EFFECT OF A FASTFES WALKING INTERVENTION ON WALKING ECONOMY POST-STROKE

by

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To my family, for all their love and support

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ABSTRACT

Introduction: Stroke survivors suffer marked gait deficits following their stroke, leading to a higher energy cost of transport during gait. Fast treadmill walking has been studied for its potential to improve walking economy in this population. Also, electrical stimulation of the plantar and dorsiflexors has been shown to improve walking speed through increased forward propulsion post-stroke. We intended to determine if a fast walking intervention that utilizes functional electrical stimulation (FES) improves walking economy among stroke survivors. We hypothesized that the intervention would improve gross walking economy indicated by downward shift of the U-shaped cost of transport vs. speed curve across all speeds.

Methods: Eight subjects (age 60 $\pm$ 9.4 years, self selected speed: 0.9 $\pm$ 0.18 ms^{-1}) visited the lab for pre-intervention VO_2assessment. VO_2 was assessed on a treadmill at self-selected and two "fast" speeds. These subjects then underwent a 12-week treadmill training regimen consisting of three, 90-minute training sessions per week. Each session consisted of five, six-minute bouts of walking at a 'training' speed determined based on their self-selected speed. Subjects wore 2x2in and 3x5in VersaStim electrodes on the tibialis anterior and gastrocnemius muscles respectively, with stimulation provided at varying intervals depending on the walking bout. Subjects returned to the lab immediately following the 12-week intervention to assess post-training VO_2. This post-

intervention VO_2 data was also assessed on a treadmill at self-selected speed, one 'slow' speed and two 'fast' speeds. VO_2data were analyzed over the last minute of each walking bout for energy cost of transport (ml $O_2 \cdot kg^{-1} \cdot m^{-1}$) and caloric unit cost (Kcal $\cdot kg^{-1} \cdot m^{-1}$) pre- and post-intervention.

Results: Despite a faster self-selected walking speed, energy cost of transport was less following the intervention ($p<0.05$). There was no difference in caloric unit cost pre- to post- intervention ($p=0.07$). Respiratory Exchange Ratio values measured at the same absolute speeds were found to decrease significantly following the intervention ($p<0.05$).

Discussion: A FastFES treadmill walking intervention improves walking economy in stroke subjects via movement of self selected speed to an area of lower energy cost of transport on the U-shaped economy curve. Treadmill training does not affect gross economy across all speeds, but reduces cost of transport at self-selected speed.

Chapter 1

INTRODUCTION

It is well understood that stroke survivors often suffer marked gait deficits following their stroke, resulting in a loss of symmetry in force production and leg kinematics during gait (3, 7, 9, 10).These deficits are associated with an increased energy cost of transport during gait(3, 7, 9, 16, 17, 28). For example, Ganley et al. (2006) reported that energy cost of transport was 40-50% higher in stroke survivors compared to normal controls(13). These deficits were most likely due to reduced oxidative capacity in the paretic muscle, and compensatory activation of additional muscle groups during gait(13).Gait deficits are also associated with reduced ambulatory activity following stroke(7, 17, 23, 28). As a result, cardiovascular fitness is often well below the level needed for functional aerobic capacity to support activities of daily living(23).

Stroke survivors' self-selected gait speed is much slower than the "preferred" gait speed range of 1.2-1.4 m/s that is associated with minimal energy cost of walking(26). This range, first described by Ralston in 1975, indicates that the central nervous system selects a "preferred" gait speed that minimizes the energy cost of transport during gait(27). This allows the individual to maximize the distance traveled on a given energy supply (27). This preferred gait speed range represents the vertex of a U-shaped relationship between gait speed and energy cost of transport(2, 7, 14, 17, 19, 20, 22, 27, 28, 30, 31). Deviations to the left or right of this “preferred” gait speed range are therefore associated with an increased energy cost of transport. (19, 27).

In a recent examination of the effect of walking speed on gait economy in those post-stroke, Reisman et al. found that energy cost of walking decreases (i.e walking economy improves) as speed increases above subjects’ initial self-selected speed(28). These decreases in energy cost were not offset by any energy penalty that may result if gait abnormalities increase with increasing speed (28). Subjects in the “slow” group (walking speeds lower than 1.2m/s) improved their energy cost of transport at faster speeds while those in the “fast” group did not (28). These results reinforce the idea that walking at speeds outside of Ralston’s ‘preferred’ (27) range results in increases in energy cost of transport, even in persons post-stroke. They also illustrate that one of the mechanisms by which walking economy may improve following an intervention post-stroke. First, walking economy could improve through movement of self-selected speed to a point of lower energy cost on the U-shaped speed/economy curve. Second, walking economy could improve if the position of the curve were shifted downward. Finally, walking economy could improve through a combination of these two mechanisms.

Treadmill training has been widely advocated as an effective and practical means of improving cardiovascular fitness and ambulatory function in the post-stroke population (3, 7, 9, 16-18, 28). Three months of 3 times/week treadmill training at speeds which kept heart rate reserve under 40% resulted in a 10% improvement in VO_2max in persons with chronic stroke(18).Treadmill training as fast as possible for four weeks resulted in improvements in walking economy (ml/kg/m) in persons post-stroke (24). However, it is not known whether these improvements represent a downward shift in the position of the entire U-shaped curve or movement of self-selected speed to a point of lower energy cost on this curve. This is important to determine because a downward shift of the U-shaped curve would indicate an improvement in gross economy across all speeds. A shift in self-selected speed would indicate that gross economy does not change with short-term training and that self-selected speed moves to a more economical portion of the U-shaped curve.

The purpose of this study was to determine if a fast walking training intervention with functional electrical stimulation (i.e. FastFES) to the dorsi- and plantarflexor muscles improved walking economy in persons post-stroke. As mentioned above, fast treadmill training has been found to improve post-stroke walking economy(24). Greater plantarflexor muscle activation has been hypothesized to improve walking speed through greater forward propulsion post-stroke (5). We tested the hypothesis that an intervention combining fast treadmill walking with plantarflexor muscle stimulation would result in an improvement in walking economy. Furthermore, we sought to determine the mechanism underlying this improvement: downward movement of the entire U-shaped curve, movement of self-selected speed to a point of lower energy cost on the unchanged U-shaped curve, or if both occurred simultaneously.

Chapter 2

EXPERIMENTAL DESIGN AND METHODOLOGY

Subjects. Thirteen men and women aged 47-72 were recruited from local physical therapy clinics and senior centers. Subjects also applied for participation in response to a news story about the study broadcast on a local public television station. All subjects voluntarily gave written informed consent approved by the Human Subjects Review Board of the University of Delaware. Subjects completed two phone medical screenings, one with the Stroke Studies Coordinator in the UD Physical Therapy Department, and another with the physical therapist coordinating the study. Subjects with a history of congestive heart failure, coronary artery disease, , cancer, lung disease, kidney disease, liver disease, orthopedic problems, insulin-dependent diabetes, as well as dizziness, angina or apnea without exertion were excluded from the study. Subjects meeting the inclusion criteria were asked to report to the lab for a clinical testing session in which range of motion, strength, sensation, proprioception, motor control, balance endurance and gait were assessed. These measures were also used to determine subject's eligibility to participate in the study. Subjects exhibiting signs or symptoms of the above exclusion criteria during this session were excluded from the study.

Experimental Protocol. Following acceptance into the study, subjects reported to the lab for two, one-hour treadmill VO2 sessions to assess pre-training VO_2. The subjects then reported for three, 90-minute treadmill training sessions per week over a period of twelve weeks following baseline data collection. Following completion of the training period, subjects returned to the laboratory for one post-training VO_2 assessment.

Training Protocol. Subjects wore two 2x2-inch Versa-Stim electrodes (ConMed Corporation, Utica, NY) on the skin above the tibialis anterior and two 3x5-inch Versa-Stim electrodes on the skin above the gastrocnemius and soleus, These were connected to a Grass Technologies Stimulator by a SIU8T lead. Stimulation intensity was set by 300ms long stimulation trains at 30Hz. The stimulation amplitude was maintained at 150 volts, with varied pulse duration in order to achieve the target responses for each muscle. Pulse duration for the ankle dorsiflexors was set to achieve dorsiflexion from a neutral ankle position with the subject in a seated position. Pulse duration for the ankle plantarflexors was set to achieve a heel rise with the subject in a runner's stretch position.

During treadmill walking, the timing of onset and termination of stimulation within each gait cycle was controlled using footswitches placed on the subjects' shoes. Two-centimeter circular force-sensitive resistor foot sensors of the MultiMode Footswitch System (Noraxon, USA Inc., Scottsdale, AZ) were placed on each subject's left shoe at the areas of the proximal and distal ends of the 5th metatarsal. A customized Labview Program (National Instruments Corporation, Austin, TX) was used to synchronize information with the proximal 5th metatarsal (at heel off) with stimulation of the plantarflexors and the distal 5th metatarsal (at toe off) with dorsiflextion stimulation.

Subjects mounted a GE T2100 Treadmill (General Electric Medical Systems, Milwaukee, WI) while wearing an overhead harness for safety purposes only. No bodyweight support was provided, though each subject was permitted to touch the front or side handrail with a fingertip. The choice of fastest or intermediate treadmill speed over the first 4-week training block was decided at the first training session. This minimized the risk of any overuse injuries caused by ambulating for 30 minutes at a speed that was chosen after 40 seconds of walking during motion analysis evaluation

Each training session was divided into five, six-minute bouts of walking. Following a two-minute warm-up bout at self-selected speed, the first four walking bouts followed the following procedures. Subjects walked for one minute at the treading speed while receiving electrical stimulation, followed by one minute of walking without stimulation. This cycle was repeated three times for a total of six minutes of walking. Subjects were allowed to rest for five minutes following each walking bout. During the final six-minute bout, subjects walked on the treadmill at training speed with continuous electrical stimulation for three minutes, followed by three minutes of over-ground walking.

Heart rate was monitored continuously throughout each training session by a Polar FS1 heart monitor (Polar Electro Oy, Kempele, Finland). Blood pressure was taken prior to and following each walking bout. During the five-minute rest period, each subject was asked about their status on achieving her stated goals and how to better achieve the goals for each subsequent bout. Feedback from the Physical Therapist was provided upon request from each subject. Each subject was also asked on her status on achieving her goals for the entire session and how to improve in future sessions following completion of each training session.

Pre and Post-Training VO_2 Testing. Subjects donned the mouthpiece of the metabolic measurement system, secured via a plastic headpiece placed on the subject's head, and a nosepiece placed over the nose. Subjects then stepped onto the treadmill and sat quietly in a chair on the treadmill belt. Five minutes of baseline expired air was collected for each subject, with the last two minutes defining the pre-exercise, zero-work VO_2. Participants then walked in five-minute bouts at each treadmill speed. Self-selected and fast speeds were selected for pre-training assessment, while self selected and three "fast" speeds were used for post-training assessment. Subjects wore an overhead harness during each bout for safety purposes only. No bodyweight support was provided, though subjects were allowed to touch either side handrail with a fingertip. Subjects were allowed to rest for at least three minutes between each walking bout. Testing was only resumed when heart rate, respiratory exchange ratio (RER), and VO_2/kg had returned to baseline levels. Walking was discontinued if heart rate exceeded 80% of the subject's age-predicted maximum (220-age) or if the Borg score exceeded 13 (indicating the subject was working at a moderately hard intensity)(4).

Heart rate was monitored continuously using a Polar Heart Rate monitor (Polar Electro Oy, Kempe, Finland). This measurement was transmitted to a wireless receiver connected to the metabolic cart, where it was displayed continuously throughout each testing session. The volume of oxygen consumed was measured using a ParvoMedics TrueOne 2400 Metabolic Meausrement System (Sandy, UT). Subjects wore a nose clip and breathed through the mouthpiece of the apparatus, which collected expired air. This expired air was then sampled by a mixing chamber, passed through a drying tube and then analyzed for CO_2 and O_2 concentration. CO_2 and O_2 analyzers were calibrated at the beginning of each session using standard calibration gases (16.00% O_2, 4.01% CO_2, balance nitrogen; Puritan Medical Products, Overland Park, KS). A pneumotachometer to assess inspired and expired gas volume (Hans Rudolph Inc. was calibrated using a 3-L syringe (Hans Rudolph, Inc.). All data were sampled over the duration of each testing session at 15-second intervals, Subjects were determined to have reached a steady state of oxygen consumption when the variability in VO_2 measurement was less than 2.0 ml/kg/min.

Data Analysis. VO_2 data collected over the last minute of each trial was averaged and normalized to body mass ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$). This data was then normalized to walking speed to yield energy cost of transport, defined as the energy cost per unit distance walked ($mlO_2 \cdot kg^{-1} \cdot min^{-1}$). Respiratory exchange ratio data averaged over the last minute of each bout were converted to their caloric equivalents using a caloric equivalent conversion chart(32). This value was multiplied by net VO_2 ($L \cdot min^{-1}$) to determine calories expended per minute ($Kcal \cdot min^{-1}$). Each data point was then normalized to bodyweight and walking speed to yield Caloric Unit Cost per meter walked ($Kcal \cdot kg^{-1} \cdot m^{-1}$)(12). Data from trials in which subjects did not achieve a steady state VO_2 were excluded from analysis. Respiratory exchange ratio values averaged over the last minute of each trial were also taken at each speed to determine the relative oxidation of lipids and carbohydrates at each speed before and after training.

Statistical Analysis. The main variables of interest were two indices of walking economy: Energy Cost of Transport ($mlO_2 \cdot kg^{-1} \cdot m^{-1}$) and Caloric Unit Cost ($Kcal \cdot kg^{-1} \cdot m^{-1}$); both were examined pre- and post training. Self-selected walking speeds were also examined pre- and post training. RER values were examined pre- and post-training at the same absolute walking speeds. Because of the small sample size, differences in both indices of walking economy were analyzed using a Wilcoxon paired rank test. Statistical significance was set at a $p<0.05$.

Chapter 3

RESULTS

Subject Characteristics. Subject demographic data are presented in table 1. Three subjects dropped out of the study following the first baseline collection period. Two subjects' degree of disability prevented them from completing pre-training VO_2 testing. These subjects were excluded from analysis. The data presented represent a sample size of 8 subjects that completed all pre- and post-testing. Self-selected speed increased following the intervention (Figure 1, $p<0.001$). The fastest self-selected speed achieved by any subject prior to the intervention was 0.9m/s and 1.1m/s post-intervention. All subjects completed >90% of all training sessions.

Table 1. Descriptive Characteristics

ID	Age	Hemiparetic Side	Time Since Stroke (Months)	LE Fugl-Meyer Score	Mono-filament Threshold	Proprioception	Pre-Training Self-Selected Speed (m/s)	Pre-Training Weight (kg)	Post-Training Weight (kg)
S1	68	Left	22	23	4.31	100%	0.67	86.8	86.4
S2	52	Left	110	24	<6.65	0%	0.86	88.2	89.1
S53	72	Right	68	13	4.31	100%	0.47	105.9	105.9
S128	65	Right	18	18	<6.65	80%	0.51	61.8	63.6
S129	55	Right	54	17	2.83	100%	0.48	70.5	73.9
S136	59	Right	12	13	6.65	40%	0.29	78.6	83.2
S137	47	Right	8	15	6.65	100%	0.44	68.2	71.8
S142	71	Left	9	19	6.65	100%	0.34	90.5	93.2

Walking Economy. No significant changes were found between pre- and post-training energy cost of transport values at one absolute speed measured pre- and post-training across all subjects (figure 2). Despite the faster self-selected walking speed, energy cost of transport was less following the intervention (p = 0.02; Figure 3). There was no difference in caloric unit cost pre- to post-training (p = 0.07; Figure 4).

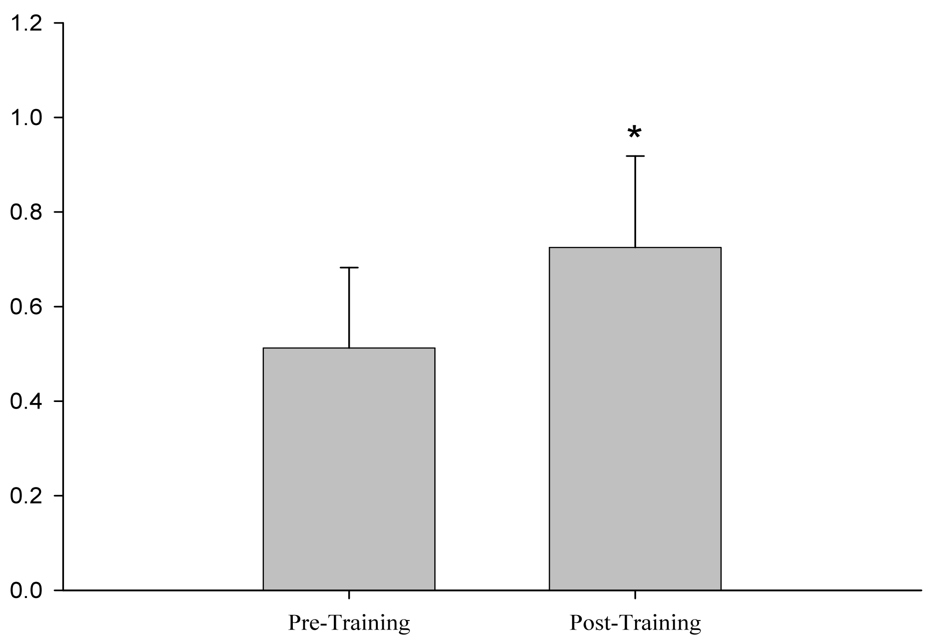

Figure 1. Self-selected speed across all subjects before and after the FAST/FES intervention. Self-selected speed increased significantly ($p<0.05$) following the intervention.

*=$p \leq 0.05$ compared to Pre-Training. Values are means ± SD.

Respiratory Exchange Ratio. RER values were examined at self-selected and 'fast' speeds pre- and post-training. RER values were 0.85 $\pm$ 0.07 at pre-training self-selected speed, and 0.86 $\pm$ 0.07 at post-training self-selected speed. RER values were 0.89 $\pm$ 0.1 at pre-training 'fast' speed, and 0.93 $\pm$ 0.1 at post-training 'fast' speed. No significant differences were found between group means at self-selected speed (p=0.34) and 'fast' speed (p=0.14) pre- to post-training.

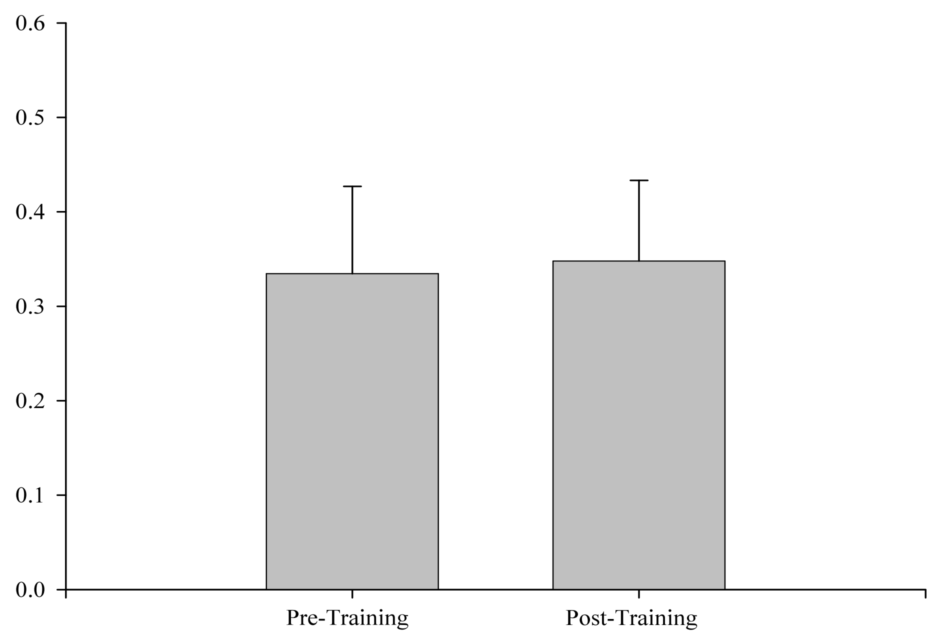

Figure 2. Energy Cost of Transport at one common speed across all subjects before and after the FAST/FES intervention. No significant differences between pre and post-intervention were found. Values are means $\pm$ SD.

Rating of Perceived Exertion. Rating of perceived exertion values were examined at self-selected and 'fast' speeds pre- and post-training. RPE vales were 8.16 $\pm$ 1.39 at pre-training self-selected speed, and 8.65 $\pm$ 2.15 at post-training self-selected speed. RPE values were 9.75 $\pm$ 1.82 at pre-training 'fast' speed, and 10.1 $\pm$ 2.65 at post-training 'fast' speed. No significant differences were found between group means at self-selected and 'fast' speeds pre- to post-training

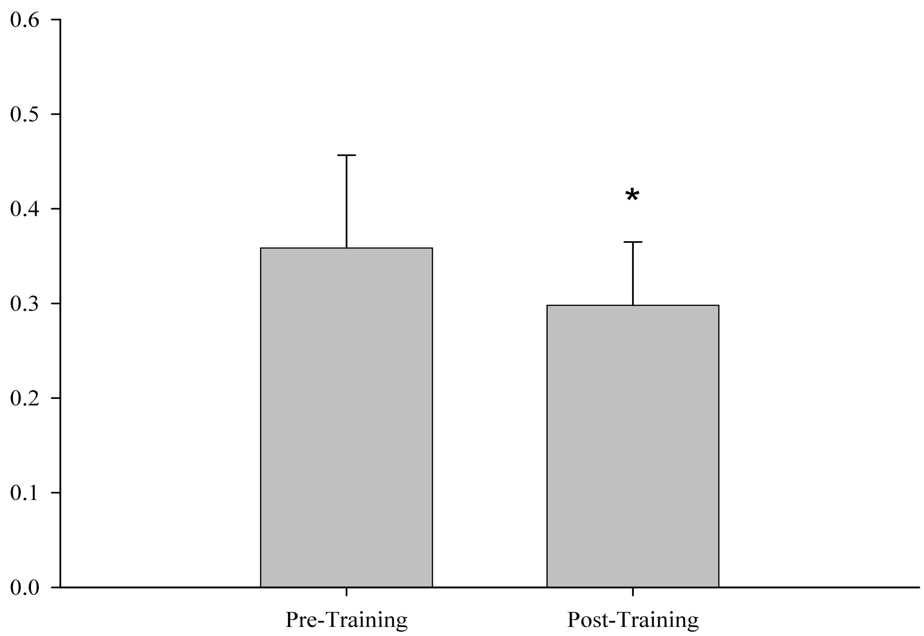

Figure 3. Energy cost of transport at self-selected speed across all subjects before and after the FAST/FES intervention. A significant decrease was found following the intervention ($p<0.05$).

*= $p \leq 0.05$ compared to Pre-Training. Values are means $\pm$ SD

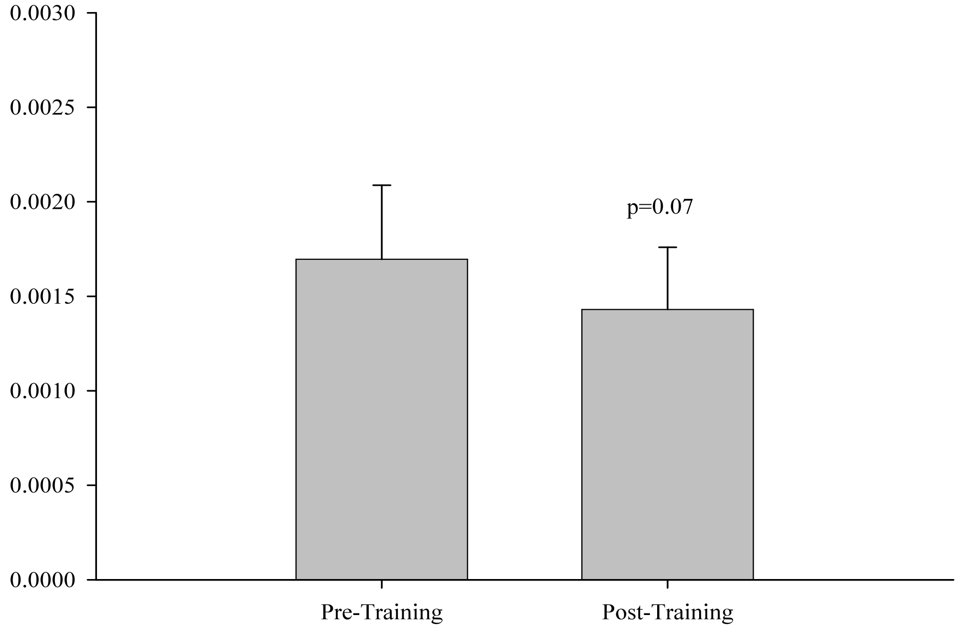

Figure 4. Caloric unit cost at self-selected speed across all subjects before and following the FAST/FES intervention. No significant differences between pre and post-intervention were found. Values are means ± SD.

Chapter 4

DISCUSSION

The primary finding of this study was that although self-selected speed increased significantly with training ($p<0.05$), energy cost of transport was significantly ($p<0.05$) lower at post-training self-selected speed compared to pre-training self-selected speed. Also, no shift in the U-shaped economy curves occurred among our subjects from pre- to post-training (figure 2).

The absence of an upward or downward shift in the U-shaped curve following the intervention suggests that the FastFES intervention does not affect gross mechanical efficiency among stroke survivors. A decrease in cost of transport at an absolute speed pre- to post-training would have indicated a shift in the entire curve as a result of the intervention (figure 2). However, we found no evidence of a significant ($p<0.05$) decrease in cost of transport at absolute speed across all subjects. Downward movement of the entire U-shaped economy curve would indicate that energy cost of transport decreases across all walking speeds, and that gross walking economy is therefore improved across all speeds. We found no consistent evidence of this phenomenon in our study. This therefore indicates that the intervention did not alter gross walking economy and that any improvement in economy must be explained by another mechanism. Ganley et al. indicated that the U-shaped curve may shift to the left at lower levels of cardiovascular fitness(13). However, Ganley et al. examined cost of transport in stroke patients compared to age-matched controls at self-selected speed without the use of any training intervention(13). To the best of our knowledge, this was the first study to examine a shift in the entire U-shaped economy curve following an exercise intervention.

Our finding that a significant increase in self selected speed was accompanied by a significant decrease in energy cost of transport following the intervention indicates that the subject's self-selected speed moved to an area of lower energy cost as a result of the intervention. This finding is consistent with several recent studies related to treadmill training and gait(16-18, 28). Recent work by Moore et al indicated that treadmill training as fast as possible over a period of four weeks resulted in improved walking economy in stroke patients(24). Also, Reisman et al. indicated that economy improves acutely as speed increases above the subjects' initial self-selected speeds(28). Movement of self-selected speed to a more economical portion of the curve indicates that economy improves through re-adjustment of self-selected speed following this intervention.

RER values significantly ($p<0.05$) decreased at the same absolute speeds from pre to post-training. Although no significant ($p<0.05$) change was found at self selected and fast speeds pre- to post-training, these values remained the same in the prescence of significantly($p<0.05$) self-selected speeds (Figure 1). The FastFES intervention therefore produced a cardiovascular training effect in our subjects pre- to post-intervention. This is consistent with traditional models of endurance training in healthy individuals, in which chronic endurance training reduces RER values across absolute speeds from pre- to post-training(8, 21). This is due to increases in the content of mitochondrial enzymes responsible for fat oxidation(29). Our result is also consistent with recent work advocating treadmill training as a means of improving cardiovascular fitness in stroke patients(16-18). These studies have reported increases in fitness reserve, 6-minute walk distance and VO_2 peak among stroke survivors who underwent treadmill training compared to healthy controls. Therefore, the FastFES intervention is also an effective means of increasing cardiovascular endurance among stroke survivors.

This decrease in RER at the same absolute speeds indicates that the training effect of the FastFES intervention alters substrate selection during gait. This may therefore build on the work of Willis et al, who indicated that Ralston's 'minimal energy hypothesis' extends not only to energy cost of transport, but also to substrate selection during gait(27, 31). Carbohydrate oxidation is minimized within the "preferred range" of 1.2-1.4 ms^{-1} , and increases sharply as gait speed deviates from this range(31). Our data revealed that the subjects' self-selected walking speeds increased towards this range from pre- to post-intervention. Therefore, improvement of walking economy by movement of self-selected walking speed to an area of greater economy may contribute to altering substrate utilization across all speeds post-intervention. However, further study is required to determine the role of economy in improving substrate utilization during gait.

One limitation of the current study is the small sample size. The degree of post-stroke cardiovascular endurance was wide among our subject pool. Nevertheless, the intent of this study was to provide pilot data for a larger, randomized controlled trial.

These findings provide insight into the role of FES and treadmill training in the improvement of mobility in stroke survivors. Improvement of economy at self-selected walking speed will work to improve functional mobility and endurance in activities of daily living that require ambulation. This will also work to improve quality of life among these individuals, allowing them to return to activities that were complicated by their hemipareisis. A next logical step in further research in this area is to examine walking economy over multiple gait speeds over ground. Although treadmill training has been shown to be an effective tool in improving post-stroke walking endurance and economy, studies of this phenomenon under conditions resembling the home environment seem to be warranted. To the best of our knowledge, no studies have examined walking economy over a range of speeds over ground. Also, the U-shaped economy curve has been observed in humans regardless of walking surface, in both healthy subjects and subjects with gait deficits (28). Such studies would provide insight into the potential benefit of utilizing a more accustomed gait pattern to improve mobility compared to the treadmill, as marked differences in gait patterns exist between both surfaces (7).

In summary, the FastFES training intervention improves walking economy in stroke survivors. This improvement occurs via movement of the self-selected gait speed to an area of lower cost of transport on the U-shaped economy curve. The position of this U-shaped curve did not appreciably change pre- to post-intervention, indicating that gross economy did not change following the intervention. Also, this intervention is an effective means of increasing cardiovascular endurance among stroke survivors.

Appendix A

REVIEW OF LITERATURE

Walking Economy and Human Gait

Optimization of energy expenditure during gait in humans is based upon the "Minimal Energy Hypothesis" first described by Ralston in 1975(27). Ralston indicated that the central nervous system selects a "preferred" walking speed that minimizes energy cost of transport, thereby allowing an individual to walk over the maximum distance on a given energy budget (Ralston). This "preferred" speed (which occurs between 1.2-1.4m/s) represents the vertex of a U-shaped relationship between energy cost of transport and gait velocity(2, 7, 14, 17, 19, 20, 22, 27, 28, 30, 31). Therefore, deviations to the left or right of this "preferred" speed will result in an increase in energy cost of walking per unit distance (19, 27). This relationship has also been defined from the adaptationist perspective, as Srinivasan stated that this economical walking speed was selected to maximize chances of survival when traveling over long distances to acquire food (30). Srinivasan defined the "preferred speed" as the "maximal range speed", or the speed that allows an animal to travel the maximum distance on a given energy budget (a single stomach full of food) without eating (30). In times of food scarcity, when the distance traveled increases with the probability of finding food, the probability of starvation is minimized by minimizing the energy cost of locomotion until a food source is found (30). Also, if a person were asked to walk a given distance in a manner that leaves her with the most unused energy after walking this distance (energy that could be used to complete some other task), the person will walk at the “preferred speed” (30).

This relationship is also thought to be more advantageous to the survival of humans than other species (6). For example, horses employ four distinct patterns of gait, each with its own U-shaped economy curve, all of which are relatively flat (6). However, these curves are characterized by relatively narrow ranges of ‘preferred’ speeds (6). This results in short transition intervals from one gait pattern to the next with increasing speed in order to minimize energy cost (6). On the other hand, humans employ a single gait pattern, with a relatively flat U-shaped curved curve at all but the fastest endurance speeds (6). This allows humans to adjust walking or running speeds continuously without change of gait or metabolic penalty over a comparatively wide range of speeds (6). Srinivasan also added that, for any given speed, humans appear to select the stride length, stride width and stride frequency that seems to minimize metabolic cost, and that stride lengths smaller or larger than preferred stride lengths tend to require greater metabolic expenditure, based on VO_2 measurement (30). This seems to agree with Ralston’s hypothesis and suggest the presence of innate neuromuscular mechanisms that control these gait factors to minimize energy economy.

Willis, et al. (2005) gave an indication of the effect of deviation in walking velocity on metabolic cost in their study of fuel oxidation during gait (31). The shape of the energy cost of transport vs. speed curve is very flat, such that large (33%) deviations in gait speed would result in relatively small (<10%) penalties in energy cost (31) (Willis et al.) However, Willis indicated that the minimal energy hypothesis pales in comparison to the selection of the metabolic fuel source as a determinant of cardiovascular endurance during gait (31). A 70-kg, healthy individual may store as much as 400,000kJ of energy as triglycerides, compared to approximately 10,000kJ as carbohydrates (31). Therefore, based on the putative relationship between carbohydrate dependence and speed, fuel selection during gait may alter walking endurance by as much as 30-fold (31) Willis et al. found that, carbohydrate oxidation is minimized at their subjects' "preferred" walking speed, and increased sharply at speeds only slightly higher than the subjects' preferred speed (13, 31). This therefore supports Ralston's minimal energy hypothesis in that the body is able to select the metabolic pathway that draws from the highest energy reserve at the lowest intensity, and increases the oxidization of carbohydrate with increasing speed. This is a result of a greater energy demand caused by increases in exercise intensity. Also, Willis indicated that the observed changes in skeletal muscle metabolic control were linked to CNS motor control (31). They proposed that their subjects' "preferred" speed is the highest achievable rate of muscle energy turnover without the redistribution of flux control from ATP oxidation sites in the myocyte, to the cell mitochondria (31). Control of low-frequency energy turnover is redistributed from the ATP oxidation sites to mitochondrial ATP production, as the contractile frequency approaches the beginning of glycolysis activation (31). The CNS is able to sense this drop in cellular energy state by comparing the efferent motor drive to afferent contractile performance signals and relinquishes control of energy flux to the mitochondrion (31). Therefore, energy flux is redistributed from the ATP-use/CNS axis toward the mitochondria when energy turnover rates are high enough to activate glycolysis (31). However, this model does not suggest that the CNS senses carbohydrate oxidation per se, but the cellular energetic milieu associated with the activation of glycolysis in fasted individuals (31). Nonetheless, the model does predict that muscle carbohydrate oxidation rate should predict the perception of effort in fasted walking subjects (31). Therefore, Willis et al. indicate that the minimal energy hypothesis accounts for both minimization of O_2 cost of transport, and the optimization of fuel selection during gait, both of which are primary determinants of walking economy.

A more recent study by Ganley et al. supported Willis' indication that "preferred" gait speed is the most metabolically efficient. Willis et al. had indicated that the "preferred" walking speed was slightly slower than the speed at which carbohydrate oxidation had increased (31). Ganley et al. also found a sharp increase in carbohydrate oxidation between "preferred" and "fast" walking speeds (13). However, they did not give an indication of the specific point at which metabolic activity increases with increasing gait speed, as they quantified walking economy based on only two fixed speeds: "preferred" and "fast" (13). Their measurement of fuel selection during gait (based on subjects' RER values) also concurred with Willis et al, as fat oxidation accounted for the majority (58%) of fuel oxidation at "preferred" speed, and carbohydrate oxidation accounted for the majority (69%) of fuel oxidation at "fast" speed (13). However, Ganley did not give an indication of the point at which fuel selection shifts from fat to carbohydrates with increasing gait speed. Mian et al. also supported Willis' findings, in their examination of the metabolic cost of walking in young and older adults (22). They reported an upward shift in the energy cost of walking vs. gait speed relationship in older adults and hypothesized that an increase in mechanical work may also explain this increase (22). However, they found no significant increases in internal or external work, but found a moderate correlation between increased antagonist muscle co-activation and energy cost of walking across all treadmill speeds in their design (22). This may indicate that antagonist muscles are activated at a greater rate at higher speed to control agonist muscle range of motion during gait, thereby leading to increased metabolic demand at higher speeds. This relationship may also occur at speeds lower than “preferred” speed as antagonist muscles may be activated to control limb range of motion and agonist muscle power during slower gait.

<u>The Effect of Hemiparesis on Human Gait Economy</u>

One of the most common neurologic deficits associated with stroke is hemiparesis, which results in marked deficits in neuromuscular function over one half of the patient’s body outward from the saggital plane. These deficits, among other factors, greatly contribute to chronic reduced ambulatory activity following stroke (7, 17, 23, 28). Michael et al. reported that the cardiovascular fitness of most stroke patients is well below the level needed for functional aerobic capacity needed to support activities of daily living (23). A strong negative relationship exists between VO_2peak, gait economy and balance, indicating that stroke patients exhibit a low level of ambulatory activity following stroke that may be the cause of deficits in mobility and cardiovascular fitness (17, 23). For the majority of stoke patients, clinical care is largely unsuccessful in restoring functional mobility post-stroke, as physical therapy tends to focus on improving only basic mobility and activities of daily living (17, 23). These patients are also not given specific home-rehabilitation instructions following discharge; beyond simply continuing to stretch and stay active (1, 25). Stroke patients are therefore greatly at risk for developing patterns of inactivity that contribute to de-conditioning and loss of functional mobility (7, 23). Also, subjects’ VO_2peak values correlated negatively with their score on the Berg Balance Scale, indicating a possible link between balance deficits and cardiovascular fitness (23). These balance deficits are most likely accompanied by an increase in physiologic workload, which may influence the outcome of restoring ambulatory activity in these patients (23).

Ganley et al. investigated these deficits further, examining the differences in muscle metabolism between stroke survivors and healthy individuals. They found that O2 cost of transport was 40-50% higher in stroke subjects than normal controls (13). They proposed that these deficits in O2 cost of transport may be caused by: specific neurological impairments (muscle spasticity), reduced oxidative capacity in the paretic muscle and compensatory activation of additional muscle groups to provide propulsion and stability during gait (13).This therefore supports Michael et al.'s findings that stroke subjects suffer deficits in cardiovascular and neuromuscular function, which account for the higher energy cost of O_2 transport during gait. Ganley et al. also expanded on the work of Willis et al., by taking measures of fuel selection during both normal and hemiparetic gait(13). RER values did not exceed 0.85 for stroke subjects, indicating that trigylceride stores was the primary fuel source utilized during gait in this group (13). Fat oxidation accounted for the majority (58%) of energy utilized at "preferred" speeds, whereas carbohydrate oxidation accounted for 68-69% of energy utilized at the "fast" speeds prescribed in their design (13). They therefore concluded that fuel selection contributed to the "preferred" gait speeds in hemiparetic individuals and that higher rates of CHO oxidation associated with "fast" speeds may prevent higher, more functional gait speeds (13). This seems to suggest that the U-shaped, minimal energy curve shifts downward at lower levels of cardiovascular fitness. Therefore, the "preferred" (most metabolically efficient) gait speed would similarly shift downward with decreasing levels of cardiovascular fitness. They also noted that progressive aerobic exercise training may allow the subjects to support greater exercise intensities and increase fat oxidation at these levels of exercise (13). Therefore, Ganley et. al seems to suggest that the U-shaped curve can shift upward and downward for an individual depending on their cardiovascular fitness.

Brouwer et al. investigated the biomechanical causes of the increased metabolic requirements of hemiparetic gait. They also examined potential differences in gait biomechanics and metabolic demand over both treadmill and overground walking. Treadmill training has gained credibility as a rehabilitation tool in hemiparetic patients as it provides for both body weight support and increased safety (as the belt speed can be controlled) during training (7). Treadmill training has also been associated with greater gait symmetry, which Brouwer et al hypothesized would lead to reduced metabolic cost and therefore improved walking economy than overground walking (7). However, despite marked differences in gait symmetry between the two surfaces, treadmill walking was associated with a higher metabolic cost than overground walking (7). This difference occurred despite greater angular displacement in the non-paretic limb of the overground subjects, indicating that the gait symmetry improvements associated with treadmill walking do not offset the increases in metabolic cost of walking on this surface (7). However, unlike other studies of hemiparetic gait on the treadmill (10, 17, 28), the study design did not allow the use of handrails or other support devices (7). This may indicate that the subjects are less stable during treadmill gait than overground gait (7). This instability and change in temporal-distance parameters may reflect the moving treadmill belt pulling back on the stance limb during the stance phase (7). This would therefore lead to an early transition to the swing phase in order to avoid excessive anterior displacement of the center of mass (7). Therefore, Brouwer et al. proposed that this higher energy cost may have reflected the elevated muscle force and power resulting from increased contribution of the muscles in the paretic limb to provide stability in the absence of handrail support (7). They also noted that push-off forces at the end of the stance phase were limited during treadmill walking (7). This lead to increased compensation from the hip flexors to move the limb through the swing phase, therefore increasing the energy cost of walking (7). This may suggest that treadmill training with handrail support may eliminate the metabolic penalties associated with treadmill walking and therefore lead to improvements in gait symmetry and therefore walking economy in hemiparetic stroke patients.

A study by Bayat et al. expanded this biomechanical perspective on hemiparetic gait, and examined maximum gait speed of stroke subjects during treadmill and overground walking to identify the temporal-distance determinants of maximal gait speed. Their results support the findings of Brouwer et al., as they found that stroke subjects were able to achieve faster gait speeds overground than on the treadmill (3). However, their healthy control group was able to achieve comparable gait speeds over both surfaces and achieved greater speed adaptation on the treadmill compared to stroke subjects (3). Treadmill walking may therefore produce a challenge to balance compared to overground walking (3). The net absence of forward progression, despite movement of the body segments responsible for production may produce a "sensory conflict" within these systems (3). This therefore presents a challenge to stroke subjects in that their deficits in sensorimotor integration may lead to difficulties integrate the conflicting sensory information (3). This therefore results in a loss of stability in the absence of support devices (handrails, weight support harnesses), which causes increased activation of the paretic limb and therefore greater metabolic demand during gait (7). Treadmill walking also induces a "mincing" gait pattern, characterized by a shorter stride length with a faster cadence (3). This gait pattern is characteristic of older, non-stroke patients with balance problems and further indicates an overall loss of stability on the treadmill (3). This biomechanical perspective on hemiparetic gait indicates that walking economy decreases on the treadmill as external support decreases. However, it is possible that the use of support structures with treadmill training such that stroke subjects are able to regain much of their functional mobility, before removing support structures on a graduated basis may result in improvements in gait stability and therefore improvements in walking economy during unsupported treadmill walking in this population.

Chen et al. investigated improvement of these gait deviations using such support systems as weight support harnesses, increased treadmill speed, support stiffness and handrail hold. They found that single limb support time on the paretic limb increased with increasing body weight support and the addition of handrail hold, thereby indicating an increase in gait symmetry (10). Furthermore, as treadmill speed increased, leg kinetic energy at toe-off increased slightly but remained low compared to the non-paretic limb (10). This may indicate an increase in walking economy with increasing treadmill speed, as increased kinetic energy in the paretic limb would indicate a greater contribution from this muscle to provide for propulsion, thus increasing gait symmetry and therefore reducing metabolic demand. These findings indicate that despite increases in instability during treadmill walking, gait symmetry increases on the treadmill with or without the presence of handrail hold or bodyweight support harnesses (10). This therefore supports the belief that the use of support structures during treadmill gait may diminish the metabolic penalty associated with this lack of stability on the treadmill, thereby increasing both cardiovascular endurance and mobility.

As a result of deficits in fitness and ambulatory activity, subjects' "preferred" gait speed decreases post-stroke, which may lead to increases in metabolic demand during gait. A recent (2009) study by Reisman et al., examined the effect of treadmill speed on walking economy in stroke patients. These patients suffered deficits in cardiovascular conditioning and mobility, such that their fastest walking speeds were slower than Ralston's "preferred" walking speed of 1.2-1.4m/s (28). Walking economy largely increased as walking speed increased above the subjects' self-selected speeds, and the energy cost of walking decreased significantly between the six treadmill speeds included in the research design (Slow, "free" and 3 "fast" speeds)(28). These findings agree with Ralston's "minimal energy hypothesis", in that as subjects increased their treadmill speed closer to the "preferred" speed of 1.2-1.4m/s, walking economy improved. It therefore follows that if subjects can be trained on the treadmill to improve their self-selected speed closer to the "preferred" speed, walking economy will continue to improve**.** Reisman et al. also indicated that although possible increases in gait deviations resulting from higher treadmill speed may have increased energy cost of walking at higher speeds, this did not offset the energy benefits of increasing treadmill speed (28). Reisman et al. also supported Ralston's hypothesis by completing a post-hoc analysis in which the subjects were divided into two sub-groups based on their maximum speed(28). Those with maximum gait speeds higher than 1.2m/s were placed into the "fast" group, and those with maximum gait speeds slower than 1.2m/s were placed into the "slow"group(28). Reisman et al. found that the "fast" group did not reduce their energy cost of walking after treadmill speed exceeded 1.2m/s(28). These findings greatly support the minimal energy hypothesis as well as the notion that the optimal range of gait velocities does not change greatly, even in the presence of impaired gait (28).

Treadmill Training and Improvement of Gait Economy

Treadmill training has recently been advocated in the literature as an effective tool for allowing stroke subjects to improve cardiovascular endurance by training them to walk at a velocity closer to the "preferred" speed for healthy individuals(7). Macko et al. began this investigation by examining improvements in fitness reserve as a result of treadmill training. They found that older patients with mild-to-moderate gait impairment who completed 3 months of treadmill training increased their VO2peak by 0.1-0.4ml/kg/min (18). They therefore concluded that treadmill training increases peak exercise capacity in these patients while decreasing the energy cost of hemiparetic ambulation, which therefore resulted in the observed improvements in fitness reserve(18). They proposed that treadmill training may enhance functional mobility in these patients by increasing ambulatory workload capacity (18). This initial data culminated in a randomized controlled trial in which Macko et al. examined improvements in ambulatory function and cardiovascular fitness following treadmill training. They demonstrated that training with the T-AEX treadmill system improves cardiovascular fitness, sustainable 6-minute ambulatory performance capacity and several measures of functional mobility following three, 40-minute treadmill training sessions per week for 6 months (17). They also demonstrated that this training protocol was superior to a reference control program in improving cardiovascular fitness and functional mobility among these patients (17). They noted that the degree of progression in T-AEX training predicted the observed gains in cardiovascular fitness, but not ambulatory function (17). Therefore, advancing training velocity may be an effective strategy for ensuring gains in cardiovascular fitness with treadmill training (17).

Luft et al. expanded on these findings by investigating the possible role of treadmill training in activating sub-cortical neural networks to improve hemiparetic gait. Gait control is managed by the integration of the cortical, sub-cortical and spinal neural networks, yet the neuromuscular basis of gait recovery post-stroke is not well understood (11, 16). Therefore, Luft et al proposed that progressive, task-repetitive treadmill training (T-EX) would improve gait function and cardiovascular fitness by promoting neural network plasticity (16). They found that, in addition to improving cardiovascular fitness by 18%, T-EX training increased activation of the posterior cerebellar lobe (72%) and the midbrain (18%) significantly ($p<0.05$) during movement of the paretic limb (16). This suggests that T-EX training activates mechanisms of neuroplasticity during activation of the paretic limb, which works to improve functional gait capacity and mobility post-stroke (16). This also suggests that the improvements in ambulatory function as a result of T-EX training may be mediated by these mechanisms (16). This increase in plasticity may therefore provide a partial explanation for increases in walking economy with speed, as increases in plasticity in these brain regions predicted a 51% increase in treadmill speed for these subjects (16).

Cortical plasticity is a primary mediator of upper-extremity movement-learning in humans, and has been shown to decrease in the months following stroke (11, 16). However, no decreases in cortical activity were observed in the treadmill group during training, indicating that the observed increases in gait speed are mediated by increases subcortical rather than cortical activation. These subcortical networks have shown increased activation during recovery (16). This increased activation of subcortical networks may indicate enhanced signaling in the red nucleus and locomotor region of the midbrain, as well as the cerebellum, which may work to enhance integration of somatosensory information into locomotion (16). Adaptations in the red nucleus that enhance locomotor recovery and inter-limb coordination have been demonstrated in several studies of non-human primates and quadrupedal animals(15). Therefore task-oriented treadmill training may enhance walking economy by promoting neural plasticity in the midbrain. This may work to enhance the processing of somatosensory information to the motor cortex, thereby promoting motor re-learning and increasing walking speed.

Dawes et al. further explored the influence of cortical mechanisms involved in hemiparetic gait by analyzing the recovery of walking performance in relation to the extent of lesion overlap in the corticospinal tract (11). They hypothesized that the degree of lesion intersection with the corticospinal tract would increase with increasing gait asymmetry and decrease with the degree of walking speed and endurance improvement as a result of treadmill training (11). They based their hypothesis on previous observation that the recovery of upper limb function following stroke was greatly influenced by this degree of overlap (11). However, only weak correlations were found between these two factors in both analyses, which seems to support the importance of sub-cortical control for highly practiced, rhythmic lower limb movements such as gait (11). Sub-cortical control mechanisms are also involved with rhythmic arm movement, but not tonic arm muscle contractions, suggesting that voluntary control of movement components may significantly engage neocortical control mechanisms (11). However, behavioral studies in which walking ability has been shown to decrease when performing cognitive tasks, seems to support the influence of sub-cortical mechanisms in controlling self-paced gait (11).

Clinical Relevance

The results of this study will further our knowledge of energy optimization during gait, and will give insight into the optimal use of the treadmill as a tool to enhance walking economy in stroke patients, thereby allowing them to increase their normal, leisurely walking velocity at home and in the community. This will therefore work to decrease the time necessary to return to activities of daily living that require ambulation. A next logical step is to examine the relative improvement in walking economy with increased speed compared to overground waling, as marked decreases have been observed between walking on the treadmill and overground, despite gait improvements on the treadmill (7). Treadmill training is an effective tool for restoring cardiovascular fitness and ambulatory function during therapy, but as individuals are often discharged without complete recovery of gait function (1, 25), devising a method to further improve gait function in the home or community seems to be warranted. No studies have investigated walking economy overground and on the treadmill over a progression of speeds (Brouwer et al. conducted their study over a single gait speed) (7). Also, Ralston's U-shaped curve has been observed regardless of walking surface, in both healthy subjects and subjects with gait deficits (28). There is no evidence to indicate that differences in gait over these surfaces would principally influence efficiency at faster speeds, because these differences were observed at self-selected speed (7, 28). Therefore, investigation of energy economy differences between treadmill and overground walking are necessary. Such work would lead to further improvement in post-discharge rehabilitation for stroke patients, thereby allowing them to return to activities of daily living.

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