Chapter 3

The combined effects of guidance force, bodyweight support and gait speed on muscle activity during able-bodied walking in the Lokomat

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Klaske van Kammen
Anne M. Boonstra
Lucas H.V. van der Woude
Heleen A. Reinders-Messelink
Rob den Otter
ABSTRACT

Background: The ability to provide automated movement guidance is unique for robot assisted gait trainers such as the Lokomat. For the design of training protocols for the Lokomat it is crucial to understand how movement guidance affects the patterning of muscle activity that underlies walking, and how these effects interact with settings for bodyweight support and gait speed.

Methods: Ten healthy participants walked in the Lokomat, with varying levels of guidance (0, 50 and 100%), bodyweight support (0 or 50% of participants’ body weight) and gait speed (0.22, 0.5 or 0.78 m/s). Surface electromyography of Erector Spinae, Gluteus Medius, Vastus Lateralis, Biceps Femoris, Medial Gastrocnemius and Tibialis Anterior were recorded. Group averaged levels of muscle activity were compared between conditions, within specific phases of the gait cycle.

Findings: The provision of guidance reduced the amplitude of activity in muscles associated with stability and propulsion (i.e. Erector Spinae, Gluteus Medius, Biceps Femoris and Medial Gastrocnemius) and normalized abnormally high levels of activity observed in a number of muscles (i.e. Gluteus Medius, Biceps Femoris, and Tibialis anterior). The magnitude of guidance effects depended on both speed and bodyweight support, as reductions in activity were most prominent at low speeds and high levels of bodyweight support.

Interpretation: The Lokomat can be effective in eliciting normal patterns of muscle activity, but only under specific settings of its training parameters.

Keywords
Electromyography; Robotics; Neurorehabilitation; Gait; Body Weight Support; Lokomat
INTRODUCTION

There is ample evidence that intensive and task-specific gait training can optimize restoration of functional walking ability [1-3]. Body-weight supported treadmill training (BWSTT) applies these principles, allowing repetitive execution of manually guided stepping movements with adjustable support of body-weight. However, BWSTT is strenuous and physically demanding for both the patient and the therapist [4-6], in particular in patients with low ambulatory status. The Lokomat was developed to automate BWSTT by replacing the manual guidance by automated guidance through a bilaterally motor driven exoskeleton [6], allowing repetitive and task specific gait training in a therapist-friendly fashion. Three adjustable parameters define the Lokomat training environment: treadmill speed, the level of bodyweight support (BWS) and the amount of guidance provided by the exoskeleton. In order to purposefully exploit the learning potential of this device, it is crucial to understand muscle activity in the Lokomat, and how it can be altered using the available training parameters.

The Lokomat exoskeleton is designed to support limb movements throughout the stepping cycle. This so called ‘guidance’ is a key feature of Lokomat training, making it possible to move along a predefined path derived from joint trajectories of healthy walkers [4,6]. Initially, guidance was realized by a position control strategy, in which the limbs were moved passively through a predefined pattern, with minimal kinematic variability [6]. To promote active involvement, an impedance controller was implemented to adjust the level of guidance according to the patient’s capacity [7]. This type of control creates a virtual coupling between the actual and the predefined joint movement, by simulating a spring that ‘pulls’ the limb to the predefined path if deviations occur [8]. Guidance levels can be set by adjusting this pulling force, allowing free walking when guidance is set to nil, and forcing a predefined gait pattern at maximum guidance.

Offering guidance makes it possible to elicit a normal gait pattern in patients that are incapable of independent stepping [4-6]. Although these conditions may limit the active contribution of patients, successful stepping induces task-specific sensory information that may inform plastic changes in the central nervous system, and stimulate unaided walking [5-7,9-11]. However, because active involvement and the production of variable movement patterns and movement errors are prerequisites for activity-dependent neuroplasticity [4,5, 12-15], guidance levels should be progressively reduced according to the patient’s capacity [5,14-16]. As such, the adjustment of guidance levels represents an important means for therapists to tailor Lokomat training to individual patients. Selective and well-dosed provision of guidance requires a good understanding of how
this training parameter affects the amount of active involvement of walkers, and the respective contributions of muscles to the production of gait.  

So far, studies on muscle activity during Lokomat walking have primarily focused on comparisons between unrestrained treadmill walking and fully guided [17-20], partially guided [20,21], or unguided [22,23] Lokomat walking, in patients [17,18,21] and healthy walkers [19,20,22,23]. Overall, the results suggest that patterns of muscle activity differ between Lokomat and treadmill walking, e.g. Lokomat walking requires less activity of the shank muscles, but more of the hamstrings and quadriceps. However, as these studies did not systematically vary guidance, they provide limited information on how these aberrations are related to the level of guidance. To the best of our knowledge, only two studies examined patterns of muscle activity under different guidance levels, showing that the modular output of synergistic muscle groups is invariant over guidance levels [20] and that reductions in guidance force do not increase muscle activity [8]. Although these insights are relevant, for purposeful employment of guidance in training, it is also important to understand whether effects of guidance depend on gait speeds and BWS, because the contribution of individual muscles to key locomotor tasks (e.g. support and propulsion) depends on both the speed of progression [24] and the level of BWS [25]. Recently, van Kammen et al. [23] showed that the nature and magnitude of the differences between Lokomat and treadmill walking depend on complex interactions with BWS and gait speed. Therefore, to gain insight in how guidance affects muscle activity, and how the nature and magnitude of these effects depend on speed and BWS, healthy walkers were studied during Lokomat walking, while guidance, BWS and treadmill speed was varied systematically.

**METHOD**

**Participants.**
Ten healthy young adults (6 females; age 20.9±2.2 years, body height 1.82±0.04 meter and body weight 77.90±9.6 kilograms), without disorders that affect gait performance or muscle activity, and no previous experience with Lokomat walking, participated in this study. All participants provided their written informed consent. The protocol was in accordance with the Declaration of Helsinki [26], and approved by the Medical Ethical Committee of the University Medical Center Groningen (METc UMCG, project number: NL42826.042.12), the Netherlands.
EFFECTS OF LOKOMAT TRAINING PARAMETERS IN HEALTHY SUBJECTS

Experimental apparatus.
The Lokomat Pro.
Participants walked in the Lokomat Pro version 6.0 (Hocoma AG, Volketswil, Switzerland) at the rehabilitation center ‘Revalidatie Friesland’ in Beetsterzwaag, the Netherlands, using the impedance control mode, allowing adjustments in guidance force (0 – 100%). The Lokomat exoskeleton exists of two actuated orthoses attached to the participant’s limbs with cuffs and straps. The hip and knee joints of the Lokomat are actuated by linear drives that move the orthoses through the gait cycle, in the sagittal plane [5]. Ankle dorsiflexion can be assisted by means of elastic foot lifters.

During this experiment, the level of guidance was varied systematically. In principle, when guidance is set to 0%, the exoskeleton only generates torques to compensate for the inertia of the exoskeleton, allowing unrestricted leg movements [4,23]. With guidance set to 100%, participants are forced to closely track the predefined pattern of the exoskeleton [4,5]. At intermediate guidance levels, the actuated exoskeleton allows for small deviations, but re-directs larger deviations towards the predefined trajectory. When deviations are too large to be re-directed, the Lokomat has a built-in safety mechanism that halts the apparatus immediately.

Electromyography and detection of gait events.
Surface electromyography (EMG) was used to record activity from the Erector Spinae (ES), Gluteus Medius (GM), Vastus Lateralis (VL), Biceps Femoris (BF), Tibialis Anterior (TA) and Medial Gastrocnemius (MG), in the right leg. Signals were recorded using self-adhesive, disposable Ag/AgCl electrodes (Kendall/Tyco ARBO; Warren, MI, USA) with a 10 mm diameter and a minimum electrode distance of 25 mm, placed according to the SENIAM protocol [27]. The electrode sites were prepared by removing body hair, and by abrading and cleaning the skin with alcohol. Gait events were detected by means of customized insoles (Pedag, international VIVA) with four pressure sensors (FSR402, diameter 18 mm, loading 10–1000 g, one under the heel and three under the forefoot), placed in the footwear of the participants.

EMG signals and pressure sensor signals were sampled simultaneously at 2048 Hz and fed to a Porti7 portable recording system (Twente Medical Systems, Enschede, The Netherlands; common mode rejection >90dB, 2µVpp noise level, input impedance >1 GV). Signals were pre-amplified and A/D converted (22 bits) before storage on a laptop for offline analysis.
Experimental procedures.
Prior to testing, hip width, length of the upper and lower limbs of the exoskeleton, and size and position of leg cuffs were fitted to match the anatomy of the participant. Lokomat gait parameters (e.g. step length, patient coefficient, knee- and hip angles and their respective offsets) were set so that walking in the device was as natural and comfortable as possible. As the present group had full functional control of their ankle movements, foot lifters were not used. Settings were not adjusted during testing and participants were instructed to ‘actively move along with the device’ when guidance was provided.

Participants walked a total of 18 trials, divided in three blocks of six trials. Each block represented a fixed level of guidance (0, 50 or 100%) and each trial within a block provided a unique combination of BWS (0 or 50% of participants’ body weight) and speed (0.22, 0.5 or 0.78 m/s). BWS was provided by means of a suspended harness and levels were chosen based on recommendations for clinical practice [6,28,29]. Gait speeds were chosen to cover most of the range of the Lokomat (i.e. 0.14 m/s to 0.89 m/s).

To control for order effects, the order of the blocks and the order of the trials within blocks, were randomized using custom-made software routines in Matlab (version 2011a: The Mathworks INC., Natick, MA). To control for transition effects between conditions, participants were allowed to practice at least one minute prior to each trial, until they indicated to be comfortable. To obtain an approximately equal number of steps for each trial, trial durations depended on speed (i.e. 120, 70 or 40 seconds for trials at 0.22, 0.5 and 0.78 m/s, respectively). When the Lokomat suddenly stopped, e.g. when unexpected movements triggered the safety mechanism, the trial was repeated until a trial of the required duration was completed.

Data analysis.
Analysis of Muscle activity.
Custom-made software routines in Matlab were used for offline analysis of the EMG data. To reduce movement artifacts, a 10 Hz Butterworth high-pass filter was applied to the data. Subsequently, the data were full wave rectified, low-pass filtered (zero lag fourth order Butterworth filter, cutoff 20 Hz), time normalized (100 data points from heel-strike to heel-strike) and amplitude normalized with respect to the maximum amplitude over all conditions, for each muscle and participant.

To compare muscle activity between conditions, the summed EMG amplitude was calculated for specified time windows. Two types of windows were defined, namely ‘typical windows’ to demark phases in the gait cycle where activity was expected based on literature, and ‘atypical windows’ to demark phases where distinct activity was observed.
in the ensemble averaged EMG outside the ‘typical windows’. As such, activity that was captured within atypical windows could be regarded as ‘abnormal’, as activity within these windows is not commonly observed during unrestrained, healthy walking. In accordance with Perry [30], the following typical windows of activity were defined: ES window 1: 40–65 % of the gait cycle and window 2: 90–15 %; GM window 1: 96–6 % and window 2: 6–29 %; BF window 1: 82–5 %; VL window 1: 90–16 %; TA window 1: 56–80% and window 2: 80–13 %; MG window 1: 9–50 %. Based on the ensemble averaged EMG, the following ‘atypical’ windows were defined: GM window 3: 29–50%, BF window 2: 5–55%, VL window 2: 16–30% and TA window 3: 13–30%.

Analysis of Gait events.
Custom-made software routines in Matlab were used for offline calculation of step phase durations, based on pressure sensor signals. Temporal symmetry was assumed in the present group, so only the relative durations of the first double support (DS1) phase and the single support (SS) phase were evaluated.

Statistical analysis.
Using SPSS version 19 for Windows (SPSS, Chicago, IL, USA), a series of three-way univariate repeated measures ANOVA’s were performed to determine the effects of Guidance (0 vs 50 vs 100%), BWS (0 vs 50%) and Gait Speed (0.22 vs 0.5 vs 0.78 m/s) on step phase durations, and levels of muscle activity, for each of the windows of activity, separately. Main effects and all two- and three-way interactions were evaluated using an alpha level of 0.05. For simplicity, no posthoc analysis was performed to test individual levels of guidance or speed. For muscles with more than one window of activity, the Benjamini-Hochberg procedure was applied to the test results, of each muscle separately, to control the false discovery rate and correct for multiple testing [31].

RESULTS
In accordance with the aims of the study, the results will focus on the main effects of Guidance, and interactions of Guidance with Speed and BWS. Tables 1 and 2 can be consulted for a complete overview of the statistical results, for muscle activity and step phase durations, respectively.
CHAPTER 3

Muscle activity.
Ensemble averaged EMG profiles, and the average activity (+standard deviation (sd)) per window, are presented in figures 1-3 (see Table 1 for an overview of the test results). The average effects of guidance reported below, represent the differences between walking with 100% and 0% guidance.

Figure 1. EMG profiles and average muscle activity per gait phase for Erector Spinae and (a,b) Gluteus Medius (c,d). a,c: Time and amplitude normalized EMG profiles during walking in the Lokomat exoskeleton without guidance (solid lines), with 50% guidance (dashed lines) and with 100% guidance (dotted lines), at 0.22 m/s (top), 0.5 m/s (middle) and 0.78 m/s (bottom), at 0% (left column) and 50% bodyweight support (right column). EMG amplitude is expressed as a percentage of peak amplitude recorded over all conditions. The gray bars represent the analyzed windows of activity. b,d: Average level of muscle activity (+ standard deviations) in all walking conditions (see above for further explanation), for the analyzed windows of activity.
Erector Spinae (ES).
Providing guidance resulted in a decrease in ES activity during the first window (40–65%; typical window) of activity by 7.4% of peak amplitude (see figures 1a+b). During the second window of activity (90–15%; typical), guidance resulted in a decrease in activity of 7.7% when BWS was provided, whereas guidance effects were attenuated during full weight bearing (average decrease 2.2%).

Gluteus Medius (GM).
Within the first window of activity (96–6%; typical), GM activity decreased by 7.6 % when guidance was provided (see figures 1c+d). Similarly, during the third window (29–50%; atypical) GM activity decreased by 14.5% when guidance was provided, although the magnitude of this effect depended on speed: the observed reductions were more pronounced at 0.22 m/s (average decrease of 22.0%), then at 0.78 m/s (4.5%). GM activity in the second window (6–29%; typical) was unaffected by guidance (p > 0.05).

Biceps Femoris (BF).
Guidance reduced BF activity (see figures 2a+b) within the first (82–5%; typical), and the second window (5-55%; atypical) by 7.4% and 15.1%, respectively. However, within the second window, a three-way interaction indicated that guidance effects were most pronounced when walking with BWS and at lower speeds. When BWS was provided, guidance reduced activity by 22.3% and 7.0% at 0.22 m/s and 0.78 m/s, respectively. During walking without BWS, the corresponding reductions were 19.6% and 8.9% at 0.22 m/s and 0.78 m/s.

Vastus Lateralis (VL).
As illustrated in figures 2c and 2d, the activity of VL was not affected by guidance (p > 0.05).
Table 1. Overview of statistical test results on Muscle Activity. Univariate results of the Repeated Measures ANOVA on the (main and interaction) effects of the factors Guidance, Speed and Bodyweight support.

<table>
<thead>
<tr>
<th>(% of Gait Cycle)</th>
<th>Guidance</th>
<th>Speed</th>
<th>BWS</th>
<th>Guidance *Speed</th>
<th>Guidance *BWS</th>
<th>Speed *BWS</th>
<th>Guidance *Speed *BWS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F(2,18)</td>
<td>\eta^2</td>
<td>F(2,18)</td>
<td>\eta^2</td>
<td>F(1,9)</td>
<td>\eta^2</td>
<td>F(4,36)</td>
</tr>
<tr>
<td>Window1 (40 – 65%)</td>
<td>9.92**</td>
<td>0.52</td>
<td>2.18</td>
<td>0.20</td>
<td>19.92**</td>
<td>0.69</td>
<td>0.79</td>
</tr>
<tr>
<td>Window2 (90 – 15%)</td>
<td>3.13</td>
<td>0.26</td>
<td>1.28</td>
<td>0.12</td>
<td>10.46*</td>
<td>0.54</td>
<td>1.64</td>
</tr>
</tbody>
</table>

**Erector Spinae**

| Window1 (96 – 6%) | 4.35* | 0.33  | 32.92*** | 0.79  | 9.27* | 0.51  | 1.46  | 0.14  | 0.58  | 0.06  | 11.78** | 0.57  | 0.30  | 0.03  |
| Window2 (6 – 29%) | 2.79  | 0.24  | 9.93**  | 0.53  | 9.87* | 0.52  | 0.86  | 0.09  | 1.60  | 0.15  | 2.07  | 0.19  | 0.28  | 0.03  |
| Window3 (29 – 50%) | 5.90* | 0.40  | 6.08*  | 0.40  | 15.65** | 0.64  | 5.57* | 0.38  | 2.44  | 0.21  | 0.64  | 0.07  | 1.17  | 0.12  |

**Gluteus Medius**

| Window1 (82 – 3%) | 10.19** | 0.53  | 5.61*  | 0.38  | 11.38* | 0.59  | 2.44  | 0.21  | 0.36  | 0.04  | 3.55  | 0.28  | 1.98  | 0.18  |
| Window2 (5 – 55%) | 26.94*** | 0.75  | 7.67*  | 0.46  | 6.25*  | 0.41  | 2.56  | 0.22  | 4.61* | 0.34  | 1.19  | 0.12  | 3.37* | 0.27  |

**Biceps Femoris**

| Window1 (90 – 16%) | 0.12  | 0.01  | 18.23** | 0.67  | 13.41** | 0.60  | 2.78  | 0.24  | 0.38  | 0.04  | 5.57* | 0.38  | 1.93  | 0.18  |
| Window2 (16 – 30%) | 0.03  | 0.00  | 0.47  | 0.05  | 23.28** | 0.72  | 0.71  | 0.07  | 0.11  | 0.01  | 1.23  | 0.12  | 2.98  | 0.25  |

**Vastus Lateralis**
**Table 1. Continued**

<table>
<thead>
<tr>
<th>Window1 (9 – 50%)</th>
<th>Guidance Speed BWS Guidance *Speed Guidance *BWS Speed *BWS Guidance *Speed *BWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial Gastrocnemius</td>
<td>( F(2,18) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(1,9) ) ( \eta^2 ) ( F(4,36) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(4,36) ) ( \eta^2 )</td>
</tr>
<tr>
<td>2.89 0.24</td>
<td>21.59*** 0.71</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Window2 (56 – 80%)</th>
<th>Guidance Speed BWS Guidance *Speed Guidance *BWS Speed *BWS Guidance *Speed *BWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tibialis Anterior</td>
<td>( F(2,18) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(1,9) ) ( \eta^2 ) ( F(4,36) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(4,36) ) ( \eta^2 )</td>
</tr>
<tr>
<td>(56 – 80%) 1.41 0.14</td>
<td>65.09*** 0.88</td>
</tr>
<tr>
<td>(80 – 13%) 1.49 0.14</td>
<td>51.23*** 0.85</td>
</tr>
<tr>
<td>(13 – 30%) 2.26 0.20</td>
<td>3.91 0.30</td>
</tr>
</tbody>
</table>

**Table 2. Overview of statistical test results on Step Phase Durations.** Univariate results of the Repeated Measures ANOVA on the (main and interaction) effects of the factors Guidance, Speed and Bodyweight support.

<table>
<thead>
<tr>
<th>Step Phase Duration</th>
<th>Guidance Speed BWS Guidance *Speed Guidance *BWS Speed *BWS Guidance *Speed *BWS</th>
</tr>
</thead>
<tbody>
<tr>
<td>First Double Support</td>
<td>( F(2,18) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(1,9) ) ( \eta^2 ) ( F(4,36) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(2,18) ) ( \eta^2 ) ( F(4,36) ) ( \eta^2 )</td>
</tr>
<tr>
<td>2.46 0.22</td>
<td>0.12 0.01</td>
</tr>
<tr>
<td>Single Support</td>
<td>2.72 0.23</td>
</tr>
</tbody>
</table>

**bold = significant; * p < 0.05; ** p < 0.01; *** p < 0.001.**
Figure 2. EMG profiles and average muscle activity per gait phase for Biceps Femoris (a,b) and Vastus Lateralis (c,d). Time and amplitude normalized EMG profiles (a,c) and the average level of muscle activity (+ standard deviations) for the analyzed windows of activity (b,d). See figure 2 for further details.
Figure 3. EMG profiles and average muscle activity per gait phase for Medial Gastrocnemius (a,b) and Tibialis Anterior (c,d). Time and amplitude normalized EMG profiles (a,c) and the average level of muscle activity (+ standard deviations) for the analyzed windows of activity (b,d). See figure 2 for further details.

**Medial Gastrocnemius (MG).**
Guidance resulted in an attenuation of speed effects on MG activity (see figures 3a+b), as speed related increases in MG activity were more prominent during walking with minimal (average increase 13.0% between 0.22 and 0.78 m/s) compared to maximal guidance (7.9%).

**Tibialis Anterior (TA).**
TA activity within the first (56–80%; typical) as well as the second window (80–13%; typical) of activity was unaffected by guidance (p > 0.05; see figures 3c+d). Within the third window (13–30%; atypical), guidance effects depended on speed, as an average reduction of 16.5% was observed at 0.22 m/s, whereas guidance effects were negligible at 0.78 m/s.
Step phase durations.
The average (+sd) relative durations of gait phases are shown in figure 4 (see also Table 2 for an overview of the test results).

The effects of guidance on DS1 durations depended on speed. When no guidance was provided, DS1 durations decreased with speed (12.1% of the gait cycle time at 0.22 m/s vs 9.7% at 0.78 m/s), whereas DS1 durations was unaffected by speed levels during fully guided walking (11.3% at 0.22 m/s vs 12.4% at 0.78 m/s). The duration of the SS phase was not significantly affected by Guidance (p > 0.05).

Figure 4. Mean duration of step phases. The mean relative duration (+ standard deviations) of (a) the double support phase and (b) the single support phase, expressed as a percentage of the total gait cycle duration, during walking in the Lokomat, for different levels of guidance (0, 50 and 100%), bodyweight support (BWS; 0 and 50%) and gait speed (0.22, 0.5 and 0.78 m/s).

General effects of BWS and Speed.
Providing BWS resulted in decreased DS1 durations and increased SS durations, whereas step phase durations were unaffected by speed. Also, amplitude generally increased with speed and decreased with BWS, in all muscles (GM$^{W1}$, BF$^{W1}$, VL, MG and TA). Notably, some muscles (GM$^{W2, W3}$ and BF$^{W2}$) showed paradoxical speed effects, i.e. decreases in amplitude with speed. Furthermore, Speed by BWS interactions in ES, GM, VL and MG showed that speed effects were more prominent during full weight bearing.

DISCUSSION

Guidance generally reduces the amplitude of muscle activity, but the magnitude of this effect depends on BWS and gait speed. Nevertheless, even when guidance is maximal, muscles showed phased activity, indicating that gait movements were still actively
controlled in conditions where the robot is in charge. It can be concluded that in healthy subjects the possibility to elicit a ‘physiological’ pattern during Lokomat guided walking strongly depends on the combined settings of guidance, speed and BWS.

**Effects of guidance on the step phase durations.**
During unrestrained walking, passive dynamics of the walker largely determine the durations of step phases [32]. To maintain energetic efficiency, the relative duration of the SS phase increases, whereas the relative duration of the DS phase decreases with speed [23, 33-35]. The present results show that this speed related modulation of phase durations was attenuated when guidance was provided. Arguably, the functional relationship between speed and step phase durations is disturbed due to alterations in the passive dynamics of the legs when walking in an (actuated) exoskeleton. Indeed, previous studies on Lokomat walking have shown that at low speeds DS1 durations are shorter than during treadmill walking [17,23], but that these durations can be partly normalized by increasing speed [23]. However, the present data indicate that when guidance is provided, such normalization does not occur and that a fixed temporal stepping pattern is used over speeds. The fixed relationship may result in a walking pattern that is less energetically efficient [18,33,36] and may induce an abnormal pattern of muscle activity [23]. However, it is important to acknowledge that the impedance controller used in the present study may have restricted step phase modifications. An important drawback of impedance control is that, due to the coupling of spatial and temporal guidance, the timing of movements is fixed when full guidance is provided [8]. Recently, a ‘path control algorithm’ was developed (see e.g. [4,5,8]), that produces a supportive force for the timing of movements, which can be set separately from the guidance force [5,8]. Lowering the supportive force allows more flexibly timed limb trajectories and step events.

**Effects of guidance on muscle activity.**
The amplitude of activity in most muscles (ER, GM, BF and MG) was lowered when guidance was offered. The muscle specific nature of these effects indicates that guidance primarily reduces muscular activity related to stability and propulsion, whereas the absence of these effects in other muscles (i.e. VL and TA) suggests that leg loading and foot clearance still require activity. It must be noted that no foot support was provided, and that use of foot lifters is known to reduce activity in the ankle dorsiflexors [19-21].

Interestingly, even when full guidance was offered, muscles showed marked and structurally phased activity, confirming findings of others [17-20]. This is noteworthy, as in this condition the exoskeleton is in charge and no voluntary activity is required.
from the walker [4,18]. However, the instructions used in the present study (i.e. ‘actively 
move along with the device’) may have affected activity, as previous studies showed that 
encouraging active involvement increases muscle activity during guided Lokomat walking 
[17,18]. Another factor to consider is that passive stepping may give rise to task specific 
sensory information that elicits and modulates step-like EMG activity [9].

Although EMG was not recorded during unrestrained treadmill walking, the 
comparison with commonly observed patterns in healthy subjects [30] revealed that some 
muscles (i.e. GM, BF, VL, and TA) showed activity in phases where this was not expected. 
Quantifying this activity separately, within ‘a-typical’ windows of activity, made it possible 
to evaluate how parameter settings affected levels of abnormal activity. The observed 
aberrations confirm earlier studies, showing that the patterning of muscle activity during 
Lokomat walking is different from regular treadmill walking [17-19,21,23]. This atypical 
activity may indicate efforts to overcome altered task constraints during exoskeleton 
walking, due to e.g. reductions in the degrees of freedom allowed by the exoskeleton 
[18,19], increased balance issues [20] or altered inertial properties of the limbs [23]. It 
is interesting to note that increases in guidance reduced activity within these atypical 
windows, indicating that in healthy walkers guidance diminishes the necessity to actively 
overcome the altered task constraints associated with Lokomat walking.

The effects of guidance depended on treadmill speed in a number of muscles, in 
particular within atypical windows of activity (GM\(^{W3}\), BF\(^{W2}\), TA\(^{W3}\)). Independent of 
guidance settings, the observed aberrations were dramatically reduced as speed increased. 
As a consequence, guidance effects were most outspoken at the lowest speed, whereas 
these effects were marginal at the highest speed (see e.g. GM\(^{W3}\) and TA\(^{W3}\)). The effects of 
guidance also depended on the BWS that was provided. During the atypical BF activity 
(BF\(^{W2}\)), the provision of BWS resulted in increased activity, but the magnitude of this 
effect reduced by providing guidance. Taken together, these results underscore that when 
setting parameters for Lokomat training, interactions between training parameters should 
be explicitly considered.

**Clinical implications.**

Although care should be taken not to overstate clinical implications derived from healthy 
participants, the present results suggest that therapists should be aware that aberrations in 
muscular control can occur when certain combinations of parameters are presented 
during training. First, as low speeds combined with low guidance levels induced
aberrations in relevant muscles, this specific combination should preferably be avoided during training. In contrast, at the highest speed, activation levels differed only marginally between fully guided and unguided walking. These findings may be particularly relevant as a likely strategy for Lokomat training is to progressively reduce guidance levels as patients become more capable of voluntary stepping [16]. If a physiological pattern is targeted, the present results should be taken into account when reducing treadmill speed to enable training at lower guidance levels. Second, as guidance and BWS both reduce muscle activity, combining high levels of BWS and guidance may result in abnormally low muscle output (see e.g. ES$^w$) and may therefore not be desirable during training.

Limitations.
We included healthy subject to enable free exploration of the training parameters in a relatively homogeneous population. In principle, the observed reductions in activity may reflect the ability of healthy walkers to consciously reduce their work against the exoskeleton. However, instructions were given to avoid such passive behavior and the present results show that muscles are still active even when fully guided. Nevertheless, generalization of the present results to patient groups is not self-evident, as neurological patients often display patterning abnormalities (e.g. [37]) that may necessitate the employment of different control strategies in response to the Lokomat training parameters. Although the present results provide relevant insights into the therapeutic potential of the device, further research needs to confirm that the observed effects are also present in patient groups that are indicated for Lokomat training.

The Lokomat environment may have induced idiosyncratic activation patterns and large inter-subject substantial variability in the presently used sample of naive Lokomat walkers. Therefore, the here reported results represent the most commonly observed activation patterns, although individual walkers may show different responses to the training parameters.

Finally, although the chosen speeds cover the range of the device (i.e. 0.14 – 0.89 m/s), walking at 0.22 m/s may not be used commonly in clinical practice. Also, such slow speeds may alter the passive dynamics of the leg and induce abnormal activation patterns, although previous research has shown that such effects primarily affect the amplitude rather than the patterning of activity [23, 24, 35]. We therefore believe that the observed aberrations at slow speeds are caused primarily by altered leg dynamics due to the (not-fully uncompensated) inertia of the exoskeleton.
CONCLUSIONS

Assessing the effects of guidance on muscular coordination is important to better understand how the Lokomat training parameters affect the production of gait, and how these effects can be exploited in the design of training protocols. The results show that guidance generally reduces muscular activity, but that the nature of these effects depends on settings for speed and BWS, and that walkers still display structurally phased activity, even when walking with full guidance. The findings also suggest that the ability of the Lokomat to elicit normal muscle activity patterns, may depend on specific settings of its training parameters. The outcomes of this study warrant further research on the effects of Lokomat parameters on muscle activity in patient groups targeted for Lokomat training.

COMPETING INTEREST

The authors declare that they have no competing interests.

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