Symmetry of corticomotor input to plantarflexors influences the propulsive strategy used to increase walking speed post-stroke

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HIGHLIGHTS

- Corticomotor asymmetry to plantarflexors influences the propulsive strategy used to increase post-stroke walking speed.
- Individuals with good corticomotor symmetry improve propulsive symmetry to achieve their fastest walking speeds.
- Rehabilitation strategies that promote corticomotor symmetry to plantarflexors may improve post-stroke gait mechanics and enhance functional walking outcomes.

ABSTRACT

Objective: A deficit in paretic limb propulsion has been identified as a major biomechanical factor limiting walking speed after stroke. The purpose of this study was to determine the influence of corticomotor symmetry between paretic and nonparetic plantarflexors on the propulsive strategy used to increase walking speed.

Methods: Twenty-three participants with post-stroke hemiparesis underwent transcranial magnetic stimulation and biomechanical testing at their self-selected and fastest walking speeds. Plantarflexor corticomotor symmetry (CS_{PF}) was calculated as a ratio of the average paretic versus nonparetic soleus motor evoked potential amplitude. The ratio of the paretic and nonparetic peak ankle plantarflexion moments (PF_{sym}) was calculated at each speed.

Results: CS_{PF} predicted the ΔPF_{sym} from self-selected and fastest speeds ($R^2 = .629$, $F(1,21) = 35.56$, $p < .001$). An interaction between CS_{PF} and ΔPF_{sym} ($\beta = .596$, $p = .04$) was observed when predicting $\Delta speed$ ($_{adj}R^2 = .772$, $F(3,19) = 20.48$, $p < .001$). Specifically, the ΔPF_{sym} with speed modulation was positively related to the $\Delta speed$ ($p = .03$) in those with greater CS_{PF}, but was not related in those with poor CS_{PF} ($p = .30$).

Conclusions: Symmetry of the corticomotor input to the plantarflexors influences the propulsive strategy used to increase post-stroke walking speed.

Significance: Rehabilitation strategies that promote corticomotor symmetry may positively influence gait mechanics and enhance post-stroke walking function.

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1. Introduction

Following stroke, the majority of survivors are unable to regain sufficient walking function to allow for ambulation at speeds that are safe and effective for community function and participation (van de Port et al., 2008). In addition to typically slower walking speeds compared to neurologically-intact individuals, persons post-stroke are left with a reduced capacity to increase walking speeds (van de Port et al., 2008). The ability to modulate walking speed is clinically meaningful because it underlies an individual's capacity for safe and effective community function (Jonkers et al., 2009; van de Port et al., 2008). Altered muscular strength and

coordination leads to asymmetrical gait patterns that underlie post-stroke hemiparesis and limit walking function (Nadeau et al., 1999; Olney et al., 1994; Den Otter et al., 2007; Turns et al., 2007). In addition to biomechanical impairments, neurophysiologic measures of corticomotor pathway integrity to the lower extremity muscles have been shown to be related to lower extremity strength (Beaulieu et al., 2014) and walking function post-stroke (Hendricks et al., 2003; Steube et al., 2001; Palmer et al., 2016).

A critical factor in producing functional walking speeds is the ability to generate sufficient propulsion to advance the body's center of mass forward (Neptune et al., 2001). In fact, the most significant biomechanical contributor to limited post-stroke walking speeds has been identified as a deficiency in propulsive force generated by the paretic limb (Bowden et al., 2006; Nadeau et al., 1999; Neptune et al., 2001; Peterson et al., 2010). Knowledge of an individual's paretic plantarflexor contribution to forward propulsion can distinguish him or her between functional ambulation classifications of limited versus unlimited community ambulators (Bowden et al., 2008; Peterson et al., 2010). Further, rehabilitation strategies that improved paretic limb propulsion have also improved post-stroke walking function (Awad et al., 2014; Bowden et al., 2013). The two main contributors to forward propulsion are trailing limb angle and ankle plantarflexion moment (Hsiao et al., 2015a,b). The plantarflexion moment represents the net torque generated by the plantarflexor muscles that cross the ankle joint. Thus, the ability to activate the plantarflexor muscles plays a critical role in generating propulsion to attain and increase gait speeds in both neurologically-intact (Hsiao et al., 2015b) and stroke populations (Olney et al., 1994; Hsiao et al., 2015a; Peterson et al., 2010).

Although impaired paretic propulsion has been shown to be related to post-stroke walking function, analyzing the biomechanical strategies that individuals use to *increase* their gait speed reveals important impairments of walking function (Jonkers et al., 2009). In the presence of an inability to recruit the paretic plantarflexors, persons with post-stroke hemiparesis utilize a variety of compensatory strategies to achieve faster walking speeds. These include utilization of the paretic hip flexors (Nadeau et al., 1999; Jonkers et al., 2009) and compensation with the nonparetic limb (Jonkers et al., 2009). Amongst a heterogeneous stroke patient population, individuals may utilize different mechanisms (e.g. increase paretic plantarflexion moment or increase reliance on nonparetic plantarflexion moment) to achieve similar walking speeds (Allen et al., 2014). Previously, Jonkers et al. (2009) found that individuals who walked at slower speeds did not use paretic plantarflexion power to increase gait speed, but instead relied on increased nonparetic plantarflexion power (Jonkers et al., 2009). In contrast, individuals who walked at faster speeds increased both paretic and nonparetic plantarflexion power to increase gait speed, which is the strategy expected in neurologically-intact individuals (Jonkers et al., 2009). However, other studies have found that propulsion asymmetry between paretic and nonparetic legs is only weakly related to walking speed and that individuals walking at the same speed exhibit varying degrees of asymmetry, with some individuals improving paretic leg propulsion contribution (improved symmetry) and others relying heavily on the nonparetic leg (worse symmetry) (Bowden et al., 2006; Allen et al., 2014). Although it is clear that individuals utilize different biomechanical strategies to increase walking speed post-stroke and that such strategies are associated with the level of functional recovery, *previous research has failed to identify the underlying factors that determine the biomechanical strategy used to increase gait speed.*

Following stroke, disuse of the paretic limb coupled with heavy reliance on the nonparetic limb for functional activities have been shown to induce major cortical neuronal reconstruction (Kleim and

Jones, 2008) and influence corticomotor input to affected muscles (Harris-Love, 2013). Transcranial magnetic stimulation (TMS) is a noninvasive brain stimulation tool that is used to investigate the neurophysiologic components underlying post-stroke motor function and recovery by quantifying the strength of corticomotor input to specific muscles (Harris-Love, 2013). In the upper extremity, the strength of corticomotor input to the paretic arm and hand has been shown to be related to muscle activation, strength and function in individuals post-stroke (Dimyan and Cohen, 2010; Harris-Love, 2013) and can be used to predict an individual's ability to regain activation of those muscles and functional outcomes in response to a rehabilitation intervention (Koski et al., 2004). Additionally, abnormally increased corticomotor input to the nonparetic limb has been observed following stroke (Harris-Love, 2013; Traversa et al., 1998). The resulting corticomotor asymmetry between the paretic and nonparetic limbs has been shown to be related to poor upper extremity motor recovery (Koski et al., 2004). Though limited at this time, evolving research in the lower extremity has indicated that decreased corticomotor input to paretic leg muscles is related to poor function (Hendricks et al., 2003; Steube et al., 2001; Palmer et al., 2016; Beaulieu et al., 2014). Additionally, a recent study from our laboratory showed that contraction of the nonparetic tibialis anterior and activation of the nonlesioned hemisphere facilitated corticomotor input to the paretic tibialis anterior in those with slow walking speeds post-stroke (Palmer et al., 2016). This suggests that there may be a maladaptive influence of the nonparetic lower extremity on paretic limb walking function. However, little is known about the role of corticomotor input to the nonparetic leg and the influence of corticomotor asymmetry between paretic and nonparetic legs on *biomechanical walking function*. Further, studies to date have failed to investigate the role of corticomotor input to the *ankle plantarflexor muscles*, the primary contributors to forward propulsion during walking.

A better understanding of possible interactions between biomechanical and neurophysiologic factors that affect walking function post-stroke could be crucial for the development of effective rehabilitation approaches. The purpose of this study was to investigate the influence of lower extremity corticomotor input on the propulsive strategy used to modulate walking speed post-stroke. Specifically, we aimed to determine (1) the relationship between the symmetry of corticomotor input to the plantarflexor muscles versus the changes in plantarflexion moment symmetry and (2) if symmetry of corticomotor input to the plantarflexors moderates the relationship between change in plantarflexion moment symmetry and change in walking speed. We hypothesized that there would be a positive relationship between plantarflexor corticomotor symmetry and changes in plantarflexion moment symmetry with increases in walking speed. Additionally, there will be an interaction between change in ankle plantarflexion moment and plantarflexion corticomotor symmetry, with individuals with the most symmetrical corticomotor input to paretic and nonparetic plantarflexors improving relative paretic ankle moment contribution with increases in walking speed.

2. Methods

Twenty-three individuals with chronic stroke (>6 mo.) (15 males, mean time since stroke 50 ± 59 mo., mean age 61.5 ± 8.4 years) and hemiparesis were recruited. All participants gave written informed consent and the protocol was approved by the University of Delaware's Institutional Review Board. Participants sustained a single cortical or subcortical stroke, were able to walk for at least 1 min without an orthotic and without the assistance of another person, and had sufficient ankle passive range of motion to allow the paretic ankle joint to reach the neutral

position with the knee extended. Exclusion criteria included >1 previous stroke, cerebellar involvement, pain in the lower extremities, and any unsafe TMS testing criteria (Rossi et al., 2009).

2.1. Gait and clinical testing

All participants underwent biomechanical and clinical evaluations. Participants performed an overground 10 m walk test to quantify self-selected and fastest walking speeds (Awad et al., 2014). An average of 3 tests for each speed was used. Kinetic and kinematic data were collected with an 8-camera motion capture system (Motion Analysis 3D Eagle, Santa Rosa, CA) while participants walked at their self-selected and fastest speeds on a dual-belt treadmill (Bertec Corp., Columbus, OH, USA) for a total of 1 min at each speed (Awad et al., 2014). The treadmill was instrumented with 2 independent 6° of freedom force platforms that measured ground reaction forces at 1080 Hz.

2.2. Assessment of corticomotor input to plantarflexors

Monophasic magnetic stimuli with a 100 μs approximate rise time and a 1.0 ms total duration were delivered using a magnetic stimulator (Magstim 200^2, MagStim Ltd., Wales, UK) through a custom batwing coil (maximal output 2 Tesla, each wing 11 cm in diameter, angle between windings 65°). Participants wore an elastic cap and were seated upright comfortably with knee and ankle angles positioned at 90° and both feet resting on the floor. EMG activity was recorded from double differential surface electrodes with integrated ground (BL-AE, B&L Engineering, Santa Ana, CA) that were carefully positioned and secured to the skin over the lateral soleus and tibialis anterior (TA) muscles of the paretic and nonparetic legs using a 6 channel active EMG system (BL-EMG-6, B&L Engineering, Santa Ana, CA). EMG data were sampled at a rate of 2000 Hz with a 330 gain set on a 16 bit data acquisition board (National Instruments NI USB-6341), band-pass filtered at 15–450 Hz and saved for offline analysis. The experimenter began with the midpoint of the coil aligned antero-posteriorly to the vertex of the skull so that the induced electrical current traveled in the anterior direction within the cortex (Devanne et al., 1997). Stimulation began at sub-threshold intensity with the coil positioned at the vertex and gradually increased to an intensity where a visible motor evoked potential (MEP) was observed within the TA on the targeted side on real-time EMG. During the search for the optimal coil position for eliciting lower extremity MEPs, the coil was moved over the scalp as magnetic stimuli of suprathreshold intensity were delivered and participants were asked to maintain a light dorsiflexion contraction of the targeted leg while real-time EMG and MEPs from the TA were observed (Palmer et al., 2016). The optimal coil location was determined to be the location that elicited MEPs of greatest amplitude at a given location. Approximately 20–30 stimuli were applied during the search for the optimal position for each targeted muscle for each participant. We chose to use the TA as a guide in the search for the optimal lower extremity coil location because paretic soleus MEPs could not be elicited in all participants, even when participants maintained an effortful plantarflexion contraction (see results section for full description). Our pilot testing indicated that no discernable difference in optimal coil locations existed between the TA and soleus muscles of the same leg.

The optimal location for eliciting an MEP for the paretic and nonparetic lower extremity was identified and carefully marked on the cap. Next, the setting and triggering of TMS pulses and EMG collection were performed using Custom LabVIEW software (National Instruments, Austin, TX). Throughout the trial, participants maintained a light plantarflexion contraction at 15% of their maximal volitional soleus EMG activity produced during a maximal voluntary isometric contraction. Real-time EMG biofeedback was provided to assist participants in maintaining a constant level of muscle activity. If a participant was unable to produce or maintain a 15% contraction, they were asked to produce an observable increase in EMG that they could maintain. Participants were allowed to rest if they reported fatigue or if a notable decrease in muscle activity was observed. TMS pulses were applied at intervals of 3% of the stimulator's output intensity from subthreshold through 100% maximum output intensity at a frequency of 0.2 Hz to produce a stimulus-response curve (Mathias et al., 2014; Needle et al., 2013). Only MEP responses to 100% MSO are presented here. An additional 3–10 pulses were delivered at 100% maximum stimulator output intensity to each muscle.

All MEP amplitudes were normalized to the maximal response to peripheral nerve stimulation (Mmax). The tibial nerve was located in the popliteal fossa and stimulated using a custom electrical stimulator to activate the soleus muscle. Surface stimulation was delivered to the nerve using 1 ms square electrical pulses of gradually increasing intensities until no increase in the M-wave was observed within the soleus muscle. The same testing procedures were performed for the paretic and nonparetic soleus muscles.

2.3. Data reduction and analyses

Cortex and Visual3D software programs (C-Motion Inc., Bethesda, MD, USA) were used for data processing. Kinematic and kinetic data were filtered using a bi-directional Butterworth low-pass filter at 6 and 30 Hz, respectively. Peak ankle plantarflexion moment resolved into the shank coordinate system was calculated for each limb during the stance phase of gait. An average of the peak plantarflexion moment for each limb was taken for all strides for each subject during two 30 s walking bouts at each speed.

Peak ankle plantarflexion moment was the biomechanical variable of interest in this study due to its temporal correlation with peak soleus muscle EMG activity during walking (Bogey et al., 2005; Buchanan et al., 2005), its relationship to self-selected and fastest walking speeds (Beaman et al., 2010), and, in contrast to plantarflexion power or anterior ground reaction forces, its relative independence from other joint segments (e.g. hip flexion moment on ankle joint power or the trailing limb position on anterior ground reaction forces) (Hsiao et al., 2015a,b). Ankle plantarflexion moment symmetry (PF$_{sym}$) was calculated for each participant at each speed as the average paretic plantarflexion moment divided by the average nonparetic plantarflexion moment. Change in PF$_{sym}$ (ΔPF$_{sym}$) was calculated for each participant as the difference in PF$_{sym}$ between self-selected and fast speeds. MEP amplitude was quantified as the peak-to-peak value of the EMG response within a 100 ms window duration beginning at 10 ms post stimulus artifact. Using this method, MEP amplitude is a continuous variable. For each participant, the average of the normalized, peak-to-peak MEP amplitudes at 100% of the magnetic stimulator output intensity (MEP$_{100}$) was determined for each the paretic and nonparetic soleus muscles. Symmetry of the corticomotor input to the plantarflexors (CS$_{PF}$) was calculated for each participant as the paretic soleus MEP$_{100}$ divided by the nonparetic soleus MEP$_{100}$. For both measures of symmetry, a value of 1.0 indicates perfect symmetry, with the paretic and nonparetic values being equal in magnitude; a value greater than 1 indicates the paretic was greater than the nonparetic; a value less than 1.0 indicates the paretic was less than the nonparetic.

Simple linear regression was first used to evaluate the relationship between the ΔPF$_{sym}$ observed between participants' self-selected and fast walking speeds and CS$_{PF}$. Next, bivariate correlations between CS$_{PF}$, ΔPF$_{sym}$, and change in walking speed were

evaluated. Subsequently, moderated multiple linear regression was used to evaluate how CS_{PF} moderated the relationship between ΔPF_{sym} and Δwalking speed. Specifically included in the model were CS_{PF}, ΔPF_{sym}, and the interaction $CS_{PF} \times \Delta PF_{sym}$. Briefly, the relationship between ΔPF_{sym} and Δwalking speed were compared for participants with good (symmetry = 1.0) and poor (symmetry = 0.0) CS_{PF}. All analyses were performed using SPSS version 22 with α set to 0.05.

3. Results

Complete data sets were obtained for all 23 participants (see Table 1). Consistent presence of MEPs, traditionally defined as MEPs with an amplitude of greater than 50 microvolts in more than 50% of trials (Schambra et al., 2015; Cacchio et al., 2011), could not be defined in the paretic soleus muscle in 7 out of the 23 participants, despite stimulation at 100% MSO. Out of these 7 participants, 4 produced small (<50 microvolts) but consistent (>50% of trials) MEPs with stimulation intensity at 100% MSO. In 3 other participants no observable MEP could be produced in the paretic soleus muscle (see Table 1). However, we thought that it was important to include these participants, as they generally represented individuals of the lowest functional levels (self-selected gait speed 0.40 ± 0.32 m/s). For this reason we chose to use a TMS outcome measure that would allow us to treat MEP amplitude as a continuous variable using a constant stimulator output intensity across all participants (i.e. 100% MSO). Thus, we were able to calculate CS_{PF} symmetry for all participants by using MEP amplitude within this time window, regardless of the size of the MEP. For the 3 participants for whom no observable MEP of any size could be elicited, the background EMG within the observed cortical silent period was used, a value very close to zero. Example data from participants with good and poor corticomotor symmetry are presented in Fig. 1. Optimal coil placement was found to be $1.8 \pm .7$ cm anterior and 1.5 ± 2.2 cm contralateral to the vertex in

the paretic leg and $2.0 \pm .8$ cm anterior and $2.5 \pm .8$ cm contralateral to the vertex in the nonparetic leg. In 2 participants (S20 and S22) the optimal coil position for the paretic leg was found to be centered over the ipsilateral (contralesional) hemisphere. Optimal coil locations for the paretic and nonparetic legs of all other participants were consistently found to be centered over the contralateral hemisphere of the targeted muscle.

Participants' CS_{PF} explained 63% of the variance in the ΔPF_{sym} observed when participants increased their walking speeds ($F(1,21) = 35.56$, $p < 0.001$, $R^2 = 0.629$) (Fig. 2). Although ΔPF_{sym} was positively correlated to Δwalking speed ($r = 0.36$, $p = 0.05$) (Fig. 3), CS_{PF} was not ($r = 0.32$, $p = 0.07$). Interestingly, neither ΔPF_{sym} ($\beta = -0.26$, $p = 0.30$) nor CS_{PF} ($\beta = -0.04$, $p = 0.89$) independently explained the observed Δwalking speed when accounting for the interaction between these two variables ($\beta = 0.60$, $p = 0.04$). Specifically, CS_{PF} was found to moderate the relationship between ΔPF_{sym} and Δwalking speed ($_{adj}R^2 = 0.77$, $F(3,19) = 20.48$, $p < 0.001$). The model predicted a strong positive relationship ($p = 0.03$) between ΔPF_{sym} and Δwalking speed in individuals with high levels of corticomotor symmetry (symmetry = 1.0), indicating that those individuals with greatest CS_{PF} increase their walking speed by improving the contribution of their paretic ankle moment relative to their nonparetic ankle moment. The model predicted a non-significant negative relationship ($p = 0.30$) between ΔPF_{sym} and Δwalking speed in those with poor corticomotor symmetry (symmetry = 0.0), indicating that those individuals with poor CS_{PF} and a paretic soleus MEP_{100} equal to zero increase their walking speed by *decreasing* the contribution of their paretic ankle moment relative to their nonparetic ankle moment (Fig. 4).

4. Discussion

This study provides novel evidence that the balance of corticomotor input to the paretic and nonparetic plantarflexor muscles is an underlying factor that influences the biomechanical strategy

Table 1
Individual participant ($N = 23$) gait speeds, MEP_{100} (% Mmax), and plantarflexion moment results.

Participant no.	Self-selected gait speed (m/s)	Fast gait speed (m/s)	Paretic MEP_{100} (% Mmax)	Nonparetic MEP_{100} (% Mmax)	CS_{PF}	Self-selected speed			Fast speed			Change PF_{sym}
						Paretic PF	Nonparetic PF	PF_{sym}	Paretic PF	Nonparetic PF	PF_{sym}	
01	1	1.1	7.3	10.0	0.726	0.127	0.156	0.815	0.126	0.161	0.782	−0.034
02[†]	1.07	1.51	1.6	15.8	0.099	0.115	0.187	0.613	0.128	0.235	0.543	−0.070
03	1	1.32	8.5	11.8	0.717	0.101	0.142	0.708	0.113	0.134	0.841	0.132
04	0.74	0.85	4.1	29.0	0.140	0.061	0.083	0.731	0.066	0.097	0.681	−0.050
05	1.13	1.37	1.3	32.4	0.040	0.142	0.162	0.876	0.124	0.160	0.777	−0.099
06	1.16	1.59	5.6	15.6	0.359	0.126	0.154	0.814	0.140	0.173	0.806	−0.008
07	1.44	1.55	4.0	6.6	0.606	0.122	0.122	1.001	0.130	0.121	1.077	0.076
08	0.94	1.11	1.1	7.3	0.152	0.122	0.118	1.031	0.121	0.129	0.935	−0.096
09	0.92	1.05	4.7	15.8	0.299	0.118	0.147	0.803	0.120	0.153	0.783	−0.019
10	1.01	1.11	17.5	25.4	0.689	0.145	0.128	1.140	0.153	0.131	1.170	0.030
11	0.35	0.83	5.4	7.4	0.728	0.072	0.131	0.547	0.108	0.162	0.665	0.118
12[†]	0.18	0.6	3.6	12.5	0.283	0.062	0.131	0.474	0.063	0.134	0.466	−0.008
13	0.26	0.38	3.4	4.5	0.753	0.061	0.083	0.736	0.068	0.095	0.721	−0.016
14[†]	0.32	0.38	5.0	16.7	0.297	0.000	0.072	0.000	0.000	0.076	0.000	0.000
15[*]	0.32	0.33	0.3	25.5	0.012	0.000	0.046	0.000	0.000	0.051	0.000	0.000
16[†]	0.09	0.24	1.8	10.0	0.177	0.001	0.055	0.016	0.000	0.055	0.000	−0.016
17[*]	0.4	0.51	0.7	11.8	0.060	0.102	0.111	0.915	0.101	0.119	0.854	−0.061
18[*]	0.43	0.96	0.9	12.6	0.068	0.115	0.161	0.715	0.116	0.169	0.686	−0.029
19	0.45	0.78	8.0	8.2	0.981	0.060	0.099	0.605	0.085	0.112	0.765	0.159
20[∞]	0.53	0.73	12.8	27.8	0.459	0.115	0.130	0.888	0.126	0.145	0.870	−0.018
21	1	1.37	15.4	13.2	1.166	0.121	0.121	0.995	0.152	0.140	1.088	0.094
22[∞]	0.6	0.9	18.3	20.9	0.876	0.131	0.163	0.806	0.158	0.175	0.901	0.095
23	0.81	1.1	6.7	9.1	0.734	0.137	0.141	0.977	0.151	0.147	1.024	0.047

CS_{PF} = corticomotor symmetry of plantarflexors; PF = plantarflexion ankle moment; PF_{sym} = symmetry of plantarflexion ankle moment.
[†] Indicates that the observable MEP was <50 microvolts.
[*] Indicates that no observable MEP was detected.
[∞] Indicates that the optimal location for stimulating the paretic leg was found to be centered over the ipsilateral hemisphere.
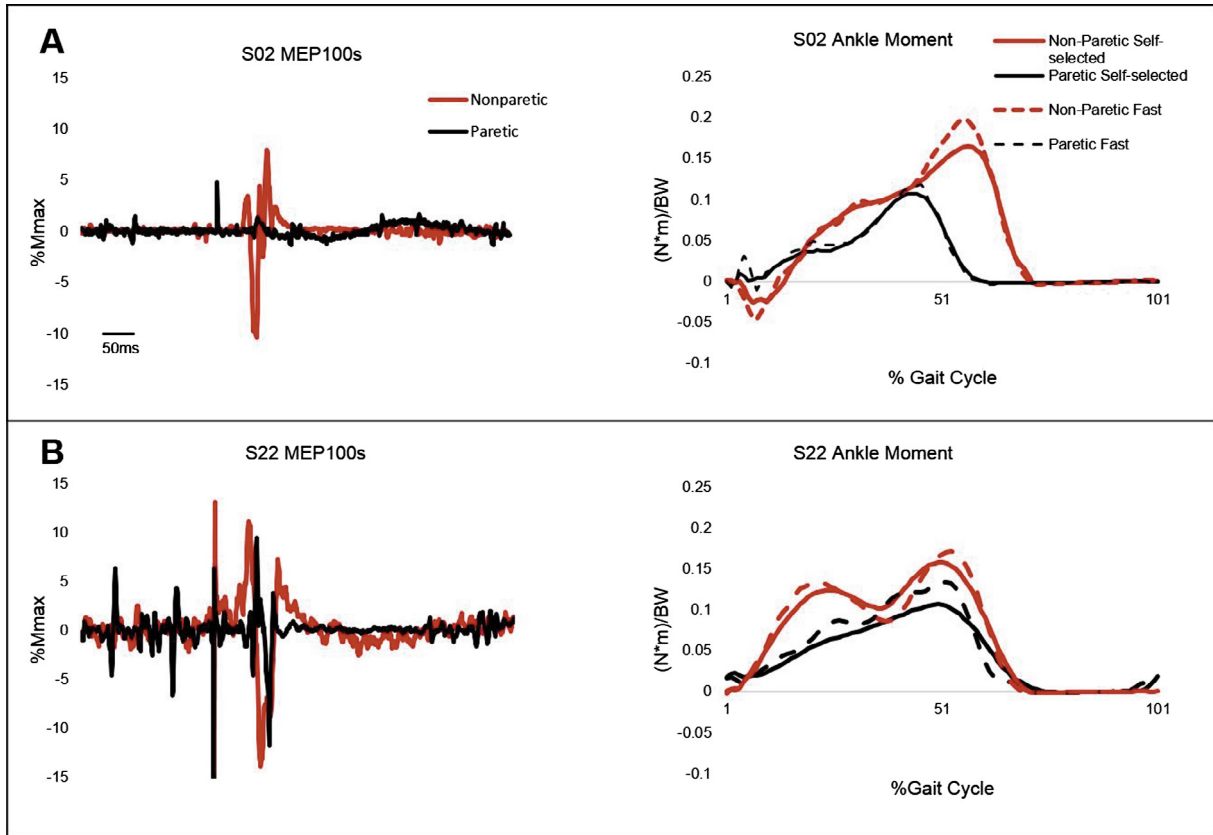
Fig. 1. Raw soleus MEP_{100} data (left column) and average plantarflexion moments over all strides for paretic and nonparetic legs (right column) are shown for a participant with poor (A) and good (B) corticomotor symmetry.
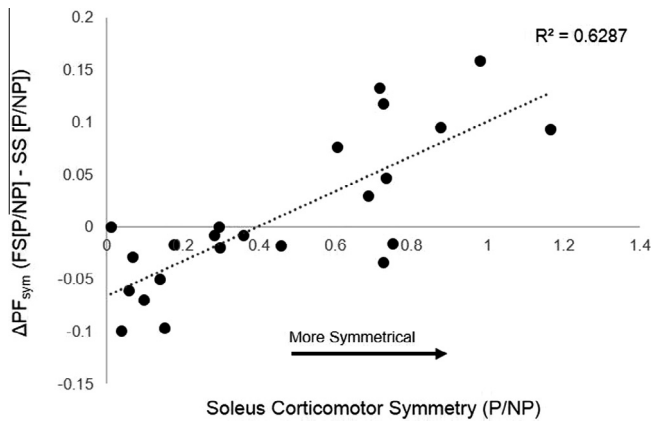

Fig. 2. The relationship between corticomotor symmetry (paretic (P) MEP_{100}/nonparetic (NP) MEP_{100}) and change in plantarflexion moment symmetry (ΔPF_{sym}) (paretic plantarflexion moment/nonparetic plantarflexion moment) from self-selected (SS) to fastest walking (FS) walking speed ($F(1,21) = 35.56$, $p < 0.001$, $R^2 = 0.629$) ($n = 23$).

Fig. 3. The relationship between change in plantarflexion moment symmetry (ΔPF_{sym}) (paretic (P) plantarflexion moment/nonparetic (NP) plantarflexion moment) from self-selected (SS) to fastest walking (FS) speed and change in walking speed (FS–SS) ($r = 0.36$, $p = 0.05$) ($n = 23$).

used to increase walking speed in individuals post-stroke. Specifically, we observed that more symmetrical corticomotor input to the paretic and nonparetic plantarflexor muscles was associated with increases in PF_{sym} when walking at faster speeds (see Fig. 2). Additionally, we found that participants with low levels of corticomotor symmetry to plantarflexors were not likely to increase walking speed through more symmetrical plantarflexor moments, but those with high levels of corticomotor symmetry to plantarflexors were (see Fig. 4). These findings reveal how the neurophysiologic characteristics of individuals with chronic stroke
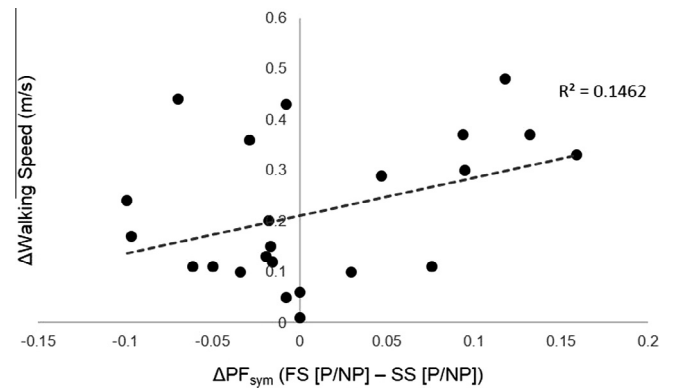
may influence the biomechanical strategies used to increase walking speed. These results thus have important implications for post-stroke rehabilitation.

Consistent with previous literature, changes in PF_{sym} were weakly correlated to changes in walking speed (Allen et al., 2014; Bowden et al., 2006). Nonetheless, change in PF_{sym} and CS_{PF} alone were not significant predictors of change in walking speed. Our data suggest that, despite having poor changes in PF_{sym} and poor CS_{PF}, some individuals were still able to sufficiently increase walking speed through reliance on the nonparetic limb (see Table 1). However, the *interaction* between change in PF_{sym} and CS_{PF} was the only significant predictor of change in walking speed. In the present study, individuals with good CS_{PF} generally
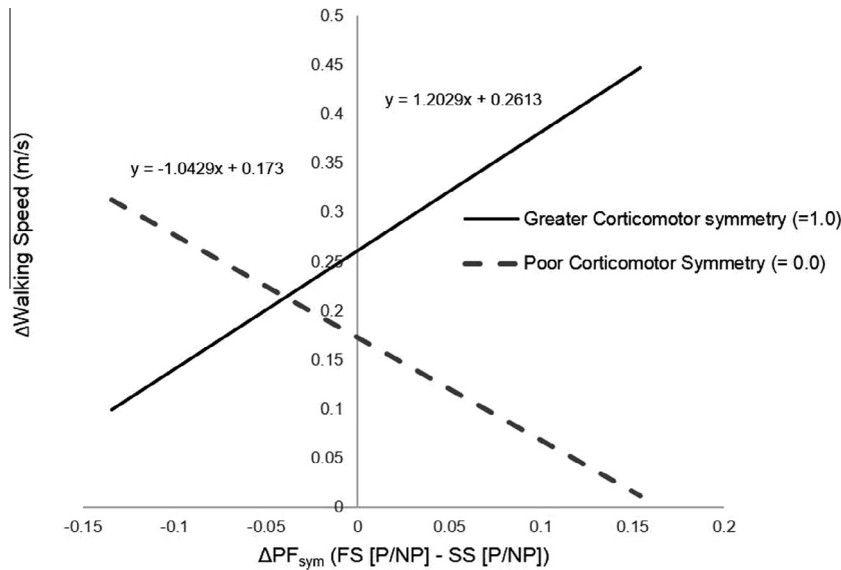
Fig. 4. Moderation effect of corticomotor symmetry on the relationship between change in plantarflexion moment symmetry from self-selected to fastest walking speed (ΔPF_{sym}) (±2 standard deviations from the mean) and change in walking speed. There was a positive relationship ($p = 0.03$) between ΔPF_{sym} and change in walking speed in individuals with high levels of corticomotor symmetry (symmetry = 1.0) and a non-significant negative relationship ($p = 0.30$) between ΔPF_{sym} and Δwalking speed in those with poor corticomotor symmetry (symmetry = 0.0).

increased their paretic plantarflexion moment (see Table 1), leading to improvements in PF_{sym} to reach their fastest walking speed (see Fig. 4). Information about the symmetry of the corticomotor input to the plantarflexors thus appears to provide information about the *capacity* to improve the paretic limb's contribution to propulsion in post-stroke ambulation. Our data suggest that those with greater corticomotor symmetry possess sufficient intact corticomotor pathways to allow for increased paretic plantarflexor recruitment to meet the increased propulsive demands required for faster walking speeds (Hsiao et al., 2015a,b). In contrast, individuals with poor corticomotor symmetry seem to possess weaker corticomotor pathways to the paretic plantarflexors and may have saturated their ability to recruit paretic plantarflexors at slower self-selected gait speeds (Jonkers et al., 2009). These individuals were, therefore, forced to rely on nonparetic plantarflexors and other compensatory strategies to increase propulsion when walking at faster speeds. The lack of significance in the relationship between change in PF_{sym} and change in walking speed in individuals with poor CS_{PF} could be because these individuals adopt a variety of compensation strategies in addition to the increased nonparetic plantarflexion moment. For example, increases in trailing limb angle (Hsiao et al., 2015a) or hip flexion power (Jonkers et al., 2009; Nadeau et al., 1999) with walking speed modulation could introduce variability to this relationship. The results of this study indicate that changes in biomechanical patterns alone are not sufficient to accurately predict changes in walking speed, but that knowledge of the balance of corticomotor input to each limb is critical for predicting functional ambulation ability.

This is the first study to investigate the relationship between plantarflexor corticomotor excitability measures and the kinetics of walking in individuals post-stroke. Indeed, this is a challenging area of research when utilizing traditional measures of corticomotor excitability. Previous studies with stroke have utilized corticomotor excitability measures that were a function of TMS motor threshold (Beaulieu et al., 2014; Prashantha et al., 2013; Dimyan and Cohen, 2010; Traversa et al., 2000). This approach has been particularly challenging in lower extremity muscles such as plantarflexors that receive less cortical input and have higher motor thresholds (Petersen et al., 2001; Capaday, 2002). Thus, likely due to methodological limitations, we are not aware of any studies that

have previously studied post-stroke corticomotor measures in the soleus, a muscle that plays a crucial role in generating propulsion during walking. Such conventional methods that rely on use of motor threshold do not allow for the inclusion of the most impaired participants, who typically have the highest motor thresholds (i.e. >90% MSO) or have or absent MEPs in the paretic leg. By utilizing a method where a constant intensity is used across subjects, we were able to collect data for all participants, including those without the presence of an MEP response in the paretic soleus muscle. For these participants, their corticomotor symmetry values were close to zero, enabling our model to predict the propulsion strategy used to increase walking speed in individuals across the full spectrum of asymmetries and levels of functional walking recovery. Future studies aiming to study post-stroke individuals of low-level function may consider utilizing such measures.

Results of this study show that symmetry of corticomotor input to the lower extremity is related to gait impairments and influences kinetics of walking function in individuals with chronic stroke. Thus, the corticomotor patterns of lower extremity motor recovery appear similar to those of the upper extremity (Koski et al., 2004; Traversa et al., 1998). Previous research has suggested that rehabilitation does not sufficiently target the function of the paretic limb and generally leads to strengthening of compensation strategies instead of learning to utilize more optimal gait patterns, limiting functional outcomes (Hall et al., 2012). Reliance on ankle-foot orthoses or assistive devices commonly used in neurologic rehabilitation immobilizes and promotes disuse of the paretic limb, leading to further degradation of paretic limb function (Kleim and Jones, 2008). Indeed, heavy reliance on one limb coupled with disuse of the other limb is related to major cortical neuroplastic changes that lead to corticomotor imbalances (Koski et al., 2004; Kleim and Jones, 2008). Interestingly, learning new motor skills can increase corticomotor input to paretic limb muscles and decrease input to the nonparetic limb muscles, promoting greater corticomotor symmetry (Koski et al., 2004; Muellbacher et al., 2001). It is possible that rehabilitation strategies that promote disuse of the paretic leg strengthen compensation with the nonparetic leg, resulting in an imbalance of corticomotor input to paretic and nonparetic plantarflexors. Future research could determine if rehabilitation strategies shown to promote corticomotor

symmetry in the upper extremity (Koski et al., 2004) can also improve corticomotor balance in the lower extremity and lead to positive changes in gait biomechanical and walking function.

4.1. Limitations

Due to the cross-sectional design of the present study, it is not clear if corticomotor imbalances lead to biomechanical impairments or if they result from observed compensation strategies. In this study, measures of plantarflexion moment were reported because of its specificity to the plantarflexor muscle contribution to propulsion. However, we did not investigate other factors that could also affect propulsion and influence gait speed, such as the position of the trailing limb during late stance, which could explain additional variability in the model. In lower extremity TMS experimentation, the anatomy of lower extremity muscle representation within the motor cortex makes it improbable that one hemisphere can be stimulated in isolation, particularly at high stimulator output intensities. Thus, it is difficult to discern differential hemispheric contributions to the observed corticomotor asymmetries. Additionally, because optimal coil locations for the paretic leg in 2 participants were found to be centered over the ipsilateral hemisphere relative to the vertex, it is possible that different corticomotor mechanisms (e.g. corticomotor pathways from the contralesional hemisphere to the paretic soleus) contributed to symmetry of corticomotor input between paretic and nonparetic plantarflexors. Future research utilizing imaging techniques could provide important and more precise spatial information about cortical origins of motor pathways to the paretic limb and its effect on walking recovery. In this study the TA muscle was used to identify the location for coil positioning. It is possible that this location was not the best for stimulation of the soleus muscle and may have decreased the actual value for soleus MEP_{100}s. However, our pilot testing showed there was no discernible difference between the optimal coil locations of the TA and soleus muscle of the same leg. If this did occur, then coil position would likely affect both the paretic and nonparetic soleus MEP_{100}s and would have minimal effect on the soleus corticomotor symmetry value. All corticomotor data in the present study were collected while participants were seated performing a sustained volitional unilateral muscle contraction and it is possible that the strength of corticomotor input could change with walking. All participants in the present study were able to walk without an orthosis or assistance of another person, making results ungeneralizable to all individuals post-stroke.

5. Conclusions

The present study provides novel evidence that symmetry of corticomotor input to the lower extremity muscles of persons post-stroke underlies gait impairments and influences walking function. Measures of corticomotor input may assist clinicians in identifying the most effective rehabilitation strategies for each individual to maximize walking function post-stroke following stroke. Post-stroke gait rehabilitation interventions should target strategies to promote symmetry of corticomotor input to the plantarflexor muscles to enhance biomechanical contributions from the paretic lower extremity during walking.

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