



## The influence of locomotor rehabilitation on module quality and post-stroke hemiparetic walking performance

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### ABSTRACT

Recent studies have suggested the biomechanical subtasks of walking can be produced by a reduced set of co-excited muscles or modules. Individuals post-stroke often exhibit poor inter-muscular coordination characterized by poor timing and merging of modules that are normally independent in healthy individuals. However, whether locomotor therapy can influence module composition and timing and whether these improvements lead to improved walking performance is unclear. The goal of this study was to examine the influence of a locomotor rehabilitation therapy on module composition and timing and post-stroke hemiparetic walking performance.

Twenty-seven post-stroke hemiparetic subjects participated in a 12-week locomotor intervention incorporating treadmill training with body weight support and manual trainers accompanied by training overground walking. Electromyography (EMG), kinematic and ground reaction force data were collected from subjects both pre- and post-therapy and from 19 age-matched healthy controls walking on an instrumented treadmill at their self-selected speed. Non-negative matrix factorization was used to identify the module composition and timing from the EMG data. Module timing and composition, and various measures of walking performance were compared pre- and post-therapy.

In subjects with four modules pre- and post-therapy, locomotor training resulted in improved timing of the ankle plantarflexor module and a more extended paretic leg angle that allowed the subjects to walk faster and with more symmetrical propulsion. In addition, subjects with three modules pre-therapy increased their number of modules and improved walking performance post-therapy. Thus, locomotor training has the potential to influence module composition and timing, which can lead to improvements walking performance.

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### 1. Introduction

Stroke is the leading cause of long-term disability in the United States [1]. Although the manifestations of disability post-stroke vary, several features of hemiparetic gait are common, including diminished speed, increased duration of stance on the non-paretic limb, increased duration of double support and asymmetric joint kinematics and kinetics [2,3]. Because improved walking ability is central to rehabilitation of stroke patients [4], assessments are needed to evaluate walking performance throughout the

rehabilitation process. Previous assessments have compared self-selected walking speed [5], propulsive and braking impulses [6], paretic leg propulsion [6], step length asymmetry [7,8] and pre-swing leg angle [9]. Since gait impairments are the result of deficient neuromuscular control, we have recently focused on quantifying the neuromuscular control deficits exhibited by individuals post-stroke. In healthy adults and persons post-stroke, we have shown that the biomechanical subtasks of walking (e.g., body support, forward propulsion, leg swing and mediolateral balance control) are produced by co-activated muscles or modules [10,11]. In healthy adults these modules are activated independently. In contrast, individuals post-stroke exhibit poor inter-muscular coordination characterized by co-activation (timing overlap) of modules that are independent in healthy individuals [12]. Given that modules control the biomechanical subtasks of movement, this finding suggests the biomechanical subtasks of

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walking are interfering with one another. Greater interference between subtasks is expected to lead to poorer walking performance while less interference is expected to lead to better walking performance. Indeed, we found a higher number of modules post-stroke was positively associated with better performance in various clinical and biomechanical assessments of walking, including walking speed, ability to change walking speed (increase from preferred to fast), dynamic gait index, step length symmetry and propulsion symmetry [12,13]. Thus, improvements in modular organization during rehabilitation may lead to a more normal gait pattern and improved walking performance.

In healthy adults, analyses of the modular organization have revealed that well-coordinated walking can be produced by exciting 4 co-activation modules: module 1 (hip and knee extensors) in early stance, module 2 (ankle plantarflexors) in late stance, module 3 (tibialis anterior and rectus femoris) during swing, and module 4 (hamstrings) in late swing and early stance, with each module providing essential biomechanical functions [11]. Persons with post-stroke hemiparesis typically have fewer modules that are less organized than in healthy individuals [12]. Even in those individuals who have four modules post-stroke, the modules differ in composition (i.e., the relative weighting of each muscle in each module) and timing (i.e., the activation of those modules over the gait cycle) from those of healthy individuals, which likely adversely affects their walking ability. Although we have shown that independent activation of modules is important, it is also necessary to ensure that the quality of modules is appropriate with regard to timing and composition. Indeed, individuals post-stroke who have an appropriate number of modules often exhibit walking deficits relative to healthy individuals [12]. Therefore, improvement of the composition and timing of their modular organization such that it better matches the organization of healthy subjects could significantly improve locomotor performance.

However, whether locomotor therapy can improve module composition and timing and if these improvements lead to better walking performance is unclear [e.g., 14]. Therefore, the goal of this study was to examine the influence of a locomotor rehabilitation therapy on module composition and timing and walking performance in post-stroke hemiparetic subjects. Specifically, we assessed whether those subjects with four modules pre-therapy improved their post-therapy module composition and timing and walking performance. In addition, we compared module composition and timing post-therapy in all subjects with four modules post-therapy, grouped by pre-therapy number of independent modules, to determine whether the number of modules an individual had pre-therapy influences their post-therapy modular organization and biomechanical measures of gait performance. Specific measures of gait performance included self-selected walking speed, paretic step length asymmetry, paretic pre-swing leg angle and propulsion asymmetry.

## 2. Methods

### 2.1. Participants

Study participants were a subset from a larger study on the effects of locomotor training post-stroke [15]. Twenty-seven post-stroke hemiparetic subjects participated in a 12-week, 36 session locomotor training program that included stepping on a treadmill with body weight support and manual assistance [15]. The inclusion criteria were: stroke within 6 months to 5 years; hemiparesis secondary to a single unilateral stroke (Fugl-Meyer LE score < 34); no significant lower extremity joint pain, range of motion limitations, or major sensory deficits; able to walk independently with an assistive device over ten meters on a level

surface; able to walk on a daily basis in the home; no severe perceptual or cognitive deficits; no significant lower limb contractures; and no significant cardiovascular impairments contraindicative to walking. Data from a single walking session were acquired from 19 aged-matched healthy subjects. All subjects provided informed consent to an institutionally approved protocol.

### 2.2. Experimental set-up and procedure

Subjects performed 30-s walking trials on a split-belt instrumented treadmill (Techmachine, Andrézieux Boutheon, France) at their self-selected speed both pre- and post-therapy. Practice trials were performed to ensure subjects were comfortable with the experimental setup. Subjects walked approximately 10-s prior to each data collection to ensure they had reached a steady-state walking pattern. Reflective kinematic markers were placed on the limbs and torso using a modified Helen Hayes marker set. Marker locations were recorded in three dimensions at 100 Hz using a twelve-camera motion capture system (Vicon Motion Systems). A 16-channel EMG system (Konigsburg Instruments, Pasadena, CA) was used to record EMG data at 2000 Hz bilaterally from the tibialis anterior (TA), soleus (SO), medial gastrocnemius (MG), vastus medialis (VM), rectus femoris (RF), medial hamstrings (MH), lateral hamstrings (LH), and gluteus medius (GM). Bilateral 3D ground reaction forces (GRFs) were recorded at 2000 Hz.

### 2.3. Data analysis

Kinematic and kinetic data were processed using Visual3D (C-Motion, Inc., Germantown, MD). Kinematic and GRF data were low-pass filtered using a fourth order Butterworth filter with cutoff frequencies of 6 Hz and 20 Hz, respectively. EMG was high pass filtered with a cutoff frequency of 40 Hz, de-meaned, low pass filtered with a cutoff frequency of 10 Hz using a 4th order Butterworth filter and normalized to its peak values. Gait cycle time was determined from the GRF data. All data were time normalized to 100% of the gait cycle.

Biomechanical and EMG measures were analyzed using Matlab (The Mathworks, Natick, MA). Pre-swing leg angle was computed as the maximum angle between a line from the pelvis center-of-mass to the foot center-of-mass and vertical (positive when foot is posterior to the pelvis) during the double support phase [9]. Propulsion asymmetry was quantified as the proportion of total anterior GRF generated by the paretic leg subtracted from 0.5 and then taking the absolute value [6]. Paretic step ratio was calculated as the ratio of the paretic step length to the overall stride length [8]. To compute step length asymmetry, this number was then subtracted from 0.5 and the absolute value of the difference was taken.

The number of modules required to account for >90% of the EMG variability was found using non-negative matrix factorization previously described in detail [12]. To assess module quality, the module composition and timing for each post-stroke participant were compared to the average module composition and timing from the control group. Pearson's correlation coefficient was used to compare the composition of each module, represented by a  $1 \times 8$  array of muscle weightings, between each stroke participant and the controls. Module composition quality was defined as the correlation coefficient, with 1.0 being a perfect association with the healthy group mean. The quality of module timing was assessed by calculating a timing error, defined as the difference in timing peaks of the hemiparetic modules relative to the control group as a percentage of the gait cycle. In module 3, where the module has two timing peaks, overall timing quality was calculated as the average of the two timing errors.

**Table 1**

Comparisons of module timing quality, module composition quality and biomechanical measures pre- and post-therapy (paired *t*-test results). Means  $\pm$  standard deviations are listed for each measure for pre-therapy minus post-therapy as well as the post-therapy means  $\pm$  standard deviations. Bold indicates rows that are significant or marginally significant.

Module	<i>p</i> -Value	Pre–post	Post
<b>Module timing quality</b>			
1	0.6346	0.04 $\pm$ 0.17	0.10 $\pm$ 0.11
2	<b>0.0132</b>	0.08 $\pm$ 0.07	0.05 $\pm$ 0.05
3	0.1926	–0.14 $\pm$ 0.24	0.25 $\pm$ 0.15
4	0.3053	–0.02 $\pm$ 0.05	0.09 $\pm$ 0.08
<b>Module composition quality</b>			
1	0.2868	–0.11 $\pm$ 0.24	0.71 $\pm$ 0.19
2	0.6904	–0.05 $\pm$ 0.32	0.79 $\pm$ 0.26
3	0.6508	0.04 $\pm$ 0.18	0.82 $\pm$ 0.17
4	0.3021	–0.12 $\pm$ 0.26	0.82 $\pm$ 0.14
<b>Biomechanical measures</b>			
Speed	<b>0.0114</b>	–0.29 $\pm$ 0.14	0.78 $\pm$ 0.26
Leg angle	<b>0.0440</b>	–5.83 $\pm$ 4.35	19.85 $\pm$ 6.07
Abs PP	<b>0.1121</b>	0.11 $\pm$ 0.11	0.15 $\pm$ 0.06
Abs PSR	0.6904	0.01 $\pm$ 0.08	0.05 $\pm$ 0.06

2.4. Statistical analysis

All statistical analyses were performed using SAS statistical software (SAS Institute, Cary, NC). For subjects with four modules pre- and post-therapy, self-selected speed, paretic step length asymmetry, paretic pre-swing leg angle, propulsion asymmetry, module timing quality and module composition quality were compared using paired *t*-tests. Using false discovery rate control to

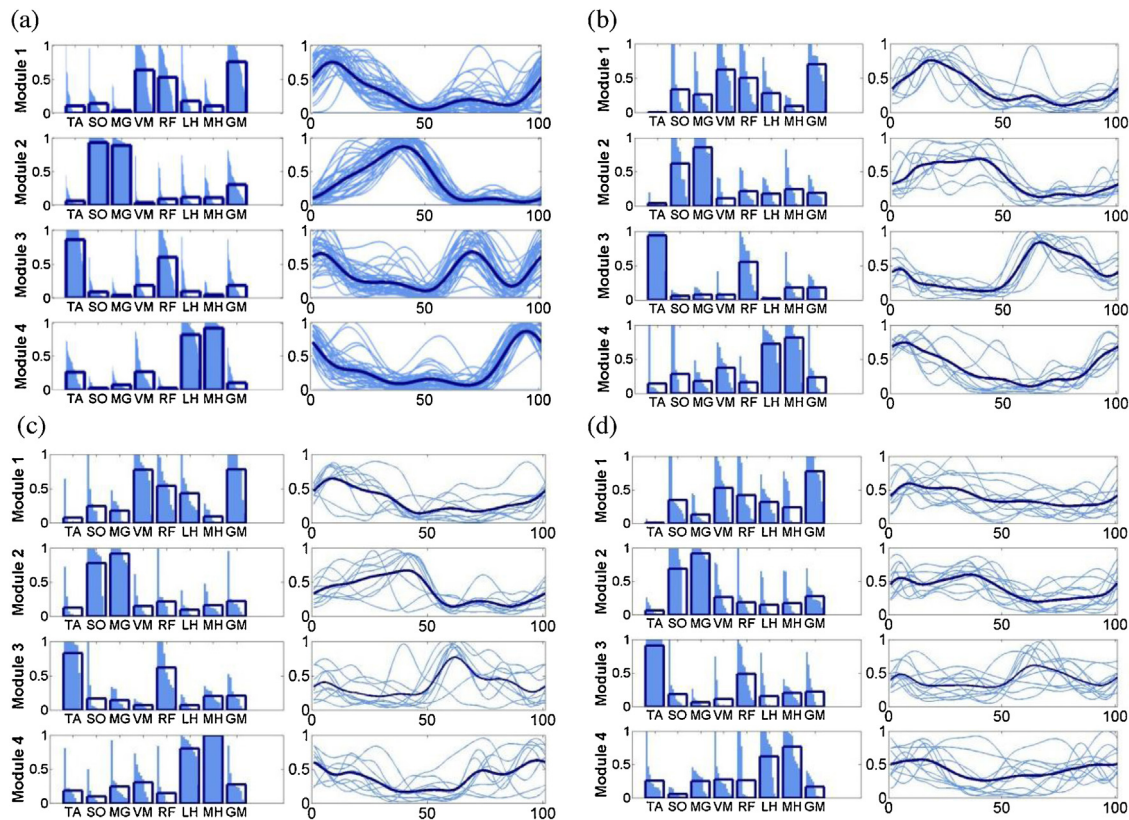
correct for multiple comparisons, additional *t*-tests were performed comparing the composition, timing and biomechanical measures for these subjects both pre- and post-therapy to the control subjects. For all subjects with four modules post-therapy, separate repeated measures ANOVAs ( $\alpha = 0.05$ ) and post hoc *t*-tests with a Bonferroni correction for multiple comparisons were used to compare (1) module timing, (2) module composition and (3) biomechanical measures for four groups: those persons with hemiparesis with 2, 3 and 4 modules pre-therapy, respectively, and the controls.

3. Results

This study includes data for all subjects in the larger study who had four modules post-therapy ( $n = 22$ ). Characteristics of the subjects include the following: 14 left hemiparesis; 15 men; age: 57.3  $\pm$  13.2 years; 19.0  $\pm$  13.0 months post-stroke; pre-therapy walking speed: 0.48  $\pm$  0.20 m/s; pre-therapy lower extremity Fugl–Meyer: 22.9  $\pm$  4.4; and pre-therapy dynamic gait index: 13.5  $\pm$  3.2.

3.1. Subjects with four modules pre- and post-therapy

Nine of the 27 hemiparetic subjects had four modules both pre- and post-therapy. When comparing the module composition and timing quality of the four modules pre- and post-therapy, the only significant change was improved timing for the ankle plantarflexor module (module 2;  $p = 0.0132$ ; Table 1). The average post-therapy timing peak of the plantarflexor module was more defined and occurred 8.45% of the gait cycle (Table 1) later in stance, which more closely resembled the control group (compare Fig. 1b and c to a). In these subjects, two walking performance measures also showed



**Fig. 1.** Module composition (left, bar plots), the relative contribution of the muscles to each module, and activation timing (right, line plots) of that module. Individual subject (lighter histograms and lines) and group average (bold bar outlines and darker lines) data are shown for: (a) control subjects, (b) pre-therapy for subjects with 4 modules pre-therapy (c) post-therapy for subjects with 4 modules pre-therapy (d) post-therapy for subjects with 3 modules pre-therapy. Abbreviations: TA, tibialis anterior; SO, soleus; MG, medial gastrocnemius; VM, vastus medialis; RF, rectus femoris; LH, lateral hamstrings; MH, medial hamstrings; GM, gluteus medius.

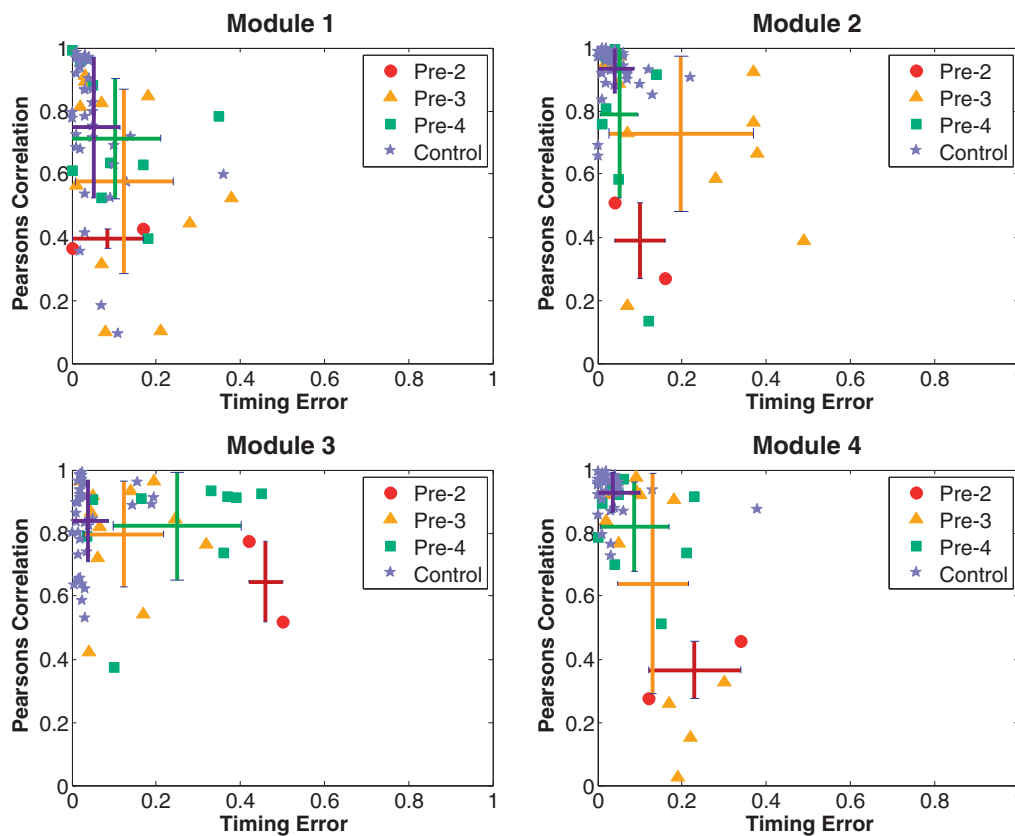
**Table 2**  
Comparisons of module timing quality, module composition quality and biomechanical measures pre-therapy and post-therapy with controls. Means  $\pm$  standard deviations are listed for each measure for pre-therapy as well as post-therapy. Bold indicates rows that are significant or marginally significant.

Module	Pre	p-Value	Post	p-Value	Control
<b>Module timing quality</b>					
1	0.14 $\pm$ 0.14	<b>0.0132</b>	0.10 $\pm$ 0.11	0.1121	0.05 $\pm$ 0.06
2	0.14 $\pm$ 0.10	<b>0.0004</b>	0.05 $\pm$ 0.05	0.6508	0.04 $\pm$ 0.05
3	0.11 $\pm$ 0.15	<b>0.0349</b>	0.25 $\pm$ 0.15	<b>&lt;0.0001</b>	0.04 $\pm$ 0.05
4	0.06 $\pm$ 0.07	0.3187	0.09 $\pm$ 0.08	0.0958	0.04 $\pm$ 0.06
<b>Module composition quality</b>					
1	0.60 $\pm$ 0.11	<b>0.1121</b>	0.71 $\pm$ 0.19	0.6904	0.75 $\pm$ 0.22
2	0.74 $\pm$ 0.17	<b>&lt;0.0001</b>	0.79 $\pm$ 0.26	<b>0.0160</b>	0.94 $\pm$ 0.08
3	0.86 $\pm$ 0.10	0.6904	0.82 $\pm$ 0.17	0.7614	0.84 $\pm$ 0.13
4	0.70 $\pm$ 0.25	<b>&lt;0.0001</b>	0.82 $\pm$ 0.14	<b>0.0052</b>	0.93 $\pm$ 0.06
<b>Biomechanical measures</b>					
Speed	0.46 $\pm$ 0.17	<b>&lt;0.0001</b>	0.78 $\pm$ 0.26	<b>0.0057</b>	1.11 $\pm$ 0.22
Leg angle	13.21 $\pm$ 3.59	<b>&lt;0.0001</b>	19.85 $\pm$ 6.07	<b>0.0625</b>	23.20 $\pm$ 2.85
Abs PP	0.27 $\pm$ 0.17	<b>&lt;0.0001</b>	0.15 $\pm$ 0.06	<b>&lt;0.0001</b>	0.01 $\pm$ 0.01
Abs PSR	0.06 $\pm$ 0.04	<b>&lt;0.0001</b>	0.05 $\pm$ 0.06	<b>&lt;0.0001</b>	0.01 $\pm$ 0.01

improvements post-therapy. Self-selected speed increased ( $p = 0.0114$ ) and pre-swing leg angle increased (i.e., was more extended,  $p = 0.0440$ ) following therapy. In addition, reduction of propulsion asymmetry post-therapy approached significance ( $p = 0.1121$ ).

Compared to the controls, plantarflexor timing was impaired pre-therapy ( $p = 0.0004$ ) and improved post-therapy such that  $t$ -tests with the control subjects no longer showed a significant difference ( $p = 0.65$ ; Table 2). The hip and knee extensor module timing was impaired pre-therapy (module 1;  $p = 0.0132$ ), and

marginally improved ( $p = 0.1121$ ) post-therapy. The tibialis anterior and rectus femoris module (module 3) timing, plantar-flexor module composition and hip and knee extensor module composition remained impaired both pre- and post-therapy (Fig. 2). These subjects had diminished speed ( $p < 0.0001$ ) and leg angle ( $p < 0.0001$ ) as well as propulsion asymmetry ( $p < 0.0001$ ) and step length asymmetry ( $p < 0.0001$ ) pre-therapy as compared with control subjects, and although most of these quantities improved post-therapy, they still remained impaired compared to the control subjects.



**Fig. 2.** Timing error and Pearson's correlation are plotted for each subject. Means  $\pm$  standard deviations are shown with error bars for each measure for each pre-therapy number of modules. Each pre-therapy number of modules is colored: red circles indicate the subjects who had two modules pre-therapy; orange triangles indicate subjects who had three modules pre-therapy; green squares indicate subjects who had four modules pre-therapy; purple stars indicate control subjects. (For interpretation of the references to color in the artwork, the reader is referred to the web version of the article.)

### 3.2. All subjects with four modules post-therapy

Twenty-two subjects had four modules post-therapy. Of these, 11 subjects had three modules pre-therapy (five with merged modules 1 and 4, two with merged modules 1 and 2, and four with merged modules 2 and 4) and two subjects had two modules pre-therapy, with only an independent module 3. Because only two subjects had two modules pre-therapy, the corresponding results had low statistical power, and therefore fewer comparisons were significant. They are not discussed further, but are included in Table 3 for completeness.

The timing error for the ankle plantarflexor module (module 2) for those subjects with three pre-therapy modules was significantly higher ( $p < 0.001$ ) compared to subjects that had four modules pre-therapy and from the control subjects (Table 3). The timing for subjects with three modules pre-therapy was less defined and had increased activity in early stance relative to the control subjects and those subjects with four modules pre-therapy (compare Fig. 1d to c and a). There was also a significant difference in the composition of module 2 in those subjects who had three modules pre-therapy as compared with the control subjects (Table 3). There was a diminished contribution from the soleus muscle in module 2 in these subjects (compare Fig. 1d and a). In addition, both the timing and composition of module 4 (hamstrings) in subjects who had three modules pre-therapy were significantly different from that of the control subjects. These modular organization differences were accompanied by an increased step length and propulsion asymmetry, slower self-selected speed and decreased pre-swing leg angle (Table 3;  $p < 0.05$ ) in subjects who had three modules pre-therapy relative to those who had four modules pre-therapy and the control subjects.

## 4. Discussion

The goal of this study was to examine the influence of a locomotor rehabilitation therapy on the quality of module composition and timing and post-stroke hemiparetic walking performance. Overall, we found that manual body-weight supported treadmill training does influence some aspects of module composition and timing quality that leads to improvements in symmetry and speed depending on pre-therapy modular organization.

**Table 3**

Comparisons of module timing quality, module composition quality and biomechanical measures at post-therapy depending on the number of modules pre-therapy (ANOVA results). Means  $\pm$  standard deviations are listed for each measure for each pre-therapy number of module grouping. Each pre-therapy number of module grouping is colored as is the marker indicating statistical significance. Red indicates the subjects who had two modules pre-therapy. Orange indicates subjects who had three modules pre-therapy. Green indicates subjects who had four modules pre-therapy. Purple indicates control subjects. This data is graphically depicted in Fig. 2. (For interpretation of the references to colors in this table, the reader is referred to the web version of this article.)

Module	ANOVA p-Value	Pre-2	Pre-3	Pre-4	Control
<b>Module timing quality</b>					
1	0.0813	0.09 $\pm$ 0.09	0.12 $\pm$ 0.12	0.10 $\pm$ 0.11	0.05 $\pm$ 0.06
2	<0.0001	0.10 $\pm$ 0.06	0.20 $\pm$ 0.17**	0.05 $\pm$ 0.05*	0.04 $\pm$ 0.05*
3	<0.0001	0.46 $\pm$ 0.04***	0.12 $\pm$ 0.09***	0.25 $\pm$ 0.15***	0.04 $\pm$ 0.05***
4	0.0002	0.23 $\pm$ 0.11*	0.13 $\pm$ 0.08*	0.09 $\pm$ 0.08	0.04 $\pm$ 0.06**
<b>Module composition quality</b>					
1	0.0635	0.40 $\pm$ 0.03	0.58 $\pm$ 0.29	0.71 $\pm$ 0.19	0.75 $\pm$ 0.22
2	<0.0001	0.40 $\pm$ 0.12**†	0.73 $\pm$ 0.25†	0.79 $\pm$ 0.26*	0.94 $\pm$ 0.08**
3	0.3244	0.65 $\pm$ 0.13	0.80 $\pm$ 0.17	0.82 $\pm$ 0.17	0.84 $\pm$ 0.13
4	<0.0001	0.37 $\pm$ 0.09**	0.64 $\pm$ 0.35*	0.82 $\pm$ 0.14*	0.93 $\pm$ 0.06**
<b>Biomechanical measures</b>					
Speed	<0.0001	0.63 $\pm$ 0.13*	0.55 $\pm$ 0.25*	0.78 $\pm$ 0.26*	1.11 $\pm$ 0.22***
Leg angle	<0.0001	16.70 $\pm$ 3.59	13.61 $\pm$ 7.52†	19.85 $\pm$ 6.07†	23.20 $\pm$ 2.85*
Abs PP	<0.0001	0.12 $\pm$ 0.09	0.25 $\pm$ 0.16*	0.15 $\pm$ 0.06*	0.01 $\pm$ 0.01**
Abs PSR	0.0003	0.02 $\pm$ 0.02	0.12 $\pm$ 0.16*	0.05 $\pm$ 0.06	0.01 $\pm$ 0.01*

†† Indicates marginal significance using Bonferroni *t*-tests.

\*\* Indicates statistical significance for the difference in means using Bonferroni *t*-tests.

### 4.1. Hemiparetic plantarflexor impairment

Plantarflexor impairment is commonly observed in hemiparetic walking. In both control and hemiparetic subjects, the soleus is an important contributor to forward propulsion during pre-swing and is critical to increasing walking speed [16]. In this study, impaired plantarflexor activity was exhibited by both reduced participation in module 2 (subjects with three modules pre-therapy) and impaired timing (subjects with three modules pre-therapy and pre-to-post-therapy four module comparison). Compared to control subjects, paretic leg ankle plantarflexor muscle activity has been shown to be reduced in hemiparetic subjects [2,17], which leads to diminished body propulsion and leg swing initiation [17].

### 4.2. Improved timing of plantarflexor module

An important finding of this study was that gait recovery post-stroke can be associated with temporal changes in motor modules. The locomotor therapy improved the timing of module 2 (plantarflexors) in those subjects who had four modules prior to therapy. This improvement was accompanied by an increased speed and pre-swing leg angle (i.e., the leg was more extended prior to toe-off). Also, greater propulsion symmetry following therapy approached significance. Improvements in these performance measures were likely due to the better timing of the plantarflexor module since the plantarflexors are essential for body propulsion [18–20]. Another important finding was that locomotor training leads to an increased leg angle in late stance, which is a more effective kinematic position for the plantarflexor force to propel the body forward [9]. This is important for gait speed and also for step length symmetry [9]. We believe that improvement in plantarflexor timing is likely the largest contributor to the improvements in the biomechanical measures. However, it is likely that the therapy also produced benefits in additional domains beyond muscle coordination (e.g., strength/power, endurance, balance and confidence) that contributed to improved walking and also correlated with improved biomechanical measures.

The important finding of improved plantarflexor module timing is in contrast with den Otter et al. [14], which suggested gait recovery is not associated with temporal changes in individual

muscle activity post-stroke. However, differences between studies are likely due to the variations in the actual rehabilitative therapies, and approaches for determining changes in timing, with our study determining peak amplitude and the previous study looking at periods of activation over the gait cycle. In addition, the previous study [14] only examined four muscles bilaterally (RF, BF, MG, and TA) and did not include the soleus. Including the soleus is important since previous modular analyses have suggested that improving soleus output during rehabilitation may provide the greatest improvement in walking performance [21].

#### 4.3. Pre-therapy module number influences response to therapy

Relative to those with fewer than four modules pre-therapy, individuals with four modules pre-therapy had better walking performance, and module composition and timing both pre and post-therapy. In those subjects who had three modules pre-therapy, module 2 timing post-therapy was worse than subjects who had four modules pre-therapy. These subjects also had poor timing and composition compared to control subjects. This is due to pre-therapy merging of non-impaired modules [12]. Only five of the eleven subjects with three modules pre-therapy and four modules post-therapy had an independent plantarflexor module pre-therapy. Although these subjects gained an independent plantarflexor module post-therapy, this module still had impaired timing. Hemiparetic gait is commonly associated with temporal abnormalities in the gait cycle, including over-activity of the plantarflexor muscles during early stance [2,22]. Although early stance soleus activity may contribute to stability, by reducing knee flexion in response to early stance loading [2], this soleus activity leads to increased braking (i.e. posterior GRF) in early stance.

We also found subjects who had four modules pre-therapy ( $n = 8$ ) did not have significant module 4 (hamstrings) timing error. However, subjects with three modules pre-therapy ( $n = 11$ , only two of whom had an independent hamstrings module pre-therapy) did have significant timing error in module 4 post-therapy. The latter results are consistent with abnormalities in temporal patterning of the hamstrings as commonly seen in post-stroke hemiparetic walking, especially regarding co-activation of the hamstrings and rectus femoris similar to merging modules 1 and 4 in subjects with three modules [22]. The hamstrings module accelerates the leg into swing in early stance and decelerates the leg in late swing in preparation for foot contact [11]. Thus, prolonged hamstring activity may interfere with propulsion generation [23], which is consistent with our finding of asymmetrical paretic propulsion in these subjects compared to the control subjects.

#### 4.4. Limitations

A potential limitation of this study is that due to recording EMG from a smaller set of muscles, we were only able to identify four modules. Recent simulation [10,11] and experimental [24] studies analyzing a greater number of muscles have found that 5–6 modules are necessary to control walking in healthy subjects, with the fifth module containing large contributions from the erector spinae and iliopsoas muscles. However, in this study, EMG data from the same set of muscles was analyzed in the hemiparetic and control subjects to allow a direct comparison between groups. Future studies will endeavor to incorporate data from a larger number of muscles and modules.

### 5. Conclusion

In subjects with four modules pre- and post-therapy, a manual body-weight supported treadmill training program resulted in

improved timing of the ankle plantarflexor module and a more extended paretic leg angle that allowed the hemiparetic subjects to walk faster and with more symmetrical (i.e., greater paretic leg) propulsion. Most subjects with three modules pre-therapy increased their number of modules and improved walking performance post-therapy, although they still had poorer walking performance than those that started with four modules. Thus, manual body-weight supported treadmill training has the potential to influence module composition and timing quality, which can lead to improvements in symmetry and speed depending on pre-therapy modular organization. These results provide rationale for selecting rehabilitation strategies that target specific aspects of modular organization depending on pre-therapy organization.

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### Conflict of interest statement

None declared.

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