Multiple Sclerosis and Related Disorders 35 (2019) 135–141

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard

Clinical trial

Adaptation to repeated gait-slip perturbations among individuals with multiple sclerosis

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ARTICLE INFO

Keywords:
Perturbation training
Fall prevention
Motor learning
Motor control
Dynamic gait stability

ABSTRACT

Background: Perturbation training, built upon motor adaptation and learning, has been increasingly used as a fall prevention paradigm in older adults. This training paradigm involves repeated externally-induced perturbations (like slips) to facilitate the error-driven learning of necessary motor skills for preventing falls. It remains unknown if people with multiple sclerosis can adapt to large-scale slip perturbations, which impedes the application of perturbation training in persons with multiple sclerosis. This study explored whether people with multiple sclerosis can adapt to large-scale repeated gait-slips.

Methods: Thirteen individuals with multiple sclerosis (the mean ± standard deviation of the Patient Determined Disability Steps: 2.27 ± 1.42) were exposed unexpectedly to a block of five repeated standard slips while walking on a treadmill. The outcome (fall or recovery) for each slip, as our primary outcome measure, was determined. A battery of secondary variables, including dynamic gait stability and gait parameters, were also calculated. Both primary and secondary variables were compared across trials.

Results: Our participants showed a rapidly reduced slip-fall rate (from 92.3% on the first slip to 30.8% on the fifth, $p < 0.001$). They mainly adopted proactive, assisted by reactive, strategies to improve dynamic gait stability, thus reducing the risk of slip-falls. The proactive adjustments, including shortened step, reduced foot landing angle, and flexed knee, shifted the center of mass anteriorly to be closer to the base of support. Such changes in center of mass position improved dynamic gait stability before the slip. Dynamic gait stability after the slip was also improved across trials, as a reactive strategy.

Conclusion: With practice, people with multiple sclerosis can adapt to large-scale, high-speed, gait-slips and acquire necessary skills against falls. Such skills primarily involve proactive strategy which is assisted by reactive strategy. The proactive strategy would shift the body's center of mass closer to the base of support, improving dynamic gait stability and reducing falls. Our findings could provide a theoretical foundation for deploying perturbation training to prevent falls in people with multiple sclerosis.

1. Introduction

Multiple sclerosis (MS) is the most common neurological disease leading to disability among young adults (Campbell et al., 2014). Falls are a significant concern in people with MS (PwMS) (Peterson et al., 2016). More than 50% of PwMS have fallen at least once in the past two months (Cattaneo et al., 2002). Despite the urgent need of fall prevention paradigms, very few effective programs are available to PwMS (Coote et al., 2014). It is imperative to develop effective fall prevention interventions aimed at this population.

Perturbation training has emerged as an alternative to the volitional performance-based intervention to prevent falls in the elderly (Gerards et al., 2017; McCrum et al., 2017; Pai et al., 2014) and stroke (Mansfield et al., 2018) populations. It involves repeated intentional and externally-induced perturbations (like slips) to facilitate the error-driven learning of necessary motor skills for preventing falls, rather than on self-motivated improvements of one's volitional performance. Perturbation training is considered an implicit learning process as it requires little explicit instruction or guidance (Pai et al., 2010). It also leverages the principle of training specificity (Aviles et al., 2019). A single session of repeated-slip exposure was shown to result in the acquisition of fall-resisting skills among young and older adults (Pai et al.,

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https://doi.org/10.1016/j.msard.2019.07.019
Received 15 February 2019; Received in revised form 30 June 2019; Accepted 22 July 2019

2010). During the training session, falls rapidly decreased within 3–5 trials for both age groups (Pai et al., 2010). Fall reduction has been attributed to both the proactive (*feedforward*) and reactive (*feedback*) strategies that participants adopted in response to repeated slips.

A proactive strategy involves the activation of postural adjustments prior to the occurrence of the perturbation-induced destabilizing forces. The proactive responses to repeated slips include a reduced step length, flat-foot landing, flexed knee, and forward-lean trunk at heel strike during gait (Cham and Redfern, 2002; Yang and Pai, 2013). These adaptative adjustments bring the body's center of mass (COM) closer to its base of support (BOS), enabling one to catch up with a forward slipping BOS without falling (Pai and Bhatt, 2007). The reactive control strategy is the activation of postural adjustments following the trigger of an external perturbation. A common reactive strategy is the effective recovery stepping after the slip occurrence (Pai and Bhatt, 2007; Mansfield et al., 2014).

The theoretical basis of perturbation training is motor adaption and learning (Gerards et al., 2017; McCrum et al., 2017; Pai et al., 2014; Bohm et al., 2015). The neural structures within the central nervous system (CNS) are fundamental for motor learning (Tomassini et al., 2011). Recovery from an external perturbation relies on the CNS's capacity for neural plasticity and its ability to acquire new motor skills. The MS-induced demyelination in the CNS may undermine the CNS's ability to learn new motor skills. As such, the capability of adapting to perturbations could be adversely impacted in PwMS. Therefore, it is essential to study if PwMS can adapt to large-magnitude external perturbations and learn new motor skills before applying perturbation training to this population.

Previous studies, based on gait rehabilitation (Baram and Miller, 2006; McGowan et al., 2017), low-intensity perturbation to a standing surface (Gera et al., 2016), and a hand movement task (Tomassini et al., 2011), have suggested that motor learning capacity is likely preserved among PwMS during the early stage of the disease. For example, a prior study exerted continuous and small-scale perturbation to the surface on which PwMS stood (Gera et al., 2016). The authors found that PwMS can acquire skills to keep the body's balance. The skills enable the body's COM to be shifted from a phase-lag to a phase-lead relationship with the moving surface (Gera et al., 2016). Another study adopting the same perturbation protocol reported that PwMS demonstrate a similar postural adaptation to healthy individuals (Fling et al., 2015). In a recent study, it was concluded that a single-session of throwing a medicine ball could lead to enhanced generations of the feedforward and feedback responses to maintain body balance in PwMS (Aruin et al., 2017). These findings raise a highly attractive prospect of applying perturbation training as a preventive tool to reduce falls among PwMS. However, a large-scale, high-speed, gait-slip is different than the tasks used previously and may require dissimilar motor planning and execution strategies. It still remains unexplored whether PwMS can adapt to gait-slips, hindering the application of perturbation training in PwMS.

Dynamic gait stability is a key risk factor of slip-related falls (Yang et al., 2009). Based on a conceptual framework (the feasible stability region theory, or FSR), dynamic gait stability is characterized by the kinematic relationship between the body's COM and BOS (Fig. 1) (Yang et al., 2008; Hof et al., 2005). Both aforementioned proactive and reactive response strategies improve dynamic gait stability and thus reduce the likelihood of falls after a slip. The examination of the adaptive changes in dynamic gait stability during repeated slips within PwMS could elucidate the mechanisms through which PwMS adaptively learn the new motor skills necessary for preventing slip-related falls.

The purpose of this study was to explore whether people with mild to moderate MS can adapt to unexpected standardized slip perturbations while walking on a treadmill within a single 5-slip session. Specifically, we investigated if PwMS, after repeated exposure to unexpected slips, have the capacity to (1) reduce the rate of falls and (2) improve their dynamic gait stability responding to the slips. We hypothesized that PwMS reduce their rate of slip-related falls after repeated slip exposure. We further hypothesized that they can learn how to proactively and reactively improve dynamic gait stability to reduce falls. The findings from this study could provide the theoretical evidence to apply perturbation training for the purpose of fall prevention in PwMS.

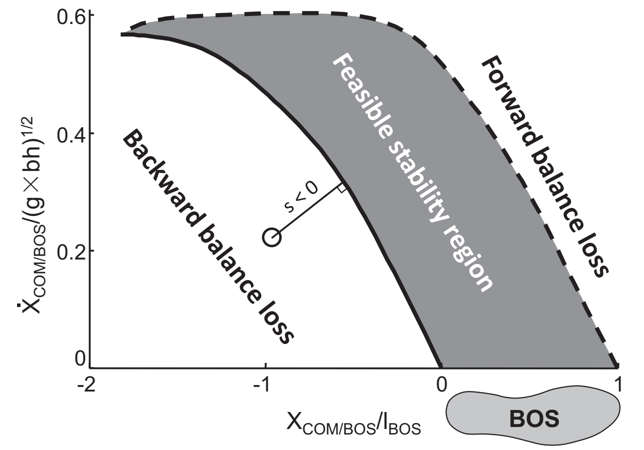

Fig. 1. Schematic illustration of the feasible stability region (FSR), which is enclosed by two boundaries: the threshold against backward balance loss (the lower boundary) and the threshold against forward balance loss (the upper boundary). Dynamic gait stability (*s*, the length of the thin line) is calculated as the shortest distance from the center of mass (COM) motion state (the combination of its position and velocity) to the threshold against backward balance loss. When a COM motion state is within the FSR, the stability is a positive value and this person is able to retain the body's balance without changing the present base of support (BOS). However, for a motion state below the threshold against backward balance loss, dynamic stability is a negative value. In this scenario, one would experience a backward balance loss possibly leading to a backward fall due to the insufficient forward momentum to carry the COM forward to the BOS. Conversely, as the motion state is above the threshold against forward balance loss, a forward fall could take place because of excessive forward momentum. Position and velocity of the COM relative to the BOS are *dimensionless* as a fraction of l_{BOS} and $\sqrt{g \times bh}$, respectively, where l_{BOS} represents the foot length, *g* is gravitational acceleration, and *bh* the body height. Dynamic gait stability is also a *unitless* quantity.

2. Materials and methods

2.1. Participants and experimental protocol

Thirteen individuals with MS were included in this cross-sectional study (Table 1). To be enrolled, participants had a neurologist-confirmed diagnosis of MS; a ≤ ·4 Patient Determined Disease Steps score; ability to ambulate independently without an assistive device; and no significant relapse within the past 8 weeks. Participants were further screened for exclusion due to cognitive impairment or bone mineral loss. Written informed consent approved by the Institutional Review Board was obtained from each participant. Participants experienced a 5-slip single-session perturbation protocol. The slips were standard across trials and participants to remove the possible confounding effect from uncontrolled perturbation intensity.

2.2. Slip perturbations

All participants walked five minutes on a treadmill as a warmup and familiarization session, in which their comfortable treadmill walking speed was determined. After a 10-min rest, they moved to the ActiveStep treadmill (Simbex, NH) and wore a safety harness tethered by ropes at the shoulders to an overhead arch (Fig. 2a) (Yang and

Table 1
Demographic and disease information of all 13 participants (8 females and 5 males) with multiple sclerosis (MS).

Parameter	Age (years)	Height (cm)	Mass (kg)	PDDS (/8)	Disease duration (years)	Cognition (/28)	Mobility (s)	Balance (/16)
Mean	48.9	166.5	81.1	2.27	12.9	3.9	10.8	12.7
SD	12.2	9.4	11.4	1.42	9.5	5.3	2.2	2.8

PDDS: Patient Determined Disease Steps.
SD: standard deviation.
Cognitive function was assessed using the Blessed Orientation-Memory-Concentration test (Folstein et al., 1975). The lower the score, the less likely the patient has cognitive disability.
Functional mobility was evaluated by the Timed-Up-and-Go test (Sebastiao et al., 2016). A shorter time used indicates a higher level of mobility.
Body balance was measured through the EquiScale test (Almeida et al., 2008). The higher the score, the better the body balance.

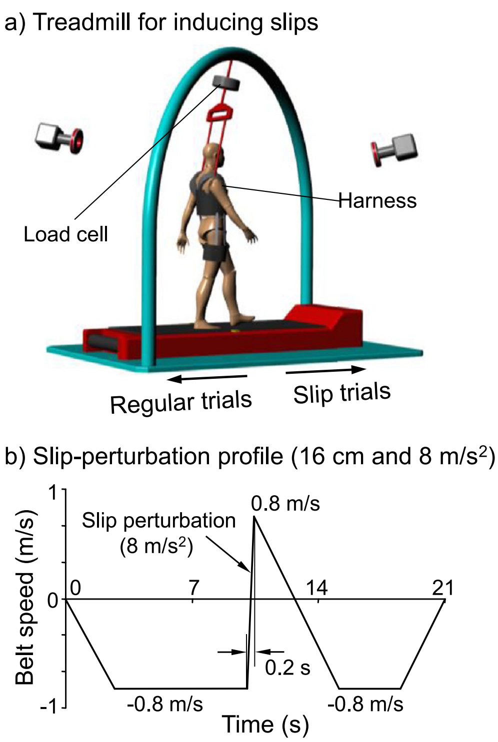

Fig. 2. Schematics of (a) the ActiveStep treadmill used to produce gait-slips and (b) a representative profile of the treadmill slip perturbation. For each participant, the perturbation level was standardized as the belt acceleration, peak slip velocity, and slip distance were 8 m/s^2, 1.6 m/s, and 16 cm, respectively. The initial belt speed was determined as each participant's self-selected gait speed on the treadmill. Following approximately 5 regular walking trials on the treadmill at their preferred gait speed, each participant was exposed to a block of 5 slip trials. Upon each slip trial, after ~6 regular steps and approximately 80–120 ms after the touchdown, the belt was suddenly accelerated to 0.8 m/s forward within 200 ms from 0.8 m/s backward. Participants were protected by a safety harness during all trials on the treadmill.

Pai, 2011). A loadcell connected to the ropes measured the force exerted on the ropes. Participants were informed that they would be performing normal walking initially and a "slip-like" movement on the treadmill later without knowing when and how that would happen. They were also told to try to recover their balance without grabbing onto the harness during any slip incidence, and then to continue walking.

After approximately five 15-second regular walking trials at their preferred speed on the treadmill, participants experienced the first slip. During the slip trial, following about 6 regular steps at the predetermined preferred speed and at the touchdown of the leading foot, without the participants' knowledge, the belt suddenly accelerated forward within 0.2 s, which induced a forward movement of the participants' BOS relative to their COM, generating an unexpected slip perturbation (Yang et al., 2013). The perturbation intensity was identical and standardized for all participants with an acceleration of 8 m/s^2, peak slip velocity of 1.6 m/s, and slip distance of 0.16 m (Fig. 2b). Following the first slip, each participant underwent four more consecutive slips. Full body kinematics data from 26 retro-reflective markers placed on participants' body were gathered using an 8-camera motion capture system (Vicon, UK), synchronized with the loadcell recording.

2.3. Data reduction and analysis

The slip outcome (fall vs. recovery), as our primary variable, was determined by the loadcell force. The slip outcome was classified as a fall if the peak loadcell force exceeded 30% body weight (*bw*) (Yang and Pai, 2011). If a fall did not occur, but the average loadcell force over any 1-second period after the slip onset exceeded 4.5% *bw*, this trial was deemed harness affected (Yang and Pai, 2011). Harness-affected trials would be removed from further analysis due to the uncertainty in determining what the outcome would have been if the harness was absent. The remaining trials were recovery (Yang and Pai, 2011). In this study, no trial was identified as a harness-affected trial.

The gait parameters, treated as our secondary outcome measure, were calculated based on marker trajectories, that were low-pass filtered at marker-specific cutoff frequencies (ranging from 4.5 to 9 Hz) using fourth-order Butterworth filters (Winter, 2005). The body COM kinematics were computed using gender-dependent segmental inertial parameters (de Leva, 1996). The two components of the COM motion state (i.e., its position and velocity) were calculated relative to the rear of the BOS (i.e. the leading heel) and normalized by foot length (l_{BOS}) and $\sqrt{g \times bh}$, respectively, where g represents the gravitational acceleration and bh the body height. Dynamic gait stability was calculated as the shortest distance from COM motion state to the threshold against backward balance loss (Fig. 1) (Yang et al., 2008). Two events: the touchdowns of the slipping foot (STD) and the recovery foot (RTD), were identified based on foot and sacrum kinematics. The STD and RTD were respectively considered pre-slip (proactive control) and post-slip (reactive control) events. The COM position, COM velocity, and dynamic gait stability were calculated at both events.

The pre-slip step length was determined as the actual distance travelled by the treadmill belt at two consecutive touchdowns (i.e., the STD and its preceding touchdown of the opposite foot). The post-slip recovery step length was obtained by subtracting the position of the recovery heel from the slipping heel at RTD in the anteroposterior direction. Both length measurements were normalized to *bh*. The trunk angle was calculated between the trunk segment and a vertical axis in the sagittal plane. A positive angle represents that the trunk leans backward against the vertical line. The knee joint angle was formed by the thigh segment and the extension line of the lower leg segment with flexion as positive. Foot angle was the angle between the sole and treadmill belt surface where a flat foot corresponded to zero degree and with toe up being positive. The foot and knee angles on the slipping side and the trunk angle were calculated at STD.

2.4. Statistical analysis

Generalized estimating equation (GEE) models were used to compare the primary and secondary outcome measures across trials to assess the adaptation performance to repeated slips. The trial was used as the factor for GEE analyses. A significant main factor effect was followed by post-hoc tests with Bonferroni correction (McNemar's tests for the primary outcome and paired *t*-tests for the secondary ones) between consecutive trials. In this study, no significant difference was detected between consecutive trials.

To further assess the adaptation throughout the entire session, we performed planned comparisons between trials one and five for all variables. McNemar's test was used for the primary variable and paired *t*-tests for the secondary. To explain the observed adaptive changes in COM position, Pearson's correlation analysis was used to examine the relationships of the COM position at STD with the pre-slip step length and foot angle at STD. All statistics were performed using SPSS 24.0 (IBM, NY) and the significance level was 0.05, unless otherwise specified.

3. Results

All thirteen participants completed the perturbation protocol and no adverse effect was reported. GEE results indicated that the fall rate exhibited a significant trial-related effect ($p < 0.001$, Fig. 3a, Table 2). It was reduced from 92.3% (12 fell among 13 participants) upon the first slip to 30.8% (4 fell) on the last slip ($p = 0.007$, Fig. 3a).

From the first to the last slip, participants shifted their COM anteriorly to be closer to the BOS at the instant of STD ($p = 0.002$, Fig. 4a). At STD, the COM was closer to the BOS at the fifth slip versus the first slip (-0.527 ± 0.224 at the first slip vs. -0.306 ± 0.305 at the fifth slip, $p = 0.004$, Fig. 4a). The COM velocity did not show significant changes across trials ($p = 0.088$, Fig. 4c). The COM velocity was comparable between the first and fifth slips (0.176 ± 0.058 vs. 0.181 ± 0.053, $p = 0.243$). As a result of the changes in the pre-slip COM position, participants shifted their COM motion state closer to the threshold against backward balance loss (Fig. 4g). Correspondingly, the pre-slip dynamic gait stability was improved significantly throughout the slips ($p = 0.006$). The stability value during the first slip was significantly smaller than during the fifth slip (-0.110 ± 0.069 vs. -0.011 ± 0.116, $p = 0.004$, Fig. 4e).

At RTD across the slips, participants showed changes in their COM motion state like at STD. The COM was continuously moved forward to be closer to the BOS throughout the five slips. The COM was significantly posterior to the BOS during the first trial versus the fifth trial (-0.246 ± 0.327 vs. -0.109 ± 0.166, $p = 0.033$, Fig. 4b). The COM velocity did not demonstrate significant changes across the trials ($p = 0.460$). Its value was -0.204 ± 0.071 during the first slip, analogous to the last slip (-0.198 ± 0.087, $p = 0.528$, Fig. 4d). The COM motion state at RTD moved closer and closer to the threshold against backward balance loss across the trials owing to the change in COM

Table 2
Detailed results of the statistical analyses for both the primary and secondary outcome measures. The generalized estimating equation (GEE) models were used to analyze the omnibus effect across trials. The planned McNemar's test and paired *t*-tests were adopted to compare respectively the primary and secondary outcome measure between the first and fifth slips.

Variable	GEE Wald χ^2	DOF	p	Planned McNemar's test or paired *t*-tests X^2 or t	DOF	p
Fall	20.81	4	< 0.001	6.13	1	0.007
COM position at STD	17.13	4	0.002	3.61	12	0.004
COM position at RTD	8.30	4	0.073	2.41	12	0.033
COM velocity at STD	8.10	4	0.088	1.23	12	0.243
COM velocity at RTD	3.62	4	0.460	0.65	12	0.528
Stability at STD	14.29	4	0.006	3.62	12	0.004
Stability at RTD	6.65	4	0.156	2.20	12	0.048
Step length	31.39	4	< 0.001	2.92	12	0.013
Recovery step length	2.56	4	0.629	1.36	12	0.198
Foot landing angle	17.22	4	0.002	2.72	12	0.019
Knee angle	6.43	4	0.169	2.01	12	0.068
Trunk angle	7.78	4	0.100	1.41	12	0.183

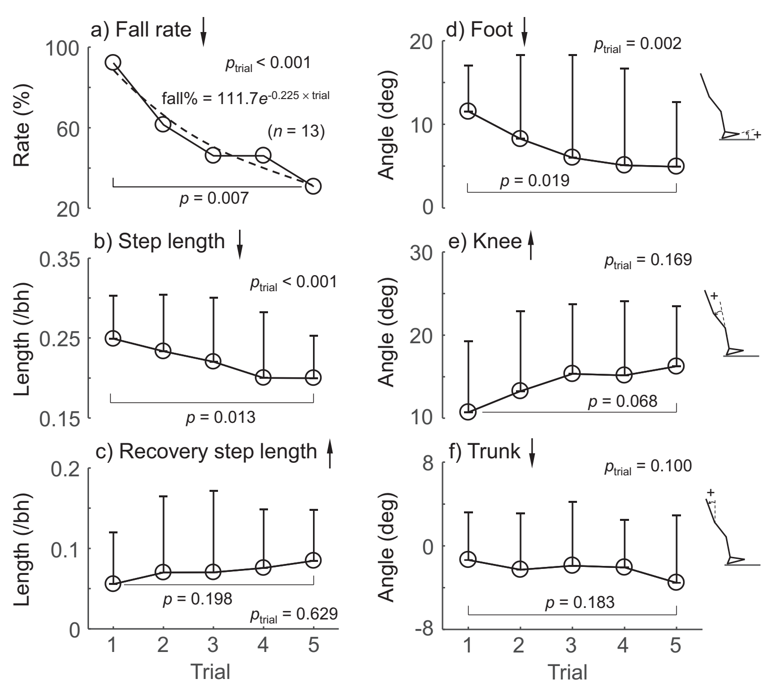

Fig. 3. Comparisons of (a) fall proportion, (b) step length prior to the slip onset, (c) the recovery step length post slip onset, (d) the foot landing angle on the slipping side prior to the slip onset, (e) knee angle on the slipping side prior to the slip onset, and (f) trunk angle before the slip onset across slip trials. The proportion of fall was calculated as the ratio of the number of fallers to the number of total participants and expressed as a percentage. The best-fit exponential relationship explained 94.5% of the variance in the percentage of falls. Both the step length and recovery step length were normalized to the body height (*bh*). p_{trial} represents the calculated probability for the main factor of trial based on the generalized estimating equation analysis. The p value is for the comparison between the first and the fifth slips. The direction of the vertical arrow specifies the desired direction of adaptative improvement of the corresponding variable.

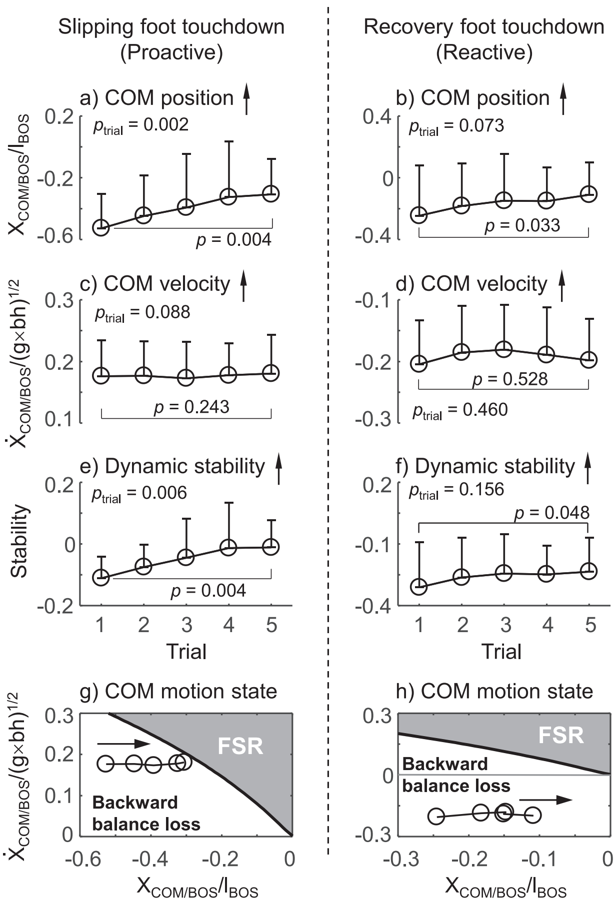

Fig. 4. Changes in the center of mass (COM) motion state across the slip trials. The left panel indicates the proactive changes (pre-slip) in the COM motion state while the right panel illustrates the reactive (post-slip) changes. The top three sub-figures in the left panel (a, c, and e) respectively represent the COM position, velocity, and stability at the instant of slipping foot touchdown. The top three sub-figures in the right panel (b, d, and f) demonstrate the same variables at the instant of recovery foot touchdown. Sub-figures (g) and (h) show the shift of the COM motion state with respect to the threshold against backward balance loss, respectively, at the slipping foot touchdown and the recovery foot touchdown from trials 1 to 5 within the feasible stability region theoretical framework. The arrow in (g) and (h) indicates the direction in which the COM motion state shifts throughout 5 trials. Both the COM position and velocity were relative to the rear edge of the base of support (BOS) and respectively normalized by foot length (l_{BOS}) and $\sqrt{g \times bh}$, where g represents the gravitational acceleration and bh the body height. Stability is calculated as the shortest distance from the given COM motion state (i.e. its position and velocity) to the threshold against backward balance loss in the FSR (Fig. 1).

position (Fig. 4h). Parallelly, dynamic gait stability significantly increased from the first to the last slip (-0.310 ± 0.220 vs. -0.235 ± 0.135, $p = 0.048$, Fig. 4f).

Participants tended to reduce their pre-slip step length across the slips ($p < 0.001$, Fig. 3b). From the first to last trial, their step length was significantly shortened (0.249 ± 0.054 vs. 0.200 ± 0.073 *bh*, $p = 0.013$). The recovery step length following the slip showed a trend of increasing across the trials, although this trend was not significant ($p = 0.629$, Fig. 3c). Across the trials, participants continuously reduced the foot landing angle at STD ($p = 0.002$, Fig. 3d). This angle was $11.6 \pm 5.5°$ during the first trial, significantly larger than during the last trial ($4.9 \pm 9.5°$, $p = 0.019$). As the trials progressed, participants appeared to flex their knee more at STD ($10.7 \pm 8.5°$ on trial 1 vs. $16.3 \pm 8.8°$ on trial 5, $p = 0.068$, Fig. 3e). Participants' trunk angle at STD did not show significant trial-related changes ($p = 0.100$) whereas displayed a trend of leaning more forward in the later trials compared

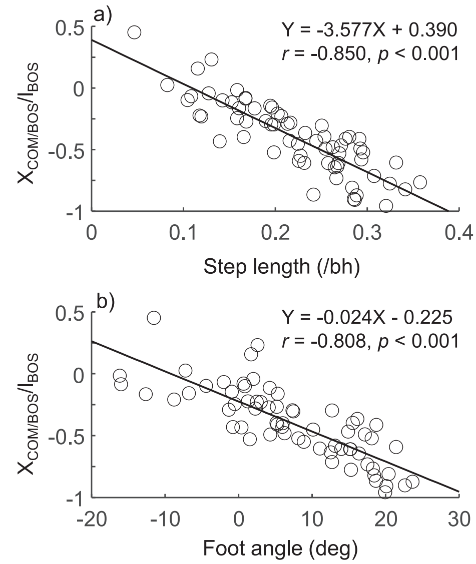

Fig. 5. Correlations between the center of mass (COM) position relative to the base of support (BOS) and (a) the step length as well as (b) the leading foot landing angle at its touchdown. Step length was calculated as the treadmill belt's actual traveling distance at two consecutive touchdowns and was normalized to body height (*bh*). Foot angle was defined as the angle between the sole and the belt surface where a flat foot corresponds to zero degree and toe up as positive. The COM position was relative to the rear edge of the BOS and normalized by foot length (l_{BOS}).

to earlier trials (Fig. 3f). At STD, the COM position related to the BOS was strongly associated with the pre-slip step length (Fig. 5a, $r = -0.850$, $p < 0.001$) and the foot landing angle (Fig. 5b, $r = -0.808$, $p < 0.001$).

4. Discussion

This study examined whether people with mild to moderate MS can quickly acquire the skills for resisting slip-related falls following repeated gait-slip perturbations. The results revealed that our participants were able to adapt to large-scale and high-speed slip perturbations within five slips. They acquired proactive and reactive strategies by adaptively adjusting the gait pattern and body posture to control stability.

The results supported our first hypothesis. About 92% participants fell upon the first slip. This rate rapidly decreased to 61.5% on the second slip and 30.8% by the fifth (Fig. 3a). Such findings are consistent with the observations among healthy adults (Pai et al., 2010). Our results suggest that the CNS among PwMS can implicitly adapt to slips and develop strategies to reduce their slip-fall risk. This implies that the capability of adapting to large-scale external perturbation is likely preserved among PwMS, at least in those with mild to moderate MS, reinforcing the findings from previous studies based on various motor tasks (Tomassini et al., 2011; Baram and Miller, 2006; McGowan et al., 2017; Gera et al., 2016). Our findings, for the first time, demonstrate that PwMS, with proper training, have the ability to improve the postural responses necessary for preventing falls induced by a large-scale gait-slip perturbation. These findings provide direct evidence prompting the application of perturbation training among PwMS.

The results also lend support to our second hypothesis. A series of gait-slips enables PwMS to adaptively improve their dynamic gait stability at both pre- and post-slip instants. These serve as the explanation of the reduced falls in the later slip trials. Based on the FSR theory, dynamic gait stability can be adjusted by altering the COM velocity and/or position relative to the BOS (Yang et al., 2008). In this study, the improvements in dynamic gait stability were primarily achieved by participants placing their COM closer to the BOS during later slips versus previous ones (Fig. 4a and b). When the COM is closer to the BOS, less forward momentum is required to allow the COM to reach BOS in order to keep body balance (Yang and Pai, 2013), thus lowering the likelihood of falling.

Our results suggest that the CNS among PwMS can proactively adjust the gait pattern in anticipation of an impending slip hazard based on prior knowledge of slips (Heiden et al., 2006). Among PwMS tested, the following strategies were adopted to translate the COM closer to the BOS: a short step, a flat landing foot, a flexed knee, and a forward-leaning trunk. Participants significantly shortened their step length from the first to the fifth slips (Fig. 3b). A reduced step length, which shifts the COM anteriorly and closer to the BOS, has been related to improved stability against backward falls (Yang and Pai, 2013; Espy et al., 2010). Our results demonstrate that the correlation between step length and COM position among PwMS is as strong as the one from healthy adults (-0.850 in the present study vs. -0.717 (Espy et al., 2010)) (Fig. 5a).

Another technique employed by our participants to transfer their COM anteriorly was the flat-foot landing. On average, participants reduced their landing angle by 6.3° during the last slip compared to the first (Fig. 3d). The reduced landing angle moves the COM closer to the BOS as it inversely correlates with the COM position (Fig. 5b), confirming the results from a past study based on analytical analyses (Yang and Pai, 2014). In previous studies, individuals who have had prior experience of a slip demonstrate a more flexed knee (Yang and Pai, 2013; Heiden et al., 2006) and a less backward (or more forward) leaning trunk segment as proactive adjustments to move the COM anteriorly (Yang and Pai, 2013; Yang and Pai, 2014). In our study, the knee flexion angle showed a marginal difference between the first and the fifth slips (Fig. 3e). Although the trunk angle did not show statistical changes from the first to the last slip, it indeed demonstrated a trend of leaning more forward in the later trials than in the earlier ones (Fig. 3f).

Participants were also able to improve their reactive control over dynamic gait stability after the repeated slips. At RTD, participants showed significantly less instability on the fifth slip than on the first. Thereby, they fell less on the fifth slip than on the first slip (Fig. 3a). The low instability on the fifth slip was achieved by shifting the COM closer to the BOS than the first slip (Fig. 4h).

After a slip, it is critical for one to take a recovery step (as a component of the reactive responses to a slip) in order to reestablish the BOS (Pai and Bhatt, 2007). The longer the recovery step, the larger the BOS and thus the more stable a person is. In this study, the recovery step length approximates a monotonical increase across the five slips, although this change did not reach a statistical significance. Such a non-significant result could be due to the small sample size. Another possible reason is that proactive adjustments serve to counteract the expected perturbation-caused destabilizing effect, reducing the reliance on reactive responses. Given the pronounced proactive improvements in stability, PwMS may not need substantial reactive modifications in the recovery step length to avert a fall.

It has been shown that PwMS, in general, can adapt to BOS perturbation with small-level forward-backward oscillation during standing (Gera et al., 2016). For example, PwMS acquired skills to anticipate the pattern of the perturbations and employ a feedforward control strategy so the body's COM shifted from a phase-lag to a phase-lead relationship with the moving surface (Gera et al., 2016). Such a finding does not necessarily apply to the postural task control after a large-scale and high-speed external perturbation, in particular a slip. Specifically, the amplitude of the support surface movement was between 7 and 15 cm and the oscillation frequency was 0.5 Hz in the previous study (Gera et al., 2016). The estimated peak velocity of the BOS was about 5 cm/s. Such a low perturbation scale does not require participants, during the adaptation process, to step and establish a new BOS in order to restore balance. In contrast, the perturbation was a 16-cm displacement with a 1.6-m/s peak velocity of the BOS in our study. Participants must take a recovery step to reestablish body balance following the perturbation. Furthermore, body posture was always bilateral and the limb movement was symmetrical in the previous study (Gera et al., 2016). Body posture is asymmetric during gait, however. These differences might require dissimilar motor planning and execution strategies. Our findings not only concur with the one from previous study (Gera et al., 2016), but extend our knowledge of the capability of CNS in PwMS to adapt to a new task (i.e., a large gait-slip perturbation).

The clinical implication of our findings is that perturbation training could be a promising fall prevention paradigm for PwMS. First, perturbation training induces involuntary gross errors that cannot be corrected solely by volitional performance. Experiencing such errors is essential for the CNS to recalibrate an existing internal representation of the environment (the FSR in this study). Second, volitional-performance based interventions lack the opportunity for someone to improve their reactive control of stability. Third, the perturbation-induced adaptive process appears to take place in just a few slips, much faster than the ones required by conventional exercise-based paradigms (weeks or months) to reduce fall risk. Last, perturbation training offers task specificity to the recovery actions required for fall avoidance (Grabiner et al., 2014). To recover body balance following a postural disturbance, the human body needs to create quick reactions. Training that targets such balance recovery actions is more effective than general exercise in improving body balance (Grabiner et al., 2014; Mansfield et al., 2010; Carty et al., 2015). Previous studies reported that task-specific training shows better outcomes when compared with other types of methods (such as strengthening or aerobic exercises) in improving body balance among PwMS (Cattaneo et al., 2007). Given that most falls occur during locomotion, like walking (Peterson et al., 2016), the perturbations induced during gait could be more meaningful than other interventions in reducing the risk of falls.

Importantly, previous studies claimed that PwMS profit more from implicit motor learning compared with explicit motor learning, possibly owing to cognitive deficits in PwMS (Tomassini et al., 2011). Motor skills acquired during implicit learning likely become automatic with practice and can be performed with little conscious awareness as opposed to explicit learning which pertains to acquisition of factual knowledge. Given that perturbation training is an implicit learning process (Pai and Bhatt, 2007), it could be more practically relevant to PwMS to prevent falls.

To make perturbation training an effective and clinically meaningful intervention for preventing falls in PwMS, the motor skills against falls learned from perturbation training should be retainable over a significant period and generalizable to different environments and contexts other than the one in which the training is completed. Earlier studies documented that healthy adults can retain the skills acquired from a single-session perturbation training in a laboratory environment for up to 12 months (Pai et al., 2014) and transfer such skills to different tasks (such as from slips to trips) (Wang et al., 2012) or contexts (such as from treadmill to overground slips) (Yang et al., 2018). As a result, perturbation training can reduce all-cause falls in the real life conditions for up to one year (Pai et al., 2014). However, due to the damage to the CNS, the capability of retaining and generalizing the adaptative motor skills acquired from perturbation training could be impaired among PwMS. Future studies should be conducted to inspect these issues for PwMS.

Our study has its limitations. First is the small sample size. This may represent a barrier for us to generalize our findings to the general MS community. Second, the lack of an age- and gender-matched healthy group may compromise our understanding of the degree to which the motor learning is preserved among PwMS in comparison with healthy individuals. Whereas, former studies adopting a similar slip perturbation protocol among healthy adults reported alike results, in which healthy individuals can drastically reduce the proportion of falls in subsequent slips by proactively and reactively improving dynamic gait stability (Pai et al., 2010). Both issues warrant more studies based on a greater sample size. This exploratory study provides a steppingstone for future research.

5. Conclusion

As an initial attempt to examine how people who are mildly to moderately affected by MS adapt to gait-slip perturbations, this study discovered direct evidence supporting the preserved ability of acquiring new motor skills in PwMS to adapt to repeated external perturbations. It sheds light on the feasibility of applying perturbation training as an intervention for fall prevention in PwMS.

Declaration of Competing Interest

None declared.

Acknowledgements

This research was partially supported by the National Multiple Sclerosis Society through a pilot Research Grant (NMSS-PP3385) and the Georgia State University Neuroscience Institute through a Seed Grant. The authors thank Edson Estrada and Maria Sanchez for assistance in data collection, and Jennifer Lees and Rebecca Ban for editing.

Role of the funding source

This study was partially supported by the National Multiple Sclerosis Society and Georgia State University Neuroscience Institute. The funding sources have no roles in study design, in the collection, analysis and interpretation of data, in the writing of the report, and in the decision to submit the article for publication.

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