

1 **Retention of improvement in gait stability over 14 weeks due to trip-**
2 **perturbation training is dependent on perturbation dose**

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26 **Abstract**

27 Perturbation training is an emerging approach to reduce fall risk in the elderly. This
28 study examined potential differences in retention of improvements in reactive gait
29 stability over 14 weeks resulting from unexpected trip-like gait perturbations. Twenty-
30 four healthy middle-aged adults (41-62 years) were assigned randomly to either a
31 single perturbation group (SINGLE, $n = 9$) or a group subjected to eight trip-like gait
32 perturbations (MULTIPLE, $n = 15$). While participants walked on a treadmill a
33 custom-built brake-and-release system was used to unexpectedly apply resistance
34 during swing phase to the lower right limb via an ankle strap. The anteroposterior
35 margin of stability (MoS) was calculated as the difference between the anterior
36 boundary of the base of support and the extrapolated centre of mass at foot touchdown
37 for the perturbed step and the first recovery step during the first and second
38 (MULTIPLE group only) perturbation trials for the initial walking session and
39 retention-test walking 14 weeks later. Group MULTIPLE retained the improvements
40 in reactive gait stability to the perturbations (increased MoS at touchdown for
41 perturbed and first recovery steps; $p < 0.01$). However, in group SINGLE no
42 differences in MoS were detected after 14 weeks compared to the initial walking
43 session. These findings provide evidence for the requirement of a threshold trip-
44 perturbation dose if adaptive changes in the human neuromotor system over several
45 months, aimed at the improvement in fall-resisting skills, are to occur.

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51 **Introduction**

52 Falls are a major cause of injuries and disability in the elderly population (Terroso et
53 al., 2014). According to epidemiological studies increased fall risk becomes detectable
54 by middle-age (i.e. about 50 years of age; Donaldson et al., 1990). Most falls in the
55 elderly result from tripping during walking (Berg et al., 1997; Talbot et al., 2005),
56 causing sudden loss of balance in the forward direction. To avoid falling, such unstable
57 body dispositions require reactive postural adjustments in order to control the position
58 and velocity of the centre of mass (CoM) relative to the base of support (BoS; Bhatt et
59 al., 2006; Bierbaum et al., 2011; MacLellan and Patla, 2006). Improving such
60 compensatory gait adjustments may be beneficial for fall prevention.

61 Perturbation training has emerged as a promising approach to reduce falls in the elderly
62 (Gerards et al., 2017; McCrum et al., 2017) since several studies demonstrate
63 significant improvements in reactive response in older adults after repeated exposure
64 to various laboratory-induced mechanical gait perturbations (Bierbaum et al., 2011;
65 Epro et al., 2018a; Lee et al., 2018; Pai et al., 2010). These improvements in reactive
66 gait stability in the elderly can be retained over several months (Bhatt et al., 2012; Pai
67 et al., 2014a) or even years (Epro et al., 2018b) without any additional training. This
68 provides evidence that repeated externally induced gait perturbations may be an
69 appropriate stimulus for the aged central nervous system to develop enhanced and
70 retainable balance control strategies through refined neuromuscular coordination
71 reducing fall risk (Pai et al., 2014b).

72 Previous studies showed that such reactive balance improvements can occur after
73 merely a single perturbation exposure (Marigold and Patla, 2002; Pai et al., 2010).
74 Though such a single trial effect seems promising, in particular for application with
75 frail older adults, it has only rarely been investigated whether reactive gait stability

76 improvements acquired through single perturbation exposure can be retained over a
77 prolonged time-period (e.g. several months) in populations which are at higher fall
78 risk. In contrast, retention of the robust effects obtained from multi-trial perturbation
79 training sessions are already well established (Bhatt et al., 2012; Epro et al., 2018b;
80 Pai et al., 2014a). However, to our knowledge only Liu et al. (2017) examined this
81 topic, demonstrating that a single slip perturbation exposure can cause long-term
82 retention effects.

83 In a previous study we were able to show retention in gait stability improvements over
84 14 weeks following a single bout of eight unexpected trip-like gait perturbations (Epro
85 et al., 2018b). As a continuation, in this study we aimed to examine whether such
86 retention effects may also be observed after single trip exposure i.e. whether the
87 retention in gait stability improvements over 14 weeks is dependent on trip_
88 perturbation dosage for a group of middle-aged.

89

90 **Methods**

91 Twenty-four healthy middle-aged adults (41-62 years; 12 of them men), with no
92 known neurological or musculoskeletal impairments, took part in this study. The
93 participants were randomly divided into two groups: (1) MULTIPLE, the reference
94 group, (eight gait-perturbations initially and after 14 weeks; $n = 15$); and (2) SINGLE
95 (a single gait perturbation initially and again after 14 weeks; $n = 9$). The two groups
96 underwent equivalent periods of treadmill walking (20-25 min). The study was
97 approved by the ethics committee of the German Sport University Cologne in
98 accordance with the Declaration of Helsinki. All participants provided written
99 informed consent after initial briefing.

100 About seven days prior to the initial measurement session all participants underwent
101 treadmill familiarisation (h/p/cosmos pulsar 4.0; Nussdorf-Traunstein, Germany)
102 consisting of ten minutes walking at 1.4 m s⁻¹. For perturbations, all participants again
103 walked at a standardised velocity of 1.4 m s⁻¹ on a treadmill and received either one or
104 eight unexpected gait perturbations using a custom-built brake-and-release system
105 described previously (Epro et al., 2018ab; see supplementary material 1 for more
106 detailed description). Note that our applied perturbation paradigm imposes *artificial*
107 trips that may not fully replicate real-life trip situations (see supplementary material 2
108 for a typical recovery response to the perturbation). Therefore, in this manuscript the
109 perturbation will be referred to as a “trip-like gait perturbation”.

110 *For electronic version: Insert supplementary material 2*

111 In order to assess dynamic stability (specifically MoS) each participant was analysed
112 before (Pre) and after 14 weeks (Post14w). Arrangements to assess dynamic stability
113 control during treadmill walking have been described previously (Epro et al., 2018ab;
114 McCrum et al., 2014; Süptitz et al., 2012, 2013). Briefly, a reduced kinematic model
115 (Süptitz et al., 2013), consisting of five retro-reflective markers (radius 16 mm) placed
116 at the seventh cervical vertebra and the greater trochanter and forefoot of the left and
117 right legs, was tracked using a 10-camera motion capture system (120 Hz; Nexus 2.6.1;
118 Vicon Motion Systems, Oxford, UK). The time-courses for the 3D coordinates of the
119 markers were smoothed using a fourth-order digital Butterworth filter (cut-off
120 frequency 20 Hz). The anteroposterior MoS was calculated at each foot touchdown
121 (TD) for baseline gait, the perturbed step (Pert) and the first six recovery steps after
122 perturbation (Reco1L-Reco6R) as the difference between the anterior boundary of the
123 base of support (anteroposterior position of the toe projection to the ground) and the
124 extrapolated centre of mass (Hof et al., 2005). TD was determined using two 2D

125 accelerometers (1080 Hz; ADXL250; Analog Devices, Norwood, MA, USA) attached
126 over the tibia of each leg (Süptitz et al., 2012). Our reduced kinematic model has been
127 validated previously (Süptitz et al., 2013) as appropriately assessing MoS for
128 unperturbed and perturbed walking and for wide ranging age groups, showing
129 significant correlations with a full-body kinematic model (average across trials $r =$
130 0.90, $p < 0.01$).

131 Independent samples t -tests were used to assess potential differences in age, height
132 and body mass between groups. A two-way repeated-measures ANOVA with factors
133 group (MULTIPLE and SINGLE) and time point (first perturbation trial at baseline
134 ($T1_{Pre}$) and after 14 weeks ($T1_{Post14w}$)) was conducted to determine retention of
135 improvements in MoS during unexpected trip-like gait perturbation, separately for TD
136 Pert and TD Reco1L. Note that only $T1_{Pre}$ and $T1_{Post14w}$ were considered for further
137 analysis as the aim of this study was principally to examine retention effects following
138 different perturbation training protocols rather than trial-to-trial adaptation within one
139 session. The focus here was set solely on the first perturbation trials since trial-to-trial
140 adaptation has been shown previously for healthy middle-aged adults (McCrum et al.,
141 2014). Note that in order to check for acute effects in MoS after single trip exposure
142 (without possibly affecting retention by adding another perturbation in group
143 SINGLE) a two-way repeated-measures ANOVA with factor trial (first and second
144 perturbation trial at initial training session, $T1_{Pre}$ and $T2_{Pre}$ respectively) and step (TD
145 Pert and TD Reco1L) was conducted for group MULTIPLE. A further two-way
146 repeated-measures ANOVA (factors: group, trial) was implemented for unperturbed
147 gait (average of 12 consecutive steps of unperturbed walking with ankle strap attached,
148 assessed prior to the first perturbation). In a case of significant main effect or
149 interaction Bonferroni *post-hoc* correction was applied. The level of significance was

150 set at $\alpha = 0.05$. All results in text and figures are presented as mean (SD). All statistical
151 analyses were conducted using Statistica software (Release 10.0; Statsoft Inc, Tulsa,
152 OK, USA).

153

154 **Results**

155 There were no significant differences in age (51.1 (6.0) years vs. 54.3 (4.0) years),
156 body height (171.9 (12.0) vs. 180.1 (12.9) cm) and body mass (76.7 (14.0) vs. 79.3
157 (14.9) kg) between the two groups (MULTIPLE vs. SINGLE). One participant from
158 group MULTIPLE was not able to cope with the task by grasping the treadmill
159 handrails to prevent a fall after the novel trip-like gait perturbation ($T1_{Pre}$); hence only
160 23 participants were considered for analysis of dynamic stability. For baseline walking
161 (12 consecutive steps), the two-way repeated-measures ANOVA revealed no
162 statistically significant effects for MoS for time point ($T1_{Pre}$ and $T1_{Post14w}$) or group
163 (MULTIPLE and SINGLE). Considering post 14 weeks, the analysis of MoS at TD
164 Pert and TD Reco1L revealed a statistically significant time point x group interaction
165 for both analysed steps ($F_{1,21} = 4.29, p = 0.05$ and $F_{1,21} = 9.66, p = 0.01$ for TD Pert
166 and TD Reco1L respectively), indicating that the time effect on MoS was dose
167 specific. Post-hoc tests revealed significantly higher MoS values ($0.001 < p < 0.01$) at
168 TD Pert and Reco1L for $T1_{Post14w}$ compared to $T1_{Pre}$ for group MULTIPLE (see figure
169 1). In contrast, no statistically significant increases in MoS after 14 weeks were found
170 for any of the analysed steps in group SINGLE (see figure 1). Regarding acute MoS
171 changes, the two-way repeated-measures ANOVA revealed a significant trial ($F_{1,13} =$
172 7.22, $p = 0.02$) and step effect ($F_{1,13} = 18.55, p < 0.001$) with higher MoS at TD Pert
173 and TD Reco1L for $T2_{Pre}$ compared to $T1_{Pre}$ and TD Reco1L compared to TD Pert for
174 both trials (see figure 2).

175 *Insert figure 1*

176 *Insert figure 2*

177

178 **Discussion**

179 We aimed to examine potential differences in retention of improvements in gait
180 stability over 14 weeks in response to single- and multiple-dose trip-like gait
181 perturbation training. The results partly support our hypothesis that higher retention
182 effects may be attained through a higher perturbation dose as significant improvements
183 in the reactive response to an unexpected trip-like gait perturbation after 14 weeks
184 were found only in the group that completed eight perturbation trials (group
185 MULTIPLE). No retention effects were found after a single trip exposure (group
186 SINGLE), indicating that there is (under our conditions) a threshold for perturbation
187 dose for provocation of adaptive changes in the human neuromotor system over several
188 months.

189 Margin of stability at TD of the perturbed step and first recovery step was significantly
190 less negative (more stable body configuration) after 14 weeks compared to the initial
191 session in group MULTIPLE (eight perturbation trials). These results are in
192 accordance with our earlier findings (Epro et al., 2018b), showing retention in gait
193 stability improvements over 14 weeks following a single bout of trip-like gait
194 perturbations in older women. Thus, although middle- and older-aged adults have a
195 higher fall risk, they are still able to improve their reactive responsiveness through
196 repeated exposure to unexpected perturbations and retain those improvements over a
197 period of months. Since for single trip exposure we found no significant differences in
198 MoS between the two measurement time points for any of the analysed steps it is likely
199 that a single perturbation may have been too low to facilitate learning effects lasting

200 for several months. This supports previous findings seen in slipping, showing that in
201 younger adults a single slip exposure without additional sessions was not sufficient to
202 yield retention effects in gait stability over four months (as compared to a higher
203 perturbation dose comprising 24 slips; Bhatt and Pai, 2009). Taken together, these
204 results indicate that perturbation dose must exceed a threshold in order to induce
205 retention of improvements in gait stability over several months acquired during single-
206 session treadmill training.

207 Repetitive exposure to unexpected trip-like perturbations may promote adaptation of
208 the central nervous system to sudden mechanical changes in the environment. The
209 current study was focused on reactive (feedback-driven) response to unexpected gait
210 perturbations. Even though predictive (feedforward-driven) adjustments of gait may
211 occur after repeated perturbations (Bierbaum et al., 2010; McCrum et al., 2016), we
212 found no differences in dynamic stability parameters at TD of the step immediately
213 before the perturbation and baseline walking for any of the perturbation trials
214 (unpublished data), indicating that the observed gait stability improvements were
215 predominantly feedback-driven. Whether the observed adaptive changes to the
216 perturbations in group MULTIPLE are driven foremost by the modulation of spinal
217 reflexes as previously seen in human infants (Lam et al., 2003; Pang et al., 2003) or
218 by automatic supraspinal postural responses (Jacobs and Horak, 2007) cannot be
219 determined from the current findings, though the issue should be examined in future
220 investigations.

221 In addition, when analysing the initial first two perturbation trials in group
222 MULTIPLE, MoS was significantly improved in the second compared to the first trial.
223 Therefore, we could assume short-term adaptive changes after single trip exposure in
224 group SINGLE without possibly affecting retention by adding another perturbation.

225 Finally, our finding that single trip exposure in group SINGLE failed to facilitate
226 adaptive changes in reactive gait stability over 14 weeks does not support previous
227 results seen for slipping (Liu et al., 2017). This group reported significant
228 improvements in reactive stability, and hence a reduction in laboratory falls, 12 months
229 after a single gait slip. Contradictions between findings requiring further investigation
230 may be related to the different perturbation types (tripping vs. slipping), numbers of
231 initially reported falls and ages of participating subjects (middle-aged vs. community-
232 dwelling older).

233 We have to acknowledge that our current protocol might not fully replicate a real-life
234 trip situation and that this may possibly restrict generalisability of the observed gait
235 stability improvements. However, despite the fact that gait-trip mechanics are highly
236 variable in nature, the common consequence of stumbling in real-life situations may
237 require similar postural corrections to regain balance to those observed in our
238 perturbation setup (i.e. effectively increasing base of support; Epro et al., 2018a;
239 McCrum et al., 2014; Süptitz et al., 2013). Although the applied perturbation
240 magnitude was equal among all analysed participants, the effect of the perturbation on
241 MoS in absolute terms appeared to differ slightly between groups (on average by 4
242 cm; see figure 1), though this difference did not reach statistical significance ($p = 0.78$).
243 Therefore, one might argue that the failure of retention for group SINGLE may be due
244 to an initially lower effect on stability. However, on analysing the relationship between
245 the MoS during the initial perturbation and its relative change after 14 weeks by
246 including our previous data on older adults (Epro et al., 2018b; total $n = 23$), we found
247 no significant correlation ($r = 0.28$; $p = 0.21$) and hence are confident that the observed
248 group differences for retention are predominately related to perturbation dose rather
249 than its initial effect on stability. Finally, the number of analysed subjects is relatively

250 low ($n = 14$ for MULTIPLE; $n = 9$ for SINGLE), possibly reducing the potential for
251 determining significant retention effects in MoS (this is reflected in low effect sizes
252 for group SINGLE: Cohen's $d = 0.33$ and 0.29 for TD Pert and Reco1L respectively).
253 However, since the observed retention effects for group MULTIPLE were large (on
254 average about 80% improvement in MoS) though the group was quite small in size,
255 we are confident that the low sample size for group SINGLE is not the primary driver
256 for the lack of functional retention effects for this group.

257 In conclusion, our results provide evidence for the existence of a threshold for
258 perturbation dose if retainable adaptive changes are to be provoked in the human
259 neuromotor system. We found that brief exposure to several unexpected trip-like gait
260 perturbations, but not a single trip, can facilitate retention in reactive gait stability
261 improvements over months, indicating that a finite number of perturbations may be
262 required for retention of fall-resisting skills over several months.

263

264 **Disclosure of Interest**

265 The authors declare no conflicts of interest.

266

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271

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360

361 **Figure 1:** Margin of stability (MoS) during unperturbed walking (Base), for
362 touchdown at perturbation (Pert) and for the following six recovery steps after the
363 perturbation (Reco1L-Reco6R) in group MULTIPLE ($n = 14$) and group SINGLE (n
364 $\equiv 9$). Data are given for the first trip-like gait perturbation trial at the initial training
365 session and post 14 weeks ($T1_{Pre}$ and $T1_{Post14w}$, respectively). Values are expressed as
366 means with SD error bars. T_M represents a statistically significant time point effect for
367 group MULTIPLE ($p < 0.01$). L: Left leg. R: Right leg.

368

369 **Figure 2:** Margin of stability (MoS) during unperturbed walking (Base), for
370 touchdown at perturbation (Pert) and for the following six recovery steps after the

371 perturbation (Reco1L-Reco6R) in group MULTIPLE ($n = 14$), after the first ($T1_{Pre}$)
372 and second ($T2_{Pre}$) trip-like gait perturbation trials at the initial training session. Values
373 are expressed as means with SD error bars. * represents a statistically significant trial
374 effect ($p < 0.05$). # represents a statistically significant difference to Pert ($p < 0.001$).
375 L: Left leg. R: Right leg.

376

377 **Supplementary material 2: Experimental setup for the assessment of the recovery**
378 **response following the first unexpected trip-like gait perturbation trial during treadmill**
379 **walking (1.4 m s^{-1}) for a typical participant.**