To fall or not to fall?
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Chapter 2

Transfer and retention effects of gait training with anterior-posterior perturbations to postural responses after mediolateral gait perturbations in older adults.

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ABSTRACT

Background  Gait perturbations, occurring in any direction in daily life, may result in a fall. In fall prevention, gait perturbation training is a promising approach. Treadmill perturbations in anterior-posterior direction can easily be applied by accelerations or decelerations of the belt, but it is unknown whether training effects transfer to reactive recovery in the mediolateral direction. We aimed to evaluate the transfer and retention effects of gait training with treadmill perturbations in anterior-posterior direction to mediolateral reactive recovery.

Methods  30 community-dwelling older adults (> 65 years) participated in this study. They were randomly assigned to a treadmill training session either with 16 anterior-posterior perturbations or with treadmill walking. The assessments contained a walking trial with 4 anterior-posterior and 4 mediolateral perturbations. Deviations in trunk velocity from unperturbed walking were summed over the first three strides after perturbation as a measure of recovery.

Findings  An exposure to gait perturbations during the baseline assessment led to significant improvement of recovery responses. For anterior-posterior perturbations, both groups showed better recovery immediately and 1-week post-intervention, but no group x time interaction. For mediolateral perturbations, both groups showed better recovery immediately and 1-week post-intervention, but no group x time interaction.

Interpretation Baseline assessment with perturbations in anterior-posterior and mediolateral directions caused significant improvements that were retained. Short-term training can be effective in the dynamic stabilization of one’s trunk, but our findings do not exclude that multi-directional perturbations may be needed.
INTRODUCTION

Falls are the leading cause of injuries in older adults (Ambrose et al., 2013; Rubenstein, 2006). Every year, one in three older adults aged over 65 years falls and this rate increases rapidly with age, leading to half of the people aged over 80 having at least one fall per year (Rubenstein, 2006; Stevens et al., 2006). Apart from injuries, falls may affect the quality of life and may result in increased fear of falling (Ambrose et al., 2013), which in turn may lead to a reduction in physical activity, loss of muscle strength and a further increased risk of falling (Scheffer et al., 2008). With demographic changes towards longer life expectancy, effective fall prevention is key for public health.

Several studies have revealed that fall incidence among older adults can be reduced by training (Gillespie et al., 2012; Sherrington et al., 2011). Conventional training programs often focus on aspects, like maintaining balance in standing tasks or safe obstacle negotiation (Sherrington and Tiedemann, 2015). In contrast, most falls are due to mechanical perturbations during walking, such as trips or slips (Krasovsky et al., 2014). Conventional training programs typically lack the training of reactive control after such perturbations.

Using advanced technology, it is possible to train reactive balance control with gait perturbations on a walkway or a treadmill and this has been shown to be effective in preventing falls (Gerards et al., 2017a; Mansfield et al., 2015; Pai et al., 2014a), with a most benefit when multiple perturbation types and directions are incorporated (Gerards et al., 2017). Gait perturbation training addresses the skills required to regain balance and avoid falls, such as reactive stepping strategies and counter-movements of the upper body (Grabiner et al., 2012; Lurie et al., 2013; McCrum et al., 2017). Older adults show improvements of these skills after repeated unexpected perturbations during standing or walking tasks that are retained (Bhatt et al., 2012; Dijkstra et al., 2015; Epro et al., 2018).

In most studies, slips or trips are simulated using sudden treadmill accelerations or decelerations to perturb the gait in anterior-posterior (AP) direction. However, in daily life, perturbations can occur in any direction like a misplaced step during a turning manoeuvre, obstacle negotiation or side bumps on a busy street. In an 8-week perturbation training study with anterior-posterior and lateral perturbations during walking, participants showed improvements in the center of mass displacement while being perturbed during quiet stance (Chien and Hsu, 2018). The study had some limitations as measurements of postural stability during perturbed walking and a control group were lacking. Moreover, it did not investigate improvements in AP and ML direction separately.

To perturb gait in mediolateral (ML) direction during treadmill walking, the treadmill itself needs to be mounted on a platform, that allows for quick and controlled sideways movement or an external apparatus has to be attached to the subject to apply lateral
pulls or pushes. Both setups require more space and more complex control and consequently entail higher costs than a 'standard' treadmill with a motor capable of delivering perturbations by quickly accelerating or decelerating the belt. If training with AP perturbations is sufficient to improve gait stability also in ML direction, this allows for a more affordable and smaller device utilizing only AP perturbations for testing and training of reactive balance control, which would be more applicable in clinical practice and accessible to a wider population.

Gait, as a motor task, should be automated when walking in daily life, as attention is needed to navigate in complex surroundings, for example, to negotiate obstacles. People with increased risk of falling often lack this automatism and have to concentrate on their gait. Adding a cognitive component to a motor-learning intervention can facilitate learning and automatization of the motor task, by distracting participants from the primary motor-task (Beaucet et al., 2009; Silsupadol et al., 2009a). Adding a virtual reality component distracts participants and provides optical flow as in a real-life situation (Mirelman et al., 2016).

If gait perturbation training can be shown effective and transfers between directions, then the question remains whether the improvement is based on changes in reactive responses or on changes in anticipatory behaviour, stabilizing the gait irrespective of perturbation direction.

In this study, we investigated the effects of a single session gait training with perturbations in AP direction on ML gait stability and assessed whether these effects are retained. Given the positive effects of perturbation training on daily-life fall incidence, we hypothesized that 1) AP gait perturbations training improves reactive balance in older adults, 2) effects transfer to ML gait stability and 3) effects are retained.

**METHODS**

**Participant recruitment**

Participants were recruited from a database of people that volunteered to participate in studies at the Department of Human Movement Sciences of Vrije Universiteit Amsterdam. Additional recruitment was done via flyers, distributed in leisure centers and online. In total, 30 older adults participated. They were healthy, had no experience with perturbation training and passed a cognition and memory test (>24 points in the Montreal Cognitive Assessment (Nasreddine et al., 2005)). Any neurological, cardiovascular or pulmonary comorbidity (i.e. stroke, heart attack, hypertension) that occurred in the past 12 months, as well as orthopaedic complications (i.e. lower extremity fractures, joint replacements) within the past 6 months, led to exclusion. All
participants provided written informed consent for this study, which had been approved by the institutional review board of Vrije Universiteit Amsterdam (VCWE-2018-026).

**Experimental setup**

Participants walked on the GRAIL (Gait Real-time Analysis Interactive Lab, Motek Medical BV, Amsterdam, The Netherlands), a 3-D instrumented dual-belt treadmill, recording ground reaction forces at 1000 Hertz, built on a platform that allows for pitch and sway movements. It is integrated into a motion capture system (Vicon Motion Systems Ltd, Yarnton, UK) with 10 infrared cameras recording at 100 Hertz. A model (Human Body Model (HBM), version 2.0, Motek Medical BV, Amsterdam, The Netherlands) based on 26 reflective markers placed on the feet, legs and trunk was used to capture the participants’ movements.

Handrails were detached to omit grasping reactions as this reduces the effects of perturbations and affects motor learning (Buurke et al., 2019). A full-body harness connected with a rope to an overhead frame allowed the participants to move freely without body weight support but prevented them from hitting the treadmill in case of falling. An immersive virtual reality experience was created by projecting a forest path on the screen and treadmill, adjusted to the walking speed and enhanced with sounds (chirping birds and steps on fallen leaves and pebbles) to distract participants from walking.

A custom-made application (D-flow version 3.30.1, Motek Medical BV, Amsterdam, The Netherlands) triggered perturbations at heel strike of either the left or right leg, using the local maxima in AP position of the heel marker relative to the pelvis (Zeni et al., 2008). ML perturbations consisted of a sideways movement of the treadmill platform to the side opposite of the foot contact. AP perturbations consisted of belt accelerations or decelerations at foot contact.

**Study design and measurement protocol**

Our participants were invited on two separate days with one week in between. They were randomly assigned to either receive the experimental (16 AP perturbations) or control (8 minutes treadmill walking only) intervention. In session 1, demographic data, as well as potential confounding variables including age, sex, height, body mass, and Timed up & go (TUG) time (Schoene et al., 2013), were assessed.

To familiarize with treadmill walking, participants started walking at 1 m/s for 6 minutes (Meyer et al., 2019; Wass et al., 2005), followed by the baseline measurement consisting of: 1) unperturbed walking at 1 m/s for 100 strides. 2) perturbed walking with 4 AP belt deceleration and 4 ML perturbations. Participants were told that perturbations could occur or not and were asked to try to recover balance and to continue walking if they experienced a perturbation. For ML perturbations, the treadmill
moved 5 cm in 0.31 seconds to the contralateral side, meaning that at right heel strike the treadmill moved to the left side and vice versa. These perturbations are likely to induce a cross over stepping strategy. For AP perturbations, the treadmill decelerated by 9 m/s\(^2\) for 0.12 seconds at heel strike, meaning the striking foot is not pulled under participant’s center of mass and therefore the center of mass stays behind the base of support. This simulates a slip, in which the striking foot slips forward, inducing backwards balance loss. The intensity and type of perturbations were based on previous work (Roeles et al., 2018), showing treadmill decelerations and contralateral sways to be the most challenging types. The order of perturbations, as well as the perturbed leg and the time between perturbations (10-60 seconds), was randomized but kept the same for all participants. This made it impossible for the participants to anticipate when on which leg and in which direction the upcoming perturbation would be applied.

After the baseline measurements, the experimental group continued with the training, during which they received 16 AP perturbations (8 belt accelerations and 8 belt decelerations) at either low (8 m/s\(^2\), 0.11s) or high (10 m/s\(^2\), 0.13s) intensity. It was shown that within one session, by the 5th slip the incidence of falls and balance loss was less than 5% and 15%, respectively (Pai et al., 2010). Another study showed that 8 slips in a single session were enough to improve dynamic stability and reduce falls (F. Yang et al., 2018). The time interval, order and leg were randomized in the same fashion as in the measurement trials. The control group continued with training consisting of walking for 8 minutes on the treadmill at 1m/s without perturbations. After a 4-minutes seated washout rest break, the participants were asked to walk again on the treadmill and the baseline measurements for unperturbed walking and perturbed walking were repeated. The same measurements were repeated 1 week later to assess retention (Fig. 1).
Figure 1: Schematic overview of the timeline and content of the measurements and interventions. AP = anterior-posterior, ML = mediolateral

DATA ANALYSIS

Data, recorded at baseline, post-intervention and retention, were processed with Nexus software (version 2.7.0, Vicon Motion Systems Ltd, Yarnton, UK) and custom-made MATLAB scripts (version R2018a; MathWorks Inc, Natick, MA, USA). Three-dimensional marker data were smoothed using a second-order 15Hz low-pass Butterworth filter and all data streams (Motion capturing and force plate) were resampled to 100 samples/s.

We calculated spatial-temporal gait parameters over 100 strides for unperturbed walking. From perturbed walking trials, the last 3 strides before a perturbation were extracted. The mean of 24 pre-perturbation strides was then used to evaluate changes in spatial-temporal parameters as a result of an anticipatory adjustment of the gait
pattern. The step time, stance time and swing time were determined from gait events, and step length and step width were calculated as the AP and ML distances between the left and right foot position at heel strike (Roeles et al., 2018).

Local dynamic stability of unperturbed walking was quantified by the local divergence exponent (LDE), reflecting the ability to cope with small internal perturbations. It was calculated for the center of mass in AP and ML directions separately (Bruijn et al., 2009). Center of mass position was approximated as the averaged position of the four pelvis markers. Briefly, 100 strides were normalized to 10000 samples (i.e. approximately 100 samples per stride) from which state spaces for all spatial dimensions were reconstructed with 5 time-delayed copies with a time delay of 10 samples. Euclidean distances between two neighbouring points were calculated and tracked over time. The slope of the average logarithmic rate of divergence was used to estimate the LDE. A lower value defines a more stable gait.

The responses to perturbations were quantified by the deviation in trunk velocity from unperturbed walking (Fig. 2). Time series of trunk velocities of unperturbed and perturbed walking were normalized to 101 samples per stride. For unperturbed gait, averages over 100 strides and their variability for each percentage of the gait cycle were calculated. Deviations in perturbed gait relative to unperturbed gait were calculated for all 6 degrees of freedom: mediolateral, vertical, anterior-posterior linear velocities and frontal, transversal and sagittal plane angular velocities (Bruijn et al., 2010). Next, the deviations were divided by the standard deviation of the unperturbed gait cycle for each dimension and then combined as the Euclidian sum over degrees of freedom into a trunk velocity deviation measure (Bruijn et al., 2010). The integral of the deviation over the first 3 recovery strides following a perturbation, shown by the area under the curve (AUC) beginning at the trigger, were used to describe recovery performance for every perturbation (Fig. 2, top right). The results were averaged over legs within perturbation directions. We used the AUC because the deviation could not
always be fitted by an exponential function (Bruijn et al., 2010). A smaller AUC indicates faster recovery.

Figure 2: Deviation of perturbed gait trunk velocity from unperturbed gait trunk velocity over time. Red vertical lines indicate the heel strikes triggering the perturbations. Top right: Close-up showing the deviation in trunk velocity after one perturbation with the area under the curve (AUC) over 3 strides starting at the trigger shaded in blue.

STATISTICS

Analyses were performed with SPSS version 25 (SPSS Inc, Chicago, IL, USA). The level of significance was set at alpha=0.05. First, we checked for normality of data using the Shapiro-Wilk test. All data were normally distributed. Next, the interquartile range rule (IQR) was used to detect outliers, with only extreme outliers (exceeding 3 times IQR) being excluded from the analysis.

To assess potential anticipatory changes, differences in the unperturbed gait pattern between groups and conditions were analyzed using repeated-measures analysis of
variance (ANOVA), with time as within-subject and group as between-subject factor. To this end, the mean values of spatial-temporal gait parameters over 100 strides were used. If ANOVA revealed significant effects, post-hoc paired samples t-tests were used to explore differences between groups or time points. The same procedure was used for the LDE. In addition, for perturbed walking, the mean values of 24 pre-perturbation strides were used to evaluate changes in spatial-temporal parameters. ANOVA’s (within-factor: time, between-factor: group), followed by post-hoc pairwise t-tests, to test for differences between groups and time points.

Recovery responses after AP and ML perturbations and transfer effects between perturbation directions were investigated using the AUC with time as within factor and group as between factor. When significant effects were found, post-hoc paired samples t-tests were used to further examine differences between groups and time points. All post-hoc tests were performed with Bonferroni correction.

RESULTS

Participant characteristics

All 30 participants (71 years (SD 4.5), [65-85]) were included in the analysis. Participants characteristics revealed no significant group difference at baseline (Tab.1).

Tab. 1: Participant characteristics, presented as means and standard deviations (SD)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Trainer (n=15)</th>
<th>Control (n=15)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.33 (SD 3.99), [66-81]</td>
<td>71.67 (SD 4.98), [65-85]</td>
<td>0.42</td>
</tr>
<tr>
<td>Gender (female)</td>
<td>8 (53.33%)</td>
<td>7 (46.67%)</td>
<td>0.72</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172.93 (SD 10.48)</td>
<td>172.33 (SD 8.77)</td>
<td>0.87</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>74.93 (SD 9.22)</td>
<td>75.40 (SD 11.17)</td>
<td>0.90</td>
</tr>
<tr>
<td>TUG (seconds)</td>
<td>7.25 (SD 1.08)</td>
<td>7.07 (SD 0.94)</td>
<td>0.63</td>
</tr>
<tr>
<td>MoCA (points)</td>
<td>27.53 (SD 1.51)</td>
<td>28.00 (SD 1.41)</td>
<td>0.39</td>
</tr>
</tbody>
</table>
Unperturbed walking

For anterior-posterior LDE, no time, group, or time x group effects were found (Fig. 3, left). Medio-lateral LDE was significantly different between time points ($F(2,56) = 3.454$, $P=0.039$), but no measurement x group interaction was found. LDE was lower at retention than immediately after training ($P=0.024$), indicating more stable dynamics, but this was not significantly different from baseline (Fig. 3, right).

Analysis of the spatial-temporal gait parameters in unperturbed walking revealed significant time effects on step time ($F(2,56) = 9.386$, $P<0.001$), step length ($F(2,50) = 8.732$, $P=0.001$), step width ($F(2,56) = 3.297$, $P=0.044$), swing time ($F(2,54) = 5.961$, $P=0.005$), stance time ($F(2,56) = 9.917$, $P<0.001$). No time x group interactions were found. Post-hoc tests revealed significant differences between baseline and immediately post-intervention for step time, step length, swing time, and stance time (all $P<0.05$), but at retention there were no differences compared to baseline. Step width had significantly changed at retention compared to post-intervention ($P=0.022$), but was not different compared to baseline (Fig. 4).

Figure 3: Local divergence exponents (LDE) of unperturbed walking for AP and ML directions. The error bars represent the standard deviation. Lower values indicate more stable gait. *indicates a significant post-hoc difference between time points.
Perturbed walking

Repeated measures ANOVA revealed significant time effects on step time ($F_{(2,56)} = 10.143, P<0.001$), step length ($F_{(2,50)} = 10.590, P<0.001$), step width ($F_{(2,56)} = 6.505, P=0.003$), swing time ($F_{(2,56)} = 8.870, P<0.001$), stance time ($F_{(2,56)} = 10.254, P<0.001$). No group effects or time x group interactions were found. Post-hoc tests revealed significant differences for all spatial-temporal gait parameters between post-intervention and baseline (all $P<0.05$). At retention, there were no significant differences compared to baseline (Fig. 5).
Figure 5: Spatial-temporal parameters of the last 3 strides before a perturbation. *indicates significant post-hoc differences between time points. The error bars represent the standard deviation.

**Perturbation responses**

For AP perturbations, AUC was significantly affected by time ($F(2,56) = 22.287, P<0.001$), indicating faster recovery immediately post-intervention and at retention, but no effect of group, nor a time x group interaction effect. Post-hoc tests revealed that in both groups recovery was significantly improved post-intervention ($P<0.001$) and at retention compared to baseline ($P<0.001$; Fig. 6, left).

For ML perturbations, AUC was significantly affected by time ($F(2,56) = 17.862, P<0.001$), but no effect of group, nor a time x group interaction effect. Post-hoc testing showed that recovery performance was significantly improved directly after the training ($P<0.001$) and at retention ($P=0.001$) compared to baseline (Fig. 6, right).
Figure 6: Deviations of perturbed gait trunk velocity from unperturbed gait, calculated as integral over 6 steps of the Euclidian sum of deviations in trunk linear and angular velocities from unperturbed walking after AP (left) and ML (right) perturbations. The error bars represent the standard deviation.

**DISCUSSION**

We investigated the effects of a single session of gait training with perturbations in AP direction and their transfer to responses to ML perturbations in older adults and assessed whether these effects were retained. Both, the control and intervention group showed improved recovery for AP perturbations in terms of trunk velocity deviations. Also, both groups similarly improved responses after ML perturbations. These effects were retained one week after training. Overall, our results suggest that exposure to the perturbations in the baseline measurement accounted for a large part of the improvement in balance recovery.

Changes observed in local dynamic stability and spatial-temporal gait parameters of unperturbed walking immediately post-intervention indicated that the gait pattern was to some extent disturbed or adapted at this time point, but the direction of these effects and the lack of effects at retention indicate that improvements in recovery were not due to anticipatory changes of the gait pattern.
Both groups of participants quickly learned from the perturbations at baseline and significantly reduced the deviation in trunk velocity after perturbations in the measurement directly post-intervention. Similar quick learning effects were shown in other studies (Pai et al., 2010; Pijnappels et al., 2008a) and similar to our findings effects were retained over weeks to months with some reduction of recovery performance over time (Bhatt et al., 2012; Pai et al., 2014b). Our results show that exposure to 4 AP belt decelerations and 4 ML perturbations during the baseline assessment already led to significant improvements that were retained. Longer training interventions (Chien and Hsu, 2018), may contribute to consolidating improvements, however, one study showed that even with a reduced amount of training in a single session intervention, improvements are still significant (F. Yang et al., 2018). Future studies on longer perturbation-based gait training should include repeated measurements to explore how many sessions are needed before effects reach a plateau.

Moreover, the fact that ML results were similar in both groups indicates that the training effect was not transferred, and suggests that multi-directional training may be needed (Gerards et al., 2017; McCrum et al., 2019, 2018). This should be investigated in future research using a protocol without ML perturbations at baseline to assess whether a transfer occurs at all and to investigate the transfer to overground walking.

With randomizing perturbation directions and perturbed leg, anticipatory adaptations of the gait pattern according to the last perturbation are ineffective for recovery after the subsequent perturbation. Most studies (Lurie et al., 2013; Pai et al., 2014a; Shimada et al., 2004; Yang et al., 2018) have used only one direction to measure and train participants, which might allow participants to anticipate to reduce the perturbation impact, making it easier to regain balance after the perturbation. Both groups showed similar changes in spatial-temporal parameters in unperturbed gait and the steps preceding the perturbation, but only immediately post-intervention. Step time and step length were increased accompanied by a reduction in step width. These changes do not clearly suggest a more stable gait pattern. Moreover, these gait changes were not retained over one week, while the improvement in recovery was. Unperturbed walking was significantly more stable in ML direction at retention compared to immediately post-intervention. At baseline and immediately post-intervention the mean stability was similar. The larger variance at baseline may suggest that some participants needed more time to familiarize with walking on a treadmill in a virtual environment. The effect at retention may then indicate that participants were more confident on the treadmill compared to the first day as they had already experienced treadmill walking and even perturbed treadmill walking without an actual fall. Our findings on unperturbed gait support the notion that reactive balance control was improved and improvements in balance recovery were not due to anticipatory adaptation of the gait pattern. While muscle strength is crucial for balance recovery after perturbations of gait (Pijnappels et al. 2008) it is unlikely that it improves within a single session of perturbation-based gait training. We suggest that changes occurred due to faster adaptations of muscle activation after the perturbation, as rapid
changes in muscle activation appear to discriminate between successful and unsuccessful balance recovery responses after gait perturbations (Pijnappels et al., 2005a) or due to selection of more appropriate recovery strategies (Bhatt et al., 2013) but our data do not allow us to differentiate between such mechanisms.

Several study limitations should be noted. First, participants were relatively fit and healthy, which may limit the generalization of our findings to more frail or patient populations. Second, the dimensions of the treadmill may have influenced the reactive movements and stepping strategies. Limited space, particularly for lateral foot placement may have led to alteration of stepping reactions. Participants may have adjusted their response to stay in the middle of the treadmill and avoid stepping on the frame lateral of the belt. However, the treadmill allowed for multiple, unexpected and standardized perturbations, which is key for successful research and may be a key for effective training (Gerards et al., 2017). The use of a fixed walking speed may cause differences in gait stability between participants (Mccrum et al., 2018) and therefore the difficulty of the perturbations may have been different between participants. However, given the comparability of the two groups, this has not likely caused a bias in the current study. Finally, assessing reactive responses as a measurement appears to have already been enough exposure to have a significant training effect that was retained. Future research should avoid measuring reactive responses at baseline. Our results support the findings that “vaccination-like” (Pai et al., 2014a) training interventions significantly improve older adults’ ability to counteract balance loss due to gait perturbations, but future research should avoid this limitation to assess transfer between perturbation directions. Our inclusion criteria may limit generalization to populations with increased fall risk. Moreover, the generalizability of improvement in trunk velocity deviation in a treadmill environment to daily life outcomes needs to be confirmed, for example in terms of transfer to daily life gait quality (Punt et al., 2019) or actual fall incidence (Pai et al., 2014a).

CONCLUSION

Our results indicate that a baseline measurement with gait perturbations in AP and ML directions caused significant improvements in balance recovery that were retained after one week. These results suggest that limited exposure to gait perturbations can be effective in terms of dynamic stabilization of the trunk during walking, but do not exclude that multi-directional perturbations may be needed. Perturbation-based gait training may enhance conventional balance training programs and may be of added value in multifactorial fall prevention in clinical practice.