

Mechanisms that stabilize human walking

A. M. VAN LEEUWEN^{1,2} | SJOERD M. BRUIJN^{1,2} | JAAP H. VAN DIEËN¹

¹ Department of Human Movement Sciences, Faculty of Behavioural and Movement Sciences, Vrije Universiteit Amsterdam, Amsterdam Movement Sciences, Amsterdam, The Netherlands.

² Institute of Brain and Behavior Amsterdam.

Correspondence to: Sjoerd M. Bruijn
 Email: s.m.bruijn@gmail.com
<https://doi.org/10.20338/bjmb.v16i5.321>

ABBREVIATIONS

| | |
|----------------------|--|
| α_i | Angular acceleration of the i^{th} Segment |
| CoM | Center of mass |
| $\ddot{C}oM$ | Acceleration of the COM |
| CoM' | Position vector of the vertical projection of the COM on the ground |
| CoP | Center of pressure (position vector of the point of application of the ground reaction force F_g) |
| com_i | Position vector of the center of mass of the i^{th} segment |
| $\ddot{c}o\dot{m}_i$ | Linear acceleration of the i^{th} segment |
| F_{gy} | Vertical component of the ground reaction force |
| \dot{H} | Change of angular momentum around the body center of mass |
| I_i | Moment of inertia of the i^{th} segment |
| m | Body mass |
| m_i | Mass of the i^{th} segment |
| n | Number of segments |
| r_e | Position vector of the point of the application of an external force F_e |

ABSTRACT

In this paper, we review what mechanisms are used to stabilize human bipedal walking. Based on mechanical reasoning, potential mechanisms to control the body center of mass trajectory are modulation of foot placement, stance leg control by modulation of ankle moments and push-off forces, and modulations of the body's angular momentum. The first two mechanisms and especially the first are dominant in controlling center of mass accelerations during gait, while angular momentum control plays a lesser role, but may be important to control body alignment and orientation. The same control mechanisms stabilize both steady-state and perturbed gait in both the mediolateral and antero-posterior directions. Control is at least in part active and is affected by proprioceptive, visual and vestibular information. Results support that this reflects a feedback process in which sensory information is used to obtain an estimate of the center of mass state based on which foot placement and ankle moments are modulated. These active feedback mechanisms suggest training approaches for populations at risk of falling, through perturbations, augmented feedback, or constraining one mechanism to train the other mechanisms.

KEYWORDS: Gait stability | Foot placement | Stance leg control | Angular momentum | Falls

PUBLICATION DATA

Received 04 11 2022
 Accepted 14 12 2022
 Published 15 12 2022

1. INTRODUCTION

Stabilizing bipedal walking to avoid falls is challenging. This is readily apparent in toddlers who learn to walk and usually master this only after many falls have occurred. At the other end of the age spectrum, age-related but also disease-related impairments often also cause problems in stabilizing gait. However, then the resulting falls are much more problematic, as they often have serious adverse consequences, such as injury, fear of falling, loss of independence, and social isolation^{1,2,3}. Training interventions have been successful at reducing fall rates in older adults⁴ and in patients at high risk of falling⁵. However, in our opinion, new training approaches to improve gait stability and methods to assess and understand changes in gait stability can be derived from a better understanding



of the mechanisms that are used to stabilize gait. In an earlier review, we covered foot placement as the most dominant mechanism used to stabilize gait⁶. In this review, we expand on this and provide an overview of gait stability control mechanisms and an outlook on how insight into these mechanisms could be used to identify potential training approaches.

For the purpose of this review, we will pragmatically define ‘stable’ gait as gait that does not lead to falls. This requires control of the position of the body center of mass relative to the base of support. In gait, the base of support is formed by those parts of the feet that are in contact with the floor at any point in time. In humans, a large part of the total body mass is located high above a small base of support, particularly in single stance. Consequently, small deviations in body orientation result in substantial gravitational moments that can easily move the center of mass away from the base of support. Therefore, even the small variations in the center of mass position that occur in unperturbed gait need to be corrected, to avoid cumulative effects over time. Thus ongoing (intermittent or continuous) stabilization is needed. When a perturbation occurs, which can here be defined as any external mechanical event that disturbs the relation between the center of mass and base of support beyond the variance observed in unperturbed gait, it is evident that stabilizing control is required. However, it is not evident that the same stabilizing mechanisms are used for the small deviations during unperturbed gait and for the larger deviations after perturbations.

Stabilization of gait can be achieved by passive and active mechanisms. Passive stabilization relies on the passive mechanical properties (stiffness, damping and inertia of the human body), whereas active mechanisms involve modulation of neural drive and muscle activity in response to sensory information. Passive mechanisms may thus be efficient, as in requiring low control effort and energy costs, but may not be amenable to change for example by training. Active mechanisms are presumably more adaptive to task requirements in the short term and may be more amenable to improvement by training in the long term. Note that active and passive mechanisms may be used in parallel.

As mentioned above, stabilization of bipedal walking is challenging. Nevertheless, a simple two-dimensional (sagittal plane) model of a bipedal walker can be stable without any form of active control. In such a model, the forward fall of the center of mass is controlled on a step-by-step basis through adequate foot placement resulting from the model’s passive dynamics⁷. The ground contact force after foot placement creates a backward moment, which catches the forward fall. However, these passive models cannot deal with perturbations of realistic magnitude and also three-dimensional versions are unstable in the mediolateral direction⁸. This indicates that additional active control must be exerted to horizontally accelerate the center of mass in the desired direction, when the center of mass deviates from its planned trajectory due to errors in control or external perturbations.

Modelling the human body as a system of linked rigid segments, we can write the acceleration of the center of mass as ($\ddot{C}oM$) the sum of three mechanisms⁹:

$$\frac{(r_e - CoM') \times F_e + (CoP - CoM') \times F_g - \dot{H}}{m(CoM - CoM')} = \ddot{C}oM \quad (1)$$

in which r_e is the position vector of the point of application of an external force F_e , CoM' is the position vector of the vertical projection of the center of mass (CoM) on the ground, center of pressure (CoP) is the position vector of the point of application of the ground reaction force F_g , \dot{H} is the change of angular momentum around the body center of mass, and m is the body mass. The coordinate system is according to the ISB recommendations: X-axis forward, Y-axis vertically upward, Z-axis to the right. Note this has effects on the sign of the contribution of each of the three terms in the numerator on the right.

The denominator of the left-hand term consists of the product of body mass and the height of the center of mass above the ground, which we will assume to be constant for now. This leaves us three terms to consider:

$$\frac{(r_e - CoM') \times F_e}{(CoP - CoM') \times F_g} \dot{H}$$

Each of these terms reflects a mechanism to horizontally accelerate the center of mass and hence a potential mechanism to stabilize gait. We will first consider the unipedal stance phase of steady-state gait for each of these terms and then consider what is different in bipedal stance.

Regarding the first term, external forces can be applied by grabbing hold of for example a handrail, but also by foot placement or stepping. We will exclude mechanisms like grabbing a handrail and focus on the only 'external force generation' that is considered part of normal walking, i.e., stepping or foot placement. R_e can be controlled by placing the swing leg's foot at the desired location and F_e can be controlled by adjusting the swing leg's stiffness when reaching that location. Foot placement can also be seen as changing the base of support and center of pressure and hence part of the second mechanism, in which case the current term does not need to be considered. From this perspective, it is obvious that foot placement has the advantage that it allows a shift of the center of pressure beyond the original base of support. Given that clearly different responses at the joint level underly these two mechanisms, we prefer to keep them separate and treat foot placement as the generation of an external force. In double support, choosing a new foot placement location is not an option.

Considering the second term, changes in the position of the CoP and the ground reaction force are largely determined by actions of the stance leg. We will therefore refer to the mechanism described by this term as stance leg control, to differentiate it from the first mechanism foot placement. The center of pressure is always underneath the stance foot, but it can be shifted within the foot contact area by means of ankle moments. Since CoP and CoM' are both on the ground, the horizontal accelerations of the center of mass due to this term are further only dependent on the vertical component of the ground reaction force (F_g in equation 2).

$$(CoP - CoM') \times F_g = \begin{bmatrix} x_{cop} - x_{com} \\ 0 \\ z_{cop} - z_{com} \end{bmatrix} \times \begin{bmatrix} Fg_x \\ Fg_y \\ Fg_z \end{bmatrix} = \begin{bmatrix} -(z_{cop} - z_{com})Fg_y \\ (z_{cop} - z_{com})Fg_x - (x_{cop} - x_{com})Fg_z \\ (x_{cop} - x_{com})Fg_y \end{bmatrix} \quad (2)$$

The vertical ground reaction force can be modified to induce horizontal accelerations as well, but this would be at the 'cost' of a vertical acceleration of the center of mass and would not allow independent control of the mediolateral and anteroposterior acceleration of the center of mass. In double support, the center of pressure can be shifted over a larger area than in single support by modulating the ground reaction forces on both legs, e.g., pushing off more or less with either leg.

The third mechanism is creating a change in angular momentum of the body, which equates to changing the moment of the ground reaction force relative to the center of mass. The rate of change of angular momentum of a system of linked rigid segments equals:

$$\dot{H} = \sum_{i=1}^n (com_i - CoM) \times m_i (\dot{c}\ddot{m}_i - C\ddot{O}M) + I_i \alpha_i \quad (3)$$

in which com_i is the position vector of the center of mass of the i^{th} segment, m_i is the mass of the i^{th} segment, $\dot{c}\ddot{m}_i$ is the linear acceleration of the i^{th} segment, I_i is the moment of inertia of the i^{th} segment, α_i is the angular acceleration of the i^{th} segment, and n is the number of segments to be considered.

As this equation shows, the horizontal acceleration of the center of mass can be controlled by accelerating body segments with respect to the center of mass. Examples of the use of this mechanism are the 'hip strategy' ¹⁰, involving trunk flexion for anteroposterior stabilization after large perturbations of standing, and the arm movements used when balancing on a slackline ¹¹. The use of this mechanism is in principle not different between single and double support, except that leg segments (of the swing leg) can only be used in single support.

In summary, horizontal acceleration of the body's center of mass can be achieved through three mechanisms: 1) generating an external force on the body by making contact with the environment, 2) shifting the center of pressure of the ground reaction force within the current base of support, 3) changing the angular momentum of body segments around the center of mass ⁹. The mechanisms described can be separated analytically, but in reality, they will often interact. For example, changing the center of pressure without simultaneously changing the direction of the ground reaction force will change the moment of the ground reaction force relative to the center of mass and hence the angular momentum.

Observations from unperturbed gait can be used to assess the usage of the three stabilizing mechanisms. In addition, perturbations of gait and changes in stabilization demands (e.g., walking on a narrow beam versus a normal surface) have been employed to probe their usage and the relevance of the observations for stabilization. This can provide a first indication of whether training each mechanism could be useful. However, not only the extent to which each mechanism plays a role, but also the extent to which this is the result of passive dynamics or of active control is an important consideration, as only actively controlled mechanisms would form a feasible target for training. Based on the model studies mentioned above, this is likely to be different for control in the anteroposterior and mediolateral directions.

In the subsequent sections of this review, we will summarize and discuss the literature on the three mechanisms to stabilize gait identified above. For each mechanism, we will first describe the evidence that it is actually used in the control of steady-state human gait. We will then assess whether and how the usage of these mechanisms changes in response to external perturbations. Next, we will discuss the sensory information and the

actuation underlying each of the mechanisms. For each of these topics, we will compare control in the mediolateral and anteroposterior directions. Finally, we propose and discuss some training approaches based on these mechanisms. We will start with foot placement as this has received more attention in the literature and is considered the dominant mechanism to stabilize gait.

2. THE THREE MECHANISMS DURING UNPERTURBED WALKING

2.1 Foot placement

Foot placement has extensively been discussed in our previous review⁶. We will therefore only briefly summarize the main findings here.

To stabilize gait in the mediolateral direction, foot placement should be lateral to the extrapolated center of mass position, that is a weighted sum of the center of mass position and its velocity¹². By placing the foot with a lateral offset relative to the extrapolated center of mass, the sideward movement of the body center of mass towards the lateral edge of the base of support will be reversed. This can of course be achieved by: (1) taking such wide steps that the feet are always placed lateral to the extrapolated center of mass position, or (2) by regulating foot placement, so that it's just lateral to the extrapolated center of mass position. For the latter, both an adequate estimate of the state of the center of mass with respect to the feet, as well as sufficient ability to control the swing leg to place it at the appropriate position are needed.

Supporting regulation of foot placement on a step-by-step basis, Wang and Srinivasan¹³ showed that as much as 80% of the variance in deviations from average mediolateral foot placement could be explained by deviations from average in mediolateral pelvis position and speed at midstance, and this was much more than could be explained from swing leg state at midstance. The pelvis state used here can be considered a reasonable proxy for center of mass state in unperturbed walking, with an offset difference between sacrum marker and center of mass position¹⁴ that does not affect the model used. Positive coefficients in the model for both state variables indicate that when the pelvis is displaced too far lateral or moves in this direction too fast, a more lateral placed step will follow, and vice versa. These results thus suggest a stabilizing feedback mechanism. In terms of equation 1, r_e is determined by foot placement and the resulting change of $(r_e - CoM)$ will correct deviations in center of mass velocity or position towards the average value. The predictive value of the model increased for center of mass states from early swing onwards and plateaued around mid-swing¹³, suggesting that foot placement location is selected based on information obtained until this phase of the gait cycle. For anteroposterior foot placement, predictors of foot placement were pelvis anteroposterior velocity plus mediolateral pelvis position and velocity. Similar to mediolateral foot placement, increased velocity of the pelvis predicts more forward foot placement. The coefficients for mediolateral pelvis state in this model indicate that for example rightward pelvis perturbations at right leg mid-swing imply shorter right steps. The variance explained by this model at mid-swing was much lower than for mediolateral foot placement, at about 40%, and increased rapidly right after foot placement, suggesting that pelvis state is adjusted to foot placement in the early stance phase. This indicates that in this phase other stabilizing mechanisms may be used for anteroposterior control of the center of mass.

The models proposed by Wang & Srinivasan¹³ were successfully applied to data

from several other studies on mediolateral control^{15,16,17,18,19,20,21,22,23} and to data from one other study on anteroposterior control^{13,24}. Jin et al.²⁴ showed that, as for mediolateral foot placement, the anteroposterior center of mass position and velocity in the corresponding direction only provide a good prediction of anteroposterior foot placement, supporting a more parsimonious model for the control of foot placement than the original model¹³. In these studies, the relative variance explained by the model and the RMS of the residual error were used as measures for the quality of foot placement coordination and these measures were shown to be sensitive to perturbations, ageing, pathology, fall risk and effects of enhanced feedback^{16,18,25}.

It is important to note, that foot placement also subserves other goals than stabilization of gait, such as achieving intentional changes in velocity (speed and direction¹²) and avoiding obstacles or selecting suitable foot holds²⁶. Some of these goals may coincide. For instance, control of gait speed may well coincide with control of gait stability²⁷ and may in fact be inseparable from it.

2.2 Stance leg control

Stance leg control can shift the center of pressure in the mediolateral and anteroposterior directions, respectively through ankle inversion/eversion and plantar/dorsiflexion. Moreover, push-off can modulate the ground reaction force. In equation 1, stance leg control thus determines the following term: $(CoP-CoM) \times F_g$. The term $(CoP-CoM)$ then reflects ankle moment control to shift the center of pressure, whereas, F_g can be modulated through push-off.

In section 2.1, we already alluded to the use of other stabilizing mechanisms to compensate for errors in foot placement. During steady-state walking, stance leg control is indeed used to (partially) correct for foot placement errors, through shifting the center of pressure and through push-off^{24,28}. As the foot extends further in the anteroposterior as compared to the mediolateral direction, more (effective) center of pressure modulation can be achieved in the anteroposterior direction. However, despite the limited width of the foot, mediolateral center of pressure modulation during single stance also functions as a stabilizing mechanism during steady-state walking^{28,29,30}.

During steady-state walking, ankle moment control is used in the mediolateral direction, since the foot placement error, i.e. the residual of the foot placement model described in section 2.1, predicts the mediolateral center of pressure shift during single stance²⁸. That these center of pressure shifts act as a stabilizing mechanism, is likely, as they disappear when walking with external lateral stabilization³⁰. So mediolateral ankle moments correct for foot placement errors to stabilize gait during the new stance phase. In addition, ankle moments in the previous stance phase can stabilize gait preceding placement of the new stance leg³¹. This allows for an early correction, before foot placement can take effect^{32,33}, but might also be used to steer foot placement. Suggesting a steering role of ankle moments, targeted stepping is preceded by an early center of pressure shift during single stance³⁴. A similar mechanism may be used during steady-state walking to steer foot placement to comply with stability demands.

Motorized push-off, perturbations and modelling results suggest that push-off modulation can contribute to mediolateral gait stability^{35,36}. External lateral stabilization seems to diminish active push-off modulation³⁷, as the vestibulomotor coherence of the medial gastrocnemius decreased during stabilized walking³⁷. But, whether push-off

modulation is indeed implemented to stabilize gait in the mediolateral direction remains to be investigated.

For the anteroposterior direction, it has been shown that foot placement errors are corrected during double stance, achieved mainly through force generated by the trailing leg, which is in turn mainly determined by the sagittal plane ankle moment²⁴. This push-off mechanism also contributes to the trailing leg's trajectory and hence to reaching a targeted location²⁶. It thus seems likely that during steady-state walking, push-off is used as a corrective mechanism for anteroposterior foot placement of the leading leg as well as to control the trajectory of the trailing leg.

Although the above-mentioned evidence shows that stance leg control contributes to stable steady-state walking, the lower relative explained variance of steady-state ankle moment control models, as compared to foot placement models^{24,28}, reflects its lesser importance compared to the foot placement mechanism.

2.3 Angular momentum changes

Formula 1 indicates that next to foot placement (section 2.1) and stance leg control (section 2.2), changes in angular momentum can be used to stabilize gait. Early work on angular momentum during unperturbed human walking has shown that it is tightly regulated, and some authors have even suggested that the goal is to keep a near zero angular momentum^{38,39}. Indeed, angular momentum has been shown to be increased in patient populations, and the increase in angular momentum was correlated with worse scores on clinical balance measures^{40,41}. However, as walking inherently requires movement of the limbs which will bring about a (change in) angular momentum, it is hard to tease apart changes in angular momentum, which are explicitly aimed at stabilizing the center of mass trajectory, from those that happen simply due to movements necessary for progression.

One way to tease these effects apart may be to make other stabilizing mechanisms less available, such that subjects must rely more on angular momentum control. Indeed, angular momentum control was largely responsible for maintaining standing balance on a beam of only 4mm width⁴². On the other hand, when standing on balance boards which could rotate in the mediolateral⁴³, or antero-posterior direction⁴⁴, the *CoP* mechanism was dominant, with contributions of angular momentum changes often in the opposite direction of the *CoP* mechanism. In a recent experiment, we tested whether subjects use angular momentum control in walking, when their other possibilities to stabilize gait are diminished⁴⁵. Subjects walked on a treadmill in a control condition, a condition wearing shoes which restrict the use of the ankle mechanism, and in a condition in which they both wore these shoes and were instructed to walk with narrow steps. The idea was that these conditions would increasingly limit use of the other stabilizing mechanisms. Results showed that indeed changes in angular momentum contributed more to center of mass accelerations during the harder conditions, but the effect of foot placement also remained substantial. From this, we concluded that the use of angular momentum changes may be limited, probably because angular accelerations ultimately need to be reversed in view of anatomical constraints and because of interference with other task constraints, e.g., interference with the gait pattern. Using changes in angular momentum to affect (linear) center of mass acceleration will inevitably lead to changes in body orientation, which may also lead to altered visual and vestibular inputs, which in and of itself may be perturbing. All in all, it seems that humans can use angular momentum changes to stabilize steady-state gait, but that they do so to a

limited extent.

3. PERTURBED WALKING

Above, we described how foot placement, stance leg control, and angular momentum are used in unperturbed gait. When gait is perturbed, it could be that control is different, because some mechanisms may be more (or less) effective for perturbed gait, or because all available means need to be used to recover from a perturbation. In this section, we will describe the use of the three mechanisms when gait is mechanically perturbed by for instance a push, pull, trip, or slip. We have chosen not to describe studies studying responses to sensory (illusory) perturbations here, and instead use these as evidence for which sensory information is used to control the three mechanisms (see section 4).

3.1 Foot placement

Foot placement has as advantage that r_e (equation 1) can be quite large, or in other words, it shifts the *CoP* over a large distance compared to stance leg control, and this of course also holds during perturbed walking. Hof et al ⁴⁶, showed that after mediolateral perturbations, foot placement does require at least 300 ms (which they estimated to be about 30% of a stride), but has a range of 20 cm. They also showed that after a perturbation, if reaction time is sufficient, the foot is placed at a more or less constant distance outward of the extrapolated center of mass. When the available reaction time was too short, further responses during the next step were observed. Later studies by Vlutters ^{47,48} showed similar results, namely that recovery from mediolateral perturbations involved mediolateral foot placement adjustments proportional to the mediolateral center of mass velocity ⁴⁷, and that the adjustments in mediolateral foot placement decreased when the perturbation onset was closer to the instant of foot contact ⁴⁸.

In the antero-posterior direction, neither forward nor backward mechanical perturbations caused an increase in the distance between the center of pressure at foot contact and the center of mass at foot placement ⁴⁷. While it is not clear whether this implies no adjustment in step length relative to the stance foot, it does indicate that swing leg control was not effectively adapted to accommodate changes in center of mass.

Like for intrinsic variations during steady-state walking ¹³, foot placement responses during perturbed walking can be predicted by a linear model with pelvis kinematic state variables as predictors ⁴⁹. Interactions between foot placement and stance leg control (push-off and ankle moments) to stabilize gait (i.e. when one mechanism is used more, another mechanism is used less) also appear to generalize across steady-state and perturbed walking contexts, at least in the mediolateral direction ³¹. This suggests that similar control strategies may underlie foot placement responses to perturbations and the intrinsic variations of a steady-state gait pattern.

3.2 Stance leg control

Reactive center of pressure shifts and the associated ankle moments have been reported for mechanical perturbations. For the sake of clarity, we will discuss these responses per dimension, and only for studies distinguishing clearly between ankle moment and foot placement control (i.e. studies that do not compute these two mechanisms as a single center of pressure mechanism).

Mediolateral pushes and pulls to the pelvis lead to fast ankle moment responses before foot placement⁴⁶. This underscores a benefit of shifting the center of pressure under the stance foot relative to foot placement; stance leg control can take effect before foot placement, and as such, ensure more continuous stabilizing control. Furthermore, Brough et al⁵⁰ showed that center of pressure shifts correct for errors in foot placement in perturbed walking²⁸. When perturbing the foot to be placed too medial, this resulted in an inversion response and vice versa. Similar ankle responses were reported in response to mediolateral pelvis perturbations⁵¹.

As mentioned in section 3.1, unlike mediolateral pelvis perturbations, mechanical perturbations in the anteroposterior direction, did not cause adjustments in foot placement with respect to the center of mass at the first foot placement after the perturbation⁴⁷. This indicates that responses in the stance phase, which are partially the result of changes in ankle moments⁵¹, accommodate anteroposterior perturbations more effectively than mediolateral perturbations. Given the difference in anteroposterior and mediolateral dimensions of the feet, this is not surprising. In response to anteroposterior perturbations at toe-off, stance leg control responded to the perturbation during single stance⁵¹ and during the double stance phase⁵², to attenuate the effect on center of mass velocity. However, when constraining such center of pressure shifts, by limiting the base of support to a point contact, foot placement was adjusted after anteroposterior perturbations⁵³. This shows that people can switch from a stance leg to a foot placement mechanism if needed, for example when stepping on a narrow ridge.

A recent model simulation study found that pelvis perturbations in anteroposterior direction at toe-off could be fully recovered by shifting the center of pressure during double stance⁵². However, humans do not appear to implement this control mechanism to its full extent, leaving part of the perturbation's effect to be attenuated later in the gait cycle⁵².

3.3 Angular momentum changes

The commonly observed flailing of the arms after large perturbations of walking would suggest that angular momentum changes do play a (major?) role in stabilizing gait at these moments. However, such arm movement may have other functions, such as reaching for support or to break an eventual fall, or to affect body orientation rather than center of mass position as more extensively discussed below. In a recent study on standing balance⁵⁴, in which participants received rotational perturbations of the platform they were standing on, we indeed found that the rate of change of angular momentum did not directly contribute to return of the center of mass within the base of support. Instead, the changes in angular momentum in that study seemed aimed at reorienting the body to an aligned and vertical configuration. Our recent findings in walking seem to agree with this; after a perturbation, changes in angular momentum contributed negatively to center of mass accelerations⁵⁵. Other studies also indicate limited use of angular momentum changes to correct perturbations. For instance, in a study in which subjects wore pin shoes while undergoing perturbations⁵³, the authors reported an increased reliance on foot placement, with no changes in trunk movements. In another study⁵⁰, in which foot placement was perturbed by means of a push to the foot, both medial and lateral foot placement perturbations led to a decrease in hip abduction moments. While such a decrease could be understood as stabilizing after a medially directed perturbation, it is harder to understand for laterally directed perturbations. Interestingly, when angular momentum itself is perturbed directly, by

a simultaneous push and pull perturbation, a recovery of the angular momentum was seen directly after the perturbations⁵⁶.

A recent study⁵⁷ showed that when the arms were bound during a slip, participants were three times as likely to fall. During a slip, angular momentum cannot be used to create horizontal accelerations of the center of mass (as there is no friction with the floor). Hence, the positive effects of having arm movements during a trip most likely stem from the fact that this limits rotation of the body, by instead rotating the arms. This would then mean that this is a strategy with a different aim. Two studies from our own group indeed have shown such an alternative aim for changes of angular momentum of the arms after a trip. The ongoing movements of the arms after a trip supported lengthening of the recovery step in both young and older adults and thus optimized foot placement^{58,59}. However, the arms did not directly contribute to acceleration of the center of mass in the desired direction. Regulating the body's angular momentum may thus be more important in terms of changes of the orientation of the body. All-in all, it seems that angular momentum changes play a minor role in controlling the center of mass after a perturbation, as we also concluded for unperturbed gait and the same limitations may apply.

4. SENSING AND ACTUATION OF THE THREE MECHANISMS

To assess the active nature of the three mechanisms, studies have combined kinematic and electromyography measures while changing stabilizing demands, such as through external lateral stabilization and by applying (sensory) perturbations. The advantage of sensory perturbations is that the first response observed is active, whilst for mechanical perturbations early active and passive responses to the mechanical perturbations can coincide. As such, sensory perturbations can provide additional understanding of the control mechanisms during steady-state walking. Mechanical perturbations on the other hand may be able to elicit larger effects, so stronger responses may be observed.

4.1 Sensing and actuation of foot placement

For steady-state walking, the correlation between center of mass state and foot placement¹³ described in section 2.1 has been interpreted as reflective of active control, but it could also result from passive coupling of movements of the leg to the movements of the upper body⁶⁰. For mediolateral foot placement, it has been shown that lowering stabilization demands, by increasing prescribed step width, decreases the strength of the coupling between mediolateral center of mass state and foot placement^{15,23}. This phenomenon is even clearer when subjects walking on a treadmill are externally stabilized by a spring-loaded construction, creating a force-field that corrects mediolateral deviations of the center of mass¹⁹. These findings suggest that the correlation between center of mass state and foot placement reflects a form of active control that is relaxed under less demanding conditions.

Mechanical simulation indicates that active control over both mediolateral and anteroposterior foot placement can be achieved by modulating activity of many muscles, including ipsilateral swing limb gluteus medius, iliopsoas, rectus femoris and hamstrings and the contralateral stance limb gluteus medius and ankle plantarflexors. These contributions are not necessarily achieved by directly driving the swing leg relative to the pelvis, but also have effect through contributions to pelvis power⁶¹. In strong support of active control of

mediolateral foot placement, studies on steady-state walking have shown associations between mediolateral foot placement and activity of stance and swing leg gluteus medius activity and swing leg adductor longus activity^{20,62,63}. The idea that active control underlies the correlation between mediolateral center of mass state and foot placement is further supported by studies on the effects of sensory illusions induced by proprioceptive¹⁶, vestibular^{33,64}, or visual stimulation⁶⁵ on this correlation. Finally, destabilizing gait by mediolateral oscillation of the visual scenery caused increased step-to-step variance of center of mass excursion and mediolateral foot placement in association with changes in variance of gluteus medius muscle activity⁶⁶. For anteroposterior foot placement, we are not aware of studies that have assessed the relation with muscle activity. We remind the reader that passive walker models can be stable in this direction through passive 'adjustments' of foot placement⁸, which implies that humans may successfully exploit their passive dynamics and actively intervene only when needed, for example after larger perturbations.

Work by Hof and Duysens⁶⁷ has focused on the neural underpinnings of mediolateral foot placement control when mechanically perturbed. They found that two quick responses in gluteus medius activity following a medial perturbation of the center of mass trajectory can be found, one at 100 and one at 170ms after perturbation onset, as well as a late response at 270ms after perturbation onset. These responses were all phase dependent, and showed facilitation during swing, and suppression during stance, both opposite to the background activity. The authors stated that this suggests premotoneural gating of these responses, and thus, rather low-level control.

If the correlations between center of mass state and swing with foot placement reflects active feedback control, this suggests that the center of mass state can be estimated from sensory information. As described above, proprioceptive, vestibular and visual information affect foot placement, and this would suggest that these sensory modalities are used to obtain such an estimate. Additional information may be provided by pressure sensors in the foot soles⁶⁸. While substantial work on the integration of sensory information for control of the center of mass in standing has been performed e.g.⁶⁹, much less is known on this process in walking. However, it has been suggested that proprioceptive information from the lower extremities is weighted less in walking than in standing⁷⁰.

4.2 Sensing and actuation of stance leg control

Ankle moments inducing center of pressure shifts during gait are at least in part actively controlled as they are associated with peroneus longus, tibialis anterior and soleus muscle activity, in both unperturbed²⁸ and perturbed^{31,32,51,65,71,72} walking. In general, ankle moment control is considered to be fast^{32,65}, and, based on muscle activity latencies, it has been attributed to phase-dependent reflexive pathways connected to visual⁶⁵ and vestibular systems³¹, likely involving supraspinal neural connections^{32,53,72,73}. Thus, ankle moment control seems to be guided by the integration of different sensory modalities. That ankle moment control is centrally regulated is underscored by ankle muscle activity in response to mechanical perturbations, despite blocking of the ankle joint, which excludes spinal level feedback-control based on local proprioceptive information alone⁷². Further evidence that stabilizing ankle moments are not (only) determined by peripheral sensory information from the ankle joint and surrounding muscles comes from a modelling study⁷³. This study showed that delayed feedback of ankle angles and angular velocities could not explain reactive ankle moments, whereas delayed feedback of the center of mass kinematic state (position and

velocity) could explain these responses. It thus seems that ankle moments are controlled based on similar sensory information as foot placement. This is in line with visual⁶⁵ and vestibular perturbations³¹ evoking both foot placement and ankle moment responses. It is especially noteworthy that, in response to such sensory perturbations, ankle moments show the earliest response⁶⁵. This is in accordance with what was observed in mechanical perturbation studies^{32,46}.

4.3 Sensing and actuation of angular momentum changes

Even though it is unclear how much angular momentum changes contribute to controlling the center of mass, it is obvious that angular momentum must be controlled in order to maintain an upright orientation. While the angular momentum strategy has also been coined the “hip strategy”, there are many more joints (and muscles) that may contribute to control angular momentum. As a matter of fact, actuation of most muscles will lead to a change in angular momentum. Using simulations, Neptune and McGowan⁷⁴ found that in early stance, hip and knee extensors (gluteus maximus and vastii), hamstrings and tibialis anterior generated backward angular momentum, while the soleus and gastrocnemii generated forward momentum. In late stance, the soleus generated primarily forward angular momentum while the gastrocnemii generated backward angular momentum.

In a follow up study, Neptune and McGowan⁷⁵ studied which muscles contribute to changes in angular momentum in the frontal plane. This study showed that in early stance, the vastii, adductor magnus and gravity tended to rotate the body towards the contralateral leg while the gluteus medius tended to rotate the body towards the ipsilateral leg. In late stance, the gluteus medius still tended to rotate the body towards the ipsilateral leg while the soleus and gastrocnemius tended to rotate the body towards the contralateral leg.

In both these studies, the head, arms and trunk were modelled as a HAT unit, and hence, no statements were made about the (potential) role of arm movements. Either way, these studies clearly shows that the angular momentum strategy entails more than simple movements at the hip.

5. TRAINING POSSIBILITIES

We have thus far discussed how foot placement, stance leg control, and angular momentum are used to stabilize healthy human walking, both unperturbed, and perturbed. We have done so in view of the fact that gait stability declines with ageing and many diseases. Thus, a better understanding of how gait is stabilized may lead to opportunities to help those with problems. In this section, we give an outlook of how our understanding of the three mechanisms might help to identify training targets and methods. Assuming, based on the preceding sections, that each mechanism is a feedback-controlled process and that the mechanisms may compensate for each other, we propose four categories of training possibilities. In unperturbed walking, stability can be maintained without optimally exploiting feedback control. For example, older adults coordinate their foot placement less well to their center of mass state than young adults, but they maintain a steady-state and hence stable gait pattern by means of a larger average step width¹⁶. It can thus be assumed that specific manipulations may be needed to trigger and train the use of these stabilizing feedback control mechanisms. The first option may be to apply perturbations of the trajectory of the center of mass that are large enough to require an active stabilizing response, which, as

shown above, will involve at least the two most important stabilizing mechanisms. Second, understanding of the feedback mechanisms can be used to specifically target the outcome of the feedback processes, e.g., perturbing foot placement away from the expected position. Third, training approaches could constrain the use of one of the three mechanisms, such that the other mechanisms must be used more and hence are trained. Fourth, training methods could augment the natural feedback process, by increasing the sensory feedback available, in the hope that subjects are then able to (re-)learn the appropriate control. Except for general perturbation-based training, there is, as yet, limited or no evidence for effectiveness of each of these training approaches, so this section merely aims to provide an outlook that may be used for future work.

5.1 Perturbation-based training

Perturbation-based training is considered a promising tool to improve gait stability and reduce fall risk, which has received rapidly growing interest in literature, for reviews on this topic we refer to ⁷⁶⁻⁷⁸. Studies have found effects on fall risk in daily life, with reductions in falls up to 50% ^{79,80}, although such effects may depend on training dosage and differ between treadmill and overground training ⁸¹.

Repeated exposure to slip- and trip-like perturbations has been shown to cause improved recovery responses in which the state of the center of mass relative to the base of support is better controlled ⁸²⁻⁸⁹. This is in part accounted for by improved foot placement, as reflected in larger margins of stability at recovery step foot placement after training ^{86,88,89,90,91,92}. However, improved recovery responses were also associated with lesser deviations in trunk movement after the perturbation ^{86,92-94}, which are most likely accounted for by improved stance leg control ^{87,95}. After slip perturbations, the improved control was also due to a reduced displacement of the base of support or slip severity ^{82,83,85,96}, which can be accounted for by changes in pro-active control and by changes in stance leg control to better maintain the body mass positioned above the sliding foot.

A single study explored sensory perturbations to perturb gait as a training tool ⁹⁷. Mediolateral shifts of the visual scenery projected in front of a treadmill perturbed foot placement, and this resulted in a decreased variability of the margins of stability in unperturbed walking after the training. This is a clear indication of an improved coordination of foot placement relative to the center of mass state. Transfer and retention of these effects remains to be studied.

All in all, perturbation-based training is a promising approach for training of gait stabilization, and its effects can be partially understood based on improvements in the stabilizing mechanisms discussed in this paper. However, none of the studies discussed was specifically designed with the aim of assessing changes in these mechanisms, so it is impossible to discern which mechanisms are best targeted with which type of perturbations.

5.2 Specific perturbation training

Specific perturbation training interferes directly with the feedback mechanisms described. This approach has been implemented by perturbing mediolateral foot placement relative to the expected foot placement based on the predictive models described in section 3.1. Improved mediolateral foot placement control was found in healthy participants ^{98,99} and in chronic stroke patients ⁹⁹. The perturbations diminished the degree of foot placement control as an immediate effect, but with prolonged exposure, the degree of foot placement

control increased^{98,99}. Since these adaptations persisted as an after-effect, it shows that the degree of mediolateral foot placement control in steady-state walking can indeed be improved, but retention has not been reported.

Another study in older adults¹⁰⁰ used leg pulls to perturb the anteroposterior trajectory of the swing leg, simulating a trip-like perturbation during training and testing. Training resulted in a further forward foot placement relative to the extrapolated center of mass at the first and second step after the perturbation. This effect was maintained after 1.5 years after only two training sessions, one at baseline and one 14 weeks later. This result indicates that perturbation training may improve anteroposterior foot placement after perturbations with long-term effects.

5.3 Constraint-based training

Constraining compensatory mechanisms can be seen as a potential to (re-)train the use of a certain mechanism. For instance, walking while other stabilizing mechanisms are constrained could be used to train foot placement. This can in part be achieved with shoes that provide a limited base of support and hence do not allow center of pressure shifts. Constraints on mediolateral center of pressure shifts, induced an initial decrease in the degree of mediolateral foot placement control, followed by a gradual increase during training²². However, despite a trend, no significant after-effects were found. It appears that this may in part be due to an additional constraint on foot placement, which was the result of training and testing on a split-belt treadmill, which forces participants to take wider steps to avoid the gap between the belts¹⁰¹.

On a single-belt treadmill, ankle moment constraints do not perturb foot placement. Instead, in young neurologically-intact adults, the degree of foot placement immediately increased above baseline during training¹⁰¹. For older adults, who walked during several training sessions with shoes constraining center of pressure shifts on a single-belt treadmill, no improvements in foot placement were seen within a session. Moreover, no consistent after-effects were demonstrated at the end of the training sessions. However, in normal walking, foot placement precision improved over sessions¹⁰². A limitation of this study was that it did not contain a control group, and hence, it cannot be distinguished whether it was the ankle moment constraint or the repeated treadmill walking that induced these effects. With this in mind, we make the cautious interpretation that constraining ankle moments may hold training potential. Furthermore, for the interventions and training interventions outlined above, it should be investigated whether the observed training effects on a treadmill translate towards over ground walking.

In the previous section, we discussed the possibility of training foot placement through constraining ankle moments. In a similar vein, one might expect that constraining foot placement would help in training center of pressure shifts. Walking on a virtual narrow beam elicited smaller mediolateral center of mass excursions at lower speed, in young as well as older adults, indicating that other stabilizing mechanisms than foot placement were enhanced to compensate for constrained foot placement¹⁰³. Unfortunately, when explicitly testing whether constraining foot placement caused improvements in the use of center of pressure shifts, no immediate effect was found²⁰. Nonetheless, constraining foot placement is a commonly used training tool^{104,105}, which has shown positive effects on gait, but mechanistic effects on gait stabilization have not been studied.

5.4 Augmented feedback

Augmented feedback aims to enhance the information used in a feedback process by providing an artificial stimulus enhancing the available sensory information. Augmented proprioception may provide a tool to enhance the degree of foot placement control²¹. Applying timed tendon vibration to either the stance, or the swing leg, depending on what complied with the current center of mass kinematic state, helped to better coordinate foot placement with respect to the center of mass kinematic state²¹. This likely entails an increased signal-to-noise ratio of the relevant sensory information. Although this improved the degree of foot placement control while the vibration was applied, it has not yet been investigated whether augmented proprioception leads to beneficial training effects. Moreover, this mechanism has thus far only been applied to improve foot placement. We can in principle envision it working to enhance the other mechanisms as well, as all would be dependent on correct use of sensory information to estimate the center of mass state.

6. DISCUSSION

We have discussed three gait stability mechanisms which can be distinguished analytically. We have shown that foot placement control is dominant and is complemented by stance leg control, either as an early response to a perturbation or to correct for foot placement errors. Moreover, changes in angular momentum do not seem to contribute directly to linear center of mass accelerations, and instead may be used to control the orientation of the body, or be used only when all else fails. Both foot placement and stance leg control are at least partly active in nature, not only in response to perturbations, but also during steady-state walking. Actively controlled mechanisms suggest trainability, and we proposed potential of perturbations, constraints, and sensory augmentation as training approaches.

6.1 Control of stability is based on center of mass state

Based on the literature reviewed above, it seems likely center of mass kinematic state information is used to control both foot placement and ankle moments. However, based on current evidence, we are unable to conclude whether it is really the center of mass or a related variable like pelvis state relative to the stance foot that is sensed. Responses to visual and vestibular perturbations, as well as modelling results discussed above show gait stabilization is not (solely) driven by local (such as hip or ankle joint angle) information. Given that proprioceptive, visual, and vestibular information all seem to contribute, humans likely use an estimate obtained through sensory integration, which provides a close proxy of the center of mass. However, it may be hard to experimentally verify whether it is really the state of the center of mass that is sensed and used to stabilize gait, or whether it is some related state variable.

Either way, it seems that the sensory information that is obtained during gait is used in a flexible manner, with changes in the information used at different timescales. For instance, stretch reflexes and vestibular coupling to muscles show modulations over the gait cycle^{37,106}, and sensory down-weighting of vestibular information over the course of seconds or minutes^{107,108}. Thus, the information that is used to stabilize gait most likely comes from multiple sensory systems, is combined in a flexible manner, and provides an estimate of the center of mass state.

Lastly, although sensory perturbations provide strong indications for the feedback nature of control mechanisms during steady-state walking, they may evoke responses larger than those required for the intrinsic variations of steady-state gait. Therefore, it is hard to interpret whether sensory perturbations trigger responses reflecting “steady-state control” or “reactive control”. Then again, the evidence presented here suggests that during perturbed and unperturbed walking similar control mechanisms are employed.

6.2 Gait speed modifies contributions of stabilizing mechanisms

Walking at different speeds influences the contribution of the available stability mechanisms. Although foot placement is dominant during walking, the degree of foot placement control decreases with decreasing speeds^{17,20}. One may argue, that given the longer stance times during slow walking, the contribution of stance leg control may increase, and thus foot placement control can be loosened. In a perturbation study, it was indeed shown that ankle moment control contributed more at lower speeds³¹. Yet, in contrast, during steady-state walking, the contribution of ankle moment control appeared higher in normal as compared to slow walking²⁸. The use of sensory information, which may contribute to gait stabilization also appears to be speed dependent. Closing the eyes had more effect on variability of foot placement in the anteroposterior direction at low speeds, while effects in the mediolateral direction were similar across speeds from 20 to 80% of maximum walking speed¹⁰⁹. Effects on balance control of illusions of mediolateral movement caused by vestibular stimulation decreased between slow (0.8 m/s) and very slow (0.4 m/s) walking^{107,110}. Some additional information can be obtained from studies on pathology. In line with experimental work, vestibular deficits and peripheral neuropathy had more effect on step time variability at low than high speeds^{111,112}. A study on bilateral vestibular loss was associated with a large mediolateral foot placement variability specifically at high speeds, and with a large anteroposterior foot placement variability at low speeds¹¹³. However, the latter study quantified variability by means of a coefficient of variation and simultaneous changes in mean values make this outcome somewhat difficult to interpret. Overall, gait stabilization appears to be more dependent on sensory feedback at low speeds. However, the speed dependence of gait stabilization is at present incompletely described and understood. Given the fact that individuals at risk of falling often change their gait speed, a better understanding of the effects of speed is warranted.

6.3 Antero-posterior and mediolateral control

Although one generally looks for mediolateral responses (e.g., changes in ankle moments) in response to mediolateral perturbations/variations and vice versa for anteroposterior responses in response to anteroposterior perturbations/variations, stabilization is not independent between these directions. Therefore, mediolateral and anteroposterior mechanisms must be coordinated to stabilize gait^{13,32,48}. For example, ankle moments can speed up anteroposterior center of pressure shifts to shorten stance, allowing foot placement control to take effect earlier in accommodating mediolateral perturbations³². Although, to our knowledge, so far, this mechanism has only been reported in relation to perturbations³², adaptations in stride frequency and the duration of specific stride phases are considered stabilizing mechanism in steady-state walking as well^{20,114,115}. Moreover, push-off, a clear antero-posterior mechanism²⁴, also has effects in the mediolateral direction, due to the moment arm of the ground reaction force with respect to the center of

mass in this direction¹¹⁶. In addition, ankle muscles causing in-/eversion (see section below), also have a plantar/dorsiflexion component and vice versa. Thus, while we (and a lot of the literature) have focused on control in one specific direction/plane, there are effects of these mechanisms in other planes as well. Perhaps, future research should focus more on such interactions.

7. CONCLUSION

We have discussed how human bipedal gait is stabilized using foot placement, stance leg control, and angular momentum changes. The first two mechanisms and especially the first are dominant in controlling center of mass accelerations during gait, while angular momentum changes play a lesser role, but may be important to control body alignment and orientation. The same control mechanisms stabilize both steady-state and perturbed gait in both mediolateral and antero-posterior directions. Control is at least in part active and is affected by proprioceptive, visual and vestibular information. Results support that this reflects a feedback process in which sensory information is used to obtain an estimate of the center of mass state based on which foot placement and ankle moments are modulated. These mechanisms suggest training approaches for populations at risk of falling, such as mechanically perturbing gait stability, specifically perturbing or augmenting the effective use of the stabilizing mechanisms, or using their complementary nature to train one mechanism by constraining the other mechanisms.

REFERENCES

1. Macintyre NJ, Dewan N. Epidemiology of distal radius fractures and factors predicting risk and prognosis. *J Hand Ther.* 2016;29:136-145. doi: 10.1016/j.jht.2016.03.003.
2. Talbot LA, Musiol RJ, Witham EK, Metter EJ. Falls in young, middle-aged and older community dwelling adults: perceived cause, environmental factors and injury. *BMC Public Health.* 2005;5:86. doi: 10.1186/1471-2458-5-86.
3. Wenning GK, Ebersbach G, Verny M, Chaudhuri KR, Jellinger K, Mckee A, et al. Progression of falls in postmortem-confirmed parkinsonian disorders. *Mov Disord.* 1999;14:947-950. doi: 10.1002/1531-8257(199911)14:6<947::aid-mds1006>3.0.co;2-o.
4. Sherrington C, Tiedemann A, Fairhall N, Close JC, Lord SR. Exercise to prevent falls in older adults: an updated meta-analysis and best practice recommendations. *N S W Public Health Bull.* 2011;22:78-83. doi: 10.1071/NB10056.
5. Allen NE, Canning CG, Almeida LRS, Bloem BR, Keus SH, Lofgren N, et al. Interventions for preventing falls in Parkinson's disease. *Cochrane Database Syst Rev.* 2022;6:CD011574. doi: 10.1002/14651858.CD011574.pub2.
6. Bruijn SM, Van Dieën JH. Control of human gait stability through foot placement. *J Royal Soc Interface.* 2018;15:20170816. doi: <http://dx.doi.org/10.1098/rsif.2017.0816>.
7. McGeer T. Passive Dynamic Walking. *Int J Robot Res.* 1990;9:62-82.
8. Kuo AD. Stabilization of lateral motion in passive dynamic walking. *Int J Robot Res.* 1999;18:917-930.

9. Hof AL. The equations of motion for a standing human reveal three mechanisms for balance. *J Biomech.* 2007;40:451-457.
10. Horak FB, Nashner LM. Central programming of postural movements: Adaptation to altered support surface configurations. *J Neurophysiol.* 1986;55:1369-1381.
11. Mildren RL, Zaback M, Adkin AL, Bent LR, Frank JS. Learning to balance on a slackline: Development of coordinated multi-joint synergies. *Scand J Med Sci Sports.* 2018;28:1996-2008. doi: 10.1111/sms.13208.
12. Hof AL. The 'extrapolated center of mass' concept suggests a simple control of balance in walking. *Human Movement Science.* 2008;27:112-125. doi: 10.1016/j.humov.2007.08.003.
13. Wang Y, Srinivasan M. Stepping in the direction of the fall: the next foot placement can be predicted from current upper body state in steady-state walking. *Biol Lett.* 2014;10. doi: 10.1098/rsbl.2014.0405.
14. Yang F, Pai YC. Can sacral marker approximate center of mass during gait and slip-fall recovery among community-dwelling older adults? *J Biomech.* 2014;47:3807-3812. doi: 10.1016/j.jbiomech.2014.10.027.
15. Perry JA, Srinivasan M. Walking with wider steps changes foot placement control, increases kinematic variability and does not improve linear stability. *R Soc Open Sci.* 2017;4:160627. doi: 10.1098/rsos.160627.
16. Arvin M, Hoozemans M, Pijnappels M, Duysens J, Verschueren SM, Van Dieën JH. Where to step? Contributions of stance leg muscle spindle afference to planning of mediolateral foot placement for balance control in young and older adults. *Front Physiol.* 2018;9. doi: 10.3389/fphys.2018.01134.
17. Stimpson KH, Heitkamp LN, Horne JS, Dean JC. Effects of walking speed on the step-by-step control of step width. *J Biomech.* 2018;68:78-83. doi: 10.1016/j.jbiomech.2017.12.026.
18. Stimpson KH, Heitkamp LN, Embry AE, Dean JC. Post-stroke deficits in the step-by-step control of paretic step width. *Gait Posture.* 2019;70:136-140. doi: 10.1016/j.gaitpost.2019.03.003.
19. Mahaki M, Bruijn SM, Van Dieën JH. The effect of external lateral stabilization on the use of foot placement to control mediolateral stability in walking and running. *PeerJ.* 2019;7:e7939. doi: 10.7717/peerj.7939.
20. Van Leeuwen AM, Van Dieën JH, Daffertshofer A, Bruijn SM. Active foot placement control ensures stable gait: Effect of constraints on foot placement and ankle moments. *PLoS one.* 2020;15:e0242215. doi: <https://doi.org/10.1371/journal.pone.0242215>.
21. Knapp HA, Sobolewski BA, Dean JC. Augmented Hip Proprioception Influences Medirolateral Foot Placement During Walking. *IEEE Trans Neural Syst Rehabil Eng.* 2021;29:2017-2026. doi: 10.1109/TNSRE.2021.3114991.
22. Hoogstad LA, Van Leeuwen AM, Van Dieën JH, Bruijn SM. Can foot placement during gait be trained? Adaptations in stability control when ankle moments are constrained. *J Biomech.* 2022;134:110990.

23. Magnani R, Van Dieën JH, Bruijn SM. Effects of vestibular stimulation on gait stability when walking at different step widths. *Exp Brain Res*. in press.
24. Jin J, Van Dieën JH, Kistemaker D, Daffertshofer A, Bruijn SM. Does ankle push-off correct for errors in anterior-posterior foot placement relative to center-of-mass states? *bioRxiv*. 2022:2022.2003.2014.484283. doi: 10.1101/2022.03.14.484283.
25. Dean JC, Kautz SA. Foot placement control and gait instability among people with stroke. *J Rehabil Res Dev*. 2015;52:577-590. doi: 10.1682/JRRD.2014.09.0207.
26. Matthis JS, Barton SL, Fajen BR. The critical phase for visual control of human walking over complex terrain. *Proc Natl Acad Sci U S A*. 2017;114:E6720-E6729. doi: 10.1073/pnas.1611699114.
27. Patil NS, Dingwell JB, Cusumano JP. Task-level regulation enhances global stability of the simplest dynamic walker. *J R Soc Interface*. 2020;17:20200278. doi: 10.1098/rsif.2020.0278.
28. Van Leeuwen AM, Van Dieën JH, Daffertshofer A, Bruijn SM. Ankle muscles drive mediolateral center of pressure control to ensure stable steady state gait. *Sci Rep*. 2021;11:21481.
29. Hof AL, Van Bockel RM, Schoppen T, Postema K. Control of lateral balance in walking - Experimental findings in normal subjects and above-knee amputees. *Gait Posture*. 2007;25:250-258. doi: 10.1016/j.gaitpost.2006.04.013.
30. Van Leeuwen AM, Van Dieën JH, Bruijn SM. The effect of external lateral stabilization on ankle moment control during steady-state walking. *J Biomech*. 2022;142:111259. doi: <https://doi.org/10.1016/j.jbiomech.2022.111259>.
31. Fettrow T, Reimann H, Grenet D, Crenshaw J, Higginson J, Jeka J. Walking Cadence Affects the Recruitment of the Medial-Lateral Balance Mechanisms. *Front sports act living*. 2019;1. doi: 10.3389/fspor.2019.00040.
32. Hof AL, Duysens J. Responses of human ankle muscles to mediolateral balance perturbations during walking. *Hum Mov Sci*. 2018;57:69-82. doi: 10.1016/j.humov.2017.11.009.
33. Reimann H, Fettrow TD, Thompson ED, Agada P, Mcfadyen BJ, Jeka JJ. Complementary mechanisms for upright balance during walking. *PLoS one*. 2017;12:e0172215. doi: 10.1371/journal.pone.0172215.
34. Zhang Y, Smeets JBJ, Brenner E, Verschueren S, Duysens J. Fast responses to stepping-target displacements when walking. *J Physiol*. 2020;598:1987-2000. doi: 10.1113/JP278986.
35. Kim M, Collins SH. Once-per-step control of ankle-foot prosthesis push-off work reduces effort associated with balance during walking. *J Neuroeng Rehabil*. 2015;12:43. doi: 10.1186/s12984-015-0027-3.
36. Reimann H, Fettrow T, Jeka JJ. Strategies for the Control of Balance During Locomotion. *Kinesiology Review*. 2018;7:18-25. doi: 10.1123/kr.2017-0053.

37. Magnani RM, Bruijn SM, Van Dieën JH, Forbes PA. Stabilization demands of walking modulate the vestibular contributions to gait. *Sci Rep*. 2021;11:13736. doi: <https://doi.org/10.1038/s41598-021-93037-7>.
38. Herr H, Popovic M. Angular momentum in human walking. *J Exp Biol*. 2008;211:467-481. doi: 10.1242/Jeb.008573.
39. Elftman H. The function of the arms in walking. *Human Biology*. 1939;11:529-535.
40. Silverman AK, Neptune RR. Differences in whole-body angular momentum between below-knee amputees and non-amputees across walking speeds. *J Biomech*. 2011;44:379-385. doi: 10.1016/j.jbiomech.2010.10.027.
41. Nott CR, Neptune RR, Kautz SA. Relationships between frontal-plane angular momentum and clinical balance measures during post-stroke hemiparetic walking. *Gait Posture*. 2014;39:129-134. doi: 10.1016/j.gaitpost.2013.06.008.
42. Otten E. Balancing on a narrow ridge: biomechanics and control. *Philos Trans R Soc Lond B Biol Sci*. 1999;354:869-875.
43. Van Den Bogaart M, Bruijn SM, Spildooren J, Van Dieën JH, Meyns P. Effects of age and surface instability on the control of the center of mass. *Hum Mov Sci*. 2022;82:102930. doi: 10.1016/j.humov.2022.102930.
44. Van Den Bogaart M, Bruijn SM, Spildooren J, Van Dieën JH, Meyns P. Limited effects of age on the use of the ankle and counter-rotation mechanism in the sagittal plane. *bioRxiv*. 2022:2022.2003.2015.484389. doi: 10.1101/2022.03.15.484389.
45. Van Den Bogaart M, Bruijn SM, Spildooren J, Van Dieën JH, Meyns P. The effect of constraining mediolateral ankle moments and foot placement on the use of the counter-rotation mechanism during walking. *J Biomech*. 2022;136:111073. doi: 10.1016/j.jbiomech.2022.111073.
46. Hof AL, Vermerris SM, Gjaltema WA. Balance responses to lateral perturbations in human treadmill walking. *J Exp Biol*. 2010;213:2655-2664. doi: 10.1242/jeb.042572.
47. Vlutters M, Van Asseldonk EH, Van Der Kooij H. Center of mass velocity-based predictions in balance recovery following pelvis perturbations during human walking. *J Exp Biol*. 2016;219:1514-1523. doi: 10.1242/jeb.129338.
48. Vlutters M, Van Asseldonk EHF, Van Der Kooij H. Foot Placement Modulation Diminishes for Perturbations Near Foot Contact. *Front Bioeng Biotechnol*. 2018;6:48. doi: 10.3389/fbioe.2018.00048.
49. Joshi V, Srinivasan M. A controller for walking derived from how humans recover from perturbations. *J R Soc Interface*. 2019;16:20190027.
50. Brough LG, Klute GK, Neptune RR. Biomechanical response to mediolateral foot-placement perturbations during walking. *J Biomech*. 2020;116:110213. doi: 10.1016/j.jbiomech.2020.110213.
51. Vlutters M, Van Asseldonk EHF, Van Der Kooij H. Lower extremity joint-level responses to pelvis perturbation during human walking. *Sci Rep*. 2018;8:14621. doi: 10.1038/s41598-018-32839-8.

52. Van Mierlo M, Vlutters M, Van Asseldonk EHF, Van Der Kooij H. Centre of pressure modulations in double support effectively counteract anteroposterior perturbations during gait. *J Biomech.* 2021;126:110637. doi: 10.1016/j.jbiomech.2021.110637.
53. Vlutters M, Van Asseldonk EHF, Van Der Kooij H. Reduced center of pressure modulation elicits foot placement adjustments, but no additional trunk motion during anteroposterior-perturbed walking. *J Biomech.* 2018;68:93-98. doi: 10.1016/j.jbiomech.2017.12.021.
54. Alizadehsaravi L, Bruijn SM, Van Dieën JH. Balance training improves feedback control of perturbed balance in older adults. *bioRxiv.* 2021.
55. Van Den Bogaart M, Bruijn SM, Van Dieën JH, Meyns P. The effect of anteroposterior perturbations on the control of the center of mass during treadmill walking. *J Biomech.* 2020;103:109660.
56. Van Mierlo M, Ambrosius J, Vlutters M, Van Asseldonk E, Van Der Kooij H. Recovery from sagittal-plane whole body angular momentum perturbations during walking. *J Biomech.* 2022:111169.
57. Lee-Confer JS, Kulig K, Powers CM. Constraining the arms during a slip perturbation results in a higher fall frequency in young adults. *Hum Mov Sci.* 2022;86:103016. doi: 10.1016/j.humov.2022.103016.
58. Pijnappels M, Kingma I, Wezenberg D, Reurink G, Van Dieën JH. Armed against falls: the contribution of arm movements to balance recovery after tripping. *Exp Brain Res.* 2010;201:689-699. doi: 10.1007/s00221-009-2088-7.
59. Bruijn SM, Sloot LH, Kingma I, Pijnappels M. Contribution of arm movements to balance recovery after tripping in older adults. *J Biomech.* 2022;133:110981. doi: 10.1016/j.jbiomech.2022.110981.
60. Patil NS, Dingwell JB, Cusumano JP. Correlations of pelvis state to foot placement do not imply within-step active control. *J Biomech.* 2019;97:109375. doi: 10.1016/j.jbiomech.2019.109375.
61. Roelker SA, Kautz SA, Neptune RR. Muscle contributions to mediolateral and anteroposterior foot placement during walking. *J Biomech.* 2019;95:109310. doi: 10.1016/j.jbiomech.2019.08.004.
62. Kubinski SN, Mcqueen CA, Sittloh KA, Dean JC. Walking with wider steps increases stance phase gluteus medius activity. *Gait Posture.* 2015;41:130-135. doi: 10.1016/j.gaitpost.2014.09.013.
63. Rankin BL, Buffo SK, Dean JC. A neuromechanical strategy for mediolateral foot placement in walking humans. *J Neurophysiol.* 2014;112:374-383. doi: 10.1152/jn.00138.2014.
64. Reimann H, Fettrow T, Grenet D, Thompson ED, Jeka JJ. Phase-Dependency of Medial-Lateral Balance Responses to Sensory Perturbations During Walking. *Front. sports act. living.* 2019;1. doi: 10.3389/fspor.2019.00025.
65. Reimann H, Fettrow T, Thompson ED, Jeka JJ. Neural Control of Balance During Walking. *Front Physiol.* 2018;9:1271. doi: 10.3389/fphys.2018.01271.

66. Stokes HE, Thompson JD, Franz JR. The Neuromuscular Origins of Kinematic Variability during Perturbed Walking. *Sci Rep.* 2017;7:808. doi: 10.1038/s41598-017-00942-x.
67. Hof AL, Duysens J. Responses of human hip abductor muscles to lateral balance perturbations during walking. *Exp Brain Res.* 2013;230:301-310. doi: 10.1007/s00221-013-3655-5.
68. Cofre Lizama LE, Pijnappels M, Verschueren S, Reeves NP, Van Dieën JH. Can explicit visual feedback of postural sway efface the effects of sensory manipulations on mediolateral balance performance? *J Neurophysiol.* 2016;115:907-914.
69. Peterka RJ, Loughlin PJ. Dynamic regulation of sensorimotor integration in human postural control. *J Neurophysiol.* 2004;91:410-423. doi: 10.1152/jn.00516.2003.
70. Courtine G, De Nunzio AM, Schmid M, Beretta MV, Schieppati M. Stance- and locomotion-dependent processing of vibration-induced proprioceptive inflow from multiple muscles in humans. *J Neurophysiol.* 2007;97:772-779. doi: 10.1152/jn.00764.2006.
71. Afschrift M, Van Deursen R, De Groot F, Jonkers I. Increased use of stepping strategy in response to medio-lateral perturbations in the elderly relates to altered reactive tibialis anterior activity. *Gait Posture.* 2019;68:575-582.
72. Vlutters M, Van Asseldonk EHF, Van Der Kooij H. Ankle muscle responses during perturbed walking with blocked ankle joints. *J Neurophysiol.* 2019;121:1711-1717. doi: 10.1152/jn.00752.2018.
73. Afschrift M, De Groot F, Jonkers I. Similar sensorimotor transformations control balance during standing and walking. *PLoS Comput Biol.* 2021;17:e1008369. doi: 10.1371/journal.pcbi.1008369.
74. Neptune RR, Mcgowan CP. Muscle contributions to whole-body sagittal plane angular momentum during walking. *J Biomech.* 2011;44:6-12. doi: 10.1016/j.jbiomech.2010.08.015.
75. Neptune RR, Mcgowan CP. Muscle contributions to frontal plane angular momentum during walking. *J Biomech.* 2016;49:2975-2981. doi: 10.1016/j.jbiomech.2016.07.016.
76. Karamanidis K, Epro G, Mccrum C, Konig M. Improving Trip- and Slip-Resisting Skills in Older People: Perturbation Dose Matters. *Exerc Sport Sci Rev.* 2020;48:40-47. doi: 10.1249/JES.0000000000000210.
77. Gerards MHG, Mccrum C, Mansfield A, K. M. Perturbation-based balance training for falls reduction among older adults: Current evidence and implications for clinical practice. *Geriatr Gerontol Int.* 2017;17:2294-2303. doi: doi:10.1111/ggi.13082.
78. Mccrum C, Gerards MHG, Karamanidis K, Zijlstra W, Meijer K. A systematic review of gait perturbation paradigms for improving reactive stepping responses and falls risk among healthy older adults. *Eur Rev Aging Phys Act.* 2017;14:3. doi: 10.1186/s11556-017-0173-7.
79. Rosenblatt NJ, Marone J, Grabiner MD. Preventing trip-related falls by community-dwelling adults: a prospective study. *J Am Geriatr Soc.* 2013;61:1629-1631. doi: 10.1111/jgs.12428.

80. Pai YC, Bhatt T, Yang F, Wang E. Perturbation training can reduce community-dwelling older adults' annual fall risk: a randomized controlled trial. *J Gerontol A Biol Sci Med Sci*. 2014;69:1586-1594. doi: 10.1093/gerona/glu087.
81. Wang Y, Wang S, Liu X, Lee A, Pai YC, Bhatt T. Can a single session of treadmill-based slip training reduce daily life falls in community-dwelling older adults? A randomized controlled trial. *Aging Clin Exp Res*. 2022;34:1593-1602. doi: 10.1007/s40520-022-02090-3.
82. Bhatt T, Pai YC. Generalization of gait adaptation for fall prevention: from moveable platform to slippery floor. *J Neurophysiol*. 2009;101:948-957. doi: 10.1152/jn.91004.2008.
83. Lee A, Bhatt T, Pai YC. Generalization of treadmill perturbation to overground slip during gait: Effect of different perturbation distances on slip recovery. *J Biomech*. 2016;49:149-154. doi: 10.1016/j.jbiomech.2015.11.021.
84. Lee A, Bhatt T, Liu X, Wang Y, Wang S, Pai YC. Can Treadmill Slip-Perturbation Training Reduce Longer-Term Fall Risk Upon Overground Slip Exposure? *J Appl Biomech*. 2020:1-9. doi: 10.1123/jab.2019-0211.
85. Lee A, Bhatt T, Liu X, Wang Y, Pai YC. Can higher training practice dosage with treadmill slip-perturbation necessarily reduce risk of falls following overground slip? *Gait Posture*. 2018;61:387-392. doi: 10.1016/j.gaitpost.2018.01.037.
86. Okubo Y, Sturnieks DL, Brodie MA, Duran L, Lord SR. Effect of Reactive Balance Training Involving Repeated Slips and Trips on Balance Recovery Among Older Adults: A Blinded Randomized Controlled Trial. *J Gerontol A Biol Sci Med Sci*. 2019;74:1489-1496. doi: 10.1093/gerona/glz021.
87. Pijnappels M, Reeves ND, Maganaris CN, Van Dieën JH. Tripping without falling; lower limb strength, a limitation for balance recovery and a target for training in the elderly. *J Electromyogr Kinesiol*. 2008;18:188-196. doi: 10.1016/j.jelekin.2007.06.004.
88. Allin LJ, Brolinson PG, Beach BM, Kim S, Nussbaum MA, Roberto KA, et al. Perturbation-based balance training targeting both slip- and trip-induced falls among older adults: a randomized controlled trial. *BMC Geriatr*. 2020;20:205. doi: 10.1186/s12877-020-01605-9.
89. Mccrum C, Karamanidis K, Willems P, Zijlstra W, Meijer K. Retention, savings and interlimb transfer of reactive gait adaptations in humans following unexpected perturbations. *Comm Biol*. 2018;1:230. doi: <https://doi.org/10.1038/s42003-018-0238-9>.
90. Bhatt T, Wang Y, Wang S, Kannan L. Perturbation Training for Fall-Risk Reduction in Healthy Older Adults: Interference and Generalization to Opposing Novel Perturbations Post Intervention. *Front Sports Act Living*. 2021;3:697169. doi: 10.3389/fspor.2021.697169.
91. König M, Epro G, Seeley J, Catalá-Lehnen P, Potthast W, Karamanidis K. Retention of improvement in gait stability over 14 weeks due to trip-perturbation training is dependent on perturbation dose. *J Biomech*. 2019;84:243-246. doi: 10.1016/j.jbiomech.2018.12.011.

92. Werth J, Epro G, Konig M, Santuz A, Seeley J, Arampatzis A, et al. Differences in motor response to stability perturbations limit fall-resisting skill transfer. *Sci Rep.* 2022;12:21901. doi: 10.1038/s41598-022-26474-7.
93. Grabiner MD, Bareither ML, Gatts S, Marone J, Troy KL. Task-specific training reduces trip-related fall risk in women. *Med Sci Sports Exerc.* 2012;44:2410-2414. doi: 10.1249/MSS.0b013e318268c89f.
94. Rieger M, Papegaaij S, Pijnappels M, Steenbrink F, Van Dieën JH. Transfer and retention effects of gait training with anterior-posterior perturbations to postural responses after medio-lateral gait perturbations in older adults. *Clin Biomech.* 2020;75:104988.
95. Pijnappels M, Bobbert MF, Van Dieen JH. Contribution of the support limb in control of angular momentum after tripping. *J Biomech.* 2004;37:1811-1818. doi: 10.1016/j.jbiomech.2004.02.038.
96. Wang Y, Bhatt T, Liu X, Wang S, Lee A, Wang E, et al. Can treadmill-slip perturbation training reduce immediate risk of over-ground-slip induced fall among community-dwelling older adults? *J Biomech.* 2019;84:58-66. doi: 10.1016/j.jbiomech.2018.12.017.
97. Richards JT, Selgrade BP, Qiao M, Plummer P, Wikstrom EA, Franz JR. Time-dependent tuning of balance control and aftereffects following optical flow perturbation training in older adults. *J Neuroeng Rehabil.* 2019;16:81. doi: 10.1186/s12984-019-0555-3.
98. Heitkamp LN, Stimpson KH, Dean JC. Application of a novel force-field to manipulate the relationship between pelvis motion and step width in human walking. *BioRxiv.* 2019. doi: 10.1101/636787.
99. Reimold NK, Knapp HA, Henderson RE, Wilson L, Chesnutt AN, Dean JC. Altered active control of step width in response to mediolateral leg perturbations while walking. *Sci Rep.* 2020;10:12197. doi: 10.1038/s41598-020-69052-5.
100. Epro G, Mierau A, Mccrum C, Leyendecker M, Bruggemann GP, Karamanidis K. Retention of gait stability improvements over 1.5 years in older adults: effects of perturbation exposure and triceps surae neuromuscular exercise. *J Neurophysiol.* 2018;119:2229-2240. doi: 10.1152/jn.00513.2017.
101. Hos M, Van Iersel L, Van Leeuwen AM, Bruijn SM. Differential effects of ankle constraints on foot placement control between normal and split belt treadmills. *bioRxiv.* 2022.
102. Mahaki M, Van Leeuwen AM, Bruijn S, Van Der Velde N, Van Dieen JH. Foot placement control can be trained: Older adults learn to walk more stable, when ankle moments are constrained. in prep.
103. Arvin M, Mazaheri M, Pijnappels M, Hoozemans MJM, Burger BJ, Verschueren SM, et al. Effects of narrow base gait on mediolateral balance control in young and older adults. *J Biomech.* 2016;43:1264-1267.
104. Timmermans C, Roerdink M, Meskers CGM, Beek PJ, Janssen TWJ. Walking-adaptability therapy after stroke: results of a randomized controlled trial. *Trials.* 2021;22:923. doi: 10.1186/s13063-021-05742-3.

105. Van Ooijen MW, Roerdink M, Trekop M, Janssen TW, Beek PJ. The efficacy of treadmill training with and without projected visual context for improving walking ability and reducing fall incidence and fear of falling in older adults with fall-related hip fracture: a randomized controlled trial. *BMC Geriatr.* 2016;16:215. doi: 10.1186/s12877-016-0388-x.
106. Sinkjaer T, Andersen JB, Nielsen JF, Hansen HJ. Soleus long-latency stretch reflexes during walking in healthy and spastic humans. *Clin Neurophysiol.* 1999;110:951-959.
107. Forbes PA, Vlutters M, Dakin CJ, Van Der Kooij H, Blouin JS, Schouten AC. Rapid limb-specific modulation of vestibular contributions to ankle muscle activity during locomotion. *J Physiol.* 2017;595:2175-2195. doi: 10.1113/jp272614.
108. Hannan KB, Todd MK, Pearson NJ, Forbes PA, Dakin CJ. Vestibular attenuation to random-waveform galvanic vestibular stimulation during standing and treadmill walking. *Sci Rep.* 2021;11:8127. doi: 10.1038/s41598-021-87485-4.
109. Wuehr M, Schniepp R, Pradhan C, Ilmberger J, Strupp M, Brandt T, et al. Differential effects of absent visual feedback control on gait variability during different locomotion speeds. *Exp Brain Res.* 2013;224:287-294. doi: 10.1007/s00221-012-3310-6.
110. Dakin CJ, Inglis JT, Chua R, Blouin JS. Muscle-specific modulation of vestibular reflexes with increased locomotor velocity and cadence. *J Neurophysiol.* 2013;110:86-94. doi: 10.1152/jn.00843.2012.
111. Schniepp R, Wuehr M, Neuhaeusser M, Kamenova M, Dimitriadis K, Klopstock T, et al. Locomotion speed determines gait variability in cerebellar ataxia and vestibular failure. *Mov Disord.* 2012;27:125-131. doi: 10.1002/mds.23978.
112. Wuehr M, Schniepp R, Schlick C, Huth S, Pradhan C, Dieterich M, et al. Sensory loss and walking speed related factors for gait alterations in patients with peripheral neuropathy. *Gait Posture.* 2014;39:852-858. doi: 10.1016/j.gaitpost.2013.11.013.
113. Mccrum C, Lucieer F, Van De Berg R, Willems P, Pérez Fornos A, Guinand N, et al. The walking speed-dependency of gait variability in bilateral vestibulopathy and its association with clinical tests of vestibular function. *Sci Rep.* 2019;9:18392. doi: 10.1038/s41598-019-54605-0.
114. Buurke TJW, Lamothe CJC, Van Der Woude LHV, Hof AL, Den Otter R. Bilateral temporal control determines mediolateral margins of stability in symmetric and asymmetric human walking. *Sci Rep.* 2019;9:12494. doi: 10.1038/s41598-019-49033-z.
115. Hak L, Houdijk H, Steenbrink F, Mert A, Van Der Wurff P, Beek PJ, et al. Stepping strategies for regulating gait adaptability and stability. *J Biomech.* 2013;46:905-911. doi: 10.1016/j.jbiomech.2012.12.017.
116. Kim M, Collins SH. Stabilization of a three-dimensional limit cycle walking model through step-to-step ankle control. *IEEE Int Conf Rehabil Robot.* 2013;2013:6650437. doi: 10.1109/ICORR.2013.6650437.

Citation: van Leeuwen AM, Bruijn SM, van Dieën JH. (2022). Walking speed does not affect age-differences in ankle muscle beta-band intermuscular coherence during treadmill walking. *Brazilian Journal of Motor Behavior*, 16(5):326-351.

Editor-in-chief: Dr Fabio Augusto Barbieri - São Paulo State University (UNESP), Bauru, SP, Brazil.

Associate editors: Dr José Angelo Barela - São Paulo State University (UNESP), Rio Claro, SP, Brazil; Dr Natalia Madalena Rinaldi - Federal University of Espírito Santo (UFES), Vitória, ES, Brazil; Dr Renato de Moraes – University of São Paulo (USP), Ribeirão Preto, SP, Brazil.

Guest editors: Dr Paulo Cezar Rocha dos Santos - Weizmann Institute of Science, Rehovot, Israel; Dr Diego Orcioli Silva - São Paulo State University (UNESP), Rio Claro, SP, Brazil.

Copyright:© 2022 Van Leeuwen, Bruijn and van Dieën and BJMB. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International License which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: MvL and SMB were funded by a grant from the Netherlands Organization for Scientific Research (016.Vidi.178.014).

Competing interests: The authors have declared that no competing interests exist.

DOI: <https://doi.org/10.20338/bjmb.v16i5.321>