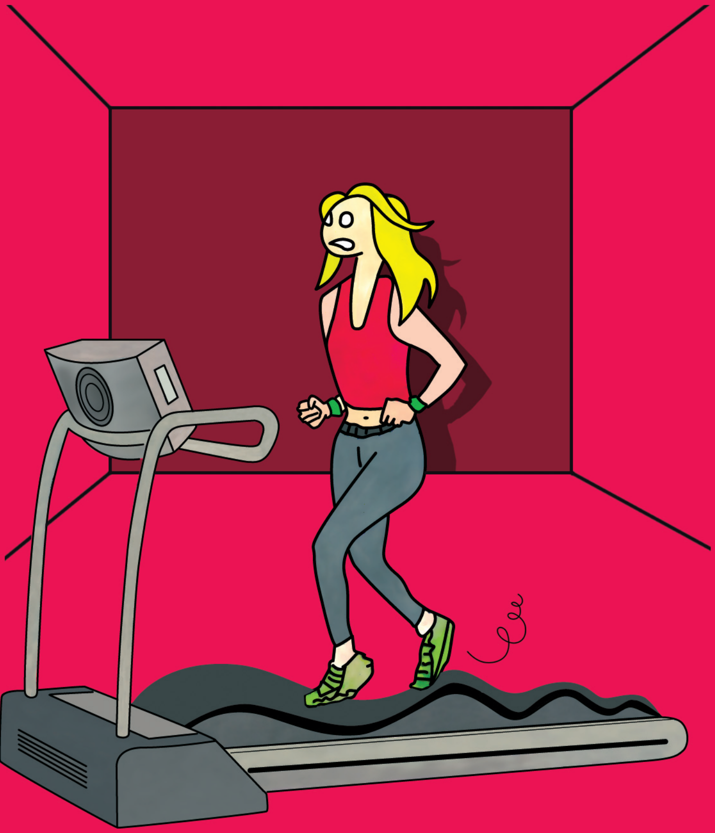
ADAPTIVE CONTROL OF DYNAMIC BALANCE IN HUMAN WALKING



TOM J.W. BUURKE

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TOM J.W. BUURKE

COLOPHON

The experiments described in chapter 2, 3, 4 and 5 were conducted at the Center for Human Movement Sciences, University Medical Center Groningen, Groningen, the Netherlands. The experiments described in chapter 6 were conducted at the Locomotor Control Lab, Division of Biokinesiology and Physical Therapy, University of Southern California, Los Angeles, CA, USA.

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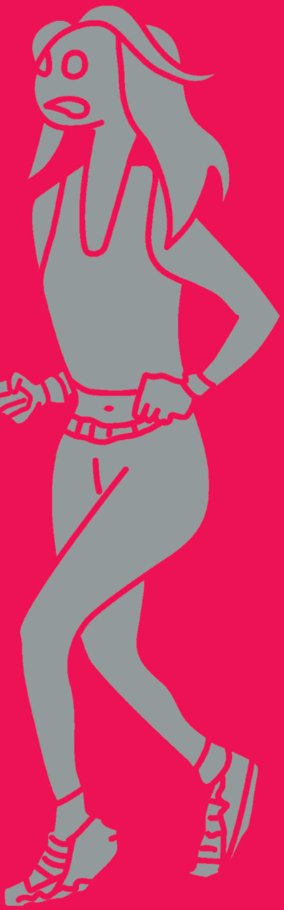

1

GENERAL INTRODUCTION

BACKGROUND

Human bipedal walking has intrigued scientists and philosophers for ages. Since Aristotle's first recorded comments (384 – 322 BCE) on vertical oscillations in human walking [1], we have come a long way until Perry's Gait Analysis [2], Winter's Biomechanics and Motor Control of Human Movement [3] and 21st century clinical and experimental gait research and analyses [4]. Humans are one of few mammals to exercise bipedal gait, and research has shown that although human bipedal gait is more energy efficient than quadrupedal gait, it is inherently unstable [5]. To stay upright while walking, humans need to be able to flexibly respond and adapt to (unexpected) changes in the environment, for instance when walking over uneven or slippery terrain, or on a rocking boat. In other words, humans need to be able to adaptively control dynamic balance to remain stable [6]. The role of adaptive control of dynamic balance in human walking becomes clear following natural ageing, disease or impairment, when people have trouble to control their balance and as a result become less mobile or more prone to falling [7-9]. However, to improve adaptive control of dynamic balance in prevention of mobility decline and gait rehabilitation, we first need to understand it. Therefore, the aim of this thesis is to increase our understanding of adaptive control of dynamic balance in human walking.

NEUROMUSCULAR CONTROL OF HUMAN WALKING

Human bipedal gait is produced by activation of muscles through the central nervous system, i.e. through neuromuscular control [10]. On many levels of human movement control, e.g. end-point control, joint angle configurations, or neuromuscular control, more degrees of freedom are available than necessary to perform a certain movement, as described in Bernstein's degrees of freedom problem. Specifically, in neuromuscular control of human walking, an almost infinite number of combinations of muscles is available to produce the same gait pattern [11]. This control problem of redundancy in available muscles for human movement can be solved by the idea that a small set of control signals, i.e. muscle synergies, can control the muscles involved in a specific task, forming functional muscle groups [12-14]. To reduce ambiguity due to different definitions of muscle synergies that are used in the literature, in this thesis we follow a definition given by Turvey (2007) [15]: '*It has been hypothesized that particular patterns of muscular activities could form a base set analogous to the concept of basis in the theory of vector spaces: a minimal number of (linearly independent) elements that under specific operations generate all members of a given set, in this case, the set of all movements*' … '*the synergies-as-basis hypothesis implies that all movement patterns share the same synergies*'. If such a synergistic structure controls all movements in human walking, by definition the same structure should be able to adaptively respond to perturbations of dynamic balance during walking. In other words, a synergistic structure for neuromuscular control of human walking needs to be flexible or adaptive, otherwise we would need a new set of synergies for each gait task, which would result in a virtually infinite instead of limited library of muscle synergies.

One of the most fundamental and frequently performed adaptations in human walking is the change of walking speed. For example, when people walk over a crowded marketplace, they continuously adapt their walking speed to avoid other pedestrians or obstacles, or to slow down before making a turn to the next stall. If neuromuscular control of human walking is regulated by a single synergistic organization, it should be able to control such speed modulations during human walking, without altering the synergistic organization itself. To test this concept and increase our understanding of adaptive neuromuscular control in human walking, we assess whether a synergistic structure can control the speed dependent modulation of muscle activity in healthy human walking in chapter 2 of this thesis.

DYNAMIC BALANCE CONTROL

Dynamic balance control is necessary to remain stable during bipedal locomotion [16]. Consider how hard it would be for one to balance a two-legged wooden stool with a 65 kg weight on top. As that task would be nearly impossible, it is amazing how healthy human adults manage to remain stable during stance [17], let alone while making over a million steps every year [18]. However, when dynamic balance control fails for even a single step in that million, the consequences can be severe. Fall related incidents in healthy adults lead to injuries, reduced quality of life, increased risk of social isolation and an estimated annual cost of 873 million euros in the Netherlands alone [19,20]. Therefore, maintaining or improving dynamic balance control is an important part of both healthy ageing and rehabilitation.

Although falling can be a serious problem in human walking, it is also a key component of normal human walking [17,21]. Dynamic balance control in human bipedal walking can be modelled after the falling movement of an inverted pendulum with a point mass on top [17,21]. In this model, the inverted pendulum represents the weightless stance leg and the point mass on top represents the body center of mass. The falling motion of the inverted pendulum during the stance phase of walking is terminated by the next step, after which the inverted pendulum motion repeats itself in the other, contralateral, stance leg. The inverted pendulum model was extended by the work of Pai & Patton (1997) [22] and Hof et al. (2005) [23], who added a center of mass velocity component to the model, improving it for dynamic situations such as walking. This led to the extrapolated center of mass concept [24], which states that stable gait can be achieved through a simple rule. As long as a step is made a minimum lateral distance from the extrapolated center of mass position, termed the mediolateral margin of stability, a person will stay upright. The margin of stability and extrapolated center of mass concept brought understanding of stepping and balance control in human gait, and inspired many studies on reactive and adaptive stepping in human walking [25-28]. In chapters 3, 4 and 6 of this thesis the margin of stability will be assessed to quantify dynamic balance control in the context of locomotor adaptation.

LOCOMOTOR ADAPTATION AND LEARNING ON A SPLIT-BELT TREADMILL

Motor adaptation is suggested to underlie motor learning, and can be seen as the basis of locomotor rehabilitation and training. Motor adaptation occurs when the intended movement and performed movement do not match, but learning occurs only when an adaptation becomes more permanent [29]. An indicator of actual motor adaptation in response to perturbations of movement in experimental settings is the emergence of after-effects once the perturbation is removed, i.e. after adaptation. Typically, these after-effects occur in the opposite direction of the adapted movement and the after-effects wash out after multiple movement repetitions in absence of the adaptation stimulus [30,31]. However, once a new movement is fully learned, after-effects no longer occur, as one is able to switch effortlessly between the different movements, without any after-effects of the adapted movement [32].

Locomotor adaptation and learning can be studied in a controlled experimental setting with split-belt treadmill walking. A split-belt treadmill is equipped with two parallel belts, the speed of which can be controlled independently. By speeding up one of the belts, it is possible to make people walk faster with one leg than the other, provoking an asymmetric gait pattern [30]. Previously, it was found that an asymmetric overground gait pattern is related to lower scores on clinical balance tests [33]. Furthermore, split-belt walking leads to a reduced frontal inclination angle [34], increased mediolateral ground reaction forces, and increased fast-leg hip moment impulse [35]. These findings indicate that, while split-belt walking is a perturbation of gait in the sagittal plane, it also challenges dynamic balance control in the frontal plane. This makes split-belt treadmill walking a suitable task to study the adaptive control of dynamic balance in reaction to a sustained perturbation of human walking.

In this thesis we utilize a common split-belt adaptation protocol to study locomotor adaptation and learning in human walking. This protocol starts with a tied-belt baseline phase, in which both belts move at the same speed, to assess baseline-walking performance. After the baseline phase, one of the belts is set at a higher speed than the other belt, called the split-belt adaptation phase. In the beginning of this phase, i.e. during early adaptation, people typically show large inter-limb asymmetries in step lengths and double support times [30]. During adaptation, these spatiotemporal asymmetries progress towards a more symmetric level over time, until late adaptation. After ten to fifteen minutes, the belts are set at tied speeds again, to wash out the adapted movement. At the start of the washout phase, after-effects are seen in the opposite direction of the spatiotemporal asymmetries in early adaptation. After-effects generally wash out within two minutes, and indicate that the spatiotemporal control of stepping was altered during split-belt adaptation [36,37]. In chapters 3, 4 and 5 a split-belt treadmill is used for continuous perturbations of dynamic balance, to study adaptive control of dynamic balance and assess the effects of external support on locomotor learning in healthy young adults.

A split-belt treadmill can be used for adaptation studies, but also to apply short and discrete perturbations during human walking. By briefly accelerating or decelerating one of the belts, a person walking on the treadmill will slip or trip [38], resulting in a reactive stepping response. The ability to precisely control the acceleration and velocity of both treadmill belts during such perturbations makes split-belt treadmills very useful to study reactive balance control in a controlled setting in both able-bodied and impaired populations. In chapter 6 a split-belt treadmill is used to selectively perturb the paretic or non-paretic leg at heel-strike during treadmill walking in people post-stroke.

ADAPTIVE CONTROL OF DYNAMIC BALANCE IN PEOPLE POST-STROKE

Approximately 43,000 people in the Netherlands suffer from a stroke annually [39]. Stroke survivors who remain ambulant often have trouble to maintain dynamic stability [40], which can lead to falls or fear of falling [8,9]. The abnormal coordination [41-45], reduced paretic leg force production [46,47], and delays in reflexes [48], that are typically seen in people post-stroke, may lead to the impaired paretic stepping responses [49], i.e. the diminished reactive and proactive balance control, that underlies these falls. During normal walking, people post-stroke unload their paretic leg, while they stabilize and propel themselves with the non-paretic leg [46,47,50], leading to asymmetric anteroposterior and mediolateral margins of stability [26]. Research has shown that people post-stroke increase their mediolateral margin of stability and decrease their anteroposterior margin of stability in response to lateral perturbations of gait, such as a push at the hip [25]. However, it is unclear how exactly reactive stepping is controlled in response to perturbations in the sagittal plane during walking post-stroke, for instance following slips or trips.

Hypothetically, an increase in the anteroposterior margin of stability in reactive stepping may come with a decrease in mediolateral margin of stability [51,52], i.e. a covariation may exist between the anteroposterior and mediolateral margins of stability. Arguably, if such a relation exists and given that people post-stroke walk with asymmetric margins of stability [26], the step length asymmetry seen in people post-stroke [46,53] could be a mechanism to improve dynamic balance on the paretic side. Therefore, to increase our understanding of adaptive control of dynamic balance in people post-stroke, we will test this hypothesis and study covariation of anteroposterior and mediolateral margins of stability in reactive balance control during walking post-stroke in chapter 6 of this thesis.

AIM AND OUTLINE OF THE THESIS

The aim of this thesis is to increase our understanding of adaptive control of dynamic balance in human walking. In all studies treadmills are used to assess human walking, in which changes in treadmill belt speed are applied to perturb participants. First, to study adaptive neuromuscular control of human walking, a synergistic structure to control the speed dependent modulation of muscle activity in human walking is assessed in **chapter 2**. Then, in

chapter 3, the adaptation of mediolateral dynamic balance control to walking with asymmetric belt speeds on a split-belt treadmill, i.e. a sustained perturbation of gait, is studied. Based on the findings in chapter 3, bilateral temporal control of stepping is proposed as a mechanism that controls mediolateral dynamic balance during symmetric, asymmetric and adaptive human walking in **chapter 4**. In chapters 3 and 4 the adaptation of dynamic balance in split-belt walking is studied, but the question remains what happens with adaptation to split-belt walking, once control of dynamic balance is no longer a problem. As adaptive control of dynamic balance was prominent in split-belt adaptation (chapters 3 and 4), we hypothesize that once the balance control problem is eliminated through external support, adaptation effects will be reduced. Therefore, in **chapter 5** the effect of external balance support, by holding on to handrails, on locomotor adaptation and learning in a split-belt walking task is assessed. We expect that chapter 5 will give more insight in the role of dynamic balance control in locomotor adaptation and learning. In **chapter 6**, the knowledge on margins of stability gained in chapters 3 and 4 is exploited to increase our understanding of impaired reactive balance control in people post-stroke. In this chapter, the covariation of anteroposterior and mediolateral stepping strategies in response to short perturbations of gait in people post-stroke is studied. Finally, a general discussion and conclusion of the findings and implications of this thesis will be provided in **chapter 7**.

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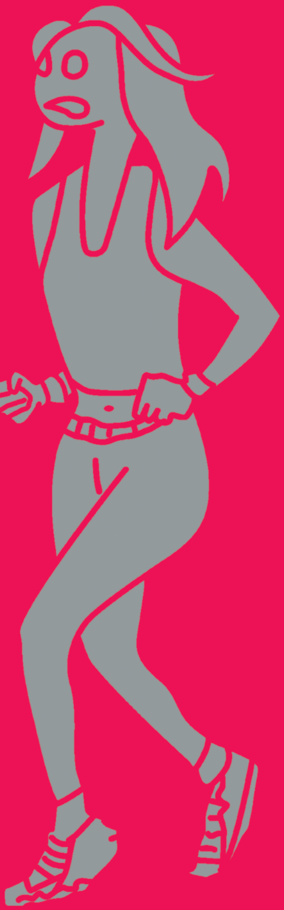

2

SYNERGISTIC STRUCTURE IN THE SPEED DEPENDENT MODULATION OF MUSCLE ACTIVITY IN HUMAN WALKING

Tom J.W. Buurke, Claudine J.C. Lamoth, Lucas H.V. van der Woude, Rob den Otter

PLoS ONE. (2016) 11(4): e0152784

ABSTRACT

Recently, a modular organisation has been proposed to simplify control of the large number of muscles involved in human walking. Although previous research indicates that a single set of modular activation patterns can account for muscle activity at different speeds, these studies only provide indirect evidence for the idea that speed regulation in human walking is under modular control. Here, a more direct approach was taken to assess the synergistic structure that underlies speed regulation, by isolating speed effects through the construction of gain functions that represent the linear relation between speed and amplitude for each point in the time-normalized gait cycle. The activity of 13 muscles in 13 participants was measured at 4 speeds (0.69, 1.00, 1.31, and 1.61 m s^{-1}) during treadmill walking. Gain functions were constructed for each of the muscles, and gain functions and the activity patterns at 1.00 m s^{-1} were both subjected to dimensionality reduction, to obtain modular gain functions and modular basis functions, respectively. The results showed that 4 components captured most of the variance in the gain functions (74.0 % ± 1.3 %), suggesting that the neuromuscular regulation of speed is under modular control. Correlations between modular gain functions and modular basis functions (range 0.58 - 0.89) and the associated synergistic muscle weightings (range 0.6 - 0.95) were generally high, suggesting substantial overlap in the synergistic control of the basic phasing of muscle activity and its modulation through speed. Finally, the combined set of modular functions and associated weightings were well capable of predicting muscle activity patterns obtained at a speed (1.31 m s^{-1}) that was not involved in the initial dimensionality reduction, confirming the robustness of the presently used approach. Taken together, these findings provide direct evidence of synergistic structure in speed regulation, and may inspire further work on flexibility in the modular control of gait.

INTRODUCTION

For the production of bipedal human gait, more muscles are available than are necessary to produce stepping, and this ‘degrees-of-freedom’ or ‘redundancy’ problem has intrigued researchers since it was first introduced by Nikolai Bernstein [1]. At the same time, the redundancy implied in the controlled system offers abundant possibilities to modify the basic locomotor pattern allowing the performance of functionally coherent movements and the accommodation to continuously changing task and environmental demands. As such, ‘complexity’ of control and behavioral ‘flexibility’ can be interpreted as inextricably connected and should eventually be explained within one unifying framework [2]. In recent years, it has been suggested that the Central Nervous System (CNS) may overcome redundancy in the locomotor system by using a single, simplified form of neuromuscular control to be employed in a broad range of task contexts [3-5]. In this approach, motor outputs are generated through activation of groups of muscles that are driven by the combined activity of a small set of control signals, so called ‘modules’. Because these signals do not activate muscles individually, but instead simultaneously drive muscle groups that are functionally related, called ‘synergies’, a dramatic reduction in the complexity of control can be achieved [6,7]. However, how this type of low-dimensional neuromuscular control can be flexibly recruited to give rise to the rich and adaptive repertoire of human stepping behaviors is still not well understood.

Arguably one the most fundamental adaptive mechanisms in human gait is the ability to modify the speed of progression, e.g. to accommodate time pressure or to enhance safety. To propel the body forward, gravitational potential energy of the center of mass (CoM) is partly transformed into kinetic propulsive energy with a speed-dependent efficiency [8,9]. The CoM momentum is controlled by activity from the calf muscles, determining the changes in step length and / or cadence that are required to alter the speed of progression [10]. At the neuromuscular level these changes are controlled by phase-specific modulations in EMG amplitude that are superimposed upon a basic activation pattern [11-17]. These adaptations in neuromuscular activity serve to control the propulsive force, the altered accelerative properties of the swinging leg, and the speed-related changes in leg loading and support demands.

If human walking is governed by a single modular architecture, the basic phasing of muscle activity and its adaptive control of speed need to be realized within a single modular control scheme. Indeed, there is evidence from a number of studies showing that the synergistic structure, and the modular activation signals it drives, are essentially preserved over gait speeds [18-21]. In these studies, the invariance of modular control is tested by recording electromyographic signals (EMG) from a set of muscles over a range of speeds, and applying pattern recognition methods to reduce the dimensionality (e.g. non-negative matrix factorization, PCA, or factor analysis), for each speed condition separately [18-21]. These procedures result in a sparse set of modular activation functions that represent the temporal properties of modular control signals, and a set of associated synergistic weightings that reflects how these control signals are distributed over individual muscles. To evaluate invariance of modular control over speeds, modular activation patterns and synergistic weightings are then compared between speed conditions. The proposed modular mechanisms responsible for the neuromuscular regulation of speed involve adjustments made to synergistic weightings [18-20], rescaling of modular activation signals [21], and shifts in a speed-dependent phase factor to account for timing differences in modular activations [19,20]. Results from these studies convincingly show that variance in the activity of large sets of muscles can be accurately captured using a small set of 4 or 5 modular activations, and that the timing properties of these activations show clear resemblances between speeds. Although these findings indicate that a single modular structure may be involved in the control of walking over a range of speeds, they may not provide direct evidence for the idea that the dynamic adjustments made to muscle activity for speed regulation are under modular control.

As EMG patterns at a given speed contain both (i) amplitude variation related to speed-independent (i.e. basis) activity of the muscle and (ii) amplitude variation that is uniquely related to the speed at which the EMG is recorded [13], it remains unclear to what extent the previously reported dimensionality reductions are the result of covariance in the speed-independent basis activity of muscles, or of speed-dependent modulations in the basis-activity (see [22] for a similar argument). As a result, the existing literature [5,18,20] provides indirect evidence for the idea that the phase specific modulation of muscle output amplitude that is involved in speed regulation, is under modular control. Arguably, more direct evidence of the modular properties of speed regulation would involve a dimensionality reduction that specifically targets these speed effects, independent of the basis activity of muscles.

Because the amplitude of muscle activity scales linearly with speed, the phase-dependent modulation of the amplitude can be described using gain functions [12,13,23]. These gain functions represent, for each moment in the time-normalized gait cycle, the linear relation between muscle activity amplitude and speed. In a study by Hof and colleagues [13], gain functions were used to successfully model recorded EMG signals over a range of speeds (0.75 to 1.75 m s^{-1}). An important finding from this study was that there were clear similarities in the basic activation of muscles as well as in their gain functions, so that an initial set of 13 basic patterns and 13 gain functions could eventually be reduced to a compact set of 6 basic muscle activation patterns and 10 related gain functions. These findings are important as they suggest that both the basic phasing of activity, as well as its modulation by speed are subject to modular control. In the present study, we elaborate on these ideas, and further explore the modular aspects of speed related changes in muscle activity during human walking. More specifically, the aims of this study were threefold. First, we assessed if speed related neuromuscular gain is subject to modular control. To this end, gain functions were determined for a group of muscles over a range of speeds. Subsequently, these gain functions were subjected to dimensionality reduction to determine if speed effects can be described using a parsimonious set of modular gain functions, indicating synergistic structure in the neuromuscular regulation of speed. Second, we determined whether the basis activation of muscles and the speed-related gains are driven by a single modular control structure. For this purpose, dimensionality reduction was performed on the muscle activations at a single walking speed (1.00 m s^{-1}), to obtain a set of modular basis functions and their associated synergistic weightings. Next, the modular basis functions and modular gain functions, as well as their associated synergistic weightings, were compared to assess their similarities. Finally, to test the robustness of the present approach, we established whether the combined set of modular basis functions and modular gain functions, and their associated synergistic weightings, can be used to predict muscle activation patterns at a speed that was not involved in the dimensionality reductions.

An important requirement for the prediction of speed-related variations in muscle activity from a set of modular activations and synergies, is that speed needs to be used as an input to the proposed modular architecture, and that it therefore needs to be made explicit which aspect(-s) of the modular architecture (e.g. the scaling of synergistic weight, phasing of modular activations, shape characteristics of modular activations) are affected by speed. Recently, Gonzalez-Vargas and co-workers [18] have shown that it is possible to produce accurate predictions for a range of speed and elevation conditions, by scaling the synergistic weightings that drive an invariant set of 4 modular activations. Such predictions can be very useful for testing ideas on flexibility within a modular framework, and for providing evidence for the robustness of the proposed approach.

MATERIALS AND METHODS

Participants

Thirteen volunteers (6 males, 7 females, 21.8 ± 2.2 years old, body height: 1.79 ± 0.07 m, body weight: 71.3 ± 9.3 kg) without any known physical or neurological impairments participated in this study.

Ethics statement

The procedures of this study were approved by the Ethics Committee of the Center for Human Movement Sciences, University Medical Center Groningen, the Netherlands, and were in accordance with the principles outlined in the Declaration of Helsinki [24]. All participants gave their written informed consent.

Experimental protocol

Participants walked on a treadmill (Enraf-Nonius, Rotterdam, the Netherlands) with a walking surface of 1.5 m long by 0.5 m wide at four different gait speeds (1.61, 1.31, 1.00, and 0.69 m s^{-1}). Prior to testing, participants walked on the treadmill for five minutes to adjust to the treadmill. At the start of each trial, participants walked on the treadmill for thirty seconds to adjust to the new speed before testing commenced. Data for each speed condition were collected for one minute, and speeds were presented in the same quasi-randomized order of gait speed conditions (1.31, 1.61, 0.69, 1.00 m s^{-1}) for all participants. No instructions were given with regard to stride length or cadence.

Data recording

EMG data was recorded using a Porti EMG unit and Portilab2 software (TMSI, Enschede, The Netherlands) at a sample frequency of 2048 Hz. Electrodes were placed unilaterally on eleven lower extremity muscles (Soleus (SO), Gastrocnemius Lateralis (GL), Tibialis Anterior (TA), Peroneus Longus (PL), Vastus Lateralis (VL), Rectus Femoris (RF), Biceps Femoris (BF), Semitendinosus (ST), Adductor Magnus (AM), Tensor Fascia Latae (TFL), Gluteus Maximus (GM)), and two back muscles (Erector Spinae (ES), and Latissimus Dorsi (LD)). Electrodes were placed according to SENIAM conventions [25], and according to Perotto [26] if a muscle was not included in SENIAM (AM, LD). Body hair was removed, and the skin was abraded and cleaned with alcohol to improve conduction. Custom-made insoles with pressure sensors (three under the forefoot, one under the heel) were used to determine initial contact and swing onset. The pressure sensors were connected to the EMG unit's auxiliary ports and the EMG and sensor data were synchronized and stored on an external hard drive for further (offline) analysis.

Data processing

EMG and pressure sensor data was processed using custom-made software routines in MATLAB (version r2015a; The MathWorks Inc., Natick, MA). EMG data was high pass filtered using a 10Hz second order Butterworth filter, then rectified, and finally low pass filtered using a 10Hz second order Butterworth filter. Next, EMG data was normalized in the time domain for stance phase (65 data points) and swing phase (35 data points) separately, to a total of 100 data points per stride. To be able to estimate the linear relationship between amplitude and speed for each moment in the normalized gait cycle, accurate temporal alignment of the EMG patterns is paramount. If 'regular' stride normalization would have been used (i.e. from initial contact to initial contact) this may lead to misalignment of functional gait phases (e.g. t = 65 % may correspond with the early swing phase at higher speeds and with late stance at slow speeds). An important consequence of this choice is that the phase shifts in modular activation patterns that are typically reported for different speeds [19,20] will be strongly attenuated or neutralized. Finally, the time normalized EMG signals were normalized for amplitude by dividing the EMG amplitude by the maximum amplitude over all speed conditions, for each muscle. Average EMG profiles were then calculated for each muscle and condition, resulting in a 13 (muscles) by 4 (speeds) by 100 (datapoints) matrix, for each participant. This matrix was then subjected to further analysis. On average 34 ± 2.5 strides were available for analysis per subject and speed condition.

Calculation of gain functions and gain modules

Our first aim was to assess if speed related neuromuscular gain is subject to modular control. In general, muscle output amplitude scales approximately linearly with speed [13], although for specific muscles this may not be the case. For example, in Rectus Femoris activity around the stance-swing transition often increases suddenly at a critical speed [27] and Semitendinosus selectively shows marked activity during this period only at very low speeds [12]. Although such non-linearities cannot be captured in the here calculated gain functions, linear approximations of the speed-amplitude relationship are known to produce accurate reconstructions of EMG patterns over a range of speeds [13,23]. To this end, for each of the m (1...13) muscles, a gain function G was calculated that represents the linear dependency of the normalized EMG amplitude on speed, for each point t in the time normalized gait cycle [12,13]. Construction of the gain functions is illustrated in Figure 1. First, the first 30 strides for each speed condition were selected for further analysis (Figure 1A). Note that for an un-biased estimate of the linear relation between speed and amplitude, an equal number of strides has to be available for each speed condition. Gain functions were calculated by performing linear approximation of EMG amplitude on speed, for each time instant t (1...100) in the time normalized gait cycle (see Figure 1B). The gain was defined as the slope of the resulting linear approximation equations, and represents the increase in EMG amplitude (µv) per unit increase in speed (m s^{-1}). Performing this operation for each t resulted in a gain function G_m for each muscle m (Figure 1C).

To assess whether the gain functions provided an accurate representation of the speed effects on EMG profiles, the averaged EMG profile of muscle m (1...13) was predicted from the gain function G_m and the averaged EMG profile of m at 1.00 m s^{-1}, for each speed v (0.69, 1.31, and 1.61 m s^{-1}, see Figure 1D), and for each participant, as follows:

$$\widetilde{EMG}_{v,m} = EMG_{1.00,m} + (v * G_m) \tag{1}$$

To assess the modular properties of the gain functions, modular gain functions were calculated for each participant. To this end, the gain functions G_m were subjected to principal component analysis (PCA) followed by varimax rotation [19,28]. This method was preferred to other methods often used, such as non-negative matrix factorization, because gain functions may contain negative values if EMG amplitude decreases with increasing speed. However, both methods generally produce similar results [5]. One of the aims of this study was to compare modular gain functions and the associated synergistic muscle weightings with modular basis functions and weightings obtained from the EMG profiles recorded at 1.00 m s^{-1} (see next section). To do so, the number of components that was extracted for the modular gain functions and modular basis functions had to be equal and needed to be defined a priori. In accordance with previous studies [18,21], the number of components that was extracted was set to 4. On average, the modular basis functions accounted for 80.1 % of the variance in the original data

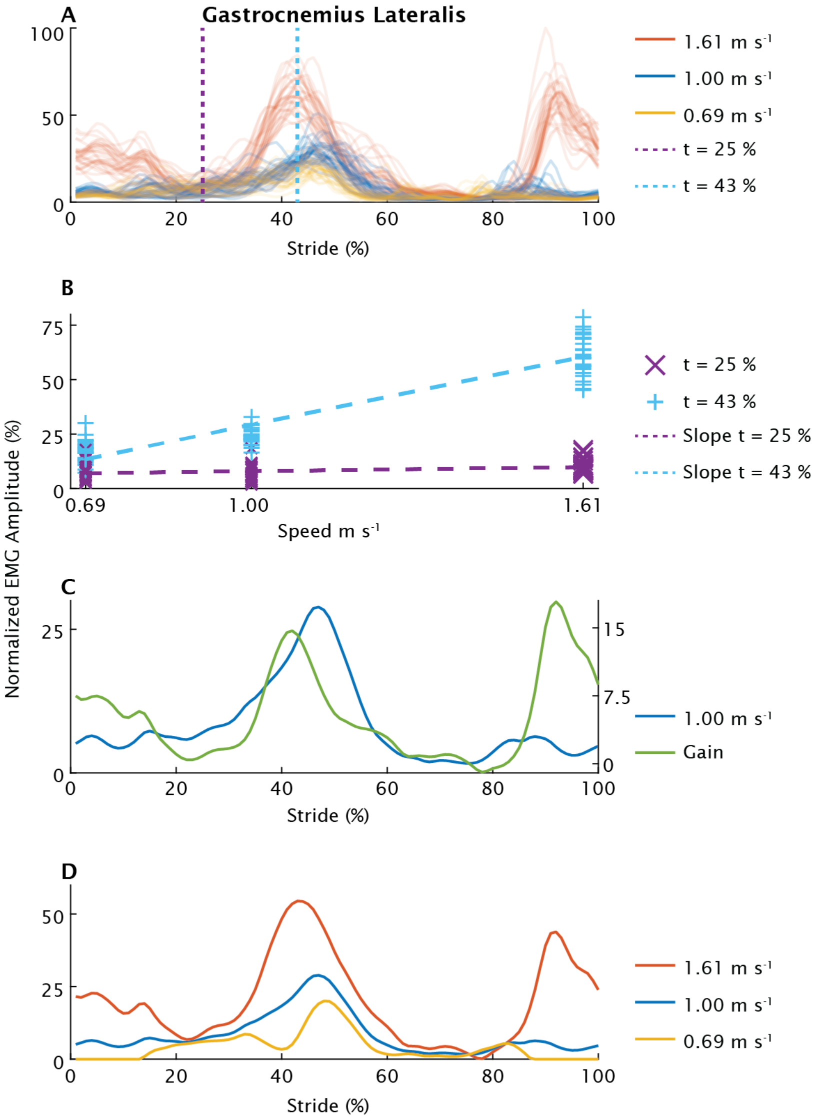

Figure 1 – Calculation of gain functions. **A)** Time and amplitude normalized EMG signals for individual strides (N = 30 per speed) of the Gastrocnemius Lateralis (GL), for a single participant at 0.69, 1.00, and 1.61 m s^{-1}. The dotted lines at t = 25 % and t = 43 % mark the points in the time normalized stride cycle which are illustrated more elaborately in Figure 1B. **B)** The linear relation between gait speed and EMG amplitude illustrated for t = 25 % and t = 43 % in the time normalized stride. For both time instants, a line is fitted to model the relation between speed and amplitude, using linear approximation. The slopes of the resulting linear approximation represents a gain factor that reflects the increase in EMG amplitude per unit increase in gait speed (m s^{-1}). The figure illustrates that for t = 43 %, the amplitude of GL activity increases with speed,

whereas for t = 25 % EMG amplitude is unaffected by speed. By calculating the gain factor for each time instant *t*(1...100) in the time-normalized gait cycle, a gain function can be constructed for each muscle. **C)** The gain function for GL and the averaged GL activity for this participant at 1.00 m s^{-1}. This illustrates that speed effects were mainly present within a specific phase (approx. between 35 % and 50 %) of the main burst of GL activity. **D)** Reconstructed EMG profiles at 0.69, 1.00, and 1.61 m s^{-1}. As the gain function represents the linear increase in EMG amplitude per unit speed, the EMG profile for each muscle can be reconstructed for any given speed, using (i) the gain function for that muscle and (ii) the averaged EMG profile for that muscle at a given speed. Figure 1D shows the reconstructed GL profiles at 0.69 and 1.61 m s^{-1} using the GL gain function and the averaged activity at 1.00 m s^{-1}.

set. In previous studies a variance accounted for > 80 % was regarded sufficient for this analysis [29,30]. This was confirmed through further analysis, showing that an additional fifth modular basis function accounted for 5.8 % of variance. Since this is less than the variance accounted for by a single muscle (7.7 %), a fifth modular basis function was left out in this model. The percentage in the gain functions of individual muscles *m* that was explained by the modular gain functions was assessed to evaluate the extent to which speed related neuromuscular gain is subject to modular control.

Comparison of modular gain functions and modular basis functions

The second aim of this study was to determine whether the basis activation of muscles and the speed-related gain are driven by a single synergistic control structure. To this end, modular gain functions and their associated muscle weightings were compared with modular basis functions and synergistic muscle weightings obtained after dimensionality reductions of the averaged activity patterns at 1.00 m s^{-1}. PCA with varimax rotation was applied to the set of 13 averaged muscle activation patterns at this speed, for each participant, to obtain modular basis activations and their associated synergistic muscle weightings. After extraction of the modular gain functions and modular basis functions for individual participants, modular functions were matched and grouped so as to allow meaningful averaging of functions and comparisons between both sets of averaged functions and their associated synergies. The grouping procedure is illustrated in Figure 2.

The varimax rotated PCA typically extracts modular functions in the order of the amount of variance they explain (i.e. function 1 explains the most variance, function 4 the least amount of variance in the original data set), but modular functions with similar timing characteristics are not necessarily extracted in the same order for different participants, as is shown in Figure 2A. Therefore, modular functions were grouped over participants according to their timing similarities (Figure 2B), so as to obtain homogeneous groups of modular functions and allow meaningful calculation of group averaged modular functions (see [31,32] for a similar approach). Here, we used K-means clustering [33] as a non-supervised method to group modular functions between participants. The number of clusters was set a priori to 4, to correspond with the number of components extracted by the PCA, so that the clustering procedure partitioned the (4 modules x 13 participants) 52 modular functions into 4 clusters. In case two modular functions of a single participant were assigned to the same cluster, the modular function with the smallest distance to the cluster centroid was assigned to that cluster, whereas the other modular function was rejected (Figure 2C). As a consequence, the number of individual modular functions assigned to a cluster could vary per cluster. This grouping procedure was applied separately for the modular gain functions and the modular basis functions.

To determine if the basis activation and speed-related gain share a similar modular structure, correlations were calculated between the cluster means of the modular basis functions and the cluster means of the modular gain functions, to obtain pairs of modular basis and gain functions with similar temporal properties. The magnitude of these correlations was interpreted as an indication of the similarity between modular gain functions and modular basis functions. To assess the similarity between the associated synergistic muscle weightings of both sets of functions, the averaged muscle weightings were calculated for each of the clustered sets of modules, for both gain modules and basis modules. Correlations between both sets of synergistic muscle weightings were used to assess their similarity.

Reconstruction and prediction of EMG using modular gain and basis functions and associated weightings

We tested the robustness of the presently used approach by reconstructing the averaged EMG profiles of individual participants using the combined set of 4 basis and gain modular activations and the associated weightings. The averaged EMG profiles at v = 0.69, 1.00, and 1.61 m s^{-1} were reconstructed as follows:

$$\widetilde{EMG}_{v,m} = H_{basis}W_{basis} + v\left(H_{gain}W_{gain}\right) \qquad (2)$$

H_{basis} and H_{gain} represent the 4 by 100 matrix of modular basis and gain functions respectively, W_{basis} and W_{gain} represent the 4 by 13 matrix of associated synergistic muscle weightings, and v represents speed (m s^{-1}).

This method was also used to achieve the third aim of this study. To determine if the combined set of modular basis and gain functions, and their associated weightings, could be used to predict muscle activation patterns at a speed that was not involved in the dimensionality reductions, EMG at v = 1.31 m s^{-1} was predicted. The amount of variance in the averaged EMG profiles that was accounted for by the reconstructions and prediction was used to assess the reconstruction and prediction quality.

To assess how well the modular gain functions can predict novel data of different subjects, we applied a bootstrapping procedure. For each of the i = 100 runs of the bootstrapping procedure, we calculated how well N = 7 randomly selected subjects were capable of predicting speed-related gain of each of the remaining N = 6 subjects. In each run, the modular gain functions of each of the 7 randomly selected subjects were used to obtain a set of 4 averaged modular gain functions. These functions were then combined with the modular basis functions of each of the remaining 6 subjects, to predict the average EMG profiles of each of these 6 subjects individually, for each muscle and speed (Equation 2). Finally, the predicted profiles were averaged over the group of 6 subjects. The average variance accounted for (with 95 % confidence interval) by the predictions was calculated for each speed condition, and averaged over all 100 bootstrap runs.

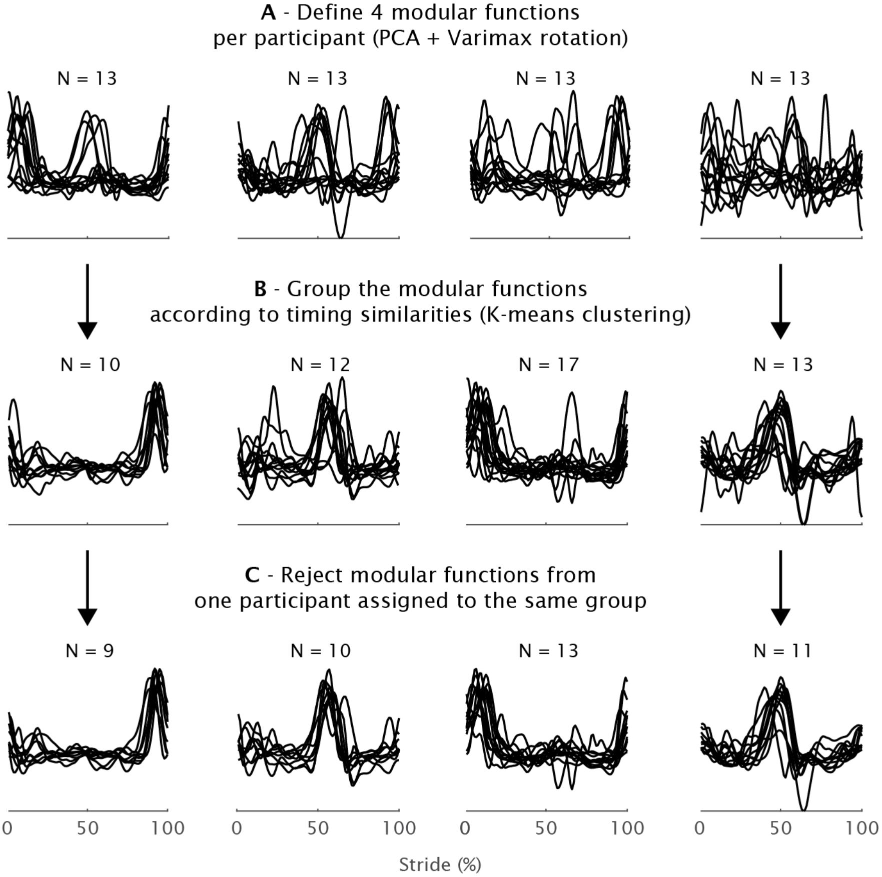

Figure 2 – Grouping and selection of modular functions. Grouping and selection of modular functions was done in 3 steps. **A)** In step 1, 4 modular functions are constructed using PCA with Varimax rotation, for all 13 participants individually. **B)** In step 2 the modular functions are clustered according to their timing similarities, using K-means clustering. **C)** If the clustered functions contained more than one function from a single participant, in step 3, only the modular function with the smallest distance to the cluster centroid was

retained, the other function(-s) within the cluster was / were rejected. Rejected gain functions were not re-assigned. Therefore, the number of functions within each cluster was typically smaller than the number of participants (i.e. N = 13). The same workflow illustrated here was used for the modular basis and modular gain functions.

RESULTS

The group ensemble averaged EMG patterns for all 4 gait speeds are shown in Figure 3. As becomes evident from this figure, for most of the 13 muscles the amplitude of activity generally increased with speed.

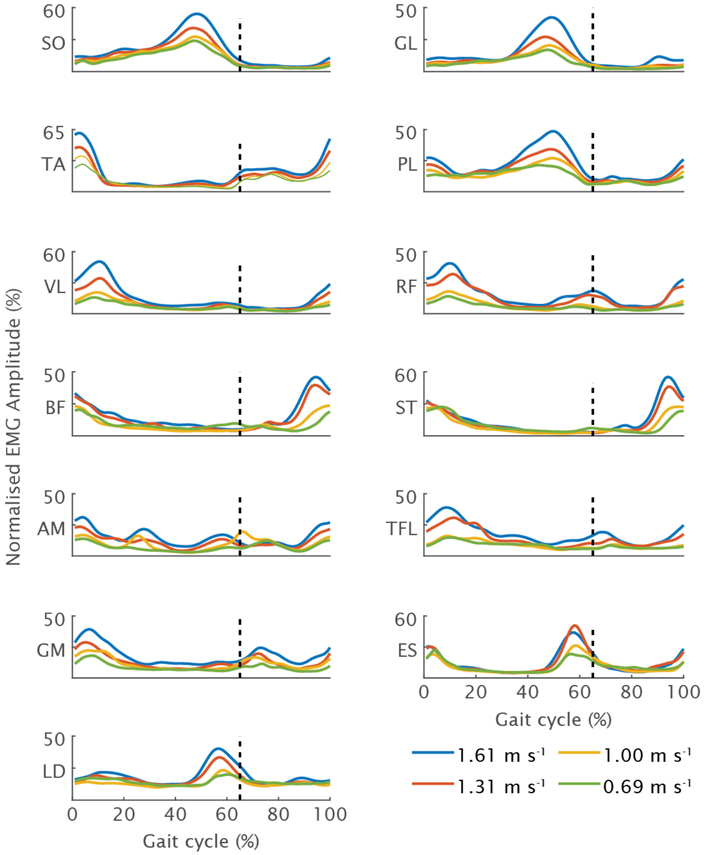

Figure 3 – Group averaged EMG profiles at 0.69, 1.00, 1,31, and 1.61 m s^{-1} for Soleus (SO), Gastrocnemius Lateralis (GL), Tibialis Anterior (TA), Peroneus Longus (PL), Vastus Lateralis (VL), Rectus Femoris (RF), Biceps Femoris (BF), Semitendinosus (ST), Adductor Magnus (AM), Tensor Fascia Latae (TFL), Gluteus Maximus (GM),

Erector Spinae (ES), and Latissimus Dorsi (LD). The dotted lines represent swing onset at 65 % of the time normalized gait cycle.

Gain functions and gain modules

Our first aim was to establish if speed related neuromuscular gain is subject to modular control. The group averaged gain functions for each muscle are depicted in Figure 4. The average gain function values were positive for all muscles, indicating that increases in gait speed generally resulted in increases in the amplitude of muscle activity, for the entire set of muscles. Visual inspection of Figure 4 also shows that increases in the amplitude of muscle activity were phase specific, and that the gain functions of particular groups of muscles share similar temporal characteristics.

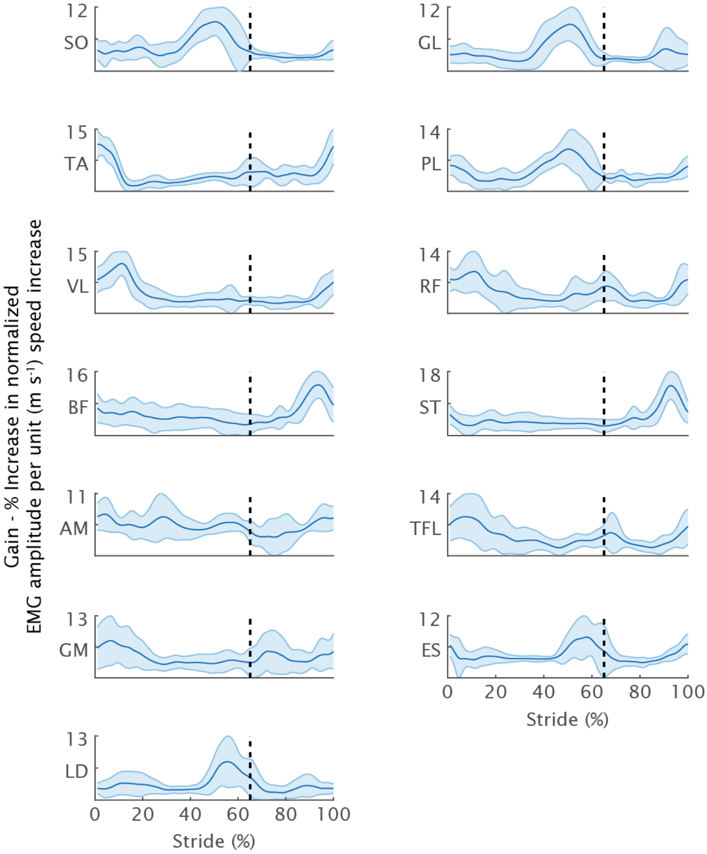

Figure 4 – The group averaged (± 1 sd) gain functions that represent the increase in normalized EMG amplitude per unit increase in speed (m s^{-1}), for Soleus (SO), Gastrocnemius Lateralis (GL), Tibialis Anterior

(TA), Peroneus Longus (PL), Vastus Lateralis (VL), Rectus Femoris (RF), Biceps Femoris (BF), Semitendinosus (ST), Adductor Magnus (AM), Tensor Fascia Latae (TFL), Gluteus Maximus (GM), Erector Spinae (ES), and Latissimus Dorsi (LD). The dotted lines represent swing onset at 65 % of the time normalized gait cycle.

To test whether the gain functions accurately represented the observed relationship between speed and EMG amplitude, the observed EMG patterns at the 1.00 m s^{-1} and the gain functions for each muscle were combined to reconstruct the group averaged EMG profiles recorded at 0.69, 1.31, and 1.61 m s^{-1}. Overall, the quality of the resulting reconstructions was good. Averaged over all muscles, the mean percentage (± sd) of variance in the observed EMG patterns that was accounted for by the reconstruction was 78.9 % (± 5.4), 93.3 % (± 2.9), and 97.4 % (± 1.4), for the EMG profiles recorded at 0.69, 1.31, and 1.61 m s^{-1}, respectively. This indicates that the effects of speed on EMG amplitude were reflected accurately in the gain functions.

To assess if there is synergistic structure in the neuromuscular regulation of speed, the gain functions were subjected to PCA with varimax rotation to extract 4 modular gain functions and a set of synergistic weightings for each of the functions. The 4 group averaged modular gain functions that were obtained, and their associated synergistic weightings, are presented in the left and right column of Figure 5. Averaged over the group, the variance accounted for by the set of modular gain functions was 74.0 % (± 1.3 %), indicating that there was communality in the gain functions, and that the major portion of variance in the set of 13 gain functions could be accounted for by 4 functions.

Comparison of modular gain functions and modular basis functions

To determine whether the basis activation of muscles and the speed-related gain are driven by a single synergistic control structure, dimensionality reduction (PCA + varimax rotation) was also performed on the EMG patterns recorded at 1.00 m s^{-1}. This resulted in a set of modular basis functions and a set of associated weightings, which are depicted in Figure 5A and Figure 5B (blue lines), respectively. Averaged over the group, the 4 modular basis functions accounted for 80.1 % (± 1.4) of the variance that was apparent in the EMG patterns at 1.00 m s^{-1}. This implies that most of the variance in the muscle activity at 1.00 m s^{-1} could be accounted for using 4 basis modules.

The number of modular functions that could be grouped using k-means clustering ranged from 11 (component B2) to 13 (component B1, B3 & B4) for the basis modules, and from 9 (component G3) to 13 (component G4) for the gain modules, indicating that the modular basis functions and modular gain functions were representative for the group. Correlations between the matched modular basis functions and modular gain functions were moderate ($r = 0.58$ and $r = 0.75$ for component B3 - G3 and B2 - G2), and high ($r = 0.84$ and $r = 0.89$ for B4 - G4 and B1 - G1). This indicates that there were clear similarities in the temporal properties of the basis and gain modular functions.

Inspection of the synergistic muscle weightings of both types of modular functions

Inspection of Figure 5 shows that the patterns of synergistic muscle weightings associated with the modular basis and gain functions, generally exhibited similar groupings of muscles. Correlations between the muscle weightings associated with the basis and modular activations were moderate ($r = 0.6$ for component B2 - G2), high ($r = 0.82$ for B3 - G3), to very high ($r = 0.95$ and $r = 0.91$ for B1 - G1 and B4 - G4), indicating that the matched modular basis and gain functions were driven by very similar synergistic weighting patterns. The muscle weightings associated with B1 and G1 were both dominated by the calf muscles (SO, PL, and GL), whereas weightings on these functions of other muscles were close to zero, resulting in a very high correlation ($r = 0.95$) between both sets of weightings. The pattern of weightings for modules B2 and G2 showed high weightings for ES and LD on both types of functions, although the calf muscles (SO, PL, and GL) showed clear weightings on the modular gain functions that were not apparent in the weightings on the modular basis functions. Patterns for modules B3 and G3 showed high weightings for the hamstrings (ST and BF), whereas TA weightings were apparent with respect to B3, but not G3. Finally, muscle weighting associated with B4 - G4, showed high muscle weightings for the quadriceps group (VF and RF), and to a lesser extend for TFL and GM.

Reconstruction and prediction of muscle activation patterns

To test the robustness of the present approach, we tested (i) the extent to which the averaged EMG profiles of individual participants could be reconstructed using the combined sets of 4 basis and gain modular activations and the associated muscle weightings, and (ii) whether these modular activations and weightings could predict the individual EMG patterns at a speed that was not used in the dimensionality reduction (i.e. at 1.31 m s^{-1}). The group average EMG, and predicted EMG per muscle are shown in Figure 6. The results confirmed the robustness of the present approach. The percentage variance accounted for by the reconstruction was 93.8 % (± 2.1), 92.8 % (± 3.1), and 79.7 % (± 5.3) for the EMG patterns at 1.61, 1.00, and 0.69 m s^{-1}, respectively. The predicted EMG patterns at 1.31 m s^{-1} accounted for 92.4 % (± 1.5; range between muscles 76.2 % - 97.9 %) of the variance in the recorded patterns at this speed, indicating that the EMG patterns at this speed were predicted quite accurately using the obtained sets of basis and gain modular activations and synergistic weightings.

To determine how well the modular gain functions were capable of predicting novel data of different subjects, we applied a bootstrapping procedure. The average percentage of variance accounted for by combining modular basis functions of N = 6 subjects with the averaged modular gain functions of the N = 7 remaining subject (with 95 % confidence interval, CI) was 80.3 % (79.6 - 81.0 %), 83.0 % (82.5 - 83.4 %), 91.1 % (90.6 - 91.5 %), and 67.8 % (66.6 - 69 %) for the predictions of EMG profiles at 1.61, 1.31, 1.00, and 0.69 m s^{-1} , respectively.

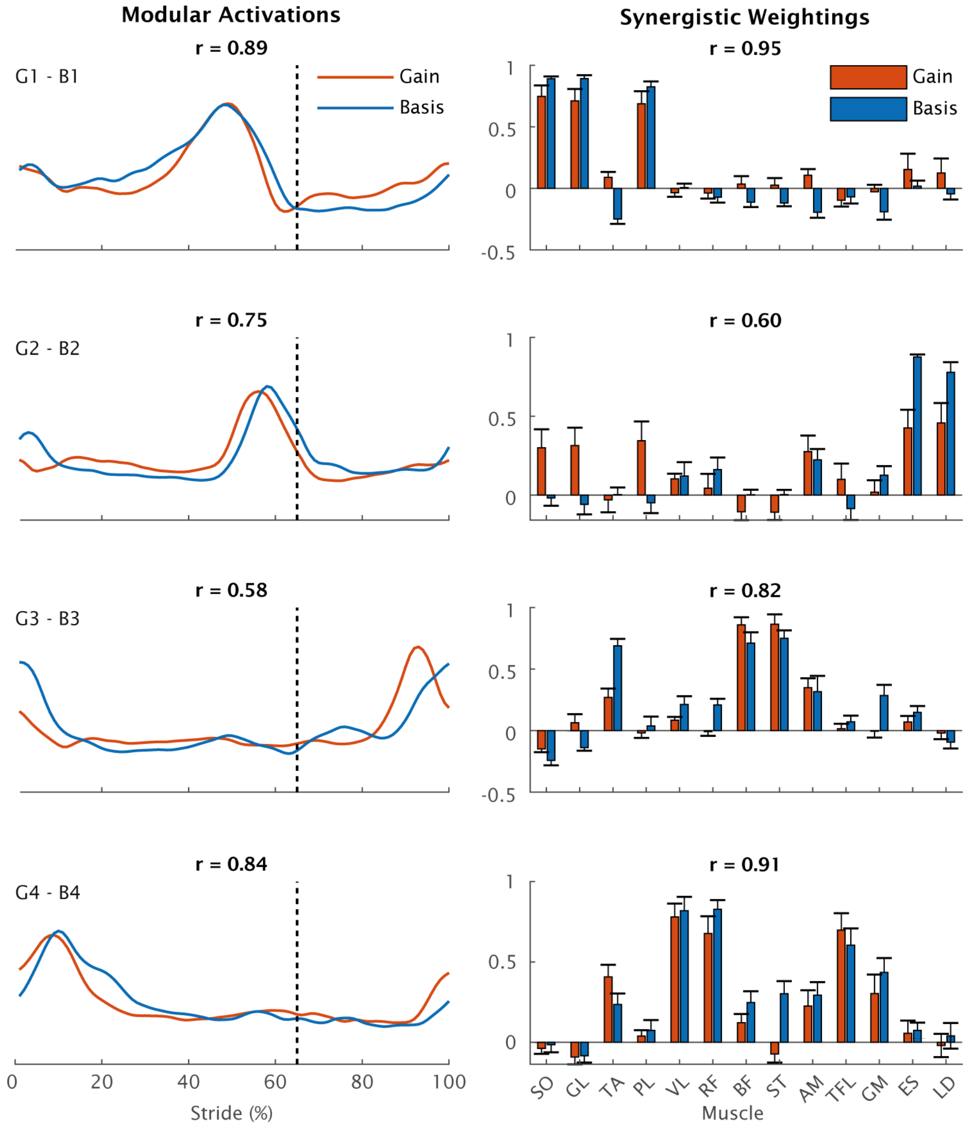

Figure 5 – Left column: Modular basis functions (blue, B1 - B4) and modular gain functions (orange, G1 - G4). In each panel, the correlation R between the corresponding modular basis and gain functions is shown. The dotted lines represent swing onset at 65 % of the time normalized gait cycle. Right column: the group averaged synergistic muscle weightings (+1 sd) associated with the modular basis functions (blue, B1 - B4) and modular gain functions (orange, G1 - G4). In each panel, the correlation between both sets of weightings is indicated as R.

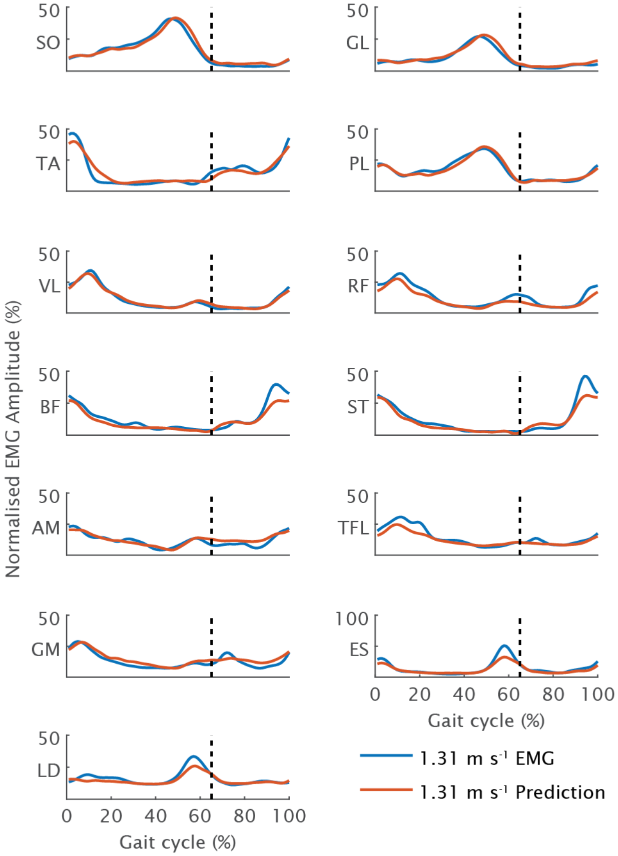

Figure 6 – The group averaged EMG patterns at 1.31 m s^{-1} (blue) and the predicted EMG patterns at 1.31 m s^{-1} based on the modular basis functions, the modular gain functions, and their associated muscle weightings. The dotted lines represent swing onset at 65 % of the time normalized gait cycle.

DISCUSSION

Previous research has shown that modular activations and (to a lesser extent) their associated synergies show clear similarities over a range of speeds [5,18,20]. However, the established similarities do not necessarily provide evidence that the dynamic regulation of speed itself is under modular control, but instead imply that muscle activations at different speed show a degree of pattern similarity. Here, we elaborated on this work and attempted to separate the 'pure' speed effects from the basis activation so as to determine if the phase-specific modulation of muscle output amplitude contains synergistic structure, as was previously implied in the work of Hof et al. [13]. To this end, gain functions were constructed, and their modular properties were assessed and compared to the modular properties of the basis activations of muscles. The results showed that the gain functions displayed a synergistic structure that was associated with clearly distinguishable muscle groups. Furthermore, the modular decompositions were similar for gain functions and the basis activity of muscles, suggesting common modular control for the basic phasing of muscle activity and its modulation by speed. The robustness of the present approach was confirmed, as for the majority of muscles a combined set of modular basis and gain functions could be used to successfully predict muscle activation patterns at a speed (1.31 m s^{-1}) that was not involved in the modular decomposition.

There is synergistic structure in the speed dependent modulation of muscle activity

The gain functions that were calculated provided a good representation of the phase dependent modulation of muscle output amplitude by speed [11-17]. By modulating the activity at 1.00 m s^{-1} with the constructed gain functions, we were able to reconstruct the EMG patterns at other speeds accurately, explaining 79.7 %, 93.8 %, and 92.8 % of the variance contained in the EMG signals collected at 0.69, 1.61, and 1.31 m s^{-1}, respectively. It is worth noting that gain values for the present speed range were mostly positive, and that no paradoxical speed effects (i.e. a decrease in amplitude with increasing speed) were apparent, as was previously reported for speeds slower than 0.28 m s^{-1} [12].

The ability to reconstruct EMG patterns from the combined set of modular basis and gain functions depended to some extent on gait speed, as the percentage of variance in EMG patterns explained by this set of functions ranged from 79.7 % at 0.69 m s^{-1} and 93.8 % at 1.61 m s^{-1}. This is likely due to the fact that at lower speeds, the signal to noise ratios are typically lower than at higher speeds. More specifically, assuming that the level of noise (or 'error variance') apparent in the EMG signal remains approximately constant over speeds, and because the amplitude of the EMG patterns increases with speed [12,13], the relative contribution of 'systematic variance' to the observed EMG signals is larger at higher speeds. Because predictions only relate to the systematic part of the EMG pattern variance, prediction quality is likely to better at higher speeds.

Previous studies [18-21] have shown that the activity of large groups of muscles over a range of speeds can be faithfully reproduced through the combined activity of a small number of modular activations. Here, we used a more direct approach to test the synergistic control of speed regulation by applying dimensionality reductions directly to the functions that represent the modulations of muscle activity through speed. The results showed that most of the variance in these functions (74.0 %) could be captured using 4 modular gain functions that were associated with clearly distinguishable synergistic muscle weightings. These findings provide direct evidence that the dynamic adjustments made to muscle activity for the regulation of speed, do not depend on individual muscle control, but instead contain synergistic structure.

Inspection of the timing properties of the modular gain functions and their associated synergistic muscle weightings, suggests that the obtained modules reflect specialized biomechanical functions involved in the regulation of gait speed. The activity of the calf muscle group is represented by function G1, with a peak between 40 and 55 % of the gait cycle. This muscle group plays a prominent role in propulsion and speed control [17,34,35], as it controls the CoM momentum during single stance, and regulates the temporal (cadence) and / or spatial (length) properties of the step that determine the speed of progression [9,10,36]. Function G2 was associated with activity of ES and LD, and to a lesser extent to the calf muscles, and may serve to accommodate speed-dependent requirements related to swing initiation [17,35,36], and trunk stability during weight shift [37,38]. Function G3 (80 - 10 % of the gait cycle) reflects modulation of activity in the hamstrings (ST and BF) and regulates leg deceleration and a feedforward mechanism to prepare for foot landing during late swing and early stance [16,17,35]. Finally, function G4 (95 % - 20 %, associated with VL and RF, and to a lesser extent TFL and GM), may reflect speed-related control of vertical support and stability during early stance as the vertical excursion of the body's CoM increases [17,35,39]. Taken together, these findings suggest that the modular gain functions reflect a parsimonious control strategy that translates higher order control signals to specific low level task commands to be implemented for the regulation of gait speed.

The basic phasing of muscle activity and the regulation of speed are part of a single modular control scheme

One of the questions we wished to address in this study was whether the basic activation of muscles, and the modulation of this basic activity by speed, are controlled by independent networks or if both are controlled by a single modular control structure. The present results clearly favor the latter scenario, as correlations between the matched modular basis functions and modular gain functions were generally high (r = 0.58 to 0.89). Importantly, these functions drive very similar muscle groups as became evident from the high correlations between the associated synergistic weightings of both types of functions (r = 0.6 to 0.95). These combined findings provide direct evidence for the claim made previously that a single set of modular activations controls walking over a range of speeds [18-21]. In this context, it is important to note that basis modules and gain modules appear to represent the same biomechanical subtasks of propulsion (B1 - G1), weight shift and swing initiation (B2 - G2), leg deceleration (B3 - G3), and vertical support and stability (B4 - G4). These findings are in line with results from a simulation study by Neptune and co-workers [17], showing that the amplitude of muscle activity changes over a range of speeds, but that the contribution of muscle groups to locomotor subtasks remains invariant over speeds.

The observed similarity between the modular basis and gain functions, and between their respective synergistic weightings, hint at two different scenarios for the modular architecture that is involved in the regulation of gait speed. First, the most parsimonious modular design would involve a single, sparse set of activation patterns, whose modular outputs are scaled approximately linearly to drive a single set of synergistic muscle groups over a broad range of gait speeds [21]. A second scenario is that the modular basis functions and modular gain functions represent higher level and lower level aspects of a hierarchical modular architecture, that together drive an invariant set of task relevant muscle synergies. The lower level modular control may involve the use of task specific afferent information to fine-tune basic modular activations to accommodate phase specific speed requirements. The importance of afferent information for the regulation of specific locomotor subtasks is well established [40-42], and the involvement of afferent mechanisms as part of a less centralized modular architecture has already been hinted at by others [31,43]. This type of hierarchical modular control can be efficient, fast and flexible, and allows higher order modular control to be adapted to a wide range of contexts and task demands. Integration of afferent information in the modular control structure may also be important for adjustments to the relative timing of modular basis and gain activations. Different speeds are associated with different relative durations of stance and swing phases [12,16] and the timing of modular activations needs to be controlled to establish functionally equivalent gait kinematics over a range of speeds [18-20]. In the present study, EMG data were time normalized separately for stance and swing phases to make possible a meaningful analysis in terms of gain functions, and as a consequence all information about possible phase shifts in the modular activations was neutralized. Nevertheless, it is well possible that the timing of the here presented modular (basis and gain) activations is subordinate to a temporal controller that is informed by afferent information on gait phase transitions [16,44].

With regard to the modular control that may govern adaptive walking, it is important to acknowledge that flexible recruitment of a single set of modular activations and synergistic weightings to accommodate speed requirements, needs to involve additional layers of control e.g. to induce phase shifts [19,20], a speed-dependent scaling of synergistic weights [18], or the construction of an additional set of functions and weights as in the present study. An important advantage of approaches like that of Gonzalez-Vargas et al. [18] and the approach described in the present paper, is that it is made explicit which elements of the modular control structure are sensitive to changes in speed. It can be argued that the here proposed mediation through an extra control layer, involving modular gain functions and their associated synergistic weights, implies an increase in the complexity of modular control. However, the observed similarities between modular gain and basis functions and their associated sets of weights, as well as the functional relatedness that is implied in this, suggests that the combined sets of functions and their synergistic weights are reflective of a parsimonious form of adaptive control.

Prediction of muscle activation patterns for a given speed

Since the modular gain functions represent the linear change in activity as a function of speed, speed can be used as an input to these functions to not only reconstruct, but also predict muscle activations at any given speed. We exploited this property to test the robustness of the presently used approach and predict muscle activation patterns for a speed (1.31 m s^{-1}) that was not involved in the construction of the (modular) gain functions. Overall, the combined set of modular basis and gain functions provided accurate predictions of the activations of individual muscles, as on average 92.4 % of the variance in the recorded EMG patterns at 1.31 m s^{-1} was accounted for by the predictions.

The good predictive properties of the combined set of modular functions and associated synergies imply that the here used modular decomposition provide an accurate representation of the basic phasing of muscle activity, and the phase-specific modulation of this basis activity by gait speed. Although recent research has shown that similarly good predictions can be produced through speed-dependent modifications in the synergistic weights that drive a single set of modular basis functions [18], the present simulations elaborate on these findings and show that a modular decomposition that is aimed directly at the speed-dependent modulation of muscle-output amplitude (i.e. the modular gain functions), provides additional evidence that for the claim made previously [18-21] that a single set of modular activations controls walking over a range of speeds.

The finding that muscle activations can be predicted for a given speed using a set of (modular) gain functions, may have interesting applications for research on neuromuscular control in special populations, e.g. in patients or frail elderly. As it is often difficult to exert experimental control over the potentially confounding effects of gait speed, the approach used here may be used to compare groups at a single, simulated speed, so as to detect differences in the patterning of muscle activity that that are not related to speed [23]. Overall, the present results also suggest that a representation of the effects of naturally varying parameters (e.g. cadence, loading) as time varying functions, and the assessment of their modular properties, may provide interesting opportunities for studying the flexibility in the modular control of gait. These findings may further inspire work on flexibility in the modular control of gait in populations with impaired walking ability [21,45].

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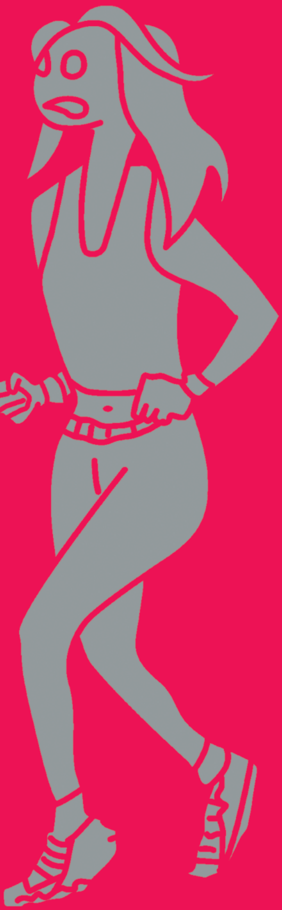

3

ADAPTIVE CONTROL OF DYNAMIC BALANCE IN HUMAN GAIT ON A SPLIT-BELT TREADMILL

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ABSTRACT

Human bipedal gait is inherently unstable and staying upright requires adaptive control of dynamic balance. Little is known about adaptive control of dynamic balance in reaction to long-term, continuous perturbations. We examined how dynamic balance control adapts to a continuous perturbation in gait, by letting people walk faster with one leg than the other on a treadmill with two belts (i.e. split-belt walking). In addition, we assessed whether changes in mediolateral dynamic balance control coincide with changes in energy use during split-belt adaptation. In nine minutes of split-belt gait, mediolateral margins of stability and mediolateral foot roll-off changed during adaptation to the imposed gait asymmetry, especially on the fast side, and returned to baseline during washout. Interestingly, no changes in mediolateral foot placement (i.e. step width) were found during split-belt adaptation. Furthermore, the initial margin of stability and subsequent mediolateral foot roll-off were strongly coupled to maintain mediolateral dynamic balance throughout the gait cycle. Consistent with previous results net metabolic power was reduced during split-belt adaptation, but changes in mediolateral dynamic balance control were not correlated with the reduction of net metabolic power during split-belt adaptation. Overall, this study has shown that a complementary mechanism of relative foot positioning and mediolateral foot roll-off adapts to continuously imposed gait asymmetry to maintain dynamic balance in human bipedal gait.

LIST OF SYMBOLS AND ABBREVIATIONS

AP	AnteroPosterior
BL	BaseLine
BoS	Base of Support
CoM	Center of Mass position
CoP	Center of Pressure position
CoP$_x$	Anteroposterior Center of Pressure position
CoP$_z$	Mediolateral Center of Pressure position
DS	Double Support time
DSS	Double Support Symmetry
EA	Early Adaptation
EE	Energy Expenditure
EE$_{Gait}$	Energy Expenditure during gait
EE$_{Net}$	Net Energy Expenditure
EE$_{Rest}$	Energy Expenditure during quiet standing
EP	Early Post-adaptation
F$_Y$	Vertical ground reaction force
g	Gravitational acceleration
GRF	Ground Reaction Force
l	Leg length
LA	Late Adaptation
LP	Late Post-adaptation
m	Body mass
M	Moment of force
M$_x$	Anteroposterior Moment of force
M$_z$	Mediolateral Moment of force
ML	MedioLateral
ML ΔCoP	Change in CoP$_z$ position during stance
MoS	Margin of Stability
MP$_{Net}$	Net Metabolic Power
RER	Respiratory Exchange Rate
SL	Step Length
SLS	Step Length Symmetry
SW	Step Width
vCoM	Center of Mass velocity
VO$_2$	Oxygen uptake
XCoM	Extrapolated Center of Mass

INTRODUCTION

Humans are one of few mammals that naturally show bipedal gait. Although human gait is more energy efficient than quadrupedal gait in mammals of equal body weight [1], maintaining mediolateral (ML) balance is more complex. Active control of balance in human gait is essential to prevent falling [2,3], as the vertical projection of the Center of Mass (CoM) is outside of the Base of Support (BoS) for 80 % of the gait cycle [4]. In order to respond to both external perturbations from the environment (e.g. being pushed or walking on uneven terrain), as well as internal perturbations from the system itself (e.g. controlling the destabilizing effect of the ankle push-off in the stride cycle), the control of balance during gait needs to be adaptive. By adaptive we refer to recalibration of motor control in response to perturbations, in order to re-establish reliable and efficient task performance, followed by after-effects once the perturbation is removed, which slowly wash out over time [5]. A good understanding of dynamic balance control requires knowledge of the adaptability of gait.

The trajectory of the CoM during bipedal human gait can be modeled with the inverted pendulum model [6,7]. In this model, the CoM of the human body is described as a single mass on top of an inverted pendulum, in which the pendulum represents the stance leg. Although both can be unstable when perturbed, anteroposterior (AP) balance is largely regulated by passive dynamics in this model, whereas the maintenance of ML balance requires more active control [3]. The importance of ML balance control has also been shown by Hilliard et al. (2008) [8], who found that poor ML balance is a key predictor of falls in older adults. Therefore, we study dynamic balance control in the ML direction. In the model, the kinematic state of the CoM can be described with the Extrapolated CoM (XCoM) concept, which is the CoM position with the addition of a CoM velocity component [9]. ML dynamic stability is maintained by active control of the ML position of the XCoM relative to the BoS [9] (i.e. relative foot positioning), known as the Margin of Stability (MoS) [10,11]. The MoS can thus be regulated by changes in CoM excursion and ML foot placement. A negative ML MoS will result in a loss of balance, necessitating the production of a sidestep to prevent a fall, whereas a positive ML MoS will result in well-balanced and safe gait [11].

Relative foot positioning and ML foot roll-off are sequential in time in a gait cycle. Recently, it has been suggested that relative foot positioning and ML foot roll-off work as a complementary mechanism (e.g. when the foot is positioned too wide relative to the XCoM, the foot will roll-off inwards in the ML direction, and vice versa) that allows for corrective control of the MoS during the stance phase [12]. The accuracy of relative foot positioning strongly depends on visual information and in general is not very precise [13-15]. However, the aforementioned complementary mechanism can change a small or large ML MoS at contralateral toe-off by rolling the foot inward or outward during stance (i.e. foot roll-off) [10], based on real time afferent information about loading [16,17] or CoM position relative to Center of Pressure (CoP) position. Because the MoS can be controlled by relative foot positioning and foot roll-off, both variables and the relationship between these variables should be measured when assessing adaptation of dynamic balance control to sustained perturbations.

To gain a better understanding of balance control in gait, ML balance has been challenged experimentally by pushing [18-20] or pulling the trunk of a participant [21], and by lateral translations of the treadmill [22]. These experiments focus on reactive balance control (i.e. balance control in reaction to perturbations from which a human recovers within a few steps), while balance control also involves adaptation to more continuous and sustained perturbations in gait (e.g. walking on a rocking ship or walking after a leg amputation). A method to perturb gait directly as well as continuously, and which has gained considerable popularity in recent years, is to let walkers adapt to imposed asymmetric gait on a split-belt treadmill.

Split-belt treadmills have two belts, one under each foot. By setting the speed of one of the belts faster than the other, a participant has to walk faster with one leg than the other, which evokes a temporally and spatially asymmetric gait pattern. Earlier research on split-belt gait in healthy individuals has shown that step lengths and double support times initially show a large asymmetry, but adapt over time to a more symmetrical ratio [23]. It has been found that spatiotemporal asymmetry in gait is associated with poor ML balance [24]. In addition, recent research in split-belt gait has shown that variability of the frontal inclination angle is reduced during sudden split-belt adaptation [25]. Furthermore, ML Ground Reaction Forces (GRF) and fast limb hip moment impulse increased during split-belt adaptation [26]. Finally, sagittal plane measures of dynamic balance during split-belt adaptation have been previously characterized, showing an increase of AP MoS on the fast compared with the slow belt [27]. These studies all show strategies to cope with the perturbed balance in split-belt gait. Split-belt gait thus provides the opportunity to examine how humans recover their ML balance in reaction to a sustained perturbation.

It has been suggested that the adaptive control of gait serves to decrease energy use [28-33]. Recent research has shown that the increase in spatial gait symmetry during split-belt adaptation is related to a decrease in metabolic power [31]. In addition, it was found that split-belt adaptation leads to an initial increase in mechanical work performed by the legs followed by a gradual decrease over the adaptation period [34]. Furthermore, research indicates that dynamic balance control and changes in metabolic power might be related [29]. To gain insight into processes underlying motor adaptation, we studied this association during split-belt adaptation. We hypothesized that adaptive control of dynamic balance in split-belt gait may be related to the reduction of metabolic power.

The primary aim of this study was to determine the effects of continuous perturbations on ML dynamic balance control, by establishing whether and how dynamic balance control adapts to split-belt gait. We hypothesized that dynamic balance parameters adapt to split-belt walking with a sudden initial increase in MoS and a gradual decrease over time, co-occurring with the adaptation of spatial and temporal gait parameters. Furthermore, we studied whether a complementary mechanism of relative foot positioning and foot roll-off controls ML dynamic balance in split-belt gait. The secondary aim of this study was to assess whether the magnitude of changes in ML dynamic balance control during split-belt adaptation coincides with the magnitude of changes in net metabolic power (MP_{net}). Based on previous research [29,31], we expected that a decrease in MoS would be related to a decrease in MP_{net}.

MATERIALS AND METHODS

Participants and ethics statement

Fourteen healthy young adults (7 males, 7 females, 23.9 ± 1.9 years old, body mass: 74.9 kg ± 11.7, height: 1.75 m ± 0.08) volunteered for this study. Participants were excluded from the study if they had any known neurological or orthopedic impairments that affect gait or balance capacity, or if they had any prior experience with split-belt treadmill walking. The procedures of this study were approved by the Ethics Committee of the Center for Human Movement Sciences, University Medical Center Groningen, The Netherlands, and were in accordance with the Declaration of Helsinki [35]. All participants gave their written informed consent prior to the experiment.

Instrumentation

Participants walked on an instrumented split-belt treadmill (M-Gait; Motekforce Link, Amsterdam, The Netherlands). Participants were fitted with a harness attached to the ceiling to secure the participants' safety, which did not provide any body weight support or constrain the participants' movements. Two handrails were attached to both sides of the treadmill for safety, but participants were instructed not to touch the handrails other than to prevent a fall. Three-dimensional GRFs (N) and moments of force (N m) were measured using two embedded force plates, one under each belt, and recorded with D-Flow software (Motekforce Link, Amsterdam, The Netherlands) at a sample frequency of 1000 Hz. The data were analyzed in an XYZ coordinate system with the X-axis along the line of gait progression, the Z-axis positive to the right, and the Y-axis pointing upwards, in accordance with International Society of Biomechanics recommendations [36]. Breath-by-breath respiratory data were measured using a portable K4b2 system (COSMED, Rome, Italy) and synchronized with D-Flow. All data were stored offline on an encrypted external hard drive for further analysis.

Protocol

Participants stood still on the treadmill for ninety seconds prior to the experiment to measure Energy Expenditure (EE) during quiet standing. Next, they were exposed to the treadmill protocol as shown in Figure 1. The treadmill session started with five minutes of warm-up at alternating slow (0.7 m s^{-1}) and fast (1.4 m s^{-1}) tied-belt gait speeds to let the participant adapt to treadmill gait [37]. After that, one minute of slow tied-belt gait (0.7 m s^{-1}) was recorded as a baseline measurement. Fast MoS and fast ML ΔCoP baseline were calculated from data of the last minute of fast tied-belt walking in warm-up. The split-belt adaptation phase lasted nine minutes. During the adaptation phase, the left belt speed was set at 1.4 m s^{-1} and right belt speed at 0.7 m s^{-1} [23]. Finally, in the post-adaptation phase both belts were set at 0.7 m s^{-1} for five minutes, to measure washout. This resulted in five experimental phases: BaseLine (BL), Early Adaptation (EA), Late Adaptation (LA), Early Post-adaptation (EP), and Late Post-adaptation (LP). The first (EA, EP), and last (BL, LA, LP) five steps of each phase were used for further analysis. Prior to and during the experiment, no instructions were given regarding the duration of the phases or the changes in gait speed. Participants were instructed to look straight ahead and remain silent for the duration of the protocol so as to not affect respiratory data.

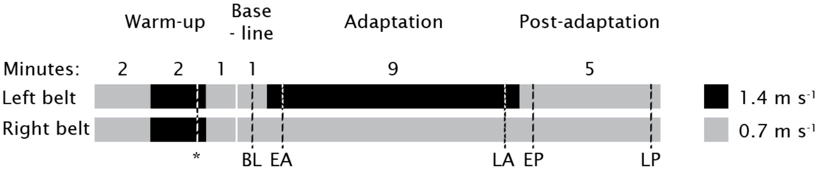

Figure 1 – Split-belt treadmill protocol. The upper bar shows left belt speed and the lower bar shows right belt speed. Phase duration is shown above the bars. Experimental phases (BaseLine (BL), Early Adaptation (EA), Late Adaptation (LA), Early Post-adaptation (EP), and Late Post-adaptation (LP)) are shown below the bars. The asterisk indicates BL measurement for the fast Margin of Stability (MoS) and the fast change in mediolateral center of pressure during stance (ML ΔCoP). Dashed vertical lines visually indicate the point in time at which the first or last five steps for each experimental phase were averaged for further analysis. Warm-up is separated from baseline in this figure to indicate the division between warm-up and baseline, in the actual experiment the belts continued to run at this point.

Data analysis

All data were analyzed using custom-made routines in MATLAB (version r2016b; The MathWorks Inc., Natick, MA, USA). GRFs and moments of force were low-pass filtered using a 15 Hz 2nd order zero phase Butterworth filter. Gait events were detected by finding the point at which GRF_Y, on either of the force plates, crossed a threshold of 50 N. For the analysis of CoP position, X and Z CoP (m) positions for each force plate were calculated using Equations 1,2,

$$CoP_X = -\frac{M_Z}{F_Y} \tag{1}$$

$$CoP_Z = \frac{M_x}{F_Y} \tag{2}$$

in which M is the moment of force (N m) and F the GRF (N). For continuous monitoring of CoP and CoM positions, the data of the two force plates were combined by summing the GRFs. Simulated single force plate CoP position data were calculated by scaling the CoP position of each force plate with the magnitude of its respective GRF (Equation 3).

$$CoP_{combined} = \frac{GRF_{Left} \times CoP_{Left} + GRF_{Right} \times CoP_{Right}}{GRF_{Left} + GRF_{Right}} \tag{3}$$

Step length symmetry (SLS) and double support time symmetry (DSS), were calculated to monitor spatiotemporal gait symmetry throughout the experiment using Equations 4 and 5 [23],

$$SLS\ (i) = \frac{SL_{Left}(i) - SL_{Right}(i)}{SL_{Left}(i) + SL_{Right}(i)} \tag{4}$$

in which SL is Step Length (meter), defined as the difference in CoP_x position between the left and right foot at toe-off. SLS was calculated as a symmetry measure between left and right SL of every stride (*i*) [23].

The DSS between the first and second DS period was calculated for every stride (*i*) using Equation 5,

$$DSS\ (i) = \frac{DS_{First}(i) - DS_{Second}(i)}{DS_{First}(i) + DS_{Second}(i)} \tag{5}$$

in which DS is the Double Support time (s), defined as the period between heel strike and contralateral toe off.

Step Width (SW) was calculated using Equation 6 for every step in the gait cycle throughout the experiment.

$$SW\ (i) = |min/max(CoP_Z(j)) - max/min(CoP_z(k))| \tag{6}$$

SW was defined as the absolute difference between the local minimum/maximum CoP_z position during ipsilateral single support phase (*j*) and the local maximum/minimum CoP_z position during the consecutive contralateral single support phase (*k*) for each left/right step (*i*) (adapted from Verkerke et al. (2005) [38]).

To determine the ML MoS (m), multiple steps were taken. First, GRF_z was divided by body mass (kg) to obtain CoM_z acceleration (m s^{-2}). The CoM_z acceleration signal was integrated twice to obtain CoM_z position (m) and high-pass filtered to prevent integration drift. Then, the absolute ML CoM position (m) was calculated by addition of the low-pass filtered CoP_z signal, and the high pass filtered CoM_z position [39]. All aforementioned filtering was done using a 0.2 Hz 2nd order zero phase Butterworth filter. The ML XCoM position (m) was calculated using Equation 7 [9],

$$XCoM = CoM + \frac{vCoM}{\sqrt{g/l}} \tag{7}$$

in which vCoM is the ML CoM velocity (m s^{-1}), l is leg length (m), and g is gravitational acceleration (9.81 m s^{-2}). Finally, the MoS was defined as the distance between the CoP_z position and $XCoM_z$ position at contralateral toe-off (*j*), for each step (*i*) using Equation 8 [9]:

$$MoS(i) = CoP_Z(j) - XCoM_Z(j) \tag{8}$$

The fast MoS was calculated for each step with the left limb (which was on the fast belt during split-belt gait), and the slow MoS for each step with the right limb (which was on the slow belt during split-belt gait).

The change in CoP_z position during single-limb stance (indicating foot roll-off, from this point on referred to as ML ΔCoP) was calculated by subtracting the CoP_z position at contralateral heel strike from the CoP_z position at the preceding contralateral toe-off. The ML ΔCoP was calculated for the fast (left) and slow (right) side separately, resulting in fast ML ΔCoP and slow ML ΔCoP. As illustrated in Figure 2, a positive ML ΔCoP corresponds with an outward ML ΔCoP, and a negative ML ΔCoP with an inward ML ΔCoP.

For the respiratory analysis, first EE (W) was calculated using Equation 9 [40],

$$EE = (4.940 \times RER + 16.040) \times VO_2 \tag{9}$$

in which RER is the Respiratory Exchange Rate, and VO_2 is oxygen uptake (L min^{-1}). Then, net EE (EE_{net}; W) was calculated by subtracting the mean EE at quiet standing from EE during the experiment. Finally, MP_{net} (W kg^{-1}) was determined by dividing EE_{net} by body mass (m; kg) [41], as shown in Equation 10.

$$MP_{Net} = \frac{(EE_{Gait} - EE_{Rest})}{m} \tag{10}$$

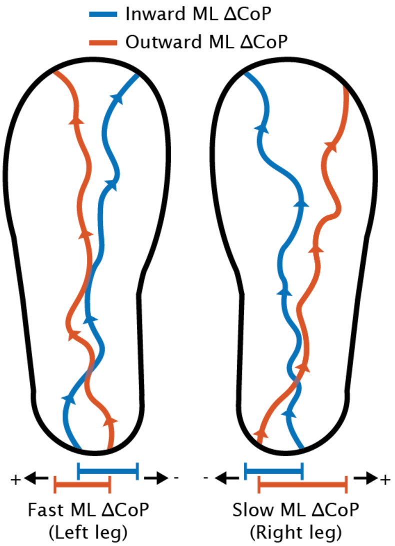

Figure 2 – Visualization of fast (left leg) and slow (right leg) change in mediolateral center of pressure during stance (ML ΔCoP). Red and blue lines indicate hypothetical CoP trajectories. Blue lines indicate inward ML ΔCoP, red lines outward ML ΔCoP. The arrows indicate the direction of the CoP trajectory. A positive ML ΔCoP corresponds with an outward ML ΔCoP, a negative ML ΔCoP with an inward ML ΔCoP. The direction of the ML ΔCoP is mirrored for the left and right foot to make interpretation of the values more intuitive.

Statistical analysis

The first minute of MP_{net} data of the EA and EP phases was left out of the analyses because of the transient change in the data from one experimental phase to the other [31]. SLS, DSS, SW, fast MoS, slow MoS, fast ML ΔCoP, and slow ML ΔCoP were averaged over the first (EA and EP) or last (BL, LA, and LP) five steps of each experimental phase for statistical analysis. MP_{net} was averaged over the first or last two minutes of each experimental phase for statistical analysis, except BL, in which MP_{net} was averaged over the last 1 minute of that phase.

To test for differences between the experimental phases, three separate repeated-measures MANOVAs (RM MANOVAs) were performed with SLS, DSS, SW, fast MoS, slow MoS, fast ML ΔCoP, slow ML ΔCoP, and MP_{net} as dependent variables. The within-subjects factor ‘phase’ had two levels in the three respective RM MANOVAs; 1) BL vs EA, 2) EA vs LA and 3) BL vs EP. When multivariate results were found to be significant, univariate results were assessed to find differences between phases. BL vs EA was tested to see whether parameters changed in reaction to split-belt gait, EA vs LA to test whether adaptation to split-belt gait occurred, and BL vs EP to test whether after-effects occurred after returning to tied-belt speeds.

To study the relationship between MoS at contralateral toe-off (from this point on referred to as initial MoS) and subsequent ML ΔCoP, a Pearson correlation coefficient was calculated between those two parameters during baseline, adaptation and post-adaptation and for the fast and slow side. This resulted in six (three experimental phases x two sides) correlations per participant. To determine whether a relationship between initial MoS and ML ΔCoP existed, Wilcoxon signed rank tests were used to test whether the group median correlation coefficient was different from zero for each of the six conditions.

To study the relationship between change in fast MoS and slow MoS from EA to LA, and the reductions in MP_{net} from EA to LA, linear regression analyses were performed. To test whether changes in spatiotemporal parameters coincided with a reduction in MP_{net}, we also investigated whether changes in SLS and DSS were related to changes in MP_{net} during split-belt adaptation with linear regression analyses, similar to Finley et al. (2013) [31].

Statistical significance was set at a Holm-Bonferroni [42] corrected alpha of 5 % for all analyses, to control the family-wise error rate. All statistical analyses were performed using IBM SPSS Statistics for Windows (Version 24, 64-bit edition, IBM Corporation, Armonk, NY, USA).

RESULTS

The group-averaged results of SLS, DSS, SW, fast and slow MoS, fast and slow ML ΔCoP, and MP_{net} are shown in Figure 3. To determine whether the participants adapted to split-belt gait in the adaptation phase and whether the learned pattern washed out during the post-adaptation phase, symmetry in step lengths (SLS) and double support times (DSS) were measured. As becomes evident from Figure 3A,B and the results from the RM MANOVAs (Figure 3G,H and Table 1), participants walked with more asymmetric step lengths and double support times in EA compared with BL, but symmetry increased during split-belt adaptation from EA to LA. During post-adaptation, participants walked with asymmetric step lengths and double support times in EP compared with BL ($p < 0.05$ for all comparisons). The participants thus showed adaptation to split-belt gait in the adaptation phase and after-effects in the post-adaptation phase.

Margin of stability adapts to split-belt gait in an asymmetric fashion

To study adaptive dynamic balance control in gait we examined whether and how the MoS changed during split-belt adaptation. Figure 3D,J shows that the fast MoS increased from BL to

EA. Subsequently, the fast MoS decreased from EA to LA, indicating adaptation to split-belt gait. All comparisons were significant in the RM MANOVA ($p < 0.05$, Table 1). No significant difference was found in fast MoS in EP compared sigh BL. Figure 3D,J shows that the slow MoS increased from BL to EA, and decreased from EA to LA, indicative of adaptation to split-belt gait. The slow MoS was higher in EP compared sigh BL, indicative of an after-effect of the learned gait pattern. All comparisons were significant ($p < 0.05$, Table 1). Interestingly, the fast MoS was higher than the slow MoS in both EA (group average: 5.4 vs 3.2 cm) and LA (group average: 3.6 vs 2.0 cm), as shown in Figure 3D,J.

Mediolateral foot roll-off shows adaptation to split-belt gait on one side

The MoS can be adjusted with ML foot roll-off, which is reflected in the change in ML ΔCoP during the stance phase of gait. Figure 3E,K shows that the fast ML ΔCoP decreased from BL to EA, indicating an inward foot roll-off. During split-belt adaptation fast ML ΔCoP increased to a value of almost zero from EA to LA, which indicates no ML foot roll-off. These comparisons were all significant in the RM MANOVA ($p < 0.05$, Table 1). In EP compared with BL, the fast ML ΔCoP showed no significant difference. The slow ML ΔCoP showed no change during the experiment ($p > 0.05$, Table 1). The ML foot roll-off thus showed significant changes and adaptation in response to split-belt gait on the fast side, but not on the slow side.

Relative foot positioning and foot roll-off represent a complementary mechanism in split-belt adaptation

To monitor ML foot placement throughout the experiment, SW was calculated. The group-averaged results for SW are shown in Figure 3C,I. The RM MANOVA results (Table 1) showed no statistically significant changes from BL to EA, and no change over time during adaptation from EA to LA. However, in EP compared with BL there was a significant increase in SW ($p < 0.05$).

To determine whether the initial MoS and subsequent ML ΔCoP during stance represent a complementary mechanism to maintain a safe MoS during gait, we studied the relationship between these two parameters. A representative example of a single participant's results is shown in Figure 4 and the group-averaged results are shown in Figure 5. Figure 4 shows that there is a strong relationship between the two parameters. When MoS decreases, the ML foot roll-off is directed outward, and when MoS increases, the ML foot roll-off is directed inward. Furthermore, this figure clearly shows the shift from high to low MoS in split-belt adaptation. Also, there was a shift from inward to outward ML ΔCoP (i.e. a change in ML foot roll-off) from EA (blue triangles) to LA (green squares). The relationship between the initial MoS and ML ΔCoP is also apparent in the group data (Figure 5), as is the shift in MoS and ML ΔCoP from EA (blue ellipses) to LA (green ellipses). The results in Table 2 show that the median correlation coefficient of this relationship was significant for all phases and sides ($p < 0.05$). The group median correlation coefficients for baseline, adaptation and post-adaptation range from 0.54 ± 0.14 to 0.79 ± 0.23, which indicates a strong relationship between initial MoS and ML ΔCoP in all phases and both sides.

Table 1 – Differences between the experimental phases: BaseLine (BL), Early Adaptation (EA), Late Adaptation (LA) and Early Post-adaptation (EP) – for all parameters.

Parameter	Phase	F (df)	p
Step length symmetry	BL vs EA	228.5 (1,13)	<0.001*
	EA vs LA	132.7 (1,13)	<0.001*
	BL vs EP	47.8 (1,13)	<0.001*
Double support symmetry	BL vs EA	9.8 (1,13)	0.008*
	EA vs LA	7.6 (1,13)	0.017*
	BL vs EP	49.9 (1,13)	<0.001*
Step width	BL vs EA	2.7 (1,13)	0.124
	EA vs LA	0.0 (1,13)	0.935
	BL vs EP	37.7 (1,13)	<0.001*
Fast margin of stability	BL vs EA	62.8 (1,13)	<0.001*
	EA vs LA	25.1 (1,13)	<0.001*
	BL vs EP	2.0 (1,13)	0.183
Slow margin of stability	BL vs EA	25.3 (1,13)	<0.001*
	EA vs LA	10.4 (1,13)	0.007*
	BL vs EP	27.6 (1,13)	<0.001*
Fast ML ΔCoP	BL vs EA	18.1 (1,13)	0.001*
	EA vs LA	32.3 (1,13)	<0.001*
	BL vs EP	4.1 (1,13)	0.064
Slow ML ΔCoP	BL vs EA	1.6 (1,13)	0.233
	EA vs LA	3.4 (1,13)	0.088
	BL vs EP	0.5 (1,13)	0.476
Net metabolic power	BL vs EA	246.3 (1,13)	<0.001*
	EA vs LA	48.7 (1,13)	<0.001*
	BL vs EP	0.4 (1,13)	0.559

Asterisks indicate statistical significance at a Holm-Bonferroni corrected alpha of 0.05.

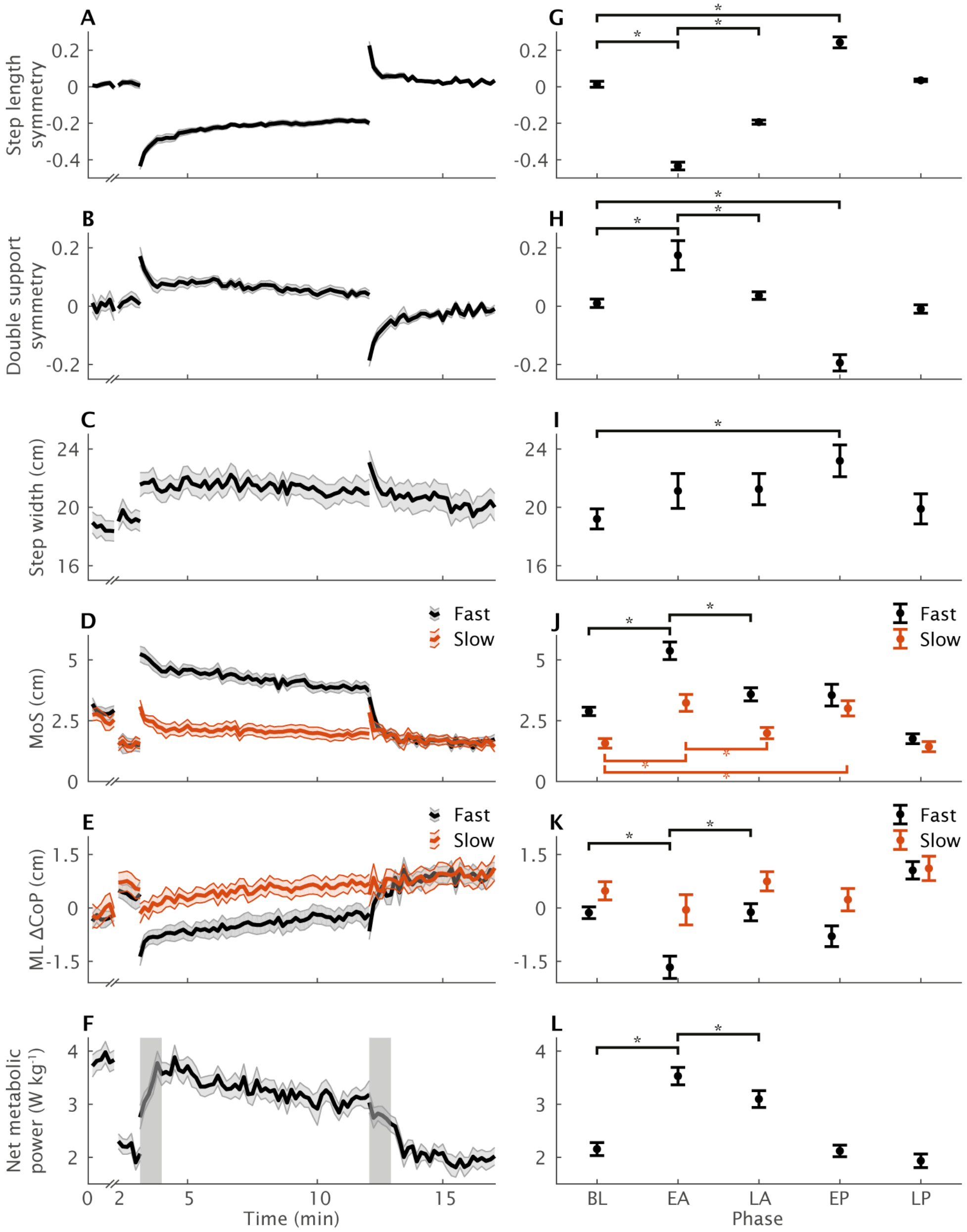

Figure 3 – Group-averaged results (N = 14). **A, B, G and H)** A value of zero indicates perfect symmetry in step length or double support time for step length symmetry and double support symmetry respectively. **A - F)** Results were averaged within ten second bins for visualization purposes. Shaded areas around the lines indicate standard error. Gaps (//) in the x-axes indicate the jump in time flow from minute one to two, i.e. from fast to slow tied-belt walking. **F)** The vertical grey shaded areas in F indicate the net metabolic power

results that have been left out of further analysis. **G - L)** Averaged results (means ± s.e.m.) and statistics (* $p < 0.05$) per experimental phase for the first (Early Adaptation (EA), Early Post-adaptation (EP)) or last (BaseLine (BL), Late Adaptation (LA), Late Post-adaptation (LP)) five steps or two minutes (net metabolic power). BL results for the fast Margin of Stability (MoS) and the fast change in mediolateral center of pressure during stance (ML ΔCoP) correspond with fast tied-belt walking.

Table 2 – Relationship between initial margin of stability and mediolateral change in center of pressure during stance for each phase and side.

Phase	Side	Median ± SD	Z-score	p
Baseline	Fast	0.79 ± 0.23	-3.233	0.001*
	Slow	0.66 ± 0.23	-3.233	0.001*
Adaptation	Fast	0.65 ± 0.11	-3.296	0.001*
	Slow	0.68 ± 0.13	-3.296	0.001*
Post-adaptation	Fast	0.54 ± 0.14	-3.296	0.001*
	Slow	0.69 ± 0.15	-3.296	0.001*

Asterisks indicate statistical significance at a Holm-Bonferroni corrected alpha of 0.05.

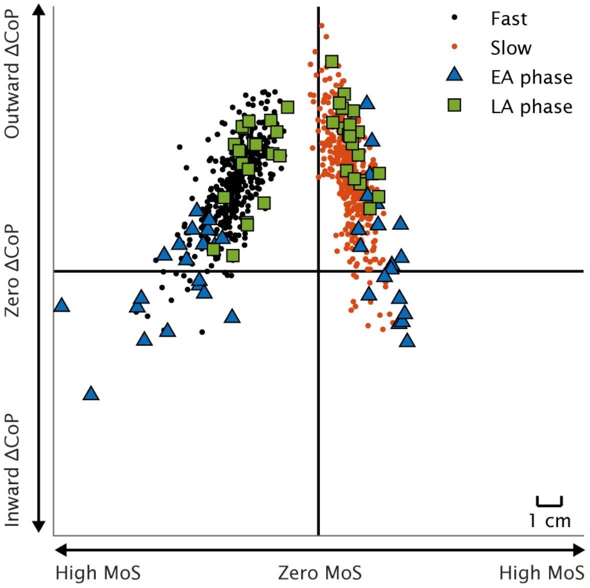

Figure 4 – Representative example of a single participant's initial margin of stability (MoS) vs change in mediolateral center of pressure during stance (ML ΔCoP) during the adaptation phase. Black and red circles represent single steps of the fast and slow leg, respectively. Blue triangles and green squares represent the first/last twenty steps from the Early Adaptation (EA) and Late Adaptation (LA) for each side, respectively. Inward ML ΔCoP indicates an inward ML foot roll-off, outward ML ΔCoP an outward ML foot roll-off, zero ML ΔCoP indicates no ML foot roll-off from heel strike to toe-off. Crossing the point of zero MoS indicates dynamic instability. A high MoS indicates dynamic stability. As this figure illustrates, a low initial MoS is typically followed by an outward foot roll-off (and vice versa) by which dynamic stability is maintained.

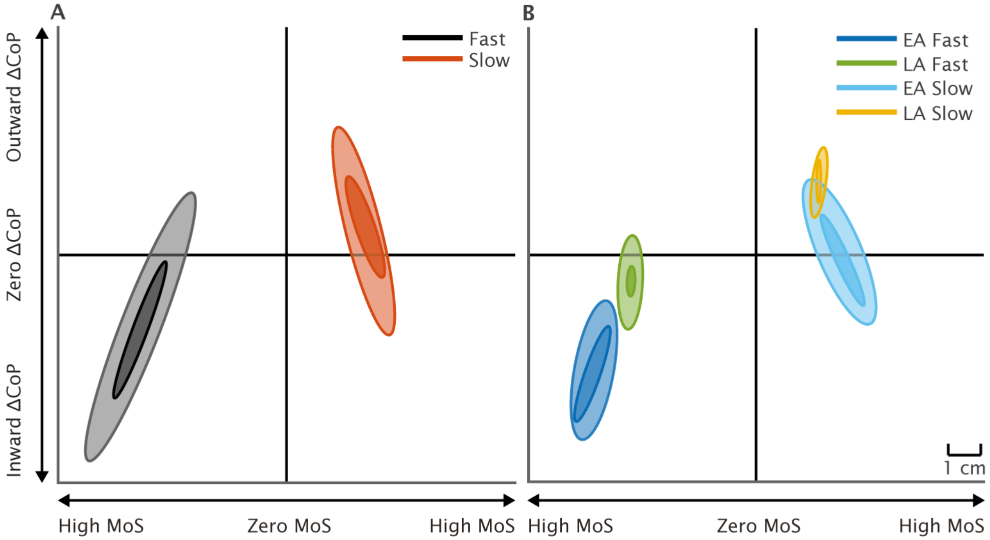

Figure 5 – Group-averaged results (N = 14) of initial margin of stability (MoS) vs change in mediolateral center of pressure during stance (ML ΔCoP) during the adaptation phase. **A)** The black (fast side) or red (slow side) ellipse shows the least squares fit through the group-averaged MoS and ML ΔCoP during the adaptation phase. **B)** The blue ellipses show the least squares fit through the group-averaged MoS and ML ΔCoP during early adaptation (EA), the green and yellow ellipses during late adaptation (LA) for the fast and slow side. The shaded outer ellipses in A and B show the least squares fit through the group-averaged data plus standard error. The Y-axis is magnified with a factor four with respect to the X-axis. Inward ML ΔCoP indicates an inward ML foot roll-off, outward ML ΔCoP an outward ML foot roll-off, zero ML ΔCoP indicates no ML foot roll-off from heel strike to toe-off. Crossing the point of zero MoS indicates dynamic instability. A high MoS indicates dynamic stability. As this figure illustrates a low initial MoS is typically followed by an outward foot roll-off (and vice versa) by which dynamic stability is maintained.

The relationship between adaptive balance control and the reduction of net metabolic power

Figure 3F,L shows an increase in MP_{net} from BL to EA, and a decrease over time from EA to LA. The gait pattern thus changed from relatively energy costly towards a more energy efficient pattern during split-belt adaptation. RM MANOVAs showed that these changes were statistically significant ($p < 0.05$, Table 1). In EP compared with BL there was no significant change in MP_{net} (Figure 3F,L and Table 1). The gait pattern was thus not more energetically costly when the belts returned to symmetrical speeds in comparison to the baseline measurement.

To study whether changes in adaptive balance control and spatiotemporal parameters coincide with a reduction of MP_{net} we performed four linear regression analyses to test whether changes in SLS (Figure 6A), DSS (Figure 6B), fast MoS (Figure 6C), and slow MoS (Figure 6D) were related to the reduction in MP_{net} during split-belt adaptation. No significant linear relationship was found between changes in any of the four parameters and the reduction in MP_{net}. Although gait became more efficient during split-belt adaptation, the amount of change in MP_{net} could not be predicted from the amount of change in dynamic balance control or spatiotemporal parameters.

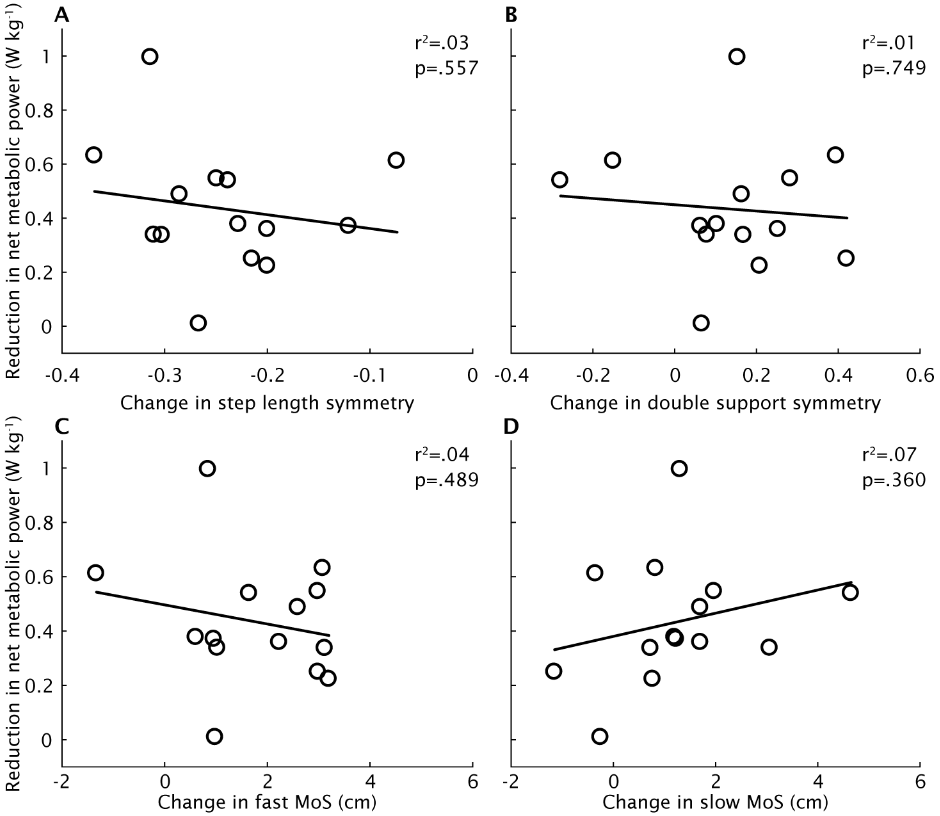

Figure 6 – Group data (N = 14) for the relationship between the reduction in net metabolic power and step length symmetry, double support symmetry, fast margin of stability (MoS), and slow MoS. Solid lines indicate the linear fit through the group data, open circles indicate results for individual participants.

DISCUSSION

Participants adapted metrics of dynamic balance control in response to the imposed gait asymmetry in multiple ways. First, fast and slow MoS were initially high and decreased over time. This shows that adaptations to sustained perturbations imposed by the split-belt treadmill include adaptations in the control of ML dynamic balance. Second, the fast MoS was larger than the slow MoS during split-belt gait, which indicates an interlimb difference in adaptive dynamic balance control. Third, the initial MoS showed a strong correlation with ML ΔCoP. This shows that a complementary mechanism of relative foot positioning and ML foot roll-off controls ML dynamic balance during split-belt adaptation. The secondary aim of this study was to determine whether changes in MP_{net} during split-belt adaptation are related to changes in dynamic balance control. Contrary to our expectations, the changes in MoS were not related to a decrease in MP_{net} during split-belt adaptation.

Dynamic balance control adapts to imposed spatiotemporal gait asymmetry

Our study is the first to examine the adaptive control of ML dynamic balance in split-belt gait. The observations we made on adaptation of spatial and temporal gait symmetry are comparable to results from previous split-belt gait studies [23,43,44]. The present study has shown that the MoS reflects the adaptive capabilities of dynamic balance control in reaction to sustained perturbations in gait. First, both the fast and slow MoS increased in the early adaptation phase, which reflects the disturbance of ML dynamic balance by split-belt gait. Second, fast and slow MoS adapted to split-belt gait and slow MoS showed after-effects when belts returned to symmetrical speeds. These dynamic balance parameters follow over time similar to that of the adaptation of spatial (i.e. SLS) and temporal (i.e. DSS) step parameters to split-belt gait, which suggests that these processes occur in parallel and are possibly governed by a common control mechanism.

Adaptive dynamic balance control shows interlimb difference depending on belt speed

A positive ML MoS is a condition for dynamic stability in gait [9]. In the present study we found that the MoS was positive during split-belt gait, but also asymmetrical between the fast and the slow side, similar to findings by Park and Finley (2017) [27], who found asymmetry in AP MoS in split-belt gait. This indicates a difference in dynamic balance control dependent on belt speed. This difference could be the result of either active control, or an indirect and more passive consequence of the spatiotemporal changes in split-belt gait.

The MoS can be actively controlled by changes in ML foot placement [10]. However, in the present study we did not find any changes in SW throughout the experiment, suggesting that the changes in MoS were not caused by altered ML foot placement. Based on the inverted pendulum model of walking, changes in ML MoS can also be caused by changes in stance time

[10]. A shorter stance time results in reduced pendulum swing time; therefore, there is less time for the CoM to move, which results in a larger MoS. The other way around, increased stance time results in increased pendulum swing time, increasing the time for CoM movement, resulting in a smaller MoS. A shorter stance time results in a higher ML MoS [45], and as stance time becomes shorter with increased gait speed, the MoS will also increase with belt speed. This leads to the question of whether the observed asymmetry in MoS is a result of active control of dynamic balance, or a passive result of spatiotemporal changes in gait (e.g. changes in stance time). In future research, a more rigorous test is necessary to determine whether the changes and asymmetry in MoS during split-belt gait are the result of active control or the passive dynamics in gait.

A complementary mechanism of relative foot positioning and foot roll-off controls ML dynamic balance during split-belt adaptation

To gain further insight in the control of adaptive dynamic balance, we studied the relationship between initial MoS and ML foot roll-off in the gait cycle. This study has shown that the initial MoS and the subsequent change in ML CoP position were strongly correlated. Recent research [12] suggests that ML foot placement and ML foot roll-off are serially coordinated (i.e. one mechanism responds to changes in the other) in the control of dynamic balance, and that without the possibility of ML foot roll-off a wider ML foot placement strategy is necessary to maintain upright balance. In line with this, Hof et al. (2007) showed that individuals who walk with an above-knee prosthetic increase their ML MoS on the affected side to compensate for the lack of ML foot roll-off in an above-knee prosthetic leg. The present study shows that a wider ML foot placement strategy is not necessary to cope with imposed spatiotemporal asymmetry in gait, when ML foot roll-off is available. Furthermore, our results show that the initial MoS and ML foot roll-off are strongly coupled, as shown by the correlational analysis. This complementary mechanism of relative foot positioning and ML foot roll-off showed its flexibility by adapting to split-belt gait. ML foot roll-off is inward in early adaptation, and returned close to baseline values during split-belt adaptation. Although the initial MoS decreased over time during adaptation, the ML ΔCoP increased to maintain stable gait. This shows that a small initial MoS does not necessarily have to result in unstable gait, as the foot roll-off can correct for this. A high initial MoS is followed by an inward foot roll-off. Although this is not necessary to prevent instability, an inward foot roll-off might be necessary to shift the direction of the CoM in time for the next step, or make gait more economical. In short, the complementary mechanism of relative foot positioning and ML foot roll-off presented here represents an active corrective mechanism for maintaining dynamic balance in reaction to sustained perturbations in gait.

Adaptive dynamic balance control is not related to a reduction of metabolic power

The secondary aim of this study was to determine whether adaptive dynamic balance control coincides with a reduction of metabolic power during split-belt adaptation. Dynamic balance control and metabolic power both changed during adaptation to the imposed split-belt perturbation; however, no relationship was found between changes in MoS and changes in MP_{net}. In a recent study [31], a relationship between changes in spatiotemporal step parameters and reduction of metabolic power was found. In contrast, in the present study we were unable to find this relationship. An explanation for this discrepancy is that different speed ratios were used in Finley et al. (2013) (3:1) and the present study (2:1). A higher split-belt ratio might evoke larger gait asymmetry, which could lead to a more distinct change in metabolic power. Two other possible causes for this discrepancy are: (1) the present study used CoP data to compute step length instead of kinematic data, and (2) the adaptation period in the present study was shorter (9 min.) than that in the study by Finley et al. (2013) (12 min). Further research is needed to determine what causes the reduction of metabolic power in split-belt gait and whether this relates to adaptive dynamic balance control.

Implications for adaptive control of human bipedal gait

Human gait is almost unique in its bipedal character and requires control of the distance between ML XCoM and ML foot placement (i.e. relative foot positioning) to maintain dynamic balance. This study has shown a complementary mechanism of relative foot positioning and ML foot roll-off that adapts to a continuously imposed gait asymmetry to maintain dynamic balance. This complementary mechanism shows an asymmetry between the fast and the slow leg in split-belt gait, which suggests that the changes in adaptive dynamic balance control might be the passive result of spatiotemporal changes in gait rather than the active control of balance. Future research should investigate the relationship between dynamic balance control and spatiotemporal control of gait to gain knowledge on adaptive dynamic balance control in human bipedal gait.

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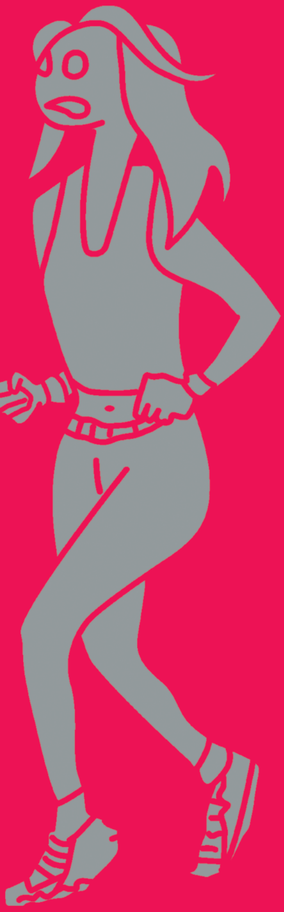

4

BILATERAL TEMPORAL CONTROL DETERMINES MEDIOLATERAL MARGINS OF STABILITY IN SYMMETRIC AND ASYMMETRIC HUMAN WALKING

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ABSTRACT

Human bipedal gait requires active control of mediolateral dynamic balance to stay upright. The margin of stability is considered a measure of dynamic balance, and larger margins are by many authors assumed to reflect better balance control. The inverted pendulum model of gait indicates that changes in the mediolateral margin of stability are related to changes in bilateral single support times. We propose updated equations for the mediolateral margin of stability in temporally symmetric and asymmetric gait, which now include the single support times of both legs. Based on these equations, we study the relation between bilateral single support times and the mediolateral margin of stability in symmetric, asymmetric, and adaptive human gait. In all conditions, the mediolateral margin of stability during walking followed predictably from bilateral single support times, whereas foot placement co-varied less with the mediolateral margin of stability. Overall, these results demonstrate that the bilateral temporal regulation of gait profoundly affects the mediolateral margin of stability. By exploiting the passive dynamics of bipedal gait, bilateral temporal control may be an efficient mechanism to safeguard dynamic stability during walking, and keep an inherently unstable moving human body upright.

INTRODUCTION

Bipedal gait (as seen in humans) is more energy efficient than quadrupedal gait (as seen in most other mammals) [1], but to stay upright it also requires active control of mediolateral dynamic balance [2,3]. During standing, the body centre of mass must be within the base of support to remain stable [4]. During walking, more complex control of balance is required, as the vertical projection of the centre of mass is outside of the base of support most of the time. To arrest the fore- and sideward fall in gait, the velocity of the centre of mass should be taken into consideration [5]. To account for the centre of mass velocity next to its position, the concept of the extrapolated centre of mass has been introduced [6]. According to this concept, to remain upright during walking, the extrapolated centre of mass must remain medial to the centre of pressure of the subsequent step [6]. The minimum distance between extrapolated centre of mass and centre of pressure, known as the margin of stability, is considered a measure of dynamic balance and larger margins are sometimes assumed to reflect a better balance control. Maintaining a constant margin of stability is often seen as an important way of balance regulation in both healthy and impaired human gait [7-9]. In the current study, we show that the temporal regulation of gait has profound effects on the mediolateral margin of stability and plays a key role in the production of stable upright bipedal gait.

The concept of the margin of stability is based on the inverted pendulum model of bipedal gait [4,10]. According to this model, centre of mass movements can be conceptualized as motions of a point mass (representing the centre of mass) on top of a single-segment massless pendulum (representing the stance leg), of which lateral oscillations passively depend on gravitational force and the body's momentum. Bipedal gait can thus be described as a series of controlled falls. Therefore, to understand how humans manage to exploit these falls and stay upright at the same time, we must understand the control of these falling motions.

According to the inverted pendulum model, the mediolateral margin of stability can be modified in two ways. First, through spatial control, i.e. through foot placement or step width regulation [7,9,11], as a wider step results in a larger mediolateral margin of stability. The second way to change the mediolateral margin of stability is through altering the temporal structure of stepping, i.e. modification of the single support time [8]. When single support time decreases, the inverted pendulum, and therefore the centre of mass, has less time to fall to the side before foot placement. In other words, this reduces the lateral sway of the centre of mass. Therefore, when single support time decreases, the extrapolated centre of mass excursion is smaller, the distance between extrapolated centre of mass and base of support increases, resulting in a larger mediolateral margin of stability. The mediolateral margin of stability can thus be increased by widening the step, but also by decreasing single support time. Multiple studies have assessed foot placement in mediolateral margin of stability regulation [7,9,11,12], indicating that foot placement after a perturbation (e.g. sideway pushes) can be predicted from the direction and magnitude of centre of mass position and velocity. To the best of our knowledge, the relation between single support time and mediolateral margin of stability has not been assessed systematically, while this relation can be studied simply by exposing humans to different treadmill belt speeds in order to induce changes in single support time.

The inverted pendulum model indicates that the relation between single support time and the mediolateral margin of stability will change once gait becomes asymmetric. As the mediolateral margin of stability at heel-strike partly depends on the preceding contralateral single support time, it follows that the observed mediolateral margin of stability is not only dictated by ipsilateral single support time, but rather by the relation between ipsilateral and contralateral single support times. If in asymmetric gait, the contralateral single support time is reduced, the mean centre of mass and extrapolated centre of mass positions shift towards the ipsilateral side, resulting in an asymmetric mediolateral margin of stability [8,13]. Understanding the relation between bilateral single support times and the mediolateral margin of stability therefore also requires understanding the effect of asymmetric single support times on mediolateral margin of stability. The properties of this bilateral mechanism will not be evident in symmetric gait, when single support times are approximately equal. However, these properties should emerge when people are forced to walk with asymmetric single support times.

Previously [7], the relation for mediolateral margin of stability b has been described as in Equation 1:

$$b = \frac{w}{e^{\omega_0 T}+1} \tag{1}$$

with the pendulum eigenfrequency $\omega_0 = \sqrt{g/l}$, in which l is leg length, w is step width and T is stance time. From this follows that the mediolateral margin of stability increases with w and decreases with T.

In the case of asymmetric walking, the respective ipsi- and contralateral mediolateral margin of stability b_1 and b_2 are closely related to w and ipsi- and contralateral stance times T_1 and T_2. Based on Hof (2008), for the mediolateral extrapolated centre of mass position ζ we find that:

$$\zeta_1(t) = b_1 e^{\omega_0 t} \text{ for } 0 < t < T_1 \tag{2}$$

$$\zeta_2(t') = w - b_2 e^{\omega_0 t'} \text{ for } 0 < t' < T_2 \text{ and } t' = t - T_1 \tag{3}$$

Now it should hold in steady state gait that:

$$\zeta_1(T_1) = w - b_2 \tag{4}$$

$$\zeta_2(T_2) = b_1 \tag{5}$$

Solving Equations 2 and 3 for conditions 4 and 5 then gives:

$$b_1 = w\frac{(e^{\omega_0 T_2} - 1)}{(e^{\omega_0 (T_1 + T_2)} - 1)} \tag{6},$$

and

$$b_2 = w\frac{(e^{\omega_0 T_1} - 1)}{(e^{\omega_0 (T_1 + T_2)} - 1)} \tag{7}$$

It follows that, the leg with the shortest stance time has the largest margin of stability. These equations seem at variance with the expression for symmetric walking in Equation 1, but if we insert $T_1 = T_2 = T$ in Equations 6 and 7, we find that these new equations are congruent with the expression for symmetric walking (see Equation 1):

$$b_1 = b_2 = w\frac{(e^{\omega_0 T} - 1)}{(e^{2\omega_0 T} - 1)} = \; w\frac{(e^{\omega_0 T} - 1)}{(e^{\omega_0 T} - 1)(e^{\omega_0 T} + 1)} = \frac{w}{(e^{\omega_0 T} + 1)} \tag{8}$$

The question remains whether humans actively exploit the relation between bilateral single support time and mediolateral margin of stability to safeguard dynamic stability. To answer this question, purposeful changes in single support time, made in response to a continuous perturbation of steady state gait should result in predictable changes in the mediolateral margin of stability. A suitable paradigm to test this prediction using a continuous perturbation of gait, is split-belt walking. In split-belt walking, people walk faster with one leg than the other. Healthy humans use self-induced changes in single support time [14,15] and mediolateral margin of stability [13,16] to adapt to these asymmetric belt speeds within 5 - 10 minutes [14]. By letting people walk at asymmetric belt speeds, we can induce asymmetric single support times and empirically test the relation between bilateral single support time and mediolateral margin of stability in symmetric, asymmetric, and adaptive gait.

To better understand dynamic balance control during gait, we empirically test whether mediolateral margin of stability and single support time are systematically related (Experiment A – tied belts), and whether the relation between single support time and mediolateral margin of stability depends on bilateral single support times (Experiment B – split belts). In addition, we assess whether changes in bilateral single support time and step width can predict changes in the mediolateral margin of stability during symmetric walking (Experiment A), asymmetric walking (Experiment B) and split-belt adaptation (Experiment C). Step width will be included in all analyses to be able to distinguish the relative contributions of single support time and step width to the mediolateral margin of stability. We predict that single support time and mediolateral margin of stability are closely related, and that this relationship depends on bilateral single support times, as will be observable in asymmetric gait. Furthermore, we hypothesize that the mediolateral margin of stability essentially depends on step width and bilateral single support times, and can be predicted from these parameters in all three experiments.

METHODS

Healthy young adults (N = 15, 8 females, mean ± s.d. age: 25.1 ± 2.9 years, weight: 75.7 ± 10.7 kg, height: 1.83 ± 0.08 m) participated in this study. Inclusion criteria were (i) no prior experience with split-belt walking, and (ii) the absence of impairments that affect gait. The ethics committee of the Center for Human Movement Sciences, University Medical Center Groningen approved the experiment protocols of this study (ECB/2018.01.15_1). The methods of this study were carried out in line with the Declaration of Helsinki [17]. All participants gave written informed consent prior to the experiments.

Instrumentation

An instrumented split-belt treadmill (Motek, Amsterdam, NL) was used in this study. 3D ground reaction forces (N), moments of force (N m) and 2D centre of pressure positions (m) were measured with two embedded force plates and recorded with D-Flow software (Motek, Amsterdam, NL) at 1000 Hz. Data were analysed in an XYZ coordinate system with the x-axis in forward direction, y-axis in vertical direction, and z-axis in left right direction [18]. All data were stored on an encrypted drive for offline analysis. To secure the participants' safety, they wore a harness that was attached to the ceiling, yet did not provide body weight support or constrain movements. Participants were instructed not to touch the handrails on the sides of the treadmill.

Experimental Protocol

In Experiments A and B, gait speed was manipulated to induce symmetric and asymmetric single support times, as a change in gait speed leads to spontaneous changes in single support times, whereas manipulating single support times through, e.g. metronome pacing may lead to confounding foot strike timing strategies. In Experiment A, participants walked at six different symmetric belt speeds, ranging from 0.50 m s^{-1} to 1.75 m s^{-1}. In Experiment B, participants walked at 5 different asymmetric belt speeds, with the left belt speed fixed at 1.75 m s^{-1} and the right belt speeds ranging from 0.50 m s^{-1} to 1.50 m s^{-1}. In Experiment C, participants were exposed to fast (1.50 m s^{-1}) and slow (0.50 m s^{-1}) tied-belt speeds, a split-belt adaptation phase (1.50 : 0.50 m s^{-1}) and a slow (0.50 m s^{-1}) tied-belt wash-out phase. All conditions are presented in detail in Figure 1.

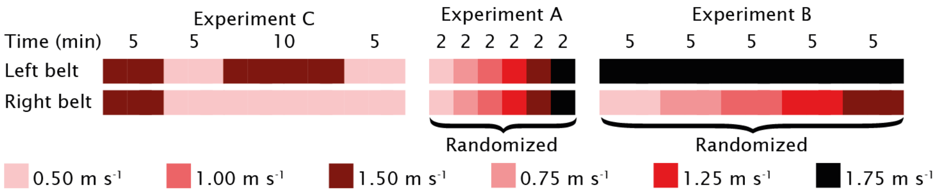

Figure 1 – Experimental protocols for Experiments A (symmetric), B (asymmetric) and C (split-belt adaptation). Upper and lower bars show left and right belt speeds. Belt speeds in Experiments A and B were randomized for each participant to reduce the chance of crossover effects. However, participants first completed Experiment A before moving on to Experiment B**.** Experiment C was measured prior to Experiments A and B to ascertain first-time split-belt adaptation effects. Belt speed was scaled to leg length for each participant.

In all conditions, belt speed was scaled to leg length by multiplying the nominal speed (v) with the square root of leg length (l) [19]; for interpretation in figures, belt speed is shown for a person with a leg length of 1 m. Experiment C was conducted prior to Experiments A and B, to ascertain first-time exposure to split-belt adaptation in Experiment C, and reduce the time required to adapt to subsequent asymmetric gait conditions in Experiment B. There was no rest between trials, therefore speed conditions were randomized between participants in Experiments A and B to avoid potential effects of fatigue, but Experiment A was always completed in full before continuing with Experiment B. Participants received no instructions regarding the duration of phases or upcoming changes in gait speed, and were instructed to look straight ahead during the experiments.

Data analysis

All data were analysed off-line in MATLAB (version r2018b; The MathWorks Inc., Natick, MA, USA). Force plate recordings were filtered with a 15 Hz low-pass second-order zero-phase Butterworth filter. Gait events were detected by finding the point at which vertical ground reaction force crossed a threshold of 50 N. Since data was recorded from two force plates, single force plate ground reaction forces were simulated by summation of left and right force plate ground reaction forces. Single force plate centre of pressure data was calculated by scaling the Centre of Pressure (CoP) of each force plate to the magnitude of its respective vertical Ground Reaction Force (GRF_Y), as shown in Equation 9.

$$CoP_{combined} = \frac{GRF_{Y,left} \times CoP_{left} + GRF_{Y,right} \times CoP_{right}}{GRF_{Y,left} + GRF_{Y,right}} \tag{9}$$

Single support time (s) was defined as the time between contralateral toe-off and contralateral heel-strike, for the left and right leg independently. Step width was defined as the difference between CoP_z (m) position at first and second toe-off in a stride, to match the definition of the mediolateral base of support in the mediolateral margin of stability calculation (see below). The mediolateral centre of mass (CoM) position (m) was calculated by combining the 1) two times high-pass filtered horizontal acceleration of the centre of mass (m s^{-2}) and 2) the low-pass filtered CoP_z position (m) [13,20,21], described in more detail in Buurke et al. (2018) [13]. The mediolateral Extrapolated Centre of Mass (XCoM) position was then calculated as in Equation 10:

$$XCoM = CoM + \frac{vCoM}{\sqrt{g/l}} \tag{10}$$

in which *l* is leg length (m), defined as greater trochanter height multiplied by 1.2 [6].The mediolateral margin of stability (m) was defined as the distance between the mediolateral extrapolated centre of mass position (m) and CoP_z position (m) at contralateral toe-off, and calculated for the left and right leg independently [6,13].

Statistical analysis

Statistical analysis was performed with the MATLAB Statistics and Machine Learning Toolbox (version r2018b; The MathWorks Inc., Natick, MA, USA). Statistical significance was set at an alpha of 5 % for all analyses. For data from Experiments A and B, single support time, step width and mediolateral margin of stability were averaged over the last minute of each condition. The final phase of Experiment A (1.75 m s^{-1} tied-belt) was also used in the analysis of Experiment B to acquire a full range of asymmetric to symmetric belt speeds. For data from Experiment C, single support time, step width and mediolateral margin of stability were averaged into bins of ten seconds.

In Experiments A and B, we examined the relation between single support time and mediolateral margin of stability, and between step width and mediolateral margin of stability. To this end, a Pearson correlation coefficient between single support time and mediolateral margin of stability, and step width and mediolateral margin of stability was calculated for every participant, and for the left and right leg independently, as a score for the relation between these parameters. Then, one-sample Wilcoxon signed-rank tests were used to non-parametrically test whether the group median correlation coefficient was different from zero.

In Experiments A, B and C, we studied whether changes in single support time resulted in predictable changes in mediolateral margin of stability based on the proposed Equations (6 and 7). To this end, individual participant's bilateral single support times and step width from these experiments and the corresponding participant's leg length were entered into Equations 6 and 7. This resulted in a predicted left and right mediolateral margin of stability for each participant and experiment. To quantify prediction quality, group-averaged differences between predicted and measured mediolateral margin of stability were calculated for the left and right leg, in all experiments.

RESULTS

Experiment A – Mediolateral margin of stability and contralateral single support time are strongly related during symmetric walking

In Experiment A we assessed whether single support time and mediolateral margin of stability are related in symmetric walking. Figure 2 shows group-averaged margin of stability (a), single support time (b), step width (c) and measured and predicted group-averaged left (d) and right leg (e) margin of stability vs contralateral single support time. Supplementary Fig. S1 shows step lengths for experiments A, B and C. The average difference ± s.d. between predicted and measured mediolateral margin of stability was 7.4 ± 3.3 mm (left leg) and 7.0 ± 4.4 mm (right leg), indicating a good prediction from the equations, however with an offset (Figure 2). Furthermore, one-sample Wilcoxon signed-rank tests showed that the median correlation coefficients between left single support time and left margin of stability (median r = -0.94, range = -0.39 – -0.99, Z = -3.408, p < 0.001), right single support time and left margin of stability (median r = -0.92, range = -0.33 – -0.98, Z = -3.408, p < 0.001), left single support time and right margin of stability (median r = -0.93, range = -0.64 – -0.99, Z = -3.408, p < 0.001) and right single support time and right margin of stability (median r = -0.94, range = -0.71 – -0.99, Z = -3.408, p < 0.001) were significantly different from zero. These correlation coefficients imply a very strong relationship between bilateral single support times and mediolateral margin of stability in symmetric walking. In addition, one-sample Wilcoxon signed-rank tests showed that the median correlation between step width and margin of stability was not significantly different from zero for the left (median r = -0.23, range = -0.98 – 0.72, Z = -1.022, p = 0.307) and for the right leg (median r = -0.29, range = -0.97 – 0.73, Z = -1.361, p = 0.173), indicating no relation between step width and margin of stability in symmetric walking.

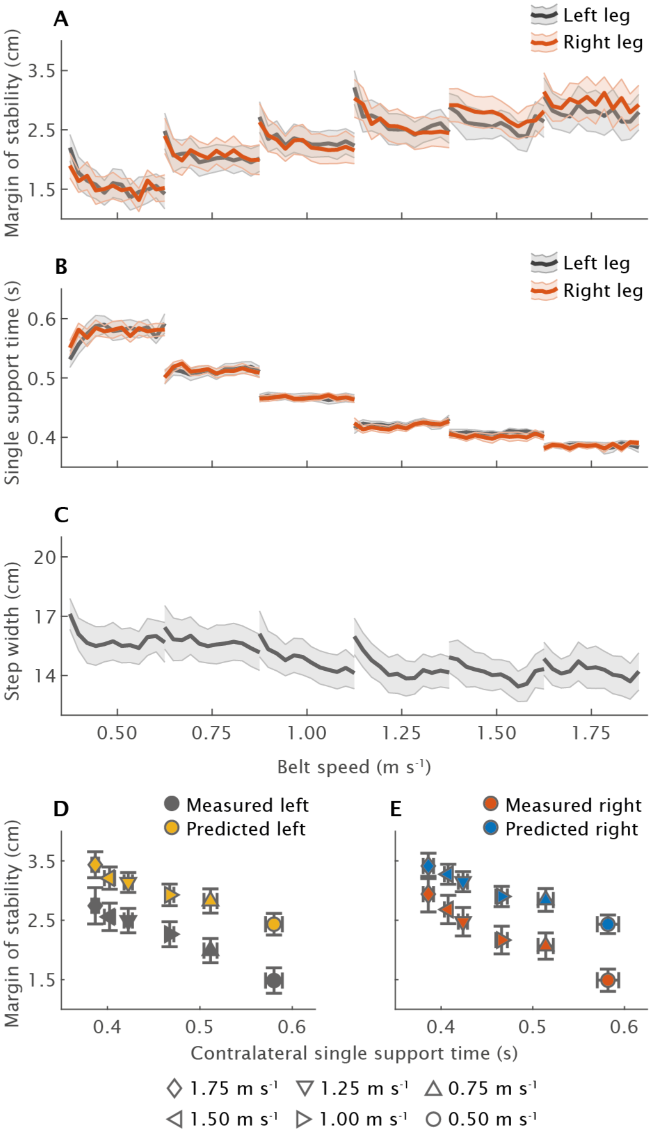

Figure 2 – Group-averaged results (N = 15) of Experiment A. This figure illustrates the relationship between margin of stability and single support time in symmetric walking. Margin of stability **(A)**, single support times **(B)** and step width **(C)** at symmetric belt speeds ranging from 0.50 m s^{-1} to 1.75 m s^{-1}. Shaded areas indicate standard error. Measured and predicted left **(D)** and right **(E)** margins of stability vs contralateral single support times. Error bars indicate standard error. Belt speed was scaled to leg length (v*√l) [19]; for interpretation, belt speed for a person with a leg length of 1 m is shown below the x-axis.

Experiment B – The mediolateral margin of stability depends on bilateral single support times during asymmetric walking

In Experiment B, we assessed the relation between single support time and mediolateral margin of stability in asymmetric gait, to determine whether the mediolateral margin of stability depends on bilateral single support times. Figure 3 shows group-averaged margin of stability (a), single support time (b), step width (c) and measured (d) and predicted (e) mediolateral margin of stability vs single support time for the left and right leg. The average difference ± s.d. between predicted and measured mediolateral margin of stability was 6.0 ± 3.2 mm (left leg) and 5.5 ± 4.5 mm (right leg), indicating a good prediction from Equations 6 and 7 in asymmetric walking. Furthermore, one-sample Wilcoxon signed rank tests showed that the median correlation coefficients between left single support time and left margin of stability (median $r = -0.95$, range = -0.73 – -1.00, $Z = -3.408$, $p < 0.001$), right single support time and left margin of stability (median $r = 0.95$, range = 0.29 – 0.99, $Z = 3.408$, $p < 0.001$), left single support time and right margin of stability (median $r = 0.88$, range = -0.58 – 0.96, $Z = 3.237$, $p = 0.001$), and right single support time and right margin of stability (median $r = -0.95$, range = -0.04 – -0.99, $Z = -3.408$, $p < 0.001$) were significantly different from zero. This indicates a strong relation between bilateral single support times and mediolateral margin of stability in asymmetric gait. In addition, one-sample Wilcoxon signed rank tests showed a significant positive relationship between step width and left margin of stability (median $r = 0.92$, range = 0.31 – 0.98, $Z = 3.408$, $p < 0.001$) and negative relationship between step width and right margin of stability (median $r = -0.64$, range = -0.96 – 0.65, $Z = -2.442$, $p = 0.015$) in asymmetric walking, indicating a moderate to strong relationship between step width and mediolateral margin of stability in asymmetric walking.

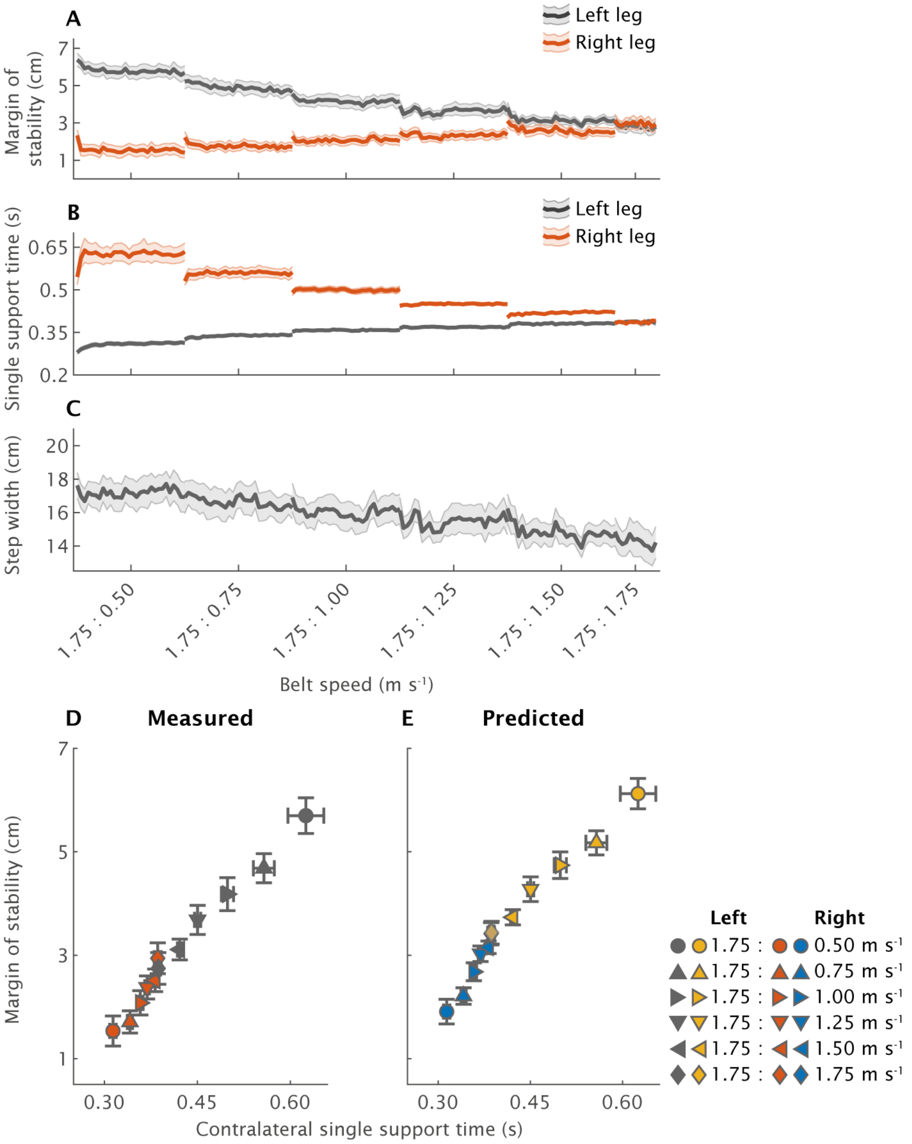

Figure 3 – Group-averaged results (N = 15) of Experiment B. This figure illustrates the bilateral relationship between margin of stability and single support time and the good quality of the predictions during asymmetric walking. Margin of stability **(A)**,single support times **(B)** and step width **(C)** at asymmetric belt speeds, with the left belt speed set at 1.75 m s^{-1} and right belt speeds ranging from 0.50 m s^{-1} to 1.75 m s^{-1}. Shaded areas around the lines indicate standard error. Measured **(D)** and predicted **(E)** left and right leg margin of stability vs contralateral single support time at all asymmetric conditions. Error bars indicate standard error. Belt speed was scaled to leg length (v*√l) [19]; for interpretation, belt speed for a person with a leg length of 1 m is shown below the x-axis.

Experiment C – The mediolateral margin of stability depends on bilateral single support times and step width during split-belt adaptation

In Experiment C, we assessed whether humans exploit the relation between single support time and mediolateral margin of stability to safeguard dynamic stability. To this end, mediolateral margin of stability was predicted from bilateral single support times and step width during split-belt adaptation (see Equations 6 and 7). Figure 4 shows the group-averaged mediolateral margin of stability (a), single support time (b), step width (c) and the observed and predicted bilateral mediolateral margin of stability adaptation curves (d, e). The group-averaged difference ± s.d. between predicted and measured mediolateral margin of stability was 5.0 ± 2.0 mm (left margin of stability) and 4.2 ± 2.8 mm (right margin of stability). This indicates a good prediction of the mediolateral margin of stability and shows that the purposeful changes in bilateral single support times and step width during split-belt adaptation result in predictable changes in the mediolateral margin of stability.

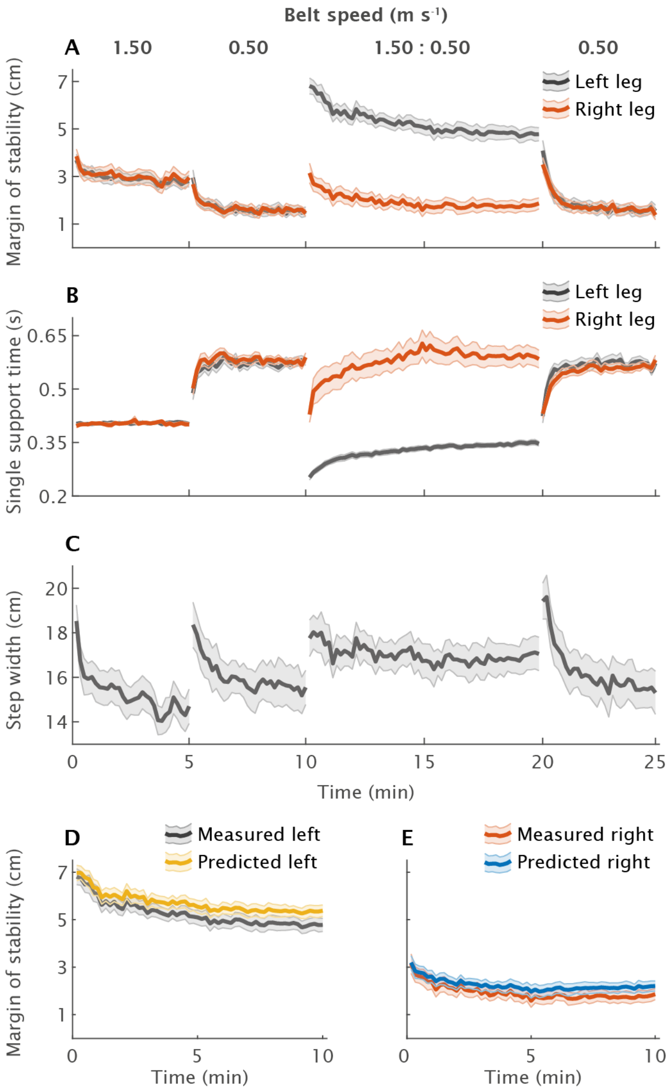

Figure 4 – Group-averaged results (N = 15) of Experiment C. Shaded areas around the lines indicate standard error. **(A)** Margin of stability, **(B)** single support times and **(C)** step width during fast (1.50 m s-1) and slow (0.50 m s-1) baseline gait, split-belt adaptation (1.50 : 0.50 m s-1) and washout (0.50 m s-1). Left **(D)** and right **(E)** leg, measured and predicted margin of stability adaptation curves are shown. Panels D & E indicate that left and right leg margin of stability adaptation curves can be predicted from bilateral single support times and step width. Belt speed was scaled to leg length (v*√l) [19]; for interpretation, belt speed for a person with a leg length of 1 m is shown above panel A.

DISCUSSION

The margin of stability is a well-known measure for dynamic balance control. The inverted pendulum model indicates that changes in the mediolateral margin of stability are related to changes in the temporal regulation of gait, however it is unclear how the margin of stability is regulated. In the present study, we predicted (Equations 6 and 7) and empirically investigated the relation between single support time, step width and mediolateral margin of stability, in symmetric, asymmetric, and adaptive human gait. The results of three present experiments show that during unperturbed gait on a split-belt treadmill, temporal control has a strong influence on the mediolateral margin of stability. According to theory (Equations 6 and 7), step width is also a determining factor, but step width was not manipulated in the present study. Furthermore, the mediolateral margin of stability depends on changes in bilateral instead of unilateral single support times. Finally, based on the adjustment of adding bilateral single support times in Equations 6 and 7 for the mediolateral margin of stability, we were able to accurately predict mediolateral margin of stability from bilateral single support times and step width in symmetric, asymmetric and adaptive split-belt walking.

It follows from the inverted pendulum model that changes in bilateral single support times correspond predictably with changes in mediolateral margin of stability. Our results show that when single support time increases in symmetric gait, the mediolateral margin of stability decreases. Previously, it has been suggested that the mediolateral margin of stability is related to ipsilateral single support time or step frequency [8,22]. However, the new Equations 6 and 7, and results show that the mediolateral margin of stability depends on both the ipsi- and contralateral, i.e. bilateral, single support times. The addition of bilateral single support times to this model allows a more comprehensive understanding of the control of the mediolateral margin of stability during symmetric and asymmetric human walking. In addition, when people purposefully changed their single support times in response to split-belt adaptation, we accurately predicted changes in mediolateral margin of stability from these bilateral single support times and step width based on Equations 6 and 7. Therefore, the adaptation of mediolateral margin of stability as reported previously during split-belt walking [13], can be interpreted as the biomechanical result of changes in the spatiotemporal stepping patterns in gait.

The results show that the mediolateral margin of stability strongly relates to bilateral single support times. Although this behaviour follows directly from the passive properties of the inverted pendulum model, this does not exclude that humans may exploit this relation purposefully to maintain dynamic stability. Humans can intentionally change the temporal structure of gait through, for instance, changes in cadence [23] or swing speed [15], thereby regulating balance control. For instance, people tend to make short, quick steps when balance is challenged, e.g. when walking in a moving train or on a rocking boat. Furthermore, active control is always required in response to perturbations, external or self-generated [24]. Active exploitation of these passive properties may be even more prominent in impaired populations.

Because even though walking with asymmetric single support times is uncommon and energy-costly in healthy humans [25], it features prominently in populations with asymmetric leg properties, such as people with a prosthesis or hemiparesis. Humans with problematic stability have possibilities to increase their mediolateral margin of stability: by taking wider steps, or, in the case of asymmetric impairment (e.g. a prosthesis [8] or hemiparesis [26]), by shortening stance time of the impaired leg. Such an increase margin of stability in itself does not provide better stability, but it gives better opportunities to correct balance, e.g. by action of the unimpaired leg. While people with post-stroke hemiparesis show similar single support times on the non-paretic side as healthy humans at equal gait speeds, they typically show a lower single support time on the paretic side [27]. This may be a direct result of reduction in muscle force production, but can also represent a timing-based strategy to safeguard mediolateral dynamic balance on the paretic side. The latter idea is supported by a study in which it was shown that when people post-stroke lower their gait speed in response to lateral perturbations, they keep their step frequency at the same level as before the perturbation [22], thereby safeguarding their mediolateral margin of stability. Thus, although the results of the present study show that large variations in the mediolateral margin of stability can be the passive result of changes in the temporal structure of gait, humans might still exploit this relationship to maintain dynamic stability.

Foot placement, as evaluated with step width, played a marginal role in the here observed variations in mediolateral margin of stability during symmetric walking in experiment A. During steady state gait, the possibilities to alter foot placement are limited, as increases in step width may induce higher energy costs associated with step-to-step transitions and lateral limb excursion [28]. In general, foot placement strategies may play a more prominent role when sudden, unexpected perturbations require a balance response under time-critical conditions. Under these circumstances, it may take one or two steps to decelerate the centre of mass through changes in single support time, which is too slow to respond adequately to perturbations such as slips [29] or pushes [9]. In contrast, deceleration of the centre of mass by means of foot placement is possible within a single step. In the current study, the influence of single support time on the mediolateral margin of stability is highlighted. There is also an effect of step width on the mediolateral margin of stability, but as the experimental results show (Figures 2, 3, 4), step width did not vary a lot in these experimental conditions. To determine the effect of step width on the mediolateral margin of stability, a different experimental set-up is necessary. It is important to note that no discrete perturbations (e.g. pushes or pulls) were applied in the present study, making employment of mediolateral foot placement strategies less likely. In addition, walking on a split belt treadmill, either in tied-belt [30] or split-belt mode [13], is associated with large step widths (approximately 17 cm in Experiment C), which limits the possibilities to utilize lateral foot placement for balance modifications and may mask the role of foot placement in this study compared to single-belt treadmill or over-ground walking. Furthermore, in the current study we neglected the role of mediolateral foot roll-off, i.e. centre of pressure displacement within the base of support during single stance [8,13,24,31]. The mediolateral foot roll-off may explain the small discrepancy between the measured and predicted mediolateral margin of stability in the current study as it defines the mediolateral base of support during single stance. To be able to assess the effect of single support time on the mediolateral margin of stability, the mediolateral margin of stability had to be defined at a discrete point in the gait cycle, in this case the start of the single support. However, it can be expected that the foot roll-off may be actively used to fine-tune deviations from the average margin of stability during stance [8,13,24,31]. In future work this can be studied, to better understand dynamic balance control throughout the gait cycle.

Originally, Hof (2008) suggested that maintaining a constant margin of stability results in stable gait. Although this holds for simulations of gait and would likely result in stable gait in humans as well, our results show that margin of stability constancy is not a requirement for stable human gait, as large variations in mediolateral margin of stability emerge predictably from changes in bilateral single support times during the experiments. Because the mediolateral margin of stability depends on bilateral single support times, inter-limb temporal coordination is crucial for maintaining mediolateral dynamic stability. This temporal regulation may be controlled by relatively simple networks in the spinal cord [32], so that regulation of dynamic stability through temporal control of gait requires minimal contribution of higher-order supra-spinal control. It can be argued that humans maintain dynamic stability through both temporal and spatial control of gait. The step width is then optimized to an energetic optimum [28], while changes in single support time are exploited to regulate the mediolateral margin of stability in unperturbed gait.

Human bipedal gait requires active control of mediolateral balance to remain stable [2] and the (magnitude of the) mediolateral margin of stability is often considered a measure of dynamic stability. This study shows that the mediolateral margin of stability during unperturbed symmetric, asymmetric, and adaptive gait follows predictably from bilateral single support times and step width. The relation between bilateral single support times and mediolateral margin of stability is especially of interest, as it is often neglected and suggests passive regulation of balance, although this relation may still be actively exploited by humans to maintain dynamic stability. These findings should be considered in future studies on dynamic balance control in both healthy and pathological populations. In conclusion, bilateral temporal regulation forms an important mechanism to exploit the passive dynamics of bipedal gait, in order to keep an inherently unstable moving human body upright, with minimal explicit control.

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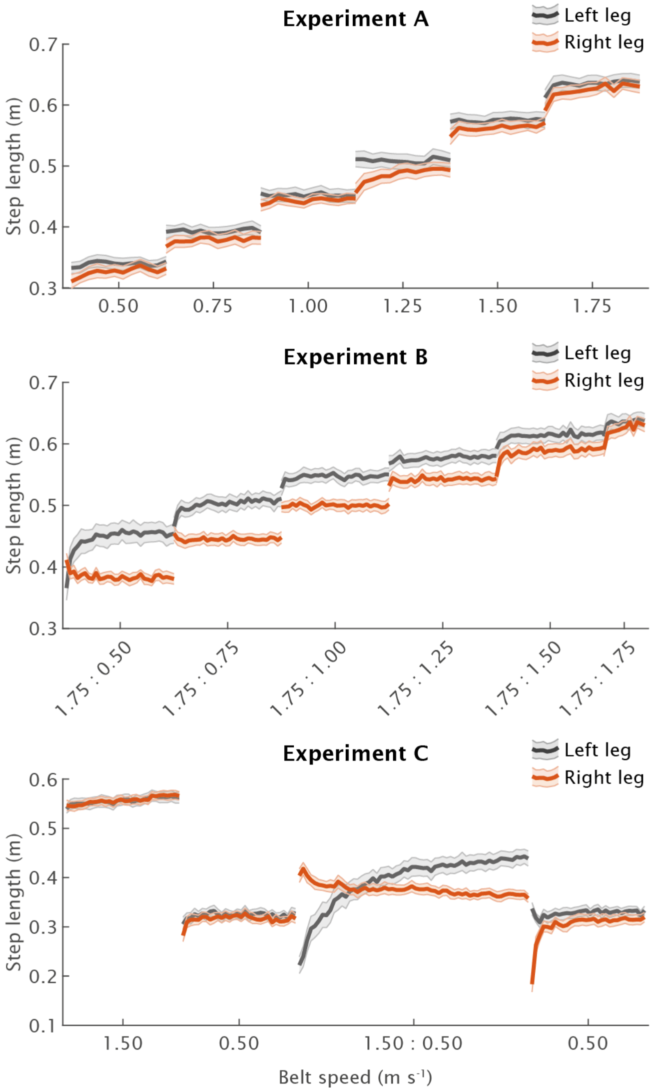
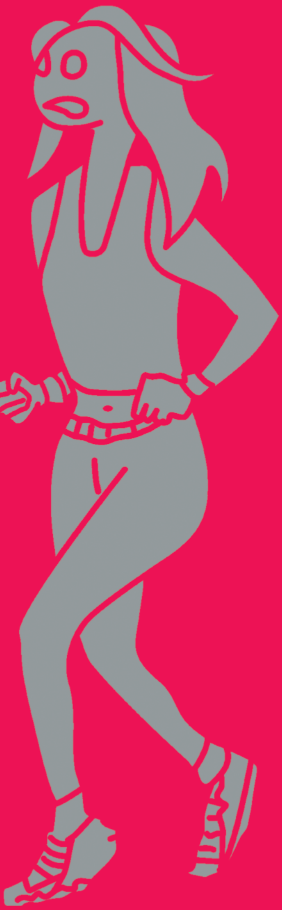
SUPPORTING INFORMATION



Supplementary Figure S1 – Group-averaged step lengths (N = 15) of all experiments. Shaded areas around the lines indicate standard error.



5

HANDRAIL HOLDING DURING TREADMILL WALKING REDUCES LOCOMOTOR LEARNING IN ABLE-BODIED PERSONS

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ABSTRACT

Treadmills used for gait training in clinical rehabilitation and experimental settings are commonly fitted with handrails to assist or support persons in locomotor tasks. However, the effects of balance support through handrail holding on locomotor learning are unknown. Locomotor learning can be studied on split-belt treadmills, where participants walk on two parallel belts with asymmetric left and right belt speeds, to which they adapt their stepping pattern within a few minutes. The aim of this study was to determine how handrail holding affects the walking pattern during split-belt adaptation and after-effects in able-bodied persons. Fifty healthy young participants in five experimental groups were instructed to hold handrails, swing arms freely throughout the experiment or hold handrails during adaptation and swing arms freely during after-effects. Step length asymmetry and double support asymmetry were measured to assess the spatiotemporal walking pattern. The results showed that holding handrails during split-belt adaptation reduces magnitude of initial perturbation of step length asymmetry and reduces after-effects in step length asymmetry upon return to symmetric belt speeds. The findings of this study imply that balance support during gait training reduces locomotor learning, which should be considered in daily clinical gait practice and future research on locomotor learning.

INTRODUCTION

Relearning to walk is an important aspect of rehabilitation after traumatic injury, as it increases a person's mobility and functioning, and thereby quality of life [1]. Locomotor learning, i.e. (re-)learning a gait task, is often done on a treadmill, allowing for longer walking sessions with more step repetitions. The addition of handrails to a treadmill allow a person to walk more safely but without the need of a walking aid or a therapist's physical support. Consequently, holding handrails enables people to start locomotor rehabilitation early, and facilitates treadmill waking for people with impaired gait function [2]. In treadmill walking post-stroke, handrail holding reduces step width and lower leg muscle co-activation, while it increases step lengths [3]. This suggests that balance support immediately enhances walking performance. However, research indicates that provision of external support or guidance in a motor learning task may ultimately reduce motor learning [4,5]. For instance, in a beam-walking experiment with a physically guided and an unguided group, the unguided group showed greater improvements than the group that received physical guidance [5]. Similarly, when behavioral performance during the learning of a visuomotor rotation task is optimized by providing full haptic guidance, the resultant learning is substantially smaller than during unguided learning [4]. This indicates that external support may decrease locomotor learning. However, the effects of balance support through handrail holding on learning a locomotor task are currently unknown [6].

A suitable paradigm to study locomotor learning in a controlled environment is split-belt treadmill walking [7,8]. During split-belt walking people are exposed to asymmetric left and right belt speeds, by which they are initially perturbed, and in response to which they adapt their step lengths, double support times [8] and balance control [9,10]. After approximately ten minutes of split-belt walking, the perturbation is removed by setting the belts at symmetric belt speeds. In this washout phase, after-effects in stepping parameters are observed in the opposite direction of the adaptations of stepping parameters that were observed in the initial split-belt phase [8]. These after-effects are considered indicative of locomotor learning [11]. Previous research has shown that split-belt walking may enforce changes in balance control [9,10,12,13]. Holding on to handrails stabilizes the body, as it increases the base of support, allows the generation of corrective forces [14], and increases somatosensory input through touch of the handrails [15]. Arguably, in split-belt walking side-mounted handrails can provide balance support by allowing the participant to slightly lift him/herself of the treadmill by pushing on the handrails with both arms, whereas front-mounted handrails may stabilize the participant by pushing and pulling the handrails to alter braking forces [16] and reduce fore-aft angular momentum [17]. This makes it easier to control dynamic balance, thereby reducing the perturbation effect of split-belt walking. By assessing how handrail holding affects split-belt adaptation and after-effects, we can empirically test if and how the imposed balance support affects locomotor learning.

The aim of this study is to determine how handrail holding affects locomotor learning during split-belt adaptation and after-effects in able-bodied persons. To appreciate the variety of handrails used in different gait laboratories and clinics, we assess one group holding handrails on the lateral sides of the treadmill, and one group holding handrails mounted on the front of the treadmill. To control for the possibility that differences between handrail holding and unsupported walking are due to a lack of arm swing rather than balance support, we assess an extra group in which arm swing is restrained. We hypothesize that holding on to handrails will reduce the perturbation of gait symmetry in early split-belt walking. In addition, we hypothesize that handrail holding will reduce locomotor learning, as visible by reduced after-effects in gait symmetry upon return to tied-belt walking (washout phase) [11]. To control for the possibility that the hypothesized lack of after-effects in the groups that hold on to handrails is due to balance support in the washout phase rather than reduced locomotor learning, we assess a fifth group. This group will hold handrails during split-belt adaptation, but not during the washout phase. We hypothesize that this group will also show reduced after-effects in gait symmetry during the washout phase.

METHODS

Participants and ethics statement

Fifty healthy young adults participated in this study and were assigned to five height-matched groups (to reduce confounding effects of leg length or body height [18]), which differed in the type of handrail support or no support. The participant characteristics are shown in Table 1. Participants were excluded from the study if they had prior experience with split-belt walking, or if they had any known impairments that may affect gait. The procedures of this study were approved by the ethics committee of the Center for Human Movement Sciences, University Medical Center Groningen, the Netherlands (ECB/2018.01.15_1), and were in line with the Declaration of Helsinki [19]. Participants gave written informed consent prior to the experiment.

Table 1 – Participant characteristics.

Group	N (males)	Age (years)	Height (m)	Weight (kg)
Side	10 (5)	21.7 ± 1.7	1.80 ± 0.11	69.8 ± 11.8
Front	10 (5)	22.4 ± 2.0	1.82 ± 0.10	72.3 ± 13.9
Control	10 (5)	21.8 ± 1.7	1.79 ± 0.08	65.2 ± 10.5
Restrained arms	10 (5)	23.6 ± 2.8	1.82 ± 0.13	73.6 ± 13.6
Switch	10 (5)	22.3 ± 1.3	1.80 ± 0.06	70.5 ± 08.8

Experimental protocol

Participants were assigned to five different groups and instructed to: Move their arms freely (Control group); Hold handrails mounted on the lateral sides of the treadmill (Side group); Hold handrails mounted on the front of the treadmill (Front group); Cross their arms across the chest (Restrained arms group); Hold handrails mounted on the lateral sides of the treadmill during baseline and split-belt adaptation, and move their arms freely during washout (Switch group). In the Switch group, the experimenter counted down from five during the last five seconds of the adaptation phase, after which participants had to let go of the handrails, exactly on the transition from split-belt to tied-belt walking.

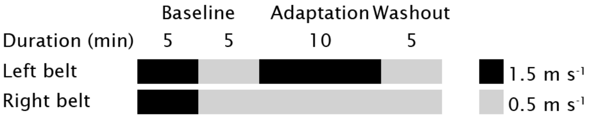

Figure 1 – Split-belt treadmill protocol. The upper bar shows left belt speed, the lower bar shows right belt speed. Phase name and duration are shown above the bars. All groups walked the same treadmill protocol.

All groups completed the same treadmill walking protocol (Figure 1). Participants walked five minutes fast tied-belt baseline (1.5 $\mathrm{m\ s^{-1}}$), five minutes slow tied-belt baseline (0.5 $\mathrm{m\ s^{-1}}$), ten minutes split-belt adaptation (1.5 : 0.5 $\mathrm{m\ s^{-1}}$), and five minutes slow tied-belt washout (0.5 $\mathrm{m\ s^{-1}}$) [8,20,21]. Participants were instructed to look straight ahead and were not informed about the duration of phases or changes in belt speed. Participants' gazing behavior was monitored during the experiment and corrected if necessary. For safety, participants wore a harness that was attached to the ceiling; however, this did not provide body weight support or restrain movement.

Data acquisition

Participants walked on an instrumented split-belt treadmill (Motek, Amsterdam, NL). Embedded force plates measured 3D ground reaction forces (N) and 2D Center of Pressure (CoP) positions (m). Data were recorded with D-Flow software (Motek, Amsterdam, NL) at 1000 Hz and saved on an encrypted drive for off-line analysis.

Data analysis

All analyses were performed in MATLAB (version r2018b, The MathWorks Inc., Natick, MA, USA). Ground reaction forces and CoP data were filtered with a 15-hz 2nd order Butterworth filter. Gait events were defined as the point at which the vertical ground reaction force crossed a threshold of 50 N. Step length (m) was defined as the difference in fore-aft CoP position at heel-strike. Double support time (s) was defined as the period between ipsilateral heel-strike and contralateral toe-off. To assess spatiotemporal gait symmetry, Step Length Asymmetry (SLA) and Double Support Asymmetry (DSA) were calculated using Equations 1 and 2 [8].

$$SLA(i) = \frac{Step\ length_{left}(i) - Step\ length_{right}(i)}{Step\ length_{left}(i) + Step\ length_{right}(i)} \tag{1}$$

$$DSA(i) = \frac{Double\ support\ _{first}(i) - Double\ support\ _{second}(i)}{Double\ support\ _{first}(i) + Double\ support\ _{second}(i)} \tag{2}$$

Statistical analysis

Statistical analysis was performed in IBM SPSS Statistics for Windows (Version 24, 64-bit edition, IBM Corporation, Armonk, NY, USA). Statistical significance was set at an alpha of 5 %. Step length asymmetry and double support asymmetry were averaged over the last 10 steps of baseline, first 10 steps of adaptation (early adaptation), last 10 steps of adaptation (late adaptation) and first 10 steps of washout (after-effects). The individual average baseline value was subtracted from early adaptation, late adaptation and after-effects for each participant for statistical analysis to control for baseline differences, from here on indicated as Δ. A MANOVA with two dependent variables (baseline step length asymmetry and baseline double support asymmetry), and between-subjects factor Group (Control, Side, Front, Restrained arms, Switch) was conducted to test whether the five groups differed from one another during baseline walking. To examine whether the Side, Front, Restrained arms and Switch groups differed from the Control group during early adaptation, late adaptation and after-effects, we performed a MANOVA. The MANOVA had two dependent variables 1) step length asymmetry and 2) double support asymmetry, in three phases relative to baseline (Δ) 1) Δ early adaptation, 2) Δ late adaptation and 3) Δ after-effects, resulting in six variables for statistical testing (two variables in three relative phases). The between-subjects factor Group had five levels: Control, Side, Front, Restrained arms and Switch. If multivariate results were significant, one-sided Dunnett's tests were assessed to compare each of the six dependent variables of the Side, Front, Restrained arms and Switch group to the Control group.

RESULTS

No significant main effect of Group on baseline step length asymmetry and baseline double support asymmetry was found (F (8,90) = 0.584, p = 0.788, $\eta^2 = 0.049$). A significant main effect of Group on step length asymmetry and double support asymmetry in Δ early adaptation, Δ late adaptation and Δ after-effects was found (F (24, 172) = 2.249, p = 0.001, $\eta^2 = 0.239$), therefore Dunnett's test were assessed (Table 2). Group averaged time-series and boxplots are shown in Figure 2, individual data of Figure 2 panels B and D are shown in supplementary files.

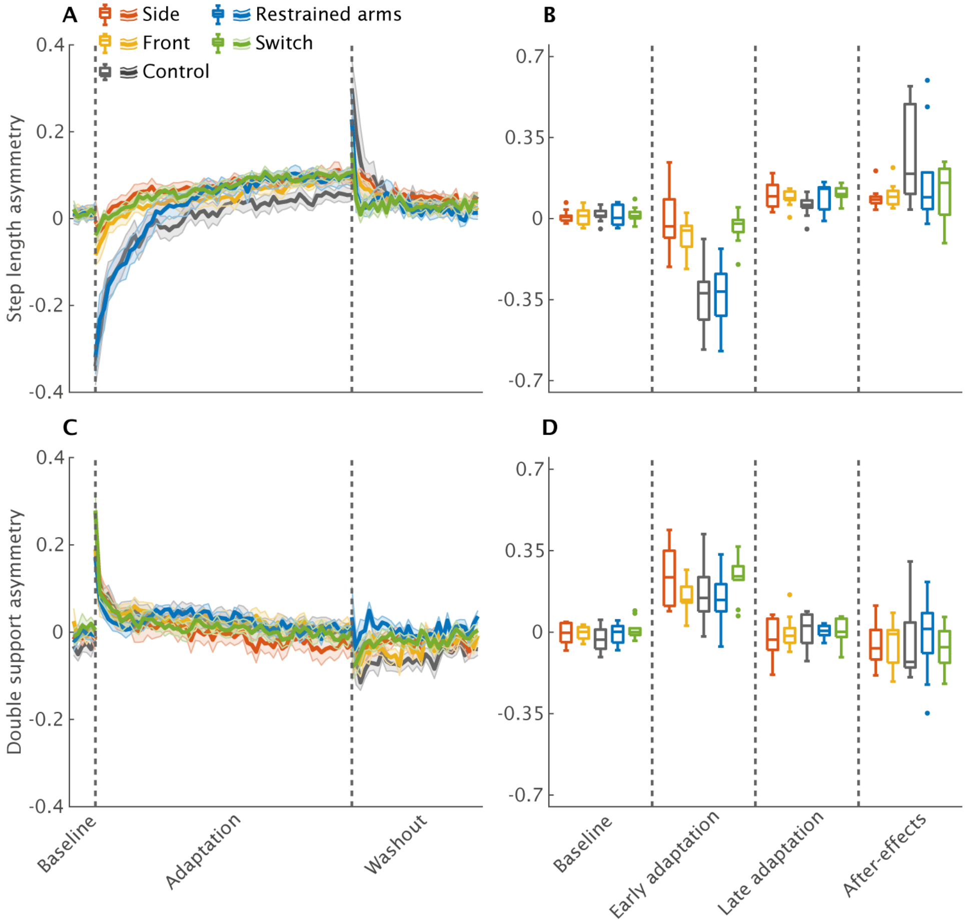

Figure 2 – Group averaged step length asymmetry (A,B) and double support asymmetry (C,D) for the Side (N = 10), Front (N = 10), Control (N = 10), Restrained arms (N = 10) and Switch (N = 10) Groups. **A, C)** Group averaged time-series for the baseline phase (final minute), adaptation phase (10 minutes) and washout phase (5 minutes). Dotted vertical lines indicate transition from one phase to the next. Shaded areas indicate standard error. **B, D)** Boxplots of the 10 step bins that were used for statistical analysis. Individual data points of panels B and D are shown in supplementary files.

Table 2 – Dunnett's tests results of step length asymmetry and double support asymmetry of all phases relative to baseline (Δ), for all groups compared to the Control group.

	Step length asymmetry			**Double support asymmetry**		
Group	**Δ Early adaptation**	**Δ Late adaptation**	**Δ After-effects**	**Δ Early adaptation**	**Δ Late adaptation**	**Δ After-effects**
Side	**p < 0.001**	p = 0.058	**p = 0.011**	p = 0.231	p = 0.984	p = 0.740
Front	**p < 0.001**	p = 0.132	**p = 0.020**	p = 0.911	p = 0.908	p = 0.714
Restrained arms	p = 0.723	p = 0.061	p = 0.195	p = 0.934	p = 0.879	p = 0.889
Switch	**p < 0.001**	p = 0.073	**p = 0.026**	p = 0.418	p = 0.957	p = 0.442

The effects of handrail holding on perturbation magnitude during early split-belt adaptation

First, we assessed whether handrail holding affects the perturbation magnitude of gait symmetry during early split-belt adaptation. To this end, we tested whether step length asymmetry and double support asymmetry during Δ early adaptation in the Side, Front, Restrained arm and Switch groups differed from the Control group. The results (Figure 2 and Table 2) show a significantly smaller step length asymmetry in Δ early adaptation in the Side ($p < 0.001$), Front ($p < 0.001$) and Switch ($p < 0.001$) groups, but not in the Restrained arms compared to Control group ($p = 0.723$). No differences were found in double support asymmetry for the Side ($p = 0.231$), Front ($p = 0.911$), Restrained arms ($p = 0.934$) and Switch ($p = 0.418$) groups compared to the Control group. These results indicate that handrail holding significantly decreases the perturbation magnitude of step length asymmetry, but not double support asymmetry during early adaptation.

The effects of handrail holding during late split-belt adaptation

Second, we assessed whether handrail holding affects the level of gait symmetry during late split-belt adaptation. Therefore, we tested whether step length asymmetry and double support asymmetry in Δ late adaptation for the Side, Front, Restrained arms and Switch groups differed from the Control group. The results (Figure 2 and Table 2) show no significant difference in step length asymmetry in Δ late adaptation in the Side ($p = 0.058$), Front ($p = 0.132$), Restrained arms ($p = 0.061$) and Switch ($p = 0.073$) groups compared to the Control group. No significant differences were found in double support asymmetry for the Side ($p = 0.984$), Front ($p = 0.908$), Restrained arms ($p = 0.879$) and Switch ($p = 0.957$) groups compared to the Control group. This indicates that holding handrails does not affect spatiotemporal gait symmetry during late split-belt adaptation.

The effects of handrail holding on after-effects during washout

Finally, we assessed whether handrail holding reduces locomotor learning. Therefore, we tested whether the magnitude of Δ after-effects in step length asymmetry and double support asymmetry in the Side, Front, Restrained arms and Switch groups differed from the Control group. The results (Figure 2 and Table 2) show significantly smaller after-effects in step length asymmetry for the Side ($p = 0.011$), Front ($p = 0.020$) and Switch ($p = 0.026$) groups, but not the Restrained arms group ($p = 0.195$) compared to the Control group. No differences were found in double support asymmetry for the Side ($p = 0.740$), Front ($p = 0.714$), Restrained arms ($p = 0.889$) and Switch ($p = 0.442$) groups compared to the Control group. This indicates that handrail holding decreases after-effects in step length asymmetry, which indicates that handrail holding reduces locomotor learning.

DISCUSSION

In both clinical and experimental settings, treadmills are often equipped with handrails to support a person during gait training. However, the effects of handrail holding on locomotor learning are unknown. Here, we determined how handrail holding affects split-belt adaptation and after-effects in able-bodied persons. Although the groups in this study had a small sample-size (N = 10), the results unambiguously show that holding handrails during split-belt adaptation reduces the perturbation magnitude of spatial, but not temporal gait symmetry. Furthermore, upon return to tied-belt walking, i.e. during washout, no after-effects in spatial gait symmetry were observed in the groups that held on to handrails. These results were not due to a lack of arm swing, or balance support in the washout phase. This indicates that balance support simplifies the task of split-belt adaptation, as seen in early adaptation, and thereby reduces locomotor learning, as seen by the lack of after-effects in washout.

Balance support reduces locomotor learning

Motor learning occurs when long-lasting adjustments in movement control are made in response to discrepancies between intended and actual task performance [22,23]. During split-belt walking, a control problem emerges because of an inefficient, asymmetric gait pattern [9,20]. This study shows that altered balance demands are an important aspect of this control problem, as the asymmetry that is typically seen in early split-belt adaptation [8,9,20] was reduced when participants were externally supported. Arguably, external support altered the task demands or simplified the task of split-belt walking, as seen by the reduced perturbation magnitude during early split-belt walking in the supported groups. In addition, continuous exposure to split-belt walking resulted in a marginal change in step length asymmetry over time in supported groups compared to the Control and Restrained Arms groups, although this could also be due to the reduced initial perturbation in the supported groups. This indicates that the amount of adaptation was reduced in the supported groups. The consequences for locomotor learning became clear upon return to tied-belt walking, when the magnitude of after-effects in the supported groups was substantially lower than in the Control group. These findings are in line with previous work on upper extremity motor learning, where the authors showed that assistance through haptic guidance in a visuomotor task directly enhanced performance, and reduced visuomotor adaptation [4]. In the current study, this suggests that groups with the largest control problem during early adaptation, i.e. the Control and Restrained arms groups, also show the largest changes in locomotor control, which enhances locomotor learning [11].

Implications for split-belt adaptation studies

The split-belt adaptation paradigm has inspired many locomotor learning and adaptation studies, with multiple studies using different set-ups [7-9,20,21,24-34]. For a better understanding of locomotor control and learning, we need to be able to compare and interpret results from different studies, and therefore research methodologies. The current study shows that handrail holding reduces the adaptation and after-effects of step length asymmetry in split-belt walking. For a good assessment of split-belt adaptation, handrail holding should be avoided or restricted throughout the experiment, provided that a participant's balance control is sufficient for unsupported walking. Furthermore, it can be argued that it should always be mentioned whether participants were allowed or instructed to hold on to handrails, and if not, how they held their arms. It should be noted that in the current study all five experimental groups show a positive step length asymmetry in late adaptation, as noted before [35]. Recent work explains this phenomenon by showing that split-belt walking with asymmetric step lengths is more mechanically efficient than symmetric step lengths, as participants learn to take advantage of the asymmetric belt speeds [36]. Finally, holding on to handrails may not only provide external balance support, but also change the kinetics of split-belt walking, i.e. participants may generate different kinetic walking patterns when split-belt walking, which should be taken into account in future work.

The role of arm swing in locomotor adaptation

The reduced perturbation magnitude and lack of after-effects in the stabilized groups were not due to a lack of arm swing in this study, as shown by the Restrained arms group. Research has shown that arm movement is coupled to contralateral leg movement in symmetric and asymmetric human walking [37], and that restraining elbow movements in split-belt walking changes inter-limb temporal coordination [38]. The effect of arm movement on dynamic stability in human gait is the theme of an ongoing discussion [39]. Some authors argue that that arm swing enhances dynamic stability [40], whereas others argue that arm swing is a passive movement that does not affect dynamic stability [41,42]. If arm swing were to enhance dynamic stability in the current study, one would expect the Restrained arms group to show larger step length asymmetries than the Control group during early split-belt adaptation and after-effects. However, the Restrained arms group did not differ from the Control group in any of these phases.

Inter-limb temporal gait symmetry is not affected by balance support

The present results provide clear evidence that external support of dynamic balance selectively affects the spatial, but not the temporal characteristics of stepping on a split-belt treadmill. While double support asymmetry is often reported to reflect inter-limb temporal coordination in split-belt adaptation studies [8,9,24], it appears to be unaffected by the differences in balance support offered in the current study. Given the role of temporal regulation in control of dynamic stability, especially in split-belt walking [9], it is remarkable that a substantial reduction of the balance control problem in split-belt walking does not result in altered adaptation of temporal stepping parameters. Previously, it was also shown that double support asymmetry is insensitive to repeated split-belt treadmill training in people post-stroke [43]. The possibilities to alter double support asymmetry are limited in bipedal walking, as only ten percent of the gait cycle is spent in double support [44], which could explain previous [43] and current findings.

Clinical implications

This study shows that balance support through handrail holding reduces locomotor learning, which has important implications for clinical gait rehabilitation practice. Maintaining dynamic stability is one of the most important obstacles in functional walking after neurological trauma, and balance assistance is often used to relearn people to walk, e.g. physiotherapists supporting the trunk, body weight support systems, exoskeletons and the use of handrails [3,6]. Walking performance in people post-stroke can be increased by both treadmill training [45], and balance assistance [3,46]. However, while handrail holding enables people to start treadmill training at an earlier point in rehabilitation, clinicians should take into account that this may reduce learning effects once balance control is at a safe enough level for unassisted walking, i.e. in ambulant patients with less severe impairments. Furthermore, a reduction in acute adaptation effects due to external balance support, may lead to reduced retention of the learned gait pattern in rehabilitation practice [22,23]. As an alternative, fall protection systems without body-weight support could be used to guarantee participant safety during gait training, ultimately benefiting the patient.

CONCLUSION

We studied the effects of handrail holding on split-belt adaptation and after-effects in able-bodied persons. The results indicate that balance support reduces locomotor learning. This reduction in locomotor learning may be due to task simplification or altered task demands, as split-belt walking poses a major challenge for balance control, which is no longer present when a person is externally supported by handrails. The findings of this study should be taken into account in future research on locomotor learning and split-belt adaptation, as well as daily clinical gait practice.

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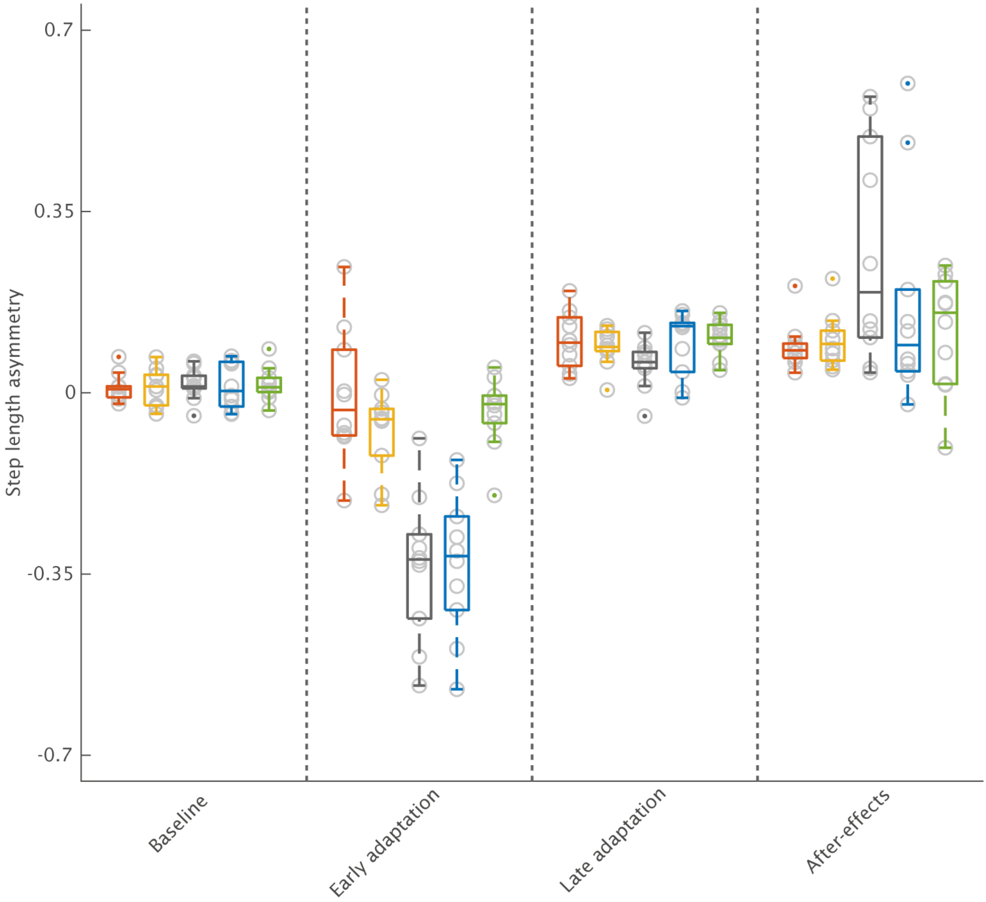
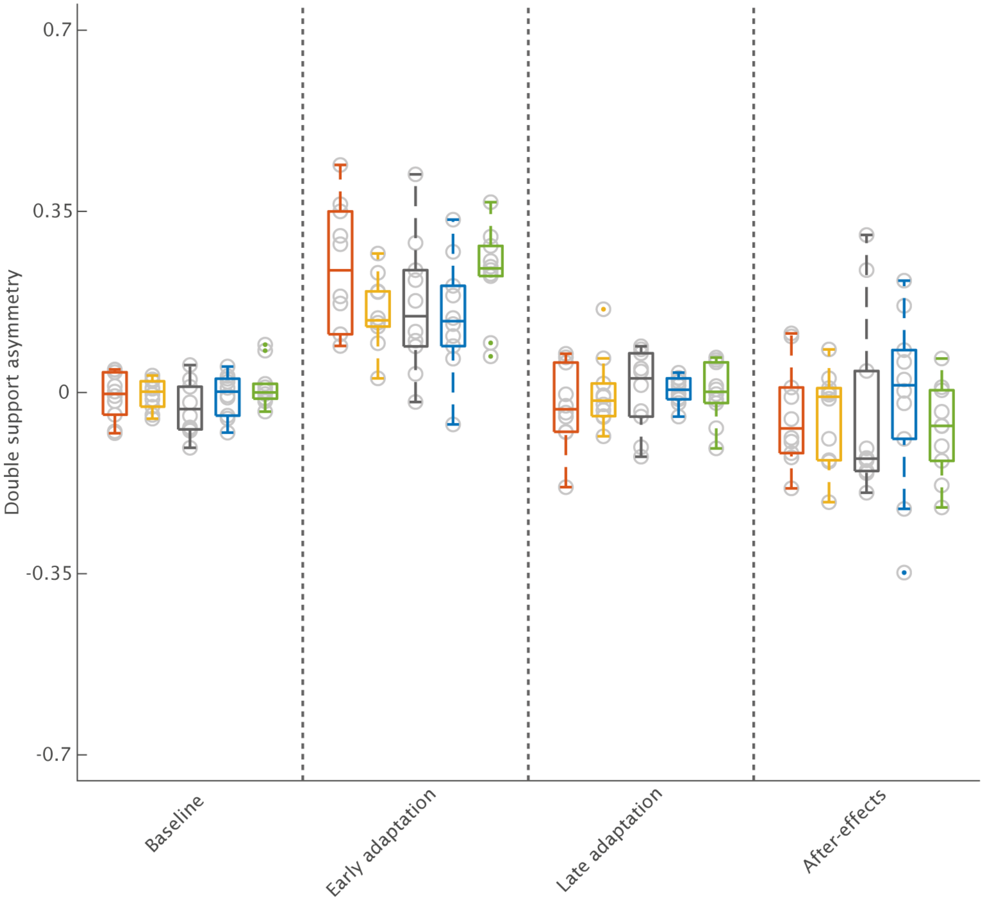
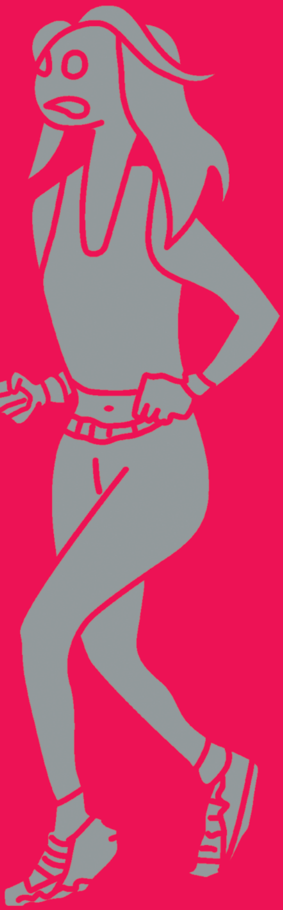
SUPPORTING INFORMATION



Supplementary Figure S1 – Expanded view of step length asymmetry box plots (Figure 2B) with individual data points.



Supplementary Figure S2 – Expanded view of double support asymmetry box plots (Figure 2D) with individual data points.



6

MAINTAINING SAGITTAL PLANE BALANCE COMPROMISES FRONTAL PLANE BALANCE DURING REACTIVE STEPPING IN PEOPLE POST-STROKE

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Submitted for publication

ABSTRACT

Maintaining balance in response to perturbations during walking often requires the use corrective responses to keep the Center of Mass (CoM) within the Base of Support (BoS). The relationship between the CoM and BoS is often quantified using the Margin of Stability (MoS). Although people post-stroke increase the MoS following perturbations, deficits in control may lead to asymmetries in the strategy used to regulate the MoS. These deficits may also cause maladaptive coupling between the sagittal and transverse planes during balance-correcting responses. We assessed how the paretic and non-paretic MoS are controlled during recovery from forward perturbations and determined how stroke-related impairments influence the coupling between the anteroposterior and mediolateral MoS. Twenty-one participants with post-stroke hemiparesis walked on a treadmill while receiving slip-like perturbations on the paretic and non-paretic limbs at foot-strike. Full-body motion capture was used to assess anteroposterior and mediolateral MoS before the perturbations and during perturbation recovery. Participants walked with a smaller anteroposterior and a larger mediolateral MoS on the paretic versus non-paretic sides. When responding to perturbations, participants increased the anteroposterior MoS bilaterally by extending the base of support and reducing the excursion of the extrapolated CoM. The anteroposterior and mediolateral MoS in the paretic limb negatively covaried during reactive steps such that increases in the anteroposterior MoS were associated with reductions in the mediolateral MoS. Balance training interventions to reduce fall risk post-stroke may benefit from incorporating strategies to reduce maladaptive coupling of frontal and sagittal plane stability.

INTRODUCTION

People post-stroke often have trouble maintaining dynamic balance while walking [1], leading to an increased risk of falls [2,3]. When responding to unexpected perturbations, dynamic balance is primarily maintained by reactive control strategies such as stepping responses. Reactive stepping may be impaired post-stroke, due to weakness in the paretic leg [4,5], delays in intra- and inter-limb reflexes [6], abnormal coordination [7-11], and impaired initiation of successful stepping responses with the paretic leg [12]. Reactive control of dynamic balance can be quantified by the Margin of Stability (MoS) [13], a variable that incorporates Center of Mass (CoM) position and velocity in the Extrapolated CoM (XCoM), and the AnteroPosterior (AP) or MedioLateral (ML) edge of the base of support. Although improving reactive dynamic balance control is an important objective in post-stroke gait rehabilitation, we do not fully understand how post-stroke impairments influence the regulation of the MoS during reactive stepping responses.

In response to perturbations during walking, non-disabled people increase the ML and AP MoS by making a stepping response that accounts for the direction and magnitude of the perturbation [14-17]. People post-stroke regulate both their AP and ML MoS in a manner that differs from non-disabled persons during unperturbed walking. For example, they have smaller bilateral AP MoS [18,19] and tend to balance their CoM over the non-paretic leg, which results in a larger paretic than non-paretic AP and ML MoS [20]. It, therefore, seems that people post-stroke unburden their paretic leg, while they stabilize and propel themselves with the non-paretic leg [4,5,21]. Control of AP and ML MoS during reactive balance responses in people post-stroke has been studied both during stance and during walking. When fore-aft perturbations occur while standing, people post-stroke have smaller paretic than non-paretic compensatory step length responses [22,23]. In response to lateral perturbations during walking [19], they increase the paretic and non-paretic ML MoS and decrease the AP MoS, regardless of whether the perturbation occurs during the paretic or non-paretic step [19]. While it is known that there are asymmetries in regulation of the AP and ML MoS, the underlying mechanisms that drive this asymmetry have not yet been determined.

The MoS can be regulated in two ways; (i) By changing the XCoM position and (ii) by changing the base of support, i.e., step length or step width. Control deficits in the paretic limb may lead to asymmetries in how these strategies are combined. While the non-paretic MoS could be controlled more via foot placement strategies, the paretic MoS might be preferentially controlled by using the non-paretic limb to modulate the position of the XCoM since foot placement control using the paretic leg may be impaired [4,5,7-10,12]. To understand how people post-stroke change their AP and ML MoS in reaction to forward perturbations during walking, it is necessary to understand how changes in each MoS are influenced by changes in XCoM position and changes in the base of support via foot placement strategies.

In addition to understanding the role of foot placement strategies and center of mass control on AP and ML MoS, respectively, there is evidence that AP and ML stability may covary systematically. For example, to increase step length in response to a forward perturbation, a transverse rotation of the pelvis is often necessary [24]. However, this rotation may result in reduced step width [25], and could, therefore lead to a decrease in the ML MoS [26], which could lead to a fall. The impact of this covariation may be particularly severe for people with post-stroke hemiparesis because paretic stepping responses are impaired [12]. This can be empirically verified by assessing whether an increase in AP MoS in the recovery step following a forward perturbation is associated with a decrease in ML MoS in the same step, due to decreased step width [26], and whether this relation differs between the paretic and non-paretic leg. Indeed, when people post-stroke increase their ML MoS in response to a lateral perturbation, they simultaneously decrease their AP MoS [19]. However, the strength of this relationship during AP perturbations has yet to be investigated.

Here, we examine the covariation between AP MoS and ML MoS in response to forward perturbations during walking in people post-stroke. Our first aim was to assess how paretic and non-paretic AP and ML MoS are controlled during unperturbed walking and the recovery steps following a forward perturbation. We hypothesized that people post-stroke would walk with asymmetric ML and AP MoS during steps before the perturbation [18-20]. Furthermore, we hypothesized that people post-stroke would increase their AP MoS and decrease their ML MoS in the recovery step following a perturbation but will show less of an increase in AP MoS on the paretic than non-paretic leg. Our second aim was to determine whether the AP MoS and ML MoS covary during the recovery step after a perturbation and to determine whether this covariation differs between the paretic and non-paretic leg. We hypothesized that the increase in AP MoS in response to a forward perturbation would negatively covary with the ML MoS and that this covariation would be stronger for the paretic than the non-paretic leg.

METHODS

Participants and ethics statement

Twenty-one chronic stroke survivors (Table 1) participated in this study. Inclusion criteria were (i) a sustained unilateral stroke more than six months prior to the experiment, (ii) paresis confined to one side, (ii) ability to provide informed consent and communicate with the experimenters, (iv) the ability to walk at least five minutes on a treadmill without assistance or walking aids. Use of an ankle-foot orthosis was permitted during the experiment. The procedures of this study were approved by the University of Southern California Institutional Review Board (Los Angeles, CA, USA) and were consistent with the Declaration of Helsinki [27]. All participants provided written informed consent before the experiment.

Table 1 – Participant demographics and clinical assessments (N = 21).

Metric	Value
Female / male	6 / 15
Left / right side hemiparesis	8 / 13
Age	59.4 ± 12.6 years
Activity-specific Balance Confidence Scale	55.0 ± 36.7
Berg Balance Scale	51.3 ± 3.7
Functional Gait Assessment	23.3 ± 4.8
10-Meter Walk Test	0.87 ± 0.23 m s^{-1}
Falls Efficacy Scale	30.4 ± 12.1
Fugl-Meyer lower extremity	28.2 ± 3.2
Self-selected walking speed	0.60 ± 0.18 m s^{-1}

Experimental protocol

Before participants walked on the treadmill, we performed a set of clinical assessments. We evaluated balance using the Berg Balance Scale [28], balance self-efficacy using the Activity-specific Balance Confidence Scale [29], walking performance using the Functional Gait Assessment [30] and 10-Meter Walk Test, fear of falling using the Falls Efficacy Scale [31], and motor impairment using the lower extremity motor domain of the Fugl-Meyer assessment [32].

After the clinical assessments, participants walked on an instrumented dual-belt treadmill (Bertec, Columbus, OH, USA) to determine their self-selected walking speed. They started with 70 % of the speed measured during the 10-Meter Walk Test, and speed was adjusted by increments or decrements of 0.05 m s^{-1} until they verbally indicated that their preferred walking speed was reached. Participants then completed a familiarization trial with at least two slip-like perturbations on each side [33].

Participants walked for three minutes at their self-selected speed to accommodate to treadmill walking, after which they completed two trials of three minutes at their self-selected speed during which they received perturbations. We used rapid accelerations of one of the treadmill's belts to act as perturbations, resulting in a slip-like perturbation [34]. During each trial, we applied six perturbations to each leg. Perturbations were triggered using Python code that predicted foot-strike timing using ground reaction forces recorded by the treadmill's embedded force plates. Each perturbation consisted of a 0.2 m s^{-1} increase in speed at an acceleration of 1.6 m s^{-2}, lasting 0.7 s and accelerating back to the self-selected speed during the swing phase of the perturbed leg. Perturbations occurred within 18 to 24 steps after the previous perturbation to let participants re-establish their normal walking pattern and minimize anticipatory responses to the perturbations. Participants had breaks of at least three minutes in between each trial to minimize fatigue. Participants did not hold on to handrails while walking on the treadmill, but they wore a harness to prevent them from falling. All participants were able to stay upright in response to the perturbations. After selection of correctly timed perturbations, we included 19 ± 5 perturbations per participant.

Data acquisition

A 10-camera motion capture system (Qualisys AB, Göteborg, Sweden) recorded 3D kinematics at 100 Hz and the treadmill embedded force plates recorded ground reaction forces at 1000 Hz. Retroreflective markers (14 mm) were placed at anatomical landmarks to create a 12-segment, full-body model. This model was based on a 13-segment model [35,36], but the pelvis segment was assumed to be rigidly connected to the trunk because the harness blocked the markers necessary to track the pelvis accurately. We validated this 12-segment model with data from a set of non-disabled participants that included the necessary markers to track the pelvis segment. The root mean square error between the 12-segment and 13-segment model was low for the CoM position (AP: 0.0041 ± 0.0034 m, ML: 0.0017 ± 0.0012 m, vertical: 0.0095 ± 0.0051 m) and CoM velocity (AP: 0.0052 ± 0.0015 m s^{-1}, ML: 0.0025 ± 0.0008 m s^{-1}, vertical: 0.0030 ± 0.0015 m s^{-1}). We placed marker clusters on the upper arms, forearms, thighs, shanks, and the back of heels. At the beginning of each trial, marker positions were calibrated during a five-second standing trial. All joint markers were removed after standing calibration.

Data analysis

Kinematic and kinetic data were processed in Visual3D (C-Motion, Rockville, MD, USA) and analyzed in MATLAB (version r2018b; The MathWorks Inc., Natick, MA, USA). Marker positions and ground reaction forces were low-pass filtered with a 4th order Butterworth filter, at a 6 Hz and 20 Hz cutoff respectively [37-39]. The timing of perturbations relative to foot-strike was re-examined post-hoc. We removed the perturbations that occurred more than 150 ms after the foot-strike. We also removed perturbations for which deceleration began before the toe-off of the perturbed leg. Load cell measured the vertical force on the harness (Litegait, Tempe, AZ, USA), and we excluded steps in which we measured more than 30 % of the participant's body weight as this would indicate that the participant relied on the harness to remain upright [23,40,41].

Step width (m) was defined as the ML distance between the 5th metatarsal marker and the contralateral foot's 5th metatarsal marker at foot-strike. Step length was defined as the AP distance between the 1st distal phalanx marker of the leading foot and the 1st distal phalanx marker of the trailing foot at foot-strike. The AP and ML MoS were calculated for the paretic and non-paretic leg independently using a modified version of the MoS which captures the nonlinearity in the CoM trajectory [42] (Equations 1 and 2).

$$MoS = l * \sin(\theta + \dot{\theta} \cdot \omega_0^{-1}) \tag{1}$$

$$\omega_0 = \sqrt{\frac{g}{l}} \tag{2}$$

We calculated the AP MoS, with leg length (l), limb angle (θ) as measured by the angle of a vector extending from the CoM to the 1st distal phalanx marker in the sagittal plane, and limb angular velocity in the sagittal plane ($\dot{\theta}$, Equation 1). We calculated ML MoS, with leg length (l), limb angle (θ) as measured by the angle of a vector extending from the CoM to the 5th metatarsal marker in the frontal plane, and limb angular velocity in the frontal plane ($\dot{\theta}$, Equation 1). AP and ML XCoM positions (m) were analyzed at foot-strike.

Statistical analysis

We conducted a series of statistical tests to assess how people post-stroke control their paretic and non-paretic AP and ML MoS in response to a forward perturbation. All statistical analyses were performed in MATLAB (version r2018b; The MathWorks Inc., Natick, MA, USA). We analyzed the last step before each perturbation (Pre-perturbation), the step during which the participant was perturbed (Perturbation) and the three subsequent recovery steps (Recovery 1-3) for each participant, leg, and perturbation side independently. Statistical significance was set at an alpha of 5 %.

First, we determined how the MoS varied from pre-perturbation through perturbation and recovery steps using two Repeated Measures ANOVAs for AP MoS and ML MoS, respectively. In each of these analyses, we included step (Pre-perturbation, Perturbation, Recovery 1-3) and leg (paretic or non-paretic) as within-subject factors and an interaction between step and leg. If main effects were significant, we performed post-hoc tests to (i) compare paretic with non-paretic MoS and (ii) determine if the MoS in the recovery steps following the perturbation (Recovery 1-3) differed from Pre-perturbation. If a step by leg interaction was significant, we performed post-hoc tests to (i) compare paretic with non-paretic MoS at Pre-perturbation and (ii) assess whether changes in the MoS from Pre-perturbation to Recovery 1-3 differed between the paretic and non-paretic leg. We used the Greenhouse-Geisser correction if the assumption of sphericity was violated and the Tukey-Kramer correction for multiple comparisons in all post-hoc testing.

We also assessed the relative contributions of non-paretic / paretic differences in XCoM position and base of support to pre-perturbation non-paretic / paretic differences in MoS. To this end we performed a multiple linear regression with predictors 1) difference in non-paretic and paretic XCoM position and 2) difference in non-paretic and paretic edges of the base of support (step length for AP and step width for ML). This analysis was performed for the AP and ML direction separately. We also used multiple linear regression to assess the relative contributions of changes in XCoM position and changes in base of support (step length for AP and step width for ML) to the change in MoS from Pre-perturbation to Recovery 1. This analysis was performed for the AP and ML direction, and paretic and non-paretic leg separately.

Finally, we determined whether the AP MoS and the ML MoS covaried during pre-perturbation steps and the first recovery step following a perturbation. We fit two linear mixed effect models to quantify the relationship between independent variables AP MoS and leg (paretic or non-paretic) and the dependent variable ML MoS. This model included main effects for AP MoS and leg, an AP MoS by leg interaction, and a random intercept for each participant. We expected to observe covariation between AP MoS and ML MoS in recovery steps but not during pre-perturbation steps. Therefore, the first model was fit with each participant's paretic and non-paretic AP MoS during Pre-perturbation steps, and the second model was fit with each participant's paretic and non-paretic AP MoS during Recovery 1 steps. Two participants were excluded from this analysis as they received less than five correctly-timed perturbations on either the paretic or non-paretic side.

RESULTS

Paretic and non-paretic margins of stability throughout perturbation recovery

For the AP MoS (Figure 1A), our repeated measures ANOVA revealed significant main effects for leg (F (1,20) = 12.503, p = 0.002) and step (F (4,20) = 24.562, p < 0.001), which indicates that the AP MoS differed between paretic and non-paretic leg and across steps. We found no interaction between leg and step (p = 0.199). Post-hoc comparisons showed a significantly smaller paretic than non-paretic AP MoS (p = 0.002), and a significant increase in AP MoS from Pre-perturbation to Recovery 1 (p < 0.001). This indicates that participants walked with a smaller paretic than non-paretic AP MoS during pre-perturbation, perturbation, and recovery steps and restored their pre-perturbation MoS after one step.

For the ML MoS (Figure 1B), we found significant main effects for leg (F (1,20) = 8.464, p = 0.009) and step (F (4,20) = 45.118, p < 0.001), and we found a significant interaction between leg and step (F (4,80) = 2.997, p = 0.040). Post-hoc comparisons showed a significantly larger paretic than non-paretic ML MoS during Pre-perturbation steps (p = 0.008), a significant decrease in ML MoS from Pre-perturbation to Recovery 1 in the paretic (p < 0.001) and non-paretic (p < 0.001) legs, and a significant increase in ML MoS from Pre-perturbation to Recovery 3 in the non-paretic leg (p = 0.008). This indicates that participants walked with larger paretic than non-paretic ML MoS before the perturbations and that they returned to pre-perturbation levels by the second recovery step for the paretic leg but were still recovering until the third recovery step with the non-paretic leg.

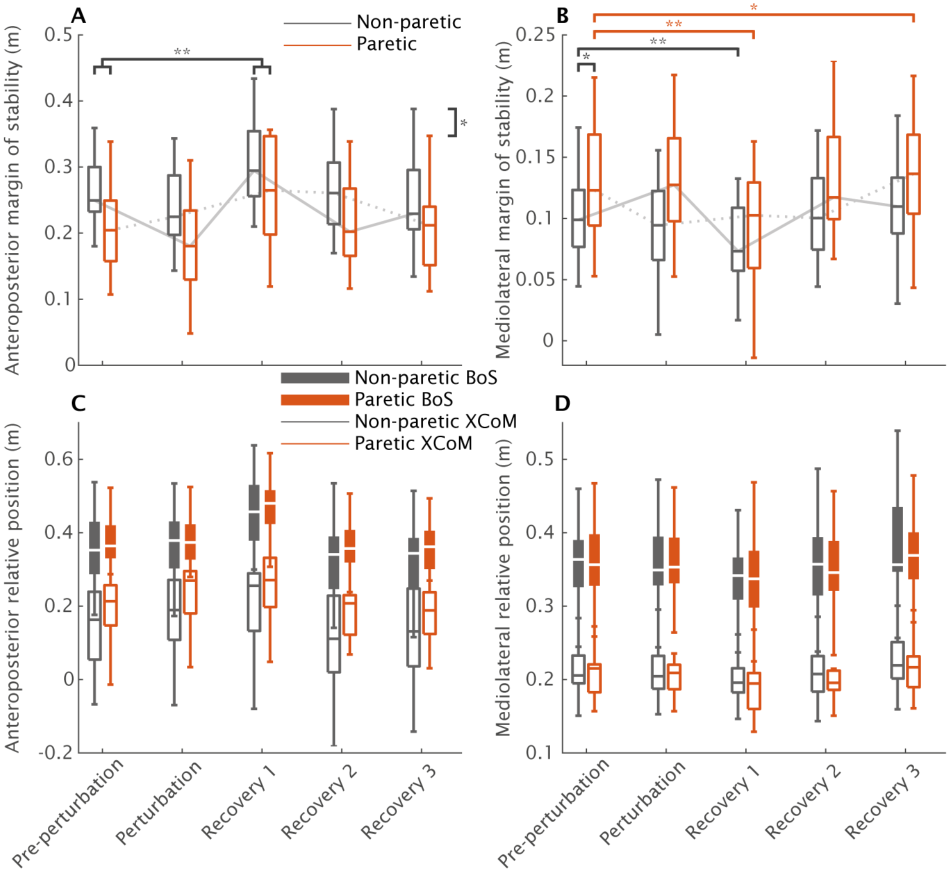

Figure 1 – Group distribution of margins of stability for pre-perturbation, perturbation and recovery steps (N = 21). **A)** Paretic and non-paretic anteroposterior Margins of Stability (MoS). **B)** Paretic and non-paretic mediolateral MoS. **C)** Paretic and non-paretic anteroposterior edge of the Base of Support (BoS; leading leg 1st distal phalanx marker) and Extrapolated Center of Mass (XCoM) positions relative to the contralateral edge of the BoS (trailing leg 1st distal phalanx marker. **D)** Paretic and non-paretic mediolateral edge of the BoS (leading leg 5th metatarsal marker) and XCoM positions relative to the contralateral BoS (trailing leg 5th metatarsal marker). Asterisks indicates significant differences in MoS between limbs or phases (* $p < 0.05$, ** $p < 0.001$). The order of steps alternates between paretic and non-paretic, based on the side that was perturbed. The grey dotted lines indicate the series of steps in which the non-paretic leg was perturbed, the solid grey lines the series of steps in which the paretic leg was perturbed.

Contributions to pre-perturbation differences between paretic and non-paretic margins of stability

The pre-perturbation difference between the non-paretic and paretic AP MoS was explained by a linear model including the difference between the non-paretic and paretic AP XCoM ($\beta = -0.071$, $p < 0.001$, Figure 2A) and the difference between the non-paretic and paretic step length ($\beta = 0.086$, $p < 0.001$, Figure 2B). This model had an R^2 of 0.675 ($F(2,18) = 18.700$, $p < 0.001$). This indicates that a smaller paretic than non-paretic AP MoS during pre-perturbation steps was explained by a more anterior paretic than non-paretic AP XCoM position and shorter paretic than non-paretic step length. The pre-perturbation difference between the paretic and non-paretic ML MoS could not be explained by a linear model including the difference between the non-paretic and paretic ML XCoM and the difference between the non-paretic and paretic step width ($p = 0.06$). This suggests that pre-perturbation differences in paretic and non-paretic ML MoS may have different contributions between participants.

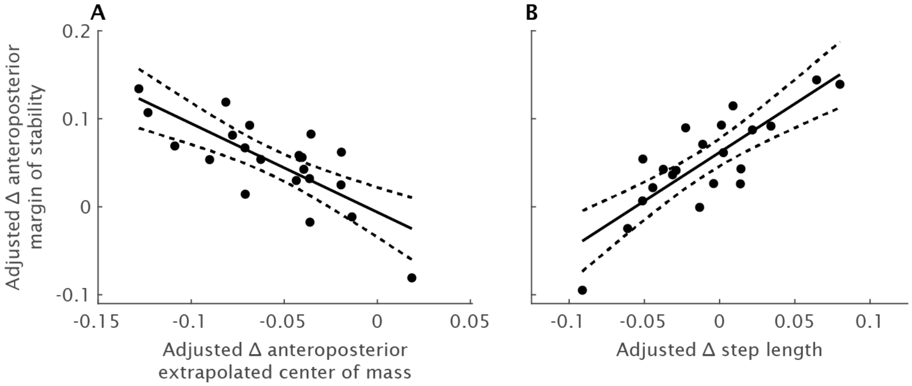

Figure 2 – Partial regression plots of pre-perturbation difference in non-paretic and paretic (Δ) Margin of Stability (MoS), Extrapolated Center of Mass (XCoM), and Base of Support (BoS) (N = 21). Δ Indicates difference between non-paretic and paretic leg at pre-perturbation. All data shown are adjusted values from the multiple regression analysis. **A)** Partial regression between Δ AnteroPosterior (AP) XCoM and Δ AP MoS. **B)** Partial regression between Δ step length and Δ AP MoS.

Contributions to changes margins of stability during perturbation recovery

The change from Pre-perturbation to Recovery 1 in paretic AP MoS was explained by a linear model including the change in paretic AP XCoM ($\beta = -0.055$, $p < 0.001$, Figure 3A) and the change in paretic step length ($\beta = 0.036$, $p < 0.001$, Figure 3B). This model had an R^2 of 0.914 ($F(2,18) = 95.1$, $p < 0.001$). The change in non-paretic AP MoS was explained by a linear model including the change in non-paretic AP XCoM ($\beta = -0.040$, $p < 0.001$, Figure 3C) and the change in non-paretic step length (β = 0.028, $p < 0.001$, Figure 3D). This model had an R^2 of 0.930 (F (2,18) = 120, $p < 0.001$). Therefore, both modulation of XCoM position by the trailing leg and increased step length by the leading leg contribute to increases in AP MoS during perturbation recovery.

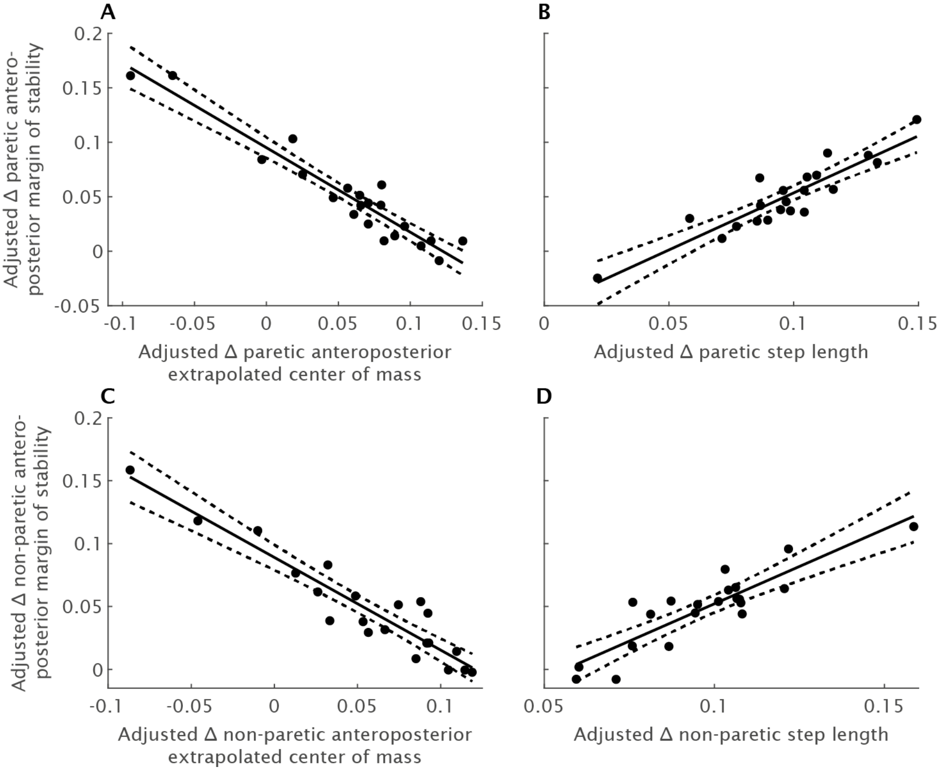

Figure 3 – Partial regression plots of change from Pre-perturbation to Recovery 1 (Δ) in Extrapolated Center of Mass (XCoM) and Δ Base of Support (BoS) vs. Δ Margin of Stability (MoS) for the paretic and non-paretic leg in the AnteroPosterior (AP) direction (N = 21). Δ Indicates change from Pre-perturbation to Recovery 1. All data shown are adjusted values from the multiple regression analysis. **A)** Partial regression between paretic Δ AP XCoM and Δ AP MoS. **B)** Partial regression between paretic Δ step length and Δ AP MoS. **C)** Partial regression between non-paretic Δ AP XCoM and Δ AP MoS. **D)** Partial regression between non-paretic Δ step length and Δ AP MoS.

The change from Pre-perturbation to Recovery 1 in paretic ML MoS was explained by a linear model including the change in paretic ML XCoM (β = -0.028, p = 0.008, Figure 4A) and the change in paretic step width (β = 0.028, p = 0.009, Figure 4B). This model had an R^2 of 0.347 (F (2,18) = 4.78, p = 0.022). The change in non-paretic ML MoS could not be explained by a linear model including the change in non-paretic ML XCoM and the change in non-paretic step width ($p = 0.290$). The model used to explain variance in paretic ML MoS had a relatively low R^2 (0.347 versus 0.914 for the paretic AP MoS), and we were unable to fit a model to the non-paretic ML MoS. This indicates that although people post-stroke decrease their ML MoS in response to forward perturbations in gait, these changes are likely caused by participant-specific changes in ML XCoM position and step width.

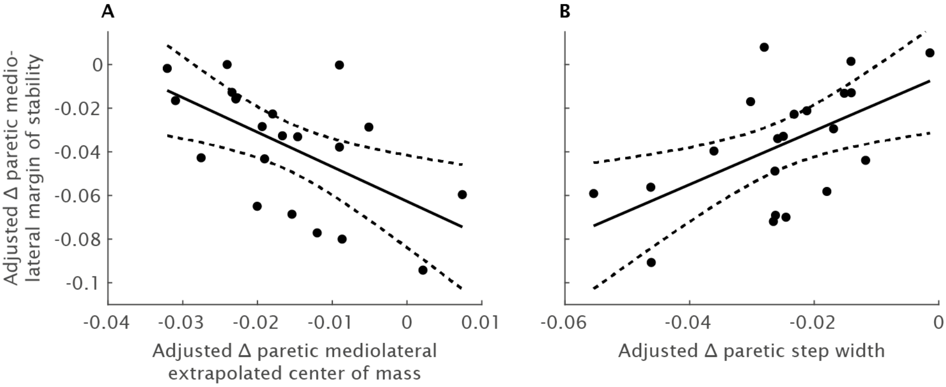

Figure 4 – Partial regression plots of change from Pre-perturbation to Recovery 1 (Δ) in Extrapolated Center of Mass (XCoM) and Δ Base of Support (BoS) vs. Δ Margin of Stability (MoS) for the paretic and non-paretic leg in the Mediolateral (ML) direction ($N = 21$). Δ Indicates change from Pre-perturbation to Recovery 1. All data shown are adjusted values from the multiple regression analysis. **A)** Partial regression between paretic Δ ML XCoM and Δ ML MoS. **B)** Partial regression between paretic Δ step length and Δ ML MoS.

Covariation between the anteroposterior and mediolateral margin of stability during perturbation recovery

There was no significant effect of AP MoS ($p = 0.089$), leg ($p = 0.917$) or interaction between AP MoS and leg ($p = 0.060$) on ML MoS during Pre-perturbation steps (Figure 5A,B). This indicates that there is no covariation between AP MoS and ML MoS during unperturbed walking in people post-stroke. In contrast, there were significant main effects of AP MoS ($\beta = -0.16$, $F(1,381) = 15.622$, $p < 0.001$) and leg ($\beta = -0.056$, $F(1,381) = 14.316$, $p < 0.001$) as well as an interaction between AP MoS and leg ($\beta = 0.14$, $F(1,381) = 8.727$, $p = 0.003$) (Figure 5C,D) on ML MoS at Recovery 1. This indicates that an increase in paretic AP MoS in response to a forward perturbation leads to a reduction in paretic ML MoS during the first recovery step (Figure 5C). In contrast, there was no significant association between AP MoS and ML MoS during Recovery 1 for the non-paretic limb ($p = 0.73$, Figure 5D).

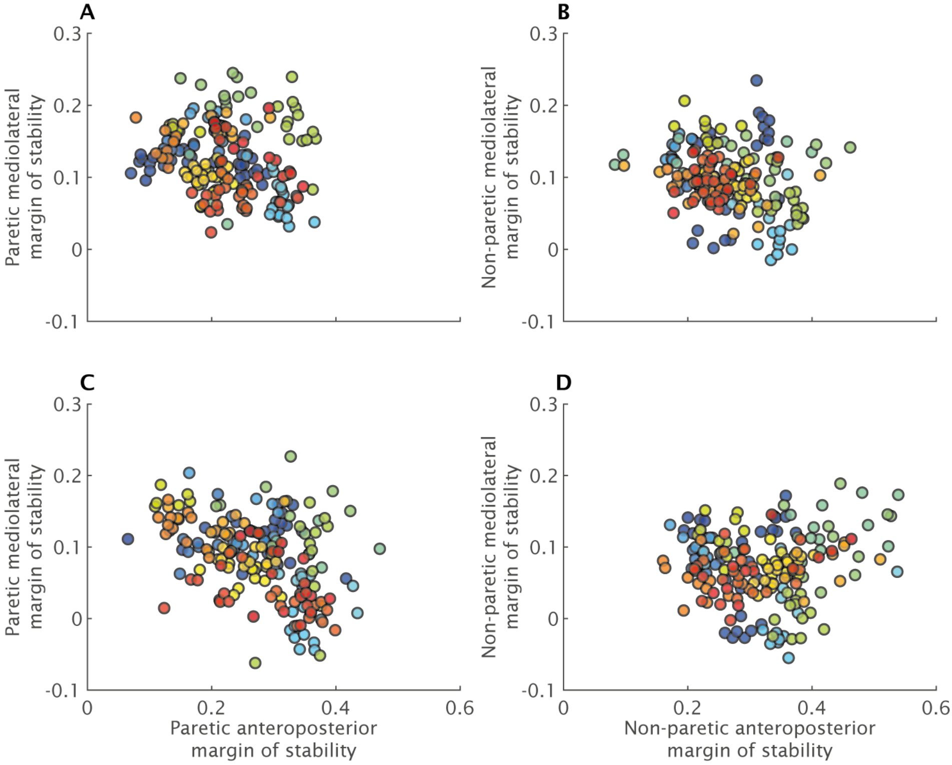

Figure 5 – Covariation between anteroposterior Margin of Stability (MoS) and mediolateral MoS (N = 19). Each color represents an individual participant. **A)** Paretic MoS at Pre-perturbation. **B)** Non-paretic MoS at Pre-perturbation. **C)** Paretic MoS at Recovery 1. **D)** Non-paretic MoS at Recovery 1. Participants who received less than five perturbations on each side were excluded from this analysis.

DISCUSSION

People with post-stroke hemiparesis are more susceptible to perturbations of dynamic balance during walking [1]. To increase our understanding of reactive balance control strategies in people post-stroke, we aimed to (i) to assess how the paretic and non-paretic AP and ML MoS are controlled in response to forward perturbations and (ii) to determine whether the AP MoS and the ML MoS during recovery steps covaried in response to a forward perturbation. We found that people post-stroke have smaller paretic than non-paretic AP MoS, and larger paretic than non-paretic ML MoS during unperturbed walking, consistent with previous studies [18-20]. In response to a forward perturbation during walking, people post-stroke increase their paretic and non-paretic AP MoS, while they simultaneously decrease their ML MoS. We also found that the paretic AP MoS and the paretic ML MoS covary during the first recovery step after a forward perturbation, which implies that improving sagittal plane balance may reduce frontal plane balance during reactive steps with the paretic leg.

People post-stroke walk with smaller anteroposterior and larger mediolateral margins of stability on the paretic side

We found that people post-stroke walk with smaller AP MoS and larger ML MoS on the paretic than the non-paretic side. The smaller paretic AP MoS at pre-perturbation was both due to a more anterior position of the XCoM relative to the trailing foot and reduced step length on the paretic side. The positive relationship between the difference in paretic and non-paretic AP MoS and the difference in paretic and non-paretic step length that was found in this study can be explained by step length asymmetry in people post-stroke. People post-stroke may either walk with a shorter paretic than non-paretic step lengths leading to a smaller paretic than non-paretic AP MoS, which was most prevalent in our sample, or a longer paretic step leading to a larger paretic AP MoS [4,43], due to reduced paretic propulsive force generation [43]. The difference between paretic and non-paretic ML MoS may be due to both impaired sensation of the CoM state [44] and stance time asymmetry [4] in people post-stroke, which have been suggested to lead to a larger paretic ML MoS [45,46]. These findings indicate that the asymmetric paretic and non-paretic AP and ML MoS in people post-stroke may be a strategy to compensate for reduced sensation of CoM state [44], unload the paretic leg during weight bearing [20] and make the paretic side less sensitive to unexpected lateral perturbations by maintaining a larger paretic ML MoS [26].

People post-stroke increase anteroposterior and decrease mediolateral margins of stability in response to a forward perturbation

We found that people post-stroke increase their paretic and non-paretic AP MoS in response to a forward perturbation, while they simultaneously decrease their paretic and non-paretic ML MoS. The increase in AP MoS during the recovery step was due to both less anterior displacement of the AP XCoM position and increased step length. This implies that the trailing limb reduces the forward momentum of the body in response to a forward perturbation, thereby achieving a larger AP MoS. Since this finding occurred in both the paretic and non-paretic leg, this suggests that people post-stroke are still capable of controlling the body's momentum with the paretic leg during late stance, despite the paretic leg's weakness [4,5] and impaired coordination [7-10].

The source of the reduction in ML MoS following a forward perturbation varied between participants, both due to more lateral displacement of the ML XCoM and reduced step width. Hak et al. (2013) showed that in response to a lateral perturbation, people post-stroke increase their ML MoS [19]. This finding and the results of the present study are in line with previous work that suggests that people increase their base of support in the direction of the perturbation [14-17], forward in the current study and lateral in Hak et al. (2013) [19].

Covariation between sagittal and frontal plane balance during reactive stepping in people post-stroke

We also found that the AP MoS and the ML MoS covaried in the paretic limb during the first recovery step following a forward perturbation, but we did not observe any associations between AP MoS and ML MoS during pre-perturbation steps or in non-paretic stepping responses. This is consistent with our hypothesis that covariation between the AP MoS and the ML MoS only occurs during reactive stepping responses, where people may have to rely more on transverse rotation of the pelvis to take larger steps than during unperturbed walking. Furthermore, this covariation was only observed in the paretic limb, which suggests that people post-stroke may rely on more transverse rotation of the pelvis to increase the paretic step length in reaction to a forward perturbation compared to when an increase of the non-paretic step length is desired.

Clinical implications of covariation in the reactive control of sagittal and frontal plane balance

Our findings have important implications for clinical practice. To prevent future falls, rehabilitation can be targeted at improving reactive stepping responses through perturbation-based training. However, to know at what to target rehabilitation practice, we must know which aspects of the stepping pattern will improve reactive balance responses in people post-stroke. We found that changes in AP MoS during reactive stepping were both due to changes in XCoM position and step length. The changes in XCoM position during reactive stepping are most likely due to control of the body's momentum by the trailing limb. Therefore, rehabilitation could be targeted at increasing the ability to bear weight on the paretic limb during perturbations of walking post-stroke to improve the paretic limb's control of the body's momentum.

Furthermore, we found covariation between the AP and ML MoS in paretic reactive stepping responses following a perturbation. This implies that an improvement in sagittal plane balance may compromise frontal plane balance in paretic stepping responses. In addition, this indicates that different relations hold during perturbed than unperturbed walking, which stresses the importance of training dynamic balance control in a task-specific fashion, e.g. by perturbation-based gait training to improve paretic stepping responses. Perturbation training could also be used to decouple the paretic AP and ML MoS in people post-stroke so that they can learn to maintain sagittal plane balance without compromising frontal plane balance. Finally, this study has shown that analysis of stability metrics during unperturbed walking may not predict how these measures change in response to perturbations. Therefore, the mechanisms that may lead to falls are likely best revealed when we challenge participants' balance during walking.

CONCLUSION

In this study, we described how people with post-stroke hemiparesis control their AP and ML MoS in response to a forward perturbation during walking. People post-stroke walk with asymmetric AP and ML MoS during normal walking and in recovery from perturbations. These asymmetries in MoS may be the result of compensatory strategies to safeguard dynamic balance against perturbations on the paretic side. We found a systematic covariation between paretic sagittal and frontal plane balance measures, which implies that frontal plane balance is compromised when sagittal plane balance is improved during paretic stepping responses. This covariation during paretic stepping responses may be due to impairment in mechanical coupling, e.g. transverse rotation of the pelvis. Future rehabilitation efforts could focus on decoupling this covariation to improve dynamic balance in people post-stroke.

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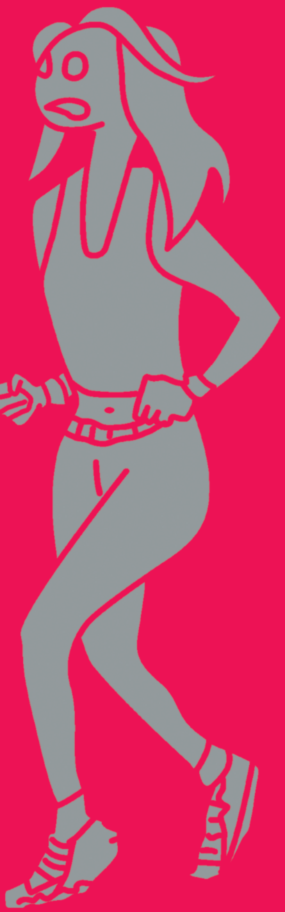

7

GENERAL DISCUSSION

MAIN FINDINGS

Adaptive control of dynamic balance is necessary to stay upright in human walking [1], and while it takes human infants over a year to learn how to walk [2], we walk autonomously for the majority of our life. It is at the point that mobility deteriorates, due to aging or pathology [3-5], that we may come to realize how being ambulant enriches our lives [6]. Although prevention programs for mobility decline and gait rehabilitation are aimed at increasing safe walking performance, we are yet unable to restore adaptive walking performance to a normal level after it deteriorates [7]. Currently, we do not fully understand the underlying mechanisms of adaptive control of dynamic balance in able-bodied and pathological populations. Therefore, the aim of this thesis was to increase our understanding of adaptive control of dynamic balance in human walking.

Through a series of five experiments, this thesis brought insight into adaptive control of dynamic balance in both able-bodied and post-stroke individuals. A synergistic structure that controls the speed dependent modulation of muscle activity was proposed as a means for adaptive neuromuscular control in human walking (chapter 2). Furthermore, mediolateral dynamic balance control was shown to adapt to walking with asymmetric belt speeds, i.e. a sustained perturbation of gait, through a complementary mechanism of relative foot placement and mediolateral foot roll-off (chapter 3). To better understand the control of relative foot placement, we proposed bilateral temporal control as a mechanism that regulates dynamic balance during symmetric, asymmetric and adaptive human walking. This mechanism may potentially explain pathological walking strategies to increase balance on an injured leg (chapter 4). When the balance control problem during split-belt adaptation was eliminated through external balance support, it was found that locomotor adaptation and learning decreased, emphasising the key role that adaptive control of dynamic balance plays in human walking and locomotor learning (chapter 5). In chapter 6, knowledge from chapters 3 and 4 was applied to understand reactive stepping in people post-stroke. There it was shown that anteroposterior and mediolateral paretic stepping strategies co-vary during the paretic recovery steps following a slip-like perturbation. This means that an improvement in frontal plane balance may come at the cost of reduced sagittal plane balance during paretic reactive stepping. The results from chapters 4 and 6 suggest that spatiotemporal stepping asymmetries in people post-stroke may not be a threat for dynamic balance, but rather a strategy to enhance dynamic balance control through unloading of the paretic leg. This thesis has shown that adaptive control of dynamic balance is an interaction between passive movement, e.g. resultant forces acting within and upon the body, and active control by the central nervous systems. In sum, learning to walk is learning to adaptively control dynamic balance and exploit the body's passive dynamic properties in an efficient manner for safe bipedal locomotion.

ADAPTIVE NEUROMUSCULAR CONTROL OF HUMAN WALKING

To generate movement, we must produce moments of force over our skeletal joints [8]. These moments can be generated by either external forces, e.g. gravity, or internal forces, e.g. muscle contractions [8]. To actively control body movement, and not be dependent on the mere gravitational forces working on our body mass, control of muscle contractions is necessary. We can record the activity of muscles through wire or surface electromyography [9,10], by which we gain insight into coordination of muscles to control joint and segmental rotations.

In chapter 2, based on surface electromyography, we found that a synergistic structure might control the speed dependent modulation of muscle activity in human walking. The adaptation of walking speed is one of the most fundamental and frequently exhibited adaptations in human movement. Therefore, if a synergistic structure of functional muscle groups regulates neuromuscular control of human walking, such a structure should reflect this adaptability. In this chapter we described a single synergistic structure that scales with gait speed [11,12] and thereby can control muscle activity during human walking at multiple gait speeds. While this structure can account for walking at a large range of velocities, the question remains whether this synergistic structure can also account for other walking tasks, such as turning or stepping over obstacles.

Although synergistic approaches to understand adaptive neuromuscular control of human walking bring a lot of knowledge to the field of locomotor control, I would like to consider three personal points of critique. First, the functional muscle groups that are found through principal component analysis or other factorization analyses could reflect neuromuscular control, but also the biomechanical constraints of human walking. Considering that human walking has an invariant task structure, muscle groups will always contribute to (sub-)tasks of gait in a consistent and predictable way. One of these sub-tasks in walking is propulsion, as without propulsion we will not progress forwards. To propel ourselves forward we generate push-off power, for which we need ankle plantarflexion. The muscles that contribute to ankle plantarflexion, the m. triceps surae [13], will then be active at the same time, resulting in a functional muscle group. One can then question whether the found muscle synergy that includes the m. triceps surae is a reflection of synergistic neuromuscular control, or rather the logical biomechanical requirement of that (sub-)task. Second, in the literature, motor synergies are often recalculated for every task, or phase of a task, after which these synergies are compared for further assessment [14,15]. However, according to the definition of muscle synergies as introduced in chapter 1 of this thesis, a true synergistic organization of muscle activity consists of a single library of patterns that controls all movements [16]. Muscle synergies are then an invariant set of control signals, reweighted for each task or condition. The problem that arises with this approach is that an extra control layer is necessary to weigh these control signals for each task. However, this additional control is often neglected in literature and reweighing synergies for every task may lead to a virtually infinite number of control possibilities rather than reduce its complexity. Indeed, in recent work on simplification of neural control through muscle synergies, Zelik, La Scaleia, Ivanenko and Lacquaniti (2014) stated that: *'The results obtained here based on simple neural architectures highlight the need for more sophisticated formulations of modular control or alternative motor control hypotheses and motivate future research to identify specific, testable neural mechanisms that can accommodate muscle coordination for disparate locomotor tasks'* [17]. Third, a cut-off criterion based on the percentage of variance accounted for by a factorization analysis is often chosen to select the number of synergies, e.g. 80 or 90 % variance accounted for [18,19] (chapter 2). This means that 10 to 20 % of variance in muscle activation is not accounted for. While muscle synergies can then describe the average behavior of individuals during a task, it can very well be that actual adaptive behavior lays in the 10 to 20 % of unaccounted variance.

To (dis)prove the theory of muscle synergies we yet need to come up with a refutable or falsifiable experimental paradigm. This experimental paradigm would have to alter the biomechanical constraints of walking, for instance through crouch gait. A single synergistic structure should then be able to describe both upright and crouch gait without recalculation or post-hoc comparison of synergies for each task. Finally, this synergistic organization of muscle activity should be able to explain adaptive behavior. The remainder of this thesis employed a more complex adaptation paradigm than the adaptation to different walking velocities, namely the adaptation to asymmetric walking velocities, i.e. split-belt walking.

ADAPTIVE CONTROL OF DYNAMIC BALANCE

In chapter 3 we showed that parameters of dynamic balance control adapt to a sustained perturbation of gait, which suggests an important role of dynamic balance in locomotor adaptations. In addition, when the balance control problem was reduced through external support during that same sustained perturbation, healthy young adults showed reduced locomotor learning (chapter 5). The findings in chapter 5 indicate an important role of dynamic balance control in locomotor adaptation. When participants were allowed to hold on to handrails during split-belt walking, balance control itself was no longer a problem because participants could stabilize themselves. Participants holding on to handrails were perturbed less during early split-belt walking, and therefore had less need to adapt their stepping pattern to the asymmetric belt speeds. Subsequently, switching back to tied-belt walking was not a problem as no adaptation took place during split-belt walking. Consequently, these participants did not learn the novel locomotor task, as was reflected by the reduced after-effects. Based on these findings, one can argue that maintaining dynamic balance is an important task goal, which shapes adaptive locomotor control and learning. As without learning to adaptively control dynamic balance, we would be able to progress forwards through space for a short period, but fall over eventually. Furthermore, while balance assistance is often used in clinical practice to relearn people to walk, clinicians should take into account that balance assistance may reduce learning effects.

A SPATIOTEMPORAL STEPPING MODEL FOR ADAPTIVE CONTROL OF DYNAMIC BALANCE

In this thesis, control of dynamic balance was described and quantified by the margin of stability [20]. The margin of stability contains valuable information about stepping strategies and center of mass control [21,22]. However, to adequately use the margin of stability, it is important to thoroughly grasp its potentials and limitations and to understand how the mediolateral and the anteroposterior margins of stability can be controlled during human walking. Therefore, a spatiotemporal stepping model for adaptive control of dynamic balance is proposed and visualized here (Figure 1).

The mediolateral margin of stability is defined as the distance between the extrapolated center of mass position and lateral edge of the base of support. Therefore, the mediolateral margin of stability can be controlled by changing the lateral base of support or by moving the extrapolated center of mass position. First, by increasing the lateral base of support, i.e. making a wider step, the margin of stability becomes larger, and logically, by making a narrower step, the margin of stability becomes smaller [21]. Second, the lateral excursion of the extrapolated center of mass can be increased, by bilaterally increasing stance time, i.e. decreasing cadence, which leads to a smaller margin of stability (chapter 4). Vice versa, bilaterally decreasing stance time, i.e. increasing cadence, decreases the lateral excursion of the extrapolated center of mass, and increases the mediolateral margin of stability [23] (chapter 4). Third, increasing the stance time on one leg, but not the other (walking with asymmetric stance times), leads to a shift in the mediolateral extrapolated center of mass position to the side with the longer stance time, and the mediolateral margin of stability becomes smaller on the side with the longer stance time. Hereby, asymmetric mediolateral margins of stability are created, with a smaller mediolateral margin of stability on the leg with longer stance time, and a larger mediolateral margin of stability on the side with the shorter stance time (chapter 4). This mechanism can be exploited, for instance to improve dynamic balance when walking on an injured leg, by standing on the non-injured leg longer and increasing the mediolateral margin of stability on the injured leg, possibly making it more robust against perturbations.

While the margin of stability is often defined at heel-strike, the margin of stability can be 'fine-tuned' through an ankle (chapter 3) [21,24] or hip strategy [25,26] during the stance phase. By using a mediolateral ankle strategy during the stance phase of gait, the location of the center of pressure under the foot can be altered after foot placement, thereby increasing the base of support when the margin of stability at heel-strike was small, or decreasing the base of support when the margin of stability at heel-strike was large. Similarly, a hip strategy can be used to move the trunk, head and arms, which generates a moment around the hip in the frontal plane [25]. By using a hip strategy, the location of the extrapolated center of mass can be moved medial or lateral, to in- or decrease the mediolateral margin of stability. For example, in narrow-ridge walking, large upper body movements are exhibited to generate a hip moment, regulate the body's center of mass and remain stable [25]. While the relation between foot placement

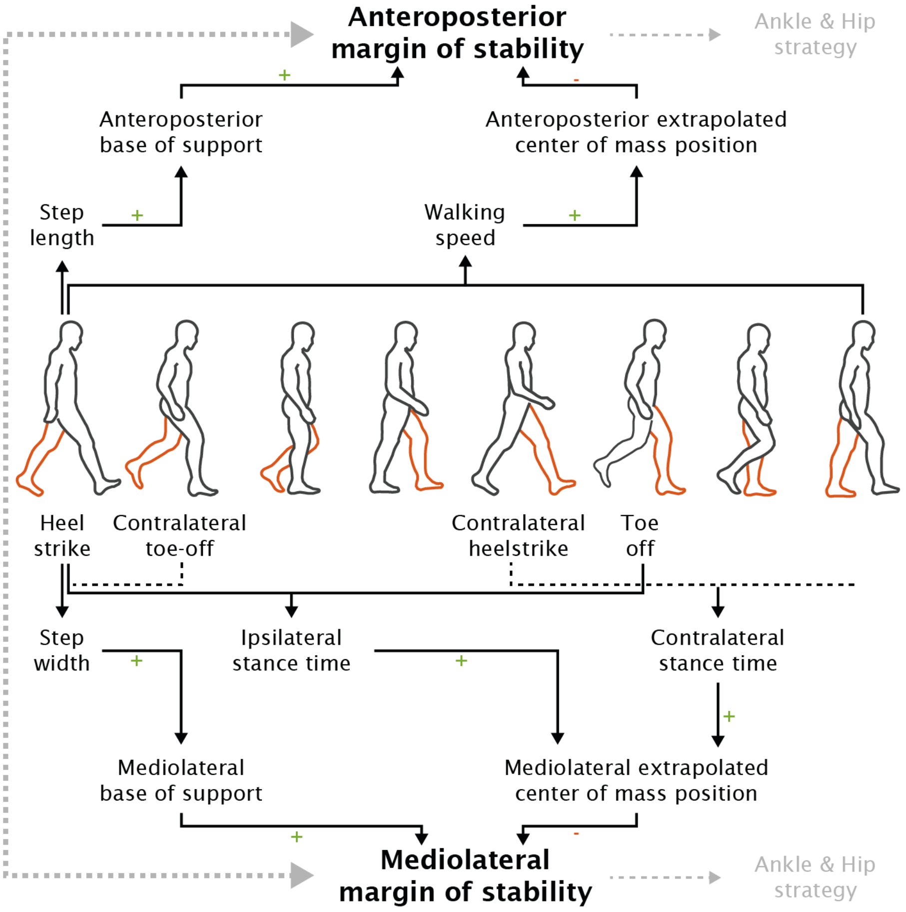

Figure 1 – A spatiotemporal stepping model for adaptive control of dynamic balance in the frontal and sagittal plane. A '+' indicates a positive effect, a '–' indicates a negative effect. The anteroposterior margin of stability is positively affected by step length and negatively affected by walking speed, and might be fine-tuned during stance by an ankle and / or hip strategy. The mediolateral margin of stability is positively affected by step width and negatively affected by bilateral stance times, and is fine-tuned during stance by an ankle and hip strategy. Note that a unilateral increase in contralateral stance time will lead to an increase in the contralateral mediolateral margin of stability (chapter 4). The large grey arrows on the left side of this figure depict the possible covariation between frontal and sagittal plane margins of stability (chapter 6).

and stance time follows logically from the linear inverted pendulum model, the model neglects the effect of an ankle or hip strategy. Previous research and this thesis (chapter 3) show that foot roll-off can be seen as an addition to this model to gain more insight in balance control strategies. For instance, Hof et al. (2017) [21] found that people with an upper leg prosthesis showed a larger margin of stability on the prosthetic than non-prosthetic side to compensate for the lack of mediolateral degrees of freedom in the prosthesis' ankle joint, and therefore the lack of mediolateral foot roll-off during stance. Interestingly, in chapter 3 we found a strong covariation between the mediolateral margin of stability and mediolateral foot roll-off. There are two hypotheses for this covariation that have yet to be investigated: (i) There is an optimal mediolateral margin of stability that can only be reached through active control of mediolateral foot roll-off after foot placement. (ii) The mediolateral foot roll-off is a product of passive dynamics in gait, which hypothetically works as follows; When we have a small margin of stability, our extrapolated center of mass position is more lateral to the edge of the base of support, resulting in an outward momentum of the body during foot roll-off, resulting in a passive outward mediolateral foot roll-off, and vice versa for a large margin of stability.

The anteroposterior margin of stability was not described in Hof's original work [20], but gained considerable interest and attention in more recent research [22,23,27,28]. Similar to the mediolateral margin of stability, the anteroposterior margin of stability can be controlled in multiple ways. First, the anteroposterior margin of stability can be increased by increasing the anteroposterior base of support, i.e. step length [23]. Second, the anteroposterior margin of stability can be increased by placing the anteroposterior extrapolated center of mass position more posterior, which can be achieved by reducing the walking speed [23]. Effects of ankle and hip strategies seem less evident, but may still be present in the anteroposterior direction. For instance, large upper body movements are made in response to a slipping or tripping perturbation (e.g. in chapter 6), generating a moment around the hip in the sagittal plane to regulate the anteroposterior position of the extrapolated center of mass. However, further research is needed to define whether the ankle and hip strategies are actively controlled or exploited to regulate the anteroposterior margin of stability during human walking.

Caution is advised when interpreting the anteroposterior margin of stability. While a negative mediolateral margin of stability would require a sidestep to prevent a fall [29], the anteroposterior margin of stability can be either positive or negative, while still resulting in stable gait [22,28] (chapter 6). When the anteroposterior extrapolated center of mass is in front of the leading leg's base of support, one can make the next step and maintain dynamic balance [30,31]. In addition, when the anteroposterior extrapolated center of mass is behind the leading leg's base of support gait can still be stable, while a person progresses forwards. Only when the extrapolated center of mass is behind the trailing leg's base of support, a backward step is necessary to remain stable [32]. Furthermore, different definitions of the anteroposterior base of support limit interpretation between studies. For example, in work by Hak et al. [22,23] the anterior base of support was defined as the posterior (heel marker) border of the leading foot. By this definition, the anteroposterior margin of stability will most often be positive during healthy unperturbed walking [22]. However, when the anterior border (toe marker) of the leading foot is chosen instead (chapter 6), the anteroposterior margin of stability can have both negative and positive values for the same behavior, and thus stable gait. Furthermore, when center of pressure positions are used to define the base of support (chapters 3 and 4), it is difficult to define a posterior or anterior border of the foot, and the center of pressure position of the leading foot will be used instead. Considering these differences between interpretations and methodologies, caution is necessary when reporting and interpreting margins of stability in human walking.

ADAPTIVE CONTROL OF DYNAMIC BALANCE IN PATHOLOGICAL WALKING

Regulation of the margin of stability contains both passive and active components (chapter 4), and exploitation of the passive properties of the margin of stability may allow for simple, yet effective adaptive control of dynamic balance in pathological populations. For example, people post-stroke show a shorter stance time on the paretic leg than the non-paretic leg [33], by which they increase the paretic mediolateral margin of stability (chapters 4 and 6). Interestingly, when we consider asymmetric margins of stabilities while walking in a straight line, the mediolateral margin of stability can only be increased asymmetrically by walking with asymmetric stance times, as increasing the mediolateral base of support on one leg and not the other, would lead to a walking in a curved path. However, unilaterally increasing the anteroposterior base of support, i.e. walking with asymmetric step lengths, would still result in walking a straight line. This implies that an asymmetric anteroposterior margin of stability can be acquired by walking with asymmetric step lengths, as is indeed commonly seen in people post-stroke [33].

In chapter 6, we examined balance strategies in reactive balance control in people post-stroke during a slipping experiment on a split-belt treadmill. There, we found asymmetric anteroposterior and mediolateral margins of stability during unperturbed walking and in the recovery steps following the perturbation. Furthermore, we found a covariation between the anteroposterior and mediolateral margins of stability in the paretic recovery step following the perturbation. This covariation implies that improving sagittal plane dynamic balance compromises frontal plane balance during reactive stepping with the paretic leg. Therefore, gait rehabilitation could be focused on decoupling the mediolateral and anteroposterior margins of stability during reactive stepping with the paretic leg, e.g. through perturbation-based training. In addition, to gain further insight in balance strategies post-stroke, it would be interesting to assess whether people post-stroke prioritize balance in one plane over the other.

THE SPLIT-BELT WALKING PARADIGM

The split-belt walking paradigm has led to advances in knowledge of locomotor adaptation [34], learning [35], retention [36], savings [37], optimization [38] and coordination [14,39]. More recently, advances in knowledge on adaptive control of dynamic balance during split-belt walking are seen (chapters 3, 4, 5 and 6) [27,40,41]. Furthermore, split-belt walking has been utilized in clinical practice to reduce pathological gait asymmetries [42]. The goal of such clinical approaches is to reduce pathological gait asymmetry and for example, results in a temporary reduction of step-length symmetry in people post-stroke [42]. However, one can question whether reduction of step length asymmetry is the right approach in post-stroke rehabilitation, as this thesis (chapters 4 and 6) indicates that the stepping asymmetry seen in people post-stroke may be a strategy that enhances adaptive control of dynamic balance in this population.

It should be kept in mind that split-belt walking is an artificial, laboratory-based task. The ecological validity of treadmill walking [43,44], let alone split-belt treadmill walking [45], compared to overground walking can be questioned. While it allows for long continuous data recording and training sessions, humans show different kinetic and kinematic parameters when walking on a regular treadmill [43,44] and walk with a wider base of support on a split-belt treadmill [45] compared to overground walking. The major benefit of studying locomotor adaptations on a split-belt treadmill is that it allows us to study how humans perform a completely novel walking task, in a controlled environment. Therefore, especially the implications from split-belt literature are deemed to find their way to rehabilitation practice. For instance, in chapter 5 the split-belt paradigm was utilized to study the effects of external balance support on locomotor learning, which lead to direct implications for gait rehabilitation.

ENERGETIC OPTIMIZATION OF HUMAN LOCOMOTION

Human walking can be described as a series of falling motions, each terminated by the next step to prevent an actual fall. Therefore, one can argue that the goal of locomotion is to progress forwards through space without falling. However, when we succeed to stay upright during walking, we still show adaptation in our walking pattern when task demands change, e.g. in split-belt walking (chapter 3). The question then comes to mind, why we change our walking pattern when we are already successful in progressing forwards while maintaining our balance. An answer to this question may lie in the energy or metabolic cost of human walking [46].

When gait is stable, humans may explore their movement possibilities to find a walking pattern that is most efficient, i.e. they optimize their walking pattern. Multiple options are available for optimization in human walking, e.g. shortest trajectory of limb motion, minimal fluctuation in center of mass height, or reduction of joint friction and impact forces. However, energetic optimization of human walking is very likely from both an evolutionary and empirical perspective. From an evolutionary perspective, all mammals, and therefore humans, may want to reduce the energy cost of movement. Since nutrition is scarce, energetic optimization of movement reduces the need for food, and thereby increases chances of survival. From an empirical perspective, there are studies showing that humans naturally walk with a step width [47], cadence [48] and velocity [49] that is at their energetic optimum. In addition, during split-belt adaptation, humans slowly reduce the energy cost of walking (chapter 3) [38,50]. Furthermore, during split-belt walking humans learn to take advantage of the treadmill's moving belts to reduce energy cost, up to the point where they cross the level of perfect step length symmetry, and go to a 'positive' step length asymmetry [51]. Ergo, an efficient stepping pattern is preferred over a spatiotemporally symmetric pattern. The knowledge that humans optimize their energy cost of walking when balance is safeguarded may help us to better understand and appreciate pathological walking.

HEAD, ARM AND TRUNK MOVEMENTS IN HUMAN WALKING

This thesis focuses on human walking; therefore, it seems logical to focus on lower-limb movements. However, human walking is not merely a movement of the legs, but rather of the whole body [52]. These movements can be captured using full-body marker sets, which contains information about the role of head, arm and trunk movements in human walking. For example, it was suggested that arm swing reduces energy cost of walking and increases stability [53]. In contrast, other studies described arm swing as a passive result of the movement of the human body, which reduces energy cost, but does not affect stability [54,55]. While many studies have described the effects of arm swing in unperturbed walking [52-55], it may also help us to better understand recovery steps in response to perturbations. In chapter 6 of this thesis, we found that regulation of the extrapolated center of mass position partially underlies changes in the anteroposterior margin of stability in reaction to slipping perturbations in walking post-stroke. This regulation may have been the result of upper-body movement, resulting in backward momentum of the body to stay upright, reducing the need for a stepping strategy to maintain dynamic balance. This illustrates that potentially valuable information lies in (the analysis of) head, arm and trunk movements in experiments on human walking, leaving room to explore in the future.

CONCLUDING REMARKS

The aim of this thesis was to increase our understanding of adaptive control of dynamic balance in human walking. The studies in this thesis have provided us with knowledge on adaptive neuromuscular control, adaptive control of dynamic balance, exploitation of passive properties of the human body, the effects of external support on locomotor learning and reactive stepping in people post-stroke. By assessment of the margin of stability, we gained insight in healthy and pathological adaptive control of dynamic balance, illustrating that this complex parameter can be regulated by simple changes in movement. The role of adaptive control of dynamic balance in locomotor learning was stressed by showing that handrail holding dramatically reduces learning outcomes. And finally, our current understanding of asymmetric strategies to control the margins of stability suggests that gait asymmetries in patient populations may enhance adaptive control of dynamic balance. In future research, a unified framework of both active and passive regulation of adaptive control of dynamic balance in human walking is necessary to further understand able-bodied and pathological human walking. This thesis brings us one step closer to understanding human walking, but many more of these small steps are necessary. In conclusion, this thesis describes adaptive control of dynamic balance in human walking as both an active and passive mechanism, utilizing temporal and spatial strategies to remain stable, while finding an efficient locomotor pattern.

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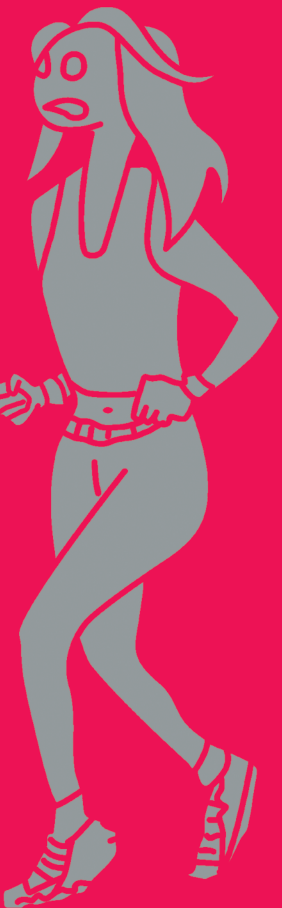

A

APPENDICES

SUMMARY

Humans are one of few mammals that exercise bipedal gait. While bipedal walking costs less energy than quadrupedal gait, it is inherently unstable. To remain stable during walking, humans need to flexibly respond and adapt to the ever-changing task-conditions, for instance when walking on a slippery surface. Humans thus need to adaptively control dynamic balance to stay upright. The importance of adaptive control of dynamic balance becomes clear after natural ageing or disease, when people have trouble to control their balance and as a result become less mobile or more prone to falling. To improve prevention of mobility decline and improve gait rehabilitation, we need to better understand adaptive control of dynamic balance. Therefore, the aim of this thesis was to increase our understanding of adaptive control of dynamic balance in human walking. In all studies a treadmill was used to assess human walking, in which changes in treadmill belt speed were applied to perturb participants (**chapter 1**).

First, in **chapter 2** we studied the adaptive neuromuscular response to changes in gait velocity in healthy adults. To generate movement, we must produce moments of force over our skeletal joints. To actively generate these moments of force, control of muscle contractions is necessary and we can record the activity of these muscles through wire or surface electromyography. Since the adaptation of walking speed is one of the most fundamental adaptations in human movement, a hypothetical synergistic structure of muscle coordination should reflect this adaptability. Based on surface electromyography, we found that a synergistic structure might control the speed dependent modulation of muscle activity in human walking, as a means of adaptive neuromuscular control in human walking.

In **chapter 3**, we studied the adaptation of mediolateral dynamic balance control during walking with asymmetric belt speeds on an instrumented split-belt treadmill, i.e. split-belt walking. Unlike a regular treadmill, the split-belt treadmill has two parallel belts, the velocity of which can be controlled independently. When exposed to split-belt walking, humans initially exhibit an asymmetric gait pattern, which they adapt towards a more symmetric gait pattern in a matter of minutes. In chapter 3 we showed that healthy young adults adapt their mediolateral dynamic balance to this task through a complementary mechanism of relative foot placement (i.e. the margin of stability) and mediolateral foot-roll off.

To better understand the control of margins of stability, we studied bilateral temporal control as a regulating mechanism of dynamic balance in **chapter 4** in healthy adults. Here we found that regulation of bilateral stance times may allow for simple, yet effective adaptive control of dynamic balance through exploitation of the passive properties of the human body. The potential exploitation of this mechanism comes to light in pathologic gait. For example, people post-stroke show a shorter paretic than non-paretic stance time, by which they unload the paretic leg and increase the paretic mediolateral margin of stability.

Then, we turned the tables in **chapter 5** and assessed what happens to locomotor learning when the balance control problem is reduced through external support. There, we found that when healthy young adults were allowed to hold on to handrails during split-belt walking, they were perturbed less during early split-belt walking, and therefore had less need to adapt their stepping pattern to the asymmetric belt speeds. Consequently, these participants did not learn the novel locomotor task of split-belt walking, as was indicated by reduced after-effects. The findings in this chapter indicate that maintaining dynamic balance is an important task goal in human walking, which shapes adaptive locomotor control and locomotor learning. Furthermore, while balance assistance is often used in clinical practice to relearn people to walk, clinicians should take into account that balance assistance may reduce learning effects.

The knowledge from previous chapters was applied to better understand post-stroke balance impairments in **chapter 6**. Here we showed that when people with post-stroke hemiparesis make a forward step with their paretic leg to increase their anteroposterior margin of stability in response to a slip-like perturbation on the treadmill, they simultaneously decrease their mediolateral margin of stability. This indicates that when people post-stroke increase forward balance, they may lose sideward balance during reactive stepping responses. Future research should indicate whether this maladaptive paretic coupling between anteroposterior and mediolateral margins of stability can be decreased in training, e.g. through perturbation training, to increase adaptive control of dynamic balance in people post-stroke.

Chapter 7 provided a general discussion of the findings in this thesis. This thesis has brought knowledge on adaptive neuromuscular control, adaptive control of dynamic balance, exploitation of passive properties of the human body, the effects of external support on locomotor learning and reactive stepping in people post-stroke. By assessment of the margin of stability, we gained insight in healthy and pathological adaptive control of dynamic balance, illustrating that the margin of stability be regulated by simple changes in movement. The role of adaptive control of dynamic balance in locomotor learning was stressed by showing that handrail holding dramatically reduces learning outcomes. Finally, our current understanding of asymmetric strategies to control the margins of stability suggests that gait asymmetries in patient populations may enhance adaptive control of dynamic balance. In conclusion, this thesis describes adaptive control of dynamic balance in human walking as both an active and passive mechanism, utilizing temporal and spatial strategies to remain stable, while finding an efficient locomotor pattern.

SAMENVATTING

Mensen zijn een van de weinige zoogdieren die op twee benen lopen, en hoewel dat weinig energie kost, is het ook instabiel. Om overeind te blijven tijdens het lopen passen mensen constant hun stappen aan op de altijd veranderende omgeving, bijvoorbeeld wanneer ze over een onregelmatige ondergrond lopen. Mensen moeten de controle van hun dynamische balans dus adapteren (aanpassen) om overeind te blijven tijdens lopen. Het belang van adaptieve controle van dynamische balans tijdens lopen wordt pas duidelijk na natuurlijke veroudering, ziekte of blessure. Mensen hebben dan moeite om hun balans te controleren en als gevolg worden ze minder mobiel en hebben ze een grotere kans op vallen. Om looptrainingen en de gangrevalidatie te verbeteren, moeten we eerst beter begrijpen hoe adaptieve controle van dynamische balans werkt. Daarom is het doel van dit proefschrift om adaptieve controle van de dynamische balans tijdens lopen bij mensen beter te begrijpen. In alle studies in dit proefschrift werd de loopband gebruikt om lopen te bestuderen, waarbij verandering in de bandsnelheid werd gebruikt om het lopen bij proefpersonen te verstoren (**hoofdstuk 1**).

Allereerst, in **hoofdstuk 2**, onderzochten we de adaptieve neuromusculaire reactie op veranderingen in loopsnelheid bij gezonde proefpersonen. Om bewegingen te genereren, moeten we momenten over onze gewichten produceren. Om deze momenten actief te kunnen produceren, hebben we spiercontracties nodig. Deze spiercontracties kunnen we meten middels draad of oppervlakte-elektromyografie. Aangezien de adaptatie van loopsnelheid een van de meest fundamentele adaptaties in het menselijk bewegen is, zou een hypothetische synergistische structuur van spiercoördinatie deze adaptiviteit moeten reflecteren. Gebaseerd op oppervlakte-elektromyografie, vonden we dat een synergistische structuur mogelijk de snelheidsafhankelijke modulatie van spieractiviteit tijdens het lopen controleert, resulterend in adaptieve neuromusculaire controle tijdens het lopen.

In **hoofdstuk 3** bestudeerden we de adaptatie van mediolaterale dynamische balanscontrole tijdens het lopen met asymmetrische bandsnelheden op een split-belt loopband, i.e. split-belt lopen. Anders dan een normale loopband heeft een split-belt loopband twee parallelle banden, waarvan de snelheden onafhankelijk gereguleerd kunnen worden. Wanneer mensen voor het eerst split-belt lopen, laten ze een asymmetrisch looppatroon zien, dat ze aanpassen naar een meer symmetrisch patroon binnen een paar minuten. In hoofdstuk 3 lieten we zien dat gezonde proefpersonen hun mediolaterale balans aanpassen aan split-belt lopen middels een complementair mechanisme van voetplaatsing (de ‘margin of stability’) en voetafwikkeling.

Om controle van de ‘margin of stability’ beter te begrijpen, bestudeerden we bilaterale temporele controle als een regulerend mechanisme van de dynamische balans bij gezonde proefpersonen in **hoofdstuk 4**. Hier vonden we dat regulering van bilaterale standtijden resulteert in een simpele, doch effectieve manier van adaptieve controle van de dynamische balans, door exploitatie van de passieve eigenschappen van het menselijk lichaam. De mogelijke exploitatie van dit mechanisme komt naar voren in pathologisch lopen. Bijvoorbeeld, mensen met een beroerte laten vaak een kortere stand tijd zien aan de aangedane zijde dan aan de niet-aangedane zijde, waardoor ze hun aangedane been ontlasten en de ‘margin of stability’ aan die kant vergroten.

Vervolgens draaiden we de rollen om in **hoofdstuk 5** en onderzochten we wat er met locomotorisch leren gebeurt, wanneer het balanscontrole probleem is verminderd door externe ondersteuning tijdens het lopen. Daar vonden we dat wanneer gezonde proefpersonen leuningen mochten vasthouden tijdens het split-belt lopen, hun looppatroon minder werd verstoord tijdens de vroege adaptatie en ze daardoor hun looppatroon niet hoefden aan te passen aan de asymmetrische bandsnelheden. Als gevolg daarvan leerden de proefpersonen niet het nieuwe patroon, herkenbaar aan de verminderde na-effecten. De bevindingen in dit hoofdstuk suggereren dat het controleren van de dynamische balans een belangrijk taakdoel is in menselijk lopen, en vormgeeft aan de adaptieve locomotorische controle en het leren. Hoewel balansondersteuning vaak gebruikt wordt in de klinische praktijk tijdens het lopen, moeten clinici er rekenen mee houden dat balansondersteuning het leren kan verminderen.

De kennis uit de vorige hoofdstukken werd toegepast om balansproblemen bij mensen met een beroerte beter te begrijpen in **hoofdstuk 6**. Hier lieten we zien dat wanneer mensen met hemiparese als gevolg van een beroerte een voorwaartse stap maken met hun aangedane been om hun voorwaartse ‘margin of stability’ te vergroten in reactie op een uitglij-verstoring op de loopband, ze tegelijkertijd hun zijwaartse ‘margin of stability’ verkleinen. Dit suggereert dat wanneer mensen met een beroerte hun voorwaartse balans verbeteren, ze hun zijwaartse balans kunnen verliezen in reactie op een verstoring van het lopen. Toekomstig onderzoek moet uitwijzen of deze koppeling tussen de voorwaartse en zijwaartse ‘margin of stability’ verminderd kan worden tijdens de revalidatie, bijvoorbeeld door middel van verstoringstraining. Daarmee zou mogelijk de adaptieve controle van de dynamische balans bij mensen met een beroerte verbeterd kunnen worden.

Hoofdstuk 7 biedt een algemene discussie van de bevindingen in dit proefschrift. Dit proefschrift heeft ons kennis gegeven over adaptieve neuromusculaire controle, adaptieve controle van de dynamische balans, exploitatie van de passieve eigenschappen van het menselijk lichaam, de effecten van externe ondersteuning op locomotorisch leren en reactieve balanscontrole bij mensen met een beroerte. Door het bestuderen van de ‘margin of stability’ kregen we inzicht in adaptieve controle van de dynamische balans bij gezonde en pathologische populaties, waarbij we lieten zien dat de ‘margin of stability’ relatief simpel gereguleerd kan worden. De rol van adaptieve controle van de dynamische balans in locomotorisch leren werd duidelijk toen bleek dat het vasthouden van handrails het locomotorisch leren sterk verminderd. Als laatste lieten we zien dat asymmetrische strategieën om de ‘margins of stability’ te controleren, de adaptieve controle van de dynamische balans tijdens pathologisch lopen zou kunnen verbeteren. In conclusie, beschreef dit proefschrift de adaptieve controle van de dynamische balans tijdens het lopen bij mensen als zowel een actief als passief mechanisme, dat gebruik maakt van temporale en spatiele strategieën om stabiel te blijven, terwijl een efficiënt looppatroon gevonden wordt.

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Tom.

ABOUT THE AUTHOR

Tom Buurke was born on September 8th, 1993 in Enschede, the Netherlands. He obtained his high school (VWO) diploma at Het Stedelijk Lyceum Zuid in Enschede in 2011, during which he did a research project on barefoot running at Roessingh Research and Development in Enschede. As part of his bilingual education in high school, he completed the International Baccalaureate English Language A2 higher level program in 2011. Tom then moved to Groningen to study Human Movement Sciences at the University of Groningen, where he obtained his bachelor's degree in 2014 and his master's degree in 2016. During his studies, Tom was a teaching assistant at Human Movement Sciences in several bachelor courses. Additionally, he was a member and chair of multiple committees at rowing club AGSR Gyas in Groningen. During his master's Tom was awarded a fully funded three-year PhD position at the University Medical Center Groningen and the University of Groningen, as part of the prestigious Master-PhD program.

During his PhD, Tom worked on multiple research studies at the Center for Human Movement Sciences in Groningen. For his research, Tom was awarded the Society for Movement Analysis Laboratories in the Low Lands award in 2016. Furthermore, he won an award for best oral presentation at the Dutch Society for Human Movement Sciences (VVBN) PhD-Day in 2017. In 2018, he received a travel award by the De Luca Foundation to attend the World Congress of Biomechanics in Dublin. In 2019, Tom won the Center for Human Movement Sciences Researcher of the Year award and a Top Publication Award from research institute SHARE for his publication on the effects of handrail holding on locomotor learning. During his PhD, Tom supervised multiple bachelor and master students during their graduation projects. Furthermore, he was a PhD representative, member of the advisory board and member of the research committee at the Center for Human Movement Sciences. In 2018, he was part of the organization for the annual conference of the Society for Movement Analysis Laboratories in the Low Lands and Tom is currently a member of the society's social media committee. In 2019 Tom was a visiting scholar at the University of Southern California in Los Angeles, CA, for which he received grants by Stichting Beatrixoord Noord-Nederland, the Groninger University Fund and Stichting De Cock-Hadders.

Currently, Tom is a post-doc researcher and lecturer at the Center for Human Movement Sciences of the University Medical Center Groningen and looking to continue his career in academia.

SCIENTIFIC OUTPUT

Journal publications

Vervoort D, den Otter R, **Buurke TJW**, Vuillerme N, Hortobágyi T, Lamoth CJC. (in press) Do gait and muscle activation patterns change at middle-age during split-belt adaptation? Journal of Biomechanics.

Buurke TJW, Lamoth CJC, van der Woude LHV, Hof AL, den Otter R. (2019) Bilateral temporal control determines mediolateral margins of stability in symmetric and asymmetric human walking. Scientific Reports. 9: 12494 DOI: 10.1038/s41598-019-49033-z

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter R. (2019) Handrail holding during treadmill walking reduces locomotor learning in able-bodied persons. IEEE Transactions on Neural Systems and Rehabilitation Engineering. 27(9): 1753-1759 DOI: 10.1109/TNSRE.2019.2935242

Vervoort D, Den Otter AR, **Buurke TJW**, Vuillerme N, Hortobágyi T, Lamoth CJC. (2019) Effects of aging and task prioritization on split-belt gait adaptation. Frontiers in Aging Neuroscience. 11:10 DOI: 10.3389/fnagi.2019.00010

Buurke TJW, Lamoth CJC, Vervoort D, van der Woude LHV, den Otter R. (2018) Adaptive control of dynamic balance in human gait on a split-belt treadmill. Journal of Experimental Biology. 221(13): jeb.174896 DOI: 10.1242/jeb.174896

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter AR. (2016) Synergistic structure in the speed dependent modulation of muscle activity in human walking. PLoS ONE. 11(4): e0152784 DOI: 10.1371/journal.pone.0152784

Submitted for publication

Buurke TJW, Liu C, Park S, den Otter R, Finley JM. Maintaining sagittal plane balance compromises frontal plane balance during reactive stepping in people post-stroke.

Other publications

Buurke TJW. (2018) Multiple balance mechanisms to keep you upright while split-belt walking. International Society for Posture and Gait Research Blog. ISSN: 2561-4703

CONFERENCE CONTRIBUTIONS

Oral presentations

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter AR. (2018) Handrail holding on a split-belt treadmill reduces locomotor learning. 6th International RehabMove State-of-the-Art Congress, Groningen, NL

Buurke TJW, den Otter AR. (2018) The margins of stability during motor learning. Part of the mini-symposium "Gait analysis and adaptations; using new ideas to tackle old problems in gait classification and training" at the Dutch Congress of Rehabilitation Medicine, Groningen, NL

Buurke TJW, Lamoth CJC, Vervoort D, van der Woude LHV, den Otter AR. (2018) Changes in mediolateral dynamic balance control during imposed gait asymmetry on a split-belt treadmill are strongly dependent on passive dynamics in gait. 8th World Congress of Biomechanics, Dublin, IE

Buurke TJW, Lamoth CJC, Vervoort D, van der Woude LHV, den Otter AR. (2018) Long-term retention of split-belt walking reveals differences in spatiotemporal gait adaptation and dynamic balance control. 22nd International Society of Electrophysiology and Kinesiology Congress, Dublin, IE

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter AR. (2017) Long-term retention of single exposure to split-belt walking: preliminary results. Dutch Society for Human Movement Sciences (VVBN) PhD-Day, Rotterdam, NL

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter AR. (2017) Relation between dynamic balance control and metabolic cost during split belt adaptation. International Society for Posture and Gait Research World Congress, Fort Lauderdale, FL

Buurke TJW, den Otter AR, Lamoth CJC, van der Woude LHV. (2016) Energieverbruik en dynamische balans controle tijdens split-belt adaptatie. 6th annual conference of the Society for Movement Analysis Laboratories in the Low Lands, Enschede, NL

Poster presentations

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter R. (2019) The effects of handrail holding on split-belt adaptation. XXVII Congress of the International Society of Biomechanics & 43rd Annual Meeting of the American Society of Biomechanics, Calgary, CA

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter R. (2019) Locomotor savings of split-belt gait adaptation indicate long-term adaptation processes. International Society for Posture and Gait Research World Congress, Edinburgh, SCT

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter R. (2019) After-effect magnitude predicts retention in split-belt gait adaptation. International Society for Posture and Gait Research World Congress, Edinburgh, SCT

den Otter R, **Buurke TJW**, Lamoth CJC. (2019) Singular Spectrum Analysis for the detection of adaptation rates in split-belt data. International Society for Posture and Gait Research World Congress, Edinburgh, SCT

Vervoort D, den Otter AR, **Buurke TJW**, Vuillerme N, Hortobágyi T, Lamoth CJC. (2019) Changes in muscle activation patterns underlie split-belt gait adaptation. International Society for Posture and Gait Research World Congress, Edinburgh, SCT

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter AR. (2018) Effects of handrail holding on split-belt adaptation. Dutch Society for Human Movement Sciences (VVBN) PhD-Day, Amsterdam, NL

Buurke TJW, Lamoth CJC, van der Woude LHV, den Otter AR. (2018) Handrail holding affects split-belt gait adaptation. 8th annual conference of the Society for Movement Analysis Laboratories in the Low Lands, Groningen, NL

Vervoort D, den Otter AR, **Buurke TJW,** Hortobágyi T, Lamoth CJC. (2018) Gait adaptation differs from explicit perception of split-belt speed differences. 8th annual conference of the Society for Movement Analysis Laboratories in the Low Lands, Groningen, NL

Vervoort D, den Otter AR, **Buurke TJW**, Vuillerme N, Hortobágyi T, Lamoth CJC. (2018) Gait adaptation differs from explicit perception of split-belt speed differences in young and middle-aged adults. 15th European Workshop on Ecological Psychology, Toulouse, Fr

Vervoort D, den Otter AR, **Buurke TJW**, Hortobágyi T, Lamoth CJC. (2017) Muscle synergies during split-belt walking in young and middle-aged adults. Dutch Society for Human Movement Sciences (VVBN) PhD-Day, Rotterdam, NL

Buurke TJW, Lamoth CJC, Vervoort D, van der Woude LHV, den Otter AR. (2017) Three week retention of a single split-belt adaptation session: Effects on gait symmetry and balance control. 7th annual conference of the Society for Movement Analysis Laboratories in the Low Lands, Leuven, BE

Vervoort D, den Otter AR, **Buurke TJW**, Hortobágyi T, Lamoth CJC. (2017) Muscle synergies during split-belt walking in young and middle-aged adults. 7th annual conference of the Society for Movement Analysis Laboratories in the Low Lands, Leuven, BE