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Somatosensory impairment of the feet is associated with higher activation of prefrontal cortex during walking in older adults

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ABSTRACT

Background: Over-activation of prefrontal cortex during walking has been reported in older adults versus young adults. Heighted activity in prefrontal cortex suggests a shift toward an executive control strategy to control walking. A potential contributing factor is degraded functioning of pattern-generating locomotor circuits in the central nervous system that are important to walking coordination. Somatosensory information is a crucial input to these circuits, so age-related impairment of somatosensation would be expected to compromise the neural control of walking. The present study tested the hypothesis that poorer somatosensation in the feet of older adults will be associated with greater recruitment of the prefrontal cortex during walking. This study also examines the extent to which somatosensory function and prefrontal activity are associated with performance on walking and balance assessments.

Methods: Forty seven older adults (age 74.6 ± 6.8 years; 32 female) participated in walking assessments (typical walking and obstacle negotiation) and Berg Balance Test. During walking, prefrontal activity was measured with functional near infrared spectroscopy (fNIRS). Participants also underwent somatosensory testing with Semmes-Weinstein monofilaments.

Results: The primary findings is that worse somatosensory monofilament level was associated with greater prefrontal cortical activity during typical walking ($r = 0.38$, $p = 0.008$) and obstacle negotiation ($r = 0.40$, $p = 0.006$). For the obstacle negotiation task, greater prefrontal activity was associated with faster walking speed ($p = 0.004$). Poorer somatosensation was associated with slower typical walking speed ($p = 0.07$) and obstacles walking speed ($p < 0.001$), as well as poorer balance scores ($p = 0.03$).

Conclusions: The study findings are consistent with a compensation strategy of recruiting prefrontal/executive control resources to overcome loss of somatosensory input to the central nervous system. Future research should further establish the mechanisms by which somatosensory impairments are linked to the neural control and performance of walking tasks, as well as develop intervention approaches.

1. Introduction

Over-activation of brain networks during cognitive and motor tasks is a common finding in older adults versus young adults (Reuter-Lorenz and Cappell, 2008; Cabeza et al., 2002), including in the prefrontal cortex during walking (Hawkins et al., 2018; Mirelman et al., 2017; Chen et al., 2017; Chatterjee et al., 2020). Over-activation means that for the same level of task difficulty, the older adult brain will have to recruit relatively more neural resources to achieve comparable task performance compared to younger brains (Reuter-Lorenz and Cappell,

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2008). For cognitive tasks, prefrontal over-activation in older adults has been attributed to neural inefficiency within that network and/or compensatory recruitment to overcome other under-performing brain networks (Reuter-Lorenz and Cappell, 2008; Cabeza et al., 2002; Pelicioni et al., 2019). However, in the context of walking, potential causes for brain over-activation are more numerous. Causes may include factors both within the brain and at lower levels of the neuraxis. One theory is that prefrontal over-activation is a compensatory strategy that emerges due to a loss of "automaticity" in the neural control of walking and balance (Clark, 2015). Automaticity refers to the use of specialized locomotor circuits in the central nervous system (e.g., in the spinal cord, brainstem, and cerebellum) that produce the complex patterns of neuromuscular coordination needed for walking and balance (Clark, 2015; Dietz, 2003; McCrea and Rybak, 2008). These circuits spare the recruitment of higher order cerebral processes to control walking. When circuits of automaticity are compromised, there may be a compensatory shift toward higher order processing in prefrontal/executive control regions (Clark, 2015).

Somatosensory afferent information is a crucial source of neural input to the aforementioned pattern-generating circuits (Fallon et al., 2005; Frigon and Rossignol, 2006; Frigon, 2017; Hiebert et al., 1996; Guertin, 2012). For example, somatosensory information from cutaneous receptors in the feet is continuously integrated with the spinal central pattern generator during walking (Pearson, 2004; Duysens and Pearson, 1976; Forssberg et al., 1975). These somatosensory signals strongly impact the timing and amplitude of events within the gait cycle (Frigon and Rossignol, 2006). Given the important role of somatosensation to control of walking, it is concerning that impaired somatosensation is common in older adults (Mold et al., 2004; Shaffer and Harrison, 2007). A prior study found bilateral somatosensory deficits in approximately 26% of individuals 65–74 years of age, 36% of individuals 75–84 and 54% of individuals age 85 and older (Mold et al., 2004). Many research studies have also reported significant associations between somatosensory impairment and deficits in gait and balance function, as well as increased fall risk (Mold et al., 2004; Resnick et al., 2000; Lipsitz et al., 2018; Cruz-Almeida et al., 2014).

The objective of the present study is to test the hypothesis that poorer somatosensation will be associated with greater levels of prefrontal recruitment during walking in older adults. Two walking tasks are assessed: typical walking and obstacle negotiation. The latter may have a stronger demand for somatosensory feedback due to the more complex coordination of the gait cycle when stepping over obstacles. This study also examines the extent to which somatosensory function and prefrontal activity are associated with performance on walking and balance assessments.

2. Methods

2.1. Participants

Participants were recruited by mailing advertisements to a research recruitment database. Telephone screening was conducted to determine eligibility. The inclusion criteria included age 65 and older, ability to walk short distances independently without a walking aid (cane, crutch, walker, braces, etc.), and agreement with the statement: "*You find it physically tiring to walk a quarter mile, or climb two flights of stairs, or perform household chores*." Based on this criterion, we intended to enroll participants with mild to moderate mobility deficits. Exclusion criteria included any prior neurological diagnosis (such as Parkinson's disease, stroke, Alzheimer's disease, etc.), significant disease of a major organ system (cardiac, pulmonary, renal, etc.), bone fracture or joint replacement within the prior six months, uncontrolled hypertension at rest, major visual impairment, lower extremity pain with walking, or difficulty communicating with study personnel. All study procedures were approved by the University of Florida Institutional Review Board and all participants provided written informed consent. The procedures were completed over two separate study visits. The first visit included paper-based questionnaires/tests of mobility and cognitive function. The second visit included the somatosensory assessment and fNIRS walking assessment.

2.2. Somatosensory assessment

Tactile somatosensory function was evaluated with Semmes-Weinstein monofilaments on the sole of both feet at the head of the first metatarsal (just proximal to the great toe). Tactile somatosensation at this site has previously been shown to be associated with walking and balance function (Cruz-Almeida et al., 2014). Participants were assessed while lying flat on their back on an examination table, and could not see when the monofilaments were applied. Five monofilaments levels were used for testing, each with a different target force: 5.07 level (10 g), 4.60 level (4 g), 4.31 level (2 g), 3.61 level (0.4 g), and 2.83 level (0.07 g). For each monofilament, two trials were conducted on each foot. The monofilament level used for each trial was randomly ordered. Prior to beginning the test, the examiner demonstrated the 10 g monofilament on the participant's hand. During testing, the examiner did not tell the participant when a monofilament would be applied to the foot. The instructions to the participant were as follows: "*Over the next few minutes I will be touching the base of your big toe with bristles of various sizes. If you feel the bristle touch the right foot say 'Right'. If you feel it touch the left foot say 'Left'. If you don't feel the bristle don't say anything.*" A participant's response was rated as correct if they appropriately answered either "left" or "right" within about 1 s of being touched by the monofilament. The lowest monofilament level with at least one correct response was recorded for each foot. If a participant did not respond correctly to the 5.07 monofilament level, we assigned a level of 5.46 (26 g), which is a subsequent monofilament level in the Semmes-Weinstein series. The monofilament levels from left and right feet were then averaged together for use in statistical analyses.

2.3. Clinical mobility assessments

Clinical mobility assessments included 10-meter walking speed, Activity Specific Balance Confidence (ABC) Scale (Powell and Myers, 1995), and Berg Balance Scale (BBS) (Berg et al., 1989). The ABC Scale is a questionnaire that assesses the participant's self-reported confidence in their ability to perform various activities without losing balance. It consists of 16 items and the score can range from 0 to 100, where 0 indicates no confidence and 100 indicates completely confident in one's balance ability. BBS is a performance-based assessment consisting of 14 balance tasks, which are scored by a trained examiner on a scale from 0 (poorest function) to 4 (highest function). The total score can range from 0 to 56.

2.4. Cognitive executive function assessment

Executive function was assessed with the Trail Making Test Part B (TMT-B). TMT-B challenges attention, working memory, inhibition, and set shifting in older adults (Sanchez-Cubillo et al., 2009). The test uses a "dot-to-dot" format on paper, requiring participants to connect a sequence of 24 consecutive targets. The targets alternate between numbers and letters (1, A, 2, B, etc.). Participants were instructed to complete the test quickly and accurately, and the time to complete the test was measured with a stopwatch.

2.5. Prefrontal activity during walking

2.5.1. Walking tasks

Walking was performed on a 19.2 m rectangular course. For the *Typical* task, participants walked around the course at their preferred comfortable speed with no assistive device. For the *Obstacles* task, the same procedure was followed except with five foam obstacles placed

evenly distanced along each of the long sides of the course. The long sides were 8.7 m, the first obstacle was placed at 1.4 m, and each subsequent obstacle was separated by 1.4 m (Fig. 1A). Obstacle dimensions (length x width x height) were 12 × 4 × 4 in. (30.5 × 10.2 × 10.2 cm). For both the Typical and Obstacles tasks, the participants performed three 30-second walking trials (see fNIRS acquisition section for additional explanation). The starting position for the first trial was at the beginning of a long side of the course. For subsequent trials, participants began walking at the same point where they had stopped after the first trial. A stopwatch was used to measure the time to walk 4 m (a straight distance within each of the longer sides of the course), and these time and distance measurements (averaged across multiple laps) were used to determine walking speed. For the *Obstacles* task, participants were instructed to step directly over the foam blocks, and to avoid circumventing the obstacles with either leg. Depending on their walking speed, the participants encountered approximately 12–18 foam blocks during each *Obstacles* trial.

2.5.2. fNIRS acquisition

Prefrontal recruitment was measured during the *Typical* task and *Obstacles* task using a commercially available multi-channel continuous-wave fNIRS unit (OctaMon, Artinis Medical Systems, Nijmegen, Netherlands). Participants wore a headband with embedded light sources that emitted near infrared light at continuous wavelengths of 760 nm and 850 nm, along with two near-infrared light detectors (Fig. 1B). Separate recording channels were distinguished by time division multiplexing. The bottom of the headband was positioned just above the eyebrows and the middle of the headband was aligned with the midline of the face. The source-detector optode location on the headband was fixed at 3.5 cm. In order to report estimated anatomical recording sites for each channel we measured the mid-point location between each light emitter-detector pair and report this location in reference to the international 10–10 system (Koessler et al., 2009). Horizontal placement was measured in the transverse plane as percentage of head circumference. Vertical placement was measured in the sagittal plane as percentage of the nasion to inion distance. The group mean recording sites relative to the nasion were as follows for horizontal and vertical direction, respectively: 4.4% ± 0.2 and 11% ± 1.8 (for the medial optodes); 8.9% ± 0.3 and 11% ± 1.8 (for the lateral optodes). The medial left and right fNIRS optodes were approximately aligned with the landmarks of Fp1 and Fp2. The lateral left and right optodes were approximately aligned with the landmarks of AF7 and AF8. The measurement locations correspond to medial and lateral sub regions of Brodmann Area 10 (Koessler et al., 2009).

fNIRS data were acquired using a block design, where 30-second active blocks of walking were alternated with reference blocks. During the reference blocks, participants stood still while counting slowly from one to thirty (approximately at the rate of 1 number per second), in order to prevent mind wandering (Holtzer et al., 2015; Holtzer et al., 2016). For each walking task, three pairs of reference/active blocks were performed. The start and end points of each block were marked manually with a wireless remote device (PortaSync, Artinis Medical Systems, Nijmegen, Netherlands), which placed event markers in a separate recording channel that was time synchronized to the fNIRS signals. The order of the two walking tasks was randomized. The data were sampled at 10 Hz and later exported to a computer for analysis.

2.5.3. fNIRS analysis

A differential pathlength factor value of 6 was used. Prefrontal O2Hb concentrations were calculated according to the modified Beer-Lambert law then analyzed with custom programs in Matlab version R2015a (Mathworks, Natick, MA, USA). Preprocessing of the raw fNIRS signals included detrending the signal and using a low-pass filter with cutoff frequency at 0.14 Hz to reduce physiological noise (Holtzer et al., 2011; Huppert et al., 2009). A wavelet filter was used to reduce the influence of motion artifacts (Herold et al., 2018). Additionally, a trained team member visually examined the data and excluded any channels with obvious deficiencies in signal quality (e.g., high amplitude artifacts inconsistent with physiological activity, or absence of any apparent change in signal). Task-related change in prefrontal O2Hb (ΔO2Hb) was calculated for each person and task. First we averaged the three blocks of active O2Hb and the three blocks of resting O2Hb, then calculated the task-related change using the formula: ΔO2Hb = Active O2Hb − Reference O2Hb. ΔO2Hb data from all channels were averaged within each participant for each task prior to all subsequent analyses.

2.6. Statistical analysis

Statistical analysis was conducted using JMP software (JMP® 15.0 SAS Institute Inc., Cary, NC, USA). Univariate associations between somatosensory monofilament level and prefrontal activity during walking were evaluated with Pearson's correlation. Multiple regression analysis was also used to examine this association after accounting for covariates of interest. Predictors of walking speed and balance score were evaluated with multiple linear regression analysis. Normality of residuals was tested with the Shapiro-Wilk test. For all tests, statistical significance

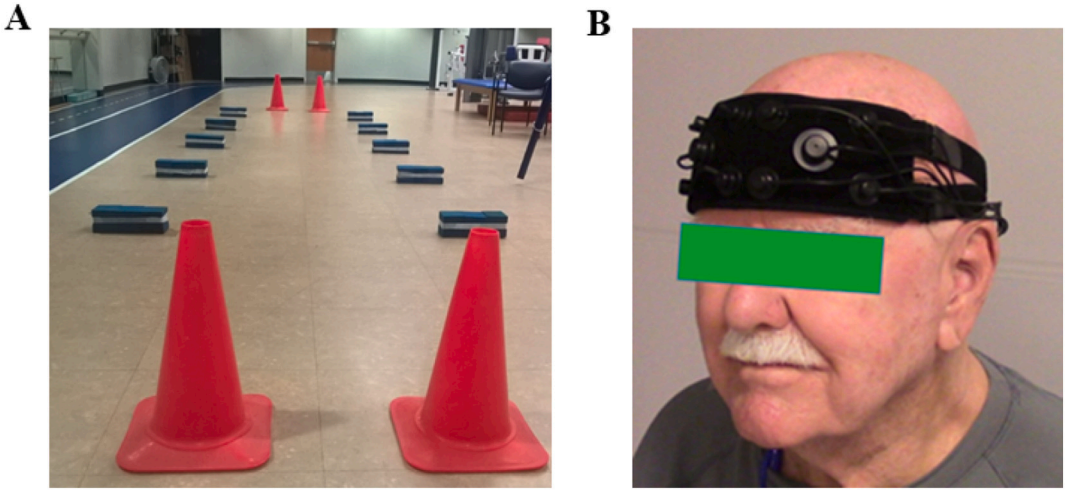

Fig. 1. Walking course and fNIRS setup. A) The course is shown set up with foam obstacles for the Obstacles walking task. The cones marked the corners of the rectangular walking course, and participants were instructed to walk just outside the cones. Walking speed was determined with a stopwatch over a 4 m distance within the straight portion of each lap. B) fNIRS was recorded from the prefrontal cortex using a commercially available device.

was set at α = 0.05.

3. Results

3.1. Participant characteristics

Fifty participants enrolled in the study, but three did not return for the second study visit and did not have complete data sets. Table 1 shows participant characteristics and mobility function for the 47 participants who were included in the analysis. Eighty percent of participants were Caucasian and 20% were Black or African American. Three participants reported being under the care of a physician for diabetes, which is known to contribute to peripheral neuropathy and may affect brain blood flow. Those participants are indicated with a triangle in Fig. 2.

3.2. Association between somatosensation and prefrontal activity during walking

Univariate regression analysis revealed a significant association between higher (worse) monofilament level and greater prefrontal cortical activity (ΔO2Hb) during the *Typical* walking task (r = 0.38, p = 0.008) and *Obstacles* walking task (r = 0.40, p = 0.006). The regression residuals for the *Obstacles* task were not normally distributed (Shapiro-Wilk W = 0.93, p = 0.008), so non-parametric correlation was also assessed and found to be statistically significant (Spearman ρ = 0.36, p = 0.014). Scatterplots are shown in Fig. 2. There were two notable data points that had the lowest scores for somatosensation and relatively low values for prefrontal activity. To examine whether these points had an excessive influence on the association, the univariate regression analysis was repeated with those two points excluded. The associations remained statistically significant for both *Typical* walking (r = 0.31, p = 0.04) and *Obstacles* walking (r = 0.32, p = 0.03).

A multiple regression analysis (with all data points included) was also run to determine if the association between somatosensation and prefrontal activity would persist after accounting for other covariates, including cognitive executive function (Trailmaking Test B), age, and sex (Table 2). For *Typical* walking the model was not statistically significant (R^2 = 0.17, p = 0.099). For *Obstacles* walking the model was significant (R^2 = 0.33, p = 0.002), including the association for prefrontal activation and somatosensation (p = 0.003).

3.3. Predictors of mobility function

Separate multiple linear regression models were used to calculate predictors of *Typical* speed, *Obstacles* speed, and Berg Balance Scale score (Table 3). For *Typical* speed the model included prefrontal ΔO2Hb (from the *Typical* task), monofilament level, TMT-B time, age, and sex. The model residuals met criteria for a normal distribution (Shapiro-Wilk W = 0.96, p = 0.10). The model was borderline statistically significant (F(5, 41) = 2.44, p = 0.05; R^2 = 0.23). Findings within the *Typical* model

Table 1
Participants demographics and clinical characteristics (n = 47).

	Mean ± SD	Range
Sex: 32 female/15 male	–	–
Age (years)	74.62 ± 6.76	65–92
Body Mass Index	30.7 ± 6.5	18.5–48.8
ABC Scale (% confidence)	81.2 ± 12.7	43.6–98.9
BBS (out of 56 points)	49.0 ± 5.10	32–56
Trailmaking Test - Part B (s)	99.3 ± 67.2	29–420
Monofilament level	4.34 ± 0.53	2.83–5.46
Typical walking speed (m/s)	1.03 ± 0.20	0.64–1.47
Obstacle walking speed (m/s)	0.83 ± 0.21	0.42–1.27

SD = standard deviation; s = second; ABC = Activity Specific Balance Confidence; BBS = Berg Balance Scale; m/s meters per second.

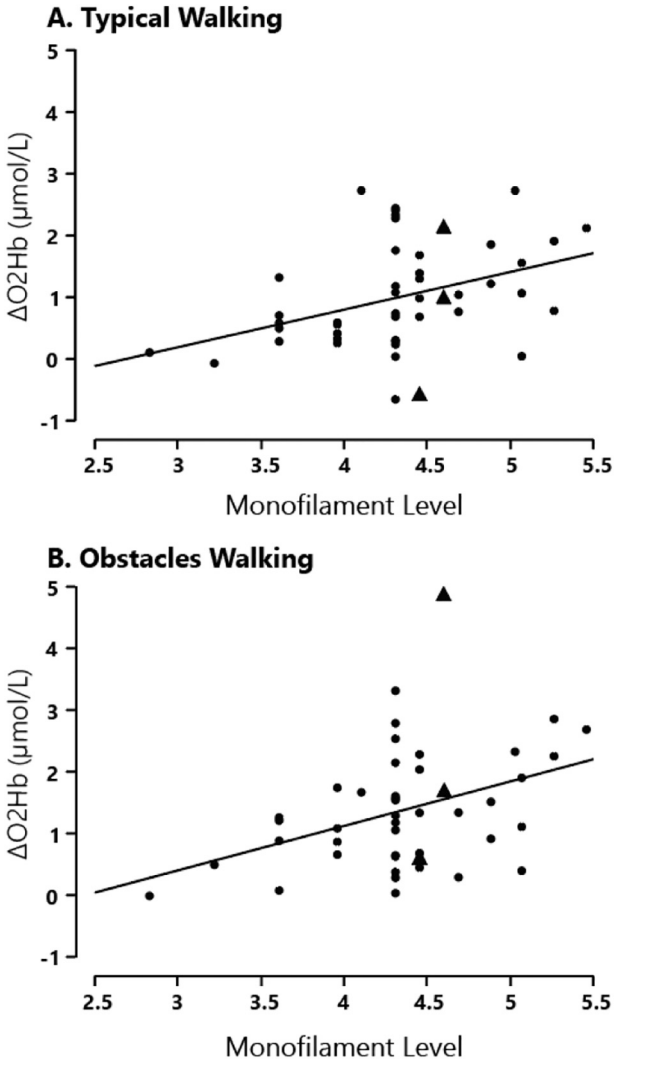

Fig. 2. Somatosensory monofilament level versus prefrontal oxygenated hemoglobin concentration (ΔO2Hb). A significant associated was observed between worse somatosensation (higher level) and greater prefrontal cortical activity during the *Typical* walking task (panel A, r = 0.38, p = 0.008) and *Obstacles* walking task (panel B, r = 0.40, p = 0.006). Triangles indicate participants who report being under the care of a physician for diabetes.

Table 2
Predictors of prefrontal activity during walking.

	Prefrontal ΔO2Hb during Typical walking			Prefrontal ΔO2Hb during Obstacle walking		
	B	t-Ratio	p	B	t-Ratio	p
Monofilament level	0.563	2.36	0.02	0.769	3.19	0.003
Trailmaking Test B	0.001	0.64	0.53	0.005	2.46	0.02
Age	−0.010	−0.51	0.61	−0.060	−3	0.005
Sex (female)	−0.120	−0.87	0.38	−0.081	−0.6	0.550

	Prefrontal ΔO2Hb during Typical walking			Prefrontal ΔO2Hb during Obstacle walking		
	R^2	F-ratio	p	R^2	F-ratio	p
Model	0.17	2.09	0.099	0.33	5.25	0.002

O2Hb = oxygenated hemoglobin concentration.

Table 3
Predictors of walking speed and balance score.

	Typical walking speed			Obstacle walking speed			Berg Balance Scale		
	B	t-Ratio	p	B	t-Ratio	p	B	t-Ratio	p
Prefrontal ΔO2Hb	0.008	0.24	0.81	0.095	3.08	0.004	–	–	–
Monofilament level	−0.104	−1.84	0.07	−0.219	−4.10	<0.001	−2.967	−2.29	0.03
Trailmaking Test B	0.000	−0.88	0.39	−0.001	−2.35	0.02	−0.017	−1.63	0.11
Age	−0.004	−0.88	0.38	0.001	0.27	0.79	−0.190	−1.78	0.08
Sex (female)	−0.079	−2.61	0.01	−0.096	−3.54	0.001	0.073	0.22	0.83

	Typical walking speed			Obstacle walking speed			Berg Balance Scale		
	R^2	F-ratio	p	R^2	F-ratio	p	R^2	F-ratio	p
Model	0.23	2.44	0.050	0.45	6.80	<0.001	0.31	4.64	0.003

O2Hb = oxygenated hemoglobin concentration.

showed that monofilament level was borderline significant ($p = 0.07$), such that walking speed decreased 0.10 m/s for each higher increment of 1 on the monofilament level. Also, walking speed was 0.08 m/s lower in women than men ($p = 0.01$).

For *Obstacles* speed the same model was used (but with prefrontal ΔO2Hb from the *Obstacles* task), and the residuals met criteria for a normal distribution (Shapiro-Wilk $W = 0.99$, $p = 0.93$). The model was statistically significant ($F\ F(5,41) = 7.26$, $p < 0.0001$), with an R^2 of 0.47. Significant findings within the *Obstacles* model showed that walking speed increased 0.09 m/s for each μmol/L increase of ΔO2Hb ($p = 0.004$), decreased 0.22 m/s for each higher increment of 1 on the monofilament level ($p < 0.001$), decreased 0.01 m/s for each 10-second increase of TMT-B time ($p = 0.02$), and was 0.10 m/s lower in women than men ($p = 0.001$). All participants performed the obstacle negotiation task safely, and obstacle strikes were rare.

For Berg Balance Scale score the model included monofilament level, TMT-B time, age, and sex. The model residuals met criteria for a normal distribution (Shapiro-Wilk $W = 0.95$, $p = 0.06$) and the model was statistically significant ($F(4,42) = 4.64$, $p = 0.003$), with an R^2 of 0.31. The model showed that Berg Balance Scale score was reduced by 3.0 points for each higher increment of 1 on the monofilament level ($p = 0.03$). Age was borderline significant ($p = 0.08$), such that Berg Balance score was reduced by 0.19 points for each higher year of age.

4. Discussion

4.1. Association between somatosensory function and prefrontal activity during walking

The primary finding of this study is that older adults who have worse tactile somatosensory function exhibit higher recruitment of prefrontal cortex during walking. Based on the results of the multiple regression analysis, this association is somewhat stronger for *Obstacles* walking than for *Typical* walking. This finding is consistent with greater importance of somatosensory feedback when walking in a complex environment. In this situation, the nervous system must create a motor plan for safely navigating each obstacle, and use real time sensory feedback and cognitive resources to monitor and/or adjust the motor plan (Brach and VanSwearingen, 2013).

Overall the results of this study are consistent with the theory that reduced somatosensory input to the central nervous system will impair automaticity of walking, and cause a compensatory shift toward executive control of walking (Clark, 2015). The exact mechanism of impaired automaticity remains unclear. Compromised performance of spinal central pattern generating circuits due to reduced sensory input is a plausible mechanism (Dietz, 2003; McCrea and Rybak, 2008). Other possible mechanisms include reduced sensory input to brainstem locomotor regions (Le Ray et al., 2011; Ryczko and Dubuc, 2013; Narita et al., 2002), cerebellar networks (Morton and Bastian, 2004), or to cerebral networks that integrate sensory and motor signals. The interplay between motor actions, cognitive function, and somatosensory information has been acknowledged in the literature, but there is a need for rigorous investigations to better understand the impact for older adults. For example, do people with cognitive impairment lack the ability to compensate for somatosensory impairment during walking, due to insufficient cognitive reserves? This example of multiple impairments within the motor-cognitive-sensory control loop might contribute to outsized risk of falls and other adverse mobility outcomes. Future research will be needed to better understand this interplay, as well as the basic neural mechanisms responsible.

4.2. Functional status of the study sample

Our intent was to enroll older adults with mild to moderate mobility deficits. All participants responded affirmatively to the screening statement "*You find it physically tiring to walk a quarter mile, or climb two flights of stairs, or perform household chores*." Group mean walking speed for the *Typical* task was 1.03 m/s, which is close to the threshold of 1.0 that is often used to define mobility deficits in older adults (Studenski, 2009). Of the 47 participants in the present study, 20 had *Typical* speed below 1.0 m/s. For the Berg Balance Scale, group mean score was 49 points (out of a maximal score of 56). This mean is somewhat lower than has been reported in a prior study of community dwelling sample of older adults who were generally healthy (Steffen et al., 2002). In that prior study, older men and women age 70–79 (similar to our group mean of 75 years) had mean BBS score of 53.5, with a 95% confidence interval of 52–56. Another study reported a heightened risk of falls in older adults with BBS scores less than 47 (Viveiro et al., 2019), which is just two points lower than our group mean. Our sample had 11 participants with BBS scores less than 47. The walking speed and BBS results are consistent with a substantial portion of our participants having mild to moderate mobility deficits.

Published guidelines are available for interpreting Semmes-Weinstein monofilament results from the plantar surface of the foot (Tanenberg and Donofrio, 2008). These guidelines report somatosensory thresholds pertaining to "normal", "diminished light touch", "diminished protective sensation", "loss of protection sensation", and "deep pressure only". Prior reports from healthy young adults have reported values ranging from 3.61 to 3.84 from the location of the foot that we measured (McPoil and Cornwall, 2006; Jeng et al., 2000), which would be classified as "normal" to slightly "diminished light touch". For our study, the group mean monofilament level was 4.34, which is at the threshold between "diminished light touch" and "diminished protective sensation". Our study included participants with a range of tactile somatosensory function, including 7 participants with "normal" sensation, 27 participants with "diminished light touch", 7 participants with "diminished protective sensation", and 6 participants with "loss of protective sensation".

Cognitive executive function was assessed with the TMT-B. Performance on this test varied widely, but the group mean of 99 s is fairly typical for this age group. Published normative data shows that the 60th percentile for people age 70–79 is approximately in the range of 95–107 s (Tombaugh, 2004). The results of our study found that greater prefrontal activity during *Obstacles* walking was associated with worse TMT-B performance. This finding might be explained by neural inefficiency, such that people with poorer cognitive function require higher levels of brain recruitment when performing complex walking tasks (Chen et al., 2017; Chatterjee et al., 2020). Nevertheless, the association between somatosensory function and prefrontal activity remained significant for *Obstacles* walking after accounting for TMT-B performance.

Three participants reported being under the care of a physician for diabetes. Diabetes contributes to peripheral neuropathy and may affect brain blood flow, but there was no obvious difference between this subset of participants and the group as a whole. All three had somatosensory function that was close to the group average, while prefrontal activity varied across these participants.

4.3. Predictors of walking and balance function

Multiple regression analysis was used to assess predictors of walking performance, including prefrontal activity, monofilament level, executive function (TMT-B), age, and sex. For *Typical* speed, the model was borderline significant ($p = 0.05$), and included a weak association between worse monofilament level and slower walking speed. Group mean walking speed for the *Obstacle* task was significantly slower than the *Typical* task ($p < 0.0001$). All but two participants had slower speed for *Obstacles* compared to *Typical*, which supports that this task was substantially more challenging. The same multiple regression model described above was used to assess predictors of *Obstacles* speed, and the model was significant ($p = 0.0001$). Within the model, higher monofilament level and higher Trailmaking test time (i.e., worse performance on each test) were associated with slower *Obstacles* speed. Both of these findings are consistent with the widely reported adverse effects of somatosensory (Mold et al., 2004; Resnick et al., 2000; Lipsitz et al., 2018; Cruz-Almeida et al., 2014) and cognitive deficits (Yogev-Seligmann et al., 2008; Allali et al., 2008; Holtzer et al., 2006; Herman et al., 2010; Chen et al., 2012; Mirelman et al., 2012) on mobility function. Female sex was also associated with slower *Obstacle* speed. This finding has been reported in prior studies, although the explanation is not fully understood (Tolea et al., 2010). The most novel finding within the model was that greater prefrontal activity was associated with faster walking speed. Heightened prefrontal activity is a task-appropriate response that should be expected to yield better performance, since obstacle negotiation requires attention and planning of movement (i.e., executive control) (Clark et al., 2014a). Higher prefrontal activity may also indicate a compensatory strategy to overcome somatosensory (or other) impairments, in order to preserve walking function. Although it is encouraging that a prefrontal control strategy can benefit task performance on the *Obstacles* task, there is a caveat. Excessive reliance on compensatory executive control of walking will encumber cognitive resources. Competition for these resources in complex real-world situations (i.e., multi-tasking) may saturate the availability of resources, which may cause performance decrements. This would pose a risk for adverse events including tripping, collisions, and falls (Fasano et al., 2012; Springer et al., 2006).

Predictors of BBS score were assessed with a multiple regression analysis that included monofilament level, executive function (Trailmaking Test B), age, and sex. Prefrontal activity was not measured during BBS tasks, so was not part of this model. The model was ($p = 0.005$), but only monofilament level was a significant predictor within the model. Prior studies have strongly linked impairments of somatosensory function to balance performance (Mold et al., 2004; Resnick et al., 2000; Lipsitz et al., 2018; Cruz-Almeida et al., 2014), so our results are in agreement with existing evidence.

4.4. Implications for clinical intervention

Given that somatosensory impairment leads to compromised mobility function and higher levels of prefrontal activation, a natural question is whether these problems can be reversed by augmenting somatosensory feedback. Prior studies on this topic have offered positive preliminary findings. Priplata and colleagues demonstrated that vibrating insoles reduced postural sway during standing balance in older adults (Priplata et al., 2003). In this case, weak (subsensory) vibratory input was delivered to increase the ability of sensory receptors and neurons to detect signals through a phenomenon called stochastic resonance (Priplata et al., 2002). Similarly, Palluel and colleagues found that static postural sway parameters improved in older adults following 5 min of walking in textured shoe insoles (Palluel et al., 2008; Palluel et al., 2009). Our own prior research found that prefrontal activity was lower in older adults when walking in textured shoe insoles versus normal shoes (Clark et al., 2014b). Vibratory and textured shoe insoles are a clinically feasible intervention approach that warrants additional research into the potential benefits to real-world walking function.

4.5. Study limitations

Our interpretation of the data is based on a theory of how somatosensory information might be used by the central nervous system to control walking. Although the theory is compelling, there may be alternative explanations and/or unknown factors influencing the relationship between somatosensory impairment and brain activity. Another limitation is that brain activity was recorded only from prefrontal cortex. There may be other brain regions used during walking that are affected by somatosensory impairment, with resultant higher or lower levels of activity. How these other brain regions might be related to walking and balance outcomes remains unknown. Another limitation is that tactile cutaneous touch is just one of multiple types of somatosensory information that are important to walking. Others include cutaneous pressure, muscle length, muscle tension, and joint motion. Impairment on the monofilament test might be a proxy for general impairment of peripheral nerve function.

4.6. Conclusions

The primary finding of an association between poorer somatosensory function and higher activity in prefrontal cortex during walking is consistent with a compensatory shift toward executive control of walking. Future research should further establish the mechanisms by which somatosensory impairments are linked to neural control and performance of walking tasks, as well as develop intervention approaches.

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CRediT authorship contribution statement

Pallavi Sood: Validation, Formal Analysis, Investigation, Data Curation, Writing – Original Draft. **Sudeshna Chatterjee:** Validation, Investigation, Data Curation, Writing – Original Draft, Writing – Review and Editing, Project Administration. **Jared Skinner:** Investigation, Writing – Review and Editing, Project Administration. **Paige Lysne:** Investigation, Data Curation, Writing – Review and Editing, Project Administration. **Chanoan Sumonthee:** Investigation, Writing – Review and Editing, Project Administration. **Samuel Wu:** Methodology, Formal

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Declaration of competing interest

There are no competing interests to disclose.

Data availability

Data will be made available on request.

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References

Allali, G., Assal, F., Kressig, R.W., Dubost, V., Herrmann, F.R., Beauchet, O., 2008. Impact of impaired executive function on gait stability. Dement. Geriatr. Cogn. Disord. 26, 364–369. https://doi.org/10.1159/000162358.

Berg, K., Wood-Dauphinee, S., Williams, J.I., Gayton, D., 1989. Measuring balance in the elderly: preliminary development of an instrument. Physiother. Can. 41, 304–311.

Brach, J.S., VanSwearingen, J.M., 2013. Interventions to improve walking in older adults. Curr. Transl. Geriatr. Exp. Gerontol. Rep. 2, 230–238. https://doi.org/10.1007/s13670-013-0059-0.

Cabeza, R., Anderson, N.D., Locantore, J.K., McIntosh, A.R., 2002. Aging gracefully: compensatory brain activity in high-performing older adults. NeuroImage 17, 1394–1402. https://doi.org/10.1006/nimg.2002.1280.

Chatterjee, S.A., Seidler, R.D., Skinner, J.W., Lysne, P.E., Sumonthee, C., Wu, S.S., et al., 2020. Obstacle negotiation in older adults: prefrontal activation interpreted through conceptual models of brain aging. InnovAging 4, igaa034. https://doi.org/10.1093/geroni/igaa034.

Chen, M., Pillemer, S., England, S., Izzetoglu, M., Mahoney, J.R., Holtzer, R., 2017. Neural correlates of obstacle negotiation in older adults: an fNIRS study. Gait Posture 58, 130–135. https://doi.org/10.1016/j.gaitpost.2017.07.043.

Chen, T.Y., Peronto, C.L., Edwards, J.D., 2012. Cognitive function as a prospective predictor of falls. J. Gerontol. B Psychol. Sci. Soc. Sci. 67, 720–728. https://doi.org/10.1093/geronb/gbs052.

Clark, D.J., 2015. Automaticity of walking: functional significance, mechanisms, measurement and rehabilitation strategies. Front. Hum. Neurosci. 9, 246. https://doi.org/10.3389/fnhum.2015.00246.

Clark, D.J., Rose, D.K., Ring, S.A., Porges, E.C., 2014. Utilization of central nervous system resources for preparation and performance of complex walking tasks in older adults. Front. Aging Neurosci. 6, 217. https://doi.org/10.3389/fnagi.2014.00217.

Clark, D.J., Christou, E.A., Ring, S.A., Williamson, J.B., Doty, L., 2014. Enhanced somatosensory feedback reduces prefrontal cortical activity during walking in older adults. J. Gerontol. A Biol. Sci. Med. Sci. 69, 1422–1428. https://doi.org/10.1093/gerona/glu125.

Cruz-Almeida, Y., Black, M.L., Christou, E.A., Clark, D.J., 2014. Site-specific differences in the association between plantar tactile perception and mobility function in older adults. Front. Aging Neurosci. 6, 1–6. https://doi.org/10.3389/fnagi.2014.00068.

Dietz, V., 2003. Spinal cord pattern generators for locomotion. Clin. Neurophysiol. 114, 1379–1389. https://doi.org/10.1016/s1388-2457(03)00120-2.

Duysens, J., Pearson, K.G., 1976. The role of cutaneous afferents from the distal hindlimb in the regulation of the step cycle of thalamic cats. Exp. Brain Res. 24, 245–255. https://doi.org/10.1007/bf00235013.

Fallon, J.B., Bent, L.R., McNulty, P.A., Macefield, V.G., 2005. Evidence for strong synaptic coupling between single tactile afferents from the sole of the foot and motoneurons supplying leg muscles. J. Neurophysiol. 94, 3795–3804. https://doi.org/10.1152/jn.00359.2005.

Fasano, A., Plotnik, M., Bove, F., Berardelli, A., 2012. The neurobiology of falls. Neurol. Sci. 33, 1215–1223. https://doi.org/10.1007/s10072-012-1126-6.

Forssberg, H., Grillner, S., Rossignol, S., 1975. Phase dependent reflex reversal during walking in chronic spinal cats. Brain Res. 85, 103–107. https://doi.org/10.1016/0006-8993(75)91013-6.

Frigon, A., 2017. The neural control of interlimb coordination during mammalian locomotion. J. Neurophysiol. 117, 2224–2241. https://doi.org/10.1152/jn.00978.2016.

Frigon, A., Rossignol, S., 2006. Experiments and models of sensorimotor interactions during locomotion. Biol. Cybern. 95, 607–627. https://doi.org/10.1007/s00422-006-0129-x.

Guertin, P.A., 2012. Central pattern generator for locomotion: anatomical, physiological, and pathophysiological considerations. Front. Neurol. 3, 183. https://doi.org/10.3389/fneur.2012.00183.

Hawkins, K.A., Fox, E.J., Daly, J.J., Rose, D.K., Christou, E.A., McGuirk, T.E., et al., 2018. Prefrontal over-activation during walking in people with mobility deficits: interpretation and functional implications. Hum. Mov. Sci. 59, 46–55. https://doi.org/10.1016/j.humov.2018.03.010.

Herman, T., Mirelman, A., Giladi, N., Schweiger, A., Hausdorff, J.M., 2010. Executive control deficits as a prodrome to falls in healthy older adults: a prospective study linking thinking, walking, and falling. J. Gerontol. A Biol. Sci. Med. Sci. 65, 1086–1092. https://doi.org/10.1093/gerona/glq077.

Herold, F., Wiegel, P., Scholkmann, F., Muller, N.G., 2018. Applications of functional near-infrared spectroscopy (fNIRS) neuroimaging in Exercise(-)Cognition science: a systematic, methodology-focused review. J. Clin. Med. 7 https://doi.org/10.3390/jcm7120466.

Hiebert, G.W., Whelan, P.J., Prochazka, A., Pearson, K.G., 1996. Contribution of hind limb flexor muscle afferents to the timing of phase transitions in the cat step cycle. J. Neurophysiol. 75, 1126–1137.

Holtzer, R., Verghese, J., Xue, X., Lipton, R.B., 2006. Cognitive processes related to gait velocity: results from the Einstein Aging Study. Neuropsychology 20, 215–223. https://doi.org/10.1037/0894-4105.20.2.215.

Holtzer, R., Mahoney, J.R., Izzetoglu, M., Izzetoglu, K., Onaral, B., Verghese, J., 2011. fNIRS study of walking and walking while talking in young and old individuals. J. Gerontol. A Biol. Sci. Med. Sci. 66, 879–887. https://doi.org/10.1093/gerona/glr068.

Holtzer, R., Mahoney, J.R., Izzetoglu, M., Wang, C., England, S., Verghese, J., 2015. Online fronto-cortical control of simple and attention-demanding locomotion in humans. NeuroImage 112, 152–159. https://doi.org/10.1016/j.neuroimage.2015.03.002.

Holtzer, R., Verghese, J., Allali, G., Izzetoglu, M., Wang, C., Mahoney, J.R., 2016. Neurological gait abnormalities moderate the functional brain signature of the posture first hypothesis. Brain Topogr. 29, 334–343. https://doi.org/10.1007/s10548-015-0465-z.

Huppert, T.J., Diamond, S.G., Franceschini, M.A., Boas, D.A., 2009. HomER: a review of time-series analysis methods for near-infrared spectroscopy of the brain. Appl. Opt. 48, D280–D298. https://doi.org/10.1364/ao.48.00d280.

Jeng, C., Michelson, J., Mizel, M., 2000. Sensory thresholds of normal human feet. Foot Ankle Int. 21, 501–504. https://doi.org/10.1177/107110070002100609.

Koessler, L., Maillard, L., Benhadid, A., Vignal, J.P., Felblinger, J., Vespignani, H., et al., 2009. Automated cortical projection of EEG sensors: anatomical correlation via the international 10–10 system. NeuroImage 46, 64–72. https://doi.org/10.1016/j.neuroimage.2009.02.006.

Le Ray, D., Juvin, L., Ryczko, D., Dubuc, R., 2011. Chapter 4–supraspinal control of locomotion: the mesencephalic locomotor region. Prog Brain Res. 188, 51–70. https://doi.org/10.1016/B978-0-444-53825-3.00009-7.

Lipsitz, L.A., Manor, B., Habtemariam, D., Iloputaife, I., Zhou, J., Travison, T.G., 2018. The pace and prognosis of peripheral sensory loss in advanced age: association with gait speed and falls. BMC Geriatr. 18, 274. https://doi.org/10.1186/s12877-018-0970-5.

McCrea, D.A., Rybak, I.A., 2008. Organization of mammalian locomotor rhythm and pattern generation. Brain Res. Rev. 57, 134–146. https://doi.org/10.1016/j.brainresrev.2007.08.006.

McPoil, T.G., Cornwall, M.W., 2006. Plantar tactile sensory thresholds in healthy men and women. Foot 16, 192–197. https://doi.org/10.1016/j.foot.2006.07.001.

Mirelman, A., Herman, T., Brozgol, M., Dorfman, M., Sprecher, E., Schweiger, A., et al., 2012. Executive function and falls in older adults: new findings from a five-year prospective study link fall risk to cognition. PloS one. 7, e40297 https://doi.org/10.1371/journal.pone.0040297 10.1371/journal.pone.0040297. Epub 2012 Jun 29.

Mirelman, A., Maidan, I., Bernad-Elazari, H., Shustack, S., Giladi, N., Hausdorff, J.M., 2017. Effects of aging on prefrontal brain activation during challenging walking conditions. Brain Cogn. 115, 41–46. https://doi.org/10.1016/j.bandc.2017.04.002.

Mold, J.W., Vesely, S.K., Keyl, B.A., Schenk, J.B., Roberts, M., 2004. The prevalence, predictors, and consequences of peripheral sensory neuropathy in older patients. J. Am. Board Fam. Pract. 17, 309–318.

Morton, S.M., Bastian, A.J., 2004. Cerebellar control of balance and locomotion. Neuroscientist 10, 247–259.

Narita, K., Murata, T., Honda, K., Nishihara, M., Takahashi, M., Higuchi, T., 2002. Subthalamic locomotor region is involved in running activity originating in the rat ventromedial hypothalamus. Behav. Brain Res. 134, 275–281.

Palluel, E., Nougier, V., Olivier, I., 2008. Do spike insoles enhance postural stability and plantar-surface cutaneous sensitivity in the elderly? Age. 30, 53–61. https://doi.org/10.1007/s11357-008-9047-2.

Palluel, E., Olivier, I., Nougier, V., 2009. The lasting effects of spike insoles on postural control in the elderly. Behav. Neurosci. 123, 1141–1147. https://doi.org/10.1037/a0017115.

Pearson, K.G., 2004. Generating the walking gait: role of sensory feedback. Prog. Brain Res. 143, 123–129. https://doi.org/10.1016/s0079-6123(03)43012-4.

Pelicioni, P.H.S., Tijsma, M., Lord, S.R., Menant, J., 2019. Prefrontal cortical activation measured by fNIRS during walking: effects of age, disease and secondary task. PeerJ. 7, e6833 https://doi.org/10.7717/peerj.6833.

Powell, L.E., Myers, A.M., 1995. The activities-specific balance confidence (ABC) scale. J. Gerontol. A Biol. Sci. Med. Sci. 50A, M28–M34. https://doi.org/10.1093/gerona/50a.1.m28.

Priplata, A., Niemi, J., Salen, M., Harry, J., Lipsitz, L.A., Collins, J.J., 2002. Noise-enhanced human balance control. Phys. Rev. Lett. 89, 238101 https://doi.org/10.1103/PhysRevLett.89.238101.

Priplata, A.A., Niemi, J.B., Harry, J.D., Lipsitz, L.A., Collins, J.J., 2003. Vibrating insoles and balance control in elderly people. Lancet 362, 1123–1124. https://doi.org/10.1016/S0140-6736(03)14470-4.

Resnick, H.E., Vinik, A.I., Schwartz, A.V., Leveille, S.G., Brancati, F.L., Balfour, J., et al., 2000. Independent effects of peripheral nerve dysfunction on lower-extremity physical function in old age: the Women's health and aging study. Diabetes Care 23, 1642–1647. https://doi.org/10.2337/diacare.23.11.1642.

Reuter-Lorenz, P.A., Cappell, K.A., 2008. Neurocognitive aging and the compensation hypothesis. Curr. Dir. Psychol. Sci. 17, 177–182. https://doi.org/10.1111/j.1467-8721.2008.00570.x.

Ryczko, D., Dubuc, R., 2013. The multifunctional mesencephalic locomotor region. Curr. Pharm. Des. 19, 4448–4470.

Sanchez-Cubillo, I., Perianez, J.A., Adrover-Roig, D., Rodriguez-Sanchez, J.M., Rios-Lago, M., Tirapu, J., et al., 2009. Construct validity of the trail making test: role of task-switching, working memory, inhibition/interference control, and visuomotor abilities. J. Int. Neuropsychol. Soc. 15, 438–450. https://doi.org/10.1017/S1355617709090626.

Shaffer, S.W., Harrison, A.L., 2007. Aging of the somatosensory system: a translational perspective. Phys. Ther. 87, 193–207.

Springer, S., Giladi, N., Peretz, C., Yogev, G., Simon, E.S., Hausdorff, J.M., 2006. Dual-tasking effects on gait variability: the role of aging, falls, and executive function. Mov. Disord. 21, 950–957. https://doi.org/10.1002/mds.20848.

Steffen, T.M., Hacker, T.A., Mollinger, L., 2002. Age- and gender-related test performance in community-dwelling elderly people: six-minute walk test, berg balance scale, timed up & go test, and gait speeds. Phys. Ther. 82, 128–137. https://doi.org/10.1093/ptj/82.2.128.

Studenski, S., 2009. Bradypedia: is gait speed ready for clinical use? J. Nutr. Health Aging 13, 878–880. https://doi.org/10.1007/s12603-009-0245-0.

Tanenberg, R.J., Donofrio, P.D., 2008. Chapter 3 - neuropathic problems of the lower limbs in diabetic patients. In: Bowker, J.H., Pfeifer, M.A. (Eds.), Levin and O'Neal's The Diabetic Foot, Seventh edition. Mosby, Philadelphia, pp. 33–74.

Tolea, M.I., Costa, P.T., Terracciano, A., Griswold, M., Simonsick, E.M., Najjar, S.S., et al., 2010. Sex-specific correlates of walking speed in a wide age-ranged population. J. Gerontol. Ser. B Psychol. Sci. Soc. Sci. 65B, 174–184. https://doi.org/10.1093/geronb/gbp130.

Tombaugh, T.N., 2004. Trail Making Test A and B: normative data stratified by age and education. Arch. Clin. Neuropsychol. 19, 203–214. https://doi.org/10.1016/S0887-6177(03)00039-8.

Viveiro, L.A.P., Gomes, G.C.V., Bacha, J.M.R., Carvas Junior, N., Kallas, M.E., Reis, M., et al., 2019. Reliability, validity, and ability to identity fall status of the Berg Balance Scale, Balance Evaluation Systems Test (BESTest), Mini-BESTest, and Brief-BESTest in older adults who live in nursing homes. J. Geriatr. Phys. Ther. 42, E45–E54. https://doi.org/10.1519/JPT.0000000000000215.

Yogev-Seligmann, G., Hausdorff, J.M., Giladi, N., 2008. The role of executive function and attention in gait. Mov. Disord. 23, 329–342. https://doi.org/10.1002/mds.21720.