis, VM: vastus medialis, MH: medial hamstrings, GM: gluteus maximus

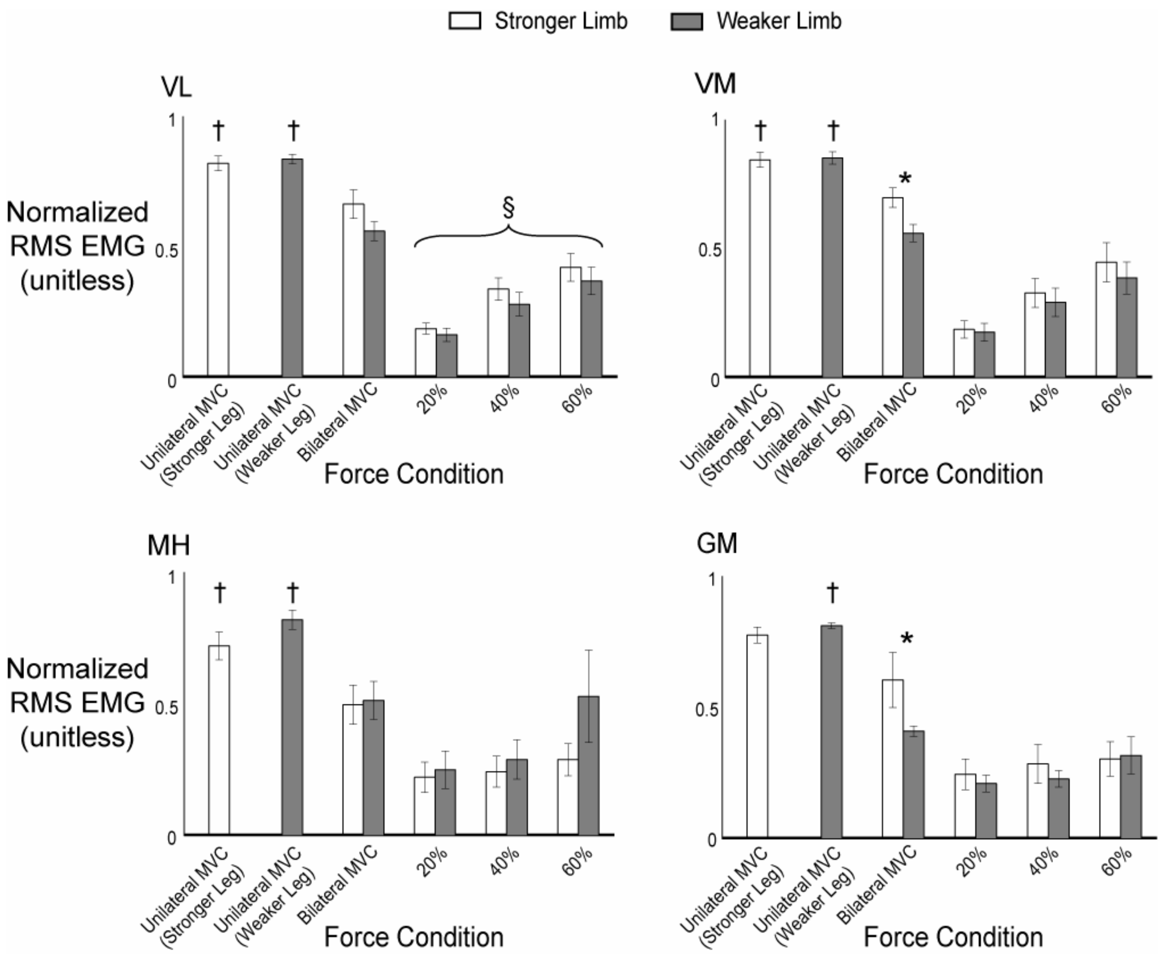


Figure 3.5. Average normalized RMS EMG for all subjects. Force conditions included unilateral MVCs on each limb, bilateral MVC, and three submaximal force matching levels. Force matching target levels were 20%, 40%, and 60% of the weaker limb peak force during the bilateral MVC condition. White columns represent forces recorded in the stronger limb and grey columns represent forces recorded in the weaker limb. Reported muscle data is for the vastus lateralis (VL), vastus medialis (VM), medial hamstrings (MH), and gluteus maximus (GM) on each side. For each muscle, RMS EMG values were normalized to the highest RMS EMG value recorded during any of the unilateral MVC trials. † indicates significant difference between EMG during unilateral and bilateral MVC conditions within each limb. * indicates significant difference between stronger and weaker limb EMG during the bilateral MVC condition. § indicates significant difference between stronger and weaker limb EMG across force levels. Error bars are standard error of the mean.

to the weaker leg during the bilateral MVC condition, there was a significant decrease in RMS EMG of the weaker leg in the vastus medialis (separate ANOVA $P = 0.0111$). Power analyses indicated power was less than 0.62 for RMS EMG data across all these tests.

When comparing RMS EMG during the force matching trials, there were significant differences between limbs and force levels for vastus lateralis (ANOVA $P < 0.0001$, limbs P = 0.0145, force levels P\0.0001) (Table 3.4). There were significant differences between force levels but not limbs for vastus medialis (ANOVA $P < 0.0001$, force levels $P < 0.0001$, limbs $P = 0.0809$) and medial hamstrings (ANOVA $P < 0.0001$, force levels $P = 0.0302$, limbs $P = 0.0611$). There were no significant differences between limbs or force levels for gluteus maximus (ANOVA $P < 0.0001$, force levels $P = 0.0914$, limbs $P = 0.3932$). No significant interaction effects were found (VM: $P = 0.6973$, VL: $P = 0.6057$, MH: $P = 0.2274$, GM: $P = 0.6307$).

Discussion

Our results clearly demonstrated that force imbalance persisted at both maximal and submaximal force levels. This suggests that the mechanisms involved in the deficit are likely the same for maximal and submaximal contractions. Interpreting these results in light of past studies on sense of effort (Gandevia and McCloskey 1977b; Carson et al. 2002; Proske et al. 2004) suggests that force production in the lower limbs is

Table 3.4. Summary of main and interaction effects of repeated measures ANOVA of RMS EMG during three submaximal force matching conditions.

		VL		VM		MH		GM	
	df	F	P	F	P	F	P	F	P
Two-way ANOVA (Limb by Force Level)									
Effect of Limb	(1,45)	6.47	0.0145	3.19	0.0809	3.69	0.0611	0.74	0.3932
Effect of Force Level	(2,45)	53.99	< 0.0001	44.95	< 0.0001	3.79	0.0302	2.52	0.0914
Limb * Force Level	(2,45)	0.36	0.6973	0.51	0.6057	1.53	0.2274	0.47	0.6307

limb: weaker/stronger, force level: 20/40/60% force matching level, *df* = degrees of freedom, VL: vastus lateralis, VM: vastus medialis, MH: medial hamstrings, GM: gluteus maximus based on sense of effort during submaximal contractions. Results of the current study should have been different if subjects were relying on their sense of force or tension rather than their sense of effort in lower limbs during the submaximal force matching tasks. If this were the case, subjects should have been able to match absolute forces between limbs because their unilateral MVC forces (and therefore individual limb strengths) were not significantly different from each other. Their lower limbs had the capacity to produce equal forces but during the submaximal force matching trials they did not generate equal forces.

Although the peak force produced by subjects during bilateral isometric maximum voluntary contractions was significantly different between limbs, the peak force during unilateral isometric maximum voluntary contractions was not. Biomechanical factors that determine muscle force include muscle length, shortening velocity, activation history and current activation (Huijing 2000). During both unilateral and bilateral maximum contraction trials, we have controlled for three of the four factors. Subjects are lying down in the same position with the shoulders firmly braced. With the same posture and joint angles, muscle lengths remain the same. Shortening velocity remains the same at ~0 cm/s as this is a maximum isometric contraction and before both trials subjects have rested and therefore have the same activation history. The only variable influencing a change in muscle force therefore is current activation neural drive (i.e. unilateral or bilateral maximum contraction). Similar peak forces between limbs during unilateral isometric maximum voluntary contractions demonstrate that the mechanical capabilities of each limb are equal. It is activating the legs at the same time (i.e. bilateral movement) that results in asymmetric limb forces. Regardless of whether humans produce maximal or submaximal forces, limb force asymmetry appears to be related to neural factors rather than differences in mechanical capabilities between the limbs.

Lower limb EMG results from the vastus medialis, vastus lateralis, medial hamstrings and gluteus maximus muscles did not explain this force asymmetry. This is likely a result of the inherent high variability in EMG amplitudes compared to force measures. Muscles act as low pass filters so that relatively large variations in EMG are not seen in muscle force (Winter 2004). As a result, our EMG measures provided low statistical power (power < 0.62). On average, more than 40 subjects would have been required to achieve statistical power greater than 0.8 for the EMG data. As a result, determining a correlating change in EMG activity is beyond the scope of our study.

The bilateral index of -35.3 ± 7.1% measured during isometric lower limb extensions reveals large bilateral deficits in our subjects. Comparisons of bilateral index to previous studies measurements are difficult due to a shortage in reported values for isometric whole lower limb extensions. Many more studies have reported bilateral indices for isometric knee extension, ranging from -24% (bilateral deficit) to +4% (bilateral facilitation) (Schantz et al. 1989; Koh et al. 1993; Jakobi and Cafarelli 1998). The large bilateral deficit demonstrated in our subjects results from several factors. First, isometric lower limb extensions involve contractions across multiple joints compared to knee extensions that only involve contractions across a single joint. When individuals have performed both isometric MVC trials of lower limb extensions (i.e. multi-joint) and isolated knee extensions (single-joint) their bilateral index changes from a bilateral deficit to a bilateral facilitation, respectively (Schantz et al. 1989). Another reason for an increase in bilateral deficit may be due to the fast rate of lower limb force development. Subjects possess a larger bilateral deficit when they are instructed to generate force as quickly as possible (BI = -24.6%) rather than generate force gradually (BI = -17.0%) (Koh et al. 1993). The bilateral index also depends upon training, such that with bilateral training the bilateral deficit is reduced (Taniguchi 1997; Taniguchi 1998; Janzen et al. 2006). Our subjects were typical university students and not specifically trained in bilateral movements.

Subjects' posture during the experiment may also contribute to the large bilateral deficit. Subjects were supine with their feet on a vertical force platform. As described in the Methods section, the lower limbs were positioned in the middle of the range of motion used for a full lower limb extension, leading to knee angles ranging from 110° to 120° (180° defined as full knee extension). Therefore, subjects had increased knee and hip extension compared to previous studies that reported knee and hip angles of 90° for knee extension trials.

Regardless of the reasons for the difference in magnitude of the bilateral deficit, an important comparison in the current study was to determine if force matching experiments in the lower limbs show similar results to upper limb force matching studies. Our results relate to a multi-joint lower limb bilateral task, whereas other studies have involved single joints of the upper limb including either the finger (distal interphalangeal joint) (Li and Leonard 2006; Park et al.

2007) or the elbow (Gandevia and McCloskey 1977b; Carson et al. 2002; Weerakkody et al. 2003; Proske et al. 2004). In several elbow joint studies, force asymmetry was induced by weakening agonist muscles through unilateral fatigue of the elbow extensors (Carson et al. 2002) or the flexors (Weerakkody et al. 2003; Proske et al. 2004). Similar to the results of the current study, subjects attempting to produce equal forces between limbs actually produced equal relative forces when individual limb forces were scaled to the instantaneous maximum strength of the muscle groups (i.e. the post-fatigued maximum strength). Different results, however, were seen in experiments involving force matching between ipsilateral fingers. When reference and matching finger forces were normalized to individual finger strength, the weaker finger produced a higher relative force (Li and Leonard 2006). Absolute forces were not significantly different when total force (instructed and uninstructed) was considered. Uninstructed fingers may produce force resulting from enslaving effects, or involuntary force production of one or more fingers when another finger is activated (Zatsiorsky et al. 1998). These findings led to conclusions that the central nervous system perceives absolute force from all fingers (Li and Leonard 2006) rather than a relative force as concluded in the current study. The contrasting results also may be due to the function of the muscles involved. Lower limb muscles are typically involved in gross motor function, whether it is producing large forces or in controlling posture, whereas smaller muscles are involved in fine motor control in order to perform accurate movements. The central nervous system may perceive absolute force when the muscles involved are used for fine motor control, such as in the finger, and relative force when the muscles involved are for gross motor function, such as in the lower limbs.

There are several neural mechanisms that could account for the changes in force observed during bilateral activation. Mechanisms proposed for causing the bilateral deficit include reduced motor neuron excitability (Vandervoort et al. 1984; Kawakami et al. 1998), interhemispheric inhibition (Gazzaniga and Sperry 1966) , and limitation of the central neural drive (i.e. ceiling effect) (Li et al. 1998; Li et al. 2001). Although these mechanisms could account for the drop in total maximum strength when a task is performed bilaterally as compared with unilaterally, they could not explain the bilateral force asymmetry described in this study.

There is another neural mechanism called common drive that may account for the neural origin of force asymmetry during bilateral activation (De Luca et al. 1982a; De Luca et al. 1982b; De Luca 1985). Common drive describes the unison behavior of the firing rates of motor units and might indicate that when homologous muscle groups are bilaterally activated, the nervous system treats them as one unit. This mechanism has been proposed to exist for both maximal and submaximal contractions (Oda and Moritani 1996). Alternatively, there could be a chronic asymmetric neural drive to the dominant and non-dominant lower limbs. Long-term potentiation could have created the asymmetry because of greater use by the dominant lower limb. Future studies relying on functional magnetic resonance or other types of brain imaging may provide more insight into the mechanisms.

The current results may have implications for other tasks and/or other populations. We examined static lower limb extensions in healthy individuals attempting to match forces between their lower limbs. Subjects with neurological disabilities typically have a mismatch between their sense of effort and force production (Bertrand et al. 2004; Mercier et al. 2004). Individuals with post-stroke hemiparesis have increased limb force asymmetry partially due to reduced strength capacity in the involved muscles of one side of the body. During upper limb submaximal matching tasks, these subjects consistently overestimate forces produced in the paretic upper limb, even though maximum voluntary force trials reveal that they have the ability to produce forces of equal magnitude (Bertrand et al. 2004; Mercier et al. 2004). These results suggest that subjects rely on their sense of effort to predict upper limb forces. More recently, Milot et al. (Milot et al. 2006) found that normalizing joint moments during gait to the maximum joint moment capabilities led to similar effort levels in the paretic and non-paretic limbs. Thus, it seems that sense of effort is an important factor in determining lower limb muscle activation in hemiparetic individuals.

The field of rehabilitation can benefit from knowing that post-stroke individuals use sense of effort in predicting force output. Current rehabilitation therapies focus on strengthening the paretic limb of these individuals. Although this is a necessary component, force matching studies would suggest that therapy also needs to address improving patients' impaired force scaling abilities. Improved results may occur with designing training techniques to address both of these components. One new strategy, symmetry-based resistance (Simon et al.

2007), has the potential to improve both the patients' force scaling abilities and limb strength. With symmetry-based resistance, task resistance increases with increasing limb force asymmetry. Lower limb extension training with symmetry-based resistance is a potential means for training subjects to recalibrate their effort to force relationship. Subjects can learn to scale muscle activation more appropriately to achieve a desired force outcome. This would enable stroke subjects to better match paretic limb forces to task requirements during activities of daily living. The results from this study demonstrate that there is a lower limb asymmetry existing even in healthy neurologically intact subjects. Therefore, future studies using symmetry-based resistance for patient populations need to consider this asymmetry as a potential factor in the study design and results.

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Chapter 4

Sense of Effort Determines Lower Limb Force Production During Supine Lower Limb Extensions in Individuals with Post-Stroke Hemiparesis

Abstract

The study's purpose was to determine if individuals who have had a stroke primarily use sense of effort to gauge force production during static and dynamic lower limb contractions. If relying on sense of effort while attempting to generate equal foot forces, subjects should produce equal percentages of their maximum voluntary strength rather than equal absolute forces in their limbs. Ten stroke subjects performed isometric and isotonic lower limb extensions on an exercise machine. When subjects attempted to produce equal bilateral isometric forces, there was a significant difference in absolute force between limbs (ANOVA, $P < 0.0001$) but no significant difference when force was normalized to each limbs' maximum voluntary contraction force ($P = 0.5129$). During bilateral isotonic contractions, subjects produced less absolute force in their paretic limb ($P = 0.0005$) and less relative force in their paretic limb (normalized to maximum voluntary contraction force) when subjects were given no force instructions on how to perform the extension ($P = 0.0002$). When subjects were instructed to produce equal forces, there was no significant difference between relative forces in the two limbs ($P = 0.2111$). For both isometric and isotonic conditions

hemiparetic subjects relied primarily on sense of effort, rather than proprioceptive feedback, for gauging foot reaction forces. This outcome indicates that sense of effort is the major factor determining force production during movements. Lower limb rehabilitation therapies should not only train strength in the paretic limb but should also train patients to recalibrate force scaling abilities to improve function.

Introduction

Humans control force production in their limbs by using an internal model of musculoskeletal mechanics to calculate appropriate neural signals (Wolpert et al. 1995; Wolpert and Ghahramani 2000; Cothros et al. 2006). The model allows the nervous system to generate predicted sensory information from the neural command and compare it to the sensory information from the actual movement. As a result, motor commands depend on the nervous system’s understanding of system mechanics and comparisons of predicted and actual afferent sensory feedback. As individuals learn a task, they update their internal model in order to generate a better prediction of the actual motion (Shadmehr and Mussa-Ivaldi 1994).

Fine control of upper limb force production is a motor task that likely uses an internal model to set efferent commands. Humans use a neural representation of their musculoskeletal system to help them determine the correct efferent commands to produce a desired motion. Individuals need to have a good internal model if they are to produce a desired force level. The internal model not only allows humans to produce accurate efferent commands but helps in interpreting proprioceptive feedback. In generating muscle force, humans can use both the scaling of the descending motor command, generally termed sense of effort (McCloskey et al. 1974), and the ascending sensory information, termed sense of force or tension (Roland and Ladegaard-Pedersen 1977).

Studies involving contralateral limb-matching paradigms have been used to determine how humans perceive muscle force and whether or not they depend more on sense of effort or sense of force. In a contralateral limb-matching protocol, subjects develop force in one limb (the reference limb) and through use of visual force feedback they are asked reach a target force level. Once they reach the target force level with the reference limb they begin producing force with their contralateral limb (the matching limb). Subjects do not receive any visual feedback regarding force in the matching limb.

If the mechanical output of an upper limb muscle is altered through fatigue (Gandevia and McCloskey 1978; Jones and Hunter 1983; Carson et al. 2002), partial curarization (Gandevia and McCloskey 1977a), or through changes in muscle length (Cafarelli and Bigland-Ritchie 1979) individuals often overestimate the force produced in that limb. Results from upper limb studies of isometric elbow flexion/extension on neurologically intact subjects with one limb in a state of fatigue showed that subjects did not produce forces of equal magnitude in their limbs (Jones and Hunter 1983; Carson et al. 2002; Weerakkody et al. 2003; Proske et al. 2004). Subjects consistently produced less force in the fatigued limb, indicating they were overestimating force in the limb. When individual limb forces were normalized to the post-fatigue maximum strength of each limb directly before testing, these normalized forces did not show any significant differences between limbs (Carson et al. 2002). These results led Carson et al. (Carson et al. 2002) to conclude that when subjects attempt to produce equal forces in their limbs they produce equal percentages of each limb's maximal voluntary strength rather than equal absolute forces.

Results from a lower limb study on the force asymmetry of neurologically intact individuals showed similar results. Subjects included in this study possessed a greater than 10% force discrepancy in bilateral foot forces during maximum voluntary contraction trials. Subjects attempting to produce equal foot forces during an isometric lower limb extension did not produce equal magnitudes of force (Simon and Ferris 2008). Instead, subjects produced equal percentages of their bilateral (not unilateral) maximum voluntary strength in each lower limb. These studies suggest that neurologically intact subjects primarily use a sense of effort originating from a corollary discharge of the motor command to the muscles (Sperry 1950; McCloskey et al. 1974; Gandevia and McCloskey 1977b; Simon and Ferris 2008), rather than relying on proprioceptive feedback to gauge force production in their limbs.

In neurological populations, such as individuals who have had a stroke, hemiparesis affects patients' abilities to approximate force production in their limbs. Proprioception is affected post-stroke, suggesting that these individuals may also rely more on their sense of effort compared with sense of force. Previous studies have demonstrated that individuals with complete loss of proprioceptive sensory abilities still have a good sense of effort and use sense of effort to gauge force production (Rothwell et al. 1982; Lafargue et al. 2003). During isometric submaximal upper extremity matching tasks, stroke subjects consistently overestimate forces produced in the paretic limb, even though maximum voluntary force trials reveal that they have the ability to produce forces of equal magnitude (Bertrand et al. 2004; Mercier et al. 2004). Because a stroke subject has reduced maximum force ability in the paretic limb, determining muscle activation based on a fixed proportion of maximum force capability will result in less force in the paretic limb. It is possible that individuals may not update their internal model of musculoskeletal mechanics to account for their post-stroke weakness (Takahashi and Reinkensmeyer 2003).

Individuals' inability to account for post-stroke hemiparesis and produce appropriate force levels with their paretic limb affects their ability to stand from a seated position, perform transfers and ambulate which may predispose a patient to falls. A mismatch between expected force production and actual force production in these situations can have serious implications for movement. Previous studies have examined force production and perception in simplified tasks of upper extremity isometric contractions (Bertrand et al. 2004; Mercier et al. 2004). Mobility tasks, however, involve force production in the lower limbs during dynamic movements.

In this study, we have investigated foot reaction forces of individuals with post-stroke hemiparesis both during isometric and isotonic movements. Results from these two experiments will provide insight into whether or not control of force in stroke subjects is the same for static and dynamic movements. The goal of this study was to determine if force asymmetry during isometric and isotonic bilateral force production of individuals with post-stroke hemiparesis both result from neural mechanisms related to sense of effort. We hypothesized that hemiparetic subjects attempting to produce equal foot forces would generate equal percentages of their bilateral maximum voluntary strength rather than equal absolute limb forces during both isometric and isotonic movement.

Methods

Subjects

We recruited 10 individuals with stroke-induced hemiparesis (5 males and 5 females; age: 56 ± 7.3 years, mean ± S.D.M.) (Table 4.1). Inclusion criteria consisted of 1) at least six months post-onset of a single neurologic insults that included ischemic or hemorrhagic type strokes (verified through MRI or CT scan data from patients' medical records), 2) between the ages of 18 and 85, 3) free of any musculoskeletal injuries or deformities, 4) presented with no spastic hypertonia in the lower limbs, and 5) adequately able to comprehend our instructions. A physiatrist at the University of Michigan evaluated and cleared each subject for participation in the study. All subjects gave written informed consent approved by the Institutional Review Board for Human Subject Research at the University of Michigan Medical School. One subject (Subject 6) participated in the study but his data were excluded from the analysis because he had great difficulty remembering and following the instructions. A physical therapist evaluated subjects' lower extremity physical performance with the lower

Table 4.1. Subject characteristics.

Subject	Age (yrs)	Gender	Paretic Side	Postonset (mos)	Lesion Location	Type of Stroke	Fugl - Meyer* Lower Extremity	Fugl - Meyer* Balance
1	69	M	L	7	Right MCA (occipital-parietal regions)	Ischemic	32	4
2	50	M	R	36	Left MCA	Ischemic	25	11
3	52	M	L	20	Right parietal lobe	Ischemic	23	10
4	69	F	R	12	Left hemisphere	Ischemic	23	8
5	50	F	L	39	Right MCA	Ischemic stroke secondary to large vessel atherosclerosis	26	10
6†	55	M	L	32	Right hemisphere	Ischemic	na	na
7	53	F	R	10	Left pons	Ischemic	27	11
8	51	F	R	39	Left frontal lobe	Ischemic	14	9
9	53	M	R	8	Left occipital and parietal lobe	Embolic	34	14
10	58	F	L	37	Temporal lobe	Ischemic	18	7

Abbreviations: Sex (F: female, M: male), Paretic Side (L: left, R: right), na: not available

*Fugl-Meyer Clinical Assessment: Lower extremity motor score (0-34), Balance motor score (0-14)

†Subject 6's data was excluded from analysis because he had great difficulty remembering and following the instructions.

limb and balance portions of the Fugl-Meyer Clinical Assessment (Table 4.1). The authors noted various sensory deficits based on comments from the subjects including reduced cutaneous sensation and impaired force perception. No subjects reported impaired sense of limb motion and position.

Experimental Design

We performed two experiments to investigate the ability of individuals with post-stroke hemiparesis to match foot reaction forces between limbs during static and dynamic force matching tasks. We performed maximum strength testing and two force matching experiments within one single testing session. Subjects received extended breaks of at least fifteen minutes between all sections of the data collection.

For the entire study, subjects exercised on a robotic exercise machine built in the University of Michigan's Human Neuromechanics Laboratory (Simon et al. 2007) (Figure 4.1). Subjects were supine on the exercise machine and placed their feet on a vertical dual force platform (Model Dual Accu-Gait, AMTI, Watertown, MA). We used foot straps to stabilize their feet.

Maximum Strength Testing

We recorded subjects' isometric (static) and isokinetic (dynamic) strength on the exercise machine. We assessed subjects' isometric strength with the machine in isometric mode. In isometric mode, the motor was turned off and the sled was locked into position such that the subject was halfway between the sled

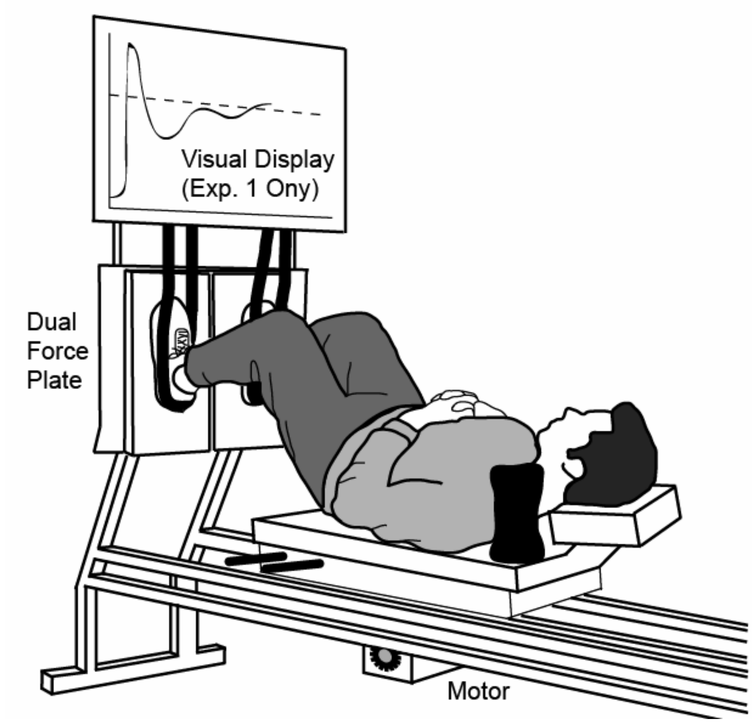

Figure 4.1. Individual with post-stroke hemiparesis using the leg press exercise machine. Subjects reclined on the machine and placed their feet in foot straps onto a dual force platform. In Experiment 1, a visual display allowed subjects to receive force feedback of the target force (dashed line) and non-paretic limb force (solid line). In Experiment 2 we removed the visual display and controlled motor resistance.

position of 90 degree knee and hip flexion and complete extension of the lower limbs. We assessed subjects' isokinetic strength with the robotic exercise machine in isokinetic mode. In isokinetic mode, the computer controlled resistance so that movement velocity remained constant at 15 cm/s during lower limb extensions. If a subject pushed hard and therefore the sled moved faster, the controller increased resistance to maintain the reference velocity. During operation of this mode, subjects received visual feedback only of movement timing (i.e. when to start and stop pushing). We instructed subjects to only push during the extension phase and relax during the flexion phase. Subjects began in a flexed position with their knee and hip angles at approximately 90 degrees and then extended their lower limbs completely being careful to not lock out their knees.

For both static and dynamic strength testing, we quantified subjects' maximum force ability with two trials each of bilateral, non-paretic limb only, and paretic limb only maximum voluntary contractions (MVC). We randomized the trial order and verbally encouraged subjects to push as hard as they could with either one foot or both feet throughout each movement. We allowed subjects to rest as long as necessary between each MVC trial (no less than three minutes).

Experiment 1: Isometric

The protocol for Experiment 1 was previously used to investigate neurologically-intact subjects' lower limb force matching ability (Simon and Ferris 2008). Subjects performed two trials of isometric lower limb force matching in isometric mode. Subjects exerted a force equal to 35% of the paretic limb isometric bilateral MVC force. This level was chosen because it represented a force level that was achievable by each subject. Subjects received visual feedback of only the target force level and the amount of force applied by the non-paretic limb. When subjects reached the target force level in the non-paretic limb, we instructed them to begin applying force with the paretic limb. No feedback was given regarding the paretic limb force. Subjects verbally signaled to the experimenter once they believed they had matched forces in both lower limbs. Upon this verbal cue, subjects held the isometric contraction for two seconds and then relaxed. Subjects rested two to three minutes between trials.

Experiment 2: Isotonic

Subjects performed two sets of six lower limb extensions in isotonic mode. In isotonic mode, the resistance for continuous lower limb extensions remained constant. We instructed subjects to extend their lower limbs completely (not locking out their knees), flex to a knee and angle of approximately 90 degrees, and match their movement speed to a metronome set at 0.33 Hz. Subjects performed both sets against a total constant resistance equal to 80% of the peak force produced by the paretic limb during the isokinetic bilateral MVC (i.e. with symmetric forces, a total resistance level of 80% would be equivalent to the paretic limb producing 40% of its MVC force). This resistance value was chosen such that it ensured that subjects had the capacity for equivalent forces throughout the extensions even if the resultant forces were not equal. In set one, no force instructions were given to subjects on how to perform these extensions (No Force Instruction). In set two, we instructed subjects attempt to produce equal forces throughout the entire movement and verbally reminded them throughout the trials (Produce Equal Forces).

Data Acquisition and Analysis

For both experiments, we recorded individual lower limb forces from dual force plate data (Figure 4.1) sampled at 1000 Hz. Each limb's MVC force, both isometric/isokinetic and unilateral/bilateral, was determined as the maximum force measured during the two trials (Jones and Hunter 1983; Proske et al. 2004). For isometric force matching trials, we calculated average foot forces applied during the two seconds following the subjects' verbal cue. For isotonic force matching trials, we identified cycle timing from motor encoder data and averaged foot forces across only the extension phase of the cycle. For all force matching trials, we normalized the averaged forces to each limbs' unilateral maximum force ability and separately to bilateral maximum force ability to determine the amount of effort subjects used in each limb.

We performed a repeated measures ANOVA (subject by limb by condition) to test for significant differences in lower limb MVC forces during bilateral and unilateral conditions for both isometric and isokinetic data (JMP IN software, SAS Institute, Inc., Cary, NC). For both experiments, we used a repeated measures ANOVA (subject by limb) to test for differences in absolute lower limb forces, as well as forces normalized to unilateral and bilateral MVC force. When the ANOVA showed significant differences ($P < 0.05$), we used Tukey-Kramer Honestly Significant Difference (THSD) post-hoc tests to further delineate differences ($P < 0.05$). Post-hoc power analyses were carried out where appropriate.

Results

Maximum Strength Testing

Bilateral isometric MVC trials showed significant differences between limbs (ANOVA $P < 0.0001$) (Table 4.2). Peak paretic limb forces were significantly lower than non-paretic by 30% during bilateral isometric MVC conditions (THSD $P < 0.05$). A significantly lower peak force was recorded within the paretic limb during the bilateral compared to the unilateral isometric MVC condition (THSD $P < 0.05$).

Table 4.2. Peak foot reaction force recorded during isometric and isokinetic maximum voluntary contractions.

Condition	Non-Paretic Limb Peak Force (N)	Paretic Limb Peak Force (N)
Isometric MVC		
Unilateral	1107 ± 143	738 ± 132*
Bilateral	901 ± 176	629 ± 115*†
Isokinetic MVC		
Unilateral	604 ± 101	491 ± 94*
Bilateral	593 ± 89	379 ± 83*†

Values are mean ± s.e.m.

*Post-hoc (THSD) analysis indicates significant decrease in paretic limb force compared with non-paretic limb force within a condition ($P < 0.05$).

†Post-hoc (THSD) analysis indicates significant decrease in bilateral peak force compared with unilateral peak force within a limb ($P < 0.05$).

During isokinetic lower limb extensions, bilateral MVC trials showed significant differences between limbs (ANOVA $P < 0.0001$) (Table 4.2). Peak paretic foot reaction forces were significantly lower than non-paretic by 36% during bilateral isokinetic MVC conditions (THSD $P < 0.05$). A significantly lower peak reaction force was recorded within the paretic limb during the bilateral compared to the unilateral isokinetic MVC condition (THSD $P < 0.05$).

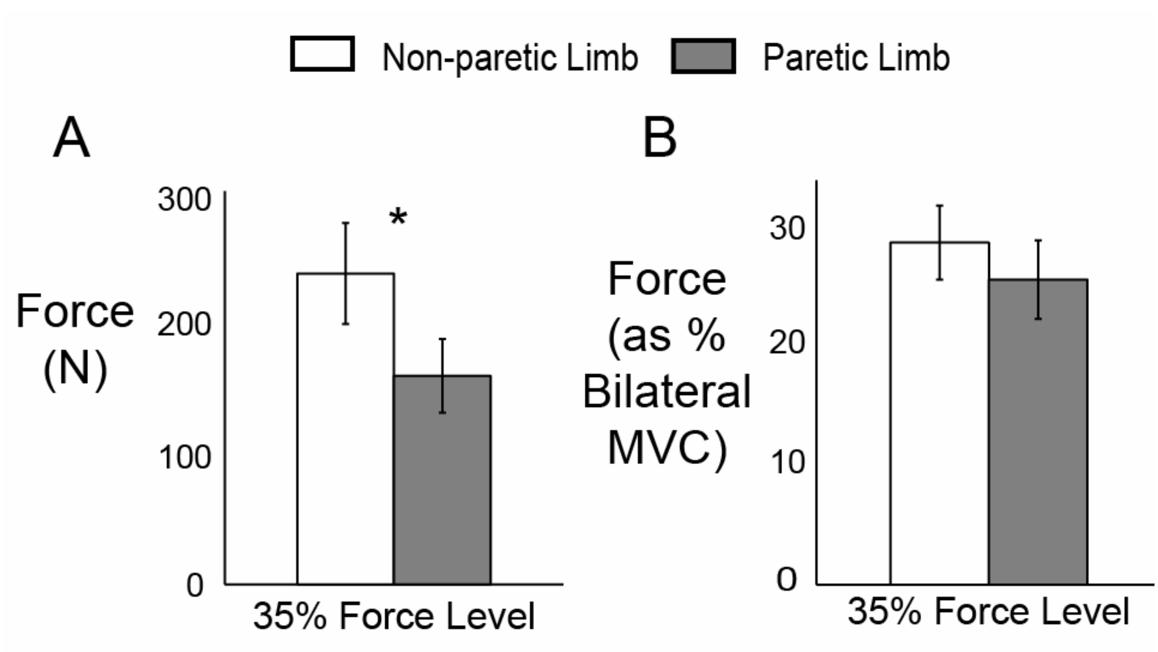

Figure 4.2. Experiment 1: Average forces during isometric force matching trials. The target force level was set to 35% of the paretic limb peak force during the bilateral isometric MVC condition. White columns represent non-paretic limb forces and grey columns represent paretic limb forces. A) Absolute foot reaction force shows significant difference between limbs (ANOVA *: $P<0.0001$). B) Force normalized to bilateral MVC shows no significant difference between limbs (ANOVA $P=0.5129$). Error bars are standard error of the mean.

Experiment 1: Isometric

Subjects were able to produce the target force with their non-paretic limb through use of visual feedback but did not produce a force equivalent in magnitude in their paretic limb. Average foot reaction force data showed that all subjects produced less absolute force in the paretic limb when compared with the non-paretic limb (ANOVA $P < 0.0001$) (Figure 4.2A) even though subjects believed the forces between their limbs were equal.

Normalizing force data to each limb's bilateral isometric MVC peak foot reaction force resulted in no significant differences between limbs (ANOVA $P = 0.5129$) (Figure 2B). The normalized force data (Figure 4.2B) indicate that the paretic limb undershot the target as the 35% force level was not achieved. Since the non-paretic limb's MVC force was greater than the paretic limb's MVC force, achieving the target force in the non-paretic limb equaled less than 35% MVC force in this limb. Post-hoc analyses revealed a least significant value of 1.96. This indicates that if there was a real difference between limbs that we did not have the power to detect, there is a 95% chance that it is no larger than 1.96% of the bilateral MVC value (Sall et al. 2001). Even if there is a Type II error the magnitude of the difference is small.

Experiment 2: Isotonic

Example foot reaction force profiles of four subjects with post-stroke hemiparesis performing isotonic lower limb extensions are shown in Figure 4.3. Compared to the No Force Instruction condition, when subjects were instructed to Produce Equal Forces in their limbs subjects' force production ranged from generating even less force in their paretic limb to one subject producing extremely large forces in their paretic limb. Overall subjects produced less absolute force in the paretic limb than in the non-paretic limb during both the No Force Instruction and the Produce Equal Forces conditions (ANOVA $P < 0.0001$ and $P = 0.0002$, respectively) (Figure 4.4A). Inter-subject variability of the

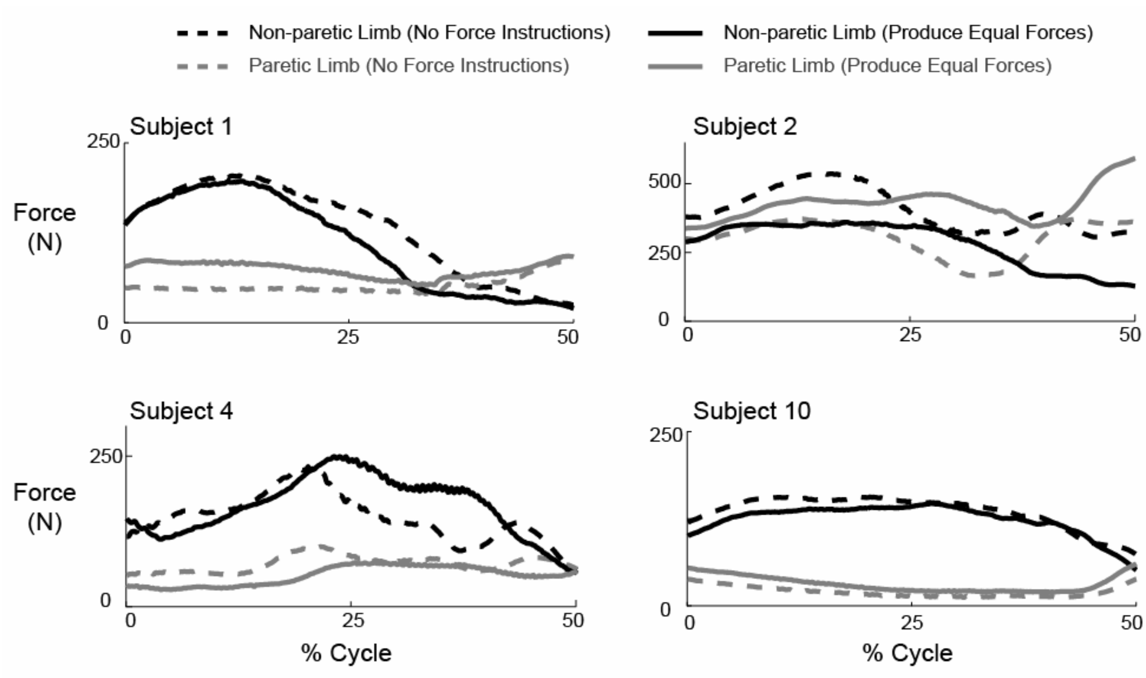

Figure 4.3. Experiment 2: Example plots of individual foot forces as a function of percentage of the isotonic cycle. From 0 to 50% is the extension phase of the cycle. Data shown are typical forces recorded for Subjects 1, 2, 4 and 10. Subject 2 was the only subject that produced much higher absolute forces in the paretic limb than in the non-paretic limb during the Produce Equal Forces condition. Black lines represent non-paretic limb forces and grey lines represent paretic limb forces. Dashed lines represent data from the No Force Instruction condition and solid lines represent data from the Produce Equal Forces condition.

movement timing was 0.34 Hz ± 0.021 Hz for the No Force Instruction condition and 0.33 Hz ± 0.011 Hz for the Produce Equal Forces condition.

Normalizing force data to each limb's bilateral isokinetic MVC peak foot reaction force resulted in a significant difference between limbs for the No Force Instruction condition (ANOVA, $P = 0.0005$) and no significant difference for the Produce Equal Forces condition (ANOVA $P = 0.2111$) (Figure 4.4B). Post-hoc analyses revealed a least significant value of 2.69. Thus, if there is a real difference between limbs, there is a 95% chance it is no larger than 2.69% of the bilateral MVC value (Sall et al. 2001). Even if there is a Type II error the magnitude of the difference is small.

Discussion

Our findings indicate that, similar to the upper limbs, control of force production in individuals with post-stroke hemiparesis is similarly reliant on sense of effort for lower limbs. During the isometric force matching of Experiment 1, subjects consistently produced less force in their paretic limb even though the target force was set low enough that subjects had the capability for equal forces. Normalizing foot reaction forces to each limbs' bilateral isometric MVC force revealed no significant differences between limbs suggesting that subjects are basing isometric lower limb forces on their sense of effort. These results for the lower limb are comparable to force matching tasks in the upper limbs of stroke subjects (Bertrand et al. 2004; Mercier et al. 2004) and in the lower limb of neurologically intact subjects (Simon and Ferris 2008).

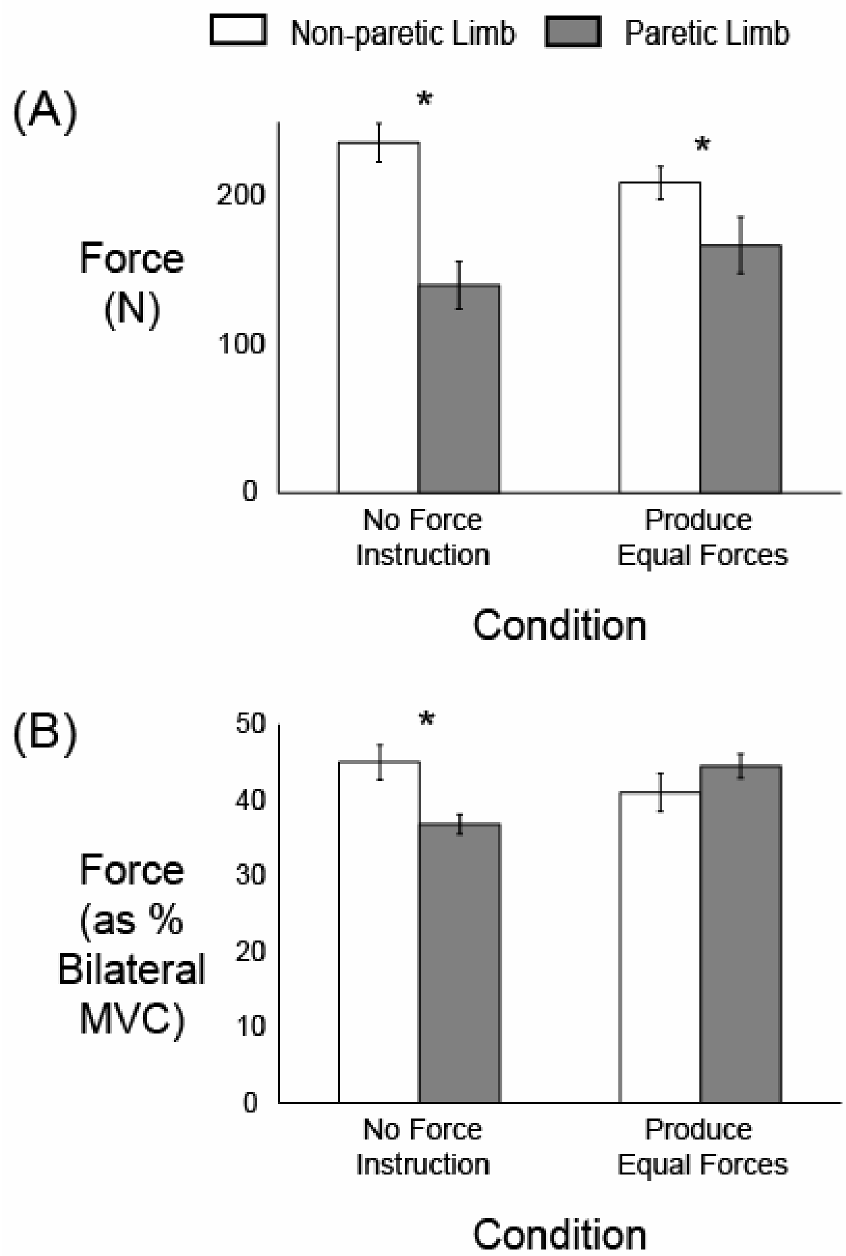

Figure 4.4. Experiment 2: Average forces during isotonic lower limb extension trials. The resistance level was set to 80% of the paretic limb peak force during the bilateral isokinetic MVC condition. White columns represent non-paretic limb forces and grey columns represent paretic limb forces. A) Absolute force shows significant difference between limbs for the No Force Instruction and Produce Equal Forces conditions (ANOVA *: P < 0.0001 and P = 0.0005, respectively). B) Force normalized to bilateral isokinetic MVC shows a significant difference between limbs for the No Force Instruction condition (ANOVA *: P = 0.0002) and no significant difference for the Produce Equal Forces condition (ANOVA P = 0.2111). Error bars are standard error of the mean.

Our study is the first to show that the sense of effort can also explain the magnitude of force generation during dynamic movements of the lower limbs in subjects post-stroke. Subjects produced asymmetric foot reaction forces even though the resistance was set low enough such that the paretic limb had the capacity to produce half of the force required. When subjects were given no force instructions, normalizing lower limb forces to bilateral isokinetic MVC still revealed significant differences between limbs whereas the Produce Equal Forces condition did not. During the No Force Instruction condition, subjects most likely relied on their non-paretic limb more because they are used to their paretic limb being weaker and did not have any incentive to try to use that limb more. During the Produce Equal Forces condition, however, we actively encouraged subjects to try to use both lower limbs equally. When subjects attempted to produce equal forces, subjects' effort was divided between the two lower limbs equally and there were no significant differences between normalized forces. Therefore, for the Produce Equal Forces condition, subjects also relied more on their sense of effort, rather than proprioceptive feedback.

These results indicate that sense of effort is not only involved in static movements (i.e. isometric force matching tasks) but also during movement. Although the task involved in Experiment 2 was isotonic lower limb extensions, results likely can be extended to other movements that are functionally relevant for activities of daily living, such as standing up from a chair or climbing stairs. Indeed, a recent study examining level of muscle activation during human walking by subjects with stroke has related findings. Milot et al. (2006) found that the level of electromyography in lower limb muscles during walking were similar percentages of the isokinetic maximum voluntary contraction electromyography value for the paretic and non-paretic limbs. This suggests that the magnitude of the efferent signal to each individual muscle was similarly scaled to the maximum force output of that muscle (Milot et al. 2006). Considering both these previously published studies and our current results, it seems that the dominant factor in gauging foot reaction forces for static and dynamic movements in individuals with post-stroke hemiparesis is sense of effort rather than proprioceptive feedback.

During normal motor behavior, however, there are a host of sensory signals that are integrated to influence muscle activation. The primary sensor signals derive from Golgi Tendon Organs, muscle spindles and cutaneous receptors. Group Ib afferents within Golgi Tendon Organs are reliable sensors of local muscle tension. It was long believed that they only inhibited muscle activation as a protective mechanism, but they can monitor muscle tension over a wide range of force levels and can also provide autogenic excitation for positive force feedback (Pearson 1995; Pearson et al. 1998). Group Ia and II afferents within muscle spindles signal changes in muscle length and velocity. Studies show that even during static muscle contractions, as in Experiment 1, muscle spindles provide the central nervous system with afferent feedback (Gandevia 1996). Cutaneous mechanoreceptors, specifically those that respond to mechanical pressure, can also affect motor commands during movement. We are not arguing that these sensory signals are unimportant and irrelevant. On the contrary, the kinesthesic information provided by these sensory receptors can be critical to movement dynamics (Gandevia 1996). Our conclusion is that, compared to afferent feedback, sense of effort dominates in the determination of efferent signal magnitude.

There have been many studies that have examined how altered sensory input affects the level of force production in humans. Chronically deafferented subjects have difficulty generating constant level forces for long durations (Rothwell et al. 1982). If the individuals are distracted or devote less attention to the force generation task (e.g. holding a cup of coffee), the forces decrease without concerted effort. However, they can grade their central commands to produce different force levels (Rothwell et al. 1982; Sanes et al. 1985). These observations are in line with our findings that sense of effort is the dominant factor determining force production. Acutely partially deafferented subjects can also judge forces accurately and have the ability to grade force production (Gandevia and McCloskey 1978; Gandevia et al. 1990). These results also support our conclusions.

There has been data and speculation that does not seem to directly support our results. Takarada et al. (Takarada et al. 2006) recently observed an overestimation of forces in neurologically intact subjects undergoing a tourniquet-induced sensory alteration. It may be that the tourniquet methodology was not an ideal simulation of deafferentation without affecting efferent signals and/or muscle force capabilities. Sanes and Shadmehr (Sanes and Shadmehr 1995) studied a position matching protocol in patients with chronic large fiber sensory neuropathy and concluded that peripheral afferents contribute partially to determining efferent signal magnitude. The difference in position matching protocol versus force matching protocol may be critical to interpreting Sanes and Shadmehr results as it is known that motor control can be different during the two types of tasks (Mottram et al. 2005). It could be that in certain situations, the nervous system re-weights the importance of afferent sensory information versus sense of effort in the determination of the descending efferent signal.

Stroke patients in general have deficits in their sensory perception. It is typical for individuals to experience the loss of touch sensation and impaired proprioception (Carey et al. 1993; Carey 1995; Hunter and Crome 2002). It seems likely that these individuals would rely on all resources available to them to accurately control muscle activation. However, our findings that both isometric and isotonic force production is equal for both limbs when normalized to the bilateral maximum force generating capabilities of the limbs clearly points to feedforward central command (sense of effort) as the dominant factor in force production.

Our subjects did not seem to have updated their neural representation of their lower limb (i.e. internal model) to account for their weakness even though they sustained this weakness anywhere from 7–39 months previously. Subjects typically commented that using their paretic limb was harder, that it felt heavier, and that they don’t have a good idea of how much force they are producing in the limb. Previous studies involving individuals with post-stroke hemiparesis have also reported an increase in sensations of heaviness or effort when trying to move the paretic limb (Gandevia 1982; Rode et al. 1996). Figure 3 illustrates that subjects do not understand the extent of their weakness. For example, compared to the No Instruction condition, when Subject 1 was asked to produce equal forces in his lower limbs, he was able to generate more force in the paretic limb but not enough to match the force produced in his non-paretic limb. Subject 2 was more aware of the extent of his weakness and ended up overcompensating for his weakness by producing more force in his paretic limb than his non-paretic limb. His awareness was confirmed after the study in discussion with the experimenter. Without knowing the purpose of the experiment, he explained that he felt his paretic limb was so weak that he had to push even harder on that side to get what he believed to be an equivalent force output. Regardless of the strategy the subjects used, they still had very poor ability to produce a given force with their paretic limb.

The results of the current study have some limitations due to the subject population and task. Although we only analyzed data on 9 subjects, statistical analysis revealed clear significant differences as predicted by our hypotheses. We could not separate out the possibility of a false negative in either experiment, but post-hoc analyses indicate that the magnitude of the differences, if there is one, is small. In relation to the experimental tasks, during both experiments only one force level was tested. Previous force matching studies have included 2-3 target force levels (Carson et al. 2002; Bertrand et al. 2004; Simon and Ferris 2008), showing similar results for either all levels or the two highest target force levels. We chose to test subjects in a simplified task of lower limb extensions that requires no upper body stabilization. This allowed us to investigate foot reaction forces in a controlled manner rather than using a more functional task which would make it harder to control for confounding factors. Finally, the current study did not include recording and analysis of electromyography. A previous lower limb force matching study that did record electromyography in neurologically intact subjects did not have enough power to make strong conclusions relating muscle activity to lower limb forces (Simon and Ferris 2008). Given the higher intersubject variability in EMG in post-stroke subjects it seems doubtful that EMG would have provided any new information.

Regardless of these limitations, it is apparent that weakness is not the only problem that stroke rehabilitation should focus on. This study shows that post-stroke individuals also have an impaired awareness of their effort to force relationship that needs to be addressed. Physical therapists can use the information presented in this paper relating to sense of effort and limb force asymmetry to design alternative training for these patients. For example, one new type of therapy could involve lower limb extensions with symmetry-based resistance (Simon et al. 2007). With symmetry-based resistance, exercise resistance increases with increasing lower limb force asymmetry. This might provide patients with a means for recalibrating their effort to force relationship (Simon et al. 2007). Regardless of approach, stroke patients need to better understand how to use a stronger effort on their paretic side in order to compensate for their weakness.

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Chapter 5

Symmetry-Based Resistance as a Novel Means of Lower Limb Rehabilitation

Abstract

Robotic devices hold much promise for use as rehabilitation aids but their success depends on identifying effective strategies for controlling human-robot interaction forces. We developed a robotic device to test a novel method of controlling interaction forces with the intent of improving force symmetry in the limbs. Users perform lower limb extensions against a computer controlled resistive load. The control software increases resistance above baseline in proportion to lower limb force asymmetry (balance between left and right limb forces). As a preliminary trial to test the device and controller, we conducted two experiments on neurologically intact subjects. In Experiment 1, one group of subjects received symmetry-based resistance while performing lower limb extensions ($n = 10$). A control group performed the same movements with constant resistance ($n = 10$). The symmetry-based resistance group improved lower limb symmetry during training (ANOVA, $P < 0.05$), whereas the control subjects did not. In Experiment 2, subjects ($n = 10$) successfully used symmetry-based resistance to alter their lower limb force production towards a target asymmetry (ANOVA, $P < 0.05$). These studies suggest that symmetry-based

resistance may hold rehabilitation benefits after orthopedic or neurological injury. Specifically, performing strength training therapy with this controller may allow hemiparetic individuals to focus better on increasing strength and neuromuscular recruitment in their paretic limb while experiencing symmetric limb forces.

Introduction

Strength training is beneficial to rehabilitation after neurological or orthopaedic injury. This training can increase muscle strength in the affected limb(s) by increasing motor neuron recruitment and muscle size (Dodd et al. 2002; Jacobs and Nash 2004; Jan et al. 2004; Patten et al. 2004). When one limb is more affected than the other limb, an imbalance in limb forces can arise during functional tasks. One way that therapists have attempted to overcome this type of limb asymmetry is to provide patients with audio and/or visual feedback about muscle activation or limb force. Neurologically impaired individuals who are provided with visual force feedback while standing and performing upper limb tasks improve stance symmetry and decrease sway compared to subjects receiving similar therapy without feedback (Sackley and Lincoln 1997; Wong et al. 1997). Sit-to-stand training with audio feedback of paretic lower limb loading shows increased improvement toward symmetric body weight distributions over no feedback controls (Engardt et al. 1993). Although these results show improvements after training with feedback, they occur over relatively long training periods. Training sessions range between 45 to 60 minutes a day, 3 to 5 days a week, for 4 to 6 weeks (Engardt et al. 1993; Bourbonnais et al. 2002). An alternative type of therapy that reduces training time could speed patients' motor recovery and decrease therapy costs.

Robotic devices can yield functional benefits for patients when training task-specific exercises (Reinkensmeyer et al. 2004). The devices can impose novel force fields to shape motor output while completing a task. During a bilateral steering task, the force-cue mode implemented in the Driver's Simulation Environment for Arm Therapy (Driver's SEAT) uses resistance torques that allow steering motions to be produced only by the paretic upper limb (Johnson et al. 2005). With these force cues, hemiplegic subjects increased the productive use of their paretic upper limb over trials without force cues. Resistive force fields can also strengthen patients' muscles. Devices such as upper extremity manipulanda and lower extremity locomotor devices are showing promise, although to date the results are very joint specific (Hesse et al. 2001; Lum et al. 2002; Krebs et al. 2005). These results suggest that multiple types of robotic exercise machines will likely be necessary for rehabilitation (Krebs et al. 2005).

We built a lower limb robotic device that uses a novel control strategy for increasing force symmetry during bilateral lower limb extensions. The device features a motor to provide real-time control of resistance and a force platform to measure limb forces. Control software calculates the difference between the target and actual center of pressure location. This difference is multiplied by a gain and then added to a baseline resistance. In effect, the motor increases resistance in proportion to lower limb force asymmetry. Subjects training with the symmetry-based resistance perform the least effort against the device when they produce symmetric forces.

This study reports initial results from neurologically intact subjects using the device. In the first experiment, two groups of ten subjects performed bilateral lower limb extensions during a single testing session. One group received symmetry-based resistance and the other group received constant resistance. Both groups were asked to perform lower limb extensions as symmetrically as possible. We hypothesized that the symmetry-based resistance group would increase lower limb symmetry within the single testing session more than the control group as a result of the variable resistance. In the second experiment ten subjects attempted to produce an asymmetry of foot forces using symmetry-based resistance, again in a single testing session. We hypothesized that these subjects would learn the appropriate relative sense of effort in the two limbs to produce the target asymmetry. Some neurologically impaired subjects perceive symmetric force production as an asymmetry. Thus, testing neurologically-intact subjects as they learn to produce a force asymmetry may provide a good indication of the learning effects using the symmetry-based resistance controller.

Methods

Robotic Device

We modified a commercially available exercise machine (Plyo-Sled, Lifestyle Sports, Dunkirk, NY) (Figure 5.1). Subjects recline on a sled resting on low friction rollers and place their feet on a vertical footplate to perform bilateral

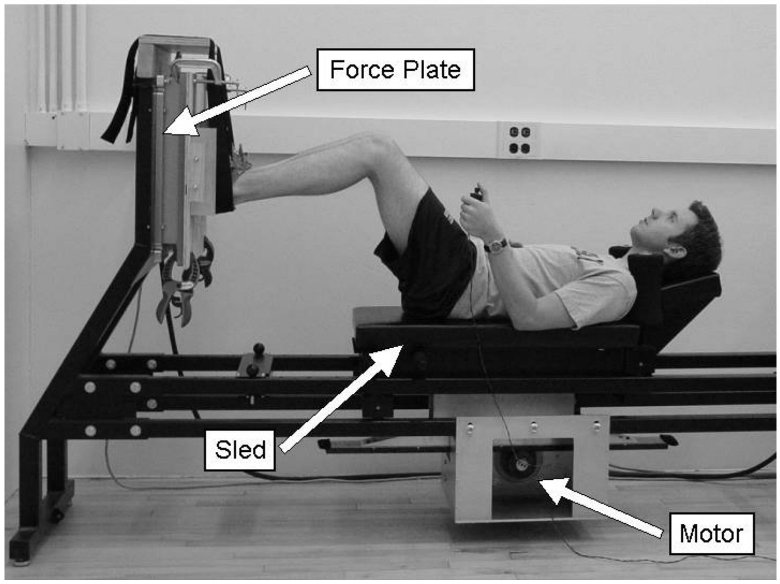

Figure 5.1 Lower limb robotic device. A force platform measured lower limb forces while a computer controlled motor adjusted resistance in real-time.

lower limb extensions. We added a computer controlled electrical motor (MT706C1-R1C1 Goldline XT Servomotor, Kollmorgen, Northampton, MA) to control resistance in real-time. A horizontal rack affixed to the sled was driven by a pinion on the motor to transform rotational motion of the motor to linear motion of the sled. We attached a force platform (Model OR6-7MA, AMTI, Watertown, MA) to the footplate to capture center of pressure during movement. From center of pressure calculations the controller determined the relative symmetry between right and left foot forces.

Real-time control of motor resistance was achieved with two desktop PCs in a host-target configuration with RT-Lab Solo software (Opal-RT Technologies, Quebec, Canada). The symmetry-based resistance controller adjusted resistance according to the location of the center of pressure detected by the force platform

(Figure 5.2A). The resistance, R, in percent body weight, was calculated according to the following equations:

$$R = K\left|COP - T\right| + B \tag{5.1}$$

$$K = \frac{S - B}{1.5\left|COP_{avg} - T\right|} \tag{5.2}$$

where COP is the instantaneous center of pressure low-pass filtered at 5 Hz, K is the controller gain, and T is the target symmetry (i.e. 50% for perfect symmetry). The symbol COP_{avg} is the center of pressure location averaged over the entire first set of extensions. The symbols B and S are the baseline and saturation resistance as a percentage of body weight. Equation 5.1 determines the motor resistance by multiplying the difference between the center of pressure and the target by a gain and adding a baseline resistance. As the center of pressure moves away from the target, motor resistance increases until saturation (Figure 5.2B). If foot forces were the same (i.e., subject's center of pressure remained directly between his/her feet), motor resistance remained at baseline. If foot forces were unequal (i.e., subject's center of pressure moved away from center towards one of the feet), the computer increased motor resistance above baseline. The resistance was proportional to the amount of asymmetry in the subject's foot forces thereby providing immediate information about force symmetry in the subject's lower limbs. Subjects could perform extensions with minimal resistance if they generated equal forces at their left and right feet.

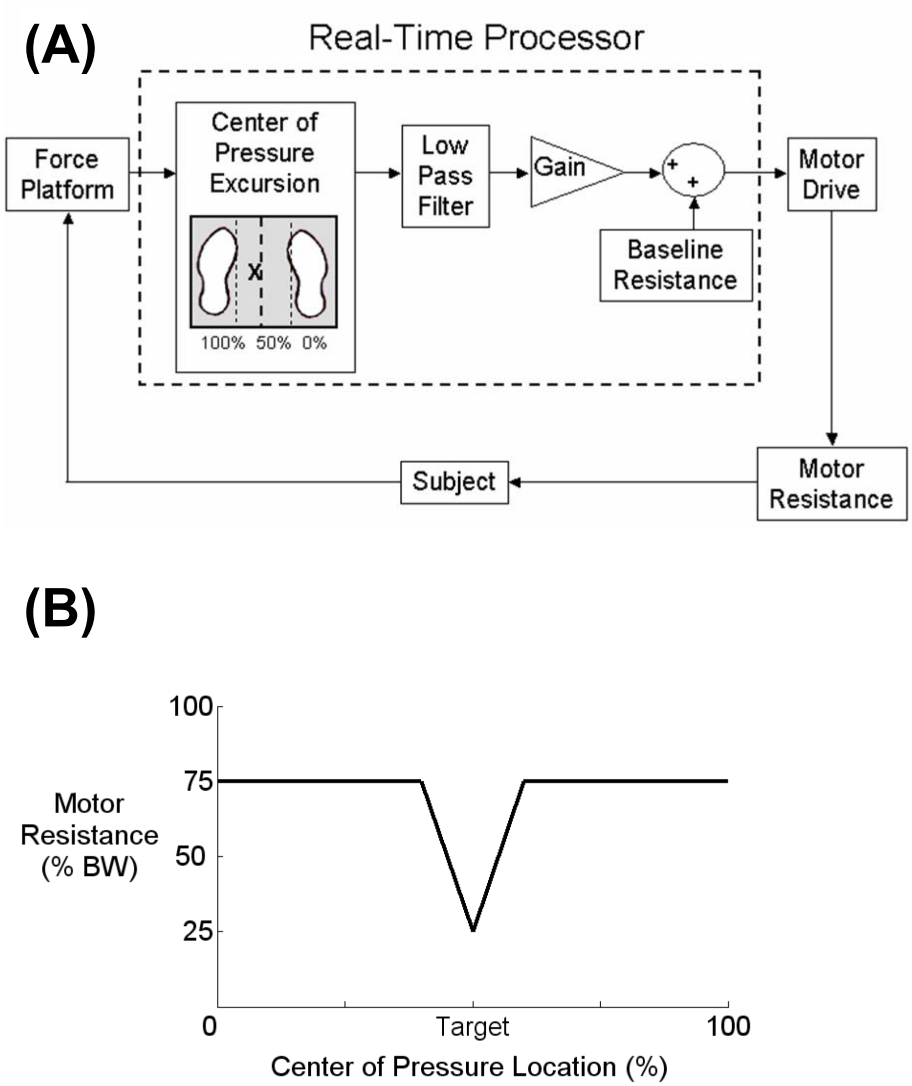

Figure 5.2 Symmetry-based resistance algorithm. A) Diagram of the symmetry-based resistance controller. A force platform recorded foot forces during bilateral lower limb extensions and sent data to a real-time processor. The real-time processor calculated center of pressure location in percent distance from the non-dominant foot (sample asymmetry of center of pressure location at 60% denoted by the X). The center of pressure excursion was calculated as the difference between the center of pressure location and the target. After low pass filtering, the signal was multiplied by the gain to produce the motor command. A baseline resistance was added to the signal before output to the motor drive. Subjects performed extensions with least effort if they generated the necessary lower limb forces to move their center of pressure to the target. B) Plot of motor resistance as a function of center of pressure location for the symmetry-based resistance controller. Motor resistance is at a minimum when the center of pressure location is at the target (i.e. 50% for perfect symmetry). As the center of pressure moves away from the target, the motor resistance increases until saturation at 75% body weight.

Subjects

Thirty neurologically-intact subjects gave written informed consent and participated in this study (14 male and 16 female; age: 26 ± 3.0 years, mean ± s.d.). The human subject review board at the University of Michigan Medical School approved the protocol.

<u>Experiment 1</u>

The purpose of Experiment 1 was to determine if subjects could become more symmetric in their lower limb force production with symmetry-based resistance. Twenty subjects were randomly placed in two groups. One group experienced the symmetry-based resistance and the other was a control group with constant resistance. All subjects performed five sets of twenty lower limb extensions with rest between sets. Subjects' foot placement had an inter-foot distance equal to their anterior superior iliac spine (ASIS) width. We tracked center of pressure location as a percentage of inter-foot distance with 0% being at the non-dominant foot center. The non-dominant foot was determined as the foot that produced the least amount of force during set one. We set the target for symmetry at 50% of inter-foot distance. Subjects extended to full knee extension and flexed to a knee angle of approximately 90 degrees, matching movement speed to a metronome set at 0.33 Hz.

(A) Experiment 1 Protocol

	Set 1	Set 2	Set 3	Set 4	Set 5
Symmetry-Based Resistance Group	25% BW	SBR	SBR	SBR	25% BW
Control Group	25% BW	43% BW	42% BW	43% BW	25% BW
No. of repetitions	20	20	20	20	20
Instructions	Symmetric	Symmetric	Symmetric	Symmetric	Symmetric

(B) Experiment 2 Protocol

	Set 1	Set 2	Set 3	Set 4	Set 5
Symmetry-Based Resistance Group	25% BW	SBR	SBR	SBR	25% BW
No. of repetitions	20	20	20	20	20
Instructions	Symmetric	Asymmetric	Asymmetric	Asymmetric	Asymmetric

Figure 5.3 Experimental protocols. All sets of extensions included 20 repetitions. A) The symmetry-based resistance group received constant resistance for sets 1 and 5. In sets 2 – 4 they received symmetry-based resistance (SBR) where the amount of resistance increased with asymmetric foot forces. The control group received constant resistance at varying percentages of their body weight (BW) for all sets. Instructions to subjects of both groups were to perform all sets of extensions symmetrically. B) Subjects received constant resistance for sets 1 and 5. In sets 2 through 4 they received symmetry-based resistance (SBR) where the amount of resistance increased as their center of pressure location moved away from the target force asymmetry. Instructions to subjects were to perform extensions of set 1 symmetrically, in sets 2 through 4 they were to learn the asymmetry in force production, and in set 5 they were asked to reproduce the asymmetry.

The symmetry-based resistance group performed the first set of lower limb extensions against a constant baseline resistance equal to 25% of their body weight (Figure 5.3A). During the second, third, and fourth sets, the symmetry-based resistance controller was turned on. Resistance increased in real-time above baseline in proportion to lower limb asymmetry. We set the saturation resistance equal to 75% body weight. We informed subjects that the resistance would vary based on their force symmetry and their goal was to perform extensions with increased symmetry and therefore decreased resistance. In the fifth set, we turned the symmetry-based resistance controller off and set the resistance to a constant 25% body weight. We included this set to assess subject performance without the controller.

The control group performed set one against a constant resistance equal to 25% body weight (Figure 5.3A). During the second, third, and fourth sets the resistance did not change with foot force asymmetry and was equal to the average resistances of the symmetry-based resistance group (43%, 42% and 43% body weight, respectively). We informed subjects of the new constant resistance levels. In the fifth set, we set the resistance to a constant 25% body weight to assess performance after training. As with the symmetry-based resistance group, we frequently verbally reminded subjects to perform extensions symmetrically.

Experiment 2

The purpose of Experiment 2 was to determine if neurologically intact subjects could learn an asymmetry of foot forces using the symmetry-based resistance controller. Ten subjects performed five sets of twenty lower limb extensions with rest between sets (Figure 5.3B). We changed the target in the symmetry-based resistance controller from 50% to 33%. During the second, third, and fourth sets when subjects received symmetry-based resistance, we informed subjects that they were to learn the asymmetry in force production by attempting to minimize device resistance. We did not explicitly inform subjects where the new target was, which foot had to produce more force, or how much more force that foot had to produce. We assessed subject performance without the controller in the fifth set by asking subjects to reproduce the asymmetry against a constant resistance of 25% body weight.

Data Collection and Analysis

For both experiments, we collected force and center of pressure readings using a force platform (Figure 5.1). We normalized center of pressure data to individual stance width to reduce intersubject variability. We identified extension cycle timing from motor encoder data. We also calculated the root mean square (RMS) center of pressure excursion to capture the variability. We normalized RMS center of pressure excursion to the average value of the first set to reduce intersubject variability. This resulted in a first set average value of 100% for all subjects. A decrease in this value represented a change in foot forces towards the target. We averaged center of pressure and RMS center of pressure excursion for the entire last ten repetitions within each set to eliminate possible high variability of initial repetitions.

For Experiment 1, we collected electromyography (EMG) data from all subjects in the symmetry-based resistance group to ensure that any changes in limb symmetry were not due to muscle fatigue. We recorded surface EMG (Model CP511, Astro-Med Inc., West Warwick, RI) from the left vastus lateralis using bipolar surface electrodes. The EMG amplifier had a bandwidth of 30 to

1000 Hz. We calculated the mean power frequency of EMG within each set by plotting the power spectral density and calculating which frequency corresponded to the mean value. As the vastus lateralis muscle fatigues, the power spectrum of EMG shifts towards lower frequencies (Arendt-Nielsen and Mills 1988). Due to equipment malfunction, we analyzed EMG data for only seven of the ten subjects.

In Experiment 1, we used a repeated measure ANOVA (subject by group by set, with subject nested within group) to test for differences in average center of pressure location and normalized RMS center of pressure excursion (JMP IN software, SAS Institute, Inc., Cary, NC). We performed a repeated measure ANOVA (subject by set) for the symmetry-based resistance group to test for differences in EMG mean power frequency. When the ANOVA indicated significant differences ($P < 0.05$), we used a Tukey-Kramer HSD post-hoc test to determine differences between sets ($P < 0.05$).

In Experiment 2, we used a repeated measure ANOVA (subject by set) to test for differences in average center of pressure location and normalized RMS center of pressure excursion. As in Experiment 1, we then used a Tukey-Kramer HSD post-hoc test to determine differences between sets ($P < 0.05$).

Results

Experiment 1

Subjects in the symmetry-based resistance group improved force symmetry as measured by average center of pressure location while control

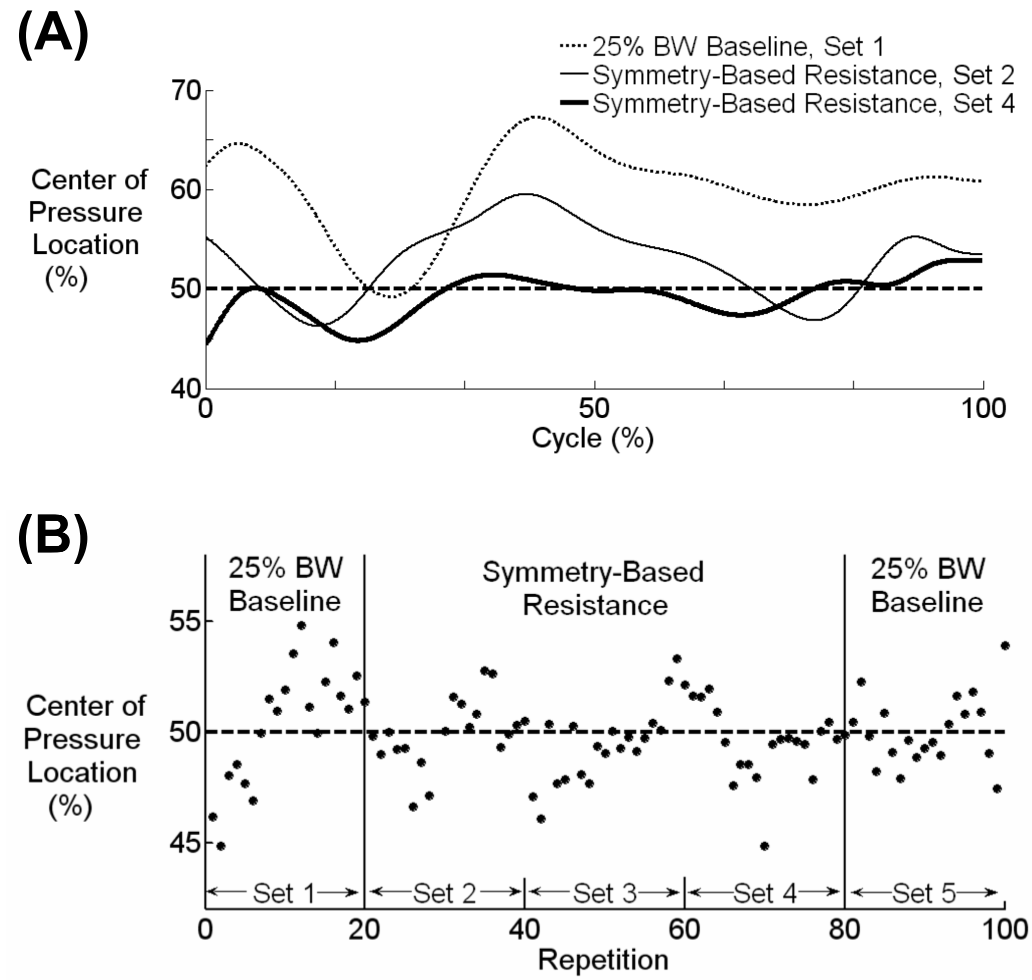

Figure 5.4 Experiment 1: Center of pressure location data for a typical subject. A) Plot of center of pressure location as a function of percent of lower limb extension for one subject throughout three repetitions. Lower limb flexion is the first 50% of the cycle and extension is the last 50% of the cycle. Data represents center of pressure location during the last repetition of set 1 against 25% body weight resistance (dotted line), first repetition of set 2 with the symmetry-based controller turned on (thin solid line), and last repetition of set 4 with the symmetry-based controller (thick solid line). The subject's center of pressure location moved closer to the target of 50% symmetry by the end of set 4. B) Average center of pressure location data for a typical subject with the symmetry-based resistance controller in Experiment 1. The dashed line represents the target for symmetry of 50%. This subject was better at producing symmetric forces about the target by set four (indicated by reduced scatter of set four compared to set one).

subjects did not (ANOVA, $P < 0.001$). Figure 5.4 shows example data from one subject in the symmetry-based resistance group. On average, the symmetry-based resistance group had center of pressure locations closer to 50% for sets three and four than for set one (THSD, $P < 0.05$) (Figure 5.5A). The average center of pressure location for these subjects was 52.5% ± 0.73% (mean ±s.e.m.) for set one and decreased to 50.2% ± 0.63% during set four. The control group did not improve with training (THSD, $P < 0.05$), perhaps due to lack of concentration. Comparing the symmetry-based resistance and control groups showed no significant difference of average center of pressure location between groups during set one (THSD, $P > 0.05$). By sets three and four, the symmetry-based resistance group was significantly closer to 50% than the control group (THSD, $P < 0.05$) (Figure 5.5A). During the last set, however, there was no significant difference between groups (THSD, $P > 0.05$).

Center of pressure excursion demonstrated similar trends as average center of pressure (Figure 5.5B). We collected this measure to further describe symmetry levels by capturing the variability in the center of pressure. In sets three and four, the symmetry-based resistance group significantly reduced their center of pressure excursion from set one (THSD, $P < 0.05$). The control group did not improve with training (THSD, $P > 0.05$). During set five, the center of pressure excursion for the control group significantly increased compared to set one (THSD, $P < 0.05$). Overall, there was a significant difference between the two groups during sets three, four, and five (THSD, $P < 0.05$).

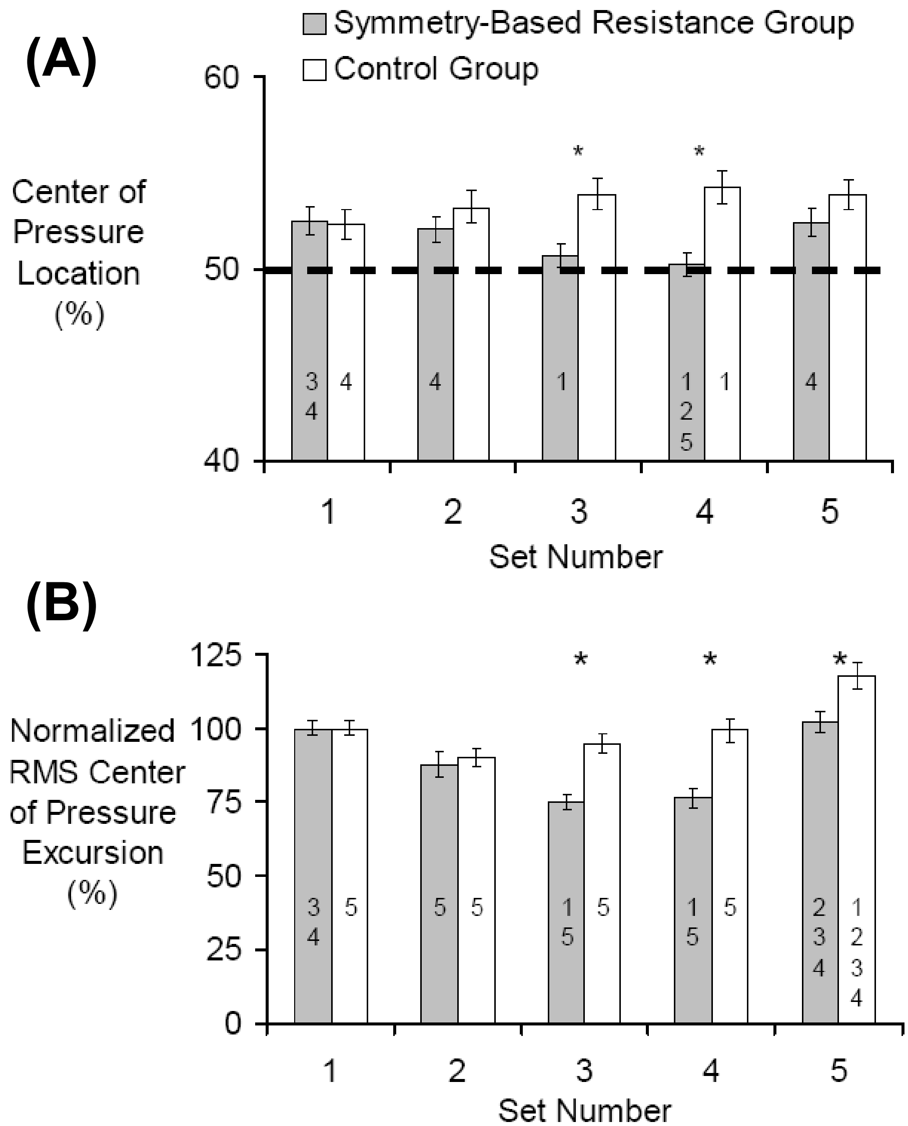

Figure 5.5 Experiment 1: Averaged center of pressure location and excursion for all subjects. Grey columns represent the symmetry-based resistance group and white columns represent the control group. Numbers within each bar indicate which sets are significantly different from the current set (THSD, $P < 0.05$). Error bars are standard error of the mean. A) Mean center of pressure location significantly decreased in the symmetry-based resistance group (THSD, $P < 0.05$). In contrast, the control group did not improve in symmetry. In sets 3 and 4, the symmetry-based resistance group was significantly better at producing symmetric forces than the control group (THSD, *: $P < 0.05$). B) Normalized RMS center of pressure excursion showed results similar to the center of pressure location with one addition. The symmetry-based resistance group was significantly better at producing symmetric forces than the control group in sets 3-5 (THSD, *: $P < 0.05$) rather than just sets 3-4.

Electromyography results from the vastus lateralis muscle of subjects in the symmetry-based resistance group showed no significant change in EMG mean frequency (ANOVA, $P > 0.05$). These results indicate that these subjects were not fatigued by the end of training. EMG mean frequencies for sets one to five were 80.6 Hz ± 4.0 Hz, 78.3 Hz ± 4.5 Hz, 79.7 Hz ± 3.8 Hz, 81.4 Hz ± 4.0 Hz, and 81.1 Hz ± 4.0 Hz, respectively.

<u>Experiment 2</u>

With the symmetry-based resistance controller on, subjects shifted their average center of pressure location towards the target of 33% (ANOVA, $P < 0.001$). Figure 5.6 shows data of one subject learning the asymmetry. The trend

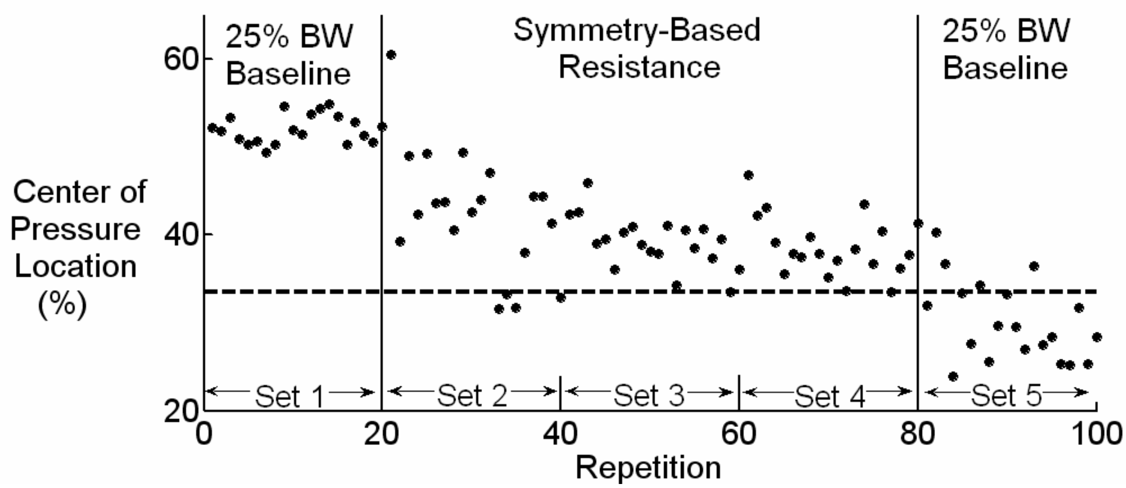

Figure 5.6 Experiment 2: Center of pressure location data for a typical subject. The symmetry-based resistance controller was active during sets 2 through 4. The dashed line represents the target for asymmetry of 33%. With training, the subject was able to produce asymmetric forces near the target. When asked to reproduce the asymmetry during set five, the subject showed carryover of the training.

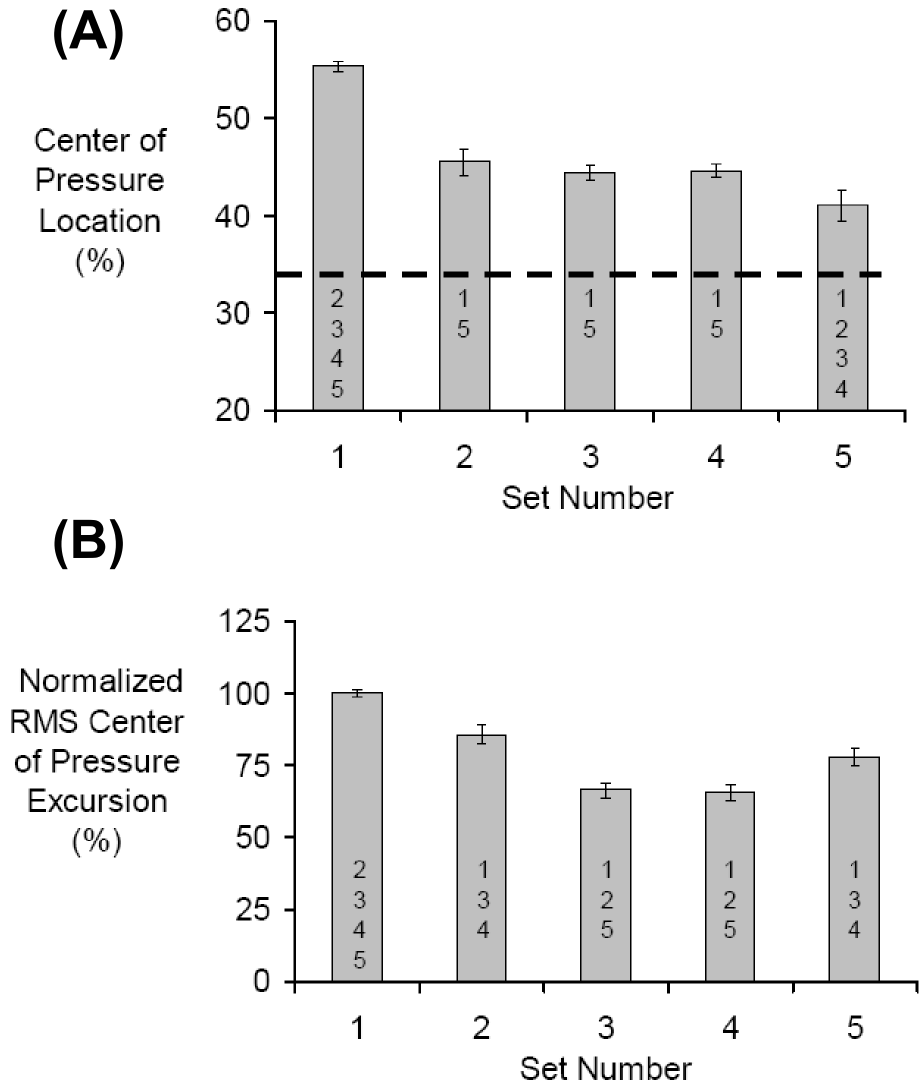

Figure 5.7 Experiment 2: Averaged center of pressure location and excursion for all subjects. During sets 2 through 4, all subjects received symmetry-based resistance about the targeted asymmetry of 33%. Numbers within each bar indicate which sets are significantly different from the current set (THSD, $P < 0.05$). Error bars are standard error of the mean. A) Mean center of pressure location shows a significant decrease towards the asymmetry with training (THSD, $P < 0.05$). In set 5, subjects showed carryover of the training and were able to reproduce the asymmetry without the symmetry-based resistance controller. B) Normalized RMS center of pressure excursion decreased in sets 2, 3, 4, and 5 from initial values in set 1 (THSD, $P < 0.05$).

towards the target is clearly evident. For all subjects, the average center of pressure location in the first set was 55.3% ± 0.5% (Figure 5.7A). The second, third, and fourth sets decreased significantly from set one towards the target (THSD, $P < 0.05$) and by set four the average center of pressure location was 44.6% ± 0.7%. In set five when the symmetry-based resistance controller was turned off and subjects were asked to reproduce the asymmetry, the average center of pressure location was 41.1% ± 1.6%. This value was significantly lower than that of set one (THSD, $P < 0.05$), demonstrating a carryover of asymmetry.

Center of pressure excursion (as calculated from the target asymmetry) also decreased with training (Figure 5.7B). With the symmetry-based resistance controller turned on, this value decreased during sets two, three, and four (THSD, $P < 0.05$). The normalized RMS center of pressure excursion for set five was significantly less than set one (THSD, $P < 0.05$), showing a carryover of training.

Discussion

Our results show that neurologically intact subjects training with the symmetry-based resistance controller shifted their center of pressure location towards the targets. In Experiment 1, the symmetry-based resistance group increased lower limb symmetry within the single testing session. This increase in symmetry, however, was not maintained when the symmetry-based resistance controller was turned off. In Experiment 2, subjects learned the appropriate relative sense of effort in the two limbs to produce the target asymmetry. When subjects were asked to reproduce the asymmetry, they did show carryover of training. Subjects altered lower limb force production towards the asymmetry without the symmetry-based resistance controller.

One explanation for why the symmetry-based resistance controller was effective in the neurologically intact subjects is the principle of least effort. The principle states that while performing a task, humans prefer movements that require the least amount of physical energy to achieve a goal (Almasbakk et al. 2000). Symmetry-based resistance directs subjects into altering limb symmetry towards the target by this principle. Subjects performed extensions against minimal resistance and therefore least effort when they increased lower limb symmetry. Symmetry-based resistance may have an advantage over audio and/or visual feedback because proprioceptive mapping to muscle recruitment is much more direct than audio/visual sensory mapping to muscle recruitment. Motor neuron activation and muscle forces are encoded at the spinal cord level (Bosco and Poppele 2001a; Bizzi et al. 2002), resulting in a more natural proprioceptive feedback loop for symmetry-based resistance. The rate of motor learning may be faster for symmetry-based resistance than for audio and visual feedback techniques.

In all likelihood, Experiment 1 did not demonstrate carryover for the symmetry-based resistance group because of the relatively small changes in symmetry required to match the target. All subjects exhibited symmetry levels close to the target in set one. The symmetry-based resistance controller was able to increase symmetry slightly, but the resolution of the training effect was not great since the change in center of pressure location was only 2% of the distance between the feet. In Experiment 2, the asymmetry target was much further away from subjects' initial symmetry levels. The subjects made a change in center of pressure location of 10% of the distance between the feet. The resolution for the second experiment was better because of the magnitude of the targeted change.

Neurologically impaired individuals may benefit from symmetry-based resistance therapy. Subjects in the second experiment demonstrated carryover to what they perceived as an asymmetry. Individuals with hemiparesis sense symmetry in force development as a perceived asymmetry and the magnitude of targeted change would likely be large. Although the principle of least effort may not hold for neurologically impaired users, practice with symmetry-based resistance may allow them to gain a better sense of relative effort for comparable forces in their paretic and non-paretic limbs (Rode et al. 1996). This could enable them to produce symmetric forces in other functional movements when they have a need (e.g. sit-to-stand transition). In addition, exercise with symmetry-based resistance may enhance recruitment of the paretic limb during therapy and lead to greater strength gains than traditional strength training with a constant resistance. Further testing on neurological populations is warranted to test these hypotheses.

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Chapter 6

Preliminary Trial of Lower Limb Training with Symmetry-Based Resistance in Individuals with Post-Stroke Hemiparesis

Abstract

The purpose of this study was to test a new control strategy for robotic rehabilitation of individuals with post-stroke hemiparesis. Symmetry-based resistance increases resistance when limb forces become more asymmetric during bilateral exercise. The underlying rationales are that it will guide patients to use their paretic limb more during therapy and also teach them how to more accurately gauge force production in their paretic limb by having an ongoing comparison to the non-paretic limb. During a one day training session, seven subjects with post-stroke hemiparesis performed lower limb extensions in symmetry-based resistance mode on a robotic exercise machine. Subjects improved lower limb symmetry from initial values of 28.6% ± 3.9% against a constant resistance pre-test to 36.2% ± 4.3% during the last set of symmetry-based resistance training (ANOVA, $P=0.03$). Subjects did not maintain the improved lower limb symmetry during the post-test against constant resistance (symmetry values were 33.2% ± 5.4%, $P>0.05$ for pre- and post-test comparison). Two subjects that showed the greatest improvements in symmetry performed longer term training. Those results suggest some patients can

demonstrate long lasting benefits with symmetry-based resistance training.

Introduction

Stroke is the leading cause of serious, long-term disability in the United States with 5.8 million patients with stroke (Rosamond et al. 2007). More than half of these individuals experience moderate to severe impairments that limit their mobility and functionality. These impairments include weakness (Patten et al. 2004), impaired coordination (Kautz and Brown 1998) and proprioception (Carey 1995).

Another neurological deficit of patients with post-stroke hemiparesis that is less understood is impaired force scaling abilities. When post-stroke patients are asked to produce a force in their paretic limbs equal to the force in their non-paretic limbs, they often overestimate the force produced in their paretic upper limbs (Bertrand et al. 2004; Mercier et al. 2004) and paretic lower limbs (Simon et al. 2008). A disparity exists between the force level patients think they are producing and the force level they are actually producing. Such force mismatches in the lower limbs can affect patients' ability to be mobile, stand from a seated position, and recover from falls. For example, if a patient with stroke needed to take a step to prevent a fall, sending too low of an efferent command to the lower limb muscles would lead to inadequate extension torques about the joints and the patient could fall.

Strength training and aerobic exercise can help post-stroke patients regain their strength and (Teixeira-Salmela et al. 1999; Weiss et al. 2000; Gordon et al.

2004b). Patients usually exercise two to three days per week and can increase motor recruitment of both the paretic and non-paretic limbs without increasing spasticity (Badics et al. 2002; Morris et al. 2004). Increasing muscle strength leads to concurrent increases in functional abilities such as sit-to-stand performance, gait speed, and dynamic balance (Weiss et al. 2000; Monger et al. 2002; Mercier et al. 2004).

Therapy may also include audio and/or visual biofeedback training about patients' muscle activation or limb forces to improve functional ability. Visual biofeedback can improve stance symmetry and decrease sway during standing compared to controls receiving similar therapy without feedback (Sackley and Lincoln 1997; Wong et al. 1997). These improvements occur over relatively long training periods of up to 60 minutes a day, 3 to 5 days a week, for 4 to 6 weeks (Engardt et al. 1993; Bourbonnais et al. 2002). However, recent systematic reviews of the literature conclude that audio/visual biofeedback of muscle activation and/or limb forces is not very effective for motor recovery after stroke (Barclay-Goddard et al. 2004; Woodford and Price 2007). One potential reason for this is that audio/visual biofeedback requires increased cognitive involvement of cortical brain regions that are not directly involved with the motor task. In contrast, proprioceptive feedback is encoded at the spinal cord level along with motor neuron activation patterns (Bosco and Poppele 2001; Bizzi et al. 2002). Thus, proprioceptive feedback loops are considerably shorter than audio or visual feedback loops. Patients may benefit more from an alternative type of therapy that acts to influence proprioceptive feedback given its proximity to the basic neural control architecture.

Symmetry-based resistance has the potential to provide mechanical biofeedback to patients without requiring involvement from audio/visual cortical centers. With symmetry-based resistance, task resistance increases with the magnitude of the limb force asymmetry during bilateral exercise. This control mode could benefit the patient by evoking enhanced muscle activation in the paretic limb during exercise. In addition, it could help patients calibrate their force production in their paretic limb with the force production in their non-paretic limb. Applied to lower limb extensions, individuals exercise with the goal of producing equal lower limb forces during movement. If they exercise with equal forces, resistance is at a baseline value and subjects perform the minimal mechanical work. If their lower limb forces become asymmetric, a real-time controller increases resistance causing subjects to perform more mechanical work. This novel control strategy has previously been tested on neurologically intact individuals that demonstrate a slight but typical asymmetry during lower limb exercise (Simon et al. 2007). Subjects altered their lower limb forces towards a target symmetry within a single training session (Simon et al. 2007).

The goal of this study was to perform a preliminary trial of lower limb exercise with symmetry-based resistance in individuals with post-stroke hemiparesis. In the current study, symmetry-based resistance training was tested as a means of addressing subjects' impaired force scaling abilities. Individuals post-stroke could use the mechanical feedback received during training to reduce the mismatch between the forces they think they are producing and the forces they are actually producing. We hypothesized that lower limb exercise with symmetry-based resistance would result in more symmetric lower limb forces when subjects performed extensions against a constant resistance. This study primarily reports results from individuals with post-stroke hemiparesis after a one day training session of lower limb extensions with symmetry-based resistance. We also performed some longer term training with two of the subjects that demonstrated the largest improvements in symmetry.

Methods

Subjects

We recruited 10 individuals (7 females and 3 males) with stroke-induced hemiparesis (age: 49 ± 17 years, mean ± S.D.M.). A physiatrist at the University of Michigan evaluated each subject for inclusion criteria and participation in the study. Inclusion criteria consisted of 1) at least six months post-onset of a single neurologic insults that included ischemic or hemorrhagic type strokes (verified through MRI or CT scan data from patients' medical records), 2) between the ages of 18 and 85, 3) free of any musculoskeletal injuries or deformities, 4) presented with no spastic hypertonia in the lower limbs, and 5) adequately able to comprehend our instructions. All subjects gave written informed consent approved by the Institutional Review Board for Human Subject Research at the University of Michigan Medical School. A physical therapist evaluated subjects' lower extremity physical performance by through use of the lower limb and balance portions of the Fugl-Meyer Clinical Assessment (Table 6.1). Based on

Table 6.1. Subject characteristics.

Subject	Age (yrs)	Gender	Paretic Side	Postonset (mos)	Lesion Location	Type of Stroke	Fugl - Meyer* Lower Extremity	Balance
1	73	F	L	156	Right hemisphere	Ischemic	22	8
2	52	F	R	11	Left basal ganglia	Hemorrhagic	31	9
3	22	M	R	37	Left thalamus extending into the pons	Hemorrhagic	21	3
4	69	F	R	12	Left hemisphere	Ischemic	23	9
5^	54	M	L	29	Right parietal lobe	Ischemic	23	10
6†	47	F	R	72	Cerebellum	PICA-AVM hemorrhagic	34	13
7†	53	M	R	28	Cerebellum	AVM-hemorrhagic	30	9
8^	22	F	L	37	Right temporal lobe	Ischemic	29	11
9	47	F	L	24	R-MCA -internal capsule/basal ganglia	Hemorrhagic	34	14
10†	54	F	L	42	Right basal ganglia	Hemorrhagic	32	12

Abbreviations: Sex (F: female, M: male), Paretic Side (L: left, R: right)

*Fugl-Meyer Clinical Assessment: Lower extremity motor score (0-34), Balance motor score (0-14)

^Subject participated in four week training protocol

†Subject's data was excluded from analysis because lower limb symmetry was greater than 45%

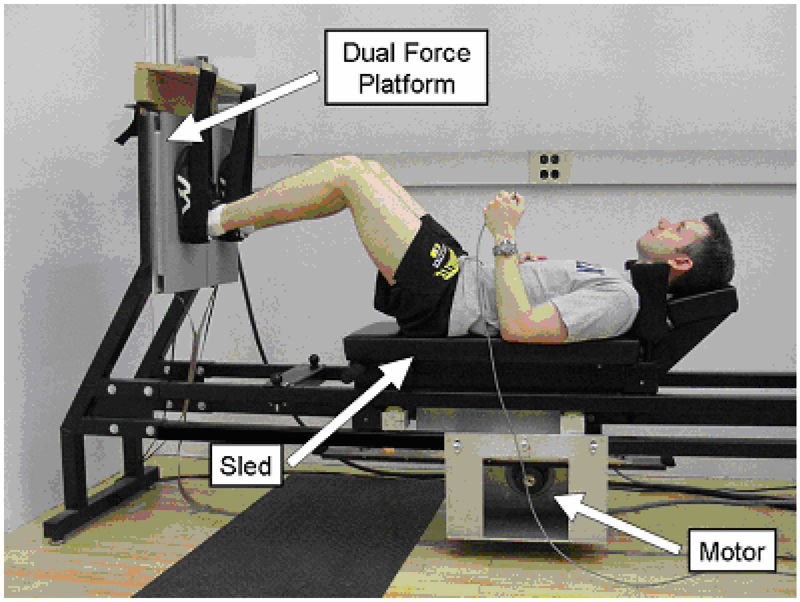

Figure 6.1. Lower limb robotic exercise machine. A dual force platform measured lower limb forces while a computer controlled motor adjusted resistance in real-time.

comments from subjects, we noted various subject sensory deficits including reduced cutaneous sensation and impaired force perception. No subjects reported impaired sense of limb motion and position.

Experimental Design

Subjects exercised on a robotic exercise machine built in the University of Michigan's Human Neuromechanics Laboratory (Figure 6.1) (Simon et al. 2007). The machine included a dual force plate (Model Dual Accu-Gait, AMTI, Watertown, MA) to capture individual foot forces during exercise.

Maximum Strength Testing

First we assessed subjects' isokinetic maximum strength during lower limb extensions on the exercise machine in isokinetic mode. In this mode, the computer controlled resistance so movement velocity remained constant. We instructed subjects to push as hard as they could only during the extension phase and relax during the flexion phase. Subjects performed two trials each of right limb only, left limb only, and bilateral maximum voluntary contraction (MVC) trials. We randomized the trial order and verbally encouraged subjects to push as hard as they could throughout each contraction. Subjects rested three minutes or more between each MVC trial.

Lower Limb Extensions

Subjects performed one set of ten bilateral lower limb extensions on the robotic exercise machine in isotonic mode pre- and post-training. In isotonic mode, the resistance for continuous lower limb extensions remained constant and was equal to 60% of the paretic limb bilateral MVC force. We instructed and frequently verbally reminded subjects to try to produce equal forces throughout the movement. Since this was a bilateral task, if subjects were able to produce equal forces in their limbs they would have only needed to produce force equal to 30% of the paretic limb bilateral MVC force in each limb (i.e. a total resistance of 60% was equal to 30% force in each limb). We instructed subjects to extend their lower limbs completely (not locking out their knees), flex to a knee/hip angle of 90 degrees, and match their movement speed to a metronome set to 0.33 Hz.

In between the pre- and post- test, subjects performed lower limb extensions on the exercise machine in symmetry-based resistance mode. During exercise with symmetry-based resistance, resistance increased when lower limb forces became asymmetric. Therefore subjects performed the least amount of work when their lower limb forces were symmetric. Movement timing and range of motion were the same as the pre- and post-test trials.

The control algorithm used for symmetry-based resistance determined resistance in real-time based on individual's instantaneous lower limb symmetry (Figure 6.2). Lower limb symmetry was calculated according to Equation 6.1.

$$Sym_i = \frac{F_{Paretic}}{F_{Paretic} + F_{Non-paretic}} \times 100\% \tag{6.1}$$

The resulting signal ranged from 0% to 100% with 50% representing perfect symmetry in lower limb forces. In symmetry-based resistance mode, resistance followed the shape of standard normal distribution curve reflected over the horizontal axis (Figure 6.3). The resistance, R, in percent maximum force ability of the paretic limb, was calculated according to Equations 6.2 and 6.3.

$$K = \frac{S - B}{\sqrt{0.32\pi}} \tag{6.2}$$

$$R = -K \times exp\left[-\frac{4.5 \times (50 - Sym_i)^2}{(50 - Sym_{RMS})^2}\right] + S \tag{6.3}$$

where K was the controller gain. B and S were baseline and saturation resistances set to 60% and 100% of the bilateral maximum force ability of the paretic limb, respectively. This limit was set to ensure that subjects had the

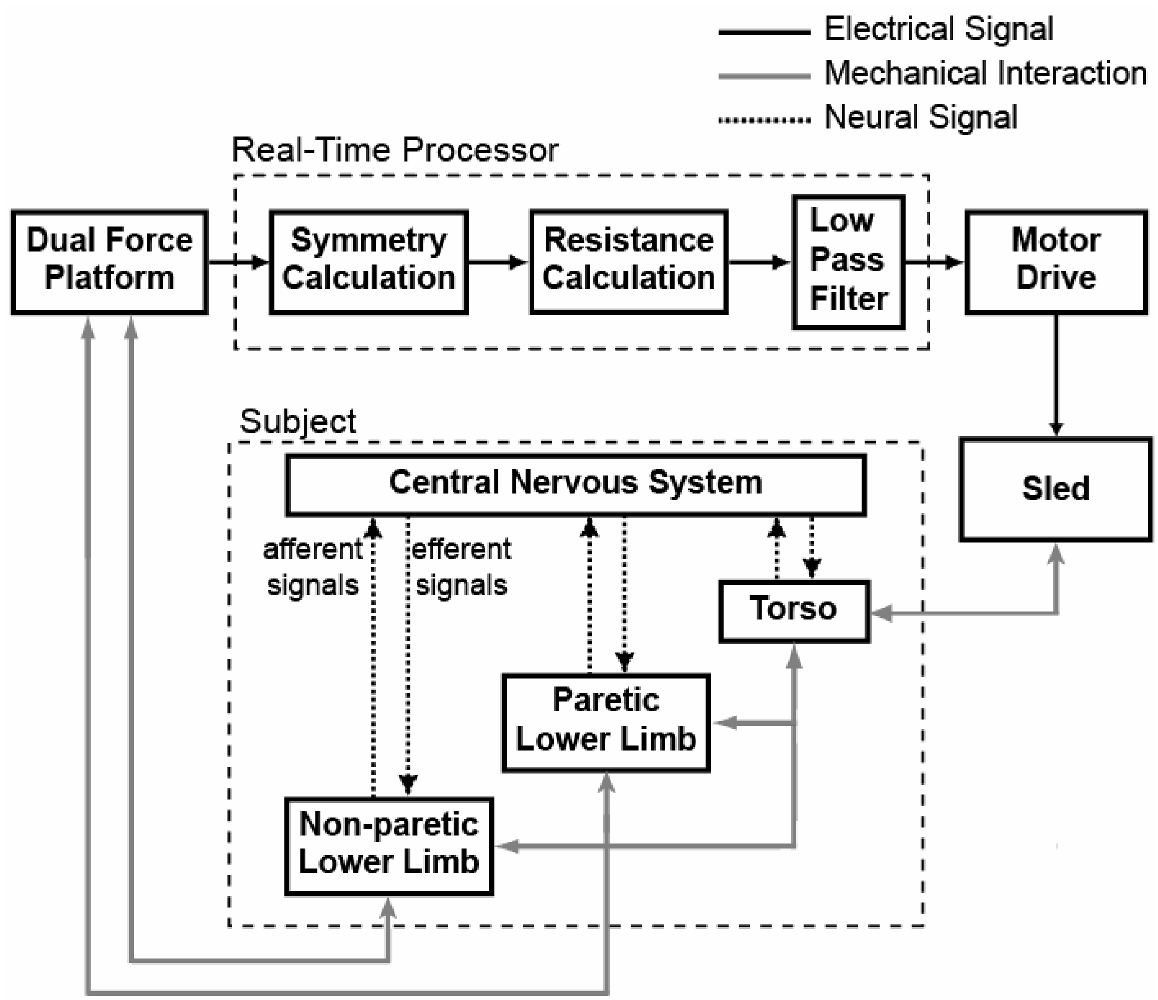

Figure 6.2. Symmetry-based resistance control algorithm. A dual force platform recorded individual limb forces during bilateral lower limb extensions and sent data to a real-time processor. The processor calculated lower limb symmetry and motor resistance based on individual limb force data. The motor command signal was low pass filtered and output to the motor drive. In real-time the motor drive commanded the motor to produce the appropriate resistance. The subject sensed resistance through afferent signals and output motor efferent signals.

capability to produce equivalent forces in their paretic and non-paretic limb. Sym_{RMS} was the root mean squared symmetry value measured for each subject during the pre-test and Sym_i was the instantaneous lower limb symmetry calculated in real-time from Equation 1. After the real-time controller calculated

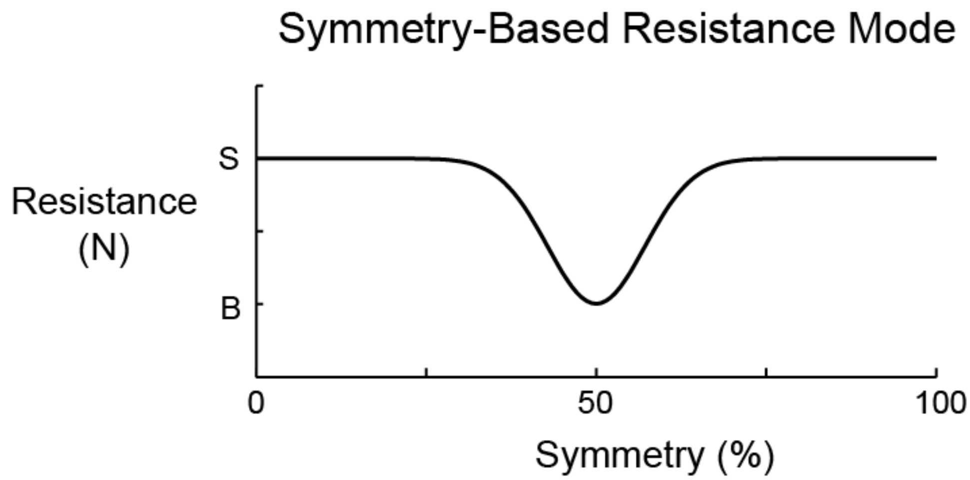

Figure 6.3. Motor resistance vs. lower limb symmetry for symmetry-based resistance mode. In symmetry-based resistance, motor resistance (R) was set to a minimum baseline value (B) when lower limb forces were equal (i.e. symmetry value of 50%). As limb forces became more asymmetric, the motor resistance increased until saturation (S).

load the signal was passed through a 2^{nd} order low pass Butterworth filter (1 Hz cutoff). The signal was then sent to the motor drive. The overall result of Equations 6.2 and 6.3 was that resistance was at a minimum with perfect lower limb force symmetry and increased to saturation as lower limb forces became asymmetric (Figure 6.3).

We allowed subjects to explore what symmetry-based resistance feels like by instructing them to produce more force or less force with their non-paretic and paretic limbs and experience the resistance feedback. The exploration lasted for two minutes and subjects were not under the constraints of movement timing or range of motion described previously. Subjects then performed four sets of ten repetitions of lower limb extensions with the symmetry-based resistance controller on. During all trials we frequently verbally reminded subjects to produce equal forces and to try to exercise against the lowest resistance. We allowed subjects to rest between sets for three minutes or longer if necessary.

4 Week Training Protocol

In order to investigate the retention affects of exercise with symmetry-based resistance, subjects who showed greater than a 30% improvement in pre- to post-test lower limb symmetry values returned to the laboratory for further training. Two of the ten subjects showed this trend and returned to the laboratory for one day a week for three additional weeks of training (four weeks total). During day one and four the protocol was the same as described above. During day two and three subjects only performed the lower limb extension protocol.

Data Acquisition and Analysis

We recorded dual force plate data sampled at 1000 Hz throughout all trials on the exercise device (Figure 6.1). Non-paretic and paretic limb MVC force was determined as the maximum force measured during the two trials (Jones and Hunter 1983; Proske et al. 2004). We calculated normal force (force vector in the direction of movement), total resultant force (sum of the normal force vector combined with shear force vectors), and total resultant force direction (0 degrees represented the normal direction). During lower limb extensions, we identified cycle timing from motor encoder data and averaged individual foot force data only across the extension phase of each cycle. We calculated root mean square

(RMS) symmetry during the extension phase to capture the variability. As this value approached 50%, it represented a change in foot forces towards perfect symmetry (i.e. producing equivalent forces in both the non-paretic and paretic lower limbs). We averaged individual foot forces and RMS symmetry for the last five repetitions within each set to eliminate possible high variability of initial repetitions. Subjects were excluded from the study if their lower limb forces during the pre-test of the lower limb extensions resulted in greater than 45% symmetry as these subjects did not properly represent the stroke population with hemiparesis. Three out of the ten subjects were excluded from the analysis for this reason.

For the lower limb extension training with symmetry-based resistance we performed a repeated measures ANOVA limb by set to test for significant differences in lower limb forces. We performed a repeated measures ANOVA by set to test for differences in RMS symmetry values. When the ANOVAs indicated significance ($P < 0.05$), we used Tukey-Kramer Honestly Significant Difference (THSD) post-hoc tests ($P < 0.05$). Post-hoc power analyses were carried out where appropriate.

Results

Lower Limb Extensions

During the pre-test when individuals with post-stroke hemiparesis attempted to generate equal lower limb forces, they produced significantly different limb forces (ANOVA $P < 0.001$) (Figure 6.4). The paretic limb produced significantly less normal force during exercise. When subjects performed lower limb extensions with symmetry-based resistance, there was no significant increase in normal force produced by the paretic limb (THSD P > 0.05). The average amount of resistance subjects exercised against increased from 474 N ± 102 N (mean ± s.e.m) during pre- and post-training to 693 N ± 71 N during exercise with symmetry-based resistance (Sets 1-4). Comparing the average normal limb force pre- to post-training within the one day session, there were no significant differences for both non-paretic and paretic limbs (THSD P > 0.05 for

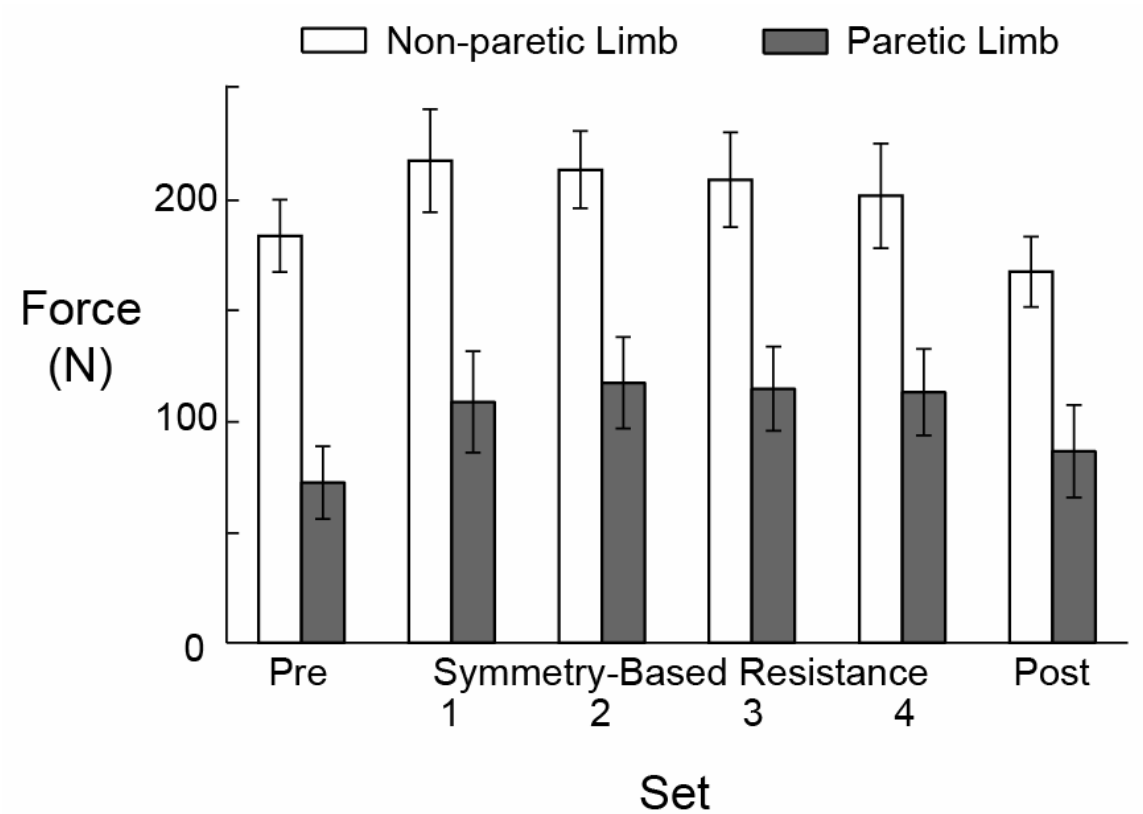

Figure 6.4. Average forces during lower limb extensions for all subjects during the one day training session. White columns represent non-paretic limb forces and grey columns represent paretic limb forces. Error bars are standard error of the mean. The non-paretic limb generated significantly more force than the paretic limb during the pre- and post-test as well as during symmetry-based resistance training (ANOVA, P < 0.001).

both limbs). Further force analysis revealed that for the normal force in the non-paretic and paretic limbs accounted for greater than 96% and 95%, respectively, of the total resultant force during all lower limb extensions. Results comparing total resultant force magnitude during the pre-test, training, and post-test showed similar trends as the normal force magnitude reported.

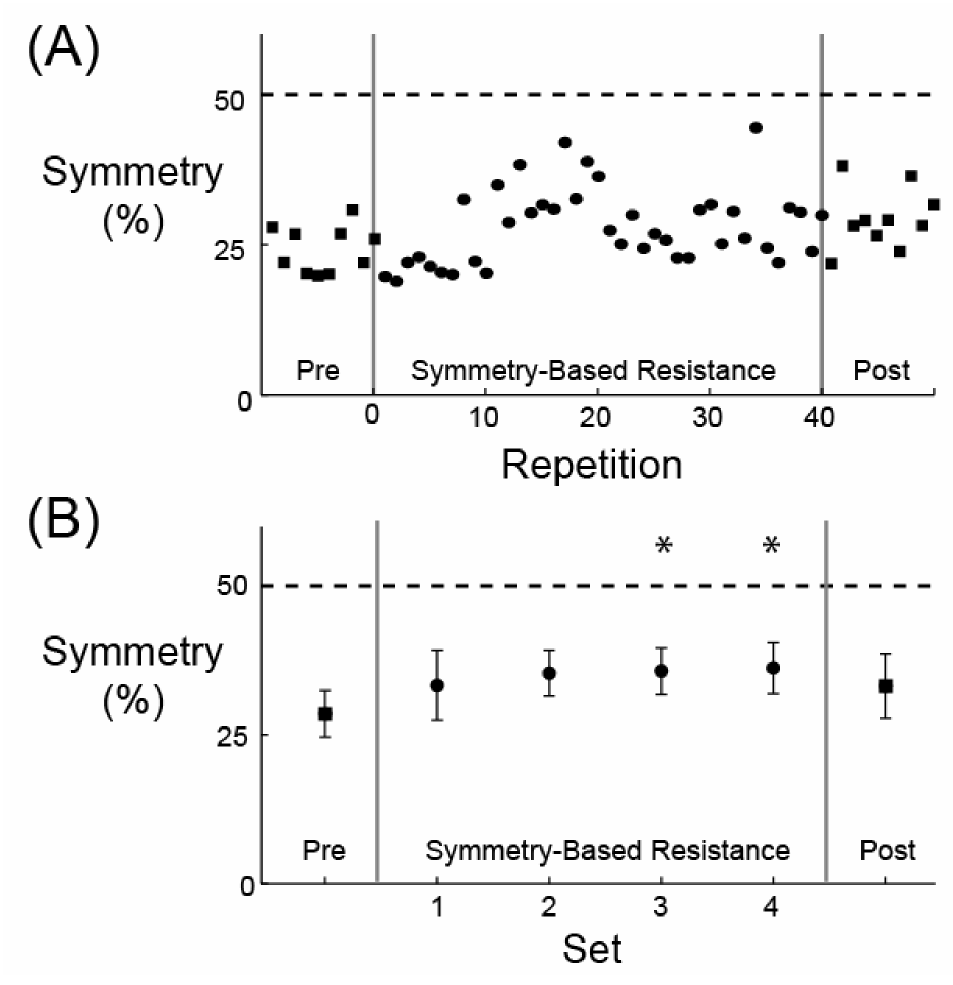

Figure 6.5. Symmetry values for subjects during the one day training session. The dashed line represents subjects' goal of 50% symmetry. The pre- and post-test lower limb extensions were against constant resistance. The symmetry-based resistance controller was turned on for Sets 1-4. A) Symmetry vs repetition for a typical subject. B) Symmetry vs. set for all subjects. Subjects exercised with significantly higher lower limb symmetry values during Sets 3 and 4 compared to the pre-test values (ANOVA, *: $P = 0.0262$).

Figure 6.5A shows one subject's lower limb symmetry during the lower limb extension pre-test, training with symmetry-based resistance, and post-test. Subjects' goal was to exercise with 50% symmetry or equal lower limb forces. On average subjects increased their lower limb symmetry values during exercise with symmetry-based resistance for Set 3 and 4 compared to the pre-test against constant resistance (ANOVA P = 0.0262) (Figure 6.5B). Lower limb symmetry values for the pre-test were 28.6 % ± 3.9 % for the pre-test, 36.2 % ± 4.3 % during the last set of symmetry-based resistance training (Set 4), and 33.2 % ± 5.4 % during the post-test.

<u>4 Week Training Protocol</u>

The two subjects with stroke-induced hemiparesis that trained for four sessions on Day 1 of training had average lower limb symmetry values of 34.2% ± 4.2%. These subjects showed improvement within Day 1 of training with post-test symmetry values equal to 48.3% ± 3.9%. The subjects also demonstrated retention of symmetry-based resistance training throughout testing Days 2-4 (Figure 6.6). During the lower limb extension pre-test against constant resistance on Day 4, subjects exercised at lower limb symmetry values of 50.7% ± 3.1%.

Discussion

During lower limb extensions, individuals with post-stroke hemiparesis did not produce equal forces during lower limb extensions even though they believed

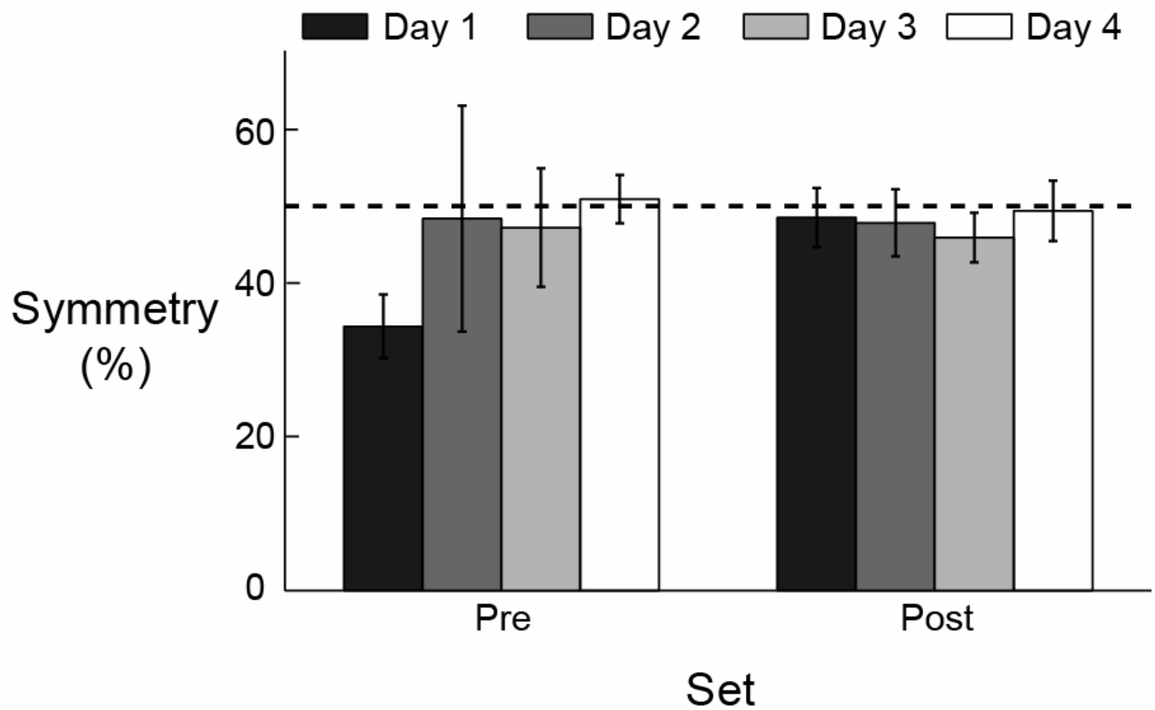

Figure 6.6. Symmetry values for the two subjects in the four week training protocol. The dashed line represents subjects' goal of 50% symmetry. Data represents on the pre- and post-test lower limb extensions against a constant resistance. Black columns represent Day 1, dark grey columns represent Day 2, light grey columns represent Day 3, and white columns represent Day 4. Subjects demonstrated retention of symmetry-based resistance training throughout testing Days 2-4.

their forces were equal. Previous studies have reported similar results in both the upper and lower limb of these patients (Bertrand et al. 2004; Mercier et al. 2004; Simon et al. 2008). Based on subjects comments, when the symmetry-based resistance controller was turned on, all subjects were able to feel the change in resistance (i.e. they knew when the resistance increased or decreased). During Set 3 and 4 of exercise with symmetry-based resistance, subjects were able to improve their lower limb symmetry. These improvements were small in magnitude for the group as a whole. The improvement in lower limb symmetry represented a smaller difference between the forces the subjects think they are producing and the forces they actually are producing. The increase in lower limb symmetry did not demonstrate carryover as subjects showed no one day changes in symmetry comparing the pre- to post-test of lower limb extensions against a constant resistance.

Analysis of the total resultant force vectors during lower limb extensions revealed that subjects did not seem to have problems with producing force in the plane of movement. A previous study has shown that individuals with post-stroke hemiparesis have coordination impairments that lead them to produce inappropriate paretic limb forces during pedaling (Rogers et al. 2004). These subjects had a hard time directing their foot forces to a given direction. The subjects in the current study did not have this problem during the task of lower limb extensions. One possible explanation is that performing lower limb extensions is a simpler task compared to pedaling. Pedaling may require more coordination in order to move the legs in different directions and constantly change force direction.

Subjects who returned to the laboratory for a total of four training sessions, did show a pre- to post-training trend of improvement in lower limb symmetry and of increased paretic limb force. These subjects also showed retention of training as their lower limb symmetry values during the pre-test improved from Day 1 to Day 4. On Day 4 of training, subjects began exercise with symmetry values close to 50%, indicating that after three weeks of training they were able to actually produce the force that they thought they were with no feedback. During training sessions Subject 5 often commented that he realized that his paretic limb was not producing as much force as he originally thought.

Our studies of exercise with symmetry-based resistance have some limitations. The studies report data for seven and two subjects for the one day and four week training protocols, respectively. Testing more subjects might reveal a stronger result, however for the one day training protocol we achieved power of 0.78. This suggests that longer training may be necessary to see pre- to post-training results. Testing more subjects for the longer training protocol seem to be warranted based on our preliminary results. Another limitation was that our subjects had a large range of functional impairments. Results may have differed if we used a stricter inclusion criteria based on functional abilities.

An advantage of training on the exercise machine, although not tested in the current study, is the potential for strength training. Strength training regimens in individuals post-stroke previously were thought to increase spasticity and decrease functional abilities (Badics et al. 2002), but studies now show that strength training has positive benefits such as increasing motor recruitment, muscle strength, and functional abilities without increasing spasticity (Mercier et al. 1999; Weiss et al. 2000; Badics et al. 2002; Monger et al. 2002). An additional benefit of strength training is that it enhances the neural component of motor abilities optimizing central motor activation (Patten et al. 2006a; Patten et al. 2006b). Therefore, one of the goals of the current line of research is to investigate whether we can design a better training regimen to enhance the neural component of strength training. A computer controlled exercise machine that provides instantaneous feedback to patients may have the potential to enhance traditional strength training protocols. Results from subjects who trained for four weeks in the current study suggest that improvements made in lower limb symmetry were not likely from morphological changes in the muscle but were neural related. The trend was that these subjects learned to more closely produce the forces they wanted to produce.

Further investigation of individuals with post-stroke hemiparesis training with symmetry-based resistance is necessary. Protocols involving more than a one day training session with more total subjects might reveal further benefits of symmetry-based resistance. Results of the current study suggest that a subpopulation of individuals post-stroke might benefit and that it might be helpful to selectively choose subjects based on percent improvement within a one day training session. Populations of individuals post-stroke are very diverse in functional abilities and impairments and targeting interventions for patients based on preliminary test may help tailor therapies to groups of patients. Additionally, comparing results from groups of subjects exercising with symmetry-based resistance, audio/visual force feedback, or pure strength training would assess which type of training, if any, could produce the most benefit in the least amount of training time for different groups of patients.

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Chapter 7

General Discussion

Neural Basis of Sense of Effort

A main finding of this dissertation is that both neurologically intact individuals and individuals with post-stroke hemiparesis mainly relied on their sense of effort more than sense of force during lower limb force production. Sense of effort could be neurally based at either the spinal or cortical level. At the spinal level Renshaw cells are inhibitory interneurons associated with alpha motor neurons. The rate of discharge of these cells therefore is proportional to the firing rate of the motor neurons. In the experiments of this dissertation, individuals believed their foot reaction forces were equal even though they were not. Unequal foot forces were a result of asymmetric muscle force and asymmetric motor neuron activation. If the sense of effort signals were originating at the spinal level, Renshaw cell output would expose the asymmetric motor neuron activation.

Therefore, it is most likely that the sense of effort is based at the cortical level. Several structures within the brain have the potential to maintain an individuals' sense of effort. The cerebellum is associated with an internal model of the motor system and may make comparisons between the predicted sensory outcome (corollary discharge) and the actual outcome to update the internal model. The basal ganglia are a collection of nuclei in the white matter of the cerebral cortex that serves as a relay station between peripheral sensory information and cortical sensory/motor areas (Shadmehr and Krakauer 2008). Finally the thalamus is a large mass of grey matter in the forebrain that processes and relays sensory information to various parts of the cerebral cortex. Future studies using functional magnetic resonance imaging or transcranial magnetic stimulation would be necessary to provide a better indication of the cortical structures involved.

Study limitations

The wide range of stroke subject characteristics (Chapters 4 and 6) in time since injury, location of stroke, and functional level might have been a limiting factor in the findings of the studies. The inclusion criteria for individuals with post-stroke hemiparesis included 1) at least six months post-onset of a single documented cortical insult, 2) between the ages of 18 and 85, 3) free of any musculoskeletal injuries or deformities, and 4) adequately able to comprehend our instructions. In terms of the time since injury subjects ranged from 7 to 156 months post-onset. Therefore some individuals have lived with and learned to compensate for their hemiparesis whereas others were most likely still adjusting and trying to regain more functional abilities. The location of the insult was not controlled for, resulting in a pool of subjects with various impairments beyond hemiparesis. These impairments included motor and sensory deficits and aphasia. Subjects with stroke who participated in these studies had various functional levels. Some were able to independently rise from a chair while others could not. All subject characteristics were reported within each study. Finally, the number of individuals tested for these experiments was only nine and seven subjects, respectively for Chapters 4 and 6. Although results from these experiments indicate a power of 0.78, a larger subject number might increase the power in our results.

A limitation in the design of the exercise machine was that the device involves leg extensions with the body positioned in the horizontal plane, whereas normal mobility tasks (i.e. standing, sit-to-stand movements, locomotion) are performed with upright postures. In these upright postures, the vestibular system assesses information about postural steadiness, involving both medial-lateral and anterior-posterior body sway. Therefore, vestibular feedback on the robotic device was different than that received while in an upright posture. While performing leg extensions, subjects did not have to completely stabilize their upper body, as the sled provided the majority of this support. The limitation of different vestibular feedback was outweighed by the fact that subjects could devote most of their attention to sensing what it felt like to produce more symmetric forces rather than focusing their attention on stabilizing their upper body. During exercise, subjects might have received sensory cues from the shoulder pads attached to the sled. If they are pushing asymmetrically, they generated a moment that is resisted by the robotic device but, in turn, might have produced more pressure on one shoulder than the other. This increase in pressure on one side might have provided additional feedback, above that of solely increased resistance levels that the subject was not producing the forces they believed they were. Pressure on one or more shoulders also may have produced subject discomfort thereby producing a larger bilateral deficit during exercise.

In regards to the protocol of the experiment involving post-stroke individuals exercising with symmetry-based resistance factors that may have limited the scope of the findings include the training time and the absence of a control group. For the preliminary trial, the training time was limited to a one-day session. When subjects showed improvements pre- versus post-exercise they then returned to the laboratory and completed a four week training period with one session per week. The results from this training period demonstrate that exercise with symmetry-based resistance may be beneficial for a subpopulation of patients with stroke. These studies, however, did not compare results against a control group of subjects that received constant resistance training. The study was used as potential pilot data for a future clinical trial. We wanted to uncover the improvements of training with symmetry-based resistance. In addition, several lower limb symmetry training studies showed only minor improvements in task performance for control groups (Engardt et al. 1993; Cheng et al. 2001). Likewise these results were observed after long training sessions which range between 45 to 60 minutes a day, 3 to 5 days a week, for 3 to 6 weeks (Sackley and Lincoln 1997; Teixeira-Salmela et al. 2001; Badics et al. 2002). Therefore, the improvements that were seen in these control groups most likely did not occur within the first few training sessions. Future training studies involving exercise with symmetry-based resistance should address this point and add a control group to compare results against.

Recommendations for Future Work

The experiments in this dissertation laid the foundation for additional studies investigating the effects of exercise with symmetry-based resistance. Recommendations for future work involve longer training protocols, software improvements to the exercise machine, and/or adopting the symmetry-based resistance controller for other tasks. Overall, the work in this dissertation opens up the possibility of creating a larger class of computer controlled exercise machines that use mechanical biofeedback to improve subject performance during a task.

Longer training protocols

Results from Chapter 4 of individuals with post-stroke hemiparesis training with symmetry-based resistance suggest that a subpopulation of these individuals might benefit from longer training protocols. Screening patients to select those who may benefit most might involve one day of symmetry-based resistance training and a calculation of pre- to post-exercise lower limb symmetry. Preliminary trials indicate that subjects who improve by greater than 30% within the one day training session might benefit the most. Alternatively, screening patients based on their functional abilities might also be beneficial, although this was not tested in the current dissertation.

Longer training times have the potential to allow subjects to gain not only the neural benefits but also strength benefits. Current rehabilitation techniques involve pure strength training and/or audio/visual force feedback. The field of rehabilitation could benefit from a study comparing results from groups of individuals with post-stroke hemiparesis participating in one of these training regimens. Training protocols would need to be matched for exercise time and for easy comparisons to existing literature should involve 45 minutes of exercise, three days a week for four weeks. Results from the three groups of subjects plus a control group receiving no additional exercise could then report on which type(s) of exercise, if any, produces the greatest improvements in strength, functional abilities, and in force scaling abilities. Likewise, results might indicate that one type of training provides the most benefits in the least amount of training time.

Software improvements to exercise machine

The performance of the hardware could be improved by software modifications. The most substantial improvements could be made for the isotonic mode. In this mode, the motor produced a constant resistance for subjects to exercise against. During continuous lower limb extensions the forces at the subject’s feet varied from the nominal value due to the inertia of both the subject and the sled. Because movement velocity was slow during the experiments in this dissertation, the resulting deviations were small compared to overall resistance. However, a relatively simple controller utilizing the forces measured by the force platform could be implemented to reduce these deviations. Furthermore, this improved controller design would allow for future protocols where these deviations may become large in relation to overall resistance. Cases

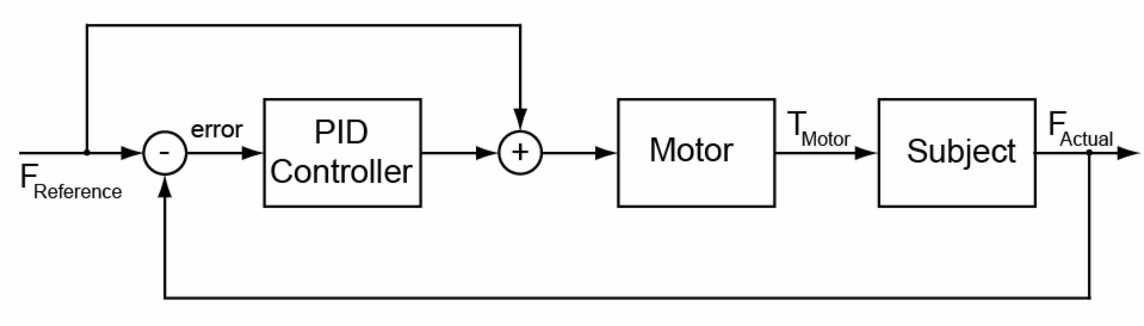

Figure 7.1. Improved isotonic controller. Using the PID controller, the motor control signal is updated to minimize error between the reference force signal and the actual force signal measured by the force plate.

where this might occur include when the resistance level is low for use with extremely weak subjects or when subjects perform faster movements.

The block diagram presented in Figure 7.1 illustrates the proposed controller for generating a more constant resistance isotonic mode. The total lower limb force measured at the force plate can be compared to the reference force to generate a force error signal. Using a PID controller, the motor torque could be adjusted to minimize the deviations between the force felt by the subject and the desired reference force.

Adopting the symmetry-based resistance controller for other tasks

The symmetry-based resistance controller has the potential to be used for various other training tasks. Adding the symmetry-based resistance controller to a body weight support system during a sit-to-stand task would provide patients with the task-specific feedback necessary to potentially improve lower limb symmetry during movement. Implementation of the symmetry-based resistance controller during this task would be very similar to its implementation during lower limb extensions. Individual lower limb force data recorded simultaneously from each limb as a subject rises from a chair could be sent to the body weight support computer. As a subject performed the movement with symmetric lower limb forces, body weight support would increase thereby allowing the subject to perform less work. As lower limb forces became asymmetric, body weight support would decrease, requiring the subject to perform more work for the same task. Since individuals post-stroke have weaker paretic limbs, body weight support should not decrease past twice the maximum force capability of the paretic limb. As in the experiments of this dissertation, symmetry-based resistance is used as a means to provide subjects with information about the forces they are actually producing. Symmetry-based resistance might allow patients minimize the disparity between the forces they think they are generating and those they are actually producing while at the same time focus on maintaining their balance and upright posture during the task of rising from a chair.

Another possible application of the symmetry-based resistance controller is during tasks such as walking with body weight support or pedaling. During locomotion, much like during the sit-to-stand task, body weight support would increase when limbs are symmetric and decrease when asymmetric. For pedaling, resistance would increase when limb forces become asymmetric.

During these tasks lower limb forces are not produced simultaneously but are out of phase with each other.

Implementation of the controller for these types of tasks would need to overcome issues of changing from a continuous to a discrete controller. One such issue is how to update the symmetry-based resistance controller. An option is to have the controller store the most recent non-paretic limb parameters for half a cycle, then in real-time compare them against the paretic limb parameters and adjust body weight support or resistance accordingly. This solution involves a phase lag and it is currently unclear how much phase lag an individual with post-stroke hemiparesis can accept and still alter their lower limb forces in response to it. Storing half cycle parameters also encounters the problem that during tasks such as walking cycle or stride duration is different between the paretic and non-paretic limbs (Chen et al. 2005) and interpolation would be necessary. However, a symmetry-based resistance controller for these tasks may help to improve individuals' lower limb symmetry and perception of forces generated during both pedaling and walking.

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Chapter 8

Conclusions

Accomplishments

The overall goals of this dissertation were to 1) design and build a computer controlled lower limb exercise machine that can be operated in a range of modes, 2) identify the physiological principles governing lower limb force asymmetry, and 3) develop and test the effects of exercise with symmetry-based resistance. The dissertation includes results from neurologically intact individuals and individuals with post-stroke hemiparesis. The main findings from the series of experiments in this dissertation are outlined below.

Computer controlled lower limb exercise machine

The robotic exercise machine used a computer controlled electrical motor to control exercise resistance in real-time. A horizontal rack affixed to the sled was driven by a pinion on the motor. A dual force platform attached to the vertical footplate captured individual lower limb forces during movement. The device was successfully programmed to be operated in one of several different custom modes: isokinetic, isotonic, or symmetry-based resistance (Chapter 2). In isokinetic mode, the computer controlled resistance so that movement velocity was held constant over the entire lower limb extension movement. This mode was used to measure subjects' isokinetic lower limb strength. During performance tests the peak force the motor could resist was 2310 N. Isotonic mode allowed subjects to perform lower limb extensions against a constant resistance. In symmetry-based resistance mode, the controller varied exercise resistance in real-time. The resistance was proportional to the amount of asymmetry in the subject's foot forces thereby providing immediate information about force symmetry in the subject's lower limbs.

Physiological principles governing lower limb force asymmetry

Neurologically intact subjects who have a greater than 10% force discrepancy in bilateral foot forces during isometric maximum voluntary contraction trials show similar force discrepancies during submaximal force matching tasks. These individuals could use both their sense of effort, or descending motor command, and their sense of force, or ascending sensory information, to control force production. Results showed that these subjects mainly relied on their sense of effort during isometric lower limb force production (Chapter 3). Electromyography results from four main lower limb muscles did not explain this force asymmetry and is likely a result of the inherent high variability in electromyograph amplitudes compared to force measures (Winter 2004).

Individuals with post-stroke hemiparesis also demonstrated lower limb force asymmetries due to their paretic limb being weaker. Although these subjects have various degrees of motor and sensory impairments, they also have their descending motor command and ascending sensory information available to them during force production. Results indicated that similar to neurologically intact subjects, subjects post-stroke mainly rely on their sense of effort during isometric lower limb extensions (Chapter 4). Further investigation revealed that control of force production in subjects with post-stroke hemiparesis is similar during static (isometric) and dynamic (isotonic) lower limb extensions.

Overall, both populations of subjects did not produce equal lower limb absolute forces even though they believed their forces to be equal. Furthermore, all subjects had the capacity to produce equal absolute forces even though they did not. This force asymmetry in neurologically intact subjects is much smaller than in individuals with post-stroke hemiparesis and likely does not affect their activities of daily living. For patients with stroke, however, an inability to account for this force asymmetry and produce the appropriate force levels with their paretic limb can affect their ability to be mobile and perform transfers.

Effects of exercise with symmetry-based resistance

Neurologically intact subjects exercising with symmetry-based resistance were able to alter their foot forces towards a target of either 50% symmetry (i.e. equal foot forces) or to a target asymmetry of 33% within a one day training session (Chapter 5). When the necessary change in foot forces was small (~5%) as it was during symmetry training, this change was not maintained during a post-test of lower limb extensions against a constant resistance. However, when the percent change was large as it was during the asymmetry training (~24%), neurologically intact subjects were able to show carryover of training. The lower limb symmetry post-test results against constant resistance demonstrated that subjects were able to alter their lower limb force production towards the asymmetry without feedback.

Individuals with post-stroke hemiparesis were able to slightly improve their lower limb symmetry during exercise with symmetry-based resistance (Chapter 6). However, this improvement of ~15% did not result in a significant improvement during the post-test when the symmetry-based resistance controller was turned off. Subjects who did show a larger improvement (greater than 30%) and participated in four training sessions spread over four weeks, showed a trend towards improvement. After four weeks of training these subjects demonstrated retention of training and were able to exercise at an average of ~51% symmetry during the pre-test of Day 4 of training. Therefore, in a subpopulation of stroke, exercise with symmetry-based resistance has the potential to allow individuals to learn to produce the forces they think they are.

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