Learning to cope with trips: retention and generalisability of fall-resisting skills across the adult lifespan

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Statutory declaration

Hereby I declare that this thesis and the work presented in it is my own original work except where acknowledged within the text. This material has not been submitted either in whole or in part for a degree at this or in any other institution. All used and paraphrased material from other sources are clearly indicated as references. I further declare that I took the guidelines for qualified scientific work of the London South Bank University into account.

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Summary

Daily-life locomotion constantly challenges our neuromotor system, requiring adjustments in motor strategies to cope with external perturbations (e.g. a trip), control stability and avoid falls. Though knowledge about the effectiveness of perturbation-based interventions for improving fall-resisting skills in older adults has grown considerably, the effects of age and different protocol parameters on the adaptability (i.e adaptation, retention, generalisability) of the balance control system are not well established. This dissertation examined the adaptability and specificity of fall-resisting skills across the adult lifespan, with the perspective that the insight gained could improve both the effectiveness and efficicency of the assessment and training of fall-resisting skills. Four studies were conducted, comprising of both cross-sectional and longitudinal (14 weeks) designs. The first part of the dissertation focused on the specificity of the assessment of reactive dynamic stability control and the second part on adaptability to trip-perturbation exposure and how this varies with practice dose or age (i.e. young, middle-aged, old). Firstly, a gradual, age-related decline in reactive stepping performance was confirmed for different stepping modes. More importantly, it appears that volitional stepping characteristics have limited potential for discriminating between individuals or groups with quite different balance recovery capabilities. Therefore, volitional stepping tasks may not be sensitive enough for clinical application. Secondly, although the adaptability of reactive gait stability control during a single bout of trip-perturbations remains highly effective across the adult lifespan (which could counteract the initially poorer ability to cope with sudden balance loss in older age), retention of these improvements over several months seems to be diminished with ageing and dependent on a specific number of perturbations. Finally, the robust adaptations in stability control could not benefit recovery performance in an untrained reactive balance task, suggesting task specificity of learning. Profound differences in the spatiotemporal organisation of muscle activation patterns, i.e. muscle synergies, indicate a diverging modular control to different perturbations, possibly preventing inter-task generalisation of adaptations in stability control.

Zusammenfassung

Während alltäglicher Bewegungen ist unser neuromotorisches System ständig dazu angehalten Änderungen in der Bewegungsstrategie in Folge von externen Störungen (oder *Perturbationen*, z.B. stolpern) vorzunehmen, die Stabilität des Körpers zu kontrollieren und so Stürzen vorzubeugen. Obwohl unser Wissen über die Effektivität sog. perturbationsbasierter Trainingsinterventionen zur Verbesserung von Fähigkeiten zur Sturzvermeidung im Alter in der Vergangenheit stetig gewachsen ist, ist der Einfluss des Alters einer Person sowie verschiedener Trainingsparameter auf die Anpassungsfähigkeit (d. h. Adaptation, Beibehaltung, Transfer) des Systems zur Stabilitätskontrolle noch weitgehend unbekannt. Diese Dissertation untersuchte die Anpassung und Spezifität von Fähigkeiten zur Sturzvermeidung über die Erwachsenenlebensspanne mit dem Ziel, die Effektivität und Effizienz von Maßnahmen zur Analyse und Verbesserung von Fähigkeiten zur Sturzvermeidung zu erhöhen. Insgesamt wurden vier Studien durchgeführt, wovon jeweils zwei ein Quer- bzw. Längsschnittdesign über 14 Wochen aufweisen. Der erste Teil der Dissertation zielte dabei auf die Spezifität von Maßnahmen zur Untersuchung der reaktiven dynamischen Stabilitätskontrolle und der zweite Teil auf den Einfluss des Alters (jung, mittelalt, alt) und der Trainingsdosis auf etwaige Anpassungen infolge wiederholter Stolperperturbationen. Die Ergebnisse bestätigten, unabhängig von den Untersuchungsbedingungen, eine altersbedingte Abnahme in der Fähigkeit einen effektiven, reaktiven Schritt auszuführen. Außerdem konnte gezeigt werden, dass die Eigenschaften eines willkürlich ausgeführten Schritts nur bedingt in der Lage zu sein scheinen, zwischen Personen bzw. Gruppen mit unterschiedlicher reaktiver Stabilitätskontrolle zu unterscheiden. Somit erscheinen Tests zur Analyse willkürlicher Bewegungseigenschaften in diesem Kontext als nicht sensitiv genug für die klinische Anwendung. Im zweiten Teil konnte gezeigt werden, dass obwohl die Anpassungsfähigkeit der reaktiven Stabilitätskontrolle in Folge wiederholter Stolperperturbationen über die Erwachsenenlebensspanne effektiv erhalten bleibt (und der reduzierten Fähigkeit Älterer auf einen plötzlichen Stabilitätsverlust zu reagieren entgegenwirkt), sich die Beibehaltung dieser Anpassungen über mehrere Monate mit dem

Alter reduziert und abhängig von einer bestimmten Anzahl an Perturbationen ist. Die Anpassungen in der Stabilitätskontrolle hatten darüber hinaus keinen positiven Effekt auf die Wiederherstellung der Stabilität während eines anderen (untrainierten) Tests der reaktiven Stabilitätskontrolle, was auf eine Spezifität der Lerneffekte hinweist. Deutliche Unterschiede in der räumlich-zeitlichen Organisation der Muskelaktivierungsmuster (*muscle synergies*) verweisen auf Unterschiede in der modularen Kontrolle der Bewegungsantwort auf unterschiedliche Perturbationen, was einem Transfer von Anpassungen in der Stabilitätskontrolle zwischen unterschiedlichen Bewegungsaufgaben vorbeugen könnte.

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1. Introduction and outline

Daily-life locomotion is a challenging task. While walking along an uneven, bricked sidewalk, stepping over a curb to cross the street or negotiating stairs, one faces countless situations that can interrupt movement, requiring our neuromotor system to adjust its motor strategies to cope with external perturbations (e.g. a trip), control stability and avoid falls. This dissertation examined the adaptability and specificity of fall-resisting skills across the adult lifespan, with the perspective that the insight gained could improve both the effectiveness and eficicency of the assessment and training of fall-resisting skills. Therefore, the present dissertation incorporates four studies to assess (i) the effects of age and testing condition on relevant performance outcomes for reactive dynamic stability control, (ii) its long-term adaptability to single session trip-perturbation training for different age groups and practice doses and (iii) the generalisability of adaptations beyond the accustomed trip-perturbation task.

The ability to manage successful and safe locomotion in a changing environment is commonly defined as gait adaptability. Key to this process is the continuous integration of sensory input and musculoskeletal mechanics by the central nervous system to produce appropriate motor action (Scott 2004). When taking the example of a sudden trip over a curb, effectiveness of the sensory systems can be considered early determinants for the quality of the recovery response (Nielsen and Sinkjaer 2002; Nutt et al. 1993; Sousa et al. 2012). Different afferents will need to be processed quickly by the cerebral cortex, brainstem or directly by the spinal cord (Jacobs and Horak 2007) and translated into muscle action via activation of α-motoneurons. This process seems to be accomplished easily in young adults, as indicated by the fact that external disturbances to gait lead to a fall in less than 6% of the cases in this age group (Heijnen and Rietdyk 2016). With increasing age, however, all these entities show a remarkable decline, which may affect older adults' motor performance. Briefly, manifold declines in vision, audition, vestibular function, proprioception and touch sensitivity have been reported (for a recent overview see Paraskevoudi et al. 2018), which may have a negative effect on sensing balance loss and guiding coordinated movement. Further, a longitudinal *in vivo* brain-imaging study has identified a non-uniform, age-related loss in volumes of specific brain regions (Raz et al. 2005) which appear to play a role in perturbed movement (Kerr et al. 2017). Tissue-based analyses of brain atrophy (i.e. gray matter or white matter volume) observed similar degeneration patterns (Allen et al. 2005; Ge et al. 2002; see Lockhart and DeCarli 2014 for a review). Rosano et al. (2008) have directly evaluated these brain structural changes in relation to functional motor performance of older adults and found significant associations between spatio-temporal gait characteristics (i.e. step length, double support time) and gray matter volume in sensorimotor and frontoparietal brain regions. Given evidence that the response to a trip may involve spinal reflex pathways (Lam et al. 2003; Pang et al. 2003; Zhong et al. 2012), one must consider age-related changes in the spinal cord circuitry as well. Several studies could observe slower stretch reflexes or reduced stretch reflex forces (Carel et al. 1979; Koceja 1993) and lower H-reflex amplitudes or maximal M-waves in older adults (deVries et al. 1985; Kido et al. 2004; Raffalt et al. 2015; see Geertsen et al. 2017 for a detailed overview on spinal cord circuitry changes in age). The latter may be mediated by the loss of spinal motor neurons with ageing (Kawamura et al. 1977; Tomlinson and Irving 1977). The loss of spinal motoneurons is paralleled further by reductions in muscle fiber size and number (Aagaard et al. 2010), which in turn may lead to a decline in muscle capacities (e.g. reduction in lower extremity muscle strength, maximal mechanical power generation and rate of force development; Frontera et al. 1991; Häkkinen and Häkkinen 1991; Izquierdo et al. 1999; Karamanidis and Arampatzis 2006; Skelton et al. 1994; Thom et al. 2005; Winegard et al. 1996). Notably, this age-related deterioration in muscle capacities has been shown to start already in middle age (i.e. approximately the age range between 40 and 60 years of age; Alcazar et al. 2020; Asmussen and Heebøll-Nielsen 1962; Lindle et al. 1997) and has often been linked to altered motor strategies (Karamanidis et al. 2006; König et al. 2018; Kulmala et al. 2014) and reduced mobility levels in older adults (Bean et al. 2002; Rantanen and Avela 1997; Suzuki et al. 2001). Additionally, a previous study of our group found diminished recovery responses to a sudden laboratory-induced trip in older adults with lower plantarflexor muscle strength compared to their stronger counterparts (Epro et al.

2018a). In summary, the overall degradation of various sites within our complex neuromotor system with ageing may limit older peoples' capability to cope effectively with sudden external challenges to gait, such as a trip, making them more prone to fall.

As a matter of fact, ageing shows a significant association with the incidence of falls (Peel et al. 2002; Schumacher et al. 2014; Talbot et al. 2005), with about 20% of all indoor falls and 60% of all outdoor falls in older adults result from a slip or stumble during walking (Luukinen et al. 2000). Recent data for the U.S. and Europe indicate that approximately every fourth to every third at the age of 65 or older is affected by a fall at least once in a year (Bergen et al. 2016; Palumbo et al. 2016; Rapp et al. 2014). This is significant for both individuals and society as a fall can have severe consequences for an older person, such as various clinical conditions, disability or even mortality (Burns and Kakara 2018; Terroso et al. 2014), causing huge economical burden (Burns et al. 2016; Florence et al. 2018; Stevens et al. 2006). Note that an inclined incidence rate for bone fractures could be identified already around middle age, though the aetiology of fractures (e.g. osteoporotic change and falls) did not form part of this study (Donaldson et al. 1990). Concerningly, when looking at the demographic shift towards an increasingly older population and higher life expectancy in both developed and developing countries (United Nations 2017), one can assume a continuation of the worldwide trend towards increasingly higher numbers of fall-related injuries (Do et al. 2015; Hartholt et al. 2010; Hong et al. 2016; Kannus et al. 2000; Olij et al. 2019; Orces and Alamgir 2014). Also, even when not leading to injury, subsequent fear of falling can cause lower physical activity levels and lower social participation, substantially affecting an individual's quality of life (Stenhagen et al. 2014; Yardley et al. 2002). In summary, falls in general, and more precisely falls during ambulation, represent a major concern nowadays not only for an individual's quality of life, but also for public health, providing an incentive to identify effective, as well as time- and cost-efficient, intervention strategies aimed at reduction of falls in individuals or groups who have impaired balance control capability.

Before tailored fall-resisting skills assessment and training can be applied, one must define the conditions for a 'stable' system and determine the mechanisms by which stability is achieved. In mechanical terms, stability or instability of the body configuration results from the relative position of the body's centre of mass (CoM) to its limits of stability, i.e. the base of support (BoS, roughly the area under and between the feet; Woollacott and Shumway-Cook 1996). In other words, stability will be achieved if the vertical projection of the body's CoM lies within the BoS as it is usually the case during quiet stance (Winter 1995). Note that for dynamic situations such as gait, however, it has been pointed out previously that the velocity of the CoM has to be accounted for (Hof et al. 2005; Pai and Patton 1997; Townsend 1985). Thus, the majority of valid metrics to analyse gait stability or the ability to recover from large perturbations, such as a trip, are centred around the relationship between the CoM and BoS during movement (for an overview of currently available measures see Bruijn et al. 2013). A common parameter to quantify the dynamic stability of the body is the margin of stability (MoS), i.e. the horizontal distance between the anterior boundary of the BoS and the extrapolated CoM, calculated as (Hof 2008; Hof et al. 2005):

$$\mathrm{X_{CoM}} = \mathrm{CoM} + \frac{\mathrm{V_{CoM}}}{\sqrt{\frac{\mathrm{g}}{\mathrm{L}}}}$$

where $\mathrm{X_{CoM}}$ is the extrapolated centre of mass, CoM is the horizontal position of the centre of mass, $\mathrm{V_{CoM}}$ is the horizontal centre of mass velocity and the denominator is the eigenfrequency of the inverted pendulum, with g representing the gravitational acceleration and L the pendulum length. Hof et al. (2005) specifically outlined three constraints on the validity of the "extrapolated centre of mass concept" that are related to the description of human walking by the inverted pendulum model: (i) the balance problem can be described completely by the movement of the whole-body CoM; (ii) the excursions of the CoM are small with respect to the pendulum length; (iii) the pendulum length from the ankle joint axis of rotation to the CoM remains constant. For this concept, instability beyond that of the characteristic inverted pendulum-like behaviour of gait occurs, if the motion state of the CoM cannot be compensated by establishing a new BoS with the next step (Bruijn and van Dieën 2018; Figure 1), i.e. the MoS is negative.

However, this definition of stability implies that the stability limits of the body are not fixed but can be modified according to the specific body mechanics or task need (Rogers et al. 1996). With this in mind, the general mechansims of gait stability control may be considered as basis for an effective fall risk assessment and reduction.

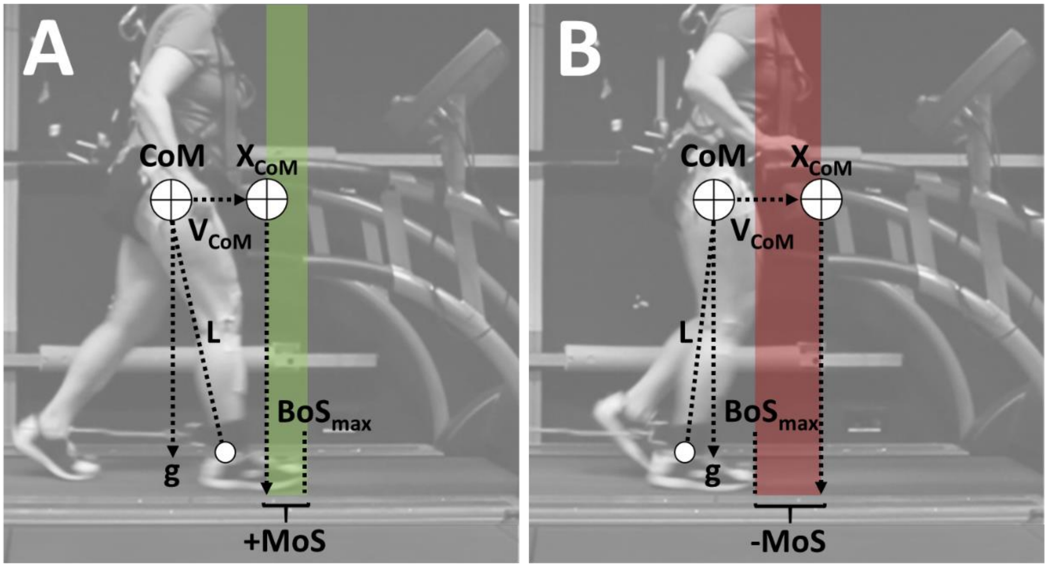

Figure 1: Schematic of the extrapolated centre of mass concept during gait (Hof 2008; Hof et al. 2005). X_{CoM} is the extrapolated centre of mass, CoM is the horizontal position of the centre of mass, V_{CoM} is the horizontal centre of mass velocity, g is the gravitational acceleration and L the length of the inverted pendulum (i.e. the distance between the CoM and the ankle joint centre of rotation in the sagittal plane). The anteroposterior margin of stability (MoS) is calculated as the horizontal distance between the anterior boundary of the base of support (BoS_{max}) and the extrapolated CoM. Note that positive MoS values indicate stable body configuration (A), whereas negative MoS values indicate unstable body configuration (B), which require compensatory motor actions, such as rapid stepping, to control stability.

As early as the 1970's and 1980's the quasi-automatic responses of the legs produced by the neuromotor system to sudden perturbation to balance were already examined and discussed in the scientific literature (Berger et al. 1984; Nashner 1979, 1980; Quintern et al. 1985). Today several concepts to categorize balance recovery mechanisms for standing balance exist according to their nature of support (Maki and McIlroy 1997) or evoked motor responses (Hof 2007). Both concepts outline responses where the body stays in place (e.g. movement of the centre of pressure under the feet) or changes its support strategy (e.g. grasping or stepping), whereby the latter are not to be seen as "strategies of last resort", but are often initiated even when the CoM is not close to the stability limits (Maki and McIlroy 1997). In the context of large mechanical perturbations to gait (i.e. high CoM displacement), such as a trip or slip, an effective increment of the BoS through stepping has been identified as being key to dynamic stability control (Hof et al. 2005; Maki and McIlroy 2006; Wang et al. 2017, 2020). In the specific case of a trip, such stepping responses can occur either in the perturbed leg (i.e. elevating strategy) or contralateral leg (i.e. lowering strategy) depending on whether the perturbation occurred early or late in the swing phase respectively (Eng et al. 1994). Note that all the above mechanisms imply a *reactive* control of stability, i.e. immediate feedback-driven responses to perturbation, though adjustments to gait to control stability can take place also in a *predictive* manner (e.g. Bhatt et al. 2006; Bierbaum et al. 2010; Bohm et al. 2012; McCrum et al. 2016; Wang et al. 2012, 2019a). Predictive adjustments to gait are made based on prior experience and/or knowledge of the external environment (e.g. shortening step length or increasing step height before an expected perturbation), whereas reactive adjustments (e.g. rapid compensatory stepping after an unexpected perturbation) rely upon continuous sensory feedback received during locomotion (Lam et al. 2006; MacLellan and Patla 2006; Marigold and Patla 2002; Pai et al. 2003). Given the unpredictable nature of most daily-life falls and hence limited possibilities to pre-plan motor responses, this dissertation focusses on the assessment and training of reactive stability control mechanisms, but the potential involvement of predictive motor adjustments to balance recovery from our applied perturbation setup is discussed in the *Limitations* (section 7.4) of this dissertation.

Given the significance of reactive stepping for maintaining stability, it may be a crucial factor in the assessment of fall-resisting skills and important for the development and evaluation of fall prevention programmes. As the topic of stability control crosses different fields, both fundamental and applied, such measures to identify individuals or groups with diminished stepping responses likely differ between different contexts. Tests can be based on various outcomes such as pure reaction times to a sensory trigger or whether a person falls after a given mechanical perturbation. For example, Carty et al. (2014) found in their prospective study that the recovery stepping performance after a simulated forward fall in the laboratory is an independent predictor of future fall risk in older adults. On the other hand, tests that are often used in physical therapy or geriatric settings involve volitional stepping to a non-destabilizing mechanical cue (i.e. "step execution test"; Halvarsson et al. 2012; Melzer et al. 2007), showing markedly longer stepping reaction times in old age (Kurz et al. 2013; Luchies et al. 2002; Melzer and Oddsson 2004) and slower intentional stepping in people with a history of falls (Lord and Fitzpatrick 2001). Thus, while both balance recovery and volitional stepping have been associated with fall risk (Okubo et al. 2017), their specific assessment may target different capacities of the neuromotor system (Luchies et al. 1999; see Tisserand et al. 2015 for a review). Knowledge of the task inherent to volitional motor control tests implies that the triggered motor responses can benefit from anticipation and be optimised by the participants, unlike most stepping actions evoked by sudden postural threats in daily life. In other words, there is no clear evidence on the extent to which tasks assessing fall-resisting skills are tailored to resemble daily life challenges to balance, i.e. as to whether volitional stepping can be used to estimate a person's balance recovery behaviour (**Study 1**). Answers to that question may be crucial to the subsequent application of tailored interventions to reduce falls in older adults.

Long-term training interventions over several months or years, combining different exercises to benefit muscle strength/power, flexibility, mobility or balance, have been shown to potentially reduce the incidence of falls (Campbell et al. 1999; Chang et al. 2004; Guirguis-Blake et al. 2018; Hamed et al. 2018; Sherrington et al. 2008, 2017; Shubert 2011) and/or fall-related injury in older adults (El-Khoury et al. 2013; Tricco et al. 2017; Zhao et al. 2017). The latest meta-analysis on exercise-based fall prevention from the Cochrane Library indicates reduced fall rates (23%) and less people experiencing falls (15%) through physical exercise with high-certainty evidence (Sherrington et al.

2019). However, it is important to point out here that these intervention programmes usually require consistent participation over longer time periods [e.g. Guirguis-Blake et al. (2018) report intervention durations of on average 12 months with a most common frequency of three exercise sessions a week], which raises the question of feasibility, in particular when dealing with older individuals. In fact, despite the predictable health benefits of physical activity and exercise, inactivity and lack of motivation are unfortunately very common among older adults (Hui and Rubenstein 2006). Together with the reportedly high drop-out rates once physical activity has been commenced (Schmidt et al. 2000; see Dishman et al. 1985 for a discussion of barriers and opportunities), these results suggest that higher efficiency is needed to increase fall prevention effectiveness. In this context, Grabiner et al. (2014) proposed the use of more *task-specific* interventions as an adjunct or an alternative to the conventional exercise-based approaches. Here, the exercise itself would mimic the actual task for which the training is conducted, in this case the reactive recovery stepping responses to slip- or trip-like events, rather than targeting surrogate variables associated with stability control (e.g. muscle strength). Such repeated exposure to unexpected mechanical perturbations during stance or gait is generally termed as “perturbation-based balance training“ (Gerards et al. 2017). Notably, it has been demonstrated by our group and others that, although the ability to cope with sudden gait perturbations appears to be initially reduced in middle and older age (Süptitz et al. 2013), coping capabilities can be improved even up to old age within only a single gait perturbation training session (Bhatt et al. 2006; Bierbaum et al. 2011; Epro et al. 2018a; Okubo et al. 2018, 2019; Pai et al. 2010; Wang et al. 2019a, 2019b; see Karamanidis et al. 2020 for a current review on the topic). Moreover, such experimental protocols have revealed retention of adaptations to gait stability control over prolonged time periods (i.e. several months to years; Bhatt et al., 2012; Epro et al., 2018b; Liu et al. 2017; McCrum et al. 2018; Pai et al., 2014a) without any ancillary training sessions, leading to a reduced real-life fall risk at least for the practiced perturbation mode (Rosenblatt et al. 2013). Given this growing body of evidence that fall prevention interventions using specific postural disturbances seem to be both effective and efficient for fall-resisting skills improvement, there is also critical need to identify the most effective practice dose.

In this dissertation, a perturbation paradigm is used that delivers large-magnitude trip-like perturbations during treadmill walking and has been shown to cause acute (Epro et al. 2018a) and long-term changes in aged human balance control (Epro et al. 2018b). In these previous experiments, eight separate perturbation trials per training session were used. However, it remains largely unknown whether such retention effects may also be observed after single trip exposure i.e. whether the retention in recovery response adaptations over months is dependent on trip-perturbation dose (**Study 2**). This is of particular importance not only for further reduction in expenditure of time, but also for potential application of perturbation training in frail, clinical populations or groups limited in their tolerance of higher perturbation doses. Furthermore, the results from that previous study (Epro et al. 2018b) indicate that adaptations observed after several months were significantly smaller than the acute effects from a single perturbation training session (i.e. there was partial retention). Since only older adults were investigated here, this raises the question whether the observed decay in training effects over time is inherent to such single session perturbation training or is dependent from an individual’s age. Support for this hypothesis comes from results in slipping, showing more rapid reduction of improvements in stability control from slip-perturbation training in older compared to younger adults after merely a short wash-out period (Pai et al. 2010). Combining these results with earlier studies demonstrating that locomotor adaptations in general may be smaller and/or occur at a lower rate in older age (Bierbaum et al. 2011; Bohm et al. 2012; Bruijn et al. 2012; McCrum et al. 2016), one has reason to believe that, although adaptability in the balance control system is preserved, various aspects of learning (i.e. adaptation rate, retention) may be diminished with increasing age (**Study 3**). Knowledge on the dynamics of learning and forgetting in different groups or individuals is required for tailored recommendations in fall prevention.

Considering that falls in daily life can result from a variety of postural threats, generalisability (i.e. the ability to transfer acquired motor strategies beyond the accustomed context of a given task) may be an important feature of fall-resisting skill learning. Partial transfer of adaptations in stability control has been reported previously, at least between different conditions of the same perturbation task, i.e. from training gait-slips on the treadmill to a ‘novel’ overground slip, or from simulated slips on a moveable platform to an untrained slip on an oily surface (Bhatt and Pai 2009a; Lee et al. 2018; Parijat and Lockhart 2012; Wang et al. 2019c; Yang et al. 2013, 2018). In other words, our neuromotor system seems to be able to generalise previously learned responses during walking to new challenges when the characteristics of the gait perturbation (e.g. direction, type) are similar. It remains largely unknown, however, whether such transfer of adaptations can occur also between two different perturbation tasks (i.e. *inter-task* generalisability) and whether this is affected by ageing (**Study 3**). To allow for a more comprehensive answer to this question, one must also define factors that determine task similarity or difference which perhaps facilitate or limit the generalisability of learning – and this is where muscle synergies come into play.

It is commonly accepted in the literature that functional movements may be generated by small sets of synergistically-active muscles, i.e. muscle synergies (Bizzi and Cheung 2013; Bizzi et al. 1991, 2008; Lee 1984; Mussa-Ivaldi et al. 1994; Singh et al. 2018; Tresch et al. 1999, 2002), which appear partially inborn and subsequently tuned and augmented throughout development, matching changes in locomotion biomechanics (Dominici et al. 2011). For example, it has been demonstrated that characteristic gait phases in adults correlate well with distinct groups of active muscles (Ivanenko et al. 2004; Janshen et al. 2017; Santuz et al. 2018). Evidence from animal (d’Avela and Bizzi 2005; d’Avela et al. 2003; Torres-Oviedo et al. 2006) and human studies (Krishnamoorthy et al. 2003; Oliveira et al. 2012; Santuz et al. 2017a; Torres-Oviedo and Ting 2007) indicate similar results across variety of muscles and motor tasks, such as running, jumping, swimming, kicking or even postural control and recovery from sudden perturbation to balance. The advantage of such motor control is that it solves the “degrees of freedom problem” of the neuromotor system (Bernstein 1967), by breaking down an endless number of output variables, i.e. possible combinations of individual muscle activations, to merely few muscle synergies generating a specific movement. This ability to choose from an abundance of "motor equivalent" solutions may explain the adaptability and robustness of biological systems (Ting et al. 2015). For researchers, the reduction in assessable output variables makes muscle synergies a suitable tool to analyse movement construction and adaptation phenomena.

Muscle synergies can be extracted from electromyographic (EMG) signals using different factorisation approaches (e.g. principal component analysis, factor analysis, independent component analysis and non-negative matrix factorisation; Tresch et al. 2006) of which non-negative matrix factorisation appears to be suited best in terms of the non-negative nature of muscle activations (Lee and Seung 1999). The general idea behind this technique is that high-dimensional non-negative data, such as complex muscle activation patterns, is compactly reduced by the linear combination of two sets of coefficients, which can be expressed as (Lee and Seung 1999):

$$\mathrm{V(t)} \approx \mathrm{V}_R\mathrm{(t)} = \mathrm{WH(t)}$$

The muscle activation matrix V can be approximated by the reconstructed matrix V_R, resulting from the linear combination of the motor modules (Gizzi et al. 2011; Santuz et al. 2017b) matrix W with the dimensions m x r and the motor primitives (Dominici et al. 2011; Santuz et al. 2017b) matrix r x n, with m representing the number of recored muscles, n the number of recorded time points and r the number of synergies. Note that the motor module matrix contains the time-invariant muscle weightings, i.e. the contribution of each muscle to a specific synergy, and the motor primitive matrix contains the time-dependent coefficients of the factorisation, i.e. the timing of basic activation patterns (Figure 2). Based on the assumption that motor primitives can be scaled and summed, the original set of EMG data can be reconstructed (Figure 2). For that purpose, the computation is repeated several times until the minimum number of synergies necessary to represent the original muscle activation matrix is identified (Lee and Seung 1999). The reconstruction quality is defined by means of the coefficient of determination (Santuz et al. 2017b; Cheung et al. 2005).

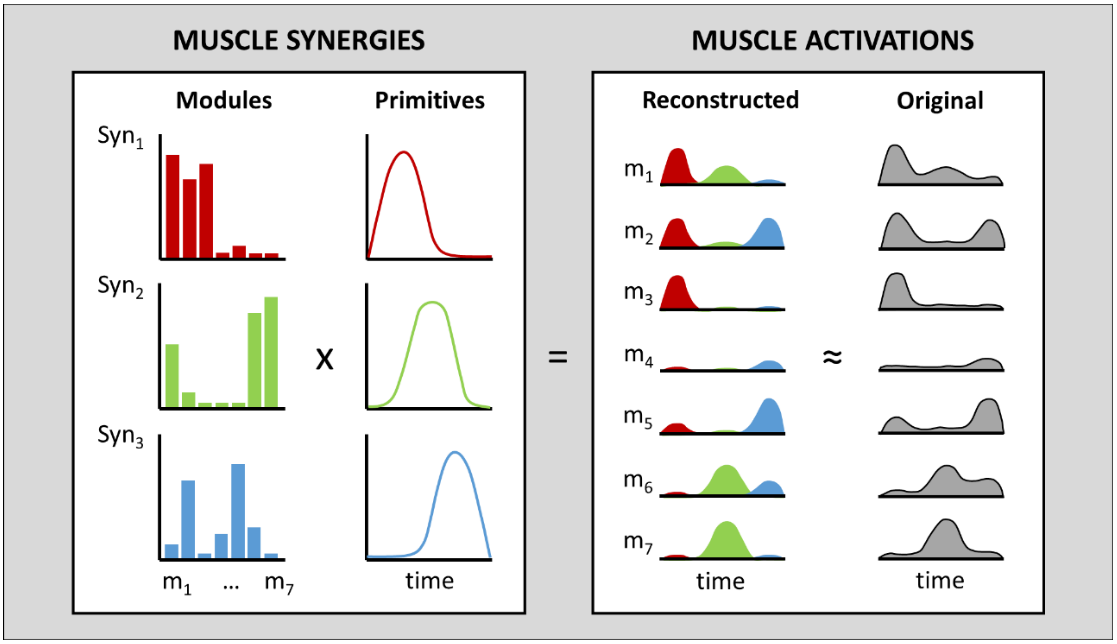

Figure 2: Schematic of muscle synergies (Dominici et al. 2011; Santuz et al. 2018). Simulated example of reconstructed muscle activations of seven muscles (m_1-m_7) as the linear combination of the time-invariant muscle weightings (i.e. motor modules) and time-dependent muscle activation patterns (i.e. motor primitives) of only three muscle synergies (Syn_1-Syn_3). The level of approximation of the original EMG data set, or reconstruction quality, is defined by means of the coefficient of determination.

Several studies have extracted muscle synergies from EMG signals using non-negative matrix factorisation to analyse adaptations in the modular organisation of the motor system in the face of various internal (e.g. proprioceptive loss or ageing; Santuz et al. 2019, 2020) or external perturbations (e.g. uneven or slippery flooring; Martino et al. 2015; Santuz et al. 2018), showing a widening in the time-dependent component of muscle synergies (i.e. motor primitives), implying a more robust motor control strategy (Kitano 2004). In this dissertation, the muscle synergy concept is used to examine the degree of similarity between different reactive balance tasks and whether this may be related to generalisability of learning from trip-perturbation training (**Study 4**). The foundation of the hypothesis is the fact that some synergies for balance control appear to be shared across different tasks, whereas others seem to be specific to match a particular biomechanical demand (Chvatal et al. 2011; Chvatal and Ting 2013; Torres-Oviedo and Ting 2010). Unravelling neuromotor correlates of responses to different perturbations seen at the macro level may help to broaden our understanding of the factors facilitating or limiting learning in the human balance control system.

Based on this background, the first objective (**Study 1**) was to analyse the relationship between volitional and balance recovery stepping measures for a large subject pool (n = 97) of different ages (i.e. young, middle-aged and older adults) in a cross-sectional design. In particular, we wished to assess whether volitional step characteristics can discriminate between individuals showing single- or multiple-stepping behaviour after sudden balance loss, i.e. between individuals with high and low balance recovery capabilities. The main concern of this experimental setup is the extent to which tasks assessing fall-resisting skills are tailored to resemble daily life challenges to balance. Two reactive stepping tasks were analysed: a volitional single step in the anterior direction in response to a mechanical stimulus to the heel and a recovery stepping response after sudden anterior balance loss in a lean-and-release protocol. The results showed shorter reaction times and faster stepping responses across all participants (on average 40%) after sudden balance loss compared to volitional stepping. The participants were classified into two groups (single-stepper and multiple-stepper) based on their recovery stepping behaviours for the lean-and-release task, which revealed a clear decline in the ability to cope with sudden balance loss with increasing age, with 24/26 older, 15/43 middle-aged and none of the younger adults required two or more steps to regain balance. Multiple steppers showed shorter step lengths (23%) and lower maximal step velocities (12%) compared to single-steppers for the lean-and-release task only and reduced rates of increase in BoS for both of the stepping tasks (14% for balance recovery and 11% for volitional stepping). Furthermore, in examining the relationship between the results of the two tasks, only weak to moderate correlations were found for step velocity and rate of increase in BoS. Prevention of falls will require sensitive, yet clinically applicable measures to identify those with limited capacity to recover from balance perturbations and to apply tailored interventions. However, these results appear to indicate that volitional step execution tasks are of restricted use in this regard, pointing towards a task-specificity in fall-resisting skills assessment.

Secondly, the adaptability of such reactive recovery response mechanisms was analysed for a specific challenge to balance resembling one of the most common causes of falls in older adults, namely tripping while walking. In two separate investigations of the same longitudinal study (**Study 2** and **3**) we analysed the effects of (i) practice dose and (ii) age on adaptation to gait stability control and its retention over several months from single session gait-trip perturbation training. The results of this second part of the dissertation have significance for our understanding of the dynamics of the human neuromotor system in relation to both acute external influences (perturbations) and to longer-term internal (ageing) constraints, which may allow tailored recommendations for fall prevention. It is also important to establish whether these learning effects can transfer between different tasks, considering that real-life falls can result from a variety of postural threats. Therefore, we further analysed whether an improvement in balance recovery mechanisms from perturbation training transfers to an untrained reactive balance task and, if so, whether this is affected by ageing. To achieve this, young, middle-aged and older adults completed two tasks. The primary task involved treadmill walking, either unperturbed (control; n = 39) or perturbed (eight unexpected trip-like perturbations; training; n = 39). A single retention test trip was repeated after 14 weeks. To test for a potential dose effect a group of middle-aged (n = 9) performed only a single trip to both measurement time points. The secondary transfer task, before and after treadmill walking or training, involved sudden loss of balance in a lean-and-release protocol. Note that the lean-and-release task is similar to the trip-perturbation task in the stability control mechanisms required, i.e. establishing a new BoS in the anterior direction and reducing the anterior velocity of the CoM, possibly facilitating transfer of adaptations. As main outcome parameter served the anteroposterior MoS at foot touchdown. The results showed that, although the ability to cope with the trip-perturbation task was initially reduced in older age (more recovery steps required to regain positive MoS compared to younger adults but not middle-aged adults), all age groups increased their MoS for the first recovery step over the course of the eight perturbations to a similar extent (up to 70%). Moreover, there was a significant retention of recovery response adaptations over 14 weeks without training, though there was a decay over time found for older adults which could not be observed in younger adults (middle-aged showing a tendency for decay: $p = 0.076$). Thus, although adaptability in reactive gait stability control remains highly effective as age increases, retention of learning over time appears to be reduced with ageing. Notably, a single trip exposure in a separate group of middle-aged adults caused no retention effects at all, suggesting that perturbation practice dose must exceed a threshold in order to induce long-term adaptive changes in the human balance control system. Despite the robust adaptations in stability control from multiple gait perturbations in all three age groups and the similar stability control mechanisms required, improvements for the untrained lean-and-release transfer task from before to after the treadmill protocol were not superior compared to those of age-matched controls not undergoing the trip-perturbation training. Thus, critical factors in neuromotor control (e.g. spatiotemporal organisation of muscle activation patterns or muscle synergies) may still discriminate perturbation types, possibly explaining failure in inter-task generalisation. Note that the experimental design of this study (i.e. the transfer task was performed twice, before and after the treadmill protocol) may not permit a general conclusion regarding the generalisability of learning in the balance control system since one may not disentangle potential transfer of recovery response adaptations from a “single trial effect” for the lean-and-release task (Ringhof et al. 2019).

The final study of this dissertation (**Study 4**) put its focus on the transfer of adaptations from trip-perturbation training using an alternative cross-sectional design and by taking into account neuromotor factors potentially regulating learning generalisability within the balance control system. Specifically, this study examined the consistency in modular organisation of motor responses to different perturbations, i.e. treadmill gait-trips and sudden loss of balance in a lean-and-release protocol. Participants ($n = 57$; age range 19-53 years) were randomly assigned either to a perturbation ($n = 39$; eight unexpected trip-like gait perturbations) or a control group ($n = 18$; unperturbed walking only). After the treadmill protocol, all participants performed a single lean-and-release. The anteroposterior margin of stability (MoS) was calculated at foot touchdown as difference of the anterior boundary of the base of support and the extrapolated centre of mass. For the perturbation group, the muscle activation of 13 ipsilateral leg muscles was recorded and muscle synergies were extracted using non-negative matrix factorisation for recovery responses to either perturbation type. After eight trip-perturbations participants significantly increased their MoS during the first recovery step ($p < 0.001$), yet the perturbation group did not show superior improvement to the untrained lean-and-release transfer task compared to controls ($p = 0.44$). This confirms our previous findings in that adaptations in stability control from single session perturbation training seem highly task-specific. The number of muscle synergies was four in recovery from tripping and three for the lean-and-release. However, only one synergy appeared to be shared between the two perturbation types, revealing profound differences in the spatiotemporal organisation of muscle activation patterns. The results indicate a diverging modular control to different perturbations, possibly preventing inter-task generalisation of adaptations in stability control.

2. Aims of the dissertation

Falls and the consequences of falls are a major health risk for our ever-growing older populations. Despite the fact that knowledge about the effectiveness of perturbation-based balance training for improving slip- and trip-resisting skills in older adults has considerably advanced over the last decades, the effect of age and different protocol parameters on the adaptability (i.e adaptation, retention, generalisability) of the balance control system is yet not well established. This dissertation examined the adaptability and specificity of fall-resisting skills across the adult lifespan, with the perspective that the insight gained could improve both the effectiveness and efficicency of the assessment and training of fall-resisting skills. Four studies were conducted, comprising of both cross-sectional and longitudinal (14 weeks) designs, with the first study focusing on the specificity of assessment of performance outcomes for reactive dynamic stability control and the last three studies examining its adaptability to trip-perturbation exposure across the adult lifespan. More concisely, the **first study** aimed

(i) to investigate the relationship between volitional and balance recovery stepping measures in young, middle-aged and older adults, i.e. whether volitional step characteristics can discriminate between individuals showing high and low recovery stepping performance (cross-sectional study).

Based on the available literature it was hypothesised that there are only moderate correlations between volitional and balance recovery stepping characteristics, and that volitional step execution tests are limited in predicting reactive balance recovery performance. This would also imply that when improvement of reactive balance control strategies are the goal, one might benefit more from specific, exercise-based approaches resembling unpredictable daily life challenges to balance (e.g. sudden trips or slips during walking) than from the general improvement of task-related volitional motor control strategies.

Hence, in order to address the questions about the adaptability of the balance control system across the adult lifespan, the **second** and **third study** aimed

(ii) to examine the effects of practice dose (one vs. eight perturbation trials) and age (young vs. middle-aged vs. old) on the retention of adaptations in stability control following single-session gait-trip perturbation training over 14 weeks (longitudinal study), and

(iii) to investigate whether adaptations in stability control made during repeated gait-trip perturbation exposure benefit the recovery performance during an untrained reactive balance (lean-and-release) task in young, middle-aged and older adults.

With regard to the existing literature, the overall hypothesis of this pair of studies was that older adults are capable of long-term adaptation in their reactive gait stability control if perturbation practice dose exceeds a certain threshold (>1 trial). However, the adaptation may occur at a lower rate, decay at a faster rate and transfer less effectively to an untrained task than for the young and middle-aged. In particular, the latter thereby appears to be an important determinant for the effectiveness of interventions aimed at the reduction of daily life falls, as these may result from a variety of postural threats.

Hence, to investigate this aspect of learning more thoroughly, a **fourth study** was conducted with the aim

(iv) to examine whether inter-task generalisability of adaptations relates to the modular organisation of the motor system in balance recovery responses during different perturbation tasks, i.e. repeated treadmill gait-trips and sudden loss of balance in a lean-and-release protocol.

It was hypothesised that the motor system uses different modular organisation in recovery responses to tripping and the lean-and-release task, preventing positive transfer of adaptations to stability control. The results of this study provide novel insight into particular factors potentially regulating learning generalisability within the balance control system.

The four conducted studies are presented separately in the following chapters, as submitted to the corresponding journal (including the reference list) with the citation style maintained as prescribed from the respective journal.

3. First Study | Volitional step execution is an ineffective predictor of recovery performance after sudden balance loss across the age range

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Key words: Aged; falls; reactive balance; motor control; geriatrics

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Version submitted to journal (*under review*)

3.1. Abstract

Rapid stepping to preserve stability is a crucial action in avoiding a fall. It is also an important measure in the assessment of fall-resisting skills. We asked whether volitional step execution is correlated with recovery stepping performance after sudden balance loss for adults of different ages. In particular, we investigated whether volitional step performance can discriminate between individuals with high and low balance recovery capabilities, i.e. between those making single versus multiple steps after balance perturbation. Healthy adults (28 young, 43 middle-aged and 26 older; 24 ± 4, 52 ± 5 and 72 ± 5 years respectively) performed a single step in the anterior direction volitionally in response to a mechanical stimulus to the heel. In a secondary stepping task, participants experienced sudden anterior balance loss in a lean-and-release protocol. For both tasks an optical motion capture system was used to assess stepping kinematics. We found shorter reaction times and faster stepping responses across all participants after sudden balance loss compared to volitional stepping (average 41%; $p < 0.001$). There was a significant age-related decline in recovery stepping performance after sudden balance loss: 24/26 older, 15/43 middle-aged and none of the younger adults required two or more steps to regain balance ($p < 0.001$). Multiple- compared to single-steppers had significantly shorter step lengths (average 23%) and lower maximal step velocities (12%) for the lean-and-release task ($p < 0.01$). Multiple steppers also had reduced rates of increase in base of support for both of the stepping tasks (14% for balance recovery and 11% for volitional stepping). Furthermore, in examining the relationship between the results of the two tasks, only weak to moderate correlations were observed for step velocity and rate of increase in base of support ($0.36 \leq r \leq 0.52$; $p < 0.001$). Thus volitional step execution appears to be of limited usefulness for research or clinical practice aimed at the assessment of reactive balance recovery capability, an assessment essential to the targeted reduction of falls in older adults.

3.2. Introduction

Falls have become a major public health issue as they can lead to severe clinical conditions, disability or even death in a growing elderly population (Burns & Kakara, 2018; Terroso, Rosa, Marques & Simoes, 2014) and result in substantial medical costs (Florence, Bergen, Atherly, Burns, Stevens & Drake, 2018). This seems even more significant given that the prevalence of fall-related injuries is already increasing by middle-age (i.e. by about the fifth decade of life; Donaldson, Cook & Thomson, 1990). Even when a fall does not cause injury, subsequent fear of falling can lead to lower physical activity levels and lower social participation, substantially affecting quality of life (Stenhagen, Ekström, Nordell & Elmståhl, 2014). Most falls in older adults result from balance loss due to incorrect shift of body weight or external hazards (Robinovitch et al., 2013; Yang, van Schooten, Sims-Gould, McKay, Feldman & Robinovitch, 2018). A major challenge for falls prevention is to establish methods that allow identification of individuals at higher fall risk who have impaired balance control capability.

The well-established condition for stable stance is that the vertical projection of the body's centre of mass (CoM) lies within the boundary of the base of support (BoS, roughly the area under and between the feet; Woollacott and Shumway-Cook 1996). Disturbances to posture involve rapid compensatory stepping responses to establish a new BoS and recover balance (Hof, 2007; Maki & McIlroy, 1997; Nashner, Woollacott & Tuma, 1979). Notably, recovery stepping performance after a sudden forward fall in a lean-and-release protocol can predict future fall risk in older adults (Carty et al., 2014), and reactive step training can produce a clinically relevant reduction in falls incidence (~50%; Okubo, Schoene & Lord, 2016 for a review). The capacity to effectively increase the BoS in a reactive manner in order to preserve stability is a crucial assessment of fall-resisting skills and important for the development and evaluation of fall prevention programmes.

Previous studies focusing on volitionally-controlled stepping actions to a non-destabilizing cue showed markedly longer stepping reaction times in older compared to younger adults (Kurz, Berezowski & Melzer, 2013; Luchies et al., 2002; Melzer &

Oddsson, 2004), which coincides with a higher falls risk for the older group. Moreover, the same experimental protocols revealed slower intentional stepping in people with a history of falls (Lord & Fitzpatrick, 2001). In these studies, however, even when the required weight shift was not known prior to the task (i.e. which stepping leg was to be used), the instructed stepping actions could be well anticipated and controlled by the participants. Given the unpredictable nature of daily life falls, one might argue that valid fall-resisting skills assessment rather must involve low levels of task certainty as for sudden postural threats, and provoke reactive stability control mechanisms. Data from a previous investigation (Luchies, Wallace, Pazdur, Young & DeYoung, 1999) do indeed suggest that the performance during a volitional step task fails to estimate older adults' ability to respond quickly to sudden balance loss due to differences in task characteristics (see Tisserand et al., 2015 for a review), i.e. the ecological validity of volitional stepping is limited. There is no clear evidence as to whether volitional stepping can be used to estimate a person's balance recovery behaviour, and hence to identify individuals or groups at higher fall risk.

The present study aimed to examine the relationship between volitional and balance recovery stepping measures for a large subject pool (*n* = 97) of varying age. In particular, we wished to assess whether volitional step characteristics can discriminate between individuals showing single- or multiple-stepping behaviour after sudden loss of balance in a lean-and-release protocol, i.e. between high and low recovery stepping performance. We hypothesized that: (i) there are only moderate correlations between volitional and balance recovery stepping characteristics; and (ii) volitional step execution tests are limited in predicting reactive balance recovery performance. Our concern is the extent to which falls risk assessment tasks are tailored to resemble daily life challenges to balance.

3.3. Methods

3.3.1. *Participants and experimental design*

Twenty eight young, forty three middle-aged and twenty six older adults took part in this study (16/28 men, 24 ± 4 yr; 20/43 men, 52 ± 5 yr; 13/26 men, 72 ± 5 yr; mean ± standard deviation is used throughout). The heights and body masses for the groups were: 177.1 ± 4.6 cm and 70.1 ± 10.7 kg for the young; 173.7 ± 11.1 cm and 75.8 ± 13.0 kg for the middle-aged; and 169.8 ± 8.4 cm and 76.0 ± 14.0 kg for the older adults. Exclusion criteria consisted of any neurological or musculoskeletal impairments of the lower limbs (e.g. joint pain during movement). The participants were generally healthy and reported comparable physical activity levels (7.0 ± 3.4, 6.4 ± 3.9 and 6.6 ± 3.2 h/week for young, middle-aged and older adults respectively). Our participants took part in two different reactive stepping tasks – a volitionally-controlled anterior step to a tap cue on the heel and a secondary lean-and-release task to test balance recovery performance (Figure 1). The study was approved by the ethics committee of the German Sport University Cologne (ethical approval number 141/2017) and met all requirements for human experimentation in accordance with the Declaration of Helsinki. All participants provided written informed consent after initial briefing.

3.3.2. *Volitional step task*

In order to examine volitional stepping, the participants had to perform a rapid forward step in response to a mechanical cue (see also Halvarsson, Franzén, Olsson & Ståhle, 2012; Melzer, Shtilman, Rosenblatt & Oddsson, 2007; Figure 1A). At the beginning of the test the participants stood on a force plate (60 x 90 cm; Kistler, Winterthur, Switzerland) with their feet shoulder-width apart, keeping a neutral posture. The experimenter then applied a distinct manual tap cue, using a standard reflex hammer, to the heel of the preferred leg for step initiation (Melzer & Oddsson, 2004). Participants were instructed to step forwards as quickly as possible after sensing the heel tap over a predefined target line (25% of individual body height). The mechanical cue did not cause pain or disturb balance enough to initiate a fall. To control for task predictability, the heel tap was applied only after any anticipatory movements had subsided, i.e. antero-posterior and medio-lateral weight shift regulation (recorded via real-time centre of pressure on the force plate). Target step length was chosen in order to require proper stepping actions of the participants, as opposed to small adjustments of foot position. With this arrangement the foot always landed on a second force plate (60 x 90 cm; Kistler, Winterthur, Switzerland) mounted in front of the first. In order to ensure novelty of the task, no practice trials were conducted.

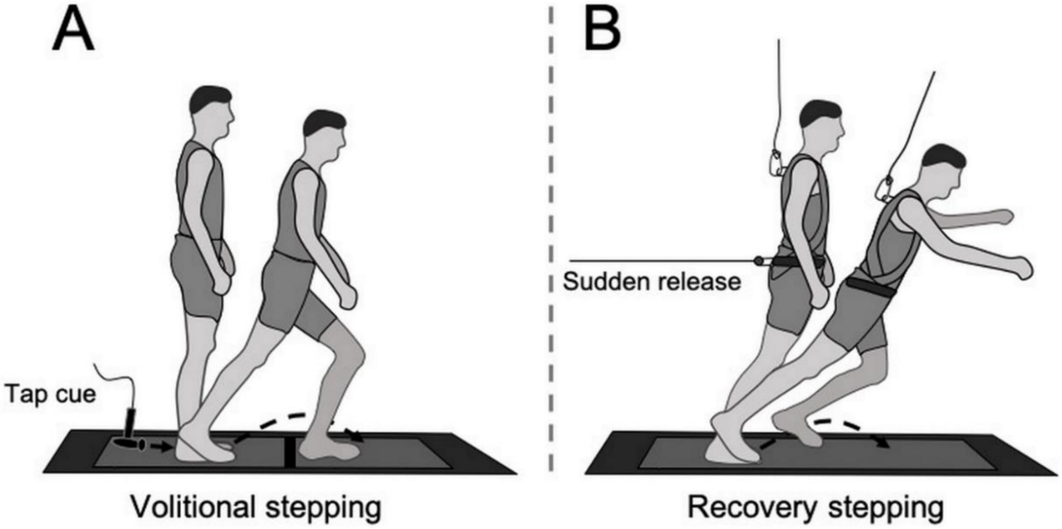

Figure 1: Stepping tasks. **(A)**: volitional stepping in response to a tap cue on the heel. Minimum anterior step length was set at 25% of the individual body height for this task. **(B)**: balance recovery stepping after sudden release from a forward inclined position (the lean-and-release task). Lean angles were normalized to individual body weights in order to standardize the level of balance loss.

3.3.3. Balance recovery step task

Balance recovery performance related to sudden anterior balance loss was analysed using a lean-and-release protocol (Figure 1B). The task protocol has been described previously in detail (Karamanidis & Arampatzis, 2007; Karamanidis, Arampatzis & Mademli, 2008;

König, Epro, Seeley, Potthast & Karamanidis, 2019). Briefly, the participants stood on the first force plate as described in *Volitional step task* (section 2.2) and, keeping their feet flat on the ground, were gradually inclined forward via a horizontal inextensible cable attached at one end to a belt around the participant's pelvis and at the other end to a custom-built pneumatic release system (see also Do, Breniere & Brenguier, 1982; Thelen, Wojcik, Schultz, Ashton-Miller & Alexander, 1997). The gradual inclination was terminated when a lean angle was achieved that corresponded to a recording of 23 ± 3% of body weight on a load cell placed in series with the supporting cable. After any anticipatory movements had subsided (i.e. antero-posterior and medio-lateral weight shift adjustments, checked via real-time cable loads and centre of pressure on the force plate), the cable was suddenly released without warning after a random time interval of 10 to 30 s. The participants were told to attempt to restore balance within a single recovery step when released, using the limb of their choice (Madigan & Lloyd, 2005). The recovery limb always landed on the second force plate mounted in front of the first one (see also section 2.2 *Volitional step task*). No practice trials were conducted to ensure novelty of the task. The exact forward lean was chosen according to our previous results of the reduced ability of older adults to regain balance within a single recovery step from cable loads of more than 23% body weight (Karamanidis et al., 2008). Participants were protected by a full-trunk safety harness connected to an overhead track, allowing for full range of motion in anterior and lateral directions while preventing contact of the body with the ground (with the exception of the feet).

Recovery stepping behaviours were classified as single- or multiple-step according to our previous description (Karamanidis & Arampatzis, 2007). Briefly, participants were classified as single-steppers if only one step was required to regain balance or if a follow-up step of the contralateral limb did not exceed the anterior displacement of the recovery limb. Accordingly, multiple-step behaviour was defined as involving any additional step of the recovery limb or if the participant took a contralateral step exceeding the anterior displacement of the recovery limb. Furthermore, multiple-step behaviour was deemed to have occurred if a participant made use of the safety harness support (i.e. > 20% of body weight, determined by a second load cell incorporated into the harness suspension cable; Cyr & Smeesters, 2009).

3.3.4. Data collection and processing

In order to determine the spatio-temporal step characteristics for the two tasks a six-camera motion capture system (Vicon Motion Systems, Oxford, UK; 120 Hz) was used. One retroreflective marker (25 mm diameter) was attached to each of the forefeet. For further processing the 3D-coordinates of the markers were smoothed using a fourth-order digital Butterworth filter with a cut-off frequency of 20 Hz. For each stepping task three events were identified as follows. (a) Test initiation, i.e. the instant of the tap cue or the release of the participant from the inclined position. The former initiation was registered by a contact sensor attached to the striking surface of the reflex hammer; the latter by a component of the pneumatic brake-and-release system. In both cases an analogue TTL signal (at 1080 Hz) was simultaneously delivered to the Vicon system. (b) Foot take-off, defined as the instant at which the forefoot marker of the stepping limb reached a threshold velocity of 0.2 m/s in the anterior direction. (c) Foot touchdown, defined as the instant at which vertical ground reaction force exceeded a threshold level of 20 N. Based on the identified events, reaction time (b-a) and swing time (c-b) were derived for each trial. The maximal step velocity during swing time and the rate of increase in BoS (anterior forefoot marker displacement of the stepping limb from take-off to touchdown divided by swing time) were also calculated.

3.3.5. Statistics

The distribution normality of variables was checked before applying statistical analysis using the Kolmogorov-Smirnov test with implemented Lilliefors correction, revealing that all analyzed parameters conformed to normal distributions ($p > 0.05$). (i) To examine the volitional and balance recovery stepping responses amongst the three age groups (young, middle-aged and older), separate two-way repeated-measures ANOVAs were used to detect differences in reaction time, maximal step velocity and rate of increase in

BoS (age and step task as factors). In case of significant main effects or interactions, Duncan post-hoc corrections were applied. Note that a target step length was used for the volitional step task (25% of individual body height) and hence the effect of age on step length was only assessed by means of one-way ANOVA for the lean-and-release task. (ii) The participants were classified into two groups (single-stepper and multiple-stepper) based on their recovery stepping behaviours for the lean-and-release task. Differences in the number of single or multiple steppers between age groups were analyzed using separate chi-squared (χ^2) tests of independence. Independent samples t-tests were used to examine differences between single- and multiple-steppers in step length (lean-and-release task only), reaction time, maximal step velocity and rate of increase in BoS for the two stepping tasks. Furthermore, Pearson product-moment correlation coefficients were computed for reaction time, maximal step velocity and rate of increase in BoS to identify the relationship between volitional and balance recovery stepping responses. The level of significance was set at $\alpha = 0.05$, with all results presented as mean and standard deviation. All statistical analyses were conducted using Statistica software (Release 10.0; Statsoft Inc, Tulsa, OK, USA).

3.4. Results

3.4.1. Comparison of volitional and balance recovery stepping responses amongst age groups

Assessment of volitional and recovery stepping responses revealed statistically significant task effects for reaction time, maximal step velocity and rate of increase in BoS [$F(1,94) = 203.88$, 1295.30 and 1643.60 respectively; $p < 0.001$], independent of age. All participants ($n = 97$) showed longer reaction times and slower stepping responses for volitional step execution compared to lean-and-release stepping (Figure 2).

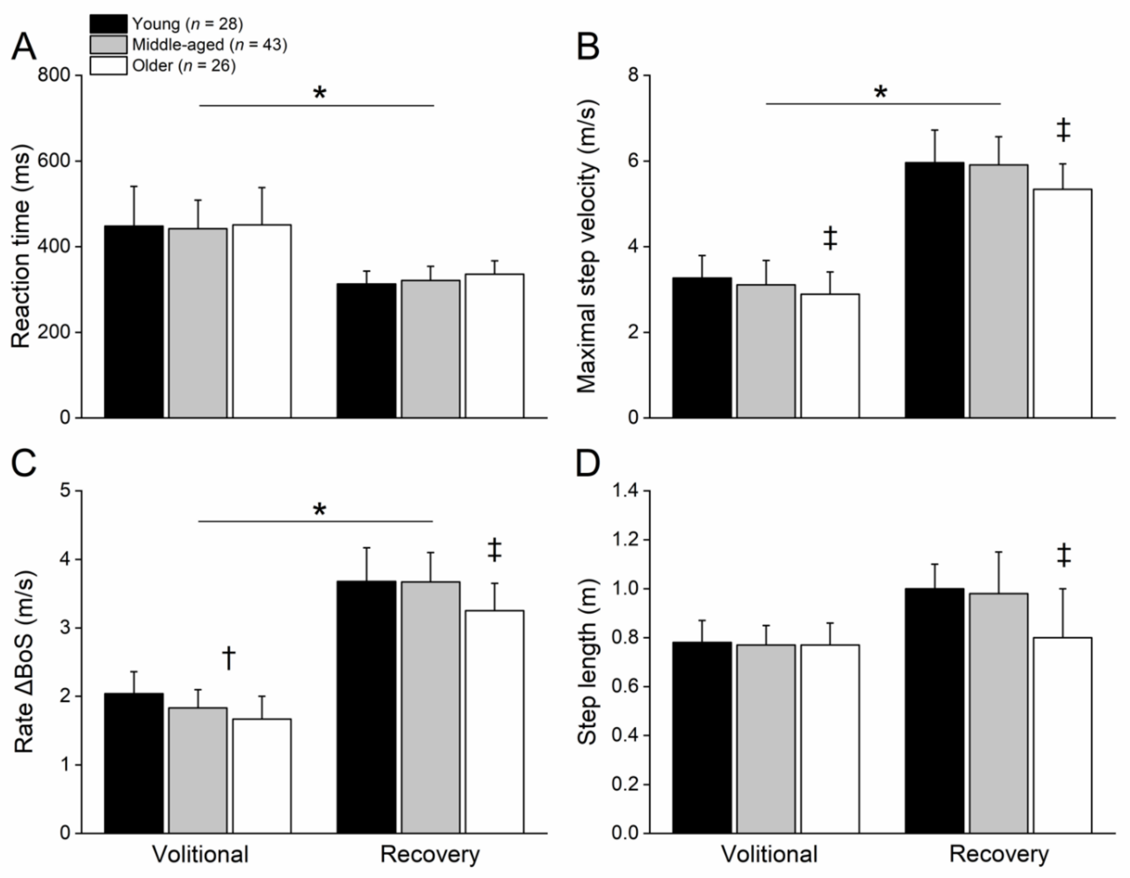

Figure 2: Spatio-temporal characteristics of volitional (VOL) and balance recovery stepping responses (REC). Data are given for reaction time **(A)**, maximal step velocity **(B)**, rate of increase in BoS [ΔBoS; **(C)**] and step length **(D)** in young (*n* = 28), middle-aged (*n* = 43) and older adults (*n* = 26). Values are expressed as means with SD error bars. Statistically significant differences at the level $p < 0.05$: * = between stepping tasks; † = compared to young adults; ‡ = compared to young and middle-aged adults.

Regarding the comparison of stepping responses amongst the three age groups, we found a statistically significant age effect for maximal step velocity [$F(2,94) = 7.95$; $p < 0.001$], independent of stepping task, with lower velocities for older compared to both younger age groups ($0.001 \leq p \leq 0.004$; Figure 2). There was a significant age x task interaction for rate of increase in BoS [$F(2,94) = 3.29$; $p = 0.04$], with lower rates for older compared to younger adults for both stepping tasks ($p < 0.001$). However, lower rates for older adults compared to middle-aged adults were found only for balance recovery stepping ($p < 0.001$). Furthermore, middle-aged adults showed lower rates of increase in BoS ($p = 0.02$) compared to younger adults for the volitional step task (Figure 2). Step length comparison was performed for the lean-and-release task only (note that minimum step length was predefined for the volitional step task) and revealed a significant age effect [$F(2,94) = 11.64$; $p < 0.001$], with lower step lengths for older compared to both younger age groups (Figure 2). Significant positive weak-to-moderate correlations between results for the two stepping tasks were found for maximal step velocity and rate of increase in BoS over all analyzed participants ($n = 97$; $0.36 \leq r \leq 0.52$; $p < 0.001$; Figure 3).

3.4.2. Comparison of the single- and multiple stepper subgroups

Thirty-nine participants (fifteen middle-aged and twenty-four older adults) were classified as multiple-steppers after sudden loss of balance in the lean-and-release protocol (all of the younger adults regained balance within a single step). Hence there was an age-related decline in the ability to cope with the task across the adult lifespan ($12.38 \leq \chi^2 \leq 46.52$; $p < 0.001$). Accordingly, only middle-aged and older adults were considered for subgroup comparisons (single-stepper versus multiple-stepper).

Assessment of stepping characteristics for the two pooled groups of middle-aged and older adults revealed statistically significant differences between single- and multiple-steppers for the recovery stepping response in the lean-and-release protocol. In detail, multiple-steppers showed lower maximal step velocities [$t(67) = 5.64$; $p < 0.001$], lower rates of increase in BoS [$t(67) = 6.29$, $p < 0.001$] as well as shorter step lengths [$t(67) = 6.43$; $p < 0.001$] compared to single-steppers (Figure 4). However, for the volitional step execution task such differences could only be observed for the rate of increase in BoS [$t(67) = 2.72$; $p = 0.01$; Figure 4].

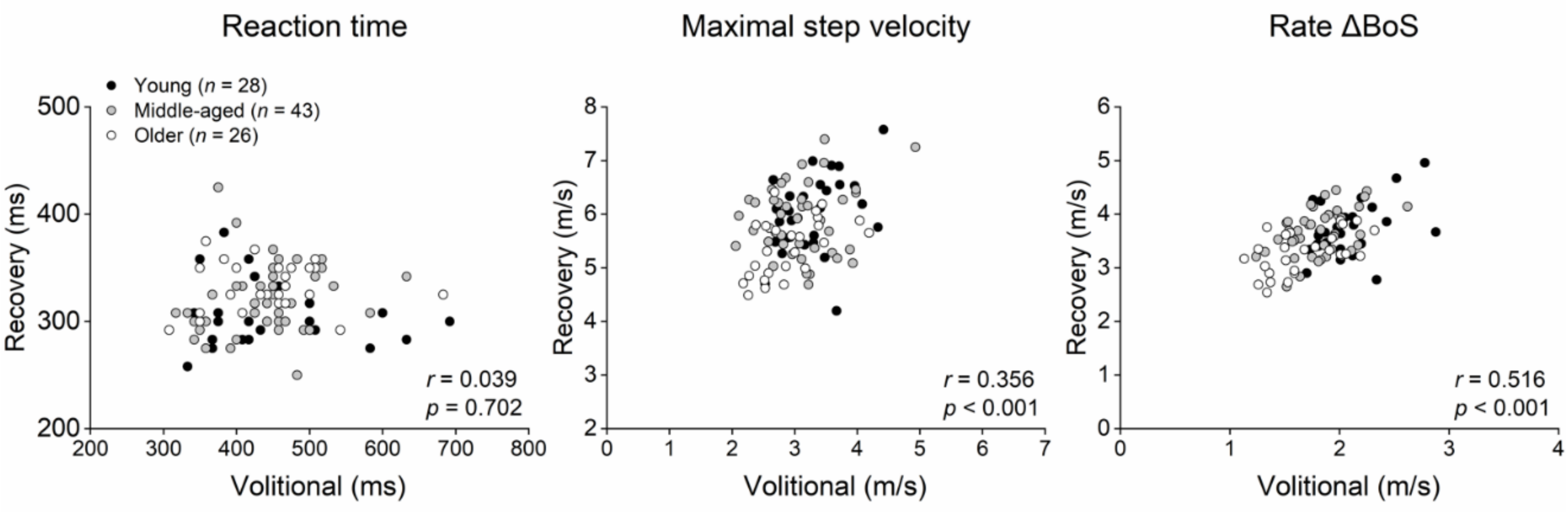

Figure 3: Relationship between volitional (VOL) and balance recovery stepping responses (REC). Data are given for reaction time, maximal step velocity and rate of increase in BoS (ΔBoS) in young (*n* = 28), middle-aged (*n* = 43) and older adults (*n* = 26).

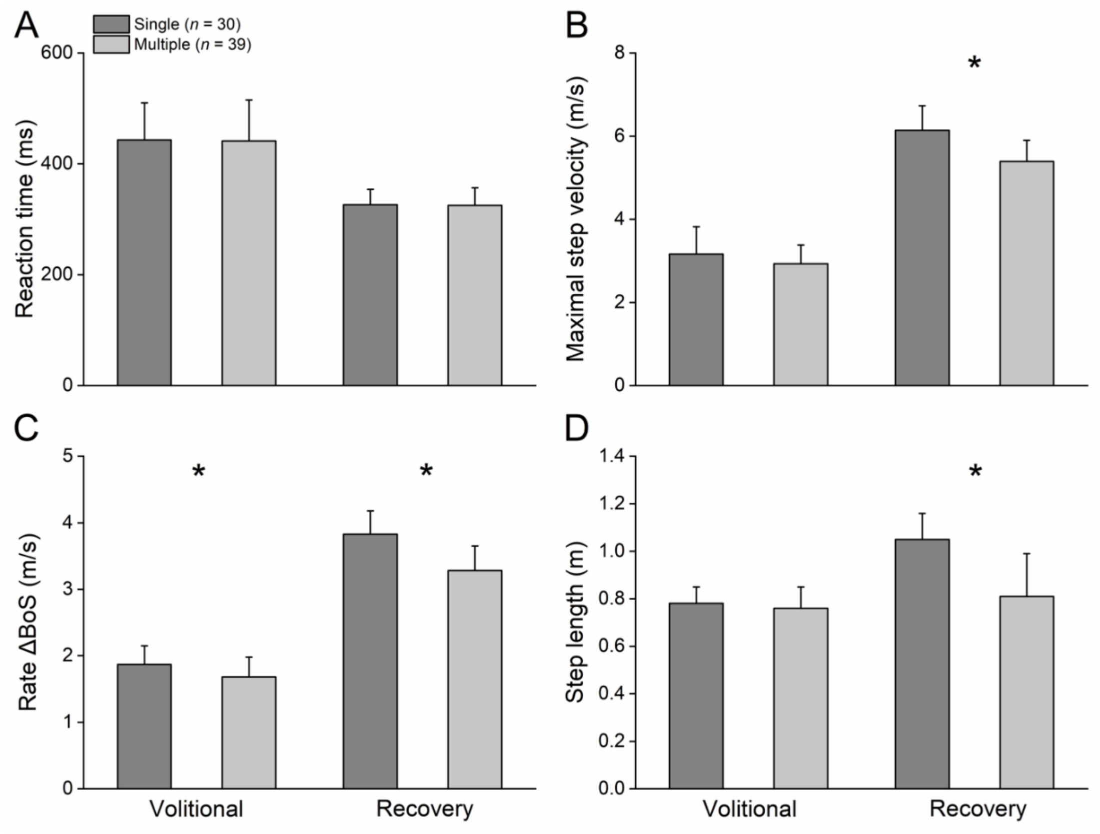

Figure 4: Spatio-temporal characteristics of volitional (VOL) and balance recovery stepping responses (REC) for the pooled groups of single- and multiple-steppers (*n* = 30 and *n* = 39 respectively). Data are given for reaction time **(A)**, maximal step velocity **(B)**, rate of increase in BoS [ΔBoS; **(C)**] and step length **(D)** with values expressed as means with SD error bars. Note that none of the younger adults failed to regain balance within a single step and therefore were not considered for subgroup comparison. * represents a statistically significant group effect ($0.001 \leq p \leq 0.01$).

3.5. Discussion

We aimed to examine the relationship between volitional and balance recovery stepping in young, middle-aged and older adults. In particular, we wished to understand whether volitional step characteristics serve to discriminate between groups or individuals with high or low recovery stepping performance after sudden loss of balance. Our hypotheses were confirmed in that (i) volitional step characteristics showed only poor correlation with balance recovery stepping and hence (ii) volitional stepping seems to have limited predictive value of an individual's recovery performance to sudden balance disturbance. Reduction in the incidence of falls will require targeted interventions that focus on individuals particularly at risk and hence will require methods, operated within a clinical setting, for identifying those with limited recovery capacities for sudden balance loss. Our results appear to indicate that volitional step execution is of quite limited usefulness in this regard.

Although the two stepping tasks appear to share distinct motor control subtasks aimed at appropriate modification of the BoS in the anterior direction, the stepping actions were remarkably slower (on average by 41%) for the volitional stepping response for all age groups. Moreover, our observed correlations between the two stepping tasks ($0.36 \leq r \leq 0.52$; $p < 0.001$) can be classified as poor to moderate associations, indicating that only 13% to 27% of the variance in volitional step characteristics can be related to the variance in balance recovery stepping performance for the analysed subject pool ($n = 97$). These results support earlier findings that demonstrate that the performance during a volitional step task fails to estimate older adults' ability to respond quickly to sudden balance loss (Luchies et al., 1999). Thus, in contrast to non-destabilizing mechanical cueing, initial perceptual information evoked by postural disturbance seems to be linked directly to the mobilization of subsequent rapid stepping responses. It is likely therefore that the two types of task require different capabilities of the human neuromotor system. Faster motor output during compensatory limb movements can be explained by reliance principally on lower brainstem and spinal circuits, as suggested by the retained capacity for righting actions in decerebrate and complete-spinalized cats (Honeycutt & Nichols, 2010; Zhong et al. 2012) and the occurrence of corrective stumbling responses in human infants before independent walking (Lam, Wolstenholme, van der Linden, Pang & Yang, 2003). In contrast, there is emerging evidence for at least some involvement of the cerebral cortex in reactive balance control (see Bolton, 2015 and Jacobs & Horak, 2007 for reviews). Identification of circuits involved in operation of the more demanding lean-and-release task cannot be determined from the present experimental setup but the issue should be examined in future investigations.

We compared subgroups of our participants based on recovery stepping performance (Figure 4). The pooled group of multiple-steppers (n = 39) showed diminished balance recovery stepping performance, i.e. they had lower step lengths, reduced step velocities and lower rates of increase of BoS compared to single-steppers (n = 30). Multiple-steppers may therefore be predisposed to higher fall risk (Carty et al., 2014). It is worth noting that we did not find differences in reaction time (time from instant of release to foot take-off) between these groups. This indicates that alterations in balance recovery capabilities do not seem to relate to diminished neuromotor control for step initiation rather to timing of muscle activation during the reactive stepping response. Similar results were found for the volitional step execution task, but only for the rate of increase of BoS were there statistically significant differences between single- and multiple-steppers. It appears therefore that volitional stepping characteristics have limited potential for discriminating between individuals with quite different reactive balance capabilities and therefore that such volitional tasks may not be sensitive enough for application in clinical practice. The limited predictive capacity of volitional stepping in relation to recovery stepping performance is reflected also in the relatively lower effect size for the difference in rate of increase of BoS for volitional stepping with Cohen’s *d* being 0.70 (versus 1.51 for recovery stepping). That being said, volitionally-controlled stepping may be promising for application to frail, clinical populations or groups who are limited in their performance capabilities and/or tolerance of larger postural threats. Volitional stepping may be a helpful addition to tasks tailored to resemble daily life challenges to balance within more holistic approaches to falls risk assessment. For example, a previous study (Lord & Fitzpatrick 2001) was able to detect longer volitional step execution times for fallers compared to non-fallers.

Our results show a diminished reactive stepping performance for older adults due to an age-related reduction in the ability to increase effectively the BoS, irrespective of task complexity. Interestingly, this reduction appears to be detectable already by middle age.

These results are in line with diminished balance recovery responses to tripping during walking in people over 40 years of age reported previously (König et al., 2019; Süptitz, Catalá, Brüggemann & Karamanidis, 2013). Reduced ability of older adults to effectively increase the BoS has been associated with muscle weakness (Karamanidis et al., 2008), though a deterioration in stability control seen for middle-aged and older adults may relate to a diminished neuromuscular control with aging rather than a general decline in leg extensor muscle strength (Arampatzis, Karamanidis & Mademli, 2008).

A potential limitation of the present study relates to predefinition of step length for volitional step execution. This may affect comparability of stepping responses. However, based on our observations from pilot studies (unpublished data), participants were not asked to place their foot at a fixed distance, rather to step over a normalized minimum target line thus provoking proper stepping actions, as opposed to small adjustments of foot position. In order to overcome this potential drawback, swing times were normalized to individual step length for both tasks. We believe therefore that our results are only affected in absolute terms and that the comparison of data sets remains valid.

3.6. Conclusions

In conclusion, we found only poor correlation between volitionally-controlled and balance recovery stepping responses over a wide range of age, suggesting that the magnitude of postural disturbance may directly affect an individual’s reactive stepping performance. Therefore these results point to task-specificity in fall-resisting skills assessment and volitional step execution tasks appear to be of restricted use for clinical practice. Effective estimation of differences in reactive balance recovery capability is required for prevention of majority incidence of falls in older adults.

3.7. Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

3.8. Competing interests

The authors declare that they have no competing interests.

3.9. Acknowledgements

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3.10. Authors' contributions

M.K. and K.K. conceived and designed the research; J.W. and M.K. performed the experiments; J.W., M.K., G.E. and K.K. analyzed data; J.W., M.K., G.E., J.S., W.P. and K.K. interpreted the results of experiments; J.W., M.K. and K.K. prepared figures; J.W. and M.K. drafted the manuscript; J.W., M.K., G.E., J.S., W.P. and K.K. edited and revised the manuscript; J.W., M.K., G.E., J.S., W.P. and K.K. approved the final text.

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4. Second study | Retention of improvement in gait stability over 14 weeks due to trip-perturbation training is dependent on perturbation dose

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Key words: Falls, perturbation training, gait, dynamic stability, motor learning

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4.1. Abstract

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

4.2. Introduction

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

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

Previous studies showed that such reactive balance improvements can occur after merely a single perturbation exposure (Marigold and Patla, 2002; Pai et al., 2010). Though such a single trial effect seems promising, in particular for application with frail older adults, it has only rarely been investigated whether reactive gait stability improvements acquired through single perturbation exposure can be retained over a prolonged time-period (e.g. several months) in populations which are at higher fall risk. In contrast, retention of the robust effects obtained from multi-trial perturbation training sessions are already well established (Bhatt et al., 2012; Epro et al., 2018b; Pai et al., 2014a). However, to our knowledge only Liu et al. (2017) examined this topic, demonstrating that a single slip perturbation exposure can cause long-term retention effects.

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

4.3. Methods

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

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

In order to assess dynamic stability (specifically MoS) each participant was analysed before (Pre) and after 14 weeks (Post14w). Arrangements to assess dynamic stability control during treadmill walking have been described previously (Epro et al., 2018ab; McCrum et al., 2014; Süptitz et al., 2012, 2013). Briefly, a reduced kinematic model (Süptitz et al., 2013), consisting of five retro-reflective markers (radius 16 mm) placed at the seventh cervical vertebra and the greater trochanter and forefoot of the left and right legs, was tracked using a 10-camera motion capture system (120 Hz; Nexus 2.6.1; Vicon Motion Systems, Oxford, UK). The time-courses for the 3D coordinates of the markers were smoothed using a fourth-order digital Butterworth filter (cut-off frequency 20 Hz). The anteroposterior MoS was calculated at each foot touchdown (TD) for baseline gait, the perturbed step (Pert) and the first six recovery steps after perturbation (Reco1L-Reco6R) as the difference between the anterior boundary of the base of support (anteroposterior position of the toe projection to the ground) and the extrapolated centre of mass (Hof et al., 2005). TD was determined using two 2D accelerometers (1080 Hz; ADXL250; Analog Devices, Norwood, MA, USA) attached over the tibia of each leg (Süptitz et al., 2012). Our reduced kinematic model has been validated previously (Süptitz et al., 2013) as appropriately assessing MoS for unperturbed and perturbed walking and for wide ranging age groups, showing significant correlations with a full-body kinematic model (average across trials $r = 0.90$, $p < 0.01$).

Independent samples t-tests were used to assess potential differences in age, height and body mass between groups. A two-way repeated-measures ANOVA with factors group (MULTIPLE and SINGLE) and time point (first perturbation trial at baseline ($T1_{Pre}$) and after 14 weeks ($T1_{Post14w}$)) was conducted to determine retention of improvements in MoS during unexpected trip-like gait perturbation, separately for TD Pert and TD Reco1L. Note that only $T1_{Pre}$ and $T1_{Post14w}$ were considered for further analysis as the aim of this study was principally to examine retention effects following different perturbation training protocols rather than trial-to-trial adaptation within one session. The focus here was set solely on the first perturbation trials since trial-to-trial adaptation has been shown previously for healthy middle-aged adults (McCrum et al., 2014). Note that in order to check for acute effects in MoS after single trip exposure (without possibly affecting retention by adding another perturbation in group SINGLE) a two-way repeated-measures ANOVA with factor trial (first and second perturbation trial at initial training session, $T1_{Pre}$ and $T2_{Pre}$ respectively) and step (TD Pert and TD Reco1L) was conducted for group MULTIPLE. A further two-way repeated-measures ANOVA (factors: group, trial) was implemented for unperturbed gait (average of 12 consecutive steps of unperturbed walking with ankle strap attached, assessed prior to the first perturbation). In a case of significant main effect or interaction Bonferroni post-hoc correction was applied. The level of significance was set at $\alpha = 0.05$. All results in text and figures are presented as mean (SD). All statistical analyses were conducted using Statistica software (Release 10.0; Statsoft Inc, Tulsa, OK, USA).

4.4. Results

There were no significant differences in age (51.1 (6.0) years vs. 54.3 (4.0) years), body height (171.9 (12.0) vs. 180.1 (12.9) cm) and body mass (76.7 (14.0) vs. 79.3 (14.9) kg) between the two groups (MULTIPLE vs. SINGLE). One participant from group MULTIPLE was not able to cope with the task by grasping the treadmill handrails to prevent a fall after the novel trip-like gait perturbation ($T1_{Pre}$); hence only 23 participants were considered for analysis of dynamic stability. For baseline walking (12 consecutive steps), the two-way repeated-measures ANOVA revealed no statistically significant effects for MoS for time point ($T1_{Pre}$ and $T1_{Post14w}$) or group (MULTIPLE and SINGLE). Considering post 14 weeks, the analysis of MoS at TD Pert and TD Reco1L revealed a statistically significant time point x group interaction for both analysed steps ($F_{1,21} = 4.29$, $p = 0.05$ and $F_{1,21} = 9.66$, $p = 0.01$ for TD Pert and TD Reco1L respectively), indicating that the time effect on MoS was dose specific. Post-hoc tests revealed significantly higher MoS values ($0.001 < p < 0.01$) at TD Pert and Reco1L for $T1_{Post14w}$ compared to $T1_{Pre}$ for group MULTIPLE (see figure 1). In contrast, no statistically significant increases in MoS after 14 weeks were found for any of the analysed steps in group SINGLE (see figure 1). Regarding acute MoS changes, the two-way repeated-measures ANOVA revealed a significant trial ($F_{1,13}$ = 7.22, p = 0.02) and step effect ($F_{1,13}$ = 18.55, p < 0.001) with higher MoS at TD Pert and TD Reco1L for T2$_{Pre}$ compared to T1$_{Pre}$ and TD Reco1L compared to TD Pert for both trials (see figure 2).

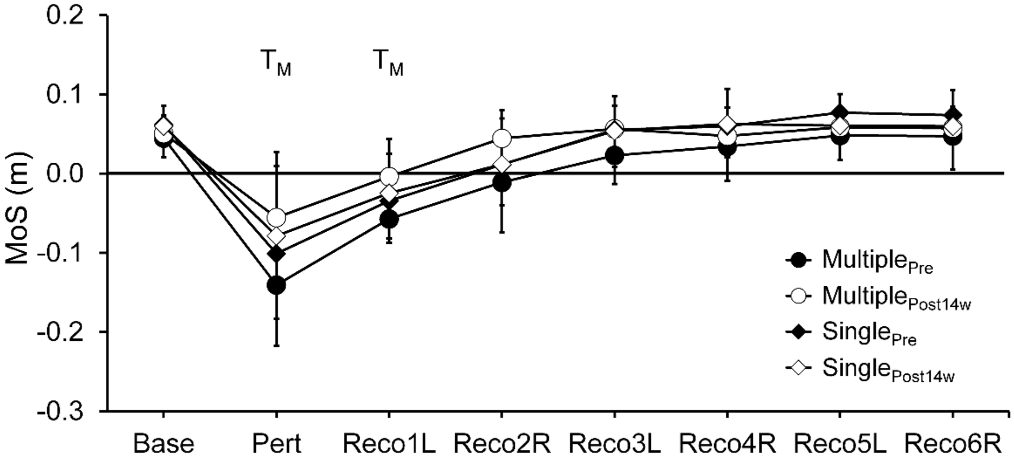

Figure 1: Margin of stability (MoS) during unperturbed walking (Base), for touchdown at perturbation (Pert) and for the following six recovery steps after the perturbation (Reco1L-Reco6R) in group MULTIPLE (n = 14) and group SINGLE (n = 9). Data are given for the first trip-like gait perturbation trial at the initial training session and post 14 weeks (T1$_{Pre}$ and T1$_{Post14w}$, respectively). Values are expressed as means with SD error bars. T$_M$ represents a statistically significant time point effect for group MULTIPLE (p < 0.01). L: Left leg. R: Right leg.

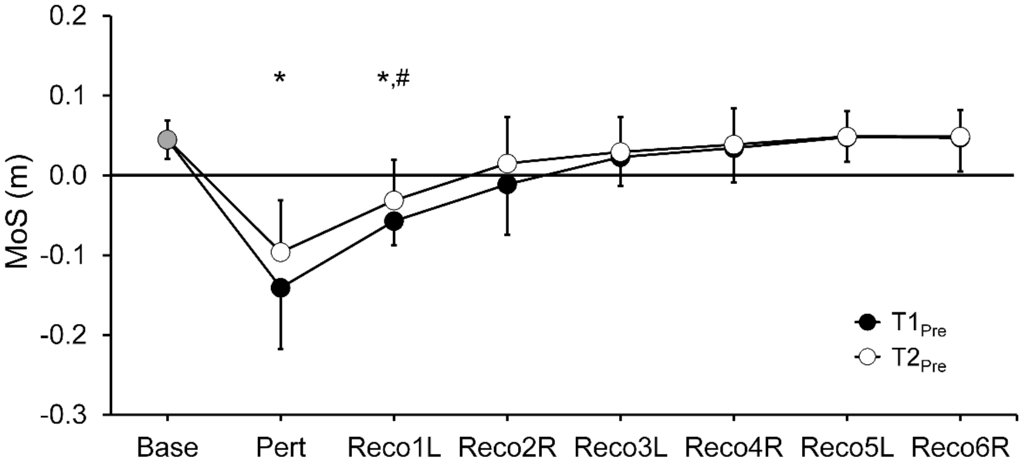

Figure 2: Margin of stability (MoS) during unperturbed walking (Base), for touchdown at perturbation (Pert) and for the following six recovery steps after the perturbation (Reco1L-Reco6R) in group MULTIPLE (n = 14), after the first ($T1_{Pre}$) and second ($T2_{Pre}$) trip-like gait perturbation trials at the initial training session. Values are expressed as means with SD error bars. * represents a statistically significant trial effect ($p < 0.05$). # represents a statistically significant difference to Pert ($p < 0.001$). L: Left leg. R: Right leg.

4.5. Discussion

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

Margin of stability at TD of the perturbed step and first recovery step was significantly less negative (more stable body configuration) after 14 weeks compared to the initial session in group MULTIPLE (eight perturbation trials). These results are in accordance with our earlier findings (Epro et al., 2018b), showing retention in gait stability improvements over 14 weeks following a single bout of trip-like gait perturbations in older women. Thus, although middle- and older-aged adults have a higher fall risk, they are still able to improve their reactive responsiveness through repeated exposure to unexpected perturbations and retain those improvements over a period of months. Since for single trip exposure we found no significant differences in MoS between the two measurement time points for any of the analysed steps it is likely that a single perturbation may have been too low to facilitate learning effects lasting for several months. This supports previous findings seen in slipping, showing that in younger adults a single slip exposure without additional sessions was not sufficient to yield retention effects in gait stability over four months (as compared to a higher perturbation dose comprising 24 slips; Bhatt and Pai, 2009). Taken together, these results indicate that perturbation dose must exceed a threshold in order to induce retention of improvements in gait stability over several months acquired during single-session treadmill training.

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

In addition, when analysing the initial first two perturbation trials in group MULTIPLE, MoS was significantly improved in the second compared to the first trial. Therefore, we could assume short-term adaptive changes after single trip exposure in group SINGLE without possibly affecting retention by adding another perturbation. Finally, our finding that single trip exposure in group SINGLE failed to facilitate adaptive changes in reactive gait stability over 14 weeks does not support previous results seen for slipping (Liu et al., 2017). This group reported significant improvements in reactive stability, and hence a reduction in laboratory falls, 12 months after a single gait slip. Contradictions between findings requiring further investigation may be related to the different perturbation types (tripping vs. slipping), numbers of initially reported falls and ages of participating subjects (middle-aged vs. community-dwelling older).

We have to acknowledge that our current protocol might not fully replicate a real-life trip situation and that this may possibly restrict generalisability of the observed gait stability improvements. However, despite the fact that gait-trip mechanics are highly variable in nature, the common consequence of stumbling in real-life situations may require similar postural corrections to regain balance to those observed in our perturbation setup (i.e. effectively increasing base of support; Epro et al., 2018a; McCrum et al., 2014; Süptitz et al., 2013). Although the applied perturbation magnitude was equal among all analysed participants, the effect of the perturbation on MoS in absolute terms appeared to differ slightly between groups (on average by 4 cm; see figure 1), though this difference did not reach statistical significance (p = 0.78). Therefore, one might argue that the failure of retention for group SINGLE may be due to an initially lower effect on stability. However, on analysing the relationship between the MoS during the initial perturbation and its relative change after 14 weeks by including our previous data on older adults (Epro et al., 2018b; total n = 23), we found no significant correlation (r = 0.28; p = 0.21) and hence are confident that the observed group differences for retention are predominately related to perturbation dose rather than its initial effect on stability. Finally, the number of analysed subjects is relatively low (n = 14 for MULTIPLE; n = 9 for SINGLE), possibly reducing the potential for determining significant retention effects in MoS (this is reflected in low effect sizes for group SINGLE: Cohen’s *d* = 0.33 and 0.29 for TD Pert and Reco1L respectively). However, since the observed retention effects for group MULTIPLE were large (on average about 80% improvement in MoS) though the group was quite small in size, we are confident that the low sample size for group SINGLE is not the primary driver for the lack of functional retention effects for this group.

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

4.6. Disclosure of Interest

The authors declare no conflicts of interest.

4.7. Acknowledgements

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4.9. Supplementary material 1: Appendix to Methods

In our current setup the perturbations were applied using a custom-built brake-and-release system described previously (Epro et al., 2018a,b). Participants walked at a standardised velocity of 1.4 m s^{-1} on a treadmill (h/p/cosmos pulsar 4.0; Nussdorf-Traunstein, Germany) when a resistance (creating a constant force field of approximately 55 N) was applied to the lower right limb via an ankle strap and Teflon cable. The rise and fall time of the pulling force of the perturbation was under 20 ms. The pulling force was activated during the stance phase of the right leg, just before the start of the swing phase and the force was first perceivable at toe off of the perturbed leg. The pulling force was turned off during the next stance phase of the same foot. Accordingly, the duration of the perturbation was the entire swing phase of the right leg and thereby individually standardised for each participant. The pulling force was turned on manually and the on- and offset of perturbation was assessed in post processing using a synchronized TTL signal, where each trial was checked (via visual expectation) to assure that the on- and offset was at the correct instant of time (for the onset during previous stance phase and offset during the following stance phase of the perturbed leg). Due to the fact that the gait velocity was relatively low with quite long ground contact and swing phases and the measurement operator was highly experienced in the timing of the onset/offset for this kind of perturbation, we did not generate any invalid trials due to erroneous perturbation switch timing.

During unperturbed walking the participants experienced negligible active resistance through the Teflon cable (resistance below 0.1 N). In a series of pilot studies prior to this investigation we also compared walking kinematics with and without the Velcro strap attached to the ankle joint and found no differences in sagittal plane joint kinematics at the instant of foot touchdown (unpublished data). Baseline measurement (25 stride cycles of unperturbed walking) was conducted after four minutes of walking (Karamanidis et al., 2003) from which twelve consecutive steps were used to determine baseline values of the analysed parameters (Epro et al., 2018a,b). Following these measurements, the resistance was applied for one step and immediately removed. Participants were not warned about the onset or removal of the perturbation, but were previously informed that at some point their gait would be perturbed. During all measurements participants wore a full-body safety harness connected to an overhead frame. In group MULTIPLE the trip-like gait perturbation was repeated eight times, separated by uneven two- to three-minute wash-out periods of unperturbed walking (Epro et al., 2018a,b; McCrum et al., 2014).

4.10. Supplementary Data References

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5. Third study | Retention and generalizability of balance recovery response adaptations from trip-perturbations across the adult lifespan

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Key words: Aging, falls, perturbation training, dynamic stability, motor learning

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5.1. Abstract

For human locomotion, varying environments require adjustments of the motor system. We asked whether age affects gait balance recovery adaptation, its retention over months and the transfer of adaptation to an untrained reactive balance task. Healthy adults (26 young, 27 middle-aged and 25 older; average ages 24, 52 and 72 years respectively) completed two tasks. The primary task involved treadmill walking: either unperturbed (control; *n*=39) or subject to unexpected trip perturbations (training; *n*=39). A single trip perturbation was repeated after a 14-week retention period. The secondary transfer task, before and after treadmill walking, involved sudden loss of balance in a lean-and-release protocol. For both tasks the anteroposterior margin of stability (MoS) was calculated at foot touchdown. For the first (i.e. novel) trip, older adults required one more recovery step (*P*=0.03) to regain positive MoS compared to younger, but not middle-aged, adults. However, over several trip perturbations, all age groups increased their MoS for the first recovery step to a similar extent (up to 70%), and retained improvements over 14 weeks, though a decay over time was found for older adults (*P*=0.002; middle-aged showing a tendency for decay: *P*=0.076). Thus, although adaptability in reactive gait stability control remains effective across the adult lifespan, retention of adaptations over time appears diminished with aging. Despite these robust adaptations, the perturbation training group did not show superior improvements in the transfer task compared to aged-matched controls (no differences in MoS changes), suggesting that generalizability of acquired fall-resisting skills from gait-perturbation training may be limited.

5.2. New & Noteworthy

The human neuromotor system preserves its adaptability across the adult lifespan. However, although adaptability in reactive gait stability control remains effective as age increases, retention of recovery response adaptations over time appears to be reduced with aging. Furthermore, acquired fall-resisting skills from single session perturbation training seem task-specific, which may limit the generalizability of such training to the variety of real-life falls.

5.3. Introduction

The aging human neuromotor system shows a gradual functional decline, which means a diminished ability to produce effective and safe gait patterns during daily life, resulting in higher fall risk. Falls in older adults can have severe functional consequences in the form of various clinical conditions, disability or even death (Burns and Kakara 2018; Terroso et al. 2014). Epidemiological studies indicate fall incidence increases by middle age, i.e. by about 50 years of age (Donaldson et al. 1990). Given the demographic transition to an expanded older population and higher life expectancy, the development of effective intervention strategies aimed at prevention of falls in populations at higher fall risk is vital for public health.

Most falls in older adults occur during walking and more than 30% of these result from a trip that causes sudden balance loss in the forward direction (Yang et al. 2018a). To ensure safe onward locomotion during such unexpected balance disturbances, rapid compensatory motor actions are required from the neuromotor system (Berger et al. 1984; Nashner 1980), but these become less effective with the onset of middle age (Süptitz et al. 2013). Hence older age groups are predisposed to higher fall risk. That being said, improvements in predictive and reactive balance control strategies can take place (Bhatt et al. 2006). It is promising that even in old age there is a capacity to enhance gait stability control following exposure to various laboratory-induced gait perturbations (e.g. sudden changes in the walking surface, slips or trips; Bierbaum et al. 2011; Epro et al. 2018a; Okubo et al. 2019; Pai et al. 2010; Wang et al. 2019a, 2019b; Yang and Pai 2013). Moreover, such experimental protocols have revealed retention of balance recovery response adaptations over prolonged time periods (i.e. several months to years), resulting from single-perturbation training sessions in middle-aged (König et al. 2019) and older adults (Bhatt et al. 2012; Epro et al. 2018b; Liu et al. 2017; Pai et al. 2014). These results provide evidence that even a very small number of external perturbations to gait can induce retainable task-specific balance control strategies in the aged neuromotor system.

Therefore older adults’ fall risk in daily life may possibly be reduced, at least for the practiced perturbation type (Rosenblatt et al. 2013).

In a previous study (Epro et al. 2018b) we found that adaptations in older adults’ reactive recovery responses to a sudden trip were retained over 14 weeks, though these responses were significantly smaller than the acute effects from a single perturbation training session (i.e. there was partial retention). It is unclear, however, whether the decay in the retention of recovery response adaptations over time is dependent on the participants’ age. Regarding this issue, Pai et al. (2010) showed more rapid reduction of improvements in balance recovery behaviour due to repeated slips in older compared to younger adults after merely a short wash-out period of unperturbed walking. Combining these results with earlier studies demonstrating that locomotor adaptations in general may be smaller and/or occur at a lower rate for older groups (Bierbaum et al. 2011; Bohm et al. 2012; Bruijn et al. 2012; McCrum et al. 2016), one might suggest that, although the capacity for adaptation in the human balance control system is preserved with increasing age, various aspects of learning (i.e. adaptation rate, retention) may be diminished.

An additional and crucial aspect of neuromotor capacity, which is generally assessed in relation to learning effects, is the ability to transfer the acquired adaptations from one situation to various alternative contexts, in this case to transfer the improvement in balance recovery mechanisms from perturbation training to different postural challenges. There is evidence to support such generalization of adaptations, at least between different conditions of the same task (e.g. from training gait-slips on the treadmill to a ‘novel’ overground slip, or from simulated slips on a moveable platform to an untrained slip on an oily surface; Bhatt and Pai 2009; Lee et al. 2018; Parijat and Lockhart 2012; Wang et al. 2019c; Yang et al. 2013, 2018b). It remains largely unknown, however, whether such adaptations are limited to a specific task or can improve recovery performance for other reactive balance tasks (inter-task transfer) and whether this is affected by age. This is of particular importance for the development of targeted fall prevention strategies in aged populations since real-life falls can result from a variety of postural threats.

The present study aimed to examine acute adaptations in reactive gait stability control due to repeated trip-like perturbations, the retention of those adaptations over several months and their transfer to an untrained reactive balance task (the lean-and-release task) in young, middle-aged and older adults. We hypothesised that older adults are capable of inducing long-term adaptation in their reactive gait stability control but that (i) the adaptation occurs at a lower rate, (ii) decays at a faster rate and (iii) transfers less effectively to an untrained task than for the young and middle-aged. The results of this study have significance for our understanding of the dynamics of the human neuromotor system in relation to both acute external influences (perturbations) and to longer-term internal (aging) constraints.

5.4. Methods

5.4.1. Participants

Twenty-six young (15 of them men; 24.1 ± 3.5 yr; mean and standard deviation), twenty-seven middle-aged (13 men; 52.4 ± 5.3 yr) and twenty-five older adults (11 men; 72.0 ± 4.4 yr) took part in this study. The height and body mass for each group were 176.8 ± 8.4 cm and 70.0 ± 11.0 kg for the young, 173.5 ± 11.0 cm and 78.3 ± 13.7 kg for the middle-aged, and 169.7 ± 7.9 cm and 75.3 ± 14.1 kg for the older adults respectively. People were excluded if they had any neurological or musculoskeletal impairments of the lower limbs (e.g. joint pain during locomotion). The participants were generally healthy and showed comparable self-reported physical activity levels (7.1 ± 3.4, 7.3 ± 4.3 and 6.5 ± 3.3 h week^{-1} for young, middle-aged and older adults respectively). The study was approved by the ethics committee of the German Sport University Cologne (ethical approval number 141/2017) and met all requirements for human experimentation in accordance with the Declaration of Helsinki. All participants provided written informed consent after initial briefing.

5.4.2. Reactive balance tasks

Our participants took part in two different tasks - a primary trip-perturbation task and a secondary lean-and-release transfer task. They were randomly assigned to one of two groups for treadmill walking (20-25 min each): to a control group (unperturbed walking only; 14 young, 13 middle-aged and 12 older adults) or to a perturbation training group (eight separate unexpected trip-like perturbations; 12 young, 14 middle-aged and 13 older adults). Before and after treadmill walking all participants were exposed to a secondary transfer lean-and-release task. In order to examine the extent of retention of recovery response adaptations from trip-perturbation and their variation across the adult lifespan, participants from the training group performed a single trip-perturbation trial after 14 weeks (see also Fig. 1). After the perturbation-training session and testing, participants experienced no other exposure to mechanically induced perturbations, but were allowed to continue with their normal physical activities.

5.4.3. Analysis of gait stability after unexpected trip perturbation

The gait-perturbation task and paradigm have been described in detail previously (Epro et al. 2018a, 2018b; König et al. 2019). Briefly, trip-like gait perturbations were applied during treadmill walking using a manually-controlled custom-built pneumatic brake-and-release system, which generates a constant restraining force of approximately 55 N (rise time about 20 ms) to the swing phase of the lower right limb via an ankle strap and Teflon cable. Treadmill-walking familiarization took place for all participants about seven days prior to the training session. After the lean-and-release task (please see *Analysis of inter-task transfer* below) the protocol began with the participants walking at a standardised velocity of 1.4 m s^{-1} on a treadmill (pulsar 4.0, h/p/cosmos; Nussdorf-Traunstein, Germany) while wearing the ankle strap and a full-body safety harness connected to an overhead frame. The strap created a negligible resistance of about 0.1 N and this had no effect on sagittal plane joint kinematics at the instant of foot touchdown (TD; unpublished data). After four minutes of walking (Karamanidis et al. 2003), a baseline measurement (25 stride cycles of unperturbed walking) was recorded in each measurement session, from which baseline values of the analyzed parameters were determined as the average over twelve consecutive steps (Epro et al. 2018b; König et al. 2019). Following this baseline measurement, the resistance was applied at an unexpected point in time for one step and immediately removed. In the present study this specific step is referred to as the *perturbed step*. The pulling force was activated during the stance phase of the right limb, just before the start of the swing phase and turned off during the next stance phase of the same foot. Resistance was first perceivable at toe-off of the perturbed step. By applying the external resistance over the entire swing phase the perturbation was standardised from participant to participant. The onset and removal of the resistance were unexpected, but participants were aware that their gait was going to be perturbed at some points during walking. The perturbation was repeated eight times in total (eight *trials*), separated by uneven two- to three-minute washout periods of unperturbed walking, and was delivered only when participants' step length returned to individual baseline levels (checked in real-time through visualization of the anteroposterior trajectories of toe markers; Epro et al. 2018a, 2018b; König et al. 2019; McCrum et al. 2014). The *trials 1* and *8* of the training session and the retention test trial post 14 weeks were used for statistical analysis. These specific trials were considered to represent the participants' initial and post-training performance, including its retention. However, as it was the aim of this study to assess adaptation rate also, the trial-to-trial changes within the training session were examined via *trials 2*, *4* and *6*.

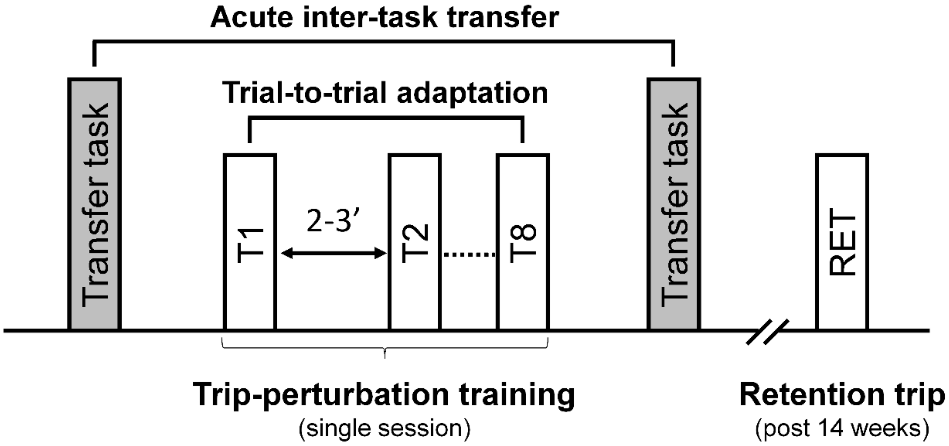

Figure 1: Experimental protocol of the two reactive balance tasks. Treadmill gait-perturbation training consisted of eight trials (T1-T8) of a trip-perturbation task, separated by uneven two- to three-minute washout periods of unperturbed walking. Before and after treadmill walking the participants were exposed to a transfer lean-and-release task. Retention of adaptations in reactive gait stability control was analyzed 14 weeks later by means of a single retention test trial (RET) of the trip-perturbation task.

To assess dynamic stability during treadmill walking a reduced kinematic model (Süptitz et al. 2013), consisting of five retro-reflective markers attached to anatomical landmarks (seventh cervical vertebra and the greater trochanter and forefoot of the left and right legs), was tracked using a 10-camera optical motion capture system (120 Hz; Nexus 2.6.1; Vicon Motion Systems, Oxford, UK). The 3D coordinates of the markers were smoothed using a fourth-order digital Butterworth filter (cut-off frequency 20 Hz). The anteroposterior margin of stability (MoS), as a valid measure for biomechanical stability of human walking (Bruijn et al. 2013), was calculated at each foot TD for baseline gait, the perturbed step and the first six recovery steps after each perturbation as the difference between the anterior boundary of the base of support (anteroposterior position of the toe projection to the ground) and the extrapolated center of mass (Hof et al. 2005). Furthermore, to account for inter-individual differences in gait stability, the change in MoS during the perturbed step and first two recovery steps relative to baseline walking during the same session was used to examine the recovery response during perturbed gait

($\Delta\text{MoS}_{\text{Step}} = \text{MoS}_{\text{Step}} - \text{MoS}_{\text{Base}}$, calculated for each individual; Epro et al. 2018a), with negative $\Delta\text{MoS}_{\text{Step}}$ values indicating a smaller MoS relative to baseline. Foot TD was detected using two 2D accelerometers (1080 Hz; ADXL250; Analog Devices, Norwood, MA, USA) placed over the tibia of each leg (Süptitz et al. 2012). The reduced kinematic model used here has been validated previously for the assessment of dynamic stability (i.e. MoS) during perturbed and unperturbed treadmill walking (Süptitz et al. 2013) with the same age groups, perturbation task and gait velocity as in the current study. There were significant correlations with a full-body kinematic model (on average $r = 0.90$, $P < 0.01$ across trials).

For evaluation of adaptations in dynamic stability control for *trial 2* and other even-numbered trials in the training session, we calculated the adaptation magnitude for MoS in a similar manner to Bierbaum et al. (2011) as follows:

$$\text{Adaptation magnitude} = \left(1 - \frac{MoS_{AdaptPhase} - MoS_{Base}}{MoS_{T1} - MoS_{Base}}\right) \text{x } 100$$

where $\text{MoS}_{\text{AdaptPhase}}$ is the MoS during the first recovery step in *trials 2*, *4*, *6* or *8*, MoS_{T1} is the MoS during the first recovery step in *trial 1* of the training session and MoS_{Base} represents baseline MoS, with positive magnitude values indicating a higher MoS relative to the first (i.e. novel) trip perturbation trial.

5.4.4. Analysis of inter-task transfer

Within a 10-to-15-minute period before and after treadmill walking and perturbation training, participants' dynamic stability was assessed in a separate laboratory via a single trial of the lean-and-release protocol involving sudden anterior balance loss. The same marker set as described above for trip perturbations was tracked by a 6-camera optical motion capture system (120 Hz; Nexus 2.6.1; Vicon Motion Systems, Oxford, UK). This secondary transfer task was conducted as described previously (Karamanidis and Arampatzis 2007). Briefly, participants stood on a force plate (1080 Hz; 60 x 90 cm; Kistler, Winterthur, Switzerland) and, keeping their feet flat on the ground, were tilted forward via a horizontal inextensible cable attached to a body harness until 23 ± 3% of their body weight (BW) was recorded on a load cell placed in series with the cable (see also Do et al. 1982; Thelen et al. 1997). After the given inclination was reached and any possible anticipatory behavior had subsided (i.e. antero-posterior and medio-lateral weight shift regulation, recorded via real-time cable force on the load cell and center of pressure on the force plate), the cable was suddenly released after a random time interval of 10 to 30 s using a custom-built pneumatic release system. Participants were instructed to attempt to restore stable stance within a single recovery step using the limb of their choice when released from the forward-leaning position (Madigan and Lloyd 2005). No practice trials were conducted to ensure novelty of the task. The exact forward lean was chosen according to the reduced ability of older individuals to regain stability with a single recovery step from greater cable loads than 23% BW (Karamanidis et al. 2008). The anteroposterior MoS was calculated at foot TD of the recovery limb after the sudden release as described above for gait perturbations. Foot TD was defined as the first instant when vertical ground reaction force exceeded a threshold level of 20 N determined by a second force plate (1080 Hz; 60 x 90 cm; Kistler, Winterthur, Switzerland) mounted in front of the first. Validity of our main outcome parameter MoS has been demonstrated in a previous study (Karamanidis et al. 2008), showing that MoS during the recovery step predicts the recovery behavior (i.e. single vs. multiple stepping) in about 96% of the cases for a large subject pool. In order to account for inter-individual differences in the recovery response to the untrained transfer task, the change in MoS during the first recovery step in the trial after the treadmill protocol relative to the first (i.e. novel) trial was used to examine inter-task transfer of training effects ($\Delta MoS_{Trial} = MoSP_{ostTrial} - MoS_{PreTrial}$, calculated for each individual), with positive ΔMoS_{Trial} values indicating a higher MoS relative to the pre-trial. Participants were secured by a full-trunk safety harness connected to an overhead track that allowed for forward and lateral motion while preventing contact of the body with the ground (with exception of the feet). The safety harness suspension cable incorporated a second load cell to ensure that the measured MoS values were not affected by potential cable assistance (i.e. > 20% BW placed on the safety harness suspension cable at TD of the recovery limb after the sudden release; Cyr and Smeesters 2009).

5.4.5. Statistics

To examine the recovery response adaptations to the trip-perturbation task amongst the three age groups (young, middle-aged and older), separate one-way ANOVAs were used to compare the number of recovery steps needed to regain positive MoS (in the present study defined as a criterion for a "stable" body configuration) in *trial 1* and *8* of the training session. For the analysis of the adaptation potential, the adaptation magnitude for MoS during the first recovery step was analyzed in *trials 2*, *4*, *6* and *8* of the training session. To assess the effect of age and perturbation trial on adaptation magnitude we used a two-way repeated-measures ANOVA with age group and trial as factors [hypothesis (i)]. The effect of age on the retention of recovery response adaptations was assessed by means of a two-way repeated measures ANOVA with age group and perturbation trial (*trial 8* of the perturbation-training session, retention test trial) as factors applied separately for $\Delta \mathrm{MoS}_{\mathrm{Step}}$ (MoS referenced to baseline) during the perturbed step and first two recovery steps [hypothesis (ii)]. For baseline MoS (average of 12 consecutive steps of unperturbed walking with ankle strap attached, assessed prior to the first perturbation trial of each measurement session), a further two-way repeated measures ANOVA with factors age group and time point (perturbation-training session, retention test) was implemented. For the analysis of inter-task transfer we calculated $\Delta \mathrm{MoS}_{\mathrm{Trial}}$ as the absolute change in dynamic stability after a sudden forward fall from before to after treadmill walking, and for the control group. To assess the effect of age and treadmill perturbation training on $\Delta \mathrm{MoS}_{\mathrm{Trial}}$ we used a two-way ANOVA with age group and intervention group (training, control) as factors [hypothesis (iii)]. In a case of significant main effects or interactions Duncan *post-hoc* corrections were applied pairwise. The level of significance was set at $\alpha = 0.05$, with all results presented as mean and SD. All statistical analyses were conducted using Statistica software (Release 10.0; Statsoft Inc, Tulsa, OK, USA).

5.5. Results

5.5.1. Changes in gait stability control to repeated trip perturbations

Four participants (one middle-aged and three older adults) had to grasp the handrails of the treadmill to cope with the tripping task and were removed from the analysis (none of the younger adults failed to cope with the task). Accordingly, 26 young, 27 middle-aged and 22 older adults were considered for the statistical analyses.

Assessment of dynamic stability during treadmill walking revealed positive MoS during baseline walking (average value over twelve consecutive steps) for all analyzed participants with no statistically significant age group or time point effects (perturbation-training session vs. retention test; Fig. 2). The unexpected gait perturbation caused a considerable decrease in MoS (lower values compared to baseline) in all age groups (Fig. 2), indicating less stable body positions. For the recovery response to the first (i.e. novel) unexpected perturbation, we found a statistically significant age effect [$F(2,32) = 2.99$, $P = 0.05$] with the older adults requiring on average one more recovery step to regain positive MoS compared to younger adults ($P = 0.03$; Fig. 2). Although not significant ($P = 0.085$), there was a tendency to require a higher number of recovery steps also in middle-aged compared to younger adults. After experiencing eight trip perturbations, there were no statistically significant differences in the required number of recovery steps to attain positive MoS amongst the three age groups (Fig. 2).

We found a significant trial effect [$F(3,96) = 4.35$, $P = 0.01$] for the adaptation magnitude (*trial 2* vs. *trials 4*, *6* and *8*; $0.01 \leq P \leq 0.02$), indicating smaller changes in MoS, and hence more complete recovery, during the first recovery step in *trials 2*, *4*, *6* and *8* relative to *trial 1* of the training session (Fig. 3). However, no significant trial by age group interaction was found, which refutes our first hypothesis.

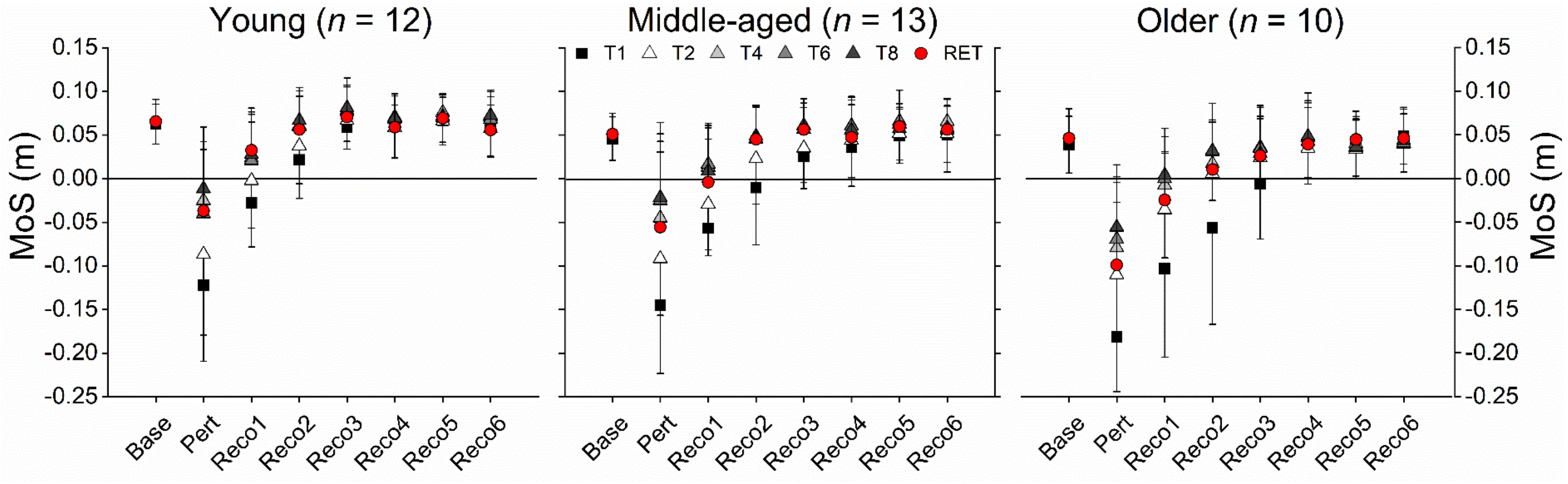

Figure 2: Margin of stability (MoS) measurements for the trip-perturbation training session and the retention test. Data are given for baseline walking (Base), for touchdown at perturbation (Pert) and for the following six recovery steps after the perturbation (Reco1-Reco6) in young (*n* = 12), middle-aged (*n* = 13) and older adults (*n* = 10). Values represent the first (T1), second (T2) and subsequent alternate trials (T4, T6 and T8) of the trip-perturbation training session and the retention trip trial (RET), and are expressed as means with SD error bars.

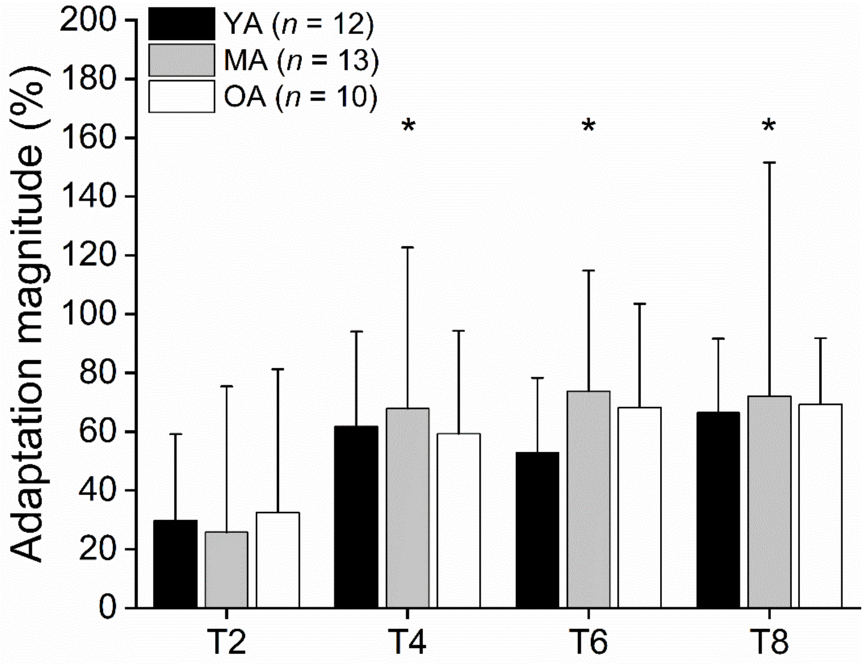

Figure 3: Adaptation magnitudes for the initial trip-perturbation training session. Values represent the adaptation in the margin of stability at touchdown for the first recovery step for the second (T2) and subsequent alternate trials (T4, T6 and T8) referenced to the first trip-perturbation trial in young (YA; n = 12), middle-aged (MA; n = 13) and older adults (OA; n = 10). Values are expressed as means with SD error bars. * represents a statistically significant difference with respect to T2 ($P < 0.05$).

5.5.2. Retention of improvement in gait stability control over 14 weeks

The retention test trial was performed on average 98 (± 4) days after the perturbation-training session and revealed an improved recovery response compared to the first (novel) trip-perturbation trial for all age groups (Fig. 2). The specific comparison of $\Delta\text{MoS}_{\text{Step}}$ (MoS referenced to baseline) during the perturbed step in *trial 8* of the training session and the retention test trial revealed a statistically significant trial effect [$F(1,32) = 18.01$, $P < 0.001$], showing lower $\Delta\text{MoS}_{\text{Step}}$ values (more negative, $P < 0.001$) after 14-weeks and hence only partial retention of recovery response adaptations, independent of age group (Fig. 4). However, when considering the same comparison for the first two recovery steps after perturbation a statistically significant trial by age interaction for both analyzed steps was found [$F(2,32) = 3.37$, $P = 0.05$ and $F(2,32) = 1.30$, $P = 0.05$ for the first and the second recovery steps respectively]. This means that the effect of single session perturbation training on long-term retention in training effects was age specific. Specifically, a significant decrease ($0.002 \leq P \leq 0.01$) in $\Delta \text{MoS}_{\text{Step}}$ during the first two recovery steps after 14 weeks (retention test trial vs. *trial 8* of the perturbation-training session) could be observed for the older but not for the young and middle-aged adults (Fig. 4), supporting our second hypothesis. Note that, although non-significant, there was a tendency ($P = 0.076$) for middle-aged adults also to have lower $\Delta \text{MoS}_{\text{Step}}$ values in the retention test trial compared to *trial 8* of the perturbation-training session (Fig. 4). Consequently, older adults showed lower ($0.03 \leq P \leq 0.04$) $\Delta \text{MoS}_{\text{Step}}$ values during the second recovery step in the retention test trial compared to the two younger age groups (Fig. 4).

5.5.3. Dynamic stability changes for the lean-and-release task

All age groups improved their recovery response to the sudden forward fall in the second trial compared to the first (i.e. novel) trial as indicated by the positive $\Delta \text{MoS}_{\text{Trial}}$ values (Fig. 5). However, contrary to our third hypothesis, the analysis of inter-task transfer of recovery response adaptations from a single trip-perturbation training session revealed no statistically significant main effects or interaction (i.e. intervention vs. control group) for $\Delta \text{MoS}_{\text{Trial}}$ for the first recovery step in the transfer lean-and-release task ($P = 0.98$ for the age group by intervention group interaction; Fig. 5).

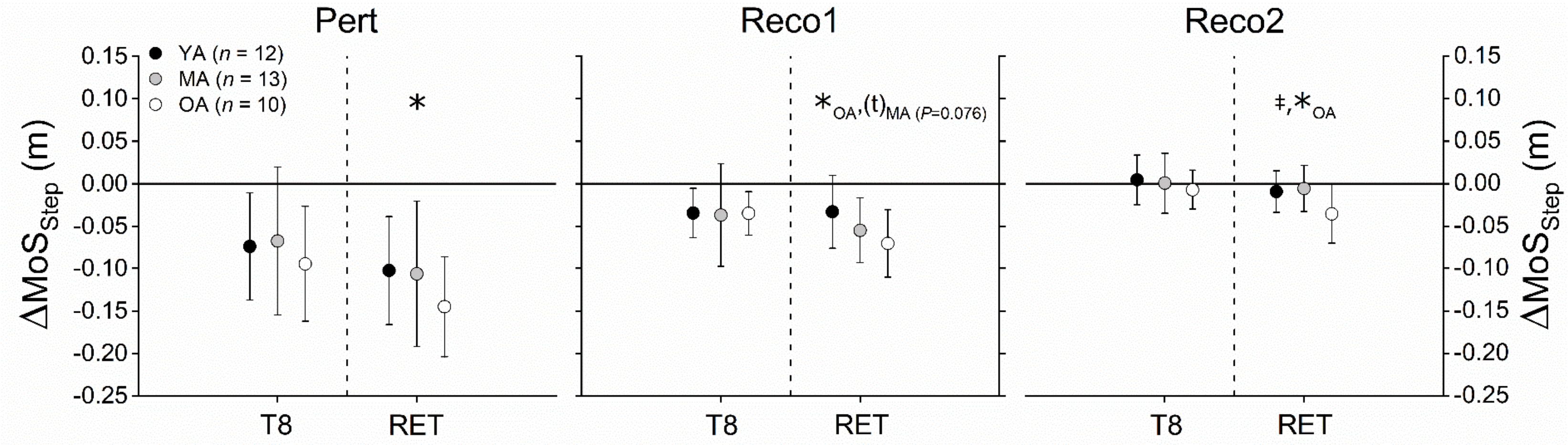

Figure 4: Margin of stability changes (ΔMoS_{Step}) for *trial 8* of the initial perturbation training session (T8) and the retention trial (RET). ΔMoS_{Step} values are referenced to baseline walking. Data are given for touchdown at perturbation (Pert) and for the following two recovery steps (Reco1 and Reco2) in young (YA; *n* = 12), middle-aged (MA; *n* = 13) and older adults (OA; *n* = 10). Values are expressed as means with SD error bars. Statistically significant differences at the level $P < 0.05$: ‡ = older compared to young and middle-aged adults; * = compared to *trial 8* of the initial perturbation training session. (t) = tendency to significance, *trial 8* of the perturbation-training session compared to the retention test trial ($P = 0.076$).

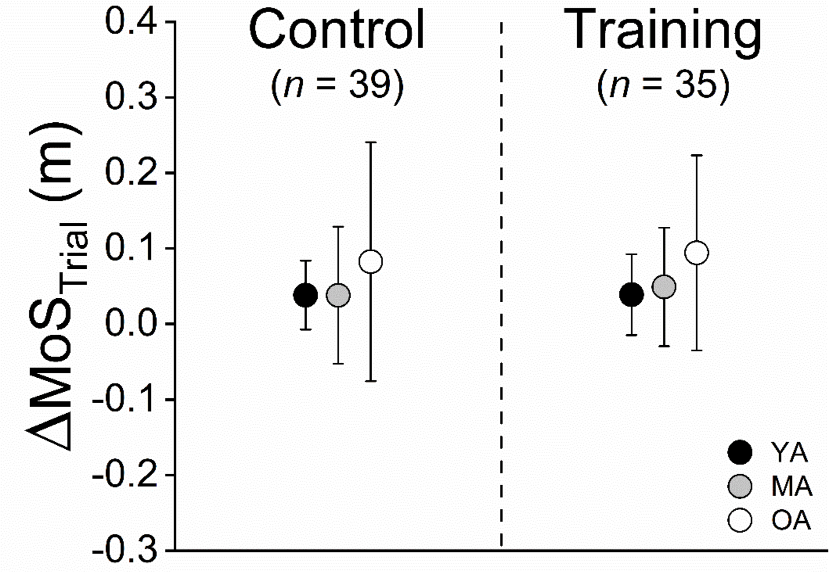

Figure 5: Margin of stability changes (ΔMoS$_{Trial}$) for touchdown of the recovery limb for the transfer lean-and-release task. ΔMoS$_{Trial}$ values are referenced to the first lean-and-release trial (i.e. before treadmill walking). Data are given for young (YA), middle-aged (MA) and older adults (OA) of the control group [unperturbed treadmill walking; *n* = 39 (14 young, 13 middle-aged and 12 older)] and perturbation-training group [single trip-perturbation session; *n* = 35 (12 young, 13 middle-aged and 10 older)]. Values are expressed as means with SD error bars.

5.6. Discussion

We aimed to examine acute adaptations of reactive gait stability control due to repeated trip-like perturbations, the retention of those adaptations over several months and transfer to an untrained reactive balance (lean-and-release) task in young, middle-aged and older adults. Our first hypothesis that adaptation to repetitive perturbation exposure would occur at a lower rate in old age was rejected since all age groups rapidly, and to a similar extent, improved their reactive gait stability control to the perturbation task (i.e. no differences in the trial-to-trial adaptation were found). However, our second hypothesis was confirmed in that older adults demonstrated a significant decrease in retention of acquired recovery response adaptations after 14 weeks (lower recovery performance in the retention test trial vs. *trial 8* of the training session), which was not observed for younger adults (though with a tendency for a decrease in the middle-aged group). Finally, despite robust gait adaptations, the perturbation training group did not show superior improvements in the untrained transfer task in comparison to aged-matched controls (no differences in ΔMoS_{Trial}). Hence, while the capacity for adaptation in reactive gait stability control remains high as people age and the acquired changes appear limited in their generalizability independent of age, retention of adapted stability improvements over a prolonged time seems reduced with aging.

5.6.1. *Balance recovery response and its adaptability to trip perturbation*

In *trial 1* of the perturbation-training session older adults needed more recovery steps (3 vs. 2) to regain positive MoS values compared to younger adults (Fig. 2), which is in line with previously reported deficiencies in the recovery response from sudden balance loss with aging (Karamanidis and Arampatzis 2007; Pai et al. 2010; Pavol et al. 2002; Süptitz et al. 2013). Note that for this study, and similar to previous work (Süptitz et al. 2013), we found a tendency for middle-aged adults to require one more recovery step to regain positive MoS compared to young adults (a difference that did not, however, reach statistical significance: $P = 0.085$), potentially indicating that the ability to cope with a sudden trip has already begun to deteriorate by middle age. The diminished recovery from tripping with increasing age has previously been associated with reduced ankle push-off for older adults (Pijnappels et al. 2005). Moreover, Epro et al. (2018a) recently found that in older adults higher triceps surae muscle strength and tendon stiffness contribute to enhanced recovery responses to an unexpected trip, highlighting a potential role in gait stability control for general age-related degeneration in leg-extensor muscle-tendon unit capacities (Karamanidis and Arampatzis 2006; Onambele et al. 2006).

After experiencing eight trip perturbations, all age groups improved their recovery response and needed fewer steps to regain positive MoS values following the trip-perturbation task (Fig. 2). More interestingly, we found no age-related differences in adaptation magnitude with respect to dynamic stability irrespective of perturbation trial with a plateau in improvement after only four perturbation trials (Fig. 3). Our results align with previous findings that show remarkable improvements in stability control after merely a single perturbation exposure (König et al. 2019; Marigold and Patla 2002; Owings et al. 2001) and similarly rapid recovery response adaptations to repetitive gait-slip perturbations for young and older adults (Pai et al. 2010). These results together suggest that although aging may reduce one's ability to cope with sudden perturbations to gait, older adults remain capable of developing robust balance control strategies after merely a few gait perturbations, which seems promising for application of trip/slip training to frail, clinical populations or groups limited in their tolerance of higher perturbation doses.

One might argue, however, that our perturbation paradigm may not permit a general conclusion regarding the effect of age on the adaptability of the human balance control system since task demand may have differed between age groups. Supporting this, we found remarkably lower MoS values during the first recovery step for older compared to middle-aged and younger adults in *trial 1* of the training session (-0.10 ± 0.10 m, -0.06 ± 0.03 m and -0.03 ± 0.05 m respectively; see also Fig. 2). To deal with this issue a subgrouping of data was arranged with young and older adults equal in MoS during the first recovery step in the initial perturbation trial. These stability-matched subgroups consisted of eight young and eight older adults with respectively the lowest and highest MoS values for the first recovery step (young, -0.06 ± 0.03 m; old, -0.06 ± 0.04 m). The subgroups still showed no differences in adaptation magnitude for dynamic stability irrespective of adaptation phase ($P = 0.75$). Thus our current perturbation paradigm revealed no evidence for age in having a negative effect on the rate of adaptation in reactive gait stability control, though the issue of (initial) task demand and its possible effects on adaptability should be examined in more detail in future investigations.

Given such rapid recovery response adaptations after merely a single perturbation trial, it seems reasonable to suggest that the observed improvements may be driven foremost by the central nervous system. Our perturbation paradigm consisted of repeated trip-like perturbations at unexpected times, provoking involuntary prediction errors that may stimulate the central nervous system to reorganise the motor programs relevant for stability control and hence increase the system’s robustness to similar future perturbations. Data from our previous study (Epro et al. 2018a) using the same setup does indeed indicate that the observed recovery response adaptations to the tripping task are accompanied by a refined neuromuscular control of the perturbed step. These may benefit performance during the subsequent recovery steps. That being said, it cannot be determined from the current findings whether the observed reactive adjustments to the external perturbation occur solely at a spinal level as in previous observations of motor output modulation, for example to repeated stumbling in complete low-thoracic spinal cats (Zhong et al. 2012) or in human infants prior to independent walking (Lam et al. 2003; Pang et al. 2003). Descending influence of supraspinal structures may also be involved (Dietz et al. 1985; Dimitrov et al. 1996; Jacobs and Horak 2007; Mochizuki et al. 2009; Wittenberg et al. 2017).

5.6.2. Retention of recovery response adaptations after single-session perturbation training

Aside from these short-term training effects, fall prevention strategies should target long-term retention of the acquired recovery-response adaptations. Previous studies demonstrated meaningful retention of improvements in reactive gait stability control over prolonged time periods (i.e. several months up to years) following exposure to a single session of gait perturbation in middle-aged (König et al. 2019) and older adults (Bhatt et al. 2012; Epro et al. 2018b; Pai et al. 2014). Nevertheless, after quite short periods of time (i.e. several minutes to days) gait adaptive changes have been shown to wane more rapidly in older compared to younger adults (Krishnan et al. 2018; Malone and Bastian 2016; Pai et al. 2010; Sombric et al. 2017). This provides evidence that, next to short-term adaptation, long-term retention of recovery response adaptations may be diminished, to some degree, by aging.

As expected, all age groups showed a retention in training effects from the single perturbation training session over 14 weeks as indicated by the improved recovery response in the retention test trial compared to the first novel trip perturbation trial (Fig.

2). However, whereas we found a minor but significant decrease in stability measures over time (*trial 8* of the training session vs. the retention test trial; Fig. 4) for the perturbed step for all age groups, only older adults demonstrated a significant drop in dynamic stability after the 14-week retention period for the first two recovery steps. Together these results indicate that, independent of age, single-session perturbation training leads to a partial retention in recovery response adaptations over several months, with a more prominent decay over time with aging. This was supported by a trend for a reduction in ΔMoS_{Step} over 14 weeks during the first recovery step for middle-aged but not younger adults ($P = 0.076$). One might argue that our result of a diminished ability to retain acquired recovery response adaptations with aging may be of limited importance in view of its marginal significance level ($P = 0.05$). Additional support for our main finding was, however, achieved when considering only young and older adults in our analysis since we found a highly significant trial by age interaction at $P = 0.01$. In order to investigate this further we analyzed additionally the recovery stepping behavior in the retention test trial, finding that older adults on average required one more recovery step to regain positive MoS compared to younger and middle-aged adults ($0.01 \leq P \leq 0.05$; note that there were no age-related differences in the number of recovery steps in *trial 8* of the training session). Therefore our results clearly suggest that although all age groups were able to adapt rapidly their reactive response to the trip-perturbation task to a similar extent (as indicated by the plateau in learning effects, Fig. 3), retention in those improvements over prolonged time seems diminished with aging. The ability to retain a learned motor skill has been shown previously to involve a distributed network within the central nervous system including the primary motor cortex (Cantarero et al. 2013; Centeno et al. 2018; Hadipour-Niktarash et al. 2007), and different to that engaged in motor task acquisition (Galea et al. 2011; Shadmehr and Holcomb 1997). Thus one possible explanation for the observed deterioration in the ability of older adults to retain perturbation training-induced adaptations may be inhomogeneous changes in brain function with aging (e.g. due to non-uniform regional brain changes; Raz et al. 2005), possibly affecting motor memory more than the ability to adapt motor behavior rapidly.

5.6.3. Transfer of recovery response adaptations to the untrained lean-and-release task

Although a vital aspect of neuromotor capacity is the ability to apply acquired adaptations from one situation to various contexts, the topic of inter-task transfer has rarely been investigated to date. In the present study we investigated potential transfer of balance recovery response adaptations after a single perturbation training session to the recovery from a sudden forward fall. The perturbation and lean-and-release tasks were chosen based on their shared stability control mechanisms (i.e. establishing a new base of support in the anterior direction and reducing the anterior velocity of the center of mass), possibly facilitating transfer of adaptations. However, despite such task similarities and the meaningful improvements (~70%) in reactive gait stability control following repeated exposure to unexpected gait-trip perturbations, participants from the perturbation-training group did not show superior adaptations to the untrained lean-and-release task compared to age-matched controls (no perturbation training, Fig. 5), meaning that inter-task transfer of acquired fall-resisting skills (at least from single-session treadmill-perturbation training) may be limited. We acknowledge that this might be achieved if the number of perturbation-training sessions were increased, though the dose-response relationship for generalizability of training effects from treadmill-perturbation training needs to be examined in future investigations. Further, given the slightly higher stability adaptations to the lean-and-release task in older adults compared to the two younger age groups (Fig. 5), one might argue that exposure to the novel transfer task required older adults to adapt more to the sudden balance loss due to possible age-related differences in task demand. Indeed we found negative MoS values during the recovery step only in the majority of older adults (whereas middle-aged and younger adults regained positive MoS already by the first step; data not shown). This is in line with our results for the trip-perturbation task. However, when excluding young and middle-aged adults from our transfer analysis we still found no differences in the stability improvements between the training and the control group ($t(73) = 0.24$; $P = 0.82$). Thus this single trial effect confirmed the above findings of a high adaptation potential of the human balance control system irrespective of age. One may conclude that the observed improvements for the perturbation training group in the ‘untrained lean-and-release task can be associated with rapid adaptability rather than transfer in recovery response adaptations from a single perturbation training session.

Transfer of acquired motor behavior across tasks has been associated previously with similarity in motor programs (i.e. the relative timings and weightings of muscle activity; Manoel et al. 2002). This is supported by the notion that generalizability of recovery response adaptations has been found for different conditions of the same task (e.g. from gait-slips on a moveable platform to an untrained slip on an oily surface; Bhatt and Pai 2009; Parijat and Lockhart 2012) assisted possibly by a more robust motor output (Santuz et al. 2018). Thus one might argue that despite certain task similarities, critical task parameters (e.g. muscle activity patterns, muscle-tendon unit lengths, body dynamics), and hence modular organization of motor output, still differ, thereby limiting inter-task transfer of training effects. A study of Rosenblatt et al. (2013) showed reductions in older adults’ trip-related, but not all-cause, falls after four sessions of treadmill trip-perturbation training. Combining those results with ours points to the need for more-specific exercise-based fall prevention training if fall risk in aged populations is to be reduced (Grabiner et al. 2014). Therefore one potential avenue of research may be to explore the neuronal correlates determining generalizability of adaptations to the balance control system in order to provide more closely targeted fall-prevention strategies. In summary, we put forward the hypothesis that motor task acquisition is rapid, task-specific and independent of age, but retention of these learning effects is age-dependent (Fig. 6).

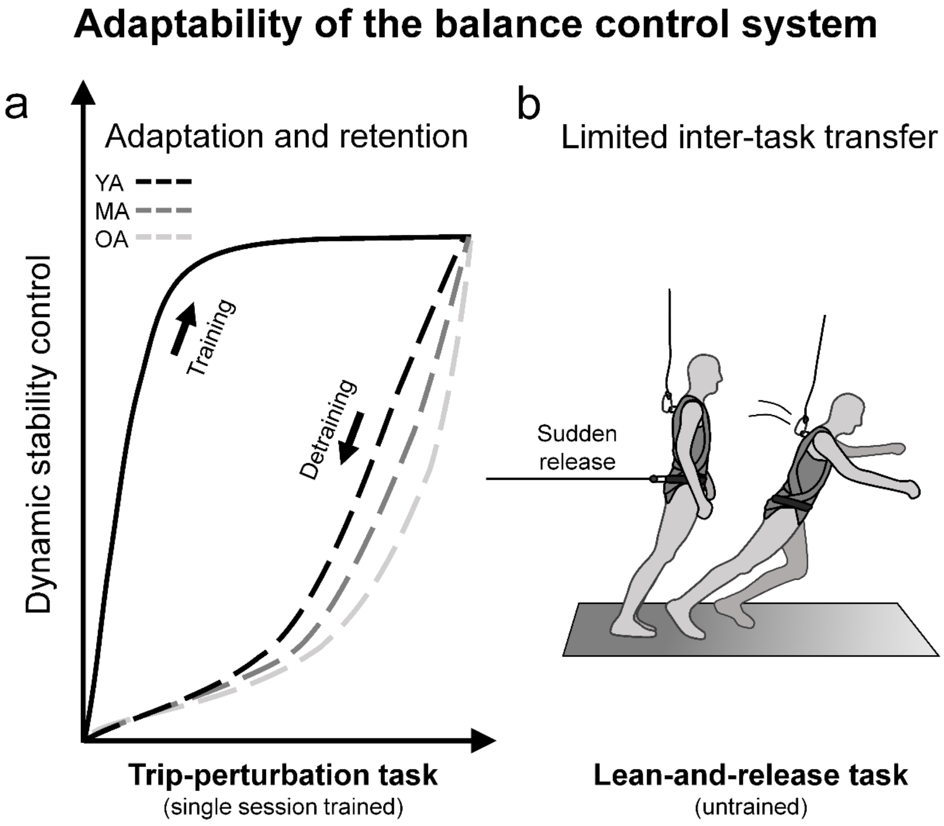

Figure 6: A schematic illustration of the adaptability of the human balance control system to trip perturbations. (a) While motor task acquisition may be independent of age as indicated by the observed similar rates and magnitudes of balance recovery response adaptations due to trip-perturbation training in young (YA), middle-aged (MA) and older adults (OA) (Training), retention of learning may diminish with increasing age (Detraining). (b) Although we observed meaningful reactive response adaptations to gait-trip perturbation training, we found no evidence for transfer of training effects to an untrained reactive balance task (the lean-and-release task), despite the similarity of the dynamic stability control mechanisms (i.e. establishing a new base of support in the anterior direction and reducing the anterior velocity of the center of mass). This suggests limited generalizability of acquired fall-resisting skills due to a single perturbation-training session.

5.6.4. Limitations

With regard to the applied perturbation paradigm, one might argue that the participants may have anticipated the perturbation onset after repeated practice of the task and thereby *predictively* modified their gait, favouring increased effectiveness of the recovery response (Pater et al. 2015). On account of this, trip perturbation was delivered only when participants' step length returned to individual baseline levels. Hence we observed no significant differences in MoS during the step prior to the perturbation (about 200 ms before perturbation) compared with baseline. That being said, while we argue that the perturbed step is primarily feedback-driven due to the short time window for possible predictive adjustments to gait after onset of the perturbation, adaptations in the subsequent recovery steps may be partially predictive. Thus we cannot fully exclude the possibility that laboratory settings involving perturbations may lead to a heightened state of awareness supporting (undetected) predictive adjustments of gait. Another potential limitation relates to a validity constraint of the MoS calculation (Hof et al. 2005), in that pendulum length (distance between axis of rotation and center of mass) may not always remain constant during perturbed walking due to possible knee joint angle changes during the ground contact phase. However, in our earlier trip perturbation studies (McCrum et al. 2014; Süptitz et al. 2013) we found no substantial changes in pendulum length during the trip perturbation trials, whereas intra and inter-individual variability in the recovery responses was large. Further, one might argue that generalizability of perturbation training effects cannot be disentangled from a 'single trial effect' to the transfer task which may vary between participants. However, the training and control groups were relatively large and homogeneous in their initial performances and therefore inter-subject variability is unlikely to have a significant effect on our main findings.

5.6.5. Conclusions

The present results indicate that although adaptability in reactive gait stability control remains effective across the adult lifespan, the retention of recovery response adaptations over time appears to diminish with aging, suggesting that initial adaptations to reactive gait stability control may not necessarily predict their long-term retention for different age groups. Moreover, these robust adaptations to trip-perturbation training did not further improve the performance in an untrained reactive balance task compared to age-matched controls. Therefore the generalizability of acquired fall-resisting skills from gait-perturbation training may be limited.

5.7. Disclosure of Interest

The authors report no conflicts of interest.

5.8. Acknowledgements

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5.9. Author contributions

M.K. and K.K. conceived and designed the research; M.K. and G.E. performed the experiments; M.K., G.E. and K.K. analyzed data; M.K., G.E., J.S., W.P. and K.K. interpreted the results of experiments; M.K. and K.K. prepared figures; M.K. and K.K. drafted the manuscript; M.K., G.E., J.S., W.P. and K.K. edited and revised the manuscript; M.K., G.E., J.S., W.P. and K.K. approved the final text.

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6. Fourth study | The inter-task generalisation of stability performance depends on the common synergies among different responses

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Key words: Locomotion, muscle synergy, perturbation training, dynamic stability, motor control

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6.1. Abstract

Generalisation of learning is key to effective stability control facing variety of postural threats in nature. We examined the dynamic stability and consistency in modular organisation of motor responses to different perturbations (i.e. unexpected gait-trip perturbations and subsequent loss of anterior balance in a lean-and-release protocol) in a group of young and middle-aged (n=57; age range 19-53yrs) to detect specific neuromotor factors regulating transfer of learning within the balance control system. We hypothesised that the motor system uses different modular organisation in recovery responses to tripping and lean-and-release, preventing positive transfer of adaptations in stability control. After eight trip-perturbations participants increased their dynamic stability during the first recovery step ($p<0.001$), yet they showed no superior improvement to the untrained lean-and-release transfer task compared to controls who did not undergo the perturbation exposure ($p=0.44$). Regarding the neuromuscular control of responses, only one synergy was shared for the gait-trip perturbation and lean-and-release tasks, revealing profound differences in both the timing and function of the recruited muscles to match the biomechanical specificity of different perturbations. Our results confirmed the hypothesis that the motor system uses different modular organisation in diverse perturbation responses, what possibly prevents inter-task generalisation of adaptations in stability control.

6.2. Introduction

Daily life locomotion is a challenging task facing countless situations that can interrupt movement consistency and stability. Thus to maintain its integrity when confronted by unpredictable perturbations the central nervous system is constantly required to modulate its motor output and hence increase the system's robustness to similar future perturbations[1–3]. Since postural threats are highly variable in nature, transfer of learned recovery mechanisms to new challenges thereby appears as particularly important for effective stability control[4]. This study aimed at unraveling neuromotor correlates of responses to sudden balance loss to broaden our understanding of factors regulating learning within the human balance control system.

Positive transfer of adaptations between different conditions of the same perturbation has been reported previously, i.e. from treadmill gait-slips to a 'novel' overground slip, or from training gait-slips on a moveable platform to an untrained slip on an oily surface[5–10]. In a recent study[11], however, we could demonstrate that this does not seem to necessarily be the case with *different* motor tasks. We found remarkable improvements in stability control from a single bout of trip-like gait perturbations. Despite this and similar required balance control mechanisms (i.e. establishing a new base of support in the anterior direction and reducing the anterior velocity of the center of mass), no benefit could be identified for the recovery performance after sudden balance loss in a lean-and-release protocol. Thus, while generalisation of learning is principally possible within the human balance control system, it may be limited if critical factors discriminate perturbation responses.

Muscle synergies have been increasingly employed over the last years for providing indirect evidence of a simplified, modular control of motor output[12–16]. By using few common activation patterns of functionally-related muscle groups or synergies, rather than muscle-specific commands, the neuromotor system may overcome the overwhelming amount of degrees of freedom available for accomplishing targeted movement[17]. An even larger simplification in motor control is reflected by the common sets of muscle synergies across different motor tasks[18,19], though 'task-specific' motor modules may occur when challenged with diverse biomechanical demands or perturbations[20,21]. Mixture of shared and specific synergies has been reported previously across different postural responses and tasks[22,23] or walking and standing perturbation responses[20]. In combination to previous findings of a rapid adaptability in basic activation patterns of the same synergies for robustness, as seen for the transition from unperturbed walking to walking on uneven or slippery ground[2,3,24], generalisation of learning may be driven by certain number of shared muscle synergies between tasks. In turn, transfer of adaptations to new challenges may be limited for tasks comprising mostly different spatiotemporal motor entities.

This study used the muscle synergy concept to examine the consistency in motor responses to different types of perturbation, i.e. trip-like gait perturbations and sudden loss of balance in a lean-and-release protocol, in order to provide answers to the question which factors are limiting inter-task generalisability of response adaptations. We hypothesised that the motor system uses different modular organisation in recovery responses to tripping and the lean-and-release task, preventing positive transfer of adaptations to stability control. This would indicate for the first time that the consistency of fundamental synergies between different motor tasks may determine the degree of learning generalisation.

6.3. Methods

6.3.1. Participants and experimental design

Fifty-seven young and middle-aged adults (36 men; age range: 19 – 53 years) took part in this study. Exclusion criteria were any neurological or musculoskeletal impairments of the lower limbs (e.g. joint pain during locomotion). The participants were healthy and regularly active (with an average self-reported physical activity level of 6.5 ± 5.7 $\text{h}\cdot\text{week}^{-1}$). The study was approved by the ethics committee of the London South Bank University (approval code SAS1826b) and met all requirements for human experimentation in accordance with the Declaration of Helsinki. All participants provided written informed consent after being informed about the procedures and possible risks of the study.

The participants took part in two different tasks – firstly a treadmill walking task and secondly a lean-and-release task. Thirty-nine participants were randomly assigned to a single session treadmill perturbation group (eight separate unexpected trip-like perturbations; PERT), and the remaining eighteen participants formed a control group (unperturbed walking only; CTRL). The two groups underwent equivalent periods of treadmill walking (20–25 min). After treadmill walking all participants were exposed to a lean-and-release task. Kinematics of the two tasks were recorded using an eight-camera optical motion capture system (120 Hz; QTM v2019.3; Qualisys, Gothenburg, Sweden). In order to examine the modular organisation of the balance recovery responses, the electromyographic (EMG) activity of 13 ipsilateral muscles was recorded for group PERT.

6.3.2. Gait perturbation task

Trip-like gait perturbations were applied during treadmill walking using a manually-controlled custom-built pneumatic brake-and-release system, similar to the one described in our previous studies[11,25–27]. To generate a trip, a constant restraining force of approximately 100 N (rise time about 20 ms) was applied to and removed from the lower left limb during swing phase via an ankle strap and Teflon cable. Treadmill-walking familiarization took place for all participants about seven days prior to the training session. The protocol began with the participants walking at a standardized velocity of 1.4 $m\cdot s^{-1}$ on a treadmill (Valiant 2 sport XL; Lode B.V., Groningen, The Netherlands) while wearing an ankle strap at each leg and a full-body safety harness connected to an overhead frame. After four minutes of walking[28], a baseline measurement (25 stride cycles of unperturbed walking) was recorded, from which twelve consecutive steps were used to determine the baseline for all analysed parameters[26]. Subsequently, the resistance was applied for one step (i.e. the perturbed step) and immediately removed during the following stance phase. The subsequent step with the contralateral right leg was defined as the first recovery step. The participants were not informed about the onset or removal of the resistance but were aware that walking was going to be perturbed at some points during walking. The perturbation was repeated eight times in total (eight *Trials*), separated by uneven two- to three-minute washout periods of unperturbed walking[11,25,26,29], with the *Trial 1* and *8* being considered for further analysis. These specific trials were considered as they represent the participants' initial and post-training performance. Note that the trial-to-trial changes within training have been reported previously in detail[11,29].

To assess dynamic stability during unperturbed and perturbed walking we used a reduced kinematic model[30], with five markers being placed to the following anatomical landmarks: seventh cervical vertebra and the greater trochanter and forefoot of the left and right legs. A fourth-order digital Butterworth filter with cut-off frequency of 20 Hz was applied to the 3D coordinates of the five markers. The anteroposterior margin of stability (MoS[31], a valid measure for biomechanical stability of human gait[32], was calculated at each foot touchdown for baseline walking, and the perturbed step and first six recovery steps after each perturbation as the difference between the extrapolated center of mass and the anterior boundary of the base of support (anteroposterior position of the toe projection to the ground). The reduced kinematic model used here has been demonstrated previously to be valid for dynamic stability assessment during trip-like perturbation to gait with the same age group and walking velocity as in the current study (with significant correlations with a full-body kinematic model of on average $r = 0.90$, $p < 0.01$ across steps)[30].

6.3.3. Lean-and-release transfer task

Directly after treadmill walking (within 10-15 minutes), participants were exposed to a single trial of the lean-and-release protocol involving sudden anterior balance loss in a separate laboratory setup. The same marker set as described above for trip perturbations was used. Arrangements to assess dynamic stability during a simulated forward fall has been described previously in detail[11,33]. Briefly, participants stood on a force plate (1080 Hz; 40 x 60 cm; Kistler, Winterthur, Switzerland) and, keeping their feet flat on the ground, were tilted forward via a horizontal inextensible cable attached at one end to a body harness and at the other end to a custom-built pneumatic release system[34,35]. Once the targeted inclination was reached (i.e. 33 ± 3% of the individual body weight, recorded via a load cell placed in series with the cable) and any possible anticipatory behavior had subsided (i.e. antero-posterior and medio-lateral weight shift regulation, recorded via center of pressure under the feet), the cable was suddenly released after a random time interval of 10 to 30 s. The instructions given to the participants were as follows: “Aim to regain balance within a single large recovery step with your right leg when released from the forward-leaning position”. The foot thereby always landed on a second force plate (1080 Hz; 40 x 60 cm; Kistler, Winterthur, Switzerland) mounted in front of the first. The right limb was pre-selected as recovery limb for every participant to allow for comparability of data to the gait perturbation task (note that resistance was applied to the left limb and hence the first recovery step was performed with the right limb for the gait perturbation task). The exact forward lean was chosen based on previous data using the same experimental setup[36], providing a balance challenging condition for the younger adults. The anteroposterior MoS at foot touchdown of the recovery limb was calculated as described above for gait perturbations. No practice trials were conducted to avoid learning effects in dynamic stability parameters and ensure novelty of the task[11,37]. Participants were secured by a full-trunk safety harness connected to an overhead track, allowing for forward and lateral motion while preventing contact of the body with the ground (with exception of the feet). The safety harness suspension cable incorporated a second load cell to ensure that measured MoS values were not affected by potential cable assistance (i.e. > 20% body weight placed on the safety device at touchdown of the recovery limb after the sudden release)[38].

6.3.4. Step cycle assessment

In order to compare the different motor tasks in group PERT, the first recovery step cycle was broken down into swing and early stance (i.e. energy absorption) by obtaining the foot toe-off, foot touch-down and minimum knee joint angle using kinematic, kinetic and accelerometer data. Foot toe-off during each task was estimated using the local maximum in the vertical acceleration of toe marker in relation to its minimum vertical position[39].

Foot touchdown was obtained via two different approaches: (1) in treadmill walking task by using the impact peaks of two 2D accelerometers (1080 Hz; ADXL250; Analog Devices, Norwood, MA, USA) placed over the tibia of each leg[40] and (2) for the lean-and-release task by determining the first instant when the vertical ground reaction force exceeded a threshold value of 20 N using force plate data. To define the termination of energy absorption, the minimum knee joint angle was determined for the right limb as the first local minima after foot touchdown of the sagittal plane angle between the greater trochanter, lateral femoral epicondyle and lateral malleolus markers[33]. The swing phase was then defined as the time period between foot toe-off and touchdown, and the early stance phase as the time period between the foot touchdown and the following minimum knee joint angle (Fig. 1).

Individual recovery step cycles were manually analysed by two independent examiners and trials were excluded from further analysis in at least one of the following cases to allow comparability of the data (either within the gait perturbation task or between different perturbation tasks): (i) the participant fell in one of the tasks or had to grasp the handrails of the treadmill in perturbed walking, (ii) elevating of the perturbed limb which itself counted as first recovery step in perturbed walking or use of the left leg as a recovery limb in the lean-and-release (iii) artefacts in the EMG signal. Then, for each of the three conditions, the remaining valid trials (28 for unperturbed walking, 27 for perturbed walking and 39 for lean-and-release) were considered for further analysis.

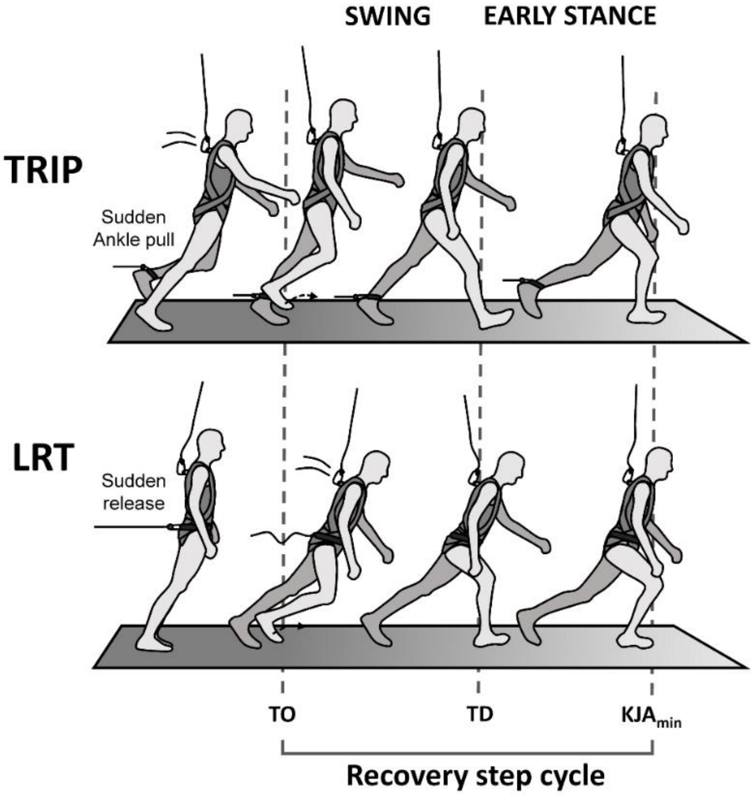

Figure 1. Step cycle assessment. In both tasks (TRIP, treadmill gait perturbation; LRT, lean-and-release) the first recovery step cycle was broken down into swing and early stance phase (i.e. energy absorption) based on the foot toe-off (TO), foot touch-down (TD) and minimum knee joint angle (KJA_{min}). The swing phase was defined as the time period between TO and TD, and the early stance phase as the time period between TD and the following KJA_{min}.

6.3.5. Modular organisation assessment

For each task, the EMG activity of the following 13 ipsilateral (right side) muscles was recorded at a sampling rate of 1080 Hz using bipolar surface electrodes with two synchronized 8-channel EMG systems (Bagnoli^{TM}; Delsys, Natick, MA, USA): *gluteus maximus* (MA), gluteus medius (ME), tensor fasciæ latæ (FL), rectus femoris (RF), *vastus medialis* (VM), *vastus lateralis* (VL), *semitendinosus* (ST), *biceps femoris* (long head, BF), *tibialis anterior* (TA), *peroneus longus* (PL), *gastrocnemius medialis* (GM), *gastrocnemius lateralis* (GL) and *soleus* (SO). The electrodes were placed over the midpoint of the muscle belly and further secured to the skin using an elastic tape to minimize motion artifacts. Before electrode placement, the skin over the muscle belly was carefully shaved and cleaned with ethanol to reduce skin impedance. Muscle synergies data were extracted from each participant for unperturbed walking, eighth perturbed walking and lean-and-release through a custom script (R v3.6.3, R Core Team, 2020, R Foundation for Statistical Computing, Vienna, Austria) using the classical Gaussian non-negative matrix factorization (NMF) algorithm[41,42]. The raw EMG signals were band-pass filtered within the acquisition device (cut-off frequencies 20 and 450 Hz). The signals were high-pass filtered, full-wave rectified and lastly low-pass filtered using a 4th order IIR Butterworth zero-phase filter with cut-off frequencies 50 Hz (high-pass) and 20 Hz (low-pass for creating the linear envelope of the signal) as previously described[2]. One randomly chosen unperturbed step cycle and the first recovery step cycle from the eighth perturbation trial and the lean-and-release trial were then selected for each participant. Note that only *Trial 8* of perturbed walking was considered for modular organisation analyses because this is the most relevant in terms of transfer, as it represents the ‘adapted’ post-training state. After subtracting the minimum, the amplitude of the EMG recordings obtained from the single trials was normalized to the maximum activation recorded for every individual muscle (i.e. every EMG channel was normalized to its maximum in every trial)[2,3]. Then, for each of the three conditions, every available cycle (28 for unperturbed walking, 27 for perturbed walking and 39 for lean-and-release; see *Step cycle assessment*) was concatenated (i.e. joined) to the others in a single EMG matrix. Each step cycle, one for every participant, was then time-normalized to 200 points, assigning 100 points to the swing (i.e. from lift-off of the right foot and until touchdown) and 100 points to the early stance phase (i.e. from touchdown and until the minimum of the knee joint angle)[2,3,43,44]. The reason for this choice is twofold[44]. First, dividing the step cycle into two macro-phases helps the reader to understand the temporal contribution of the different synergies, diversifying between swing and stance. Second, normalizing the duration of swing and stance to the same number of points for all participants makes the interpretation of the results independent from the absolute duration of the gait events. Synergies were then extracted through NMF as previously described[2,3,44]. For the analysis, we considered the

13 muscles described above (ME, MA, FL, RF, VM, VL, ST, BF, TA, PL, GM, GL and SO). The m = 13 time-dependent muscle activity vectors of all participants were grouped in a matrix V with dimensions m × n (m rows and n columns). The dimension n represented the number of normalized time points (i.e. 200*number of participants). The matrix V was factorized using NMF so that $V \approx V_R = WH$. The new matrix V_R, reconstructed multiplying the two matrices W and H, approximates the original matrix V. The motor primitives[42,45] matrix H contained the time-dependent coefficients of the factorization with dimensions r × n, where the number of rows r represents the minimum number of synergies necessary to satisfactorily reconstruct the original set of signals V. The motor modules[42,46] matrix W, with dimensions m × r, contained the time-invariant muscle weightings, which describe the relative contribution of single muscles within a specific synergy (a weight was assigned to each muscle for every synergy). H and W described the synergies necessary to accomplish the required task (i.e. treadmill walking or lean-and-release). The quality of reconstruction was assessed by measuring the coefficient of determination R^2 between the original and the reconstructed data (V and V_R, respectively). The limit of convergence for each synergy was reached when a change in the calculated R^2 was smaller than the 0.01% in the last 20 iterations[42], meaning that with this amount of synergies, the signal could not be reconstructed any better. This operation was first completed by setting the number of synergies to 1. Then, it was repeated by increasing the number of synergies each time, until a maximum of 10 synergies. The number 10 was chosen to be lower than the number of muscles, since extracting a number of synergies equal to the number of measured EMG activities would not reduce the dimensionality of the data. Specifically, 10 is the rounded 75% of 13, which is the number of considered muscles[3,47]. For each synergy, the factorization was repeated 10 times, each time creating new randomized initial matrices W and H, in order to avoid local minima[19]. The solution with the highest R^2 was then selected for each of the 10 synergies. To choose the minimum number of synergies required to represent the original signals, the curve of R^2 values versus synergies was fitted using a simple linear regression model, using all 10 synergies. The mean squared error48 between the curve and the linear interpolation was then calculated. Afterwards, the first point in the R^2-vs.-synergies curve

was removed and the error between this new curve and its new linear interpolation was calculated. The operation was repeated until only two points were left on the curve or until the mean squared error fell below 10^{-4}. This was done to search for the most linear part of the R^2-versus-synergies curve, assuming that in this section the reconstruction quality could not increase considerably when adding more synergies to the model.

The EMG dataset was created by joining together (i.e. concatenating) trials from different participants. The concatenation process suffers from a major drawback: the order of the concatenated trials can influence the extracted synergies. To account for this potential issue, we used a bootstrapping approach to create 1000 concatenations, each with randomly chosen individual trials, picked from those available and resampled with replacement (meaning that the trial from the same participant could be sampled more than once)[47].

We compared motor primitives by evaluating the full width at half maximum (FWHM) and the center of activity (CoA), two metrics useful to describe the timing of activation patterns[2,3,47,49–51]. The FWHM was calculated cycle-by-cycle as the number of points exceeding each cycle's half maximum, after subtracting the cycle's minimum and then averaged[51]. The CoA was also calculated cycle-by-cycle as the angle of the vector in polar coordinates that points to the center of mass of that circular distribution[50]. The polar direction represented the cycle's phase, with angle $0 \leq \theta \leq 2\pi$. The FWHM and CoA were calculated only for the motor primitives relative to fundamental synergies. A fundamental synergy can be defined as an activation pattern whose motor primitive shows a single main peak of activation[2]. In a case of two or more fundamental synergies are blended into one (or when one synergy is split into one or more synergies), a combined synergy appears. Combined synergies usually constitute, in locomotion data, 10 to 30% of the total extracted synergies. While fundamental synergies can be compared given their similar function (i.e. motor primitives and motor modules are comparable since they serve a specific task within the step cycle), combined synergies often differ from one another making their classification impossible. Due to the lack of consent in the literature on how to interpret them, we excluded the combined synergies from the FWHM analysis. The recognition of fundamental synergies was carried out by clustering similar motor primitives through NMF, using the same algorithm employed for synergy extraction with the maximum number of synergies set to the maximum factorization rank plus one. The obtained “principal shapes” (four for unperturbed and perturbed walking and three for lean-and-release) were then compared to the motor primitives in order to cluster similar shapes. A primitive was considered similar to one of the principal shapes if the NMF weight was equal at least to the average of all weights. Of all the primitives that satisfied this condition, we then calculated the R^2 with the relevant principal shape. If the R^2 was at least the 25% (or four times if the R^2 was negative) of the average R^2 obtained by comparing all the remaining primitives with their own principal shape, we confirmed the synergy as fundamental and classified it based on function. Primitives that were not clustered, were labeled as combined.

6.3.6. Statistical analysis

To assess the recovery response to gait perturbation for both analysed trials (*Trial 1* and *Trial 8*), separate one-way ANOVAs were performed to compare the MoS during baseline walking to the perturbed and following six recovery steps. To assess adaptations in the recovery response to repeated gait perturbation exposure, a two-way repeated measures ANOVA, with gait event (perturbed step and recovery steps 1-6) and perturbation trial (*Trial 1* and *Trial 8*) was applied for MoS at foot touchdown. In a case of significant main effects or interactions Bonferroni *post-hoc* corrections were implemented. The effect of repeated gait perturbations on balance recovery performance for the lean-and-release task was assessed by comparing MoS at touchdown of the recovery limb after sudden forward fall for groups PERT and CTRL using a t-test for independent samples. Further independent-samples t-tests were implemented to identify possible group-differences in age, body mass, body height and self-reported physical activity level. To evaluate differences in modular organisation of recovery responses for the two perturbations, we estimated the 95% confidence interval of the bootstrapped relevant parameters (i.e. factorization rank, reconstruction quality, FWHM and CoA) using the 2.5% sample quantile as the lower bound and the 97.5% sample quantile as the upper bound. Ten thousand resamples with replacement for each parameter were used to estimate the confidence intervals[47]. Moreover, we calculated the effect size Hedges' g. The approximate distribution of the effect size g was calculated from the bootstrapped sample pairs and confidence intervals (CI) were taken from this distribution as described above. Differences were considered significant when the zero was lying outside each CI. The level of significance was set at $\alpha = 0.05$, with all results presented as mean and SD. All statistical analyses were conducted using custom R scripts or SPSS software (26.0; IBM, Armonk, NY, USA).

6.4. Results

6.4.1. Dynamic stability changes to different types of perturbation

Four young participants fell after gait perturbation was applied (none of the participants failed to cope with the lean-and-release). Further eight gait perturbation trials did not meet the criteria to assure comparability of the data (see *Step cycle assessment*). Hence, the participants were removed from the dynamic stability analysis (both tasks). Accordingly, twenty-seven participants of group PERT and eighteen CTRL remained for adaptation and generalisation analyses. No significant differences were detected in participants' age (31 ± 9 vs. 30 ± 10 years), body height (177 ± 12 vs. 178 ± 9 cm), body weight (78 ± 15 vs. 79 ± 14 kg) or physical activity level (5.7 ± 4.7 vs. 5.4 ± 3.9 $\text{h}\cdot\text{week}^{-1}$) between PERT and CTRL groups.

For both analysed gait perturbation trials, the unexpected trip caused significantly lower (i.e. more negative; $p < 0.01$) MoS during the perturbed step compared to baseline (average value over twelve consecutive steps; Fig. 2), indicating less stable body configuration. In *Trial 1* the participants slowly increased their MoS (still different to baseline; $p < 0.05$) within the following three recovery steps and regained their baseline MoS at touchdown of the fourth recovery step (Reco4; Fig. 2). In *Trial 8* the participants regained baseline MoS already during the second recovery step (Reco2; Fig. 2). Assessment of adaptations in the recovery response to repeated gait perturbation exposure revealed a statistically significant trial x gait event interaction [$F(6,21) = 7.72$, $p < 0.001$]. When comparing *Trial 8* with the first (i.e. novel) unexpected perturbation, we found a significantly higher ($0.001 \leq p < 0.01$) MoS during the perturbed step and the following two recovery steps for all analysed participants (Pert and Reco1-2 respectively; Fig. 2), indicating smaller changes in MoS, and hence more complete recovery following repeated exposure to gait perturbations. The analysis of inter-task transfer of recovery response adaptations from repeated gait perturbation exposure revealed no statistically significant differences in MoS at touchdown of the recovery limb in the untrained lean-and-release transfer task between PERT and CTRL ($p = 0.44$; Fig. 2). Note that there was no difference in task demand (i.e. MoS at the instant of release) between groups.

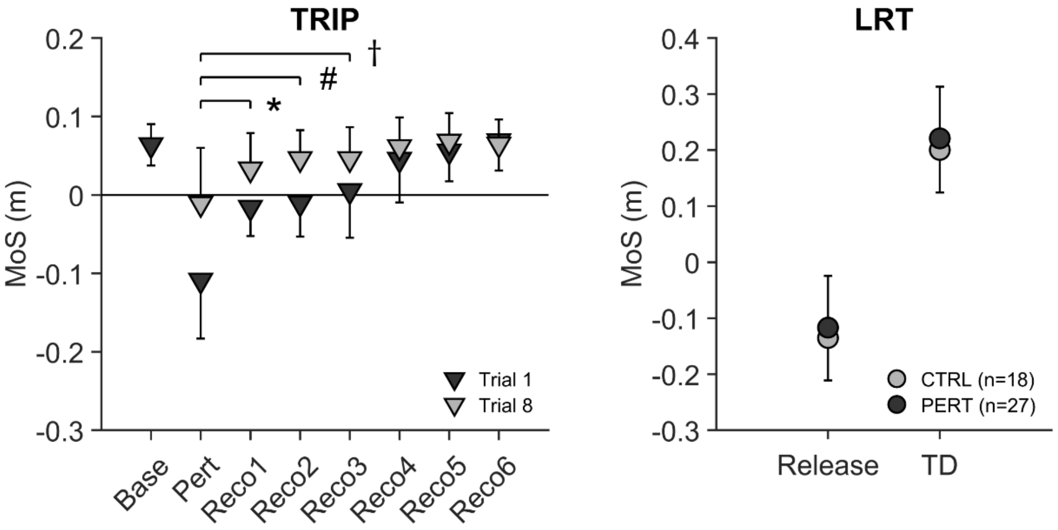

Figure 2. Margin of stability (MoS) during repeated gait perturbations (TRIP) and lean-and-release (LRT). Data for the TRIP task are presented for unperturbed baseline walking (Base), for foot touchdown (TD) at perturbation (Pert), and the following 6 recovery steps after the perturbation (Reco1-Reco6) in Trial 1 and Trial 8 for the PERT group. Data for the LRT task are given for the time points of release and TD of the recovery limb for the control (CTRL) and PERT groups. Values are displayed as mean with SD as error bars. † statistically significant ($P < 0.05$) difference between Trial 1 and Base; * statistically significant ($P < 0.05$) difference between Trial 8 and Base. $^{\#}$ statistically significant ($P < 0.05$) difference between Trial 1 and Trial 8.

6.4.2. *Modular organisation of recovery responses to different types of perturbation*

The minimum number of synergies necessary to reconstruct the resampled concatenated EMG data (i.e. the NMF factorization rank) was 4.1 ± 0.4 for unperturbed walking, 3.8 ± 0.4 for perturbed walking and 3.9 ± 0.6 for lean-and-release, with a significant difference only between unperturbed and perturbed walking (-6.7%, CI [-0.50%, -0.07%], g=-3.6). The average reconstruction quality (i.e. the R^2 or the EMG variability accounted for by the factorization) was 0.648 ± 0.031, 0.615 ± 0.03 and 0.510 ± 0.057 for the three tasks, respectively, with significant differences between all three (-4.9%, CI [-0.02%, -0.00%], g=-5.7 between the two walking tasks; -20.7%, CI [-0.20%, -0.11%], g=-15.9 between unperturbed walking and lean-and-release -16.6%, CI [-0.10%, -0.08%], g=-11.9 between perturbed walking and lean-and-release). The percentage of combined synergies was 15.2%, 8.9% and 26.6% for the three tasks, respectively.

Four fundamental synergies were clustered in both walking conditions, while three were clustered for the lean-and-release (Fig. 3). In walking, the first synergy functionally referred to the late swing, highlighting the relevant influence of knee flexors in unperturbed walking and of the hip abductors and flexors and the foot dorsiflexors in perturbed walking. The second synergy was associated with the touchdown, with a major involvement of the foot dorsiflexors to counteract the plantarflexion at heel strike and the mediolateral foot stabilizers. The third synergy identified the weight acceptance and showed the involvement of knee and hip extensors. The fourth and last synergy reflected the propulsion phase, highlighting the relevant influence of the foot plantarflexors. In the lean-and-release task, the first two synergies covered the early and late swing phase, respectively. The early swing was predominantly characterized by the contribution of foot dorsiflexors and hip abductors and flexors, similarly to what we found in the late swing phase of perturbed walking. The late swing saw the contribution of almost all recorded muscles. Note that the spatiotemporal characteristics of this specific synergy do not reflect the typical patterns of a late swing synergy (i.e. the primitive expands over the analysed stance phase, negligible contribution of foot dorsiflexors and hip flexors, and comparably high contribution of plantarflexor muscles), and hence has to be considered as different to unperturbed or perturbed walking). The third and last synergy, that of weight acceptance, included the contribution of knee and hip extensors, similarly to the weight acceptance synergy of the walking tasks. The synergy-by-synergy variability of individual bootstrapped motor modules is reported in Table 1. FWHM and CoA results are reported in Table 2 and Table 3. When comparing unperturbed and perturbed walking, primitives were narrower (i.e. lower FWHM) in the latter. The CoA shifted later in time in the late swing primitive and earlier in the weight acceptance and propulsion in perturbed walking (Tab. 2). The only comparable primitive of perturbed walking and lean-and-release (i.e. the one related to the weight acceptance) was wider in the latter.

6.5. Discussion

This study used the muscle synergy concept to examine the consistency in motor responses to different perturbations in order detect potential neuromotor factors limiting inter-task generalisability of fall-resisting skills. We found no benefit of improved stability control from repeated gait perturbations for the recovery performance in an untrained lean-and-release task. Profound differences in the spatiotemporal organisation of muscle activation patterns indicated a diverging modular control to the different perturbations (i.e. only one synergy was shared). These results confirm our hypothesis in that the consistency in modular organisation, i.e. the number of common synergies, in different perturbation responses may determine the degree of learning generalisation.

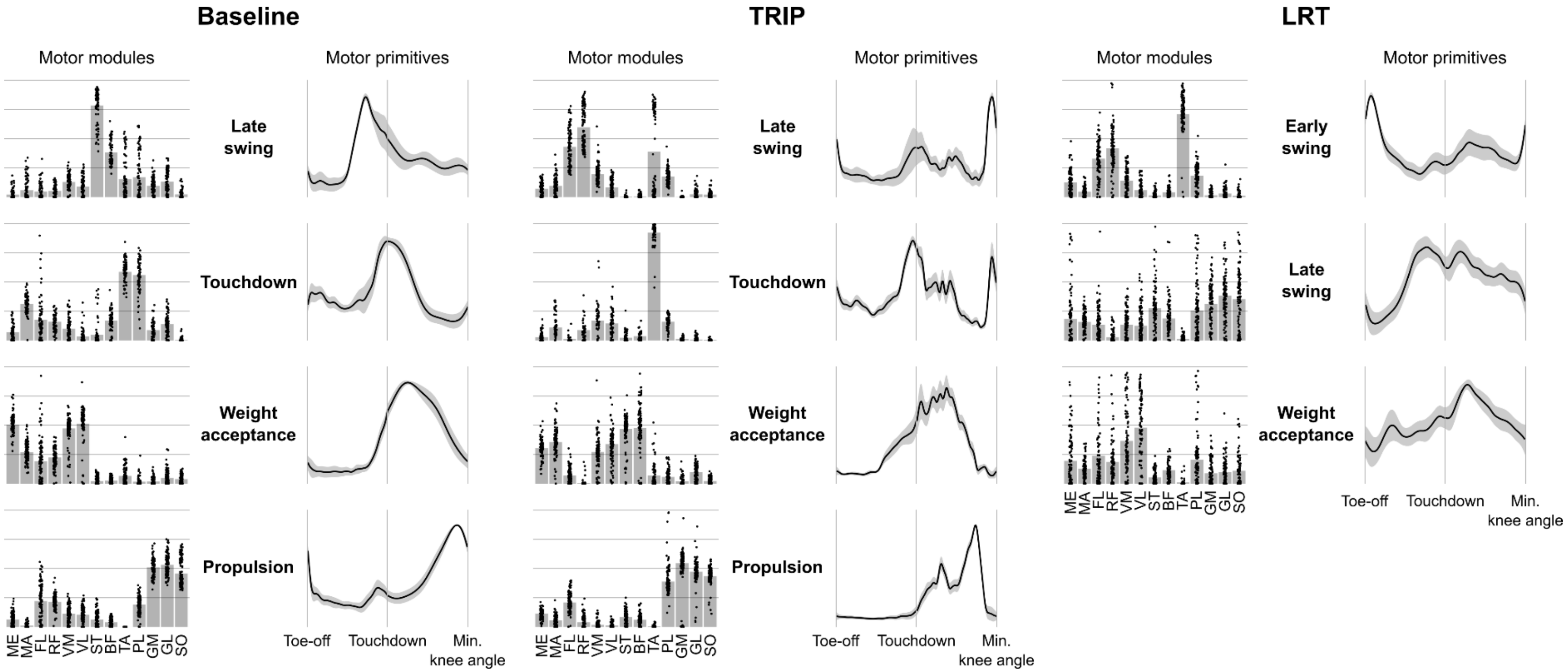

Figure 3. Bootstrapped motor modules and motor primitives of the fundamental synergies for unperturbed walking (Baseline), gait perturbation (TRIP) and lean-and-release (LRT). The motor modules are presented on a normalized y-axis base. Each muscle contribution within one synergy can range from 0 to 1 and each point represents 10 of the 1000 bootstrapped trials. For the motor primitives, the x-axis full scale represents the averaged step cycle (with swing and stance until the minimum of the knee angle normalized to the same amount of points and divided by a vertical line) and the y-axis the normalized amplitude. Muscle abbreviations: MA = *gluteus maximus*, FL = *tensor fasciæ latæ*, RF = *rectus femoris*, VM = *vastus medialis*, VL = *vastus lateralis*, ST = *semitendinosus*, BF = *biceps femoris*, TA = *tibialis anterior*, PL = *peroneus longus*, GM = *gastrocnemius medialis*, GL = *gastrocnemius lateralis*, SO = *soleus*.

Table 1. Estimating the variability of the motor modules for unperturbed (Baseline) and perturbed walking (TRIP) and the lean-and-release (LRT). Data are reported as the average of the standard deviation of all 13 muscles over the 1000 bootstrapped trials.

	Average variability		
Motor module	Baseline	TRIP	LRT
Early swing	Not present	Not present	0.084
Late swing	0.089	0.088	0.149
Touchdown	0.088	0.055	Not present
Weight acceptance	0.071	0.085	0.157
Propulsion	0.071	0.061	Not present

Table 2. Comparing bootstrapped full width at half maximum (FWHM) and center of activity (CoA) of motor primitives for unperturbed and perturbed walking. Data are reported as percentage differences between unperturbed and perturbed walking ($\Delta_{U,P}$ ± standard deviation). Positive differences ($\Delta_{U,P} > 0$) denote bigger values in perturbed walking, whereas negative differences imply the contrary. The Hedges' g effect size shows the bias-corrected standardized differences between unperturbed and perturbed walking means. Asterisks highlight the 95% confidence intervals (CI) which do not contain the zero.

	FWHM		CoA	
Motor primitive	$\Delta_{U,P}$	95% CI	$\Delta_{U,P}$	95% CI
Late swing	-34.7 ± 3.9%	[-20.9%, -13.4%]* (g = -12.7)	+26.6% ± 3.6%	[+30.7%, +53.4%]* (g = 10.3)
Touchdown	-41.3% ± 2.2%	[-27.2%, -22.1%]* (g = -26.9)	+1.5% ± 1.8%	[-2.2%, +5.3%] (g = 1.2)
Weight acceptance	-37.8% ± 2.1%	[-31.2%, -25.1%]* (g = -25.7)	-8.3% ± 0.6%	[-13.1%, -9.6%]* (g = -18.1)
Propulsion	-37.3% ± 2%	[-22.7%, -18.5%]* (g = -27.2)	-10.8% ± 0.7%	[-21.0%, -16.2%]* (g = -21.5)

Table 3. Comparing bootstrapped full width at half maximum (FWHM) and center of activity (CoA) of motor primitives for perturbed walking and lean-and-release. Data are reported as percentage differences between perturbed walking and lean-and-release ($\Delta_{P,L}$ ± standard deviation). Positive differences ($\Delta_{P,L} > 0$) denote bigger values in lean-and-release, whereas negative differences imply the contrary. The Hedges' g effect size shows the bias-corrected standardized differences between perturbed walking and lean-and-release means. Asterisks highlight the 95% confidence intervals (CI) which do not contain the zero.

	FWHM		CoA	
Motor primitive	$\Delta_{P,L}$	95% CI	$\Delta_{P,L}$	95% CI
Early swing	Not present in walking			
Late swing	+56.9% ± 3.2%	[+42.9%, +53.3%]* (g = 25.3)	-18.7% ± 3.7%	[-40.9%, -18.0%]* (g = -7.1)
Touchdown	Not present in lean-and-release			
Weight acceptance	+31.2% ± 2.8%	[+18.9%, +26.8%]* (g = 15.9)	-1.6% ± 1.5%	[-5.8%, +1.8%] (g = -1.5)
Propulsion	Not present in lean-and-release			

Repeated exposure to sudden gait perturbations led to a significant improvement of reactive balance control mechanisms, providing evidence to the hypothesis that changes in the natural environment stimulate our neuromotor system to rapidly adapt its motor output relevant for stability control, and hence increase the system's robustness to similar future perturbations[2,3]. While generalisation of adaptations in stability control between different conditions of the same perturbation (e.g. from treadmill gait-slips to a 'novel' overground slip) have been reported quite frequently in the past[7–10], this does not seem to be the case with all kinds of daily life postural threats. In line with our previous study[11], no benefit from repeated gait perturbation exposure could be observed for the recovery performance in an untrained reactive balance task, though similarity in required balance recovery mechanisms (i.e. establishing a new base of support in the anterior direction and reducing the anterior velocity of the center of mass) and demands for stability (Fig. 2). However, critical components in neuromotor control (e.g., module composition and time-coordinated recruitment of motor modules) may still discriminate perturbation types, possibly explaining the discrepancy between findings for learning generalisation from repeated gait perturbation exposure. Thus, although generalisation of learning is principally possible within the human balance control system, it requires a certain degree of similarity, if not consistency, between tasks which may be determined by factors other than shared limb mechanics seen at the macro level.

Here, we demonstrate that, while the two walking conditions showed a comparable modular organisation, as evidenced by similar amounts and characteristics of fundamental synergies, the lean-and-release task had only one common synergy with unperturbed or perturbed walking (i.e. the weight acceptance). In addition to limited similarity in modular control between walking and lean-and-release, for the latter we found a doubled variability in the motor module of the weight acceptance synergy. Thus, while the ability to choose from abundant 'motor-equivalent' solutions reflects adaptability, i.e. robustness, of biological systems[1,52], it may further aid to adapt different modular control to different perturbations.

Muscle synergies represent coordinated muscle activation patterns for functional movement[12–16]. While it is reasonable to suggest that the neuromotor system uses common sets of synergies to effectively and flexibly construct movement[18,19], also task-specific motor modules may occur when challenged with diverse biomechanical demands or perturbations[20–23]. The most important phase for balance recovery performance during the lean-and-release is the one from release until foot touchdown, because the MoS at touchdown determines the stability during stance[36,53]. Therefore, the ability to generate a hip joint moment in an appropriate temporal framework in the beginning of the swing phase is very important[54]. This biomechanical requirement is visible in the early swing synergy of the lean-and-release, showing a dominant contribution hip- and ankle flexor muscles. Therefore, we argue that from a neuromechanical point of view, this synergy is most important for successful balance recovery in the lean-and-release. However, it is absent in unperturbed and perturbed walking. Further, it is worth pointing out that the late swing synergy of perturbed walking shows a similar spatial (i.e. time-independent) profile to the early swing synergy of the lean-and-release, indicating different temporal recruitment of common motor modules for the two perturbations, and hence distinct modular control via modifications in activation timing. The observed discrepancies in the spatiotemporal organisation of the motor system reflected the neuromechanical specificity of perturbed walking and lean-and-release and may, therefore, explain the absent performance transfer between tasks. Hence, failure in learning generalisation may be driven by the limited similarity (i.e. number of common muscle synergies and temporally coordinated recruitment of motor modules) between perturbation responses. Though proof-of-concept via the assessment of generalisation between tasks sharing their modular organisation is yet to be performed.

Perturbation to gait was applied to unexpected time points, affecting the normal locomotor pattern. We found that, while both locomotion conditions, i.e. unperturbed and perturbed walking, showed a similar modular organisation, there was a substantial shift in time-dependent activation signals evoked by the perturbation. Specifically, we found a delay in the CoA of the first synergy (i.e. late swing) and earlier CoA in the weight acceptance and propulsion synergies when comparing perturbed with unperturbed walking, indicating that perturbation is unpredictable in its timing facilitating reactive stability control mechanisms for quicker step execution. This might explain also the lower FWHM in perturbed as compared to unperturbed walking possibly due to a bigger signal-to-baseline ratio in perturbed walking. These results align with the changes in activation signals but preserved motor modules during the unperturbed recovery step in unexpected slipping[55], providing evidence to the hypothesis that the central nervous system flexibly modulates the temporal activation pattern of a retained set of motor modules via descending commands[2,3,56,57], to respond to altered conditions of the same motor task.

A potential limitation of the present design may be the concatenation of trials from different participants because the order of the concatenated trials may influence the extracted synergies. One possibility to overcome this issue is to resample many times the order of concatenation. A solution that, for the present data set, led to an average number of extracted synergies lower than that obtained by concatenating the trials following the order given by the recording date (4 vs. 5 extracted synergies per condition; unpublished data). This clearly indicates that the order of concatenated cycles plays a role in the factorization process. Finally, the relatively low number of controls (n = 18) may foster inter-subject variability in recovery responses to the novel transfer perturbation task, and thereby reduce the potential for determining statistically significant generalisation. However, we found similar variability levels in MoS for group PERT (Fig. 2) though the group was quite large in size, and hence the size of the investigated sample may not be the primary driver for failure of generalisation from repeated gait perturbation exposure.

In conclusion, with this study using the muscle synergies concept, we shed new light onto potential factors regulating learning within the balance control system. Profound differences in the spatiotemporal organisation of muscle activation patterns, i.e. muscle synergies, indicate a diverging modular control to different perturbations, possibly preventing inter-task generalisation of adaptations in stability control.

6.6. Data Availability Statement

The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

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6.9. Author contributions

M.K., A.A. and K.K. conceived and designed the research; M.K. and J.W. performed the experiments; M.K., A.S., G.E., A.A. and K.K. analyzed data; M.K., A.S., G.E., J.W., A.A.

and K.K. interpreted the results of experiments; M.K., A.S., G.E. and K.K. prepared figures; M.K., A.S., A.A. and K.K. drafted the manuscript; M.K., A.S., G.E., J.W., A.A. and K.K. edited and revised the manuscript; M.K., A.S., G.E., J.W., A.A. and K.K. approved the final text.

6.10. Additional Information

Competing Interests Statement

The authors declare no competing interests.

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7. Main findings and discussion

This dissertation examined the adaptability and specificity of fall-resisting skills across the adult lifespan, with the perspective that the insight gained could improve both the effectiveness and efficicency of the assessment and training of fall-resisting skills. Taking the results of the individual studies together, a number of conclusions related to this overall aim will now be drawn. Subsequently, the limitations, practical relevance and perspectives for future research will be discussed.

7.1. Comparison of volitional and balance recovery stepping tasks for fall-resisting skills assessment

Prevention of falls will require sensitive, yet clinically applicable measures to identify those with limited capacity to recover from balance perturbations and to apply tailored interventions. The first part of this dissertation addressed the extent to which tasks assessing fall-resisting skills are tailored to resemble daily life challenges to balance. The results of the first study showed a gradual decline in the ability to perform a rapid, effective step in the anterior direction across the adult lifespan, independent of task complexity (i.e. volitional step execution vs. balance recovery stepping). These results are in line with diminished reactive stepping responses of middle-aged and/or older adults to a non-destabilising cue (Kurz et al. 2013; Luchies et al. 2002; Melzer and Oddsson 2004), sudden anterior balance loss (Karamanidis and Arampatzis 2007; Karamanidis et al. 2008; Thelen et al. 1997; Wojcik et al. 1999), slipping (Lockhart et al. 2005; Pai et al. 2010; Pavol and Pai 2007; Pavol et al. 2002; Tang and Woollacott 1998) and tripping (Joshi et al. 2018; Pijnappels et al. 2005; Schillings et al. 2005; Süptitz et al. 2013). However, although the two stepping tasks appear to share distinct motor control subtasks aimed at appropriate modification of the BoS in the anterior direction, volitional step execution outcomes could only partly explain differences in the balance recovery performance after sudden forward fall. When combining the present results with an earlier finding that volitional step characteristics fail to estimate older adults' ability to respond quickly to sudden balance loss (Luchies et al. 1999), it appears that volitional stepping tasks have only limited potential for discriminating between individuals with quite different reactive balance capabilities. Therefore, such volitional tasks may not be sensitive enough for application in clinical practice. This was further supported with the poor to moderate detected correlations between the results of the two tasks (only 13% to 27% of the variance in volitional step characteristics were related to the variance in balance recovery stepping performance), suggesting that the two types of task require different capabilities of the human neuromotor system. For example, faster motor output during compensatory limb movements may be explained by reliance principally on lower brainstem and spinal circuits, as suggested by the retained capacity for righting actions in decerebrate and complete-spinalized cats (Honeycutt and Nichols 2010; Zhong et al. 2012) and the occurrence of corrective stumbling responses in human infants before independent walking (Lam et al. 2003). However, there is emerging evidence for at least some involvement of the cerebral cortex in reactive balance control (Dietz et al. 1985; Dimitrov et al. 1996; Mochizuki et al. 2009; see Bolton 2015 and Jacobs and Horak 2007 for reviews) and therefore the issue should be examined in future investigations. This would also imply that when improvement of reactive balance control strategies are the goal, one might benefit more from specific, exercise-based approaches resembling unpredictable daily life challenges to balance (e.g. sudden trips or slips during walking) than from the general improvement of task-related volitional motor control strategies.

7.2. Retention and generalisability of recovery response adaptations to repeated trip-perturbation

The second part of this dissertation aimed to expand our knowledge about the adaptability of the human balance control system to both acute external influences (perturbations) and to longer-term internal neuromotor constraints (ageing), which may allow tailored recommendations for fall prevention. A gait-trip perturbation paradigm was used (Epro et al. 2018a, 2018b) in line with trips being one of the most common causes of falls in older adults (Luukinen et al. 2000). As expected based on the results of **Study 1**, older adults showed an initially reduced ability to cope with the tripping task, with a trend that this deterioration had already started by middle age. Diminished recovery from tripping with increasing age has previously been associated with a reduced ankle push-off function for older adults (Pijnappels et al. 2005) and hence with reduced triceps surae muscle-tendon unit capacities (Epro et al. 2018a). However, there is evidence that diminished neuromuscular control with aging may be the primary driver for the diminished dynamic stability control in older adults rather than a general decline in leg extensor muscle capacities (Arampatzis et al. 2008; Karamanidis et al. 2020).

Over the course of eight gait-trip perturbation trials, all age groups rapidly improved their recovery responses to a similar extent (up to 70%), with markedly improved MoS values already after single trip exposure and a plateau in training effects after four perturbation trials. Moreover, there was a significant retention of recovery response adaptations over 14 weeks, though there was a decay over time found for older adults which was not observed in younger adults (middle-aged showing a tendency for decay). These results suggest that, while the adaptability in reactive gait stability control remains highly effective as age increases, retention of recovery response adaptations over time seems to be diminished with ageing. This novel and important finding requires some elaboration - it has previously been pointed out that the ability to retain a learned motor skill involves a distributed network within the central nervous system (e.g. the primary motor cortex; Cantarero et al. 2013; Centeno et al. 2018; Hadipour-Niktarash et al. 2007), different to that engaged in motor task acquisition (Galea et al. 2011; Shadmehr and Holcomb 1997). Thus, one possible explanation for the observation that older adults can learn fall-resisting skills as well as young adults but retain less, may be inhomogeneous changes in brain function with ageing (e.g. due to non-uniform regional brain changes; Raz et al. 2005), possibly affecting motor memory more than the ability to adapt motor behaviour rapidly. Note that, next to ageing, perturbation practice dose seems to affect various aspects of learning. Specifically, the present results provide evidence for the hypothesis that to achieve such long-lasting adaptations in stability control, a certain amount of practice is required. Significant improvements in the recovery response to the trip perturbation task after 14 weeks could only be observed in a group of middle-aged that completed eight perturbation trials, but not after single trip exposure. This supports previous findings seen in slipping, where a single slip exposure without additional sessions was not sufficient to yield retention effects in gait stability over four months in younger adults (as compared to a higher perturbation dose comprising 24 slips; Bhatt and Pai 2009b). Although such retention of the “single trial effect” after slipping could be demonstrated for a group of community-dwelling older adults, these effects were significantly lower (~50%) than after training sessions with higher perturbation practice doses (i.e. 24 slips; Liu et al. 2017). In addition to that, ancillary “booster” sessions appear to further aid to these superior retention effects (Bhatt et al. 2012). Taken together, these results indicate that, whereas brief perturbation exposure may be sufficient to yield acute improvements to stability control, there seems to be a threshold for perturbation practice dose for provocation of adaptive changes in the human neuromotor system over several months.

Since postural threats are highly variable in nature, transfer of learned recovery mechanisms to new challenges is particularly important for effective stability control. While generalisation of adaptations in stability control between different conditions of the same perturbation task (i.e. from training gait-slips on the treadmill to a ‘novel’ overground slip, or from simulated slips on a moveable platform to an untrained slip on an oily surface (Bhatt and Pai 2009a; Lee et al. 2018; Parijat and Lockhart 2012; Wang et al. 2019c; Yang et al. 2013, 2018) have been reported quite frequently in the past, this does not seem to be the case with all kinds of daily life postural threats. Here, we found no benefit of improved stability control from single session gait-trip perturbation training for the recovery performance in an untrained lean-and-release task, independent of the investigated age group or study design. In **Study 3** of this dissertation young, middle-aged and older adults were exposed to the lean-and-release transfer task before *and* after the treadmill protocol, whereby one may not disentangle potential transfer of recovery response adaptations from a “single trial effect” for the lean-and-release task (Ringhof et al. 2019). Therefore, in **Study 4** the very same transfer task was carried out only after the treadmill trip-perturbation protocol. Yet no inter-task generalisation could be confirmed, though the similarity in required balance recovery mechanisms (i.e. establishing a new BoS in the anterior direction and reducing the anterior velocity of the CoM) and task demand. However, critical factors in neuromotor control (e.g. spatiotemporal organisation of muscle activation patterns or muscle synergies) may still discriminate perturbation types, possibly explaining the discrepancy between findings for learning generalisation from perturbation training. This would suggest that, although generalisation of learning is possible within the balance control system, a certain degree of similarity, if not consistency, is required between perturbation tasks, which may be determined by factors other than shared limb mechanics seen at the macro level. Together, this provides evidence for the hypothesis that more-specific exercise-based fall prevention interventions are required if fall risk in aged populations is to be reduced (Grabiner et al. 2014).

In this dissertation, the muscle synergy concept was used to examine the consistency in motor responses to different perturbation tasks in order detect potential neuromotor factors limiting inter-task generalisability of fall-resisting skills. Muscle synergies have been increasingly employed over the last years for providing indirect evidence of a simplified, modular control of motor output (Bizzi and Cheung 2013; Bizzi et al. 1991, 2008; Dominici et al. 2011; Lee 1984; Ivanenko et al. 2004; Janshen et al. 2017; Martino et al. 2015; Mussa-Ivaldi et al. 1994; Oliveira et al. 2012; Santuz et al. 2017a, 2018, 2019, 2020; Singh et al. 2018; Tresch et al. 1999, 2002). While it is reasonable to suggest that the neuromotor system uses common sets of muscle synergies to effectively and flexibly construct targeted movement (d’Avella et al., 2003; d’Avella and Bizzi, 2005), also motor modules may occur specific to the biomechanical demands of a given motor or perturbation task (Chvatal and Ting 2013; Chvatal et al. 2011; Munoz-Martel et al. 2019; Torres-Oviedo and Ting 2010). When investigating the consistency in modular organisation of the motor system during the recovery responses to tripping and sudden loss of balance from a forward-inclined position, we found that the different perturbation tasks had only one synergy in common (i.e. that of weight acceptance). However, since it has been pointed out previously that the MoS at touchdown of the recovery limb determines the stability performance in the lean-and-release task (i.e. single vs. multiple stepping behaviour; Arampatzis et al. 2008; Karamanidis et al. 2008), the ability to effectively generate appropriate hip joint moment during the phase from release until touchdown appears to be most important for this task (Arampatzis et al. 2011). While this biomechanical requirement was reflected in the early swing synergy of the lean-and-release task, it was absent in the recovery from tripping. Moreover, there was a shift in the temporal recruitment of similar motor modules (i.e. time-independent muscle activation profiles) for the different perturbation tasks, indicating distinct modular control via modifications in activation timing. From these results one may suggest that the discrepancies in the spatiotemporal organisation of the motor system stemmed from the neuromechanical specificity of investigated perturbation tasks and may therefore explain absence in performance transfer. Hence, learning generalisation within the balance control system may be driven by the similarity (i.e. number of common muscle synergies and temporally coordinated recruitment of motor modules) between perturbation responses. Though proof-of-concept via the assessment of generalisation between tasks sharing their modular organisation is yet to be performed.

7.3. Main conclusions

In conclusion, the results of this dissertation provide strong evidence that the adaptability of reactive gait stability control to single perturbation training session remains highly effective across the adult lifespan, counteracting the initially reduced abilities to cope with sudden perturbation to balance in older age. Further, it was found that these adaptations can be retained over prolonged time periods, though the degree of retention seems to be dependent on perturbation practice dose and age. We found that brief exposure to several unexpected trip-like gait perturbations, but not a single trip, can facilitate retention of improvements in reactive gait stability control over months, indicating that a finite number of perturbations may be required if long-term adaptive changes are to be provoked in the human neuromotor system. Following a training stimulus above this ‘threshold’, retention of recovery response adaptations over time was found to be diminished for adults older than 40 years, suggesting that initial adaptations to reactive gait stability control may not necessarily predict their long-term retention for different age groups. Finally, the robust adaptations in stability control could not benefit recovery performance in an untrained reactive balance task, suggesting task specificity of learning. Profound differences in the spatiotemporal organisation of muscle activation patterns, i.e. muscle synergies, indicate a diverging modular control to different perturbations, possibly preventing inter-task generalisation of adaptations in stability control.

7.4. Limitations

With regard to the applied perturbation paradigm, one might argue that it does not replicate a real-life trip situation and that this may possibly restrict generalisability of the observed improvements to gait stability control. Given the fact that gait-trip mechanics are highly variable in nature (i.e. depending on the obstacle and how and at which time point of the swing phase the foot hits the obstacle), makes it quite challenging to cover all different trip or stumbling events encountered during daily life with any single perturbation set-up. However, although the present results point to the fact that acquired adaptations in stability control from single session perturbation training appear to be limited in their generalisability, it cannot be inferred that such an intervention is not valuable for fall prevention in daily life. Several previous studies were able to demonstrate at least partial transfer of recovery response adaptations from single session treadmill slip- or trip-perturbation training to an actual (untrained) slip or trip during overground walking (Bieryla et al. 2007; Grabiner et al. 2012; Wang et al. 2019c; Yang et al. 2013). Combining these results with the ones of Rosenblatt et al. (2013), showing a reduction in trip-related falls after four sessions of treadmill trip-perturbation training over two weeks, one can assume transfer of learning from our treadmill-delivered trip-surrogate to (at least) trip situations in daily life. Nevertheless, this issue requires further investigation.

Concerning our analysis of gait stability control, there is reason to suggest that the participants may have anticipated the perturbation onset after repeated practice of the task and thereby predictively modified their gait (Bhatt et al. 2006; Marigold and Patla 2002;

Pavol et al. 2004; Wang et al. 2012; Wang et al. 2019a, 2019b), perhaps increasing the effectiveness of the recovery response (Oludare et al. 2018; Pater et al. 2015). In an attempt to account for this, trip-perturbations were separated by unequal two- to three-minute washout periods of unperturbed walking, delivered only when participants' step lengths returned to baseline levels on an individual basis (monitored in real-time with the anteroposterior movement trajectories of the toe markers). Hence, we observed no significant differences in MoS during the step prior to the perturbation (touchdown of the left leg; about 200 ms before perturbation) compared with baseline for any subject group or perturbation trial. Note that a relatively short window for potential predictive gait adjustments was used, since a functionally relevant effect of any anticipatory changes to the recovery performance from a sudden gait-trip would be expected during the step prior to the perturbation rather than two or three steps beforehand (normally > 1 s before perturbation). Unpublished data from previous experiments of our research group (Epro et al. 2018a) also indicate no significant differences in EMG activity of the main leg extensors (m. soleus, m. gastrocnemius medialis and m. vastus lateralis) between baseline walking and the two steps prior to the unexpected gait-trip perturbation. Notably, when comparing the modular organisation of step cycles from baseline walking and the recovery response in the *eighth* perturbation trial, we found a substantial shift in time-dependent activation signals evoked by the perturbation (i.e. centre of activation delayed in the late swing synergy and earlier in the weight acceptance and propulsion synergies), indicating that the perturbation is unpredictable in its timing facilitating reactive balance control mechanisms for quicker step execution. That being said, while the perturbed step appears to be primarily feedback-driven due to the short time window for possible predictive adjustments to gait after onset of the perturbation, it cannot fully be excluded that adaptations in the subsequent recovery steps due to repeated practice may be partially predictive. Moreover, it is worth noting that laboratory settings involving perturbations may lead to a heightened state of awareness and concentration supporting (undetected) predictive adjustments of gait.

Another potential limitation relates to a validity constraint of the MoS calculation (for a description see the *Introduction and outline* section and Figure 1 of this dissertation; Hof et al. 2005), in that pendulum length (distance between axis of rotation and CoM) may not always remain constant in the applied gait perturbation task (as for unperturbed walking) due to possible knee joint angle changes during the ground contact phase of the perturbed step and subsequent recovery steps. This may result in an alteration of pendulum length and hence pendulum mechanics. However, in previous experiments of our research group (McCrum et al. 2014; Süptitz et al. 2013) no substantial pendulum length changes could be observed during the trip-perturbation trials, whereas intra- and inter-individual variability in the recovery responses was large. Thus, this constraint does not present a substantial limitation. Further, it is mandatory to address the fact that in the present set of studies, an adapted simplified kinematic model was used, firstly introduced by Süptitz et al. (2013), where the anteroposterior position and velocity of the CoM is calculated by the trochanter markers and by accounting for the velocity of the trochanter markers and the trunk (defined by a marker placed on the seventh cervical vertebra) respectively. This previous study of our research group (Süptitz et al. 2013) demonstrated that a reduced kinematic model is able to assess the differences in recovery performance (changes in MoS at foot touchdown) during perturbed treadmill walking for the same three age groups, perturbation task and gait velocity as in the present setup in a similar manner to a twelve-segment, full body kinematic model (26 markers). No differences in the analysed dynamic stability parameters (extrapolated CoM and MoS) were found between the simplified reduced kinematic model and the full body kinematic model. The relative agreement between the full body kinematic model and the reduced kinematic model was supported by significant and relatively high correlations between these two methods to assess the extrapolated CoM at touchdown of unperturbed walking, of the perturbed step and the following six recovery steps (across steps and conditions in all age groups on average $r = 0.90$, $p < 0.01$).

Finally, one might argue that predefined rather than individualised maximal lean angles were used to determine stability performance in the lean-and-release task, possibly affecting our transfer analysis (**Study 3** and **4**). However, the specific study design was chosen to assess the benefit of adaptations from repeated gait-trip perturbations for a *novel* (i.e. untrained) challenge to balance. In contrast, in order to identify maximal lean angle (i.e. the threshold at which the recovery behaviour shifts from single- to multiple-stepping behaviour) large amounts of practice trials are required for every individual. Note that the participants were strongly encouraged to perform a single large recovery step after the sudden release and the same lean angles were used in both training and control group. It is worth pointing out that we found significant improvement in stability performance for lean angles of approximately 23% of the individual body weight (**Study 3**), indicating that the use of maximal forward-leaning angles would not have significantly affected our main findings. Further, when analysing performance-related parameters other than MoS (e.g. rate of increase in BoS) in **Study 4**, still no difference between perturbation training and control group could be observed (4.48 ± 0.57 vs. 4.21 ± 0.49 m s^{-1}; $p = 0.10$). Moreover, in a current multi-centre reliability study of our research group and others (manuscript *in preparation*), inter-day reliability of dynamic stability parameters was found to be low for the maximal lean angle protocol in older adults. The MoS values at touchdown of the recovery limb were 0.17 ± 0.01 m (average across trials; range -0.14 to 0.85 m; $n = 13$) during maximally obtained lean angles, suggesting that the protocol may be highly susceptible to both instructions given to the participants and intra-subject variability in motivation.

7.5. Practical relevance and perspectives for future research

The results of this dissertation shed new light on the specificity and adaptability (i.e. adaptation, retention and generalisability) of fall-resisting skills across the adult lifespan, which may have a major impact on the conceptualisation and implementation of future fall risk assessment and prevention measures. In the following sections, practical implications and possible avenues for future research are outlined.

7.5.1 Implications for assessing fall-resisting skills

The basis for tailored and effective prevention of falls are sensitive, yet clinically applicable measures to identify those with limited capacity to recover from balance perturbations. In that regard, different approaches to test a key strategy for balance recovery, namely rapid stepping, were considered in this dissertation. The present results appear to indicate that common volitional step execution tasks are of restricted use to predict one's balance recovery capability, i.e. task-specificity in assessing fall-resisting skills. Valid assessments therefore should include tasks involving sudden loss of balance and hence provoke reactive balance control mechanisms and/or low levels of task certainty, as is the case for many daily-life postural threats. In their prospective study on community-dwelling older adults, Carty et al. (2014) indeed could demonstrate good predictability for future fall risk of recovery stepping performance after a sudden loss of balance in the anterior direction. However, it is worth noting that volitional step tasks may be a helpful addition to tasks tailored to resemble daily-life challenges to balance for application to frail, clinical populations or within more holistic approaches to fall risk assessment.

7.5.2 Gaining knowledge on fall-resisting skills learning

The present dissertation expands our current knowledge on the adaptability of the human balance control system during perturbation training. When combined with the data from Epro et al. (2018a, 2018b), it can be concluded that single session treadmill trip-perturbation training comprising several repetitions can facilitate rapid adjustments in gait stability control in adults of different ages, which can be retained well over one year. A major finding of the present investigation was that this retention of improvements in stability control seems to be dependent on a person's age and perturbation dose, with a greater decay in adaptations over time with older ages and lower amounts of practice. Accordingly, from a practical point of view, ancillary "booster" sessions of only a few perturbation trials may be essential for both middle-aged and older adults, to counteract the greater decay in training effects or even cause superior enhancement (Bhatt et al.

2012). In this context, previous results in slip-resisting skills training (Bhatt and Pai 2009b) indicate that frequent ancillary sessions may be unnecessary for retention of recovery response adaptations up to four months, if the perturbation practice dose in the initial training session is sufficient (i.e. > 20 slips). On the other hand, this previous study could demonstrate preservation of training effects from single slip exposure over months, but only when regular ancillary sessions were completed by the participants. This seems promising for application of trip-/slip-resisting skills training to frail, clinical populations or groups limited in their tolerance of higher perturbation doses. However, more precise information about the dose-response relationship for various type perturbation training (e.g. amount, duration and magnitude of perturbation) is still required today (Karamanidis et al. 2020), which may help provide more effective and efficient perturbation paradigms for fall prevention.

Also, it is important to define whether and to what degree adaptations in stability control can transfer beyond the trained condition or task or can actually benefit recovery from daily-life trips or slips. Although many studies have investigated and confirmed generalisation of adaptations to the same perturbation task (i.e. *intra*-task-transfer) in the last years (Bhatt and Pai 2009a; Bieryla et al. 2007; Grabiner et al. 2012; Lee et al. 2018; Parijat and Lockhart 2012; Wang et al. 2019c; Yang et al. 2013, 2018), the topic of *inter*-task transfer has rarely been investigated to date. Hence, in two different studies of this dissertation we elaborated on this issue, demonstrating failure of transfer between different reactive balance tasks, independent of age and experimental design. Contradictions between findings requiring further investigation may be related to the diverging modular control to different perturbations, possibly preventing inter-task generalisation of adaptations in stability control. An issue that should be addressed in future research is the proof-of-concept via the assessment of generalisation between perturbation tasks sharing their modular organisation.

7.5.3 Implementing fall-resisting skills assessment and training

Successful application of task-specific slip- or trip-resisting skills training already has been frequently reported for older and older old adults living in the community (Grabiner et al. 2012; Liu et al. 2017; Okubo et al. 2019; Pai et al. 2010, 2014a; Wang et al. 2019a, 2019b), revealing remarkable reduction of daily-life falls risk of up to 50% (Pai et al. 2014b; Rosenblatt et al. 2013). Furthermore, such perturbation-based training approaches seem promising for application in frail or clinical populations at higher fall risk (e.g. Parkinson's disease, stroke, cerebellar or vestibular patients; Bhatt et al. 2019; McCrum et al. 2014; Nevisipour et al. 2019; Rand et al. 1998; van Duijnhoven et al. 2018; see Gerards et al. 2017 for a review), though the dose-response relationship in these individuals or groups may differ to those of healthy adults (Karamanidis et al. 2020). Given these positive examples of both effectiveness and efficiency of perturbation-based balance training aimed at the reduction of fall risk in specific population groups, considerations for application in society more broadly can be made.

With regards to the results of the present dissertation, showing that the deterioration in fall-resisting skills starts already with onset of middle age, one might argue that this population group specifically will not be covered by the above described fall prevention measures. However, middle-aged adults constitute the major age group of our ever-growing older populations (European Commission 2015). Considering that they form increasingly higher proportions of workforces among different countries (European Commission 2010), this may become a central socioeconomic aspect in two ways – falls in the workforce may considerably increase in the future, leading to (i) a reduced work output and (ii) an increased number of working days lost, challenging the occupational health care sector. In 2025, the EU's workforce is proposed to reach its oldest age, with twice as many workers at the age of ≥ 50 years as those aged ≤ 25 years (Ilmarinen 2001). As a possible consequence of this age shift, trip- or slip-related falls were already recognised in the literature as a common health risk to working populations worldwide (Chang et al. 2016). Specifically, such "falls on the same level" have been identified as the most common cause (14.4%) of all non-fatal accidents in the EU (European

Commission 2009), with higher frequency and/or severity (i.e. the number of working days lost) of work-related falls with increasing age (Bentley 1998; Buck and Coleman 1985; Kemmlert and Lundholm 1998; Yeoh et al. 2013). To prevent this major incidence of accidents at work, common occupational fall-prevention measures have focussed on a comprehensive environmental risk assessment and management, i.e. the elimination or mitigation of specific hazards associated with tripping or slipping (Bell et al. 2008; Haslam and Stubbs 2005; Verma et al. 2011). However, it is noteworthy that, despite a general reduction of non-fatal work-related injuries in the EU over the last decade (in-between 2008 and 2017 by about 13%; European Statistical Office 2019a), the relative proportion of fall-related accidents (including falls to a lower level) remained relatively stable (European Statistical Office 2016, 2019b). Similar observations can be made for the U.S. (Bureau of Labor Statistics 2017), pointing towards a pressing need for new, i.e. individual-based, approaches in future occupational health care.

The results of this dissertation clearly indicate that merely a single 25-min-session of repeated trip practice could be an effective and time-efficient add-on to existing fall prevention measures in occupational health care, strengthening one’s capacities against unavoidable or overseen external risk factors over several months. Further, such interventions appear to benefit different age groups, representing the whole working lifespan from career entrant to early retirement stage and, hence, young and middle-aged adults more broadly, which may not have been directly addressed by current fall prevention interventions. Therefore, it may be worth implementing single session trip- or slip-perturbation training within future occupational health care strategies. In this regard, definite recommendations can be made based on the present findings:

(i) regular fall-resisting skills assessment should provoke dynamic stability control mechanisms through balance loss and be conducted on a regular basis to identify individuals with limited capacity to recover from perturbations;
(ii) workers or occupations at higher fall risk may benefit from single session gait perturbation training on a yearly basis (e.g. in the context of a regular occupational health check);

(iii) middle-aged and older workers should be exposed to single ancillary sessions every four months to overcome the slightly greater decay in training effects;
(iv) single gait perturbation training should comprise different perturbation types (i.e. trips, slips) to match the multiple nature of daily-life falls.

In this context, it is mandatory to address the fact that an investigation of potential impact of the applied trip-perturbation setup in the sense of a proof-of-concept is still outstanding, though beneficial effects can be assumed here based on the observations derived from community-dwelling older adults (Rosenblatt et al. 2013). In that regard, future investigations should inform the utilisation of such long-term training effects not only within the context of standardised laboratory settings but also in daily life situations. These trials will require large sample sizes to have enough statistical power to detect the effects of training on daily life falls, in particular when evaluating the effects of training on specific types of falls (e.g. falls due to trips or slips).

8. References

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