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Impaired interlimb coordination is related to asymmetries during pedaling after stroke

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HIGHLIGHTS

- Pedaling performance in chronic stroke is enhanced when asymmetries are permitted.
- When asymmetry is prevented, impaired paretic output and interlimb coordination degrade performance.
- Impaired interlimb coordination is a stronger predictor of asymmetry than paretic motor impairment.

ABSTRACT

Objective: To understand whether lower limb asymmetry in chronic stroke is related to paretic motor impairment or impaired interlimb coordination.
Methods: Stroke and control participants performed conventional, unilateral, and bilateral uncoupled pedaling. During uncoupled pedaling, the pedals were mechanically disconnected. Paretic mechanical work was measured during conventional pedaling. Pedaling velocity and muscle activity were compared across conditions and groups. Relative limb phasing was examined during uncoupled pedaling.
Results: During conventional pedaling, EMG and mechanical work were lower in the paretic than the non-paretic limb (asymmetry). During unilateral pedaling with the paretic limb, muscle activity was larger, but velocity was slower and more variable than during conventional pedaling (evidence of paretic motor impairment). During uncoupled pedaling, muscle activity increased further, but velocity was slower and more variable than in other conditions (evidence of impaired interlimb coordination). Relative limb phasing was impaired in stroke participants. Regression analysis suggested that interlimb coordination may be a stronger predictor of asymmetry than paretic motor impairment.
Conclusions: Paretic motor impairment and impaired interlimb coordination may contribute to asymmetry during pedaling after stroke.
Significance: Rehabilitation that addresses paretic motor impairment and impaired interlimb coordination may improve symmetry and maximize improvement.

1. Introduction

In people with stroke, the work of locomotion and other functional behaviors of the lower limbs is accomplished primarily by the non-paretic lower limb. For example, during walking, the non-paretic limb generates approximately 60% of the work or power for forward translation (Olney et al., 1991; Bowden et al., 2006; Turns et al., 2007). These and other asymmetric movement strategies are useful in acute stroke because they enable goal directed behavior despite paralysis or severe weakness of the stroke-affected limb (Levin et al., 2009). However, repeated and prolonged use of the non-paretic limb instead of the paretic limb alters cortical representation and worsens movement of the paretic limb in rats (Allred et al., 2005, 2008) and limits functional recovery (Nadeau et al., 1999; Jonkers et al., 2009) and impairs quality of life in humans (Mayo et al., 2002). Nevertheless, asymmetric contributions (non-paretic > paretic) to bilateral lower limb movements persist in chronic stroke even when the paretic limb has regained considerable motor function (Bohannon et al., 1985; Brown et al.,

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1997, 1998; Clark et al., 2016; Hsiao et al., 2016). This behavior is curious because walking, standing, and other lower limb movements are inherently bilateral and offer many opportunities to use the paretic limb. This study examined the possibility that motor impairments of the paretic limb and impaired interlimb coordination contribute to this phenomenon.

Asymmetric contributions to bilateral lower limb movements in chronic stroke may be due to residual impairment in motor output of the paretic limb. Even well recovered stroke survivors exhibit weak descending drive to spinal motor neurons (Palmer et al., 2017) and impaired motoneuronal rate coding (Frontera et al., 1997; Chou et al., 2013). Muscles on the stroke-affected side of the body have lower cross sectional area (English et al., 2010) and force generating ability than normal (Bohannon et al., 1995; Newham et al., 2001; Klein et al., 2010). The paretic limb also displays abnormal muscle phasing, whereby muscle activity is initiated and terminated at inappropriate phases in the movement cycle (Knutsson et al., 1979; Kautz et al., 1998; Den Otter et al., 2007). These impairments may prevent the stroke-affected limb from producing adequate torque, in the correct direction, at the appropriate point in the movement cycle to advance the limb or support the weight of the body. Consequently, contributions from the partially recovered limb may not enhance movement and may even make it worse.

Even if the paretic limb can produce sufficient and appropriately phased motor output unilaterally, it may be unable to do so in a reciprocal alternating fashion with the non-paretic limb. During hip flexion and extension, reflex-related torque in the paretic limb is more abnormal during bilateral than unilateral movement (Hyngstrom et al., 2010). Kautz et al. (2005b) have shown that stroke survivors can produce adequate muscle force to rotate the crankshaft during unilateral pedaling with the paretic limb, but the timing of muscle activation is less appropriate when the non-paretic limb pedals at the same time. Moreover, interlimb phasing is abnormal and more variable during walking in stroke as compared to control subjects (Roerdink et al., 2007; Meijer et al., 2011). Hence, the tendency to perform bilateral lower limb movements primarily with the non-paretic limb may be an emergent pattern to reduce the undesirable neural impact of the paretic limb on the non-paretic limb or to reduce the need to coordinate the output of the two limbs.

The goal of this study was to better understand relationships among paretic motor impairment, impaired interlimb coordination, and asymmetric contributions to bilateral movements of the lower limbs in chronic stroke. We compared conventional, unilateral, and bilateral uncoupled pedaling in people with chronic stroke and age-matched controls. Pedaling involves continuous, reciprocal, multi-joint movement of both limbs and, therefore, is a useful model of functional lower limb movement. During conventional pedaling, the right and left crank arms are mechanically coupled by a solid crank shaft, allowing forces applied to one side to be transferred to the other. People with stroke can pedal with minimal contributions from the paretic limb. Thus, conventional pedaling exposes asymmetric contributions to bilateral lower limb movement as seen during walking. Because pedaling does not require body weight support, it can be done unilaterally. Each limb can be examined in isolation without the confounding influence of the contralateral limb. Thus, unilateral pedaling exposes paretic motor impairments. When the crankshaft is split into a left and right half, as was done during the bilateral uncoupled condition, pedaling can be performed bilaterally with no mechanical connection between the pedals. This task requires that each limb rotate its respective crankshaft and that the two limbs maintain a 180° phase relationship. The mechanical characteristics experienced by each limb are the same during unilateral and bilateral uncoupled pedaling. Thus, by comparing unilateral and bilateral uncoupled pedaling in stroke survivors and controls, we were able to distinguish motor impairments of the paretic limb from impairments in interlimb coordination. We then examined the relationship between these impairments and asymmetry during conventional pedaling. Direct relationships with asymmetry would suggest that residual impairments in motor output of the paretic limb and interlimb coordination contribute to asymmetric contributions to bilateral lower limb movement in chronic stroke. Portions of this work have been presented previously in abstract form (Cleland et al., 2016; Schindler-Ivens et al., 2016).

2. Methods

2.1. Participants

Twenty-one individuals with chronic stroke and eleven age-matched controls participated. All were free of neurological disease or injury other than stroke. All provided written informed consent according to the Declaration of Helsinki and the Institutional Review Boards at Marquette University and the Medical College of Wisconsin. See Table 1 for participant demographics. 12 individuals had cortical lesions affecting: parietal lobe ($n = 9$), temporal lobe ($n = 6$), frontal lobe ($n = 5$), and insular cortex ($n = 2$). Some participants had cortical lesions that extended into subcortical regions including the basal ganglia ($n = 3$), external capsule ($n = 1$), and thalamus ($n = 1$). 9 individuals had subcortical lesions affecting: internal capsule ($n = 3$), thalamus ($n = 3$), cerebellum ($n = 2$), basal ganglia ($n = 1$), corona radiata ($n = 1$), and pons ($n = 1$).

2.2. Clinical measures

People with stroke underwent a battery of assessments to characterize sensory and motor impairment of the lower limbs. Tests included the 8 m comfortable walk test for walking velocity and the lower extremity Fugl-Meyer Assessment ($FM_{LEtotal}$), which was subdivided into motor ($FM_{LEmotor}$), sensory (FM_{LEsens}), balance (FM_{LEbal}), range of motion (FM_{LErom}), and pain (FM_{LEpain}) components. $FM_{LEmotor}$ included tests for reflex activity, synergy, and coordination. FM_{LEsens} included light touch and proprioception. Values are reported in Table 1.

Table 1
Participant demographics. Demographic characteristics for the stroke and control group. Values are Mean (SD). $FM_{LEtotal}$: Fugl Meyer Assessment total score; $FM_{LEmotor}$: motor score; FM_{LEsens}: sensory score; FM_{LEbal}: balance score; FM_{LErom}: range of motion score; FM_{LEpain}: pain score.

	Control ($n = 11$)	Stroke ($n = 21$)
Age (years)	64 (7)	60 (11)
Sex (M/F)	3/8	13/8
Time since stroke (years)		9.2 (3.7), Range: 1.7–15.8
Stroke type (ischemic/hemorrhagic)		16/5
Stroke location (cortical/sub-cortical)		12/9
Paretic limb (L/R)		12/9
$FM_{LEtotal}$ (max: 96)		79 (9), Range: 61–91
$FM_{LEmotor}$ (max: 34)		25 (6), Range: 15–33
FM_{LEsens} (max: 12)		10 (3), Range: 2–12
FM_{LEbal} (max: 10)		7 (1), Range: 6–9
FM_{LErom} (max: 20)		18 (3), Range: 14–20
FM_{LEpain} (max: 20)		20 (0)
Walking velocity (m/s)		0.83 (0.33)

2.3. Equipment and procedures

All participants performed conventional, unilateral (right, left, paretic, non-paretic), and bilateral uncoupled pedaling. Tasks were enabled by a custom-designed, split-crank pedaling device (Fig. 1). As the name suggests, the crankshaft of the device was split into a left and right half. The two halves could be fastened together with a coupler to create a conventional, unitary crankshaft. Or, the coupler could be removed to eliminate the mechanical connection between the pedals. Each half of the crankshaft turned an eccentric pulley that enabled unilateral pedaling despite no mechanical contribution from the contralateral limb. Recall that during conventional pedaling, forces applied by the downstroke limb counteract forces generated by the upstroke limb that tend to retard forward crank progression (Kautz et al., 2002). If the contribution from the downstroke limb is not simulated, unilateral pedaling is difficult to accomplish, even in people without stroke. During the downstroke of the pedaling cycle, the eccentric pulley stretched an elastic band. Energy stored in the band was released during the upstroke to help return the limb to the top-dead-center position, thus simulating the contribution of the contralateral limb. The stiffness of the eccentric pulley system was adjusted on an individual basis to achieve unilateral pedaling, as described below. During conventional pedaling, the coupler was in place to hold the right and left pedals in a fixed position 180° apart. Because the feet were secured to the pedals and the non-paretic limb was mechanically coupled to the paretic limb it could compensate for impaired paretic motor output. During unilateral and bilateral uncoupled pedaling, the coupler was removed, and there was no mechanical connection between the right and left pedals. Thus, to perform unilateral pedaling, the paretic limb had to rotate its crankshaft without a mechanical contribution from the non-paretic leg. During bilateral uncoupled pedaling, the two limbs had to work in a coordinated fashion to maintain a 180° phase relationship. The mechanical load experienced by each limb was the same during unilateral and bilateral uncoupled pedaling.

Each participant completed a setup and a test session. During both sessions, participants lay supine with their feet secured to the pedals with a strap around the heel and the dorsum of each foot. Feet were secured to the pedals because many stroke survivors could not otherwise keep their paretic foot on the pedal. The ankle could still move freely. The skin was prepped, and muscle activity was recorded bilaterally from the tibialis anterior (TA), rectus femoris (RF), biceps femoris (BF), and medial gastrocnemius (MG) as described by Hermens et al. (2000). These muscles were selected because pilot work showed that they were prime movers in supine pedaling with the custom device. Reference electrodes were placed on the medial malleolus.

The purpose of the setup session was to identify an elastic load on the eccentric pulley system that approximated the downstroke contribution of the contralateral limb and enabled unilateral and bilateral uncoupled pedaling. Loads were adjusted by changing the number of elastic bands arranged in parallel around the eccentric pulley. Up to six loads were examined on the right and left limb. Loads were presented in order of decreasing stiffness. After a load was in place, participants were asked to pedal forward with their right (or left) limb. During the setup session, participants also performed conventional pedaling. Here, the instruction was to pedal forward with both limbs. Bilateral uncoupled pedaling was not performed during the setup session.

Elastic loads for unilateral pedaling were selected by observing pedaling performance to rule out excessively low and high loads and then analyzing pedaling velocity quantitatively. During the setup session, excessively low loads were identified visually as those with inadequate elastic force to return the limb to top-dead-center (i.e. the limb got stuck in upstroke). Excessively high loads were identified by observation as those that were so stiff that a) participants were unable to accomplish the downstroke or b) the

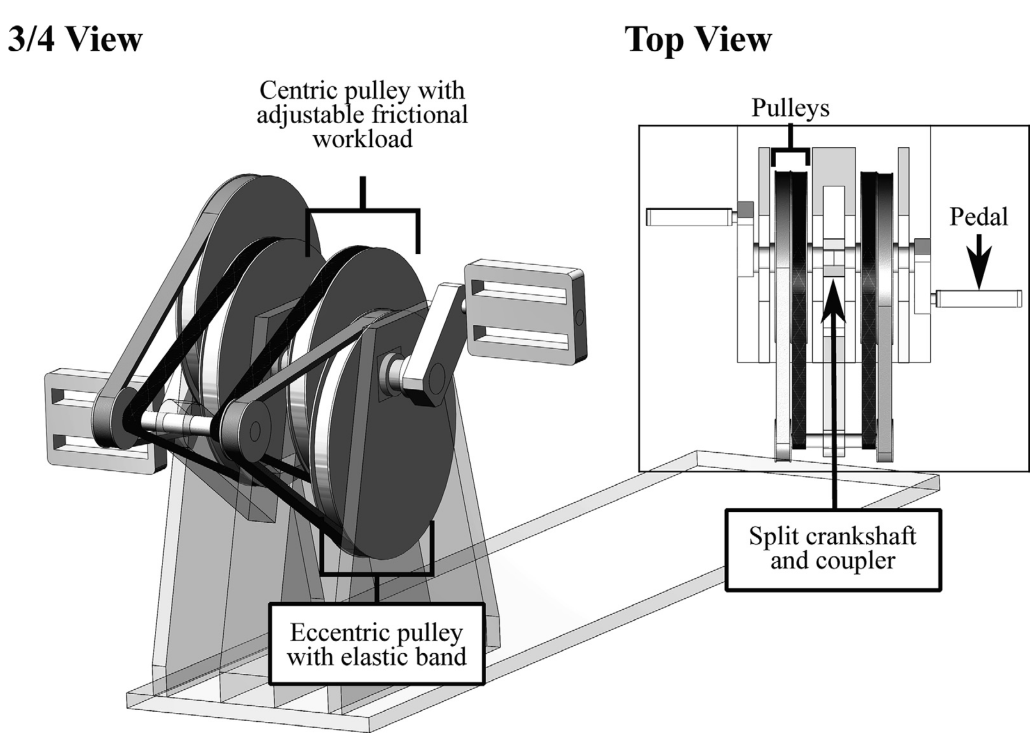

Fig. 1. Pedaling device with split crankshaft. The top view depicts the split crankshaft and coupler. The coupler allowed conventional pedaling when fastened in place and unilateral or bilateral uncoupled pedaling when removed. The ¾ view depicts the pulley systems of the pedaling device. An eccentric pulley with elastic band was used during unilateral and bilateral uncoupled pedaling to simulate the contribution from the contralateral downstroke limb during conventional pedaling. The elastic band was stretched during the downstroke of the pedaling cycle, and energy stored in the band was released during the upstroke. A centric pulley applied a frictional load.

limb raced back to top-dead-center such that participants or experimenters felt like it was moving uncontrollably. Typically, after eliminating excessively low and high loads, two or three loads remained. At this point, we computed the mean pedaling velocity as a function of crank position for all remaining loads. The difference between these values and analogous values recorded during conventional pedaling was computed. The elastic load with the smallest mean difference in pedaling velocity from conventional pedaling was selected. Loads were selected for the right and left leg individually.

During the test session, participants performed conventional, unilateral (right, left, paretic, non-paretic), and bilateral uncoupled pedaling. The elastic loads identified from the setup session were used during both unilateral and bilateral uncoupled pedaling. During bilateral uncoupled pedaling, participants were asked to pedal forward using both limbs and to keep the limbs 180° apart as in conventional pedaling. Instructions for unilateral and conventional pedaling were the same as in the setup session.

For each pedaling condition in each session, one 45-sec exposure period was provided after which one 60-sec bout of data were collected. During the exposure period, we repeated the instructions and gave verbal feedback. During the 60-sec data collection, neither instructions nor feedback were provided. Participants were asked to match their pedaling rate to an auditory pacing cue at 45 rpm. The purpose of the cue was to control pedaling rate across groups and conditions, thus minimizing rate differences that could confound interpretation of results. Moreover, if participants were unable to match the cue, differences between actual and prescribed pedaling rate could be used as a measure of task success. Despite its usefulness, we were also concerned that the cue could introduce its own confound. People with stroke might have impairments in sensorimotor processing that make it difficult to match movement rate to an external cue; they may be unable produce movement fast enough to match the cue. If this were the case, then between-group differences in pedaling performance could be attributed to stroke-related impairments in sensorimotor processing and/or movement rate, not paretic motor output and/or interlimb coordination. To address this concern, participants repeated each condition with no cue and an instruction to pedal at a comfortable rate. Trials with and without cues were counterbalanced to avoid ordering effects. Participants were always able to see the pedals.

Rotary optical encoders (MR318, Micronor Inc., Newbury Park, CA) were used to measure the position of the crankshaft. One encoder was connected to each half of the crankshaft via a chain and sprocket assembly. Fiber optic cables carried signals from each encoder to controller units (MR310, Micronor Inc., Newbury Park, CA). The zero position of the crank cycle (i.e. top-dead-center) was defined for each limb as the position where the crank arm was parallel to the plinth and the foot was nearest the hip. EMG was recorded with bipolar surface electrodes (Bagnoli-8, Delsys Inc., Natick, MA, Inc.). Signals were amplified 10 X at the electrode site before remote differential amplification (common mode rejection ratio 92 dB, gain 1,000 X, frequency response 20–450 Hz). Position and EMG signals were sampled at a rate of 2000 Hz using a 16-bit analog-to-digital convertor and data acquisition software (micro 1401 mk II, Spike 2, Cambridge Electronic Designs, UK) housed on a desktop computer.

2.4. Data processing and dependent variables

Position data were low pass filtered at 20 Hz, and the derivative of the position trace was computed to obtain pedaling velocity. EMG data were rectified and low pass filtered at 25 Hz. Velocity and EMG data were referenced to the crank position in 1° increments as described previously (Schindler-Ivens et al., 2004). Ensemble averages were created for each subject and condition. From these data, we computed the mean and coefficient of variation (COV) of pedaling velocity. Both values served as quantitative measures of pedaling performance, with COV of velocity providing a measure of smooth, continuous crank progression. In cases where group or condition-related changes in mean and/or COV of velocity were detected, we examined the velocity traces to determine the pedaling position(s) where these changes occurred. Ensemble averaged velocity data for each subject were smoothed and the derivative of velocity was calculated. Points of interest were identified by zero crossings of velocity and acceleration.

To further describe pedaling performance during bilateral uncoupled pedaling, we calculated the time relative position and velocity for the average revolution of each limb. For every complete revolution (0–360°) of each limb, we determined the mean position and velocity at every 1/500th of each revolution and averaged these 500 data points across all revolutions. We also calculated the time relative position and velocity for the contralateral limb during the average revolution of the ipsilateral limb.

For the bilateral uncoupled condition, we computed the mean and COV of continuous relative phase (CRP), defined as the absolute value of the difference in position between the right and left crankshaft as a function of time. We adapted methods from Plotnik et al. (2007) to calculate phase coordination index (PCI), which incorporates aspects of both the mean (phase accuracy) and COV of CRP (phase consistency). As shown in the equation, PCI was obtained by summing the COV of CRP and the mean of the minimum absolute difference from a 180° phase relation. Thus, PCI evaluates the accuracy and consistency of interlimb phasing. The accuracy term was normalized to 180° to convert to the same units as the consistency term. Plotnik et al. (2007) suggest that PCI represents a distinct feature of gait because it is not strongly correlated with other common measures such as gait symmetry, speed, and variability.

$$\mathrm{PCI}(\%) = \left[\frac{\sigma(\mathrm{CRP})}{\mu(\mathrm{CRP})} \times 100\right] + \left[\frac{\mu(|\mathrm{CRP}\text{ - }180|)}{180} \times 100\right]$$

Mean EMG amplitude and EMG modulation index (MI) were computed for each muscle across conditions and subjects. MI was computed as the difference between maximum and minimum EMG amplitude as a percent of maximum EMG amplitude (i.e., [EMGmax – EMGmin]/EMGmax * 100) (Zehr et al., 2000). Between-group and between-limb comparisons of EMG amplitude are difficult in pedaling because a normalization factor (e.g. M-wave, background EMG) is not available. For example, a maximal EMG value measured at one joint position is not an appropriate normalization factor for muscle activity at different joint positions (Mirka, 1991). Hence, MI was used to compare muscle activity between groups and limbs. Given that muscles are phasically active in pedaling, we reasoned that limbs and/or groups with higher muscle output would also display higher values for MI. Both the mean EMG amplitude and MI were used for within-limb comparisons of muscle activity across conditions.

Percent mechanical work performed by the paretic limb during pedaling was assessed using a pedaling device with a solid crankshaft (PowerTower with EMC Ergometric Multi Cycle attachment, Total Gym, San Diego, CA) and equipped with force and position sensors (force: Delta 660-60, ATI Industrial Automation, Apex, NC; position: BEI Model EX116-1024-2, BEI Sensors, Thousand Oaks, CA). The device and methods for quantifying work have been described previously (Kautz et al., 1998; Schindler-Ivens et al., 2008; Fuchs et al., 2011). In brief, the feet were secured to the pedals with straps around the heel and dorsum of the foot. Participants pedaled with an auditory pacing cue at 45 rpm against a moderate load (half the maximal load the participant could perform at

45 rpm). We measured the forces applied to each pedal and the position of the crank and the pedals and computed the forces oriented tangentially to the crank arm because these forces produce angular rotation of the crank. Data were referenced to crank angle and ensemble averaged. The area under the resulting curve yielded the mechanical work done by the limb. Positive and negative areas were computed to measure the propulsive (positive area) and retarding (negative area) work of each limb. Percent work done by the paretic limb [propulsive [%Work(+)], retardant [%Work (−)], and net [%Work(net)]] were computed as: Work(paretic)/ Work(total) * 100, where Work(paretic) was the work done by the paretic limb and Work(total) was the sum of the work done by both legs. A value of 50% indicated equal sharing of the work between limbs, as is typical for able-bodied individuals.

2.5. Statistics

SPSS Statistics 24 (International Business Machines Corporation, New York, NY) was used for all analyses. Effects were considered significant at $P < 0.05$ with no corrections for multiple comparisons. Before examining group and condition effects, data were tested for normality (Shapiro Wilk test) and equality of variance (Levene's test). Non-parametric statistics were applied as indicated. Analysis of variance (ANOVA) with a within subject factor of limb was used to test for differences between the left and right limb of control participants. No effects were detected for any dependent measure in any condition ($P \geq 0.10$). The average of the limbs was used in subsequent analyses.

ANOVA was also used to examine the effect of the auditory pacing cue on mean and COV of pedaling velocity. In the conventional pedaling condition, group (control, stroke) was a between subject factor and auditory cue (cue, no cue) was a within subject factor. The presence of an interaction triggered simple effects analyses consisting of pairwise comparisons at each level of group (paired samples t-tests) and each level of cue (independent samples t-tests). A single omnibus test examining the effect of cue during unilateral and bilateral uncoupled pedaling was not possible. The control vs. non-paretic and the control vs. paretic comparisons were between-subject comparisons, whereas the non-paretic vs. paretic comparison was a within-subject comparison. We ran three separate ANOVAs; one each for the following comparisons: control vs. paretic, control vs. non-paretic, and paretic vs. non-paretic. For the first two comparisons, group was treated as a between-subject factor. In the last comparison, group was treated as a within-subject factor. Finding no evidence that cue confounded the data, cued data were used in subsequent analyses.

Remaining hypothesis testing focused on our primary hypotheses that examined group and condition effects in pedaling performance. Omnibus tests were performed to identify main effects and interactions. Where global effects were detected, simple effects and/or post hoc analyses were applied. To test for effects of group and condition on velocity and COV for velocity three ANOVAs were performed. Each had a within subject factor of condition (conventional, unilateral, bilateral uncoupled). Two of the ANOVAs had a between-subject factor of group (paretic vs. control, non-paretic vs. control), and one of the ANOVAs had a within-subject factor of limb (paretic, non-paretic). Following a significant interaction, groups (independent samples t-tests and Mann-Whitney U tests) or limbs (paired sample t-tests and Wilcoxon signed rank tests) were compared. Following a significant main effect for condition or interaction, ANOVAs were performed with condition as a within subject factor. Following a main effect of condition, conditions were compared (paired sample t-tests and Wilcoxon signed rank tests).

To test for effects of group, condition, and muscle for EMG MI, three ANOVAs were performed. Each had within subject factors of condition (conventional, unilateral, bilateral uncoupled) and muscle (TA, RF, MG, BF). Two of the ANOVAs had a between-subject factor of group (paretic vs. control, non-paretic vs. control), and one of the ANOVAs had a within-subject factor of limb (paretic, non-paretic). Significant group X condition X muscle interactions was followed by ANOVAs performed for each muscle with factors of condition and group/limb. Significant interactions involving group or condition were followed by additional ANOVAs and/or paired comparisons as warranted by significant effects. Comparisons between groups/limbs were not performed for mean EMG amplitude because of limited ability to normalize EMG responses. Instead, ANOVAs were performed for each group/limb with condition (conventional, unilateral, bilateral uncoupled) as a within subject factor, followed by paired comparisons if there was a main effect of condition.

PCI, phase accuracy, and phase consistency were compared between groups (independent sample t-tests and Mann Whitney U tests). One sample t-tests and Wilcoxon signed rank tests were used to (1) compare mean velocity to the rate of the auditory cue and (2) compare %Work(+), %Work(−), and %Work(net) to a fixed value of 50%. To help describe the range of behaviors we observed during unilateral and bilateral uncoupled pedaling, stroke participants were separated into 3 groups for each condition. We tested for differences in FM scores and walking velocity between subgroups with one-way ANOVAs.

Pearson and Spearman correlations were used to examine the relationship between %Work(net) and COV of velocity, PCI, change in mean EMG amplitude, and change in EMG MI between conditions. We also tested the correlations between these variables and walking velocity, $FM_{LEtotal}$, $FM_{Lemotor}$, and FM_{LEsens}. Variables that were significantly correlated with %Work(net) were entered into a stepwise linear regression model with backward elimination to predict the dependent variable %Work(net). Variables were removed from the model in succession if the F value for that variable was the least significant of remaining variables and was $\geq$0.10. Adherence to regression-related assumptions (linearity, normality, minimal multi-collinearity, homoscedasticity, and no autocorrelation) was confirmed prior to conducting linear regressions.

3. Results

Group mean (SD) values and significance tests for velocity, EMG, and interlimb phasing are provided in Tables 2 and 3. Representative examples of pedaling behavior across groups and conditions are shown in Figs. 2 and 3.

In our evaluation of the effect of the auditory pacing cue, we found a significant main effect of cue on mean velocity during conventional pedaling ($P < 0.001$), wherein participants pedaled more slowly during cued than non-cued pedaling. There was no effect of group ($P = 0.73$) or group X cue interaction ($P = 0.36$). For COV of velocity, there was no significant main effect of cue ($P = 0.08$) or group ($P = 0.12$), but there was a group X cue interaction ($P = 0.03$). Simple effects analyses revealed that controls had a lower COV of velocity during non-cued than cued pedaling ($P = 0.003$). They also had a lower COV of velocity than participants in the stroke group during non-cued but not cued pedaling ($P = 0.03$). During unilateral and bilateral uncoupled pedaling, mean velocity was lower during cued than non-cued pedaling, regardless of group ($P \leq 0.003$). Cue had no significant effect on COV of velocity ($P \geq 0.13$).

Overall, these results suggest that pedaling performance in people with stroke was not adversely affected by the external auditory cue (i.e., no difference in COV of velocity with or without a cue). The rate of the cue was well within the movement ability of stroke

Table 2
Velocity and muscle activity across conditions and between groups. The top section shows mean and coefficient of variation of velocity for the stroke and control group during conventional pedaling and for the average control, non-paretic, and paretic limb during unilateral and bilateral uncoupled pedaling. The bottom section shows EMG modulation index and mean amplitude for the average control, non-paretic, and paretic limb during all conditions. Comparisons between groups/limbs were not performed for EMG mean amplitude. Significance notations for each condition are shown below each respective column. Values are Mean (SD). BF: biceps femoris; COV: coefficient of variation; EMG: electromyography; MG: medial gastrocnemius; MI: modulation index; RF: rectus femoris; TA: tibialis anterior.

Pedaling velocity		Conventional			Unilateral			Bilateral uncoupled		
Mean (deg/s)		*Control* 270 (1)		*Stroke* 288 (48)	*Control* 273 (6)	*Non-Paretic* 286 (43)	*Paretic* 264 (45)[bc]	*Control* 274 (14)	*Non-Paretic* 226 (72)[acde]	*Paretic* 204 (61)[acde]
COV (%)		11 (6)		11 (4)	11 (6)	12 (7)	25 (14)[abc]	23 (10)[cd]	51 (28)[acd]	65 (28)[abcd]
EMG		*Control*	*Non-Paretic*	*Paretic*	*Control*	*Non-Paretic*	*Paretic*	*Control*	*Non-Paretic*	*Paretic*
MI (%)	*TA*	58 (17)	64 (23)	60 (27)	74 (12)[c]	71 (18)[c]	75 (20)[c]	75 (10)[c]	75 (14)[c]	75 (19)[c]
	RF	79 (11)	79 (15)	54 (26)[ab]	83 (11)	83 (7)	70 (23)[abc]	87 (8)[cd]	87 (8)[cd]	76 (20)[abc]
	MG	77 (8)	77 (19)	55 (23)[ab]	77 (12)	68 (24)[c]	56 (22)[ab]	81 (7)[cd]	81 (13)[cd]	66 (20)[abcd]
	BF	81 (11)	75 (15)	51 (28)[ab]	72 (13)	56 (22)[ac]	54 (23)[a]	78 (10)	87 (9)[acd]	62 (24)[abcd]
Mean amplitude (μV)	*TA*	1.9 (1.7)	4.0 (5.2)	6.7 (6.3)	5.0 (3.7)[c]	6.7 (5.6)[c]	20.8 (17.6)[c]	5.9 (6.0)[c]	16.5 (3.2)[cd]	21.1 (21.5)[c]
	RF	3.2 (2.8)	5.2 (5.4)	2.8 (4.2)	7.0 (4.1)[c]	10.4 (10.5)[c]	8.2 (9.1)[c]	7.7 (4.8)[c]	10.6 (12.9)[c]	9.2 (12.0)[c]
	MG	5.6 (2.7)	9.5 (9.4)	2.3 (2.3)	4.7 (2.4)	6.7 (8.4)[c]	2.7 (3.2)	7.7 (3.3)[cd]	14.6 (13.8)[cd]	4.5 (5.3)[cd]
	BF	4.1 (2.5)	4.4 (5.3)	2.4 (3.2)	2.4 (1.7)[c]	2.3 (3.4)[c]	2.1 (3.2)	4.1 (2.6)[d]	13.0 (20.4)[cd]	4.0 (4.5)[cd]
		[a] $p < 0.05$ vs. control [b] $p < 0.05$ vs. non-paretic			[a] $p < 0.05$ vs. control [b] $p < 0.05$ vs. non-paretic [c] $p < 0.05$ unilateral vs. conventional			[a] $p < 0.05$ vs. control [b] $p < 0.05$ vs. non-paretic [c] $p < 0.05$ bilat. uncoupled vs. conventional [d] $p < 0.05$ bilat. uncoupled vs. unilateral [e] $p < 0.05$ rate vs. 270 deg/s		

Table 3
Interlimb phasing and coordination. Values are shown for phase accuracy and phase consistency, which are summed to produce values for PCI. Higher values represent worse performance. The stroke group had worse phase accuracy and phase consistency, and thus worse interlimb coordination as represented by PCI. Interlimb phasing and coordination values are also shown for three stroke subgroups as identified by pedaling strategy during the bilateral uncoupled condition. Values are Mean (SD). PCI: phase coordination index. [*] $P < 0.05$ stroke vs. control.

	Control	Stroke			
		All	*Slowing (n = 10)*	*Pausing (n = 6)*	*Unstructured (n = 5)*
Phase accuracy (%)	18 (5)	39 (12)[*]	34 (12)	43 (9)	46 (9)
Phase consistency (%)	15 (5)	43 (16)[*]	34 (16)	50 (11)	53 (10)
PCI (%)	32 (10)	82 (27)[*]	68 (28)	93 (19)	98 (19)

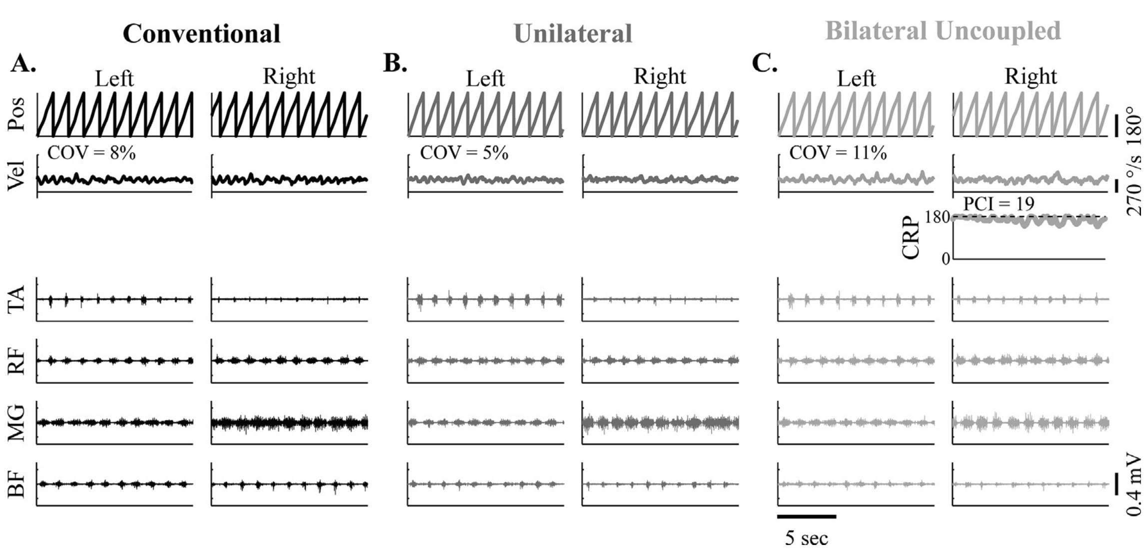

Fig. 2. Representative data from one control participant. Position, velocity, and EMG data are shown for (A) conventional (black lines), (B) unilateral (dark gray lines), and (C) bilateral uncoupled (light gray lines) pedaling for both the left and right limb. For bilateral uncoupled pedaling, continuous relative phase is also shown. The time interval of data shown (~13.7 sec) is the same across conditions. For unilateral pedaling, data for each leg are shown together despite being from different conditions. COV of velocity and PCI values that are displayed represent those values calculated for the entire data collection period. BF: biceps femoris; COV: coefficient of variation of velocity; CRP: continuous relative phase; MG: medial gastrocnemius; PCI: phase coordination index; Pos: position; RF: rectus femoris; TA: tibialis anterior; Vel: velocity.

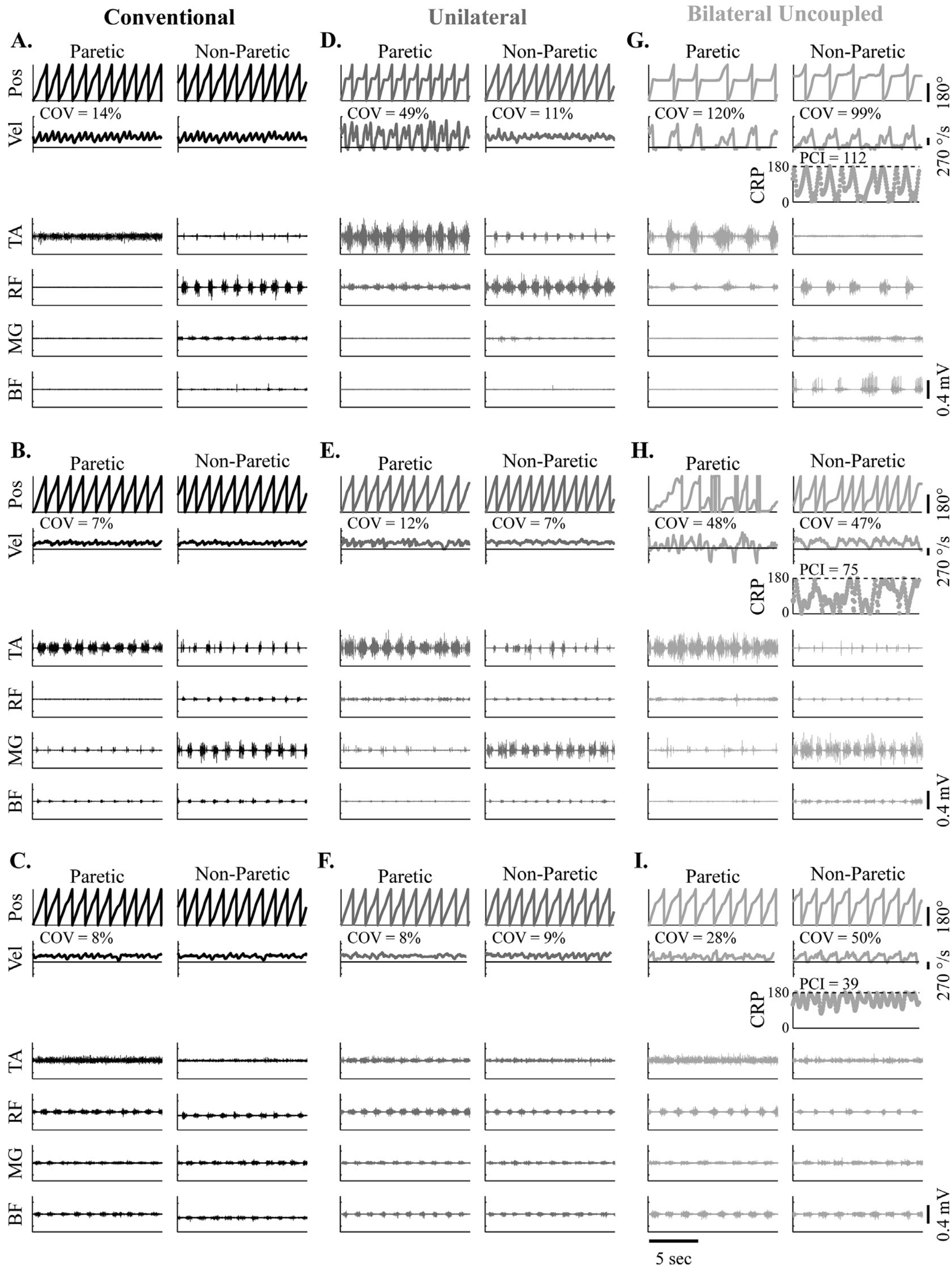

Fig. 3. Representative data from three participants with stroke. Position, velocity, and EMG data are shown for (A-C) conventional (black lines), (D-F) unilateral (dark gray lines), and (G-I) bilateral uncoupled (light gray lines) pedaling for both the paretic and non-paretic limb. Each row (ADG, BEH, and CFI) shows one representative example from each of the three subgroups identified during unilateral and bilateral uncoupled pedaling. For bilateral uncoupled pedaling, continuous relative phase is also shown. The time interval of data shown (~13.7 sec) is the same across conditions. For unilateral pedaling, data for each leg are shown together despite being from different conditions. COV of velocity and PCI values that are displayed represent those values calculated for the entire data collection period. BF: biceps femoris; COV: coefficient of variation of velocity; CRP: continuous relative phase; MG: medial gastrocnemius; PCI: phase coordination index; Pos: position; RF: rectus femoris; TA: tibialis anterior; Vel: velocity.

participants (i.e., mean velocity cued < non-cued). Moreover, during conventional pedaling, the control group was less smooth with the cue than without it. Given that stroke participants were expected to pedal less smoothly than controls, the cued data provided a more conservative estimate of this effect and reduced risk of Type I error. Together, these observations allayed our concerns that using a cue would confound the data. Cued data were used in subsequent analyses that examined group and condition effects in pedaling performance.

3.1. Velocity, work, and interlimb phasing

For velocity and COV of velocity, respectively, there were significant condition X group effects for the non-paretic limb compared to controls ($F = 3.7$, $P = 0.04$; $F = 6.4$, $P = 0.005$), the paretic limb compared to controls ($F = 8.4$, $P = 0.001$; $F = 12.7$, $P < 0.001$), and the paretic limb compared to the non-paretic limb ($F = 5.6$, $P = 0.01$; $F = 10.1$, $P = 0.001$). In follow-up ANOVAs there was an effect of condition for velocity and COV of velocity for the non-paretic limb ($F = 6.3$, $P = 0.008$; $F = 26.2$, $P < 0.001$) and the paretic limb ($F = 14.7$, $P < 0.001$; $F = 51.8$, $P < 0.001$) and an effect of condition for COV of velocity for controls ($F = 17.5$, $P = 0.001$). Paired comparisons (between groups and conditions) and significance values are presented below and in Table 2.

During conventional pedaling, both groups displayed continuous, forward crank progression (Figs. 2A and 3A, B, C). There were no between-group differences in the mean or COV of pedaling velocity ($P \geq 0.10$). In both groups, mean pedaling velocity was not significantly different from the pace of the auditory cue ($P \geq 0.10$). Consistent with asymmetric contributions to bilateral lower limb movement post-stroke, the paretic limb performed 41 (8)% of the positive work, 64 (12)% of negative work, and 16 (24)% of the net mechanical work of pedaling (all different from 50%, $P < 0.001$). Fig. 4 displays torque profiles for the non-paretic and paretic limb.

During unilateral pedaling, the mean and COV of pedaling velocity were not different from conventional pedaling in the control group and the non-paretic limb of people with stroke ($P \geq 0.13$). However, in the paretic limb, mean velocity during unilateral pedaling decreased, and COV of velocity increased ($P \leq 0.006$). Both values were significantly different from the non-paretic limb during unilateral pedaling ($P \leq 0.01$). COV of velocity was significantly higher than for unilateral pedaling in controls ($P < 0.001$). In the control group, the paretic limb, and the non-paretic limb, mean pedaling velocity was not significantly different from the pace of the auditory cue ($P \geq 0.09$). Decreased mean velocity and increased COV in the paretic limb during unilateral pedaling were due to a transient decline in pedaling velocity during the extension-to-flexion phase transition (Fig. 3D, E, F). On average, velocity began to decrease at 127 (32)° in the pedaling cycle, reached a nadir of 165 (86) deg/sec at 202 (26)°, and returned to baseline at 293 (36)°. However, there was considerable inter-individual variation in the behavior of the paretic limb with respect to velocity fluctuations during unilateral pedaling. To help describe the range of behaviors, we separated stroke participants into 3 groups based upon their performance during unilateral pedaling. In most participants ($n = 10$, Fig. 3E), the rate of forward crank progression decreased. In others ($n = 6$, Fig. 3D), there was a pause and/or a brief reversal in pedaling direction. In the remaining individuals with stroke ($n = 5$ Fig. 3F), there was little to no change in mean velocity. Individuals with stroke who were less successful with unilateral pedaling had more motor impairment ($FM_{LEtotal}$: $F = 3.4$, $P = 0.05$; $FM_{LEmotor}$: $F = 4.1$, $P = 0.03$; walking velocity: $F = 8.0$, $P = 0.003$.

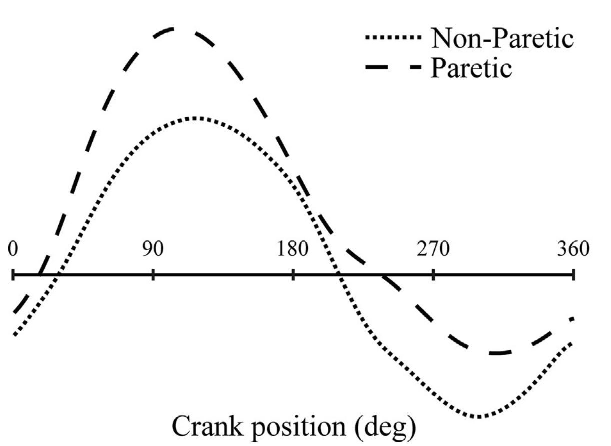

Fig. 4. Torque profiles for the non-paretic and paretic limb. Ensemble average torque data from conventional pedaling are displayed for the non-paretic (dotted lines) and paretic limb (dashed lines) across the pedaling cycle. Propulsive work is represented by the positive area under the curve, retarding work is represented by the negative area under the curve, and net work is represented by the difference between the positive and negative area under the curve. Note that torque data were collected from a pedaling device equipped with force and position sensors.

During bilateral uncoupled pedaling, control participants rotated each crankshaft forward in a manner consistent with the representative example in Fig. 2C. Mean pedaling velocity was not different from the other two conditions; COV of velocity increased significantly from conventional and unilateral pedaling ($P < 0.001$). Increased COV was due to variations in velocity across the pedaling cycle. On average, velocity rose to 385 (55) deg/s at 148 (22)° and declined to 182 (50) deg/s at 281 (43)° (Fig. 5A). Because the downstroke limb moved faster than the upstroke limb, neither the accuracy nor the consistency of interlimb phasing was ideal. This observation is reflected in group mean values for PCI, phase accuracy, and phase consistency (Table 3).

When people with stroke performed bilateral uncoupled pedaling, mean pedaling velocity in the paretic and non-paretic limb was significantly lower than the control group ($P \leq 0.04$), the other pedaling conditions ($P \leq 0.005$) and the auditory cue ($P \leq 0.02$).

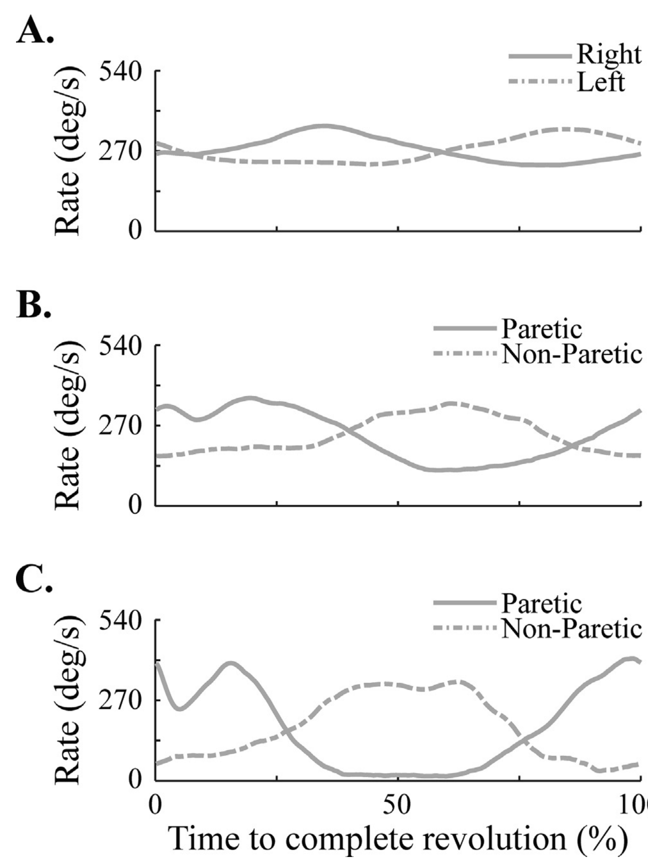

Fig. 5. Time relative velocity during bilateral uncoupled pedaling. Average time relative velocity profiles for the right or paretic limb (solid lines) and for the left or non-paretic limb (dashed lines) are shown for (A) the control group, (B) the stroke subgroup who displayed an exaggerated version of the control strategy, and (C) the stroke subgroup where one limb stopped pedaling while the other advanced the crank. Time relative velocity was determined by calculating the mean velocity at every 1/500th of every complete revolution (0–360 degrees). The resulting time relative velocity data were averaged across all revolutions and subjects within the group or subgroup of interest. The time relative velocity for the contralateral limb during the average revolution of the ipsilateral limb was determined in the same way with respect to complete revolutions of the ipsilateral limb.

COV of velocity in both limbs increased beyond the values for the control group and the other pedaling conditions ($P \leq 0.003$). COV of velocity was higher in the paretic than the non-paretic limb ($P = 0.01$). PCI during bilateral uncoupled pedaling in people with stroke was significantly higher than in controls ($P < 0.001$). Elevated PCI was due to changes in phase accuracy and phase consistency, both of which were significantly different from control values ($P < 0.001$). Unlike control participants who displayed a uniform strategy for bilateral uncoupled pedaling, people with stroke exhibited a range of behaviors that contributed to the observed deficits in velocity and interlimb phasing. To help describe the range of behaviors as done for unilateral pedaling, stroke participants were separated into 3 groups based upon their performance during bilateral uncoupled pedaling. Most stroke participants ($n = 10$) displayed an exaggerated version of the control strategy wherein velocity rose to 373 (122) deg/s at 138 (31)° and declined to 71 (34) deg/s at 245 (44)° (Fig. 5B). As with the control group, the downstroke limb moved faster than the upstroke limb (Figs. 5A, B and 3I). In 6 people with stroke, one limb stopped pedaling while the other advanced the crank. In these individuals, forward crank progression stopped at 195 (18)° in the pedaling cycle, while the contralateral limb moved from 217 (49)° in the pedaling cycle to 25 (88)°. This behavior alternated between limbs (Figs. 5C and 3G). The remaining 5 stroke survivors had considerable difficulty with bilateral uncoupled pedaling. As shown in the representative example in Fig. 3H, some would complete more than one revolution of one crank while holding stationary or occasionally rotating the other crank. Crank rotations were often incomplete and interrupted by backward crank progression. There was no repeatable pattern of motor output and no evidence of a reciprocal, alternating strategy between limbs. As seen in unilateral pedaling, individuals with stroke who were less successful with bilateral uncoupled pedaling had more motor impairment ($FM_{LEtotal}$: $F = 5.9$, $P = 0.01$; $FM_{LEmotor}$: $F = 4.8$, $P = 0.02$).

3.2. Muscle activity

For mean EMG amplitude, there were significant effects of condition for all muscles in all limbs ($F \geq 3.5$, $P < 0.05$). For EMG MI, there was a significant condition X muscle X group effect for the non-paretic limb compared to controls ($F = 6.3$, $P < 0.001$). In follow-up ANOVAs, there was a group X condition interaction for BF ($F = 9.3$, $P = 0.001$) and effects of condition for TA, MG, and RF ($F \geq 6.8$, $P \leq 0.004$). ANOVAs to compare conditions for TA, MG, RF (regardless of group), and BF (separate for each group) found significant effects of condition for TA, MG, and RF ($F \geq 9.0$, $P \leq 0.001$) and BF in the non-paretic limb ($F = 21.8$, $P < 0.001$). For the paretic limb compared to controls, there were significant interactions for group X muscle interaction ($F = 3.1$, $P = 0.04$) and condition X muscle ($F = 2.6$, $P = 0.04$). In follow-up ANOVAs, there were significant effects of condition for all muscles ($F \geq 6.1$, $P \leq 0.006$). For the non-paretic compared to the paretic limb, there was a significant condition X muscle X group effect ($F = 6.0$, $P = 0.002$). In follow-up ANOVAs, there was a limb X condition effect ($F \geq 6.0$, $P \leq 0.01$) for the RF and BF, an effect of condition for the TA and MG ($F \geq 3.9$, $P \leq 0.04$), and an effect of limb for MG ($F = 14.4$, $P = 0.001$). ANOVAs to compare conditions for TA and MG (regardless of group) and RF and BF (separate for each limb) found significant effects for all muscles ($F \geq 5.8$, $P \leq 0.01$). Paired comparisons (between groups and conditions) and significance values are presented below and in Table 2.

Group results for EMG are shown in Figs. 6 and 7. During conventional pedaling, control participants showed no significant between-limb difference in MI for any muscle examined. In people with stroke, MI in the RF, BF, and MG was lower in paretic than non-paretic limb and control limbs ($P \leq 0.002$). There was no difference in MI between the paretic, non-paretic, and control TA ($P \geq 0.79$) (Figs. 6 and 7).

During unilateral pedaling, both groups displayed significantly higher mean EMG in TA and RF as compared to conventional pedaling ($P \leq 0.009$). MI in the TA was higher during unilateral as compared to conventional pedaling for all groups ($P \leq 0.006$). MI in the paretic RF was also higher during unilateral than conventional pedaling ($P = 0.02$) but remained significantly lower than in the non-paretic limb and controls ($P = 0.007$). Also, during unilateral pedaling, mean EMG decreased in the BF of control and non-paretic limbs and in the MG of the non-paretic limb ($P \leq 0.01$). There was no change in the mean EMG in the paretic MG and BF ($P \geq 0.52$). MI in the non-paretic MG and BF was lower during unilateral than conventional pedaling ($P \leq 0.01$), dropping below controls in BF ($P = 0.03$). MI in the paretic MG remained below the control and non-paretic values ($P \leq 0.001$). In the paretic BF, MI

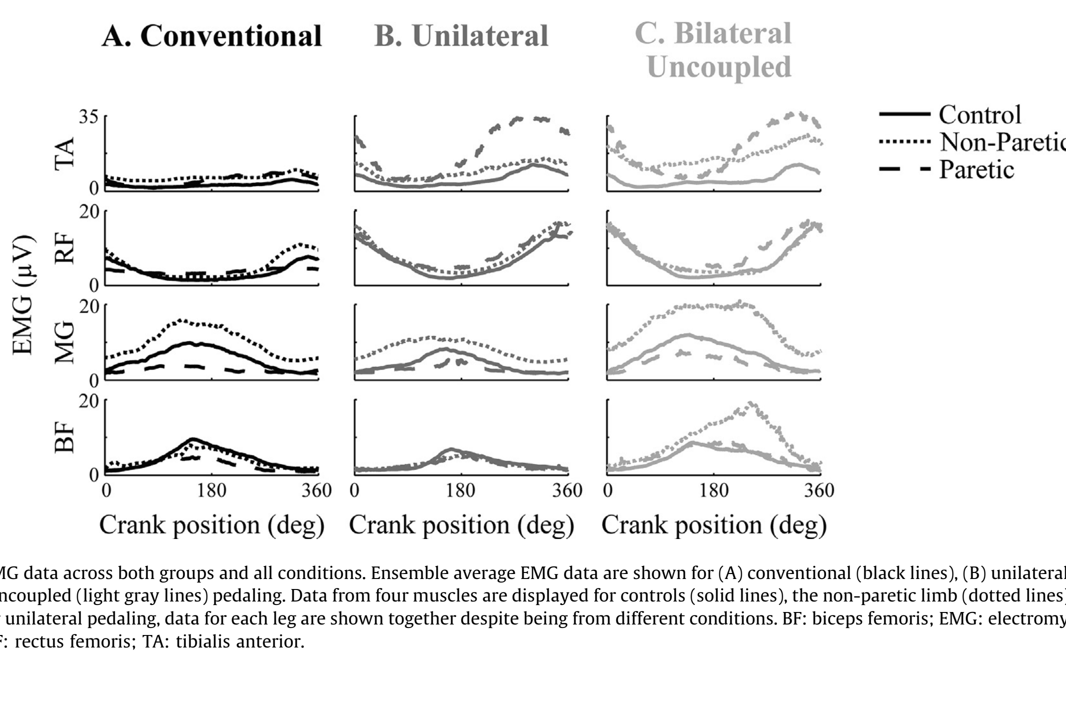

Fig. 6. Average EMG data across both groups and all conditions. Ensemble average EMG data are shown for (A) conventional (black lines), (B) unilateral (medium gray lines), and (C) bilateral uncoupled (light gray lines) pedaling. Data from four muscles are displayed for controls (solid lines), the non-paretic limb (dotted lines), and the paretic limb (dashed lines). For unilateral pedaling, data for each leg are shown together despite being from different conditions. BF: biceps femoris; EMG: electromyography; MG: medial gastrocnemius; RF: rectus femoris; TA: tibialis anterior.

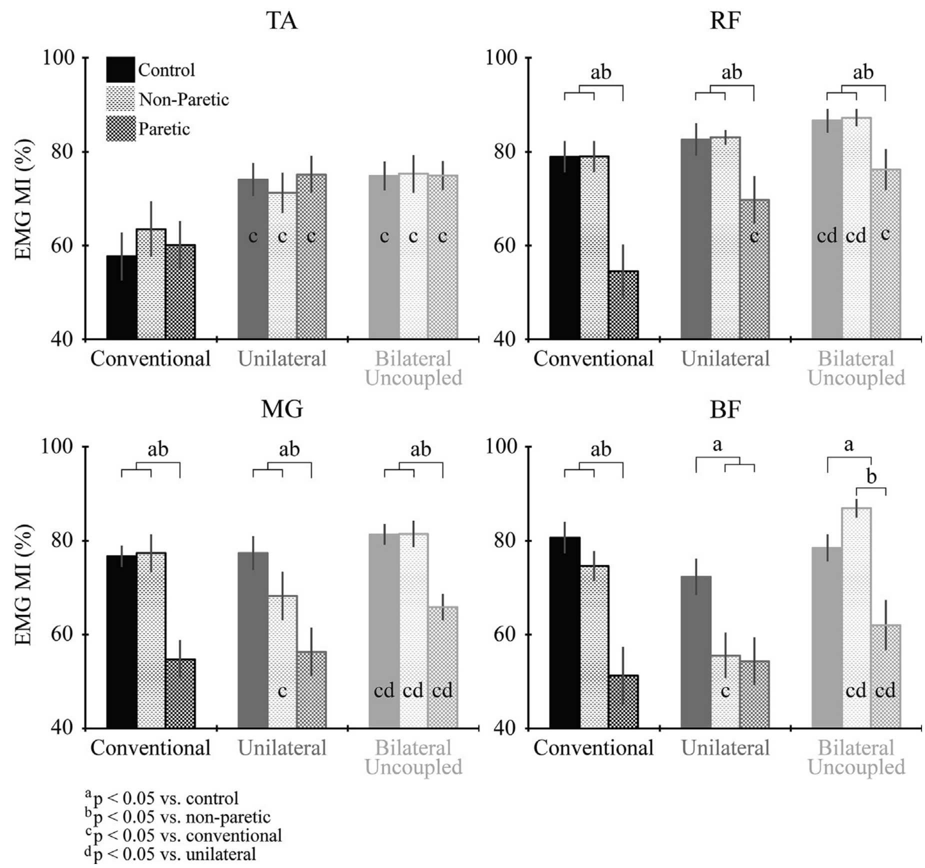

Fig. 7. EMG modulation index across both groups and all conditions. Modulation index is shown for conventional (left columns, black bars), unilateral (middle columns, medium gray bars), and bilateral uncoupled pedaling (right columns, light gray bars). Values are shown for all four muscles and from the control group, the non-paretic limb, and the paretic limb. Differences between groups and limbs are indicated by significance lines. Differences between conditions are indicated by letters within the bars. Nomenclature for significance lettering is provided. BF: biceps femoris; EMG: electromyography; MG: medial gastrocnemius; RF: rectus femoris; TA: tibialis anterior.

was lower than in the control group ($P < 0.001$) but not different from the non-paretic limb ($P = 0.82$).

During bilateral uncoupled pedaling, mean EMG amplitude in the paretic, non-paretic, and control MG and BF was higher than during unilateral pedaling ($P \leq 0.01$). Mean EMG in these muscles was also higher than during conventional pedaling for all cases ($P \leq 0.007$) except the control BF ($P = 0.43$). MI in the paretic and non-paretic MG and BF and control MG was higher than in conventional and unilateral pedaling ($P \leq 0.04$). However, in the paretic limb, these values were still lower than in control and non-paretic limbs ($P \leq 0.001$). In the non-paretic BF, MI was higher than controls ($P = 0.03$). Regardless of group, mean EMG amplitude in the RF did not increase beyond values observed during unilateral pedaling ($P \geq 0.12$). However, MI in the paretic, non-paretic, and control RF was significantly higher than during conventional pedaling ($P \leq 0.02$), and in the non-paretic and control RF, MI was higher than during unilateral pedaling ($P \leq 0.02$). MI in the paretic RF was significantly lower than in the non-paretic RF ($P = 0.008$). Regarding the TA, only the non-paretic limb displayed a significant increase in mean EMG as compared to unilateral pedaling ($P < 0.05$). Neither group showed a further increase in MI in the TA from unilateral pedaling ($P \geq 0.41$).

3.3. Relationships with mechanical work and clinical measures

In the stroke group, %Work(net) was negatively correlated with PCI ($R^2 = 0.45$, $P = 0.003$) and with COV of velocity in the paretic limb during unilateral ($R^2 = 0.25$, $P = 0.04$) and bilateral uncoupled ($R^2 = 0.29$, $P = 0.02$) pedaling. %Work(net) was not significantly correlated with the change in mean EMG amplitude or EMG MI in the paretic limb between unilateral and conventional pedaling ($P \geq 0.15$). When the three significantly correlated variables were entered into a stepwise linear regression with backward elimination, only PCI made a significant contribution to the prediction of %Work(net) ($F = 13$, $R^2 = 0.44$, $P = 0.003$). If we forced the model to include both PCI and COV of velocity during unilateral pedaling with the paretic limb, there was no improvement in the model ($F = 7$, adjusted $R^2 = 0.42$, $P = 0.006$).

With respect to clinical measures, $FM_{LEtotal}$ was positively correlated with %Work(net) ($R^2 = 0.45$, $P = 0.003$) and negatively correlated with PCI ($R^2 = 0.50$, $P < 0.001$), but was not correlated with COV of velocity in the paretic limb during unilateral pedaling. Likewise, $FM_{LEmotor}$ was also positively correlated with %Work(net) ($R^2 = 0.50$, $P = 0.001$) and negatively correlated with PCI ($R^2 = 0.61$, $P < 0.001$). Walking speed was positively correlated with %Work(net) ($R^2 = 0.28$, $P = 0.02$) and negatively correlated with PCI ($R^2 = 0.23$, $P = 0.03$). FM_{LEsens} was not significantly correlated with any outcome measure of pedaling performance.

4. Discussion

The aim of this study was to better understand why asymmetric contributions (non-paretic > paretic) to bilateral lower limb movements persist in chronic stroke. We considered that motor impairment of the paretic limb and impaired interlimb coordination may contribute. A novel, split-crank pedaling device enabled conventional, unilateral, and bilateral uncoupled pedaling. Unilateral and bilateral uncoupled pedaling were performed to identify and distinguish between impairments in paretic motor output and interlimb coordination. Conventional pedaling served as a nominal condition to which the other conditions were compared; it also provided measures of asymmetry during continuous, reciprocal, flexion and extension movements involving both lower limbs. While we found evidence of both impairments, results suggest that impaired interlimb coordination may be a more important factor than paretic motor impairment in chronic asymmetry. Below we discuss these findings in the context of prior work, examine physiological underpinnings, and consider implications for rehabilitation.

4.1. Conventional pedaling

Consistent with prior reports (Landin et al., 1977; Brown et al., 1998; Kautz et al., 1998; Perell et al., 1998; Chen et al., 2005; Alibiglou et al., 2011; De Marchis et al., 2015; Promjunyakul et al., 2015), conventional pedaling exposed asymmetries in mechanical work and muscle activity in the stroke group that were not apparent in controls. In the current study, the paretic limb of people with stroke produced only 16% of the net mechanical work for crank rotation. Muscle activity in RF, MG, and BF was significantly less modulated in the paretic limb than non-paretic and control limbs. While quantitative comparisons of EMG amplitude between the paretic and non-paretic limbs were not made, visual inspection of the data revealed many examples in which no task-related EMG was observed in the paretic limb during conventional pedaling (e.g. Fig. 3A). These observations support the conclusion that conventional pedaling is accomplished primarily by the non-paretic limb in people with stroke.

Regarding the ability to accomplish the task, people with stroke performed conventional pedaling as rapidly and smoothly as controls. Both groups matched the rate of the auditory cue, and there were no between-group differences in COV of velocity. These observations suggest that the pedaling pattern that stroke survivors used, albeit asymmetric, was sufficient to meet the demands of conventional pedaling. Moreover, groups were well matched with respect to task performance and completion during the nominal condition.

4.2. Unilateral pedaling

When the paretic limb performed unilateral pedaling, task performance was worse (pedaling was slower and less smooth) than during the conventional condition. Importantly, no such decline in performance was observed during unilateral pedaling in the control group or the non-paretic limb of people post-stroke. We conclude that these deficits represent stroke-related motor impairment in the paretic limb. Specifically, unilateral pedaling with the paretic limb was slower and less smooth than conventional pedaling. Deficits were driven by a transient decline in pedaling rate, a pause in forward crank progression, and/or a reversal of pedaling direction during the extension-to-flexion phase transition. Impairments in paretic motor output were not related to power generation, which occurs during the downstroke (Neptune et al., 1998). Rather, performance deficits expressed during unilateral pedaling were due to difficulty executing the extension-to-flexion phase transition when the limb transitions from the downstroke (where power is generated) to the upstroke (where recovery occurs). During this transition, which is also known as the posterior transition, the hip extends while the knee flexes so that the whole limb translates posterior with respect to the trunk. EMG data support that motor output associated with the posterior transition was impaired. EMG activity in the paretic BF was significantly less modulated than in controls, and BF EMG amplitude did not increase from conventional to unilateral pedaling. If we assume that BF is representative of other hamstring muscles involved in the posterior transition (Raasch et al., 1999), we can conclude that insufficient activation of these muscles contributes to the paretic lower limb movement impairments seen during unilateral pedaling.

Unilateral pedaling also provides evidence that the paretic limb may have motor ability that is neither evident nor fully utilized during conventional pedaling. Mean EMG amplitude in the paretic TA and RF increased approximately threefold from conventional to unilateral pedaling. Values for MI in these muscles also increased, with the MI for the TA reaching control values. Thus, the tendency not to use the paretic limb in conventional pedaling (or to use it less than in unilateral pedaling) may represent learned non-use, a phenomenon whereby stroke survivors can move the paretic limb but fail to do so spontaneously in real world situations (see Taub et al., 2006 for review). However, pure learned non-use requires the ability to acutely increase the motor output of the paretic limb while maintaining good task performance (Sunderland et al., 2005). We found that pedaling velocity was slower and more variable during unilateral pedaling with the paretic limb. Thus, in its purest form, learned nonuse may not fully explain increased motor output from the paretic limb. Importantly, although increased EMG during unilateral pedaling suggests that the paretic limb may have residual unused motor ability, it is not certain that this additional capability is available for use under the mechanics of conventional pedaling.

4.3. Bilateral uncoupled pedaling

Participants in the control group were successful with bilateral uncoupled pedaling as evidenced by no change in mean pedaling velocity, as compared to conventional or unilateral pedaling. However, COV of velocity increased in controls during bilateral uncoupled pedaling. This effect was driven by a decrease in pedaling velocity during the posterior transition; this suggests that controls had more difficulty with this phase transition during bilateral uncoupled pedaling than during the other two conditions. That these changes occurred during bilateral uncoupled but not unilateral pedaling (which had the same mechanics) suggests that the posterior transition is more difficult to execute when simultaneous and coordinated output of both limbs is required. These data also provide insight into how neurologically intact individuals alter their pedaling pattern to fulfill the demands of bilateral uncoupled pedaling. To keep pace with the auditory cue, the control group adjusted their pedaling rate in each limb. Pedaling rate was above average in the downstroke and below average during upstroke. Because pedaling involves simultaneous and reciprocal movement of both limbs, these adjustments could be achieved only by coordinating the output of the two limbs. Thus, bilateral uncoupled pedaling exposed decrements in pedaling performance that represent challenges to interlimb coordination, but it also provided evidence that people without stroke can overcome this challenge with a pattern reliant on interlimb coordination.

In the stroke group, bilateral uncoupled pedaling revealed evidence of impaired interlimb coordination. Observations from this condition also suggest that impaired interlimb coordination may be a more substantial impediment to bilateral movement than paretic motor impairment alone. During this condition, the stroke group was unable to match the rate of the auditory cue. Crank progression was less smooth, and interlimb phasing was less appropriate than in control participants. Some stroke survivors slowed their pedaling rate during the posterior transition while the contralateral limb moved more rapidly through downstroke. Others stopped pedaling during the posterior transition while they advanced the other limb. Some were unable to achieve any sort of bilaterally coordinated movement of the limbs. Those who slowed or stopped one limb while advancing the other were most successful with the task. Their strategy resembled the one employed by controls wherein participants adjusted pedaling rate in each limb so that they could slow down for the posterior transition and still achieve the desired mean pedaling velocity. The observation that most stoke participants displayed behaviors similar to controls (e.g. slowing during posterior transition) suggests that they have some residual ability to produce reciprocally coordinated movement of the lower limbs. However, because stroke survivors were less successful than controls with bilateral uncoupled pedaling (e.g. stopping, slowing more than controls), our data also suggest that strategies available for interlimb coordination and their underlying mechanisms are degraded in chronic stroke. The observation that some people with stroke displayed no evidence of interlimb coordination during the bilateral uncoupled condition and were unable to move the limbs in a reciprocal fashion further supports this conclusion. Neural circuits responsible for interlimb coordination may be severely disrupted in these individuals.

Of note, pedaling performance in the non-paretic limb was impaired during bilateral uncoupled as compared to unilateral pedaling. Similarly, both limbs experienced performance deficits during bilateral uncoupled pedaling in the control group. These findings suggest that impaired interlimb coordination may cause performance deficits in both limbs. In healthy controls, the bilateral influence of the sensorimotor state of one limb on the contralateral limb has been demonstrated during pedaling (Ting et al., 1998; 2000; Alibiglou et al., 2009). After stroke, it has been suggested that interlimb effects are enhanced, potentially through supraspinal disinhibition (Kautz et al., 2005b, 2006). Interestingly, performance of the non-paretic limb becomes worse and more like the paretic limb during bilateral movements of the upper limb (Dickstein et al., 1993; Steenbergen et al., 1996; Rice et al., 2001). Some of these authors have suggested that the non-paretic limb adapts its motor performance to allow motor output that is better coordinated with the paretic limb. Such an effect might constrain the limbs to function as a unit to maximize performance bilaterally.

4.4. Interlimb coordination vs. Paretic motor impairment

In this study, we detected stroke-related performance deficits during unilateral and bilateral uncoupled pedaling. These data suggest that both paretic motor impairment and deficiencies in interlimb coordination may contribute to reduced use of the paretic limb and asymmetric contributions to conventional pedaling. It is plausible that difficulty completing the posterior transition with the paretic limb alone could contribute to asymmetry. Indeed, the paretic and non-paretic limbs are mechanically coupled, and the feet are secured to the pedals in conventional pedaling, allowing torque applied by the non-paretic limb to compensate for inadequate contributions from the paretic limb. The observation that COV of velocity during unilateral pedaling was associated with asymmetry further supports this conclusion. However, our data also suggest that impaired interlimb coordination may be a more important factor in asymmetry than paretic motor impairment alone. Most people with stroke displayed some deficiencies in unilateral pedaling, but all could produce repeated crank rotations. Hence, the inability to produce adequate torque in the correct direction at the correct time to rotate the crank cannot explain asymmetry. In contrast, not all stroke survivors could do bilateral uncoupled pedaling. Those who could produce reciprocal movement during this task displayed more substantial performance deficits than in unilateral pedaling. Finally, once a regression model accounted for movement deficits in bilateral uncoupled pedaling, impairments associated with unilateral pedaling made no further contribution to the prediction of asymmetry during conventional pedaling. Together, these observations suggest that asymmetric work during conventional pedaling may be due to the inability to coordinate the output of the paretic and non-paretic limbs, especially during the extension to flexion (i.e. posterior) phase transition.

After stroke, multiple studies suggest that altered descending supraspinal signals may contribute to impaired interlimb coordination. When the non-paretic limb performs static contractions or pedaling, regardless of the timing of activation, paretic EMG phasing gets worse during pedaling (Kautz et al., 2005b; Rogers et al., 2011). These findings suggest that the cause of impairment is descending commands associated with movement of the non-paretic limb. Consistent with this explanation, stroke survivors who are worse at bilateral antiphase ankle movements also have greater descending ipsilateral conductivity (Madhavan et al., 2010). Therefore, this may be one reason why interlimb coordination is impaired after stroke.

4.5. Clinical significance

During both unilateral and bilateral uncoupled pedaling, we identified a wide variety of responses across stroke participants. Variability of responses is evident in the representative examples (Fig. 3) and in the large standard deviations for measures such as mean pedaling velocity. To help organize these findings we identified three subgroups during both unilateral and bilateral uncoupled pedaling based on the pedaling pattern used during each condition. We also considered whether stroke-related motor function was related to these subgroups, as might be expected. We found that subgroups defined during both unilateral and bilateral uncoupled pedaling were related to Fugl-Meyer total and motor scores; individuals with greater difficulty achieving the task had poorer motor function. Greater difficulty during unilateral pedaling was also related to slower walking velocity. These findings suggest that both paretic motor impairments and impaired interlimb coordination are important for overall motor function. Interestingly, unilateral and bilateral subgroup classification were not related ($P = 0.13$). Although no participant had better performance during bilateral uncoupled than unilateral pedaling, having greater performance impairments during unilateral pedaling was not predictive of having greater performance impairments during bilateral uncoupled pedaling. It is likely that the influence of paretic motor impairments and impaired interlimb coordination varies on a subject-by-subject basis. However, conclusions must be tempered because comparisons were made between artificial subgroups, not across a continuous variable.

In this study, we found evidence that TA retains substantial motor output in chronic stroke. Mean EMG activation in TA and MI both increased substantially during unilateral as compared to conventional pedaling. Muscle activation was also high during bilateral uncoupled pedaling. These findings are interesting because TA is typically one of the last muscles to recover, and exhibits substantial impairment, including reduced activation during walking (Knutsson et al., 1979). The large activation of TA during unilateral and bilateral uncoupled pedaling raises the possibility that these tasks could be used to improve spontaneous TA activity during functional movements of the lower limb. Such an effect could positively influence functional recovery. However, motor output in TA may be contingent upon the activation of a flexion synergy; muscle activation in TA occurs with a similar phasing as in RF. Consequently, the rehabilitative benefits and detriments of training in-synergy or out-of-synergy movements must be considered. For example, promoting flexion synergies might be useful during the swing phase of walking, but be detrimental during other lower limb tasks.

4.6. Limitations

Although there were a range of Fugl-Meyer scores and walking speeds, participants in this study had relatively high levels of function, as was necessary to perform pedaling. People with lower functioning may have greater impairments in paretic motor output and/or interlimb coordination. Therefore, conclusions from our findings may not generalize to the entire population of stroke survivors. Furthermore, our sample included individuals with both cortical and subcortical strokes. Results may differ depending on stroke location. Another limitation of this study is that our measures of asymmetry are imperfect. MI is an indirect measurement of the amplitude of muscle activity but was used because of limited ability to normalize EMG responses. Percent mechanical work was evaluated on a different pedaling device than was used to assess interlimb coordination and paretic motor impairment because the bike with a split crankshaft was not instrumented to measure force/torque. Thus, mechanical work symmetry on the instrumented device may not directly relate to the value of that construct on the other device.

During unilateral and bilateral uncoupled pedaling, the eccentric pulley system of our pedaling device may not have matched the mechanics experienced during conventional pedaling. Most deficits in unilateral and bilateral uncoupled pedaling across both groups occurred near the posterior transition of the pedaling cycle, where elastic resistance was the highest. EMG in the TA and RF increased during unilateral pedaling, perhaps because the stored elastic energy was insufficient to aid the anterior transition of the pedaling cycle. Consequently, differences in performance and muscle activation during unilateral and bilateral uncoupled pedaling as compared to conventional pedaling may have resulted from mechanical differences between tasks. However, it is worth noting that deficits in task performance during unilateral pedaling only occurred in the paretic limb. Thus, this condition may still provide insight into paretic motor impairments. Deficits in unilateral pedaling performance may occur because the mechanics of the device accentuate post-stroke alterations in activation of muscles involved in the posterior transition. Namely, excitation is phase advanced in BF and semimembranosus, making the posterior transition more difficult (Kautz et al., 1998). Because both groups had deficits in pedaling performance during bilateral uncoupled pedaling, the device mechanics likely have a larger effect during this condition. This coincides with previous work that has shown altered muscle activation and increased braking torque during bilateral as compared to unilateral pedaling in both stroke survivors and controls (Ting et al., 1998, 2000; Kautz et al., 2005a). However, limitations of the device likely do not negate the conclusions from this study. The mechanics required to perform unilateral and bilateral uncoupled pedaling were the same. Thus, differences in muscle activation and pedaling performance between unilateral and bilateral uncoupled pedaling likely result from the coordination of movements of each limb.

Impaired proprioception may have contributed to our results. Specifically, the inability to maintain an antiphase relation between the pedals may have resulted from an inability to sense the position of the leg, not interlimb coordination. However, subjects were positioned so they could see their feet while pedaling, and we did not find a relation between FM_{LEsens} and any measure of pedaling performance. Differential levels of upper limb motor activity also may have affected our results. It is well documented that motor activity in the upper limb has a significant impact on motor activity in the lower limb (for review see Zehr et al., 2009). Although we did not collect any upper limb data, anecdotally, we did not observe any noticeable upper limb motor activity in any participant.

4.7. Conclusions

Conventional pedaling performance after stroke was similar to controls but was performed asymmetrically and with minimal paretic motor output. During unilateral and bilateral uncoupled conditions, pedaling was slower and less smooth, but paretic muscle activity was increased. These observations suggest that asymmetric work during conventional pedaling may be due to impaired paretic motor output and the inability to coordinate the output of the paretic and non-paretic limbs. Rehabilitative interventions that address both causes may elicit more symmetry and improved movement.

Declaration of Competing Interest

None of the authors have potential conflicts of interest.

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All authors conceived and designed the study; performed experiments; analyzed and interpreted results; drafted, edited, and revised the manuscript; and approved the final version of the manuscript.

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