Single Session of Functional Electrical Stimulation-Assisted Walking Produces Corticomotor Symmetry Changes Related to Changes in Poststroke Walking Mechanics

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Background. Recent research demonstrated that the symmetry of corticomotor drive with the paretic and nonparetic plantarflexor muscles was related to the biomechanical ankle moment strategy that people with chronic stroke used to achieve their greatest walking speeds. Rehabilitation strategies that promote corticomotor balance might improve poststroke walking mechanics and enhance functional ambulation.

Objective. The study objectives were to test the effectiveness of a single session of gait training using functional electrical stimulation (FES) to improve plantarflexor corticomotor symmetry and plantarflexion ankle moment symmetry and to determine whether changes in corticomotor symmetry were related to changes in ankle moment symmetry within the session.

Design. This was a repeated-measures crossover study.

Methods. On separate days, 20 people with chronic stroke completed a session of treadmill walking either with or without the use of FES of their ankle dorsi- and plantarflexor muscles. We calculated plantarflexor corticomotor symmetry using transcranial magnetic stimulation and plantarflexion ankle moment symmetry during walking between the paretic and the nonparetic limbs before and after each session. We compared changes and tested relationships between corticomotor symmetry and ankle moment symmetry following each session.

Results. Following the session with FES, there was an increase in plantarflexor corticomotor symmetry that was related to the observed increase in ankle moment symmetry. In contrast, following the session without FES, there were no changes in corticomotor symmetry or ankle moment symmetry.

Limitations. No stratification was made on the basis of lesion size, location, or clinical severity.

Conclusions. These findings demonstrate, for the first time (to our knowledge), the ability of a single session of gait training with FES to induce positive corticomotor plasticity in people in the chronic stage of stroke recovery. They also provide insight into the neurophysiologic mechanisms underlying improvements in biomechanical walking function.

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Restoration of walking function following stroke is a primary goal of patients following stroke.[1] However, despite often intensive rehabilitation efforts, the majority of people never achieve poststroke walking speeds that allow for safe and effective community function.[2] The failure of conventional rehabilitation strategies to allow people to regain poststroke walking ability results in part from our lack of understanding of the neural mechanisms underlying motor recovery[2] combined with inadequately targeting key biomechanical factors that limit walking speed and economy.[3–5]

Despite the current focus of conventional post stroke gait rehabilitation on ankle dorsiflexion dysfunction, reduced paretic limb propulsive force and ankle power have been consistently identified to be the most significant contributors to walking speed impairments[6,7] and can determine whether an individual is categorized as a limited community or unlimited community ambulator.[8] In the presence of lost paretic limb function following stroke, many people increase their reliance on the nonparetic limb to generate propulsive force to achieve reduced walking speeds.[9] The resulting asymmetrical gait patterns continue into the chronic phase of poststroke motor recovery, even when the capacity to regain paretic limb function may exist.[10] When effectively improved, paretic limb propulsion can increase poststroke walking function.[11,12] However, the neural factors limiting these biomechanical determinants of poststroke walking ability and the capacity for walking recovery are poorly understood and create a barrier to current rehabilitation approaches.

Nonuse in 1 extremity coupled with heavy reliance on the contralateral extremity has been shown to result in major imbalances of cortical excitation and inhibition.[13,14] In the upper extremity, a decrease in corticomotor activity in the lesioned hemisphere coupled with over-activity in the nonlesion hemisphere has been consistently observed.[15–17] The resulting hemispheric imbalance and asymmetry of corticomotor drive to the paretic and nonparetic arm and hand has been shown to be related to poor motor recovery.[18–20] Additionally, poststroke disruptions in interactions between the somatosensory cortex and the primary motor cortex can profoundly influence the balanced pattern of cortical excitation and inhibition within and between hemispheres that is essential for normal motor function.[21] Recently, work from our laboratory found that corticomotor symmetry to the paretic versus nonparetic plantarflexor muscles predicted the biomechanical propulsive strategy that people with chronic stroke used when asked to increase walking speed.[22] Specifically, people with the greatest corticomotor symmetry between limbs increased their walking speed by improving the propulsive contribution of the paretic leg, reducing propulsive asymmetries between limbs. People with the least corticomotor symmetry increased their walking speed by increasing reliance on propulsive contribution of the nonparetic leg, magnifying their gait asymmetries.[22] It is conceivable that rehabilitation strategies that promote improvements in corticomotor balance between limbs could improve biomechanical factors that limit poststroke walking speed.

Functional electrical stimulation (FES) is a rehabilitation strategy that temporally couples electrical stimulation of motor and sensory nerve fibers during performance of a functional motor task and may target neural pathways that could restore poststroke hemispheric imbalances.[23–26] Recently, studies using neuroimaging and noninvasive brain stimulation techniques have investigated the effect of FES on corticomotor function. Specifically, the long-term use of FES during rehabilitation activities improved motor function, increased corticomotor drive to the paretic limb, and shifted the focus of brain activity from the nonlesion to the lesion sensorimotor cortex during a paretic hand motor task.[23–26] In the lower extremity, an increase in corticomotor input to the tibialis anterior[27] and improved timing of paretic dorsiflexor activation during walking have been observed following long-term use of FES of the paretic dorsiflexors.[28] Gandolla et al[29] demonstrated that FES coupled with volitional dorsiflexion increased the sensitivity of the primary somatosensory cortex selectively to primary motor cortex projections. Together these studies provide strong evidence for the potential effectiveness of the use of FES to induce positive neuroplasticity and show that FES targets the potentially maladaptive corticomotor pathways associated with poor motor function following stroke. However, though single session corticomotor changes can be predictive of poststroke long-term functional improvements,[19] no previous studies have investigated FES-induced corticomotor plasticity in response to a single session of rehabilitation in either upper or lower extremities in people with stroke. Additionally, previous research using FES in poststroke gait rehabilitation has focused on the paretic dorsiflexors. Although it has been shown that plantarflexor motor impairments are more likely to limit poststroke walking function than that of dorsiflexors, few previous studies have investigated corticomotor excitability of the plantarflexor muscles after stroke and no previous studies have investigated how the changes in corticomotor excitability to the plantarflexor muscles relate to changes in walking mechanics.

Thus, there is a substantial gap in our understanding of the neurophysiologic underpinnings of the salient biomechanical limitations of poststroke walking function, and how changes in neural mechanisms might affect these gait mechanics. Further, previous research in the upper extremity has demonstrated the important prognostic ability of corticomotor response to a single session of rehabilitation in predicting individual poststroke functional outcomes to a long-term intervention.[19] However, to date no previous studies have investigated FES-induced corticomotor plasticity in response to a single session of rehabilitation in people with poststroke walking disability. Additionally, little is known about the immediate neural effects that may occur when an individual adopts his or her own biomechanical walking pattern, particularly compared to those that may be induced with specific gait intervention strategies such as FES. Therefore, the purposes of this study were to test the effectiveness of a single session of FES gait training for

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improving plantarflexion ankle moment symmetry and corticomotor symmetry of plantarflexor muscles compared to a session of walking without stimulation and to determine the relationship between changes in corticomotor symmetry and changes in ankle moment symmetry within the session.

Methods

For this study we recruited 20 people with chronic stroke (>6 months) (16 men, mean time since stroke=42 months [SD=35], mean age=59.5 years [SD=12.0], mean self-selected walking speed=0.67 m/s [SD=0.24], range of walking speed=0.14–1.0 m/s, lower extremity Fugl-Meyer score=22 [SD=6]). All participants gave written informed consent, and the experimental protocol was approved by the University of Delaware Institutional Review Board. All participants had lower extremity hemiparesis with visually detectable gait deficits as determined by the license physical therapist, sustained a single cortical or subcortical stroke, sufficient ankle range of motion to reach neutral with the knee fully extended, and were able to walk for at least 6 minutes on a treadmill without an orthotic and without the assistance of another person. Exclusion criteria included more than 1 previous stroke, cerebellar involvement, pain in the lower extremities, and any unsafe TMS testing criteria.[30]

Biomechanical Testing

All participants performed a 10-m walk test to quantify their self-selected walking speeds. The walk test was completed 3 times, and the average was used to the participant's treadmill walking speed during biomechanical testing and gait training. Handrail use was discouraged but participants were permitted to use a light touch on lateral handrails if necessary for balance and safety. If a handrail strategy was used, this was held constant pre- and posttesting and between sessions. Kinetic and kinematic data were collected with an 8-camera motion capture system (Motion Analysis 3D Eagle; Motion Analysis Corp, Santa Rosa, California) while participants walked on a dual-belt instrumented treadmill (Bertec Corp, Columbus, Ohio) for a total of 1 minute immediately before and after each gait training session. The treadmill was instrumented with 2 independent 6-degree-of-freedom force platforms that measured ground reaction forces at 1,080 Hz.

Assessment of Corticomotor Excitability to Plantarflexors

A magnetic stimulator (Magstim 200^2; The Magstim Company Ltd, Carmarthenshire, United Kingdom) was used to deliver monophasic magnetic pulses with an approximate 100-microsecond rise time and a 1.0-millisecond total duration through a custom batwing coil (maximal output=2 T, diameter of each wing=11 cm, angle between windings=65°). All participants were seated upright in an arm chair with both feet resting on the floor and knees and ankles positioned at approximately 90 degrees. Electromyographic (EMG) activity was recorded from each participant's plantarflexor and dorsiflexor muscles using a 6-channel active EMG system (BL-EMG-6; B&L Engineering, Santa Ana,California) and double differential surface electrodes that had an integrated ground (BL-AE; B&L Engineering) and that were carefully positioned and secured to the skin over the lateral soleus and tibialis anterior (TA) muscles of the paretic and nonparetic legs. EMG data were sampled at a rate of 2,000 Hz with a 330 gain set on a 16-bit data acquisition board (NI USB-6341; National Instruments, Austin, Texas) and band-pass filtered at 15 to 450 Hz. The coil was aligned posterior-anteriorly to the vertex of the skull so that the induced electrical current traveled in the anterior direction within the cortex.[31] Using a suprathreshold stimulus intensity, the optimal coil position for eliciting lower extremity motor evoked potentials (MEPs) of maximal amplitude was located using standard procedures and carefully marked on the cap.[31,32] We detected no discernable difference in hotspot locations between the TA and soleus muscles of the same leg in our pilot testing for this study. Thus, we chose to use the TA as a guide in the search for the common TA and soleus lower extremity hotspot for each leg because TA MEPs were more pronounced than soleus MEPs, particularly in the most impaired participants. Only data from the soleus muscles were processed and used in the analysis for the present study. 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 encouraged to rest if they reported fatigue or if a notable change in muscle activity was observed. Ten to 15 TMS pulses at 100% maximum stimulator output intensity were delivered to each the paretic and nonparetic soleus muscle.[22,32] All TMS testing procedures for each limb were performed immediately before and immediately following each gait training session.

All MEP amplitudes were normalized to the maximal response to peripheral nerve stimulation collected prior to the start of each training session (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.

Gait Training Session With Functional Electrical Stimulation

A licensed physical therapist administered all gait training sessions. Participants completed a session of walking with FES (FESW) and a session of walking without FES (NoFESW) approximately 1 week apart. The order of each session was randomized. The FESW session consisted of five 6-minute treadmill walking bouts at the participant's self-selected gait speed. FES was delivered through self-adhesive surface stimulation electrodes in an alternating pattern for 1 minute on

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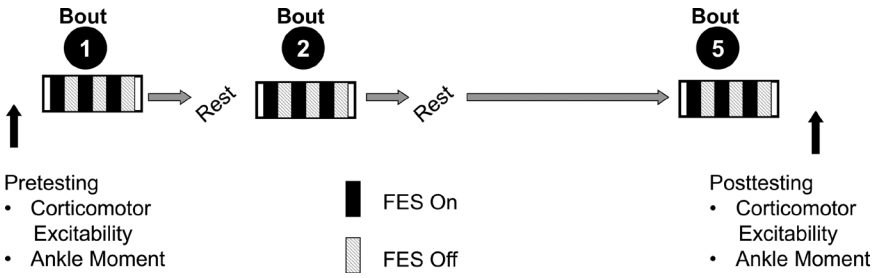

Figure 1.
Schematic of functional electrical stimulation (FES) gait training session.

and 1 minute off to the paretic ankle dorsi- and plantarflexor muscle groups (Fig. 1). Two compression foot switches were attached to the sole of the shoe of the paretic limb under the lateral aspect of the fifth metatarsal head and the lateral portion of the heel. These foot switches were used to control the delivery of FES from a custom built stimulator. During gait, FES parameters for stimulation used variable frequency trains that consisted of a high-frequency (200-Hz) 3-pulse burst followed by a lower-frequency, 30-Hz constant-frequency train.[33] The pulse duration was set at 300 microseconds, and the pulse amplitude was set at the intensity needed to reach an ankle neutral position (dorsiflexors) and heel rise with staggered stance and weight bearing (plantarflexors). FES of the dorsiflexors was delivered during the swing phase of gait as determined when the forefoot switch was turned off (paretic toe off) until the hind foot switch was turned on (paretic heel strike). FES of the plantarflexors was delivered during the terminal-stance phase, when the hind foot switch was turned off (indicating paretic heel off) and ended when the forefoot switch was turned off (indicating paretic toe off). Further details regarding the customized FES system and methods can be found in a previous study put forth by our laboratory.[33] Procedures for the NoFESW session were identical to those for the FESW session, without administration of the FES. Two 30-second bouts of posttest biomechanics were collected at the same initial walking speed immediately following the fifth bout of walking during each session. FES remained off during all biomechanical testing. TMS posttesting was completed immediately after the participant was seated in a chair following each training session.

Data Reduction and Analyses

Kinematic and kinetic data were filtered using a bidirectional Butterworth low-pass filter at 6 and 30 Hz. Biomechanical data processing was performed using Cortex and Visual3D software programs (C-Motion Inc, Bethesda, Maryland). We calculated peak ankle plantarflexion moment resolved into the shank coordinate system 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 participant during the two 30-second walking bouts at pre- and posttesting for each session. Ankle plantarflexion moment symmetry was calculated for each participant at each speed as the average paretic plantarflexion moment divided by the average nonparetic plantarflexion moment.

We quantified prestimulus EMG from the paretic and nonparetic soleus muscles during pre- and posttesting to ensure that all participants met appropriate EMG activity during muscle facilitation. We calculated the average root-mean-squared amplitude of the prestimulus EMG during a 100-millisecond window prior to the stimulus artifact for each MEP. Trials were discarded from analysis if the EMG activity of the targeted soleus muscle was less than 15 μV in amplitude or less than 2.5 standard deviations greater than that during the resting condition or if the EMG activity in the contralateral muscle was 2.5 standard deviations greater than that during the resting condition.

The MEP amplitude was treated as a continuous variable and quantified as the peak-to-peak value of the EMG response within a 100-millisecond window duration beginning at 10 milliseconds after the stimulus artifact.[22] 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 of the paretic and nonparetic soleus muscles. Symmetry of the corticomotor input to the plantarflexors 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; and a value of less than 1.0 indicates the paretic was less than the nonparetic.[22]

Two-way repeated-measures analyses of variance were used to determine whether plantarflexor corticomotor symmetry and ankle moment symmetry differed from pre- to posttesting for each session (FESW and NoFESW). We then tested the differential interlimb contributions to corticomotor and ankle moment symmetry. Two-way repeated-measures analyses of variance were used to test whether soleus MEP amplitude and plantarflexion ankle moment differed between limbs (paretic and nonparetic) and between pre- to posttesting within each session. For all significant interactions, post hoc testing using a Bonferroni method was performed for within-session comparisons. If interactions were not significant, main effects were tested. The relationship between change in corticomotor symmetry and change in plantarflexion ankle moment symmetry was tested for each session using a Pearson product moment correlation coefficient. Relationships between change in paretic and nonparetic MEP amplitudes versus change in paretic and nonparetic plantarflexion ankle moments were also tested. All analyses

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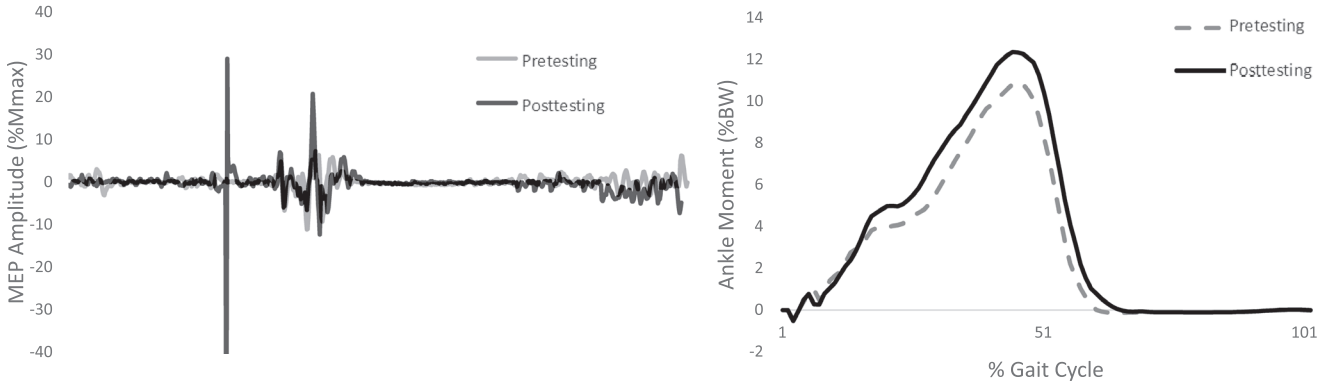

Figure 2.
Examples of pre- and posttesting paretic motor evoked potential (MEP) (left) and paretic ankle moment (right) data for the walking with functional electrical stimulation (FESW) session from a participant showing positive corticomotor and biomechanical responses. %BW=percentage of body weight, %Mmax=percentage of maximal electromyographic (EMG) response to peripheral nerve stimulation.

were performed using SPSS version 23 (IBM SPSS, Chicago, Illinois). An alpha level was set a priori at P=.05.

Results

Complete data sets were obtained from 19 participants. Data for 1 participant who could not return for the second session of NoFESW due to transportation problems were discarded from analysis. Similar levels of EMG were observed within and between sessions for the paretic soleus (pre: FESW=34.82 ± 6.51 μV, NoFESW=35.23 ± 6.09 μV; post: FESW=28.39 ± 7.78 μV, NoFESW=33.27 ± 5.87 μV) and the nonparetic soleus (pre: FESW=52.81 ± 7.04 μV, NoFESW=51.96 ± 7.23 μV; post: FESW=51.67 ± 5.79 μV, NoFESW=53.90 ± 6.58 μV).

Following gait training with FES, we observed an increase in corticomotor and ankle moment symmetry that was driven by an increase in paretic soleus MEP amplitude and paretic plantarflexion ankle moment (Fig. 2). For corticomotor symmetry, there was a significant time (pre versus post) by session (FESW versus NoFESW) interaction ($F_{1,18}$=13.80, P<.01). Post hoc testing revealed significant changes in corticomotor symmetry from pre- to posttesting following FESW (P<.01) but not following NoFESW (P=.22) (Fig. 3A). For MEP amplitude measures, no significant limb (paretic versus nonparetic) by time (pre versus post) interaction was observed following the FESW session ($F_{1,18}$=2.28, P=.14) or the NoFESW session ($F_{1,18}$=3.90, P=.06) (Figs. 3B and 3C). However, there were significant main effects for limb ($F_{1,18}$=14.27, P<.01) and time ($F_{1,18}$=4.89, P=.04) following the FESW session and a main effect of limb ($F_{1,18}$=11.81, P<.01) but not time ($F_{1,18}$=0.97, P=.34) following the NoFESW session.

For ankle moment symmetry, there was a significant time (pre versus post) by session (FESW versus NoFESW) interaction ($F_{1,18}$=9.57, P<.01). Post hoc testing revealed significant changes in symmetry from pre- to posttesting following FESW (P=.05) but not following NoFESW (P=.11) (Fig. 4A). For ankle moment measures, no significant limb by time interaction was observed following the FESW session ($F_{1,18}$=2.25, P=.15), but significant main effects were observed for limb ($F_{1,18}$=12.04, P<.01) and time ($F_{1,18}$=5.76, P=.02) (Fig. 4B). There was a significant limb by time interaction following the NoFESW session ($F_{1,18}$=5.63, P=.02) for the ankle moment measure (Fig. 4C). However, post hoc testing revealed no significant pre- to posttest differences for paretic ankle moment (P=.15) and nonparetic ankle moment from pre- to posttesting (P=.07).

There was a significant positive relationship between change in plantarflexion corticomotor symmetry and change in plantarflexion ankle moment symmetry in response to FESW (Pearson r=0.64, P<.01, n=19) but not to NoFESW (Pearson r=−0.31, P=.20, n=19) (Fig. 5). Interlimb correlation analysis of paretic and nonparetic symmetry components following FESW revealed a positive relationship between change in paretic soleus MEP amplitude and change in paretic ankle moment (Pearson r=0.62, P<.01, n=19) and no relationship between change in nonparetic soleus MEP amplitude and change in nonparetic ankle moment (Pearson r=0.27, P=.24, n=19) (Fig. 6).

Discussion

This study provides novel evidence that a single session of gait training with FES targeting paretic plantarflexor muscles can induce improvements in corticomotor symmetry and related improvements in ankle moment symmetry between limbs in people in the chronic stage of poststroke motor recovery. This shows for the first time that rehabilitation strategies that effectively promote corticomotor balance to lower limb muscles could improve poststroke biomechanical walking function and potentially enhance functional walking outcomes in response to intervention.

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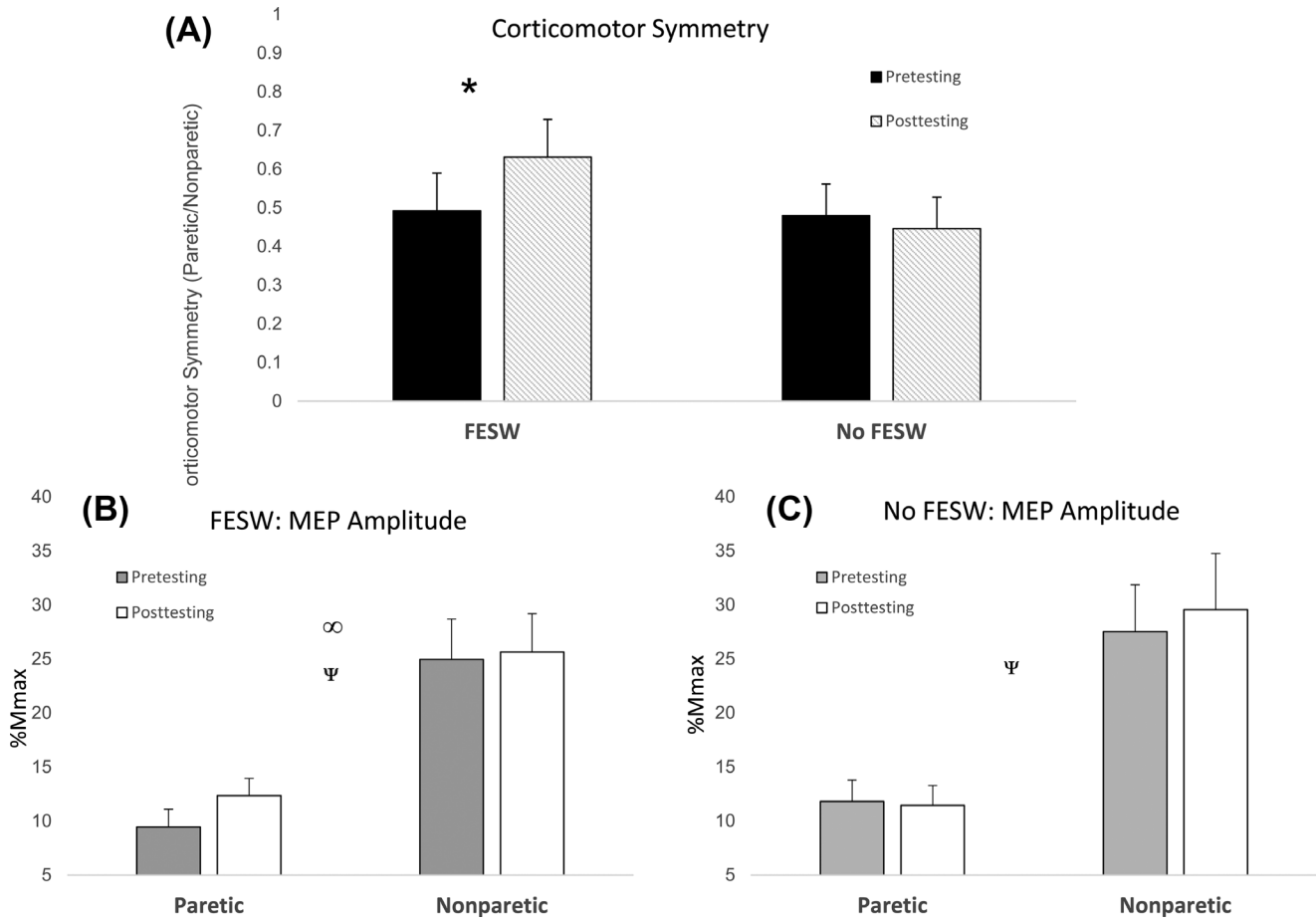

Figure 3.
Corticomotor symmetry (A) and motor evoked potential (MEP) amplitude (mean and SE) for the paretic (P) and nonparetic (NP) limbs during pre- and posttesting for the walking with functional electrical stimulation (FESW) (B) and walking without functional electrical stimulation (NoFESW) (C) sessions. There was a significant session × time interaction for corticomotor symmetry (A). * indicates a significant difference between pre- and posttesting. There was no significant limb × time interaction for MEP amplitude for either FESW (B) or NoFESW (C) sessions. ∞ indicates a main effect of time (pre and post). ψ indicates a main effect of limb. %Mmax=percentage of maximal electromyographic (EMG) response to peripheral nerve stimulation.

The relationship between changes in plantarflexor corticomotor symmetry and changes in plantarflexion ankle moment symmetry in response to gait training with FES may offer novel insight into the neurophysiologic mechanisms underlying changes in poststroke lower extremity biomechanical function that can be achieved during a single session of rehabilitation. FES-induced corticomotor plasticity has been reported in the upper extremity to be related to poststroke motor function,[24–26] in the paretic lower extremity in response to prolonged dorsiflexion-targeted interventions,[27] and in people who are neurologically intact within a single session.[29,34,35] However, to our knowledge, there have been no previous studies that have investigated FES-induced corticomotor plasticity in response to a single session of rehabilitation in people with stroke despite the potential importance this could have for predicting an individual's functional outcome in response to long-term intervention.[19] Importantly, the relationship between corticomotor responses to rehabilitation and changes in walking mechanics has not been studied. In environments where FES is coupled with volitional motor contraction during a functional task in people with stroke, neuroimaging studies have consistently demonstrated shifts in the balance of cortical activation towards the contralateral lesioned primary motor and sensorimotor cortices and away from the same areas in the ipsilateral nonlesion hemisphere that were associated with improvements in upper extremity motor function.[24,26] Similar findings have not been found after passive stimulation paradigms[35,36] and after walking without stimulation.[34] Similarly, in the present study, we observed improvements in the balance of corticomotor excitability to the paretic and nonparetic plantarflexors following a session of FES gait training but not following gait training without FES. These improvements in corticomotor symmetry were associated with improvements in ankle moment symmetry and were driven by strengthened corticomotor drive to the paretic limb, as seen in Figure 3B. Following FESW, there was a significant increase

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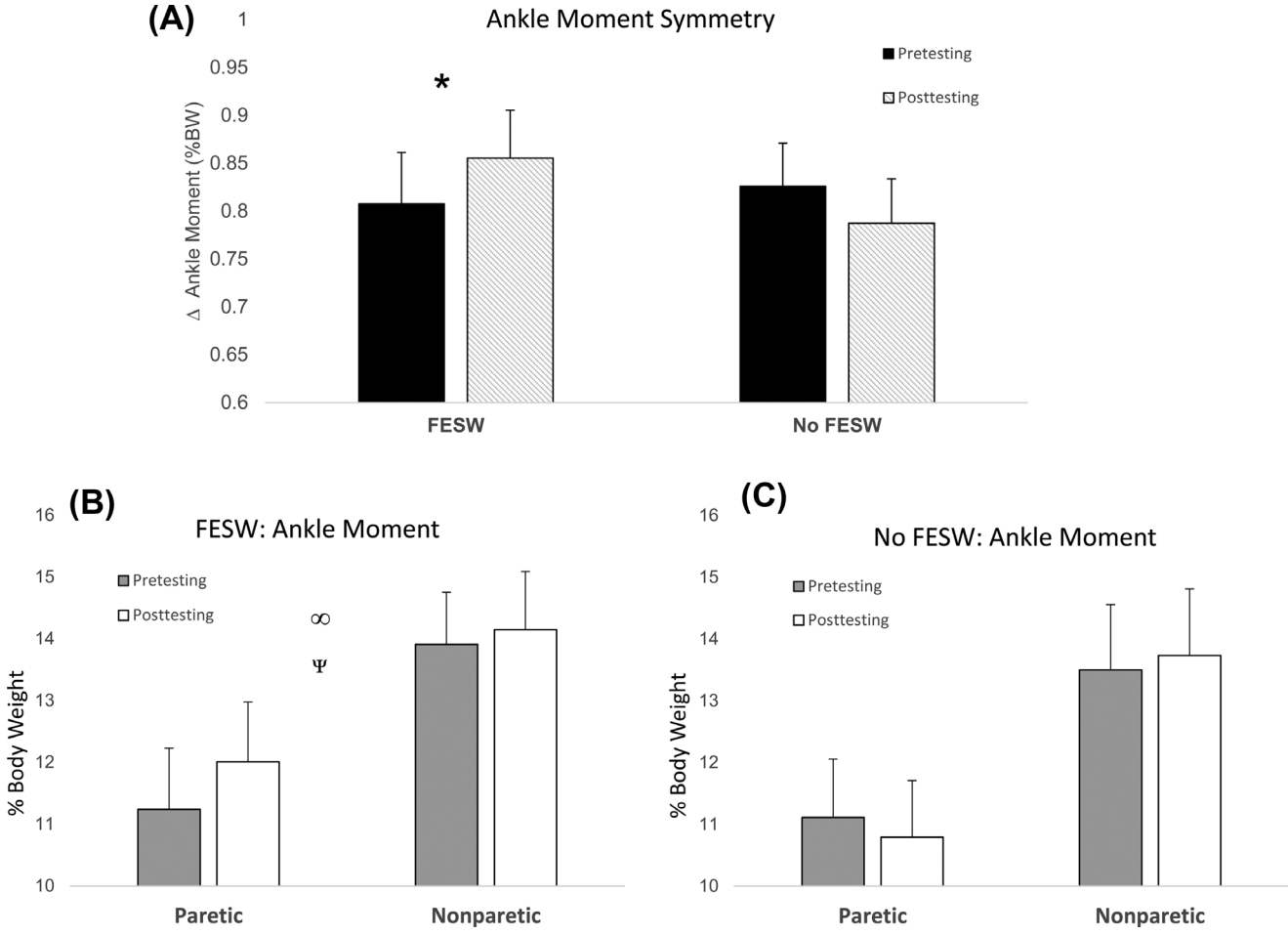

Figure 4.
Ankle moment (Mom) symmetry (A) and peak ankle moment (mean and SE) for the paretic and nonparetic limbs during pre- and posttesting for the walking with functional electrical stimulation (FESW) (B) and walking without functional electrical stimulation (NoFESW) (C) sessions. There was a significant session × time interaction for ankle moment symmetry (A). * indicates a significant difference between pre- and posttesting. There was no significant limb × time interaction for ankle moment for the FESW (B) session, but there were main effects of time (∞) and limb (ψ). There was a significant limb × time interaction for ankle moment for the NoFESW session (C). There was no significant difference within the nonparetic limb between pre- and posttesting (P=.07). Δ=change, %BW=percentage of body weight.

in paretic MEP amplitude and a related increase in paretic ankle moment (Fig. 6). The observed increase in corticomotor excitability to the paretic limb following FESW could be a result of increased coupling between neuronal activity in lower extremity regions of primary motor and somatosensory cortices found in previous neuroimaging studies following FES therapy,[24–26,29] leading to increased cortical activity in the lesioned lower extremity primary motor cortical area. Further, despite receiving less corticomotor input than the dorsiflexor muscles,[37,38] these changes were observed in plantarflexor muscles in response to a single session of rehabilitation in people in the chronic stage of poststroke motor recovery. These findings demonstrate that FES gait training targeting paretic plantarflexor muscles may be an effective rehabilitation tool to promote corticomotor balance between paretic and nonparetic lower limbs and symmetry of clinically meaningful poststroke walking mechanics.

In response to FESW, the MEP amplitude showed a main effect of time for both the paretic and nonparetic limb (Fig. 3B). The mean increase in paretic limb MEP amplitude was greater than that of the nonparetic limb (Fig. 3B), but there was a small observed increase in nonparetic MEP amplitude mean. As observed in Figure 5, change in nonparetic corticomotor drive was variable between people. Though unrelated to changes in nonparetic ankle moment, we observed an increase in corticomotor drive to the nonparetic plantarflexors in a few participants following gait training with FES; interestingly, increases in corticomotor drive to the nonparetic plantarflexors has not been reported in previous literature. Unlike upper extremity motor task training,[24,26] or simple ankle pumping tasks in the

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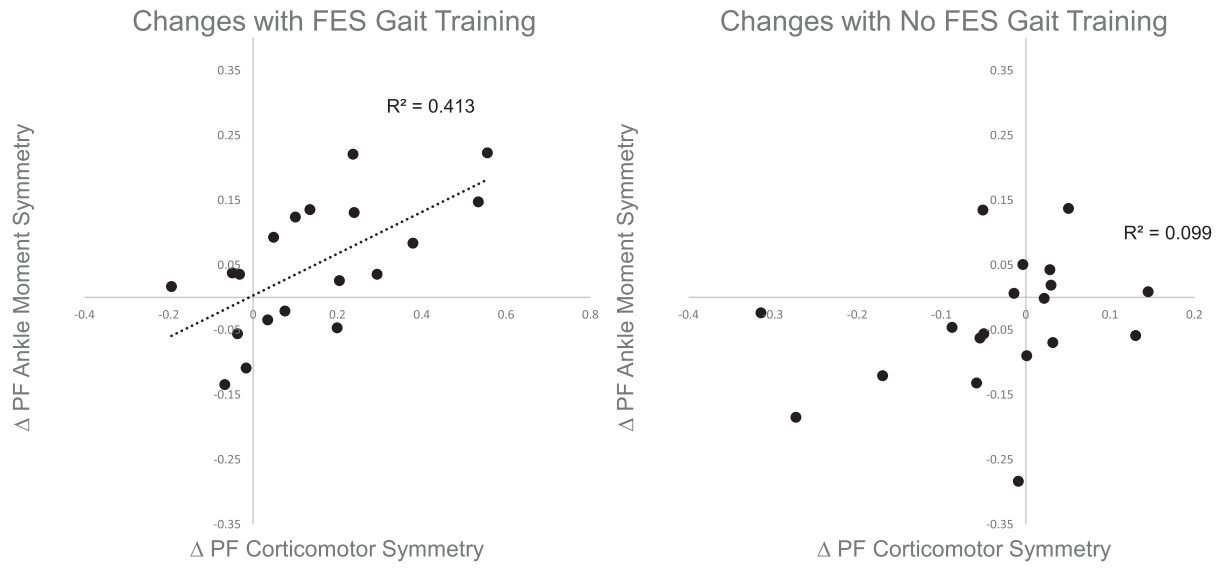

Figure 5.
Positive relationship between change in plantarflexor (ΔσPF) corticomotor symmetry and ΔPF ankle moment symmetry with functional electrical stimulation (FES) gait training (r=0.64, P<.01) (left). In response to gait training without FES (NoFES), no relationship was observed (r=–0.31, P=.20) (right).

seated position previously reported in FES literature,[29,35] in the present study the nonparetic limb was required to be continuously active during walking and tied to the antiphasic stepping patterns of the paretic limb. As such, both the lesioned and nonlesioned sensorimotor cortexes likely remained continuously active during the walking sessions, which could have resulted in neuroplastic changes in both hemispheres.[39] Alternatively, because a greater mean nonparetic corticomotor input was observed in response to walking without FES, the FES gait training session could have actually reduced the enhancement of corticomotor drive to the nonparetic leg that may occur during typical walking patterns over time in people with poststroke lower extremity hemiparesis. It is possible that this could result from the reduced demand placed on the nonparetic extremity due to the increased contribution to forward propulsion by the paretic extremity.

Although both corticomotor and ankle moment symmetry showed overall increases in response to FESW, we observed high variability between people in response to this gait training session. As evident in Figures 5 and 6, FESW was not an effective strategy for inducing corticomotor or biomechanical changes in some people. A range of responses is consistent with the variability in biomechanical responses[40] and corticomotor changes induced by FES in the upper extremity.[24,41] This variability could explain inconsistencies between previous studies investigating the effectiveness of FES gait training[42,43] and for small group effect sizes following FES gait training interventions.[42,43] It is conceivable that the people in the present study who showed a positive response to FESW may have possessed a neural substrate that allowed them to be responsive to the FESW.[19,39] Though baseline measures of corticomotor function generally show poor prognostic ability for rehabilitation outcomes in the chronic stage of stroke recovery,[19] these findings suggest individual corticomotor response to a single session of rehabilitation could potentially be an important indicator for response to a long-term intervention, similar to findings in the upper extremity.[19] Specifically, if corticomotor response to a single session of FES gait training revealed that an individual possessed good potential for improvement, then subsequent training sessions could use that strategy to focus on improving paretic limb function. In contrast, if corticomotor response to a single session indicated no potential for improvement, then rehabilitation efforts could focus on nonparetic limb compensation to maximize walking function. In this way, measurements of corticomotor response to a single session could provide a useful clinical tool to quantify individual neuroplastic responses to rehabilitation strategies that could ultimately help to individualize poststroke rehabilitation among a heterogeneous patient population and maximize poststroke walking function.

Interestingly, results of this study suggest that a session of walking without FES could actually magnify corticomotor and ankle moment asymmetries during gait. Though decreases in corticomotor symmetry and ankle moment symmetry following NoFESW were not statistically significant, consistent patterns of change were observed for corticomotor and biomechanical measures. Following a gait training session without FES, we observed an overall decrease in paretic corticomotor drive and paretic ankle moment and an overall increase in nonparetic corticomotor drive and nonparetic

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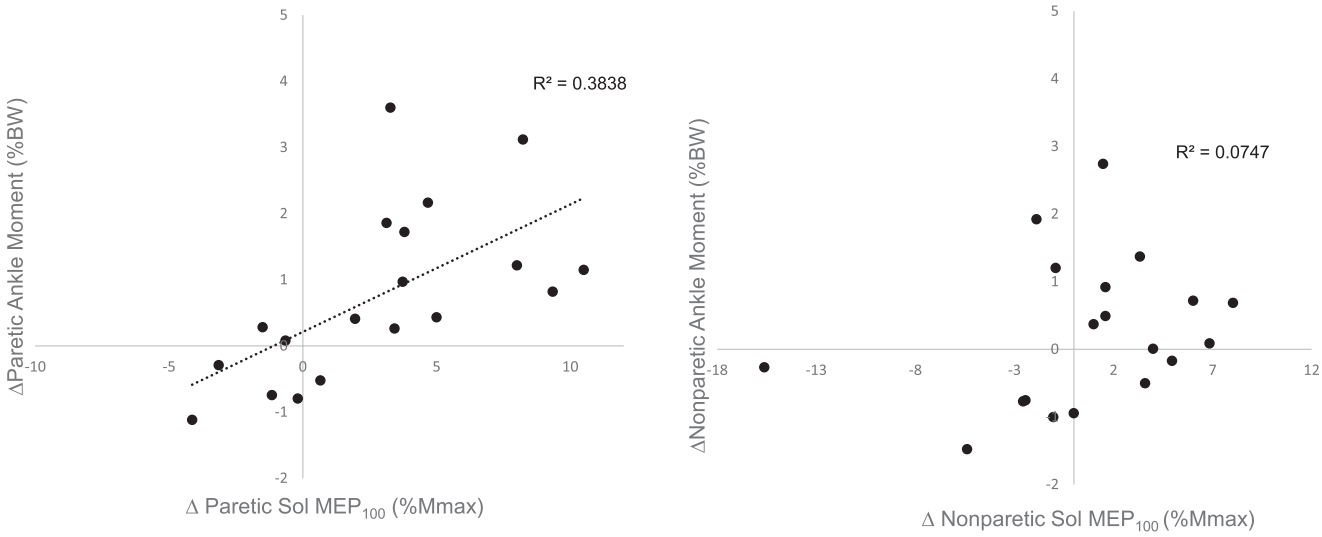

Figure 6.
Positive relationship between Δ paretic MEP_{100} and Δ paretic ankle moment with functional electrical stimulation (FES) gait training (r=0.62, P<0.01) (left). No relationship was observed between Δ nonparetic MEP_{100} and Δ nonparetic ankle moment (r=0.27, P=.24) (right). Δ=change, MEP_{100}=100% of the magnetic stimulator output intensity, %Mmax=percentage of maximal electromyographic (EMG) response to peripheral nerve stimulation., NP=nonparetic, P=paretic, PF=plantarflexor, Sol=soleus.

ankle moment (Figs. 3C and 4C). These results may suggest that typical poststroke asymmetrical walking patterns may strengthen corticomotor imbalances between hemispheres and could potentially amplify gait asymmetries in some people. Gait training with FESW may have interfered with underlying neural mechanisms of these patterns in those same people, both enhancing corticomotor drive to the paretic leg and reducing the typical enhancement of corticomotor drive to the nonparetic leg following typical gait, as posited above. The lack of relationship between change in corticomotor symmetry and change in ankle moment symmetry in response to the NoFESW (Fig. 5) may be because, in the absence of a specific learning strategy, people adopted different biomechanical strategies (ie, increased trailing limb angle to increase propulsion)[44] during walking over time to achieve the same speeds. Thus, the relationship between change in corticomotor measures and change in biomechanical gait patterns may only exist when induced by specific targeted interventions that activate specific neural pathways.[29]

Limitations

Some limitations of the present study are important to consider in the interpretation of the results. Due to the correlational analysis of the present study, it is uncertain whether changes in corticomotor balance led to changes in gait mechanics or whether they resulted from the observed changes in walking pattern itself. The sample size of this study was too small to determine specific characteristics of responders versus nonresponders to each of the training session. Interestingly in exploratory analyses we found no relationships between change in plantarflexion ankle moment metrics and walking speed, baseline plantarflexion ankle moments, baseline corticomotor excitability or Fugl-Meyer scores. Because of the close proximity of the lower extremity motor representations of each hemisphere within the primary motor cortex, the specific hemispheric origin of corticomotor excitability to the paretic and nonparetic plantarflexors cannot be determined. Future research using neuroimaging could help elucidate specific neural origins of corticomotor symmetry.

Conclusions

Findings of this study advance our understanding of the effectiveness of FES gait training to induce corticomotor plasticity to plantarflexor muscles limiting poststroke walking function and demonstrate that neuroplastic changes in the lower extremity are detectible following a single session of rehabilitation. Though it is difficult to determine causality of the reported relationships, results may provide insight to mechanisms of corticomotor plasticity underlying biomechanical improvements that can be made within a single session of rehabilitation in people in the chronic stage of poststroke motor recovery. Findings from this study may provide a basis for future studies to test whether measures of early corticomotor responses to a specific rehabilitation strategy provide a good predictor of the potential for long-term gains in functional walking ability. Future research in this area could lead to the development of effective and individualized rehabilitation strategies that may interrupt learned corticomotor imbalances underlying poststroke walking dysfunction and maximize walking ability in people with poststroke walking disability.

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Ethics Approval

All participants gave written informed consent, and the experimental protocol was approved by the University of Delaware Institutional Review Board.

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Disclosures and Presentations

All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest, and none were reported.

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References

1 Pollock A, St George B, Fenton M, Firkins L. Top ten research priorities relating to life after stroke. *Lancet Neurol*. 2012;11:209.

2 Charalambous CC, Bowden MG, Adkins DL. Motor cortex and motor cortical interhemispheric communication in walking after stroke: the roles of transcranial magnetic stimulation and animal models in our current and future understanding. *Neurorehabil Neural Repair*. 2016;30:94–102.

3 Hall AL, Bowden MG, Kautz SA, Neptune RR. Biomechanical variables related to walking performance 6-months following post-stroke rehabilitation. *Clin Biomech (Bristol, Avon)*. 2012;27:1017–1022.

4 Combs SA, Dugan EL, Ozimek EN, Curtis AB. Effects of body-weight supported treadmill training on kinetic symmetry in persons with chronic stroke. *Clin Biomech*. 2012;27:887–892.

5 Little VL, McGuirk TE, Patten C. Impaired limb shortening following stroke: what's in a name? *PLoS One*. 2014;9:e110140.

6 Jonkers I, Delp S, Patten C. Capacity to increase walking speed is limited by impaired hip and ankle power generation in lower functioning persons post-stroke. *Gait Posture*. 2009;29:129–137.

7 Awad LN, Binder-Macleod SA, Pohlig RT, Reisman DS. Paretic propulsion and trailing limb angle are key determinants of long-distance walking function after stroke. *Neurorehabil Neural Repair*. 2014;29:499–508.

8 Bowden MG, Chitralakshmi CK, Behrman AL, Kautz SA. Validation of a speed-based classification system using quantitative measures of walking performance. *Neurorehabil Neural Repair*. 2008;22:672–675.

9 Hsiao H, Awad LN, Palmer JA, et al. Contribution of paretic and nonparetic limb peak propulsive forces to changes in walking speed in individuals post-stroke. *Neurorehabil Neural Repair*. 2016;30:743–752.

10 Allred RP, Maldonado MA, Hsu And JE, Jones TA. Training the "less-affected" forelimb after unilateral cortical infarcts interferes with functional recovery of the impaired forelimb in rats. *Restor Neurol Neurosci*. 2005;23:297–302.

11 Awad LN, Reisman DS, Kesar TM, Binder-Macleod SA. Targeting paretic propulsion to improve poststroke walking function: a preliminary study. *Arch Phys Med Rehabil*. 2014;95:840–848.

12 Bowden MG, Behrman AL, Neptune RR, et al. Locomotor rehabilitation of individuals with chronic stroke: difference between responders and nonresponders. *Arch Phys Med Rehabil*. 2013;94:856–862.

13 Avanzino L, Bassolino M, Pozzo T, Bove M. Use-dependent hemispheric balance. *J Neurosci*. 2011;31:3423–3428.

14 Jones TA, Kleim JA, Greenough WT. Synaptogenesis and dendritic growth in the cortex opposite unilateral sensorimotor cortex damage in adult rats: a quantitative electron microscopic examination. *Brain Res*. 1996;733:142–148.

15 Takatsuru Y, Fukumoto D, Yoshitomo M, et al. Neuronal circuit remodeling in the contralateral cortical hemisphere during functional recovery from cerebral infarction. *J Neurosci*. 2009;29:10081–10086.

16 Manganotti P, Acler M, Zanette GP, et al. Motor cortical disinhibition during early and late recovery after stroke. *Neurorehabil Neural Repair*. 2008;22:396–403.

17 Traversa R, Cicinelli P, Pasqualetti P, et al. Follow-up of interhemispheric differences of motor evoked potentials from the `affected' and `unaffected' hemispheres in human stroke. *Brain Res*. 1998;803:1–8.

18 Butler A, Wolf S. Putting the brain on the map: use of transcranial magnetic stimulation to assess and induce cortical plasticity of upper-extremity movement. *Phys Ther*. 2007;87:719–736.

19 Koski L, Mernar TJ, Dobkin BH. Immediate and long-term changes in corticomotor output in response to rehabilitation: correlation with functional improvements in chronic stroke. *Neurorehabil Neural Repair*. 2004;18:230–249.

20 Calautti C, Naccarato M, Jones PS, et al. The relationship between motor deficit and hemisphere activation balance after stroke: a 3T fMRI study. *Neuroimage*. 2007;34:322–331.

21 Borich MR, Brodie SM, Gray WA, et al. Understanding the role of the primary somatosensory cortex: opportunities for rehabilitation. *Neuropsychologia*. 2015;79:246–255.

22 Palmer JA, Hsiao H, Awad LN, Binder-Macleod SA. Symmetry of corticomotor input to plantarflexors influences the propulsive strategy used to increase walking speed post-stroke. *Clin Neurophysiol*. 2016;127:1837–1844.

23 Koyama S, Tanabe S, Warashina H, et al. NMES with rTMS for moderate to severe dysfunction after stroke. *NeuroRehabilitation*. 2014;35:363–368.

24 Hara Y, Obayashi S, Tsujiuchi K, Muraoka Y. The effects of electromyography-controlled functional electrical stimulation on upper extremity function and cortical perfusion in stroke patients. *Clin Neurophysiol*. 2013;124:2008–2015.

25 Shin HK, Cho SH, Jeon HS, et al. Cortical effect and functional recovery by the electromyography-triggered neuromuscular stimulation in chronic stroke patients. *Neurosci Lett*. 2008;442:174–179.

26 Sasaki K, Matsunaga T, Tomite T, et al. Effect of electrical stimulation therapy on upper extremity functional recovery and cerebral cortical changes in patients with chronic hemiplegia. *Biomed Res*. 2012;33:89–96.

27 Everaert DG, Thompson AK, Chong SL, Stein RB. Does functional electrical stimulation for foot drop strengthen corticospinal connections? *Neurorehabil Neural Repair*. 2010;24:168–177.

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28 Pilkar R, Yarossi M, Nolan KJ. EMG of the tibialis anterior demonstrates a training effect after utilization of a foot drop stimulator. *NeuroRehabilitation*. 2014;35:299–305.

29 Gandolla M, Ferrante S, Molteni F, et al. Re-thinking the role of motor cortex: context-sensitive motor outputs? *NeuroImage*. 2014;91:366–374.

30 Rossini PM, Burke D, Chen R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. *Clin Neurophysiol*. 2015;126:1071–1107.

31 Devanne H, Lavoie BA, Capaday C. Input-output properties and gain changes in the human corticospinal pathway. *Exp Brain Res*. 1997;114:329–338.

32 Palmer JA, Needle AR, Pohlig RT, Binder-Macleod SA. Atypical cortical drive during activation of the paretic and nonparetic tibialis anterior is related to gait deficits in chronic stroke. *Clin Neurophysiol*. 2016;127:716–723.

33 Kesar TM, Perumal R, Jancosko A, et al. Novel patterns of functional electrical stimulation have an immediate effect on dorsiflexor muscle function during gait for people poststroke. *Phys Ther*. 2010;90:55–66.

34 Kido Thompson A, Stein RB. Short-term effects of functional electrical stimulation on motor-evoked potentials in ankle flexor and extensor muscles. *Exp Brain Res*. 2004;159:491–500.

35 Khaslavskaia S, Sinkjaer T. Motor cortex excitability following repetitive electrical stimulation of the common peroneal nerve depends on the voluntary drive. *Exp Brain Res*. 2005;162:497–502.

36 Yamaguchi T, Sugawara K, Tanaka S, et al. Real-time changes in corticospinal excitability during voluntary contraction with concurrent electrical stimulation. *PLoS One*. 2012;7:e46122.

37 Petersen NT, Butler JE, Marchand-Pauvert V, et al. Suppression of EMG activity by transcranial magnetic stimulation in human subjects during walking. *J Physiol (Lond.)*. 2001;537:651–656.

38 Bo Nielsen J. Motoneuronal drive during human walking. *Brain Res Rev*. 2002;40:192–201.

39 Rushton DN. Functional electrical stimulation and rehabilitation: an hypothesis. *Med Eng Phys*. 2003;25:75–78.

40 Kesar TM, Perumal R, Reisman DS, et al. Functional electrical stimulation of ankle plantarflexor and dorsiflexor muscles: effects on poststroke gait. *Stroke*. 2009;40:3821–3827.

41 Page SJ, Harnish SM, Lamy M, et al. Affected arm use and cortical change in stroke patients exhibiting minimal hand movement. *Neurorehabil Neural Repair*. 2010;24:195–203.

42 Kafri M, Laufer Y. Therapeutic effects of functional electrical stimulation on gait in individuals post-stroke. *Ann Biomed Eng*. 2015;43;451–466.

43 Pereira S, Mehta S, McIntyre A, et al. Functional electrical stimulation for improving gait in persons with chronic stroke. *Top Stroke Rehabil*. 2012;19:491–498.

44 Hsiao H, Knarr BA, Higginson JS, Binder-Macleod SA. Mechanisms to increase propulsive force for individuals poststroke. *J Neuroeng Rehabil*. 2015;12:40.

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