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## Neuromuscular control of Lokomat guided gait

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## Chapter 5

# Lokomat guided gait in hemiparetic stroke patients: the effects of training parameters on muscle activity and temporal symmetry

*Submitted*

Klaske van Kammen

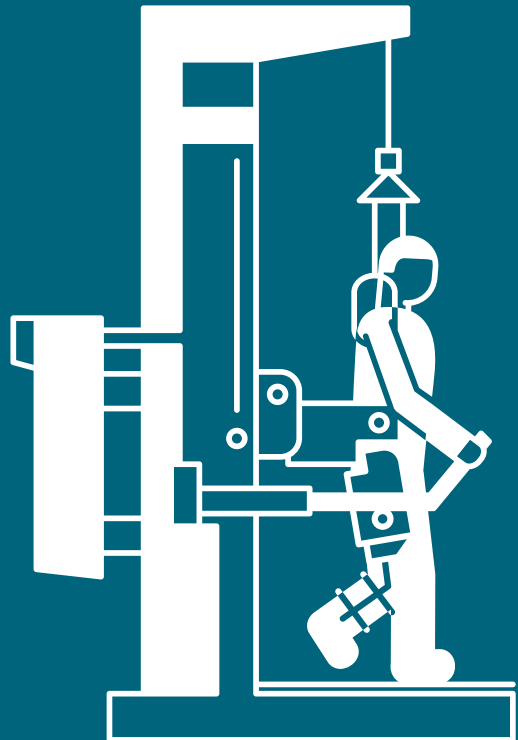
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**ABSTRACT**

**Background:** The Lokomat is a commercially available robotic gait trainer that can be used for gait rehabilitation in post-stroke hemiparetic patients. Selective and well-dosed clinical use of the training parameters of the Lokomat, i.e. movement guidance, treadmill speed and bodyweight support, requires a good understanding of how these parameters affect the neuromuscular control of post-stroke hemiparetic gait.

**Methods:** Ten stroke patients (unilateral paresis, 7 females,  $64.5 \pm 6.4$  years, >3 months post-stroke, Functional Ambulation Categories scores 2-4) walked in the Lokomat under varying parameter settings: 50% or 100% guidance, 0.28 or 0.56 m/s, 0% or 50% bodyweight support. Electromyography was recorded bilaterally from Gluteus Medius, Biceps Femoris, Vastus Lateralis, Medial Gastrocnemius, and Tibialis Anterior. Pressure sensors placed under the feet were used to determine durations of the first double support and the single support phases of both legs to evaluate the level of temporal gait symmetry.

**Findings:** Varying guidance and bodyweight support had little effect on muscle activity, but increasing treadmill speed led to increased activity in both the affected (Biceps Femoris, Medial Gastrocnemius and Tibialis Anterior) and unaffected leg (all muscles). The level of temporal symmetry was not affected by the parameter settings.

**Interpretation:** The Lokomat training parameters are generally ineffective in shaping the muscle activity and step symmetry in patients with hemiparetic stroke, as speed seems to be the only parameter that significantly affects muscular amplitude.

**Keywords**

*Stroke; Electromyography; Robotics; Neurorehabilitation; Gait; Lokomat*

## INTRODUCTION

Walking dysfunction is one of the most common consequences of stroke [1], characterized by asymmetrical step durations and length [2-5], reduced walking speed [2], and increased risk of falling [6]. The Lokomat is a commercially available robotic gait trainer that can be used for gait rehabilitation in this population. The Lokomat combines a treadmill with a bodyweight support (BWS) system and an actuated exoskeleton [7]. The exoskeleton can support leg movements throughout the gait cycle, along a predefined pattern [7,8]. This so called 'guidance' can be varied, allowing free exploration of patterns when guidance is set to zero, and forcing a predefined gait pattern when walking with full guidance (i.e. 100%) [7,9]. The level of guidance, combined with the selected treadmill speed and the level of BWS, determines the parameter space that is available to physically affect the gait pattern. Selective and well-dosed use of these parameters to tailor Lokomat training requires a good understanding of how they affect gait-related neuromuscular control.

Treadmill speed and BWS are training parameters that are also applied in more conventional gait training strategies. There is ample evidence that during treadmill walking the increase of speed induces increased muscle activity in both healthy subjects [11-13] and post-stroke hemiparetic patients [14,15], whereas an increase of BWS reduces muscle activity in both populations [11,16-18]. Recently, these effects have been confirmed for Lokomat guided walking in healthy subjects [10,19]. Robotic guidance is a unique training parameter of robotic gait trainers, and it was recently shown in healthy walkers that increasing guidance during Lokomat walking reduces muscle activity [10]. The magnitude of the effect of guidance depended on a complex interaction with both BWS and speed, as reductions in muscular amplitude of healthy subjects were most prominent at high levels of BWS and low speeds [10]. Yet, the question remains whether the effects are similar for stroke patients that are targeted for Lokomat training, as generalization of results found in healthy walkers towards stroke patients is not self-evident.

Motor control in post-stroke hemiparetic patients is changed due to muscle weakness, impaired selective control and spasticity [3,20,21], resulting in abnormalities in the neuromuscular control of both the affected and unaffected leg [3,22-24]. Stroke patients may thus respond differently to the Lokomat training parameters in terms of neuromuscular control, then previously observed in healthy subjects. In addition, the altered motor control may result in different usage of the settings. Where free exploration of the full range of settings (i.e. 0 – 100% guidance, 0 – 100% BWS and 0.14 – 0.89 m/s) is possible in healthy walkers, patients may not tolerate all levels. To the best of our

knowledge, no studies have been conducted on how clinically relevant settings of the training parameters affect neuromuscular control in hemiparetic stroke patients.

In addition, the hemiparesis that typically occurs after stroke often results in an asymmetrical temporal structure of the gait pattern. Most often stroke patients display a pattern that unburdens the affected side [25], either because of balance control issues during single leg support on the affected side [2], or because of a limited ability to generate push-off power to swing the affected leg [16]. As gait asymmetry may also be associated with inefficiency, risk of musculoskeletal injury to the unaffected leg and loss of bone mass density in the affected leg [27-29], restoration of symmetrical patterns is often targeted during gait rehabilitation. Although it was recently shown that post-stroke hemiparetic gait was more symmetrical in the Lokomat than on the treadmill [30], no knowledge is available on whether the level of symmetry can be targeted purposefully by varying the training parameters.

To determine whether varying guidance, BWS and treadmill speed can be purposefully employed in Lokomat therapy, the present study aimed to establish the effects of these parameters, and their mutual interactions, on the muscular control of post-stroke hemiparetic gait. In addition, a second aim was to study how these parameters affect temporal step symmetry.

## METHODS

### Participants.

Ten chronic stroke patients (7 females,  $64.5 \pm 6.4$  years) volunteered to participate, see Table 1 for patient characteristics. To be eligible, patients had to have unilateral paresis of the leg as a result of a clinically first ever unilateral stroke (infarction or hemorrhage), at least 3 months before inclusion. Patients had Functional Ambulation Categories (FAC) [31] scores of 2 (*'patient needs continuous or intermittent support of one person to help with balance or coordination'*) to 4 (in our study operationalized as: *'patient can walk independently in and around the house (< 200 m) with use of walking aids on level ground, but requires help when walking > 200 m on stairs, slopes and uneven surfaces'*). Exclusion criteria were (1) severely impaired cognitive functions (Mini Mental State Exam [32], score  $\leq 25$ ), (2) severe speech, language or communication disorders (i.e. patient is unable to understand instructions and provide informed consent), (3) severe visual problems or neglect, (4) comorbidities that are known to affect gait, and (5) incapable to walk under the experimental conditions. None of the participants had previous experience with Lokomat walking, and

all participants provided their written informed consent. The Medical Ethical Committee of the University Medical Centre Groningen, the Netherlands, approved the protocol in accordance with the Declaration of Helsinki [33] (project number: NL46137.042.12).

**Table 1** Overview of participant characteristics.

Subject	Gender	Age (years)	Weight (kg)	Length (m)	Affected Side (L/R) <sup>a</sup>	Type stroke	Post stroke (months)	FAC <sup>b</sup>	Walking aids
<b>Stroke patients</b>									
1	Female	57	66	1.76	L	Hemorrhage	5	2	Wheelchair, AFO <sup>c</sup>
2	Female	72	68	1.69	R	Hemorrhage	70	4	Cane, AFO <sup>c</sup>
3	Female	70	70	1.63	L	Infarction	12	3	Cane
4	Female	72	68	1.68	R	Infarction	216	4	Cane
5	Male	68	78	1.79	L	Infarction	13	4	Cane, wheelchair, AFO <sup>c</sup>
6	Female	55	86	1.70	L	Hemorrhage	53	3	Eifel cane, wheelchair
7	Male	57	72	1.76	R	Hemorrhage	5	4	Cane, adjusted shoes
8	Female	65	65	1.59	L	Hemorrhage	148	4	Rolling walker
9	Male	66	91	1.83	L	Infarction	27	4	Cane, AFO <sup>c</sup>
10	Female	63	60	1.57	L	Infarction	4	3	Cane, wheelchair, AFO <sup>c</sup>
<i>Mean (std)</i>		64.5 (6.4)	72.4 (9.8)	1.70 (0.09)				55.3 (72.2)	

<sup>a</sup>Left/Right; <sup>b</sup>Functional Ambulation Classification Score; <sup>c</sup>Ankle Foot Orthoses

### Experimental protocol.

Participants visited the rehabilitation center ‘Revalidatie Friesland’ in Beetsterzwaag, the Netherlands twice. The first session was used to familiarize patients with the Lokomat and to adjust the device to the anthropometry of the subject. During this session, the ability to walk under the experimental conditions was determined to evaluate exclusion criteria (5).

The second session was the test session, during which participants walked a total of eight trials in the Lokomat, divided in two blocks of four trials. During each block the level of guidance was fixed (50 or 100%) and during each trial within a block the level of BWS (0 or 50% of participants’ body weight) and selected treadmill speed were varied (0.28 or 0.56 m/s). BWS was provided using a suspended harness, and the levels of BWS were chosen in accordance with clinical practice [8,34]. The levels of guidance and speed were chosen

based on earlier research [35-37] and on clinical experience of physiotherapists working with stroke patients in the rehabilitation center. Participants rested their hands on the side bars of the Lokomat for stability, wore their own (adjusted) footwear and Ankle Foot Orthoses, and ankle movements were stabilized by the elastic foot lifters of the Lokomat.

The order of the blocks and of the trials within each block was randomized among participants to control for order effects. Prior to each trial, participants were allowed practice time, until they indicated to be comfortable with the specific experimental settings. To obtain an approximately equal number of steps for each trial, trial durations depended on treadmill speed (i.e. 120 or 60 seconds for trials at 0.28 and 0.56 m/s, respectively). When needed, patients were allowed resting time between trials.

### **Apparatus.**

#### *The Lokomat Pro.*

For this study, the Lokomat Pro version 6.0 (*Hocoma AG, Volketswil, Switzerland*) was used. The Lokomat exoskeleton includes two actuated orthoses that are moved through the gait cycle in the sagittal plane by linear drives [7]. As the hip and knee joints of the Lokomat are actuated, the participant's legs are 'guided' along a predefined path based on joint movements derived from healthy walkers [8,9].

The guidance provided in the present study, was generated by an impedance controller that allows a variable deviation from the predefined path [38]. The limits of the allowed deviation are determined by the level of guidance. As long as the patient moves along the predefined pattern, the impedance controller does not interfere, but once the limits are exceeded, joint torques are applied to guide the leg back towards the desired trajectory [7,39,40]. When deviations are too large to be redirected, the safety mechanism of the device is triggered, which immediately halts the apparatus [7]. During the present study, guidance was set to its maximum (i.e. 100%), forcing patients to strictly follow the predefined pattern, and to 50%, which allows small deviations and increases the demand of active involvement of the walker to keep their legs on the predefined path.

#### *Electromyography and detection of gait events.*

Self-adhesive, disposable Ag/AgCl electrodes (*Kendall/Tyco ARBO; Warren, MI, USA*), diameter 10 mm and minimum electrode distance 25 mm) were used to measure surface electromyography (EMG) bilaterally of Gluteus Medius (GM), Biceps Femoris (BF), Vastus Lateralis (VL), Medial Gastrocnemius (MG) and Tibialis Anterior (TA). Sensor placement conformed to the SENIAM guidelines [41], after shaving, abrading and cleaning the electrode sites to improve skin conduction.

To detect heel strike and toe off for both legs, custom-made insoles equipped with 4 pressure sensors (FSR402, diameter 18 mm, loading 10 – 1000 g, one under the heel and three under the forefoot) were used.

Pressure sensor and EMG signals were simultaneously sampled at 2048 Hz and fed to a Porti7 portable recording system (*Twente Medical Systems, Enschede, The Netherlands*). The unit (common mode rejection of >90dB, a 2µVpp noise level and an input impedance >1 GV) pre-amplified and A/D converted (22 bits) the signals before storage on a computer for offline analysis.

### **Signal analysis.**

#### *Muscle activity.*

Offline analysis of pressure sensor and EMG data was done using custom-made software routines in Matlab (version 2015b; *The Mathworks Inc., Natick, MA*). To reduce movement artefacts, EMG data were high-pass filtered (10 Hz 4th order Butterworth). Subsequently, the data were full wave rectified and low-pass filtered (10 Hz 4th order Butterworth). The summed (rectified and filtered) EMG data was calculated for four sub-phases of the gait cycle, based on pressure sensor data: the first double support (DS1), the single support (SS), the second double support (DS2) and the swing (SW) phase, for both legs. Subsequently the EMG data was averaged over all strides, for each participant and each condition. For visual presentation of the data only, the filtered EMG data of each individual step were time-normalized with respect to gait cycle time (i.e. 0 – 100%, heelstrike to heelstrike), and averaged over strides.

EMG amplitude of each muscle, of each participant, was normalized with respect to the maximum observed amplitude of the specific muscle of the participant during unrestrained treadmill walking at 0.56 m/s without BWS (study protocol and data published elsewhere [30]), for further statistical processing. To allow interpretation of EMG amplitude of patients with respect to healthy gait, mean data of ten healthy subjects during unrestrained treadmill walking at 0.56 m/s without BWS (study protocol and data published elsewhere [30]) was used to calculate a peak amplitude ratio for each muscle of each leg, representing the ratio between maximal activity in stroke patients and maximal activity in healthy subjects:

Amplitude ratio (% of healthy peak amplitude) =

$$\frac{\text{mean}(\text{maximum amplitude of patients over all Lokomat conditions})}{\text{mean}(\text{maximum amplitude of healthy treadmill walking})} \times 100\%$$



with a value of 100% indicating the same maximal amplitude for the patients and healthy subjects. Values >100% indicate higher maximal amplitude for patients, whereas values <100% indicate higher maximal amplitude for healthy walkers.

#### *Temporal symmetry.*

Relative durations (expressed as a percentage of total gait cycle time) of the DS and SS phase were calculated for each step, for both legs, and subsequently averaged over all strides. A temporal symmetry index [42] was calculated for each phase, as follows:

$$\text{Symmetry index} = \frac{\text{phase duration affected leg} - \text{phase duration unaffected leg}}{\text{phase duration affected leg} + \text{phase duration unaffected leg}}$$

with a value of zero indicating perfect temporal symmetry. Values > 0 indicate asymmetry with longer phase duration of the affected leg, and values < 0 indicate asymmetry with longer phase duration of the unaffected leg.

#### *Statistical analysis.*

Using SPSS version 20 for Windows (*Chicago, IL, USA*), a series of three-way univariate repeated measures ANOVA's were performed to determine the main and interaction effects of within-subject factors Guidance (50 vs 100%), BWS (0 vs 50%) and Speed (0.28 vs 0.56 m/s) on muscle activity and temporal symmetry. For muscle activity, the analyses were done for each of the 4 sub-phases (DS1, SS, DS2, and SW) of each muscle and each leg, separately. For temporal symmetry the analyses were done for the symmetry index of DS and SS, separately. For the symmetry index, the intercept of the General Linear Model was evaluated to indicate whether temporal asymmetry was present (i.e. symmetry index  $\neq$  0). All statistical results were evaluated using an alpha level of 0.05. The Benjamini-Hochberg procedure [43] was applied to the test results to control the false discovery rate (Type I error) and to correct for multiple testing.

## **RESULTS**

### **Muscle activity.**

Figure 1 and 2 show the mean EMG profiles and mean EMG values (+ standard deviation (SD)) for the muscles of the affected and unaffected leg, with a secondary axis showing the amplitude ratio's (expressed as % healthy peak amplitude). Significant effects are presented

in Figure 1 and 2, and will be discussed in upcoming sections. For a full overview of the statistical results, Tables S1 and S2 in 'supplementary material 1' can be consulted.

#### *Guidance.*

In general, increasing the level of guidance had little effect on muscle activity. Only the main effect of Guidance on unaffected GM activity during the SS phase was significant. More specifically, decreasing the level of guidance from 100% to 50% resulted in an increase of unaffected GM activity of 5.3% of peak amplitude.

#### *Bodyweight support.*

The provision of BWS generally had little effect on muscle activity, as only one significant main effect for BWS was observed. In the unaffected leg, VL activity during the DS1 phase was higher during full weight bearing, then when 50% BWS was provided (average difference of 2.9% of peak amplitude).

#### *Speed.*

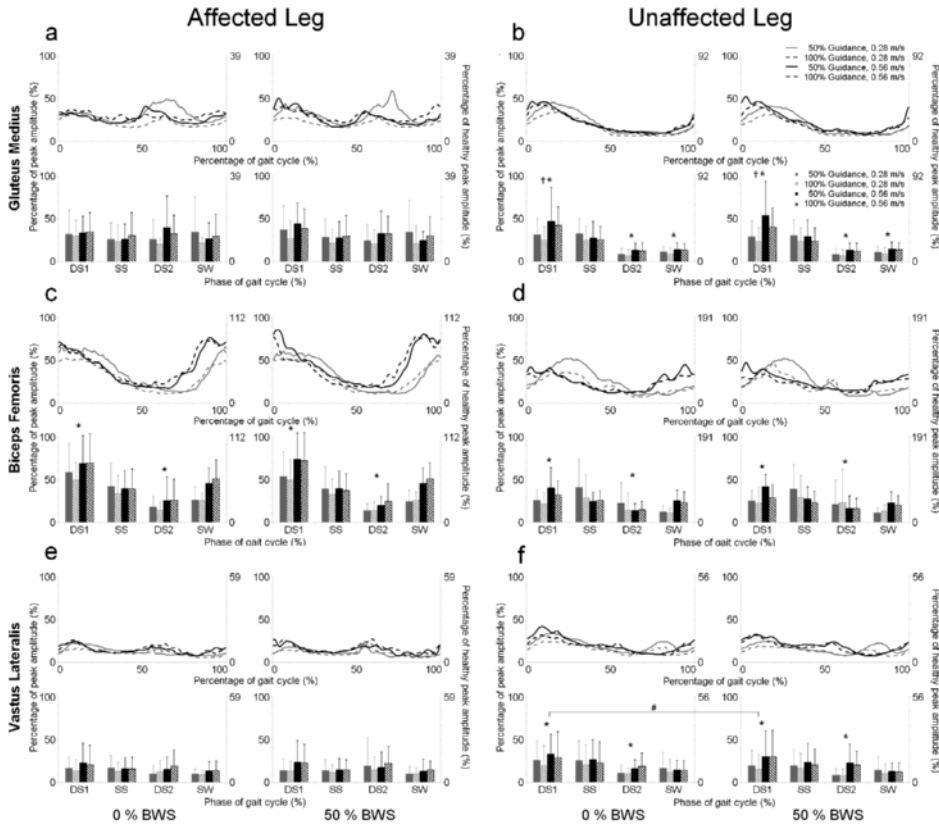
Muscle activity increased when treadmill speed was increased from 0.28 to 0.56 m/s, with significant main effects of Speed found in BF, MG and TA of the affected leg, and in all muscles of the unaffected leg.

More specifically, in the affected leg, increased speed resulted in increased BF activity during the DS1 and SW phase (average increase of 18.2 and 12.6% of peak amplitude, respectively). Similarly, TA activity increased with speed during the DS1 phase (average increase of 9.3%). MG activity was increased by increasing speed during all phases (average increase of 21.2, 15.6, 16.5 and 16.4% for DS1, SS, DS2 and SW, respectively).

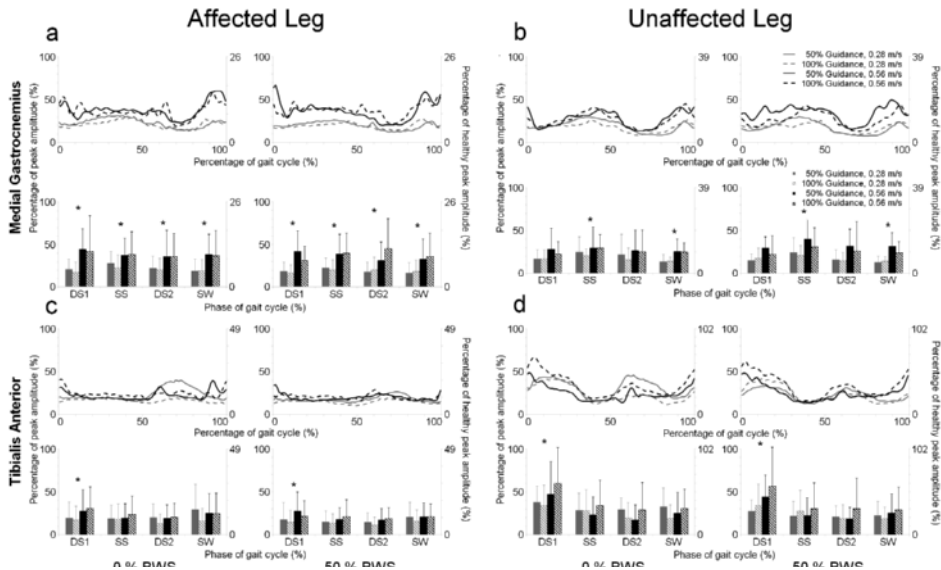
In the unaffected leg, increasing speed led to an increase of GM activity during the DS1, DS2 and SW phase (average increase of 18.4, 5.0 and 4.0 % of peak amplitude, respectively). Similarly, BF activity increased by increasing speed during the DS1 and SW phases (average increases of 12.1 and 11.1%, respectively), VL activity increased during the DS1 and DS2 phases (10.4 and 10.1%, respectively), MG activity was increased in the SS and SW phase (9.7 and 12.6%, respectively) and TA activity increased during the DS1 phase (18.9%).

#### *Interactions.*

No significant interactions were found in any of the muscles, indicating that the observed effects of Guidance, BWS and Speed occurred independent of one another.



**Figure 1.** EMG profiles and average EMG per gait phase of (a,b) Gluteus Medius, (c,d) Biceps Femoris and (e,f) Vastus lateralis. *Upper panels:* Time and amplitude normalized EMG profiles (% peak amplitude) of both the affected (a,c,e) and unaffected (b,d,f) legs of stroke patients during walking in the Lokomat under varying guidance levels (50% = solid; 100% = dashed), bodyweight support levels (0% = left panel; 50% = right panel) and speeds (0.28 m/s = grey; 0.56 m/s = black). *Lower panels:* mean EMG (+SD) (% peak amplitude) for four gait phases, i.e. the first double support (DS1), single support (SS), second double support (DS2) and swing (SW), of both the affected (a,c,e) and unaffected (b,d,f) legs of stroke patients, during walking in the Lokomat under varying guidance, bodyweight support and speed (see above for further explanation). The secondary axes represent the amplitude ratios (% healthy peak amplitude). Statistical results of the univariate Repeated Measurements ANOVA are indicated: † = significant effect of Guidance; # = significant effect BWS; \* = significant effect Speed.



**Figure 2.** EMG profiles and average EMG per gait phase of (a,b) Medial Gastrocnemius and (c,d) Tibialis Anterior. *Upper panels:* Time and amplitude normalized EMG profiles (% peak amplitude) for the affected (a,c) and unaffected (b,d) legs of stroke patients and *Lower panels:* mean EMG (+SD) per gait phase (% peak amplitude) for the affected (a,c) and unaffected (b,d) legs of stroke patients. See Figure 1 for further details. Statistical results of the univariate Repeated Measurements ANOVA are indicated: † = significant effect of Guidance; # = significant effect BWS; \* = significant effect Speed.

**Table 2. Amplitude ratios.** Amplitude ratios for both the affected and unaffected leg, indicating the ratio between maximal amplitude of each muscle in stroke patient during Lokomat guided walking and the maximal amplitude of each muscle in healthy subjects during regular treadmill walking (data used from [30]), expressed in % healthy peak amplitude.

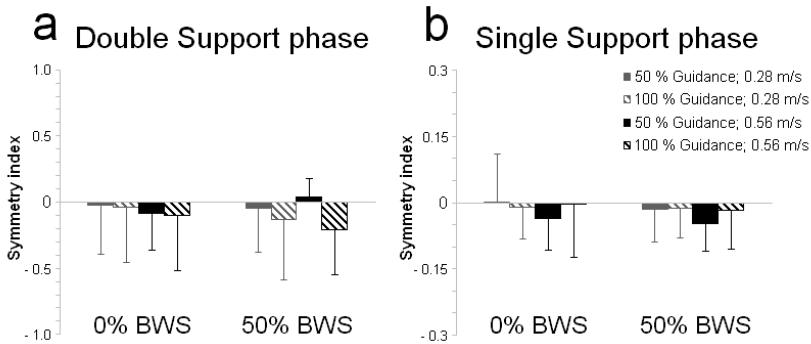
	Affected leg	Unaffected leg
	<b>Amplitude Ratio</b>	
Gluteus Medius	39 %	92 %
Biceps Femoris	112 %	191 %
Vastus Lateralis	59 %	56 %
Medial Gastrocnemius	26 %	39 %
Tibialis Anterior	49 %	102 %

### Amplitude ratios.

Table 2 shows the peak amplitude ratios, indicating the ratio between maximal activity in stroke patients and maximal activity in healthy subjects (see section ‘Signal analysis - Muscle activity’ for calculation). Peak activity of unaffected GM and TA was approximately similar to healthy walking, whereas peak activity of both the unaffected and affected BF was abnormally high. For all other muscles, peak activity was lower in stroke patients than in healthy walkers.

### Temporal symmetry measures.

Figure 3 show the mean symmetry index (+SD) for DS and SS. See Table S3 in ‘supplementary material 1’ for a full overview of the statistical results. Inspection of the intercept of the ANOVA model indicated that no significant asymmetries were found in both DS and SS phase duration. In addition, no significant main or interaction effects of Guidance, BWS and Speed were found for both the symmetry index for DS and SS phase.



**Figure 3. Mean values for symmetry index of step phases.** The mean (+SD) symmetry index for a: double support phase duration and b: single support phase duration of stroke patients during Lokomat guided walking under varying guidance levels (50% = solid; 100% = dashed), bodyweight support levels (0% = left; 50% = right) and speeds (0.28 m/s = grey; 0.56 m/s = black).

## DISCUSSION

The present study examined the effects of the Lokomat parameters, i.e. guidance, BWS and treadmill speed, on muscle activity and step symmetry in post-stroke hemiparetic patients. The results showed that both guidance and BWS had limited effect on muscle activity, whereas the increase of speed had significant positive effect on muscular output in both the affected and unaffected leg. No significant interactions between the parameters were found. In addition, the level of temporal symmetry was not affected by altering training parameters. In sum, it can be concluded that the Lokomat training parameters are generally ineffective in shaping muscle activity and step symmetry in post-stroke hemiparetic patients.

### The effects of training parameters on muscle activity.

Speed appears to be the main parameter that can be used to influence muscular output of stroke patients. The majority of muscles of stroke patients showed maximal outputs below 100% of healthy peak amplitude, as indicated by the amplitude ratios. This confirms previous research that stroke patients show reduced muscular amplitude during Lokomat

guided walking [30,35], which may negatively affect the outcome of Lokomat therapy, as active contribution to the production of a task is an important component of activity-dependent learning [44-46]. Since present results showed that speed can be used to promote increased muscular output in both the affected (BF, MG and TA) and unaffected (all muscles) leg of stroke patients, this parameter may be used to promote voluntary active control and therefore possibly enhance therapy outcome.

Although earlier research with healthy walkers showed that lowering the level of guidance increased muscular amplitude [10], current results show that in stroke patients lowering guidance level may not induce increased activity. More specifically, only GM activity of the unaffected leg was increased when guidance was reduced to 50%, whereas activity of all other muscles remained relatively constant over guidance levels. Possibly, levels lower than 50% may necessitate more active contributions of the muscles. However, extremely low levels of guidance (e.g. 20% or below) may induce unwanted abnormalities in neuromuscular control [10, 47] and 50% guidance is representative for clinical practice [35]. As such, it can be concluded that the ability to influence muscular activity in stroke patients is limited when varying guidance within a clinical relevant range.

BWS also seems to have little effect on the muscular output of stroke patients during Lokomat guided gait, as, with exception of unaffected VL, no muscles were sensitive to changes in the level of BWS. This is in contrast to literature on the use of BWS during regular treadmill walking, showing reduced muscle activity in hemiparetic patients when BWS is provided [17,18], as BWS reduces task demands related to leg support and trunk stability. During Lokomat guided walking, the task components related to leg support are assisted, e.g. by stabilizing the knee during weight acceptance. In addition, mediolateral stability is guaranteed as the exoskeleton fixates the legs, restricting movements to the sagittal plane [7,8]. This may explain why little effect of BWS was found.

### **The effects of training parameters on step symmetry.**

Previous research has shown that BWS and treadmill speed can be used during treadmill training to influence step symmetry in post-stroke hemiparetic gait. More specifically, both the provision of BWS [17,18,55,56] and increase of speed [14,15] led to prolonged single support duration of the affected leg, resulting in more symmetrical stepping patterns. However, the present study could not provide evidence to confirm these effects during Lokomat guided walking. Also, varying guidance had no effect on the level of step symmetry. The limited ability of training parameters to affect temporal symmetry may be a result of the already more symmetrical pattern of stroke patients during Lokomat guided walking, compared to treadmill walking [30]. In addition, the herewith used impedance

controller provides movement guidance with fixed timing of movements [39] and in healthy subjects phase durations were barely affected by training parameters when the impedance controller was used [10]. The recently developed path controller may possibly increase the ability of parameters to affect temporal symmetry, as it allow the walker more freedom in the timing of movement [7,9,39]. Nonetheless, it can be concluded that within the range of settings used in present study, varying the training parameters of the Lokomat did not affect the level of step symmetry in stroke patients.

### **Clinical implications.**

Present results showed that treadmill speed is the main parameter to influence muscular output in stroke patients. Clinically relevant settings of guidance and BWS do not result in alterations in the muscle activity in post-stroke hemiparetic patients. The results additionally showed that the amplitude of the majority of the muscles was lowered compared to healthy treadmill walking. As the reduced active participation may possible limit motor learning [44-46], it is advised to increase treadmill speed as early as possible during Lokomat therapy. In addition, although earlier research in healthy walkers showed complex interactions between the effects of Lokomat parameters [30], the present study did not find such interactions in stroke patients within the range of settings used. This may indicate that the benefit of varying speed occurs independent of the level of guidance and BWS. For example, increasing speed can be used under conditions that may provoke passive behavior (e.g. combination of high guidance and high BWS levels [10]), to enhance active contribution of the walker. Also, other training strategies can be incorporated during Lokomat guided walking to increase active involvement, such as motivational instructions [48,49], bio- or augmented feedback [50,51] or virtual reality [52,53]. In addition, a newly developed FreeD-module for the Lokomat adds degrees of freedom to the pelvis [54], requiring active control of hip- and trunk stability. Such developments in the mechanical set-up of the Lokomat may be exploited to increase active participation of patients.

### **Limitations.**

There are a few limitations that should be taken into account when interpreting present findings. First, the result may not be representative for a therapy session with the Lokomat, as it was chosen not to provide instructions or feedback. Studies on the effect of motivational instruction during Lokomat guided walking, however, showed that the level of muscle activity may depend on the type of instructions provided by the therapist [48,49]. Also, foot straps were used which have been shown to reduce lower leg muscle activity [35,57].

Second, patients had no experience with Lokomat walking and muscle activity was only measured during a single session. Arguably, muscular responses may change after a few sessions, e.g. as patients get familiar with the gait pattern of the Lokomat, and it can be argued that found results may not apply for multi-session therapy. Finally, although the patient group was representative of the target group for Lokomat therapy, there was large variation in gait function between patients, as indicated by FAC scores (see table 1). In order to establish whether the effects of the training parameters depend on the level of gait function, future research should focus on subgroups of patients.

## CONCLUSIONS

The present study examined the effects of Guidance, BWS and Speed on muscle activity and step symmetry in post-stroke hemiparetic patients. When using a clinically relevant range of settings for the training parameters of Lokomat therapy, only treadmill speed had a significant effect on muscular output in both the affected and unaffected leg. The level of temporal symmetry was not affected by altering training parameters. To conclude, apart from speed, the Lokomat training parameters may have limited use to affect muscle activity and step parameters and thereby to tailor Lokomat therapy.

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**Competing Interest:** The authors declare that they have no competing interests.



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## SUPPLEMENTARY MATERIAL 1

**Table S1: Overview of statistical results on muscle activity in the affected limb of hemiparetic stroke patients.** Univariate results of the Repeated Measures ANOVA on the (main and interaction) effects of the within subjects factors Guidance, Bodyweight support (BWS) and Speed on muscle activity during 4 phases of gait.

	Guidance	BWS <sup>a</sup>	Speed	Guidance * BWS <sup>a</sup>	Guidance * Speed	BWS*Speed	Guidance * BWS* Speed
	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)
<b>Gluteus Medius</b>							
DS1 <sup>b</sup>	0.98	1.88	5.38	1.38	1.27	2.53	0.00
SS <sup>c</sup>	0.10	0.00	6.38	0.48	2.82	0.00	0.21
DS2 <sup>d</sup>	2.26	0.45	7.89	0.32	0.17	0.15	0.10
SW <sup>e</sup>	1.04	0.16	0.00	0.10	3.02	0.01	0.10
<b>Biceps Femoris</b>							
DS1 <sup>b</sup>	0.34	0.00	<b>11.36**</b>	0.03	0.74	1.36	0.81
SS <sup>c</sup>	0.58	1.06	0.32	0.02	3.89	0.08	0.67
DS2 <sup>d</sup>	0.04	1.69	3.59	1.42	6.82	0.04	0.01
SW <sup>e</sup>	2.48	0.39	<b>40.79***</b>	0.29	2.14	0.01	0.48
<b>Vastus lateralis</b>							
DS1 <sup>b</sup>	0.73	0.00	4.63	0.66	0.07	2.77	0.07
SS <sup>c</sup>	1.00	3.82	1.61	0.32	3.09	1.37	0.66
DS2 <sup>d</sup>	0.34	2.09	2.27	0.35	2.10	0.26	1.05
SW <sup>e</sup>	0.12	0.49	3.50	1.85	0.42	0.01	0.00
<b>Medial Gastrocnemius</b>							
DS1 <sup>b</sup>	2.68	1.63	<b>22.66**</b>	0.28	0.31	0.52	0.73
SS <sup>c</sup>	0.02	0.80	<b>27.95**</b>	1.06	0.94	2.61	0.76
DS2 <sup>d</sup>	1.68	0.00	<b>13.04**</b>	3.15	3.80	1.50	2.89
SW <sup>e</sup>	0.01	0.55	<b>14.40**</b>	4.24	0.51	0.05	1.48
<b>Tibialis Anterior</b>							
DS1 <sup>b</sup>	0.85	4.43	<b>9.93*</b>	2.38	0.48	0.32	1.86
SS <sup>c</sup>	0.56	3.19	4.23	0.68	5.70	0.81	.06
DS2 <sup>d</sup>	0.34	4.87	2.94	0.65	2.53	0.31	0.47
SW <sup>e</sup>	5.23	5.87	0.65	1.28	3.41	0.01	1.23

<sup>a</sup> Bodyweight Support; <sup>b</sup> first double support phase; <sup>c</sup> single support phase; <sup>d</sup> second double support phase; <sup>e</sup> swing phase; **bold = significant**; \* < 0.05; \*\* < 0.01; \*\*\* < 0.001

**Table S2: Overview of statistical results on muscle activity in the unaffected limb of hemiparetic stroke patients.** Univariate results of the Repeated Measures ANOVA on the (main and interaction) effects of the within subjects factors Guidance, Bodyweight support (BWS) and Speed on muscle activity during 4 phases of gait.

	Guidance	BWS <sup>a</sup>	Speed	Guidance * BWS <sup>a</sup>	Guidance * Speed	BWS <sup>a</sup> * Speed	Guidance * BWS <sup>a</sup> * Speed
	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)
<b>Gluteus Medius</b>							
DS1 <sup>b</sup>	1.31	0.00	<b>15.46**</b>	0.61	0.45	1.16	1.51
SS <sup>c</sup>	<b>18.02**</b>	0.68	0.87	0.58	3.98	2.22	3.72
DS2 <sup>d</sup>	4.79	0.12	<b>9.79*</b>	0.00	0.18	0.00	0.03
SW <sup>e</sup>	2.39	0.70	<b>18.78**</b>	0.00	1.76	0.95	0.64
<b>Biceps Femoris</b>							
DS1 <sup>b</sup>	4.09	0.19	<b>24.16**</b>	0.14	5.42	0.15	0.90
SS <sup>c</sup>	9.65	0.00	1.16	0.67	5.34	0.18	3.88
DS2 <sup>d</sup>	0.33	1.75	0.39	0.70	0.92	0.19	7.34
SW <sup>e</sup>	0.34	3.06	<b>36.35***</b>	0.14	2.43	3.39	1.16
<b>Vastus lateralis</b>							
DS1 <sup>b</sup>	2.30	<b>11.52**</b>	<b>8.03*</b>	1.48	0.96	1.62	0.10
SS <sup>c</sup>	4.13	4.87	2.96	1.74	0.30	2.33	0.36
DS2 <sup>d</sup>	0.07	1.87	<b>12.09**</b>	0.81	0.08	7.51	2.25
SW <sup>e</sup>	2.39	4.00	0.00	0.00	9.25	0.21	0.05
<b>Medial Gastrocnemius</b>							
DS1 <sup>b</sup>	1.37	0.27	4.25	0.01	8.74	0.29	0.25
SS <sup>c</sup>	2.43	0.74	<b>13.52**</b>	0.91	0.06	3.82	2.73
DS2 <sup>d</sup>	1.43	0.02	5.37	0.00	0.00	2.92	1.65
SW <sup>e</sup>	0.56	0.54	<b>35.87***</b>	0.77	2.10	1.01	2.33
<b>Tibialis Anterior</b>							
DS1 <sup>b</sup>	0.45	2.54	<b>9.71*</b>	0.52	1.15	0.15	0.66
SS <sup>c</sup>	0.63	3.06	0.07	0.21	2.33	0.40	4.31
DS2 <sup>d</sup>	0.48	0.71	0.10	0.84	9.57	3.17	1.28
SW <sup>e</sup>	0.39	2.49	1.71	0.91	6.63	1.67	3.61

<sup>a</sup> Bodyweight Support; <sup>b</sup> first double support phase; <sup>c</sup> single support phase; <sup>d</sup> second double support phase; <sup>e</sup> swing phase; **bold = significant**; \* < 0.05; \*\* < 0.01; \*\*\* < 0.001

**Table S3: Overview of statistical results on symmetry index in hemiparetic stroke patients.** Univariate results of the Repeated Measures ANOVA on the (main and interaction) of the within-subject factors Guidance, Bodyweight support (BWS) and Speed on the symmetry index of double support phase duration and single support phase duration, calculated according to method of Mukherjee et al (2015).

	Guidance	BWS <sup>a</sup>	Speed	Guidance * BWS <sup>a</sup>	Guidance * Speed	BWS <sup>a</sup> * Speed	Guidance * BWS <sup>a</sup> * Speed
	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)	F(1,9)
<b>Symmetry Index</b>							
Double Support phase	1.42	0.30	0.15	1.65	0.82	0.32	1.93
Single Support phase	1.23	1.07	3.63	0.10	0.78	0.11	0.16

<sup>a</sup> Bodyweight Support; **bold = significant**; \* < 0.05; \*\* < 0.01; \*\*\* < 0.001



