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# Comparing Executive Function, Evoked Haemodynamic Response, and Gait as Predictors of Variations in Mobility for Older Adults

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## Abstract

**Objective:** Falls represent a major concern for older adults and may serve as clinically salient index events for those presenting in the prodromal stages of Mild Cognitive Impairment. Declines in executive function performance and in gait consistency have shown promise in predicting fall risk, however associated neurophysiological underpinnings have received less attention. In this study, we used a multimodal approach to assess fall risk in a group of older adults with and without a previous fall history.

**Method:** Processing speed, inductive reasoning, verbal fluency, crystallized ability, episodic memory and executive functioning were assessed using standardized neuropsychological tests. Cognitive interference was assessed using the Multi-Source Interference Task. Spatiotemporal gait parameters were assessed with and without cognitive load using a 6.4m instrumented walkway. Haemodynamic responses were measured using functional near infrared spectroscopy.

**Results:** Whereas no group differences were observed in cognitive behavioural performance, during a cognitive interference task fallers displayed more oxygenated haemoglobin across the prefrontal cortex relative to non-fallers, suggesting that engaging in the cognitive task was more effortful for them overall, therefore eliciting greater cortical activation. Between group differences in spatial as well as temporal gait parameters were also observed.

**Conclusions:** These results are in keeping with assertions that diminished executive control is related to fall risk. Notably, the group differences observed in prefrontal cortical activation and in gait parameters may ultimately precede those observed in cognitive behavioural performance, with implications for measurement sensitivity and early identification.

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**Keywords**

fall risk; aging; multimodal assessment; functional near infrared spectroscopy (fNIRS); variability

Falls are a leading cause of injury amongst older adults, potentially resulting in loss of functional mobility and disrupted daily routines (Kearney, Harwood, Gladman, Lincoln, & Masud, 2013). A fall (i.e., an instance in which an individual comes to rest involuntarily on a lower surface, such as the ground or floor) may also serve as a clinically salient index event for those presenting in the prodromal stages of dementia, due to neurodegeneration that affects cognitive and postural control. The risk for falling is greater in older adults with Mild Cognitive Impairment (MCI) than in those without (Delbaere et al., 2012; Liu-Ambrose, Ashe, Graf, Beattie, & Khan, 2008), and individuals with MCI are more likely to incur serious injury as a result of a fall, resulting in admission to a long-term care facility (Kallin, Gustafson, Sandman & Karlsson, 2005). The cognitive, physiological and neurophysiological mechanisms associated with both increased fall risk and MCI are therefore important to understand, as detecting changes in these domains may facilitate an earlier identification of those at risk of falls as well as inform targeted early intervention strategies.

Changes in the consistency of walking patterns (e.g., more variable swing time) and in executive functions (EF) (e.g., in EF-related task performance) have been well-established as predictors of falls in older adults (Kearney et al., 2013). Although EF (i.e., everyday goal management) and walking ability decline with increasing age (Atkinson et al., 2007), less is understood about how the neural substrates underlying these functions differ between those at high vs. low risk of falling. A number of spatial (e.g., step length) and temporal (e.g., swing time) gait parameters have been shown to differentiate fallers from non-fallers (Brach, Perera, Studenski, Katz, Hall & Verghese, 2010; Springer et al., 2006; Verghese, Holtzer, Lipton, & Wang, 2009) and the most reliable differences seem to emerge during dual-tasking conditions. In gait studies, dual-tasking involves walking while engaging in a cognitive task (e.g., repeatedly subtracting 7s from a given starting number) and typically increases variability in both spatial and temporal parameters, which have been linked to reduced overall gait stability and to fall-risk. Springer and colleagues (2006) found increases in swing time variability during several dual-tasking conditions in elderly fallers, but not in elderly non-fallers or young adults. Furthermore, poorer colour-naming performance on the Stroop test correlated with increased dual-tasking swing time variability in elderly fallers only (Springer et al., 2006), suggesting that swing time variability may be mediated by EF declines in elderly fallers.

Falls are not just associated with physical functioning; they share a strong association with cognitive functioning as well. An individual’s ability to successfully shift attention, inhibit interfering information and to engage other components of EF may make the difference between falling and avoiding a fall. Declines in EF have previously been characterized using standardized neuropsychological measures (e.g., Trail Making Test-A/B) for those at increased fall risk (Liu-Ambrose et al., 2008). More recently, poorer performance on computerized EF measures has been linked prospectively with later fall outcome. In a series of studies, researchers demonstrated that lower EF performers were up to three times more likely to fall than higher EF performers at 2-year follow up (Herman, Mirelman, Giladi, Schweiger, & Hausdorff, 2010); an effect that remained stable across a longer, 5-year interval (Mirelman et al., 2012). In keeping with claims that EF mediates gait stability (Springer et al., 2006), a recent review by Kearney and colleagues (2013) concluded that those who had had near-falls (e.g., a trip in which recovery occurred and the person did not come into involuntary contact with the ground), showed better scores on EF measures relative to those who had had a fall. Overall, these results suggest that a cognitive process, specifically EF, may mediate the relationship between reduced physical function, balance and fall outcome.

Although recent efforts examining fall risk in older adults have focused on the relationship between declines in EF and gait, differences in functional brain activity remain relatively unexplored (Holtzer, Epstein, Mahoney, Izzetoglu & Blumen, 2014). Importantly, differences observed in brain activity may precede the behavioural manifestation of an underlying pathology related to fall risk (e.g., neurodegeneration affecting postural and cognitive control) and therefore facilitate an earlier identification of those at greater risk. Several patterns of functional activity have emerged in the cognitive aging literature that distinguish older from younger adults, and may be extended to differentiate fallers from non-fallers; namely compensation and dedifferentiation (Grady, 2012). Compensation occurs with greater activation (e.g., cerebral oxygenation) in the absence of performance differences (i.e., successful compensation) or in conjunction with impaired performance (i.e., negative compensation). Similarly, dedifferentiation refers to the recruitment of more widespread (as opposed to localized) neural tissue to perform a task (Townsend, Adamo & Haist, 2006). Functional near infrared spectroscopy (fNIRS) has been used effectively to demonstrate dedifferentiation (more widespread recruitment of neural tissue as opposed to localized recruitment) in prefrontal cortex during working-memory performance (Vermeij, van Beek, Olde Rikkert, Claassen, & Kessels, 2012) as well as recruitment of additional regions of prefrontal cortex during EF tests (Hagen et al., 2014; Müller et al., 2014). Accordingly, it can be anticipated that older adults at high fall risk will show greater and/or more widespread cortical activation relative to older adults at low fall risk during EF tasks. Interference tasks combine elements of set shifting and response inhibition and have been shown to reliably activate the cingulo-frontal-parietal (CFP) cognitive attention network (Bush, Shin, Holmes, Rosen, & Vogt, 2003; Bush & Shin, 2006). Given the relevance of mitigating interfering information to avoid a fall, as well as the sensitivity of functional neuroimaging during interference task performance, there is reason to explore the utility of neuroimaging during interference tasks with regard to differentiating high- from low-risk fallers.

The present study employs a multivariate approach to characterizing fall risk, and includes measures of physical, cognitive and neurophysiological functioning. In doing so, we are able to examine the contribution of indices from each domain as predictors of fall risk. In addition, we are able to better characterize the relationship between EF and gait functioning at both the behavioural, and neurophysiological levels. A priori hypotheses include that fallers will show greater variability in gait parameters under cognitive load, and that fallers will show patterns of cortical haemodynamic responses consistent with high-risk older adults (e.g., dedifferentiation).

# Method

## Participants

This study was approved by the University of Victoria Human Research Ethics Board and was conducted in accordance with institutional guidelines. Participants were healthy, community dwelling older adults recruited from the community. Exclusionary criteria included self-report of (a) a physician-diagnosed major medical illness with residual motor or sensory deficits (e.g., Parkinson's disease, stroke, heart disease, dementia, cancer, brain tumour), (b) severe sensory impairment (e.g., difficulty reading newspaper sized print, difficulty hearing a normal spoken conversation, difficulty writing or pressing buttons), (c) drug or alcohol abuse, (d) a history of inpatient psychiatric treatment, (e) significant cognitive impairment (i.e., Mini Mental State Examination - MMSE score below 24), or (f) English as a second language.

History of falls was obtained by participants' self-report, pertaining to the two-years leading up to their first study visit. The number of falls within this two-year period was recorded, with a fall defined as any instance in which the participant came to rest involuntarily on a lower surface (e.g., ground or floor). In total, 12 participants had had at least one fall within this period ($m = 1.92$, $SD = 1.24$). Testing was completed at the University of Victoria and participants came onsite twice to complete, first a cognitive, followed by a physical assessment session (each session lasted approximately 90 minutes). We report here on a subset of measures from a larger battery within an ongoing longitudinal study. For the purposes of the present analyses, data from 27 participants (15 females, 12 males) aged 71–81 ($m = 76.07$, $SD = 3.26$) were included (12 fallers and 15 non-fallers). Demographically, the groups were equivalent. There were no significant differences (all $p$s>.05) in total number of years of education (fallers: $m = 17.47$, $SD = 3.31$; non-fallers: $m = 17.17$, $SD = 2.25$), chronological age (fallers: $m=76.25$, $SD=3.19$; non-fallers: $m=75.93$, $SD=3.41$), biological sex (fallers: 8 females, 4 males; non-fallers: 7 females, 8 males), or crystallized ability (Vocabulary - fallers: $m=41.17$, $SD=6.16$; non-fallers: $m=42.60$, $SD=5.67$ ). 92.6% of participants were right-handed.

## Procedures

**Functional Near Infrared Spectroscopy data acquisition.—**Participants completed a series of standardized, paper-and-pencil neuropsychological measures, as well as a computerized cognitive task (described in Cognitive assessment). During the computerized tasks, participants wore custom-built fNIRS headgear consisting of an array positioned over prefrontal cortex containing 10 channels (8 at 3cm separation, 2 at 1.5cm separation), and were tested using a TechEn CW6 system (TechEn Inc., Milford, MA), using wavelengths of 690nm and 830nm to index deoxyhaemoglobin (HbR) and oxyhaemoglobin (HbO), respectively. We positioned the optical array relative to key 10–20 landmarks (Fpz, Fz, F7 and F8), and then obtained 3D coordinates of scalp reference as well as optode locations using a Polhemus Fastrak digitizer system (Polhemus, Colchester, VT), in order to perform probabilistic spatial registration (Singh, Okamoto, Dan, Jurcak, & Dan, 2005). Following this procedure, we generated Montreal Neurological Institute (MNI) coordinates for the mid-point of each source-detector pair (i.e., channel) for each participant, as well as average and composite standard deviation values across the group. Last, we converted the MNI coordinates to Brodmann's areas (BA) using Talairach Client software (Lancaster et al., 2000). The lateral most channels in both hemispheres recorded over BA 46, with all remaining channels recording over BA 10. The medial-most short-separation channels (4 and 8) were not used in the current study, and were therefore excluded from analyses.

Preprocessing of the fNIRS data was performed using Homer 2 software (Huppert, Solomon, Franceschini, & Boas, 2009). After converting the raw wavelengths to optical density values, we corrected for motion using a wavelet transformation algorithm (Molavi & Dumont, 2012) using an interquartile range of 0.1 (Brigadoi et al., 2014; Cooper et al., 2012). Next, we applied bandpass filtering to correct for physiological noise using a high-pass filter value of 0.02Hz and a low-pass filter value of 0.5Hz. We then converted from optical density to haemoglobin concentrations by applying the Modified Beer-Lambert Law, and then block averaged across conditions within the experiment. Finally, we computed average HbO and HbR estimates within these blocks. Conditions were block averaged using a window of 1 second before and 30 seconds after the onset of each condition (control and interference), and 1 second before and 20 seconds after the rest periods. After applying exclusionary criteria based on accuracy, we retained a total of 27 cases for the control condition (12 fallers, 15 non-fallers) and 21 cases for the interference condition (10 fallers, 11 non-fallers ). One participant (faller) did not undergo fNIRS recording because of personal reasons and 3 additional cases (fallers) were excluded from fNIRS analyses based on pre-processing, resulting in 11 fallers and 15 non-fallers in the control condition and 7 fallers and 11 non-fallers for the interference condition.

**Gait data acquisition.—**Gait patterns were measured using a 6.4m instrumented walkway with embedded 1cm$^2$ pressure sensors (GAITRite; CIR Systems, Sparta, NJ). Sensors are activated under pressure of initial foot contact and deactivated upon toe-off, enabling the detection of footfalls as a function of time with a sampling rate of 120Hz. Additionally, spatial information between two subsequent footfalls is captured, allowing for an analysis of both spatial and temporal properties of gait. Partial footfalls at the beginning and end of the mat were removed, and each pass of the mat was visually inspected for abnormalities.

## Measures

**Neuropsychological assessment.—**Given the scope and time commitment of the overall assessment protocols, we limited the neuropsychological assessment to the following measures. Perceptual speed (Digit Symbol - Wechsler, 1981), inductive reasoning (Letter Series – Thurstone, 1962), verbal fluency (Similarities - Ekstrom, French, Harman, & Dermen, 1976), crystallized ability (Vocabulary - Ekstrom et al., 1976) and episodic memory (Word Recall – Hultsch, Hertzog, & Dixon, 1990) were examined using a battery of standardized neuropsychological tests. The outcome variables for each task were as follows: Digit Symbol - total number correct in 90 seconds and number of symbols recalled; Letter

Series - total number correct in 6 minutes; Similarities - total number correct across 4 target words in 6 minutes; Vocabulary - total number correct in 15 minutes; Word Recall - total number correct produced in 5 minutes, after 2 minutes of studying. For a detailed description of the tests, the reader is referred to Dixon et al. (2007). In addition, we administered the Mental Alternation Test (MAT – Jones, Lee Teng, & Folstein, 1993) as a brief measure of executive function. In targeting these neuropsychological constructs, we endeavoured to span a range of cognitive processes (e.g., perceptual speed) to cognitive products (e.g., crystallized ability), in order to differentiate between areas of early decline that may be sensitive to fall risk (processes) from areas that show relative stability into late-life (products). The measures were also selected due their robust psychometric properties and widespread usage in the cognitive aging and neuropsychology literatures (Strauss, Sherman & Spreen, 2006).

**Cognitive assessment.—**The Multi-Source Interference Task (MSIT) is a computerized task of cognitive interference, and was designed to activate the CFP cognitive attention network in subjects while undergoing functional neuroimaging (Bush et al., 2003; Bush & Shin, 2006). Participants were presented with an array of three numbers (ranging in value from 0 – 3), one of which was a different numeric value than the others. Using a response input device with spatially mapped keys (i.e., numeric values 1, 2 and 3 corresponded to the first, second and third locations on the input device), participants were instructed to respond to the numeric value of the odd target (as opposed to the location of the target) as quickly as possible while remaining accurate, across a total of 15 trials within a 30-second block (see Figure 1). Participants were counterbalanced to begin with either the control (location and value of the target were congruent) or interference condition (location and value of the target were incongruent), and completed a total of four blocks for each of the conditions, which alternated. Accuracy as well as response latency were computed as the outcome measures.

**Gait assessment.—**During gait assessment, participants completed a task including cognitively unloaded and cognitively loaded conditions. During the unloaded condition, participants simply walked along the walkway, whereas during the loaded condition, they were asked to repeatedly subtract 7s from a given three-digit starting number while walking along the walkway. For both conditions, participants were instructed to walk at a self-selected, normal walking speed, while wearing comfortable walking shoes. The participants walked 1.5m before and after the mat ended, in order to account for acceleration and deceleration in gait velocity, with a total recorded walking distance of approximately 6.10m. A total of 10 passes were completed for each condition, and data were analyzed using GAITRite platinum software (GAITRite; CIR Systems, Sparta, NJ). Group mean and intra-individual variability of spatiotemporal gait parameters were computed. We selected swing time as a temporal parameter of gait, which was computed as the time (in seconds) between the last contact of the current footfall to the first contact of the next footfall on the same foot. Additionally, we selected step length as a spatial gait parameter, which was computed as the distance (in centimeters) from the heel center of the current footprint to the heel center of the previous footprint on the opposite foot.

# Results

## Neuropsychological Tests

A series of independent samples t-tests were performed to compare groups across each of the neuropsychological tests In general, non-fallers outperformed fallers across the battery, however, no significant group differences were observed (all *p*s > .05). Table 1 summarizes the results.

## Cognitive Computerized Test

MSIT scores were screened for blocks with accuracy performance less than 50%. Given the nature of the task and potential EF difficulties experienced by the participants, there were several blocks of interference results in which participants appeared to have reversed the criteria, responding to location instead of value. These blocks were removed from behavioural and fNIRS analyses, yielding a total of 21 cases with two or more valid blocks of interference responses. Next, we examined the effect of group status on MSIT accuracy and response latency (based on correct trials only), as well as number of valid trials (maximum = 60) for both the control (fallers, $n$=15; non-fallers, $n$=12) and interference (fallers, $n$=10; non-fallers, $n$ =11) conditions, using a series of independent samples t-tests. No significant differences were observed as a function of fall status (all *p*s > .05; see Table 2).[1]

## fNIRS Data

**Channel-wise within group comparison.—**We compared HbO and HbR within each group (fallers and non-fallers) and condition (control and interference) to identify active channels using paired-samples t-tests. Active channels were identified as those in which the average HbO concentration was significantly greater than the average HbR concentration. Within the group of non-fallers, no channels displayed significant differences for the control condition [#A1: $t$(14)=.24, $p$=.816; #A2: $t$(14)=1.14, $p$=.274; #B2: $t$(14)=−.57, $p$=.581; #B3: $t$(14)=−.19, $p$=.850; #C5: $t$(14)=1.53, $p$=.149; #C6: $t$(14)=.79, $p$=.441; #D6: $t$(14)=1.73, $p$=.106; #D7 $t$(14)=.86, $p$=.406] and only one channels (#D6) emerged as significant one-tailed in the interference condition [#A1: $t$(10)=.54, $p$=.600; #A2: $t$(10)=1.76, $p$=.109; #B2: $t$(10)=1.79, $p$=.105; #B3: $t$(10)=1.36, $p$=.204; #C5: $t$(10)=1.24, $p$=.243; #C6: $t$(10)=1.43, $p$=.184; #D6: $t$(10)=1.90, $p$ < .05, one-tailed; #D7 $t$(10)=1.41, $p$=.190]. Cohen’s d was also computed for the control (A1=0.08; A2=0.49; B2=0.21; B3=0.08; C5=0.55; C6=0.27; D6=0.72; D7=0.43) and interference conditions (A1=0.23; A2=0.81; B2=0.81; B3=0.61; C5=0.52; C6=0.64; D6=0.92; D7=0.62).

Within the group of fallers, several channels emerged as significant in both the control [#A1: $t$(10)=2.44, $p$ < .05; #A2: $t$(10)=3.34, $p$ < .01; #B2: $t$(10)=2.96, $p$ < .05; #B3: $t$(10)=2.98, $p$ < .05; #C5: $t$(10)=2.46, $p$ < .05; #C6: $t$(10)=1.76, $p$=.109; #D6: $t$(10)=3.10, $p$ < .05; #D7:

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[1] Although the p-value associated with the between-group differences in accuracy for the control condition approached significance and the corresponding effect size was large ($d$ = 0.83), these values were likely driven by restriction of range and heterogeneity in the non-faller group. Specifically, most non-fallers and fallers alike performed at ceiling for the control condition; however, 3 non-fallers performed slightly lower (85, 90 and 92% accuracy), which resulted in the larger SD for this group relative to the fallers (4.64 vs. 1.04).

$t(10)=2.01$, $p < .05$, one tailed], and interference conditions [#A1: $t(6)=1.35$, $p=.226$; #A2: $t(6)=2.69$, $p < .05$; #B2: $t(6)=3.14$, $p < .05$; #B3: $t(6)=1.43$, $p=.204$; #C5: $t(6)=1.01$, $p=.350$; #C6: $t(6)=1.02$, $p=.349$; #D6: $t(6)=1.87$, $p=.111$; #D7: $t(6)=.68$, $p=.522$]. Figure 2 displays the group by condition activation patterns. Relative to non-fallers, Cohen's d was comparatively larger across the control (A1=1.02; A2=1.50; B2=1.28; B3=1.22; C5=0.96; C6=0.80; D6=1.41; D7=0.53) and interference conditions (A1=0.71; A2=1.54; B2=1.66; B3=0.76; C5=0.55; C6=0.54; D6=1.05; D7=0.19).

**Relative HbO group-wise comparison.—**Next, the relative amount of HbO between groups across the control and interference conditions was compared using independent samples t-tests. We computed the amount of HbO in each of these conditions relative to the rest condition, as well as between the interference and control conditions. This approach has been recently shown to effectively compare activation between groups using continuous-wave fNIRS techniques (Hagen et al., 2014).

The largest effects were observed in the relative amount of HbO between control and rest, with all 4 channels in the left hemisphere [#A1: $t(24)=2.15$, $p < .05$, $d=0.89$; #A2: $t(24)=2.62$, $p < .05$, $d=1.07$; #B2: $t(24)=4.23$, $p < .001$, $d=1.72$; #B3: $t(24)=2.44$, $p < .05$, $d=1.02$) and 3 channels in the right hemisphere (#C5: $t(24)=1.52$, $p=.142$, $d=0.61$; #C6: $t(24)=1.78$, $p < .05$, $d=0.74$, one tailed; #D6: $t(24)=2.54$, $p < .05$, $d=1.00$; #D7: $t(24)=2.12$, $p < .05$, $d=0.81$) showing significant group differences. In these channels, fallers recruited a greater amount of relative HbO than non-fallers. The relative amount of HbO between interference and rest yielded one significant group difference in the lateral-most channel in left hemisphere (#A1: $t(16)=1.81$, $p < .05$, one tailed, $d=0.95$), such that fallers recruited a greater amount of relative HbO than non-fallers. Cohen's d for the relative interference contrast was uniformly smaller (less than 0.8) for the non-significant channels (A2=0.74; B2=0.71; B3=0.14; C5=0.05; C6=0.00; D6=0.31; D7=0.37). The relative amount of HbO between interference and control conditions did not yield any significant group differences, all $p$s > .05. Figure 2 summarizes the results.

**Gait—**We computed mean-level and variability estimates to examine step length and swing time gait parameters in both the unloaded and loaded conditions. Coefficient of variation (CV) was used to estimate variability in a given parameter, independent of mean group differences. Fallers were more variable in step length than non-fallers in the loaded ($t(23)=3.05$, $p < .01$, $d=1.178$), but not the unloaded condition, $p > .05$. Group differences were also observed in mean step length during the loaded ($t(23)=1.95$, $p < .05$, one tailed, $d=0.758$), but not the unloaded condition, $p > .05$. Additionally, group differences were observed in swing time variability (CV) during the loaded ($t(23)=2.10$ $p < .05$, $d=0.786$), but not the unloaded condition, $p > .05$. No group differences were observed in mean swing time for either the loaded or unloaded conditions, $p$s > .05. For both swing time and step length, larger magnitude effects were observed for the loaded condition and for the indicator of variability. Figure 3 summarizes these results.

### Predicting Fall Risk

We examined the odds ratios associated with the most influential marker (i.e., the one that exhibited the largest group differences) from each of the domains of interest; cognitive (MSIT Control RT), gait (step length variability in the loaded condition) and neurophysiological (#B2 Control - relative HbO between control and rest). To facilitate direct comparison, we standardized each predictor (T-score metric) and then entered them in a logistic regression analysis to examine whether individual differences were associated with an increased risk of falling (see Table 3). The overall model was significant $X^2$ (3) = 20.35 $p < .001$, explained 74.6% (Nagelkerke $R^2$) of the variance and correctly classified 88% of the cases. Given our a priori hypotheses regarding expected directional effects, we employed one-tailed tests for specific, planned comparisons. Of the variables included in the model, the neurophysiological index showed the strongest effect ($p < .05$), such that a one-unit increase in the amount of HbO during the control task relative to baseline (i.e., rest) was associated with a 38% greater likelihood of being classified as a faller, controlling for differences in the cognitive and gait indices. The gait index also showed a significant effect ($p < .05$, one tailed), such that a one-unit increase in step width variability during the loaded condition was associated with a 16% greater likelihood of being classified as a faller, controlling for differences in the cognitive and neurophysiological indices. The cognitive index did not yield a significant effect, $p > .05$.

## Discussion

In this study, we examined physical, cognitive and neurophysiological functioning in older adults with and without previous fall histories. Participants were community dwelling older adults with no previous neurological trauma or psychiatric impairment, who were otherwise cognitively intact. They completed a comprehensive, multimodal assessment comprising neuropsychological, cognitive-computerized, neurophysiological and gait measures.

We observed only a single group difference in neuropsychological test performance, such that fallers performed less accurately on a measure of inductive reasoning. Non-fallers showed slightly better performance on a measure of semantic memory, however the difference was not statistically reliable. Behavioural performance on a computerized test of cognitive-interference also yielded non-significant group differences. In contrast, several trends were observed in the haemodynamic responses evoked by the cognitive-interference test (an index of EF), which were recorded using fNIRS. During the control task, fallers displayed activation in each of the left hemisphere channels, and in 3 of the right hemisphere channels. By contrast, no active channels were observed for non-fallers. Despite minimal differences observed in behavioural performance, fallers recruited additional neural tissue in order to perform the task accurately. This pattern is in keeping with a dedifferentiation effect (e.g., Grady, 2012); that is, fallers displayed more widespread cortical activation relative to the non-fallers. Further, in comparing the relative amount of oxyhaemoglobin between groups, fallers displayed greater concentrations, bilaterally across the prefrontal cortex, to perform at similar levels to the non-fallers.

During the interference condition, fallers again displayed widespread activation across left prefrontal cortex, while non-fallers displayed relatively little activation, with only a single channel in medial right prefrontal cortex showing activation. In comparing the relative amount of oxyhaemoglobin between groups during the interference condition, fallers recruited greater concentrations in a single channel in left prefrontal cortex to perform at similar levels of behavioural performance to non-fallers. In contrast to the simpler control task, the interference task required the recruitment of additional oxyhaemoglobin in both groups, such that the group differences in the relative amount of oxyhaemoglobin were minimized. Overall, the additional recruitment of oxyhaemoglobin that is more widely distributed, particularly for the simpler control task, may be indicative of a potential pathophysiology associated with fall risk (e.g., dedifferentiation).

In addition to the group differences observed in neurophysiology, several notable effects were observed in the obtained gait patterns. Whereas no differences were observed while participants were simply walking along the instrumented walkway, fallers were more variable in two gait parameters (swing time and step length) while under cognitive load. In keeping with recent findings suggesting that variability in gait under cognitive load may be the most sensitive gait indicator for predicting fall risk (Verghese et al., 2009), these results further the assertion that the executive control associated with dual tasking is uniquely associated with the decreased stability in gait associated with fall risk.

## Limitations

Several limitations to the present study should be noted. The optical array used in the current study was limited to coverage of a portion of the frontal cortex (BA 10 & 46), and interpretations cannot be extended to other potential regions of interest. Given that the use of MSIT with fNIRS is relatively unprecedented in the literature, our results are limited to a comparison with fMRI findings, which although limited in time resolution, benefit from superior spatial resolution. We used a relatively liberal definition of fall status (falls within a 2-year time frame), and participants did not undergo clinical assessment for MCI. Therefore, we remain cautious in offering strong claims regarding disease-specific mechanisms that may be related to falls and to MCI. With a greater sampling density of those at greater fall risk and follow-up testing of the reported sample (currently underway), we may be able to examine a narrower time frame (e.g., falls within 6 months) as well as recurrent versus one-off fallers. The sample size for the current study is small, thereby limiting statistical power to detect group differences. Recognizing this shortcoming, we augmented the inferential tests by computing corresponding measures of effect size (Cohen's *d*) that indicated sizeable differences between groups. Despite several tests of statistical significance yielding trends, the combination of directional hypotheses, one-tailed tests of significance, and the corresponding large magnitude effect sizes suggests a reasonably robust pattern of group differences that are in keeping with the extant literature. Further, although each class of predictor was subject to the same sample size limitations, the neurophysiological and gait markers emerged as significant indicators of group status in contrast to the behavioural cognitive measures. Replication of these findings in future investigations will be important to increase confidence in the conclusions reported. With more comprehensive neuropsychological tests of executive functioning (e.g., D-KEFS), group differences in performance may also be detected. Lastly, as we aggregated haemoglobin estimates across

30 second task blocks, our effects are likely a conservative estimate of the haemodynamic response relative to other techniques used in fNIRS analysis (e.g., peak detection).

## Conclusion

Falls are a leading cause of injury amongst older adults (Kearney et al., 2013) and are more prevalent in individuals with MCI than in healthy older adults (Delbaere et al., 2012; Liu-Ambrose et al., 2008). Falls, especially when recurrent, may serve as clinically salient index events for older adults at risk for MCI. Early identification of those at risk for falls is essential, and early intervention efforts stand to benefit from an understanding of which domains of functioning show the earliest and most significant decline, in order to intervene before the potential conversion of MCI to dementia. Differences in gait stability appear to be mediated by executive control (Springer et al., 2006) and it appears that there are differences in neurophysiology between those at higher- vs. lower-risk of falls, which are uniquely associated with performance on a cognitive interference task. In comparing physical, cognitive and neurophysiological modalities, both gait and haemodynamic response markers were associated with a significant increased risk of experiencing a fall. In contrast, standardized neuropsychological measures, although well-established in clinical practice, may lack the sensitivity required to detect early declines in cognitive function (e.g., in EF), with impairment detected only after an underlying pathophysiology has manifest in behaviour.

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Further information about the study may be obtained by contacting Dr. MacDonald at smacd@uvic.ca

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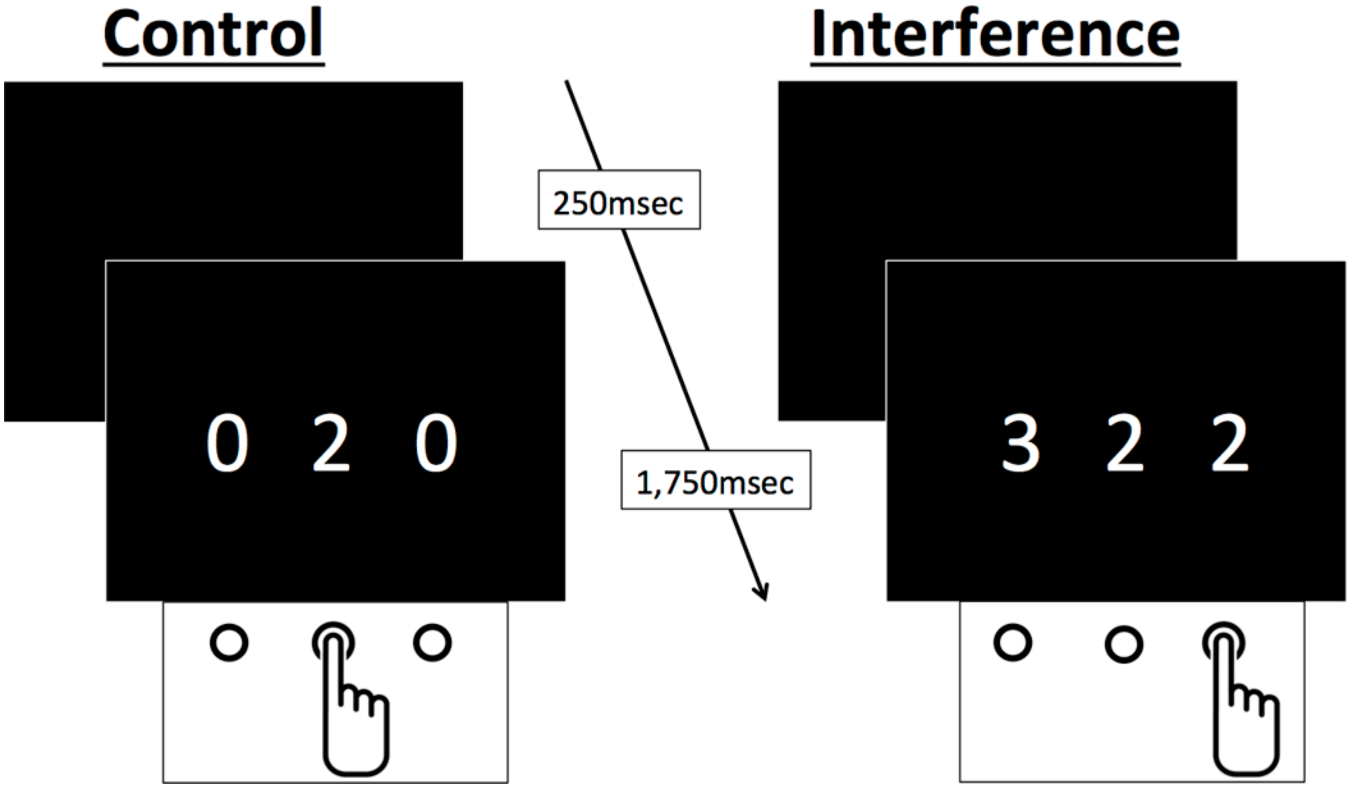


**Figure 1.**

The Multi-Source Interference Task (MSIT). Participants are presented with three numbers and indicate the value of the number that is different than the other two. The value is congruent in the control condition, and incongruent in the interference condition.

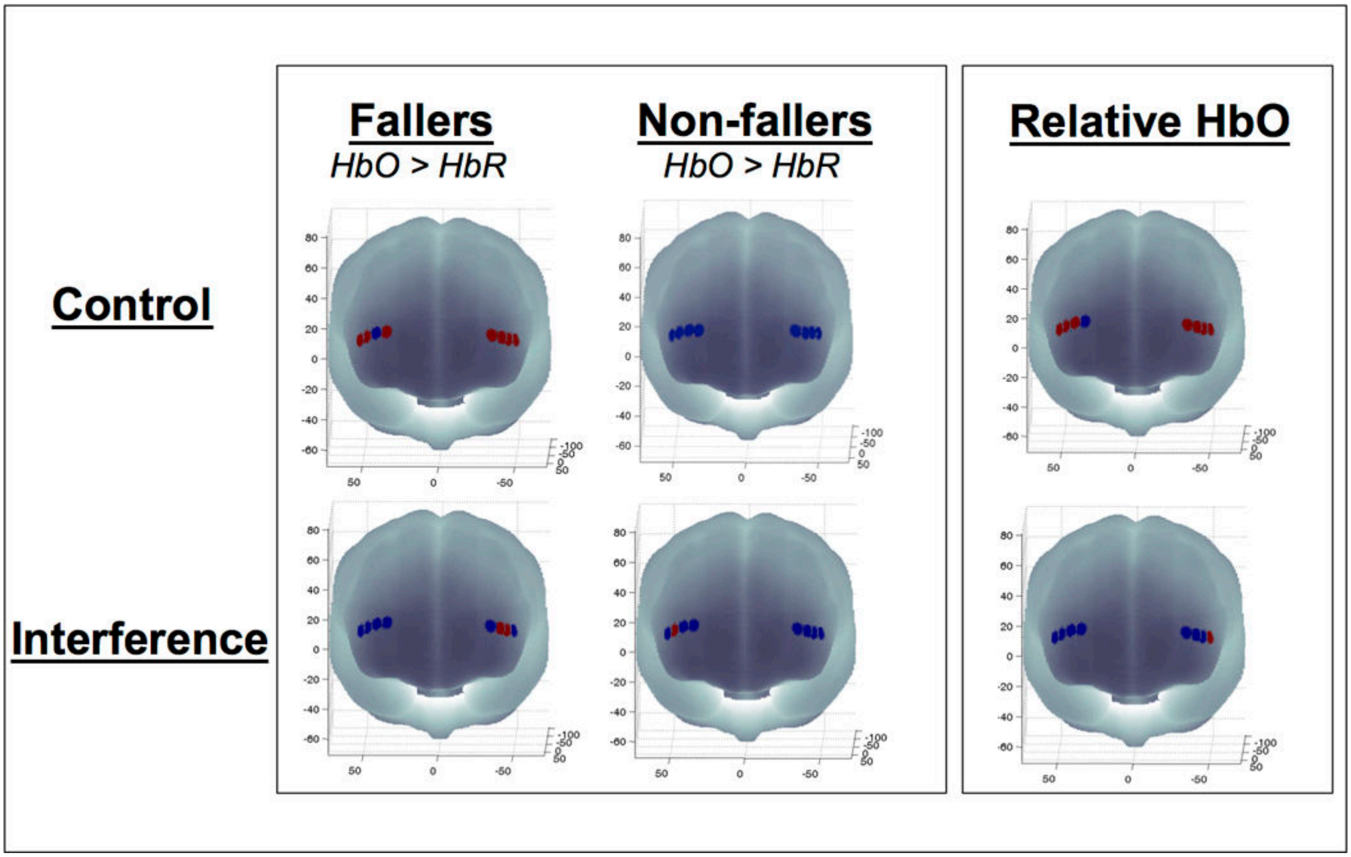
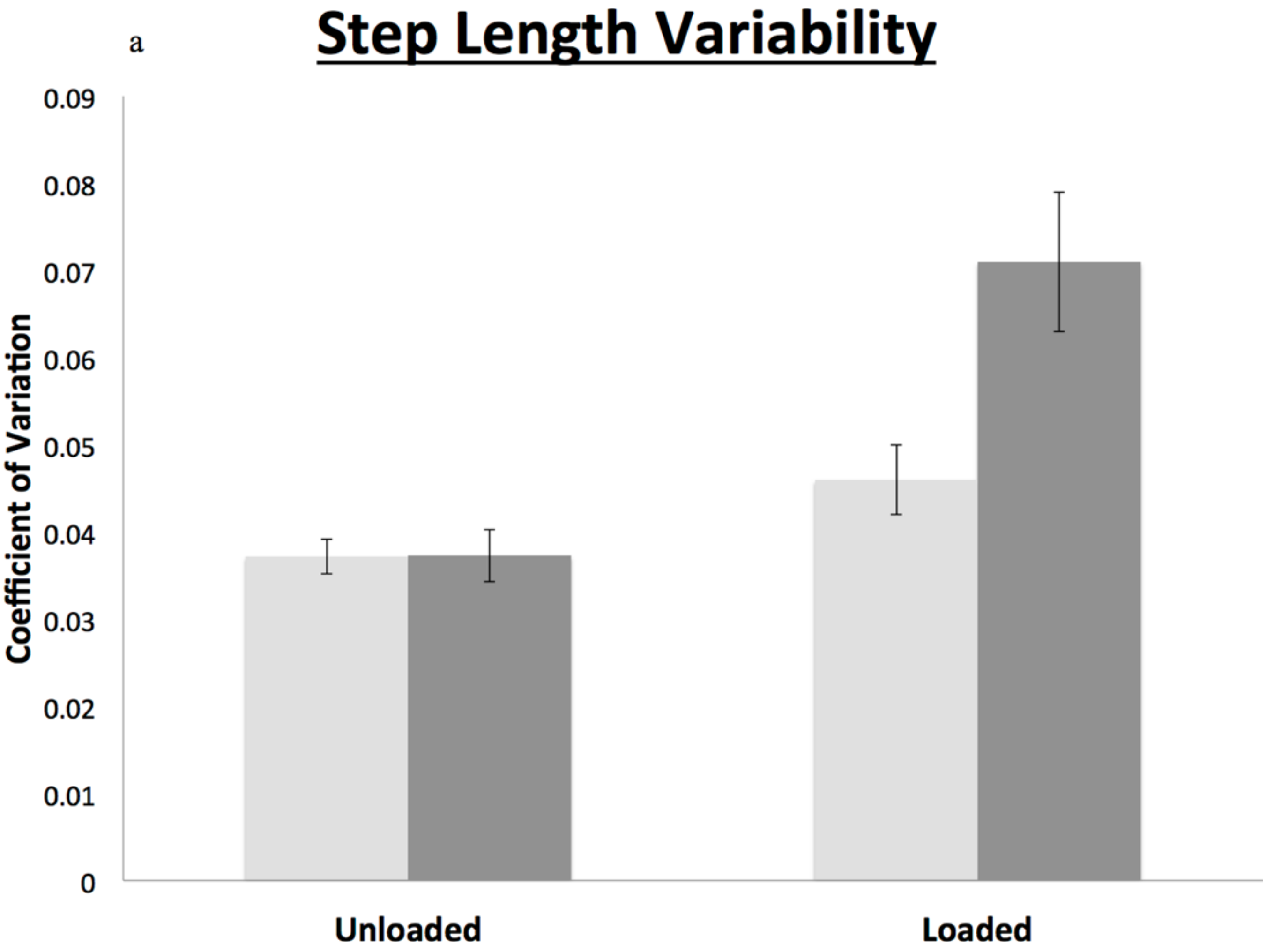


**Figure 2.**

*Left panel:* Active channels (i.e., where mean oxyhaemoglobin (HbO) concentration is greater than mean deoxyhaemoglobin (HbR) concentration) for Multi-Source Interference Task (MSIT) control and interference conditions. Red channels indicate where the difference between HbO and HbR was significant. *Right panel:* Relative oxyhaemoglobin (HbO) between group comparisons for Multi-Source Interference Task (MSIT) control and interference conditions, computed as the difference between experimental conditions (control and interference) and rest. Red channels indicate significant between-group (fallers vs. non-fallers) differences.


a
Step Length Variability
Coefficient of Variation
0.09
0.08
0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
Unloaded
Loaded

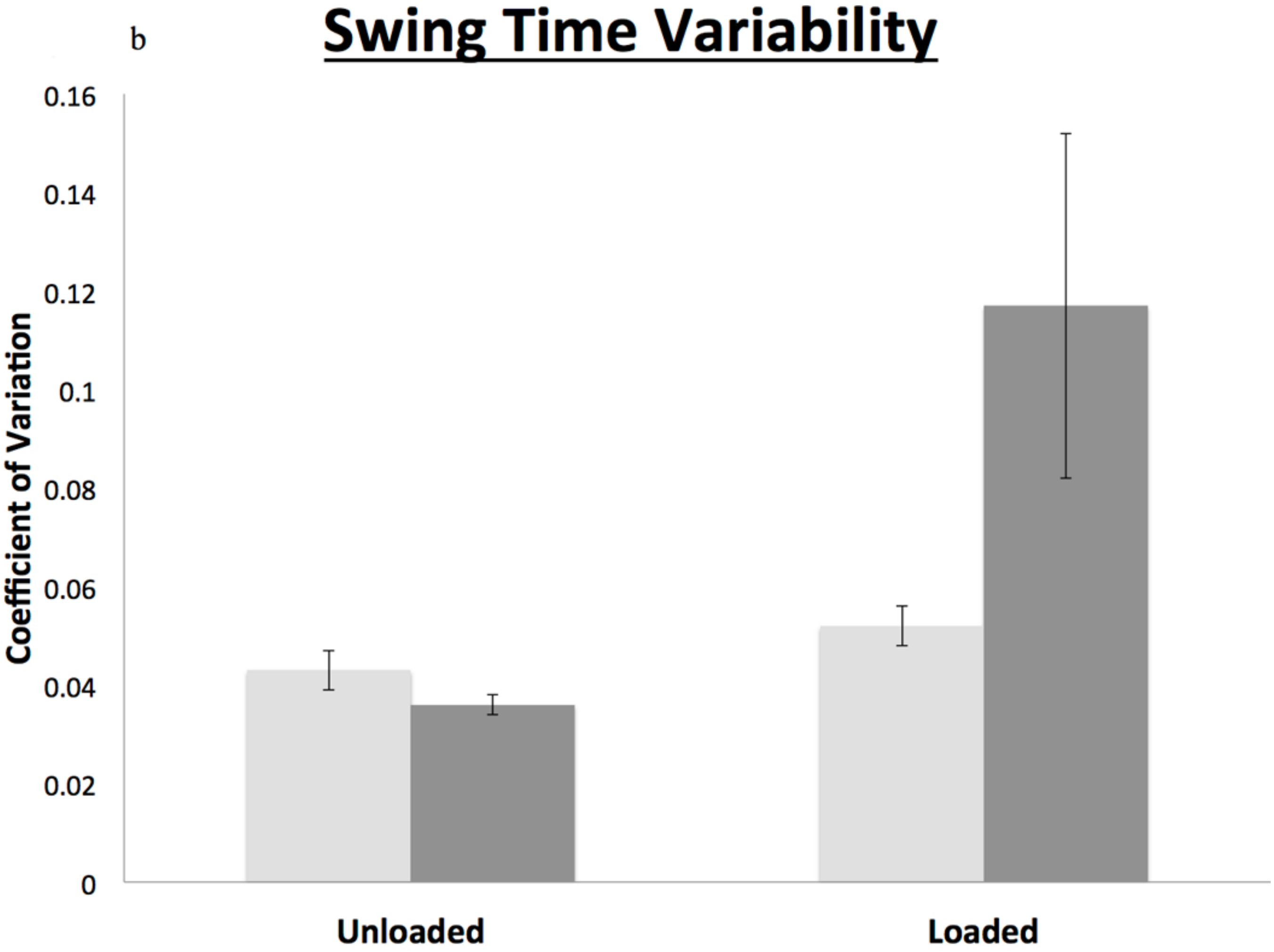


**Figure 3.**

Variability in (a) step length and (b) swing time in both the unloaded (walk-only) and loaded (walk + count backwards by 7s) conditions. Fallers (dark grey) were more variable than nonfallers (light grey) in both gait parameters during the loaded condition only.

## Table 1.

Group differences on neuropsychological tests.

| ***Task and outcome variable*** | ***Group Status*** | | | | |
|---|---|---|---|---|---|
| | **Non-Fallers** | **Fallers** | ***t* value** | ***p* value** | **Cohen's *d*** |
| *MAT* - Accuracy | 29.33 (11.32) | 24.42 (12.80) | 1.059 | 0.300 | 0.406 |
| *Digit Symbol* - Accuracy | 46.27 (9.93) | 43.92 (10.66) | 0.591 | 0.560 | 0.228 |
| Digit Symbol- Symbols Recalled | 6.27 (1.98) | 6.17 (2.59) | 0.114 | 0.910 | 0.043 |
| Letter Series- Arruacy | 11.80 (4.07) | 9.00 (4.05) | 1.780 | 0.087 | 0.690 |
| Similarities- Accuracy | 16.53 (5.82) | 16.50 (7.87) | 0.013 | 0.990 | 0.004 |
| Vocabulary- Accuracy | 42.60 (5.67) | 41.17 (6.16) | 0.628 | 0.535 | 0.242 |
| Word *Recall* - Accuracy | 13.93 (5.11) | 13.25 (6.85) | 0.297 | 0.769 | 0.113 |

Mean values are reported for each group, with standard deviations in parentheses.

## Table 2.

Group differences on the Multi-Source Interference Task (MSIT).

| ***Task*** | ***Group Status*** | | | | |
|---|---|---|---|---|---|
| | **Non-Fallers** | **Fallers** | ***t* value** | ***p* value** | **Cohen's *d*** |
| Accuracy: Control | 96.78 (4.64)<br>*n*=15 | 99.58 (1.04)<br>*n*=12 | 2.043 | 0.052 | −0.833 |
| RT: Control | 639.34(153.09)<br>*n*=15 | 618.70 (77.43)<br>*n*=12 | 0.425 | 0.675 | 0.170 |
| Number of Trials: Control | 58.47 (2.45) | 59.83 (0.39) | 1.909 | 0.068 | −0.775 |
| Accuracy: Interference | 82.68 (13.53)<br>*n*=11 | 80.67 (13.41)<br>*n*=10 | 0.342 | 0.736 | 0.149 |
| RT: Interference | 1118.45 (122.51)<br>*n*=11 | 1157.07 (125.42)<br>*n*=10 | 0.714 | 0.484 | −0.312 |
| Number of Trials: Interference | 53.93 (6.78) | 49.92 (11.32) | 1.144 | 0.263 | 0.430 |

RT = response time; mean values are reported for each group, with standard deviations reported in parentheses.

### Table 3.

Fall risk as a function of cognitive (MSIT Control RT), gait (step length variability in the loaded condition) and neurophysiological (#B2 Control - relative HbO) predictors.

| | | 90% CI for Odds Ratio | | | |
|---|---|---|---|---|---|
| **Variable** | ***B* (SE)** | **Odds Ratio** | **Lower** | **Upper** | ***p* value[*]** |
| Control RT | 0.005 (0.06) | 1.005 | 0.908 | 1.112 | 0.47 |
| Step Length Variability (*Loaded*) | 0.151 (0.08) | 1.163 | 1.019 | 1.328 | 0.03 |
| #B2 HbO[a] (*Control vs. Rest*) | 0.319 (0.16) | 1.376 | 1.061 | 1.786 | 0.02 |

[a] oxyhaemoglobin

[*] one-tailed