

1 **Improving trip and slip-resisting skills in older people: perturbation dose**
2 **matters**

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16 **Short title:** Improving fall-resisting skills in aging

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25 **Abstract**

26 Aging negatively affects balance recovery responses following trips and slips. We
27 hypothesize that older people can benefit from brief treadmill-based trip and slip-
28 perturbation exposure despite reduced muscular capacities, but with neuropathology
29 their responsiveness to these perturbations will be decreased. Thus, to facilitate long-
30 term benefits and their generalizability to everyday life, one needs to consider the
31 individual threshold for perturbation dose.

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34 **Summary:** Improving trip and slip-resisting skills in older people requires a
35 consideration of individual thresholds for perturbation practice dose.

36

37 **Key Words:** Falls; Balance; Perturbation Training; Gait Stability; Neurological
38 Disorders; Locomotion; Aged.

39

40 **Key Points:**

- 41 • Aging and neuropathology negatively affect balance recovery responses
42 following sudden gait perturbations like trips and slips.
- 43 • Older adults can adapt and retain trip and slip-resisting skills through brief
44 exposure to repetitive treadmill gait perturbations despite age-related muscular
45 changes, but pathology of the sensory and neuromotor systems reduce the
46 responsiveness to such practice.
- 47 • In order to facilitate trip and slip-resisting skills and long-term reduction in fall
48 risk, there is a need to consider the individual threshold for practice dose
49 (number of perturbations).

50 INTRODUCTION

51 Balance control during human biped locomotion in constantly changing
52 environments requires a continuous correspondence between perceptual information
53 and motor responses. This is achieved by the central nervous system governing the
54 musculoskeletal system according to visual, vestibular and proprioceptive feedback
55 received from the environment (e.g. terrain and walking surface) in which the
56 movement occurs. Locomotor adaptability resulting from these systems is essential
57 for successful and safe mobility. Although this process can be accomplished easily
58 by healthy young adults, it becomes more demanding and less effective with
59 increasing age, especially in the presence of neurological disorders (e.g. Parkinson's,
60 stroke, vestibulopathy), which coincides with the increased risk of falls in these
61 groups (1). Environmental perturbation-related falls while walking due to trips or
62 slips are responsible for about 60% of outdoor falls among older adults (2).

63 Long-term exercise interventions over several months aimed at increasing older
64 adults' balance and/or muscle strength have been shown to be effective in reducing
65 fall risk (3). However, according to the concept of training specificity, the motor
66 skills required for avoiding a trip- or slip-related fall may be improved most
67 effectively and efficiently (within several training sessions) with skill-specific
68 training (4), which represents a departure from conventional long-term fall-
69 prevention interventions. Treadmill-based perturbation training using cable-trip
70 systems (5–8) or belt accelerations/decelerations (9–11) can simulate slip- or trip-like
71 perturbations and trigger error-driven motor learning in the control of postural
72 balance. The perturbation-induced motor error stimulates the central nervous system
73 via sensory feedback to adapt the motor programs relevant for gait and balance to
74 increase the system's robustness to similar future balance disturbances; a process that

75 includes acquisition, retention and generalization of the fall-resisting skills. This has
76 been supported by evidence that treadmill-based trip-perturbation training targets
77 specific balance recovery mechanisms that may be beneficial when an actual trip is
78 experienced during daily life (12). An advantage of the treadmill in relation to
79 overground setups, is that predicting when a perturbation will be applied is more
80 difficult, which ensures that mainly reactive balance control strategies are involved.
81 Furthermore, practice dose (defined as the total amount of perturbation trials
82 experienced over a given exercise period) and perturbation intensity can be easily
83 and quickly manipulated in a safe, controlled environment. This is of particular
84 relevance for the conceptualization of fall prevention interventions because the
85 hypothesis of the dose-response relationship implies that adaption may not be
86 directly related to the applied practice dose (i.e. non-linear relationship) and that a
87 dose threshold exists beyond which any additional stimuli may not induce further
88 changes. Since there is a growing body of evidence that fall prevention interventions
89 using treadmills to deliver large postural disturbances (relatively high perturbation
90 magnitude) seem to be both effective and efficient for improving fall resisting skills,
91 there is also a critical need to identify the most effective practice dose (4). It is quite
92 likely that the extent for immediate (within the same training session) or long-term
93 gains and, hence, the effectiveness of the applied practice dose will depend on the
94 specific skills and neuromotor capacities of an individual or population.

95 *Insert Figure 1*

96 This review hypothesizes that older people can benefit from brief treadmill-based trip
97 and slip-perturbation exposure despite reduced muscular capacities, but with
98 neuropathology their responsiveness to these perturbations will be decreased,
99 reflecting a rightwards shift in the practice dose-response relationship (Fig. 1). The

100 perturbation practice dose-response relationship here refers to the relationship
101 between the number of perturbations and long-lasting changes in balance responses
102 generalizable to daily life trip and slip situations, for which we propose that a critical
103 threshold exists. Note that our hypothesis includes both middle-aged (i.e. about 40-
104 59 y) and older adults (i.e. ≥ 60 y), covering the ages in which various age-related
105 changes have been observed (we have used 60 years as a cutoff as this is deemed
106 appropriate by the United Nations for classifying older adults in international
107 contexts (13). Our recent data suggest that the potential for improvement following
108 repeated perturbations is independent of changes in lower limb muscle-tendon unit
109 capacities, and we hypothesize here that, as opposed to the general age-related
110 decline in muscular capacities, neurological deterioration (often age-related) in
111 which the sensory inflow or motor control is affected, may lead to a decreased
112 responsiveness to treadmill-based perturbations (Fig. 1). As such, in neuropathology,
113 lower practice doses possibly limit the retention and the generalizability of the
114 beneficial adaptations (the extent to which adaptations are maintained over time and
115 can be translated to improvements in performance in daily life trip and slip
116 situations). This would support our view that disruptions in locomotor control,
117 stability and learning (e.g. adaptation rate and magnitude) may be more apparent in
118 sensory or neuromotor decline than in age-related deterioration of muscular
119 capacities. Due to the majority of falls occurring as a result of trips and slips during
120 walking, as well as the practical and feasibility-related advantages of a treadmill-
121 based setup, this review focusses on information derived from studies of balance
122 control and training from treadmill trip and slip perturbations, in both healthy adults
123 as well as those with neurological disorders affecting the sensory or neuromotor
124 systems.

125

126 **MAINTAINING BALANCE FOLLOWING TRIPS AND SLIPS**

127 Human walking is partly controlled by central pattern generators, which are spinal
128 cord neurons, providing near autonomous control of basic locomotor rhythms (14).

129 Afferent feedback to the spinal cord allows reactive adjustments whereas feedback to
130 the supraspinal structures facilitates predictive adjustments in the locomotor patterns

131 (14), potentially aiding postural balance and stability during locomotion. When gait

132 stability is unexpectedly disturbed, the neuromotor system applies a series of reactive

133 corrections to re-establish postural equilibrium. In mechanical terms according to

134 Hof (15), this can be achieved by adjusting the application of force to the ground, by

135 counter rotating body segments around the center of mass (CoM) or by applying

136 forces other than the ground reaction force (e.g. by grasping a handrail).

137 In case of an unexpected slip or trip during gait, the relationship between the body's

138 CoM and the base of support is suddenly disrupted either by a disturbance of the

139 swing limb (trip) or unwanted displacement of the stance limb (slip). Due to the high

140 displacement of the CoM, it is not surprising that during tripping, a large anterior

141 step is typically required to recover balance, either initiated by the perturbed leg

142 when the disturbance occurs early in the swing phase (raising the perturbed limb over

143 the obstacle; elevating strategy), or by the contralateral leg when the disturbance

144 occurs later in swing (placing the perturbed limb quickly on the ground, aborting the

145 step, and stepping with the unperturbed limb; lowering strategy; (16)). In both cases,

146 the leg taking the compensatory recovery step needs to rapidly move forward (in

147 particular via high moment generation by the hip flexors) to be able to generate a

148 moment at landing to effectively counteract the forward angular momentum of the

149 trunk (17). The joint moment generation of the support limb (trailing leg) also plays

150 an important role, as during the push-off, the moments generated by the ankle plantar
151 flexors and knee extensors, as well as the hip extensors, provide enough time for
152 clearance and positioning of the stepping limb (leading leg) and counteract the
153 forward angular momentum of the CoM (18). In contrast, slipping can occur in
154 multiple directions to one or both limbs. However, slips leading to an anteriorly-
155 directed displacement of the stance limb resulting in a backwards loss of balance
156 have been most often studied. Once a backward balance loss is initiated, the primary
157 motor response is to act against the sliding motion of the foot by generating knee
158 flexion and hip extension joint moments in the slipping (leading) limb to minimize
159 the vertical descent of the body (19). In addition, a compensatory step by the trailing
160 limb posterior to the CoM is required to recover balance (20), initiated after the onset
161 of the slipping limb motor responses by generating an extension moment at the hip
162 and flexion moment at the knee joint in the trailing limb in order to cause foot
163 clearance and to interrupt the anterior displacement of the foot after toe-off, followed
164 by an knee extension moment to lower the trailing limb onto the ground (21). It can
165 be concluded that both slipping and tripping typically require the effective use of
166 dynamic stability control mechanisms (i.e. counter rotation of body segments and
167 adjusted application of ground reaction forces), although the contribution of each to
168 balance recovery following trips and slips likely differ.

169

170 **BALANCE CONTROL DURING TRIPS AND SLIPS IN HEALTHY AGING** 171 **AND NEUROPATHOLOGY**

172 It is widely acknowledged that the aging process leads to a general deterioration of
173 the neuromuscular system, including a gradual loss in motor neurons and impaired
174 muscle activation, leading to loss in muscle mass and decreases in strength and

175 power (22). These degradations are frequently related to diminished locomotor
176 performance. Age-related deficiencies in the recovery from many kinds of sudden
177 balance loss have been demonstrated, including tripping and slipping (5,23,24) and
178 can already be detected in middle age (5). Epidemiological studies showing an
179 increasing fall risk across the adult lifespan also highlight the need for targeted fall
180 prevention strategies in these age groups (25). In previous studies, we found a
181 significant but only moderate association between leg-extensor muscle-tendon unit
182 capacities (muscle strength, tendon stiffness), in particular of the triceps surae
183 muscle, and the ability to increase the base of support following a sudden anterior
184 loss of balance from forward leaning positions and unexpected treadmill trip
185 perturbations (7,26). These findings may provide an explanation for the reduced
186 ability to generate a large anterior balance recovery step with aging (5) and align
187 with other earlier studies showing that the diminished ability to regain stability
188 during perturbed walking is related to older adults' reduced ability to generate
189 appropriate joint moments in the trailing limb during push-off (18). Like gait-trip
190 perturbations, previous studies have demonstrated that muscle weakness of the lower
191 limbs seems to be associated with the frequency of laboratory based slip-like falls in
192 older adults (27).

193 Even though the muscle activity patterns (sequencing and timing) in the lower limbs
194 following trip and slip perturbations are similar in young and older adults, the
195 magnitude and rate of development of muscle activity is considerably lower in older
196 adults (23,28), indicating deficits in the neuromuscular control and reactive response
197 (including reaction time) in older adults during the recovery task. In line with this,
198 Arampatzis *et al.* (29) demonstrated that a less effective motor response during the
199 push-off phase of the trailing limb was related to unsuccessful recovery from a

200 forward fall, irrespective of leg-extensor muscle-tendon unit mechanical properties,
201 which emphasizes the importance of neuromuscular control for balance. This
202 supports our view that a disruption in key functions of locomotor control for
203 maintaining stability in middle-aged and older adults may arise predominantly from
204 neuromotor decline rather than from age-related muscular changes.

205 Successful recovery from balance loss not only requires precise neuromuscular
206 control, but also requires accurate detection and processing of balance loss. One of
207 the sensory systems providing important information for balance control is the
208 vestibular system, which monitors angular and linear accelerations of the head in
209 space (30). In our previous study in middle-aged adults, we exposed participants to
210 trip-like perturbations via a cable system similar to our other studies (5,7,8,31). We
211 found that, compared to healthy controls, people with unilateral vestibulopathy
212 showed a diminished recovery response to the first unexpected perturbation and
213 required at least six steps (versus four in controls) to recover stability (6); Fig. 2B).

214 Thus, next to the above described alterations accompanied with aging (i.e. altered
215 neuromuscular control) these results indicate a potential role of the vestibular
216 apparatus in postural corrections during an unexpected perturbation to gait. Other
217 studies using slightly different paradigms that still require the same recovery
218 mechanisms (rapid increase of the base of support) also provide some insight. For
219 example, Moreno Catalá *et al.* (32) found that people with Parkinson's disease, as
220 opposed to healthy controls, were not able to significantly increase their base of
221 support after a sudden change in ground surface compliance during walking. In
222 people with stroke, anterior surface translation perturbations (initiating backward
223 balance loss similar to a slip) to stance result in more falls compared to age-matched
224 controls and young healthy adults (71% of trials vs. 0% in the other groups) and

225 patients have poorer stability control during recovery, and require more recovery
226 steps (33). In summary, aged populations and in particular multiple neurological
227 patient groups appear to have a reduced ability to cope with a sudden, unexpected
228 mechanical perturbation to balance and gait predominately due to their inability to
229 rapidly increase the base of support.

230

231 **IMPROVING TRIP AND SLIP-RESISTING SKILLS**

232 It is well established that the human neuromotor system can adapt its motor behavior
233 to intrinsic (e.g. growth, muscle fatigue) and extrinsic changes (e.g. changes in the
234 mechanical environment), creating a complex interaction between sensory feedback
235 information from the periphery and motor output (34). Unexpected perturbations to
236 balance will provoke involuntary sensory prediction errors, which may not be
237 mitigated solely by volitional corrective motor responses and hence stimulate the
238 central nervous system to reorganize its internal representation of the body within the
239 mechanical environment (35). Previous studies have indeed demonstrated significant
240 improvements in reactive gait stability following repeated exposure to unexpected
241 slip or trip-like perturbations (24 or 8 repetitions, respectively) not only in young and
242 middle-aged adults (6,31), but even up to old age; i.e. 60-90 y (7,24). Notably, we
243 recently found remarkable adaptations in reactive gait stability in healthy older adults
244 (mean age and standard deviation: 65 ± 7 y) to eight repeated unexpected treadmill-
245 based trip-perturbations due to a refined neuromuscular control (Fig. 2; (7)).
246 Interestingly, participants' adaptation potential to these perturbations was
247 independent of their triceps surae muscle-tendon unit capacities (7) and similar to
248 that reported for middle-aged in the same laboratory setup (31). These results support
249 our hypothesis that an age-related degeneration of muscular capacities seems not to

250 affect one's ability to adapt and improve such fall-resisting skills following repeated
251 gait perturbations (7). Moreover, when considering the trial-to-trial adaptation over
252 the eight trip perturbations we were able to demonstrate a gradual increase in reactive
253 gait stability with increasing perturbation practice dose in middle-aged and older
254 adults, with no further improvements after only four to five perturbation trials (6,7).
255 Combined with the results seen for overground slip-perturbation training showing
256 similar rapid improvement (i.e. 'single trial effect') and plateauing of training effects
257 after merely a few slip trials in healthy young and older adults (24), these findings
258 support the notion that a small number of slip or trip perturbation trials is sufficient
259 to facilitate large refinements in the locomotor-balance control system, irrespective
260 of age. Nevertheless, whether the adaptation rate and amount, and hence the
261 perturbation dose-response relationship, are comparable across the adult lifespan
262 remains unclear and needs further investigation and a lack of knowledge regarding
263 the dose-response relationship in exercise based falls prevention has been highlighted
264 recently (4,36).

265 *Insert Figure 2*

266 Given the fact that successful motor learning depends on the function of the
267 neuromotor system, this review proposes the hypothesis that difficulties in improving
268 fall-resisting skills will be seen when the normal flow of information within the
269 nervous system is altered due to pathology (Fig. 1). In our previous study in
270 unilateral vestibulopathy using eight repeated trip perturbations on a treadmill as
271 described above, we found significant improvements in reactive gait stability during
272 the perturbed step in healthy age-matched controls but not in the vestibulopathy
273 patients (Fig. 2B; (6)). This suggests that a lack of accurate vestibular sensory
274 feedback may result in diminished locomotor adjustments and may negatively affect

275 the modification of internal models of the external environment (35), which could
276 lead to diminished corrections and adaptations of the reactive response to repeated
277 perturbations. However, we found improvements in the number of steps required to
278 recover balance in the vestibulopathy group, though not to the same extent as the
279 healthy age-matched controls. Based on these findings, we propose that patients with
280 vestibulopathy can still make improvements in their balance recovery responses, but
281 an increased practice dose (by increasing the total amount of perturbation trials
282 experienced over a given exercise period) may be needed. Looking beyond the
283 sensory systems themselves, another structure that plays a critical role in motor
284 control and sensory integration is the cerebellum. One study (37) examined how
285 cerebellar lesion patients ($n=5$; age range 20 to 56 y) and age-matched controls deal
286 with 60 repeated, sudden deceleration-acceleration perturbations during treadmill
287 walking. In line with our observations in vestibulopathy, patients improved their
288 response over time, with fewer multistep recoveries towards the end of the session,
289 but these improvements were faster, less variable and more apparent in the healthy
290 control group.

291 While not necessarily directly influencing sensory input, other neurological disorders
292 that disrupt sensory integration or neuromotor control could be expected to influence
293 the adaptation to perturbations such as in stroke. Nevisipour *et al.* (38) reported that,
294 in people with stroke, a training session of 15 posterior treadmill translation
295 perturbations during stance resulted in reduced trunk flexion during recovery from a
296 similar but untrained perturbation, indicating a training-related improvement, but
297 trunk flexion velocity, reaction time, step duration, step length and stability did not
298 improve. Bhatt *et al.* (39) applied repeated anterior surface translation perturbation
299 (initiating backward balance loss) to stance in people with stroke with both higher

300 and lower motor impairment. Both groups improved in their ability to cope with the
301 perturbations (fewer falls and better stability control), but there was a slower rate of
302 adaptation over the trials in people with more severe motor impairment. Consistent
303 with our hypotheses, these data suggest that the response to training is affected by
304 neuromotor function and that there is a need to consider the individual threshold for
305 practice dose. While not applying trip or slip perturbations, both Moreno Catala *et al.*
306 (32) and Martelli *et al.* (40) have demonstrated, a lack of improvement in the balance
307 recovery responses of people with Parkinson's disease following repeated
308 perturbations (6 sudden surface compliance changes or 72 anteroposterior and
309 mediolateral waist pulls, respectively) during gait. These findings indicate that with
310 neurological disorders, it may be difficult to stimulate the improvements of fall-
311 resisting skills that are commonly observed in healthy middle-aged and older adults
312 as described above, at least within a single gait perturbation training session or with a
313 similar number of perturbation trials. In summary, there are some early indications
314 that slip or trip-like perturbations on the treadmill would potentially provide
315 sufficient stimulus to trigger improvements in fall-resisting skills in middle-aged or
316 older adults with stroke, vestibulopathy and cerebellar lesions, although impairment
317 severity will likely influence both the tolerance to perturbations and the adaptive
318 response to the perturbations. This suggests that the perturbation practice dose-
319 response relationship is shifted to the right, but it could be harder to reach sufficient
320 practice doses within single training sessions to trigger substantial adaptations (Fig.
321 1). Further investigation is needed to detect thresholds for practice dose required to
322 induce robust gait modifications (indicated by a plateau in learning effects) as seen
323 for healthy middle-aged and older adults, which also may have important
324 consequences on their retention and/or generalizability to different conditions.

325

326 **RETENTION AND GENERALIZABILITY OF IMPROVED TRIP AND SLIP-**
327 **RESISTING SKILLS**

328 It is well known that adaptation of locomotion in response to repeated perturbation
329 exposure can occur quite rapidly in healthy middle-aged and older adults, even
330 within a single treadmill perturbation training session consisting of only a few
331 perturbation trials. Importantly, for overground walking previous slip-perturbation
332 studies have demonstrated that the acute adaptations in reactive gait stability
333 acquired during a single slip-perturbation training session (up to 24 slips) can be
334 partly retained for both short-term (a few weeks) and long-term (up to 12 months)
335 time periods by older adults in the same laboratory settings (41–43). One of our gait-
336 trip treadmill perturbation studies (eight trips at baseline, eight trips at 14 weeks)
337 supports these findings as we found that the improved recovery responses can be
338 partly retained over 1.5 years in older adults (65 ± 7 y (8)), but that these
339 improvements decay over time in this age group (Fig. 3). This suggests that even at a
340 higher age, repeated exposure to gait perturbations that mimic real-life slips or trips
341 seems to be an appropriate stimulus for the human central nervous system to improve
342 and retain balance control strategies specific to the practiced perturbation type.
343 Enhancing triceps surae muscle-tendon unit capacities through controlled resistance
344 exercise over 1.5 years did not lead to further meaningful improvements in older
345 adults' recovery response following a trip (Fig. 3; (8)). Thus, older adults seem to
346 benefit more from specific exposure to unexpected gait perturbations than from
347 improving presumed fall risk-related factors (i.e. muscle strength), as this alone
348 seems to result in sufficient improvement in performance of the targeted task.

349 The identified decay in reactive gait stability improvements over time (8) raises the
350 question whether this decay is influenced by the person's age. The comparison of
351 different studies from our laboratory on retention over several months indicates
352 lower retention of adaptations in older compared to middle-aged adults for the same
353 treadmill trip perturbation paradigm (8,31). Future studies should therefore
354 investigate whether long-term retention (i.e. several months or years) of exercise-
355 induced improvements in gait stability control may diminish across the adult
356 lifespan.

357 *Insert Figure 3*

358 Next to aging, the amount of practice seems to affect various aspects of learning.
359 Specifically, there is a growing body of evidence that to achieve such long-lasting
360 refinement of balance control strategies, certain practice doses may be required. For
361 instance, even though experiencing only one overground-slip during walking can
362 facilitate long-term retention of the acquired fall-resisting skills in older adults, these
363 effects were approximately 50% less than after interventions with higher practice
364 doses (i.e. 24 slip perturbations; (42)). Furthermore, specific ancillary 'booster'
365 sessions consisting of only a single slip have been found to further aid to these
366 superior retention effects (43). In agreement with these results, we recently found
367 evidence of a critical threshold for the amount of treadmill-based trip-like
368 perturbation trials required to provoke retainable adaptive changes in the human
369 neuromotor system (31). Specifically, we found a retention of reactive gait
370 adaptations over several months in healthy middle-aged adults only when they were
371 exposed to repeated (eight) gait-trip perturbations and not if they only experienced a
372 single perturbation (31). Thus, whereas brief exposure to treadmill-based gait
373 perturbations appears to be sufficient to achieve acute improvements in fall-resisting

374 skills in aging, retention of learned skills seems to require a minimum perturbation
375 practice dose facilitating robust gait modifications (i.e. reaching a plateau in the
376 dose-response-relationship).

377 In order to have a beneficial impact on daily life, these treadmill-based perturbation
378 training paradigms must result in fall-resisting skills that can positively benefit
379 recovery from an actual trip or slip. At least partial generalizability of adaptations to
380 repeated treadmill-delivered trip or slip perturbations to the recovery response
381 following an untrained trip/slip during overground walking has been reported (9,44).
382 Moreover, one study could show reductions in trip-related falls incidence (but not all
383 cause falls) during everyday life after experiencing over a two weeks period four
384 sessions of treadmill-based trip perturbation training (12). When combining these
385 results with recent findings in younger adults (10,11) indicating an increased
386 generalizability of treadmill perturbation training effects (i.e. improved transfer to
387 overground slips) with higher practice dose, it can be suggested that one primary
388 driver of a person's ability to cope with gait perturbations during everyday life may
389 be the total amount of perturbation trials experienced in the laboratory. However,
390 there seems to be a certain threshold for perturbation practice dose (>24 perturbation
391 trials) beyond which additional stimuli do not further increase transfer to the
392 overground condition in healthy older adults (45), indicating a critical optimum in
393 the perturbation practice dose-response relationship for generalizability to daily life
394 situations.

395 It is important to highlight that there is currently very little information in the
396 literature regarding the retention and generalizability of fall-resisting skills in
397 neurological populations. Using multidirectional perturbations to stance, Van
398 Duijnhoven *et al.* (46) found that people with stroke could improve the percentage of

399 trials recovered in a single step over five weeks of training, an effect that was
400 retained 6 weeks post-intervention. These findings indicate an intact ability of
401 retaining perturbation exposure mediated adaptations in people with stroke if the
402 number of practice sessions are sufficiently high enough, supporting our proposed
403 hypothesis. In line with this, some preliminary studies on long-term perturbation
404 training over several months in Parkinson's and stroke have shown promising (but
405 often not significant, potentially due to small samples) effects on daily life falls
406 incidence, implying a longer benefit and generalizability of the training (for a review
407 see (47)), but no study known to the authors has directly assessed this in a similar
408 manner to the studies discussed above in healthy middle-aged and older adults.
409 Given the potential deficits in gait stability and adaptability in response to repeated
410 perturbations in neurological populations (rightwards shift in the practice dose-
411 response relationship), it is reasonable to assume that retention and generalizability
412 of such improvements will also be negatively affected (Fig. 1).

413 Our proposed hypothesis of a minimum required perturbation practice dose to most
414 effectively facilitate learning (i.e. adaptation, retention and generalizability) in the
415 reactive balance control system requires consideration of the tolerability of training
416 for older adults. It may be that the minimum required dose exceeds the tolerance
417 threshold of participants, leading to anxiety or inability to physically cope with the
418 perturbations. This may be of particular importance when using this training
419 approach with frail or clinical people or groups. One possible solution might be to
420 progressively increase the complexity, unexpectedness or magnitude of perturbations
421 to initially increase training tolerance so that the minimum required dose can be
422 achieved after a certain period. Such approaches have recently been shown to induce

423 significant improvements in reactive stability control in community-dwelling older
424 adults (48,49).

425 One obvious limitation for the field is that conducting large enough trials to have
426 enough statistical power to detect the effects of such training on daily life falls
427 incidence will need high financial and high time commitments. The required sample
428 size would increase even further if researchers wished to reliably evaluate the effects
429 on specific types of falls (e.g. falls due to slips or trips), to increase the number of the
430 specific type of fall of interest in the assessed sample. But it is this information that
431 would provide more definitive answers to questions regarding the most effective
432 interventions. For instance, whereas remarkable reductions in trip-related falls
433 incidence (but not all cause falls) after experiencing four sessions of treadmill-based
434 trip perturbation training within a 2 weeks training period have been observed by one
435 study (12), this task specific transfer to everyday life could not be observed in
436 slipping (50) potentially due to the low statistical power for this outcome of the
437 study. In this context, it is important to note that the present review does not allow
438 for a general conclusion regarding the optimum number of perturbations needed in
439 order to facilitate retainable and transferable fall resisting skills in older adults, as
440 differences in perturbation paradigms (i.e. perturbation types and magnitude) may
441 also affect the dose-response-relationship. For these reasons, steps towards aligning
442 and standardizing perturbation training protocols and methodologies, as well as
443 assessment methods are critical to facilitate larger, multicenter, collaborative studies.

444

445 **CONCLUSION**

446 Healthy middle-aged and older adults can benefit from specific treadmill slip and trip
447 perturbation training interventions triggering large balance recovery responses (i.e.

448 high perturbation magnitudes), regardless of lower limb muscle-tendon unit
449 capacities. Neuropathology in aging appears to disrupt locomotor control, stability
450 and learning, leading to a higher risk of falls in these populations, and more notably,
451 resulting in a decreased responsiveness to treadmill-based perturbations. We propose
452 that a critical threshold for perturbation dose (number of perturbation trials) exists to
453 facilitate long-term adaptive changes and their generalizability to everyday life
454 situations in older adults. This implies that retention of adaptations to perturbation
455 exposure in older people with neuropathology can be achieved if the number of
456 perturbation trials or training sessions fulfill their increased need for training
457 exposure, due to a rightwards shift in the practice dose-response relationship. As
458 such, a longer period of perturbation training will be required to stimulate beneficial
459 improvements in fall-resisting skills in older adults with neurological impairments.

460

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610

611 **FIGURE CAPTIONS**

612 **Figure 1:** Schematic illustration of the proposed hypothesis: A brief exposure to high
613 magnitude gait perturbations, which mimic real-life slip or trip-like perturbations
614 (Task-specific training), can stimulate long-term adaptive changes (Long-term
615 retention) within the locomotor system. These changes lead to improved resistance to
616 treadmill trips/slips and reduced incidence of trip/slip-falls in daily life situations in
617 older adults, given that a critical threshold (dark circle) for perturbation practice dose
618 (number of perturbation trials) is reached. These improvements in fall-resisting skills
619 can be partly retained in healthy older adults over several months up to years without
620 additional training (Post-Training Retention). In neuropathology, in which the
621 sensory systems or motor control are affected, it is proposed that, due to a rightwards
622 shift in the practice dose-response-relationship for perturbation training, a greater

623 total amount of perturbation trials experienced over a given exercise period will be
624 required to reach the critical practice dose threshold to stimulate beneficial
625 improvements in fall-resisting skills. Experiencing perturbation practice dose below
626 the critical threshold will lead to a lower improvement and generalization of the fall-
627 resisting skills, whereas additional stimuli beyond this threshold have no further
628 benefit (steady state).

629

630 **Figure 2: A:** Electromyographic (EMG) activity of m. gastrocnemius medialis (GM)
631 and m. soleus (SOL) during the ground contact phase during unperturbed walking
632 and of the perturbed step (trailing limb) during first (T1) and eighth (T8) perturbation
633 trial of a single perturbation training session in a group of healthy older adults ($n =$
634 22). EMG activity was normalized to the maximal activity during unperturbed
635 walking for the corresponding muscle. **B:** Margin of stability (MoS; means and SD)
636 at touchdown (TD) of the perturbed leg in the first (T1) and eighth trial (T8) of a
637 single perturbation training session in a group of healthy older adults (OLD; $n = 22$)
638 and middle-aged unilateral peripheral vestibular disorder patients (UPVD, $n = 13$).
639 Note that whereas healthy middle-aged adults show rapid adaptation to the repeated
640 perturbation exposure, these adaptations seem dependent on an intact sensory inflow.
641 ^aStatistically significant difference between groups OLD and UPVD ($P < 0.05$);
642 ^bStatistically significant difference to T1 for group OLD ($P < 0.05$). (Adapted from
643 Epro *et al.* (7) and McCrum *et al.* (6)).

644

645 **Figure 3:** Margin of stability (MoS; means and SD) at touchdown (TD) of the
646 perturbed leg during first (T1) and eighth (T8) perturbation trial of a single
647 perturbation training session (8 unexpected gait-trip perturbations) at baseline (Base),

648 post 14 weeks (Post 14w) and post 1.5 years (Post 1.5y) measurement time points in
649 a group of older female adults experiencing trip-gait perturbation training (PERT
650 group; $n = 13$) and a second group of older female adults, who in addition underwent
651 a triceps surae muscle-tendon unit (MTU) specific exercise over 1.5 years (MTU
652 group; $n = 12$). Note that the training-induced enhancement of the triceps surae MTU
653 capacities did not benefit the recovery response from a sudden trip. ^aStatistically
654 significant difference to T1Base ($P < 0.05$); ^bStatistically significant difference to
655 T8Base ($P < 0.05$); ^cStatistically significant difference to T1Post14w ($P < 0.05$);
656 ^dStatistically significant difference to T8Post14w ($P < 0.05$); ^eStatistically significant
657 difference to T1Post1.5y ($P < 0.05$). (Adapted from Epro *et al.* (8)).