Exercise interventions, postural control, and prefrontal cortex activation in older adults

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Abstract

Abbreviations: PFC = prefrontal cortex; fNIRS = functional near-infrared spectroscopy; ML = medial-lateral; AP = anterior-posterior~~; HBR = deoxygenated blood; HBO = oxygenated blood~~

Improving postural control in older adults is necessary for reducing fall-risk, and prefrontal cortex activation may also play a role. We sought to examine the impact of exercise interventions on postural control and prefrontal cortex activation during standing balance tasks. We hypothesized that balance would improve and prefrontal control would be reduced. We assessed a subset of participants enrolled in a randomized trial of two exercise interventions. Both groups completed strength and endurance training and the experimental treatment arm included training on timing and coordination of stepping. Postural control and prefrontal cortex activation were measured during dual-task standing balance tasks before and after the intervention. Eighteen participants in the standard strengthening and mobility training arm and 16 in the timing and coordination training arm were included. We examined pre- to post-intervention changes in each study arm, and compared them between interventions. Results did not show any pre- to post-intervention changes on standing postural control nor prefrontal cortex activation in either arm. In addition, there were no differences between the two intervention arms in either balance or prefrontal activation. While exercise interventions can improve mobility, we do not demonstrate evidence of improved standing balance or prefrontal control in standing.

Keywords: prefrontal cortex; exercise intervention; postural control; older adults

1 Introduction

The United States incurs $50 billion annually in fall-related healthcare costs (Florence et al., 2018). One third of people aged 65 and older fall every year, accounting for the majority of

injury-related hospitalizations and deaths in older adults (Stevens et al., 2006). Even non-fatal falls are associated with decreased independence and lower life expectancy (Stevens et al., 2006). Poor postural control is strongly associated with higher fall risk in older adults (Graafmans et al., 1996; Pua et al., 2017; Rogers et al., 2003). Contributing factors that result in age-related reduced postural control include A) reduced proprioceptive and vestibular sensory input, B) increased reliance on visual information, C) increased muscle stiffness, and D) increased cognitive requirements during postural control (Dominguez, 2020).

Postural control, the control of bodily position for the purpose of balance, was previously considered an entirely automatic process (Woollacott & Shumway-Cook, 2002). However, postural control is a complex motor task that involves brain regions responsible for sensory integration, motor planning, and attention (Mierau et al., 2017; Redfern et al., 2019). Attention is part of the "executive processes" that are performed by brain regions primarily in the frontal lobe like the prefrontal cortex (PFC). Cognitive tasks that require attention may cause competition for neural resources and lead to postural control disruptions. Additionally, automaticity of postural control decreases with age and requires more attentional demand. PFC activation has been shown to be higher in older adults than in younger adults during dual-task balance and cognition conditions (Rosso et al., 2017), suggesting increased requirements of attention in older adults perhaps influenced by reduced decision-making speed and sensory integration inhibitory processes (Redfern et al., 2019). These age-related changes in cognition and postural control may contribute to increased fall risk in older adults (Rosso et al., 2017; Woollacott & Shumway-Cook, 2002), but this relationship is not well understood. Most mobility

interventions focus on muscular and cardiovascular improvements and disregard the underlying neuronal processes (Brach et al., 2022).

To target the neural component, an exercise intervention employed motor skill training in addition to endurance training, strength training, and behavioral lifestyle intervention (Brach et al., 2020). In this intervention primarily aimed at improving gait, motor skill training used timing and coordination walking tasks to induce a motor learning effect (Brach et al., 2013; Macaluso & De Vito, 2004). This motor learning is essentially a "neurological exercise" that was hypothesized to increase neural efficiency, and thus improve automatic motor control required for gait (Brach et al., 2013). Gait is a complex motor skill that has overlapping physical requirements to standing postural control. Both require an individual to remain upright by activating specific lower limb and trunk musculature, not to mention they both heavily rely on sensory inputs (proprioceptive, vestibular, visual). We could then infer that the neural requirements for gait and standing postural control also overlap. Motor skill training would, therefore, assist older adults in improving not only their mobility (Brach et al., 2020) but also their postural control, particularly during dual-task conditions when higher attentional demands require postural control to be more automatic (Woollacott & Shumway-Cook, 2002).

We propose that improvements in balance after exercise interventions are in part due to changes in neural control mediated by the prefrontal cortex. We can monitor changes in postural control and neural activity simultaneously using accelerometers and functional near-infrared spectroscopy. Functional near-infrared spectroscopy (fNIRS) is gaining popularity as a

non-invasive tool for measuring real-time brain activity during balance studies (Karim et al., 2013; Rosso et al., 2017). This neuroimaging modality uses light to measure changes in cortical blood flow – changes which are driven by neural activity as described by neurovascular coupling (Scholkmann et al., 2014). Higher PFC activation in older adults has been shown to be related to worse balance performance, suggesting neural inefficiency (Lehmann et al., 2022). Few fNIRS studies have employed quiet standing, or static balance, in their experimental design, other than as a baseline condition. Instead, participants often perform more difficult tasks such as dynamic posturography perturbations (Rosso et al., 2017), standing on a wobble board (Herold et al., 2017; Lehmann et al., 2022), or employing a tandem stance (Chen et al., 2018; Marusic et al., 2019). We are interested in quiet standing because it requires minimal physical demand and no additional equipment. This would make quiet standing a safer and more accessible balance assessment condition, particularly for individuals with poor balance, that could be more easily translated into clinical settings.

We sought to examine the impact of exercise interventions on postural control and prefrontal cortex activation in older adults. We hypothesized that older adults that received specific timing and coordination motor skill training compared to those in a standard intervention would increase postural control automaticity during dual-task standing conditions, resulting in better balance performance as measured by accelerometry. We anticipated that, with this improvement in balance performance, we would also see reduced PFC activity as measured by fNIRS, indicating increased neural efficiency. Previous motor learning interventions have displayed the plasticity of PFC function with similar, or less, training time. These studies

reported that PFC fNIRS signals decreased with training of the motor task (Eggenberger et al., 2016; Ono et al., 2015). While we acknowledge that this analysis of a randomized clinical trial is limited due to sample size, we also point out that the benefits of the exercise interventions may be present in the whole sample. Accordingly, we hypothesized that older adults in either intervention arm would exhibit improved single- and dual-task balance performance and reduced PFC activity following participation in exercise interventions.

2 Methods

2.1 Sample

Data for this research comes from participants that we recruited from the "Program to improve mobility in aging" (PRIMA) intervention study (Brach et al., 2020). There were 249 participants in the parent study, 43 of whom were enrolled in the PRIMA-NIRS ancillary study on which the present analysis is based. To be eligible for the PRIMA intervention study, participants had to be at least 65 years old, have a gait speed in the range of 0.60 to 1.2 m/s, be able to walk unassisted, and be cleared by a physician to participate (Brach et al., 2020). Exclusion criteria focused on inability to participate in testing or exercise programs and safety concerns. Gait speed was the primary outcome for the main study. The primary results of the intervention showed that gait speed increased for the whole sample, but no differences were found between the treatment arms (Brach et al., 2022).

No additional eligibility criteria were required for the PRIMA-NIRS ancillary. Participants were scheduled to be assessed four times, at weeks 0 (pre-intervention), 12 (immediate post-

intervention), 24, and 36. Analyses presented here use data from before the intervention (~~PRE~~pre-intervention) at week 0 and after the intervention (~~POST~~post-intervention) at week 12. Therefore, participants must have completed at least the 0- and 12-week visits to be included in these analyses. 34 of the 43 participants were thus eligible for this study (**Figure 1**). Accelerometry data from 7 participants and fNIRS data from 1 participant were excluded due to recording errors or poor signal quality. Therefore, our final analytic sample included 33 participants for fNIRS analyses of prefrontal cortical activation and 27 participants for accelerometry analyses of balance performance (Figure 1). The University of Pittsburgh Institutional Review Board approved the study and all ~~subjects~~ participants provided informed consent.

We report metrics collected in the parent study to characterize the study population. During the clinical screening step of participant recruitment, the following metrics were recorded: age, gender, race, education, height, weight, body-mass index, comorbidities, Modified Mini-Mental State scores (Teng & Chui, 1987), Short Physical Performance Battery scores (Guralnik et al., 1994), and falls history questionnaire. Gait speed (details below) and Trail Making Test times for parts A and B (Bowie & Harvey, 2006) were collected at each visit.

2.2 Interventions

The interventions have been previously described in detail (Brach et al., 2020). Briefly, all participants completed 12-weeks of exercise training with two in-person physical therapist-led sessions per week that included lower extremity strength training, endurance training, and a

behavioral lifestyle intervention. The goal for lower extremity strength training and endurance training is to exercise in a perceived effort range that is "somewhat hard" (Rating of Perceived Exertion 10-13) (Borg, 1970). The aim of the parent PRIMA intervention study was to examine whether specific timing and coordination exercises improved skillful, or smooth, automatic control of walking beyond standard training (Brach et al., 2020). Therefore, participants were randomly assigned to either the Standard therapy group or the Standard plus timing and coordination group (Standard+ group) (Brach et al., 2020). The timing and coordination exercises consisted of progressively more difficult stepping and walking patterns such as alternate forward and backward stepping and walking while tossing a ball. Training time between two groups were kept equal by reducing endurance training time for the Standard+ group (Brach et al., 2022).

2.3 Dual-Task Paradigms

We assessed both postural control performance and PFC activity under the quiet standing condition (single-task) and standing while simultaneously completing a cognitive task. These data are extracted from a larger mobility protocol, of which the details have been described previously (Hoppes et al., 2020). The single- and dual-task components of the standing protocol were each 20 seconds long, with the single-task preceding the dual-task. The cognitive task instructed participants to recite every other letter of the alphabet starting with the letter 'B'. This cognitive dual-task was selected because it is thought to be a good parallel to carrying a conversation and is commonly used in other fNIRS studies that examine walking and cognition (Holtzer et al., 2011, 2016; Holtzer, Schoen, et al., 2017; Holtzer, Yuan, et al., 2017; Hoppes et

al., 2020). No instructions were given to the participants on which task to focus or how to place their feet; they were simply told to stand quietly. Participants performed the dual-task protocol twice per trial over four trials for a total of eight repetitions per visit. Cognitive task performance was quantified as alphabet performance by dividing the number of correct letters by the duration of the task (20 seconds), as essentially the rate of correct letters generated per second. Eight trials were averaged together for each visit. Gait speed for each visit was averaged from four trials of timed 15-meter walks on a flat straight pathway on the track.

2.4 Accelerometry

Postural control performance was monitored by a tri-axial accelerometer placed over the L3 segment of the lumbar spine, used to approximate the center of mass. The accelerometer measures linear accelerations of the center of mass in the medial-lateral (ML), vertical, and anterior-posterior (AP) axes. Lower back accelerometry has been validated as an effective method to evaluate postural control performance (Whitney et al., 2011). Acceleration signals were sampled at 100 Hz; although 33% were incorrectly sampled at 30 Hz and were then up-sampled to 100 Hz during signal preprocessing. Effects of gravity on the signals were removed by correcting for accelerometer tilt using the transformations defined in Moe-Nilssen 1998 (Moe-Nilssen, 1998). Preprocessing of the signals began by removing outliers using a 5^{th} order median-filter (Sejdić et al., 2016). The signals were then passed through a 4th order, zero-phase, low-pass Butterworth filter with a cutoff frequency of 2 Hz (Alkathiry et al., 2018; Alqahtani et al., 2017, 2020). Accelerometry signals were parsed by task and visit type into four

different conditions: ~~PRE~~ pre-intervention single-task, ~~PRE~~ pre-intervention dual-task, ~~POST~~ post-intervention single-task, ~~POST~~ post-intervention dual-task.

We then calculated a variety of accelerometry features for each signal segment. We initially extracted 12 accelerometry features which we had demonstrated previously as being sensitive to this standing dual-task paradigm (Bohlke et al., 2021). In addition, we computed the root-mean-square of the accelerometry signal in ML and AP directions due to their prevalence in the literature (Alqahtani et al., 2017, 2020; Maurer & Peterka, 2005; Prieto et al., 1996; Whitney et al., 2011). To reduce redundancy across our features, we then examined associations between these 14 features. Accelerometry features with high correlation with one another were removed (n=7). The remaining seven signal features were root-mean-square ML, root-mean-square AP, centroid frequency AP, bandwidth ML, entropy rate AP, wavelet entropy ML, and cross-correlation between ML and AP signals. This set of features covers time, frequency, and time-frequency domains as well as statistical and information theory aspects of the accelerometry signals (Sejdic et al., 2014). We used Matlab version 2020a (MATLAB, The MathWorks, Inc., Natick, MA) to preprocess signals, extract variables, and run correlations for data reduction.

Some accelerometer data included signal drops when the sensors detected low levels of activity and activated a battery saving mode which resulted in flat traces. If there was more than 2 seconds of signal drop, the trial for that task was removed and not used in postural analysis. Of the 34 participants that completed the 0- and 12-week visits, seven participants did not have

sufficient accelerometry data for each of the four experimental conditions (PRE single-task, PRE dual-task, POST single-task, POST dual-task). Those participants were not included in analyses involving accelerometry features; therefore, the total sample size for balance performance accelerometry metrics is 27 (14 in Standard group, 13 in Standard+ group).

2.5 Functional Near-Infrared Spectroscopy

During the mobility tasks, participants wore a wireless fNIRS system (OctaMon, Artinis Medical Systems, Einsteinweg, Netherlands) on their forehead to monitor PFC hemodynamic response. Our fNIRS protocol follows recommendations for data collection, analysis, and reporting (Menant et al., 2020). The fNIRS system utilizes eight light emitting sources and two detectors covering the forehead symmetrically (**Figure 2**). Distance between source and detector is 35 mm. The center of the fNIRS system was aligned with the center of the nose and placed such that the lower optodes were just above the eyebrows for each participant to maintain consistent placement. The 10-20 EEG coordinate system was also used to measure relative placement of the fNIRS probes. The detectors and sources cover the left and right PFC, more specifically Broca's areas BA9, BA44, BA45, and BA46. The two near-infrared wavelengths used by this system are 760 nm and 850 nm, which target deoxygenated ~~(HBR)~~ and oxygenated hemoglobin in the blood ~~(HBO)~~, respectively.

To process the fNIRS data, signals were first trimmed to keep only two seconds of data before and after mobility tasks to reduce baseline noise. Flagged tasks and data channels with flat signals, due to equipment malfunction or saturation, were identified and removed from

analysis. We then converted raw light intensity data to optical density, down-sampled from 10 Hz to 4 Hz, and converted the optical density data to hemoglobin concentrations using the modified Beer-Lambert Law (Santosa et al., 2018). A canonical general linear regression model was used to estimate hemoglobin concentrations for each task relative to the global baseline of the signal. Physiological artifacts and motion artifacts were removed using an autoregressive iteratively reweighted least squares method. This method works by repeatedly applying an autoregressive filter to the generalized linear model that attenuates slow drifting effects from physiological and motion artifacts (Santosa et al., 2018). This autoregressively filtered generalized linear model ~~model~~ is then iteratively weighted to strongly attenuate large errors like motion artifacts.

We ran Student's t-tests to compare the estimates from the generalized linear model between tasks (Santosa et al., 2018). The quiet standing (single-task) fNIRS signal was used as the control condition to which the dual-task fNIRS signal was compared. Positive t-statistic values indicate the likelihood that the concentration of ~~HBO~~ oxy-hemoglobin or ~~HBR~~ deoxy-hemoglobin ~~increased~~increased, and negative values indicate decreases from single- to dual-task standing. Raw fNIRS data were processed using Matlab version 2021b (MATLAB, The MathWorks, Inc., Natick, MA) using the NIRS Brain AnalyzIR Toolbox (Santosa et al., 2018). In this analysis, t-statistic values for the four source-detector pairs were ~~first~~ averaged to give right and left PFC oxy-hemoglobin~~HBO~~ and ~~HBR~~PFC deoxy-hemoglobin. ~~We then averaged the right and left PFC values to give whole PFC HBO and HBR because correlations between the two hemispheres~~

~~were strong (r = 0.865 for HBO, r = 0.539 for HBR).~~ For the 33 participants in the fNIRS analysis, 17 were in the Standard group and 16 were in the Standard+ group.

2.6 Statistical Analysis

We used descriptive statistics to summarize participant characteristics. We compared the baseline participant characteristics between the two intervention groups using independent samples t-, chi-square and Fisher's exact tests. To test our hypothesis that Standard+ group would exhibit greater improvements in postural control performance and lower PFC activation during dual-task standing conditions, we fitted a series of analysis of covariance (ANCOVA) type models with each pre- to post-intervention change in fNIRS feature, ~~or~~ accelerometry feature, gait speed, or alphabet performance as the dependent variable, intervention group as the independent factor of interest, and baseline pre-intervention value (of the change being analyzed) as a covariate. Magnitude, 95% confidence interval, and statistical significance of the treatment group coefficient was used for the main findings. We then tested the hypothesis that exercise interventions, regardless of type, would improve postural control and reduce PFC activity during single- and dual-task standing conditions. We used paired samples t-test to assess pre- to post-intervention changes in accelerometry and fNIRS measures for all participants without consideration of study arm. SAS® version 9.4 (SAS Institute, Inc., Cary, North Carolina) was used for statistical analysis.

3 Results

Table 1 summarizes baseline characteristics of the 34 participants. The sample was 59% female and 85% White. Average age was 76.0 $\pm$ 6.4 years with a range of 65 to 92 years. Average baseline gait speed and alphabet performance during standing dual-task were 0.96 $\pm$ 0.15 m/s and 0.63 $\pm$0.13 correct letters/s respectively. The demographic breakdown of our sample was similar to that of the parent intervention study; however, we did have a higher percentage of male participants, a higher Duke comorbidity index on average, and slightly faster Trails A and B times on average (Brach et al., 2022). There were no significant differences between treatment groups at baseline except alphabet performance (Standard+ = 0.68, Standard = 0.59, p=0.04).

Table 2 provides the results of the series of ANCOVA models that tested for differences between treatment groups. Differences between treatment arms for changes in single-task standing features from pre- to post-intervention were not significant. There was weak evidence of differences in the pre- to post-intervention changes in dual-task features between the two intervention groups for root-mean-square AP (p = 0.09), WE ML (p = 0.09), and ~~BND~~ ML bandwidth ~~ML~~ (p = 0.05). For AP root-mean-square ~~AP~~, the treatment group differences were due to the Standard treatment group significantly decreasing from pre- to post-intervention (p = 0.02) whereas the Standard+ group did not. ~~WE~~ ML wavelet entropy~~ML~~ for the Standard+ group showed weak evidence of increasing between visits (p = 0.06), whereas the Standard group exhibited no changes. For ML bandwidth~~BND ML~~, while the intervention arms are significantly different (p = 0.05), neither group showed significant changes in dual-task features from pre- to post-intervention. As with the primary trial results (Brach et al., 2022), our smaller sample lacked differences in gait speed between treatment groups but showed improvements

when analyzing the whole sample. Additionally, the fNIRS features (left and right PFC oxy-hemoglobin ~~HBO~~ and ~~PFC HBR~~ deoxy-hemoglobin) and alphabet performance did not differ between treatment groups ~~but the Standard+ group showed weak evidence of pre- to post-intervention increases (p = 0.08)~~.

There were no significant pre- to post-intervention changes for single-task standing features, dual-task standing features, ~~or~~ fNIRS features, or alphabet performance when we analyzed the sample as a whole (**Table 3**).

4 Discussion

We found no significant differences between exercise arms in change in balance performance or prefrontal activation from pre- to post-intervention. Pre- to post-intervention changes in dual-task AP root-mean-square ~~AP~~ and in ~~WE~~ ML wavelet entropy ~~ML~~ and ML bandwidth ~~BND ML~~ seemed to show minor between-group differences. When analyzing the whole sample for intervention-related changes, no changes were found in single-task standing features, dual-task standing features, or fNIRS features. Only AP root-mean-square ~~AP~~ of the Standard group showed significant decreases from pre- to post-intervention. ~~PFC HBR of the Standard+ group had an increasing trend from pre- to post-intervention.~~

These interventions were specifically designed for improving walking, with gait speed as the primary outcome. Gait speed showed improvements across the whole sample in the parent study but lacked between-arm differences. The authors suggest that using treadmill walking,

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which reduces gait variability and encourages consistent step patterns, instead of stationary cycles for endurance training may have dampened potential differences between the treatment arms (Brach et al., 2022). Gait speed could have improved in different ways for the two arms. The authors of the parent study also discuss improvements in capacity versus efficiency (Brach et al., 2022). Differences may be detected in other components of motor control like neural activity and postural control of upright standing balance. Postural control is a complex motor task with similarities to walking and therefore could also benefit from this type of intervention. The intervention included strength and endurance training to increase muscle strength. As well as providing social interaction, the intervention required participants to leave their home, and focused on mobility practice that may have improved balance confidence and reduced fear of falling (Singh et al., 2012). Social engagement (Rosso et al., 2013), time outside of home (Suri et al., 2021), and fear of falling (Hadjistavropoulos et al., 2011; Singh et al., 2012; Young & Mark Williams, 2015) are all factors that contribute to fall-risk.

Most postural control intervention studies focus on strength training, endurance training, or a combination of both, but few have shown robust improvements to postural control (Low et al., 2017). Single-task postural control training has not been shown to improve dual-task postural control performance; specific dual-task training must be included in the intervention to see improvement. Specific dual-task training, however, is not necessarily generalizable to other dual-tasks which suggests that the neurological component involved in postural control is not effectively addressed by this task-specific training (Agmon et al., 2014). The Standard+ treatment arm not only targeted single-task physical improvements with strength and

endurance training, but also covered broad dual-task training with timing and coordination practices, which were thought to actively improve automatic motor control (Brach et al., 2020). Improvements in these complex motor tasks, particularly during dual-task conditions, could indicate increased motor control automaticity and reduced voluntary control that requires attention. In the context of postural control, we would expect improvements in automaticity to result in increases for some variables (ML bandwidth~~BND ML~~, ~~WE~~ ML wavelet entropy~~ML~~, and ~~CORR~~ ML-AP cross-correlation~~ML-AP~~) and in decreases for other variables (both root-mean-square variables, AP centroid frequency~~-AP~~, and ~~ENTR~~ AP entropy rate~~AP~~) (Bohlke et al., 2021). Automatic functions are more efficient than those with higher attentional demands because they require fewer neural resources (Brach et al., 2020). We would expect lower PFC activation in alignment with higher automaticity and lower attentional demand.

Accelerometry is a useful tool for monitoring accelerations of the center of mass (Moe-Nilssen & Helbostad, 2002). Various signal features can be extracted to evaluate different balance characteristics like sway, stiffness, adaptability, and regularity (Bohlke et al., 2021). Root-mean-square measures the amount of sway, centroid frequency informs about the stiffness of movements, bandwidth ~~BND~~ is an indication of adaptability, ~~ENTR~~ entropy rate measures local signal randomness, ~~WE~~ wavelet entropy measures global signal disorder, and ~~CORR~~ cross-correlation measures similarity between ML and AP movements (Bohlke et al., 2021; Sejdic et al., 2014). The exercise interventions did not result in any significant differences in these characteristics except for AP root-mean-square ~~AP~~ in the Standard group. The lack of significant changes in balance performance with this intervention aligns with other fall-risk intervention

programs that have suffered from lack of transferability or generalizability of learned skills. For example, trip perturbation practice does not improve performance on a lean-and-release balance perturbation task, regardless of age (König et al., 2019). Mobility exercises focused on improving gait, a dynamic action, may just not be transferable to static standing balance.

Dual-task ~~RMS~~ AP root-mean-square~~AP~~, or anterior-posterior sway, did decrease over the course of the Standard treatment intervention. This would indicate that standing balance while performing a cognitive task improved, as the participants are swaying less. This could also suggest improved balance automaticity post-intervention, as AP sway was reduced while participants attended to the additional cognitive task (Huxhold et al., 2006; Potvin-Desrochers et al., 2017; Prado et al., 2007; Richer & Lajoie, 2020; Soames & Atha, 1982; Swan et al., 2004). However, it is not clear why ~~RMS~~ AP root-mean-square ~~AP~~ would improve with the Standard intervention and not the Standard+ intervention.

Dual-task ~~WE~~ ML wavelet entropy~~ML~~, or global signal disorder in the medial-lateral direction, showed tendency for changes only in the Standard+ group. These participants had higher post-intervention ~~WE~~ ML wavelet entropy ~~ML~~ compared to pre-intervention ~~WE~~ ML wavelet entropy~~ML~~. Higher global signal disorder means that more frequencies contribute more equally to the signal (Sejdic et al., 2014). One study found that during cognitive tasks, the frequency contribution shifted to a more even distribution as opposed to a more peaked distribution around ultra-low frequencies (Richer & Lajoie, 2020). The authors discussed how the shift towards the higher frequencies indicates more automatic behavior as higher frequencies are

associated with cerebellar and vestibular responses (Richer & Lajoie, 2020). In other words, postural control signals moved from a less disordered signal to a more disordered signal with more equal frequency contributions during dual-task conditions which indicated balance was more automatic with the addition of a cognitive task. So for the Standard+ group, participants had higher signal disorder during the dual-task after the intervention than before. Importantly, the Standard group did not show changes, and the large standard deviations may have obscured significance of average change.

We had also hypothesized that the exercise interventions would improve neural efficiency by increasing the automaticity of static standing postural control. In general, older adults have higher PFC activation than younger adults during standing balance, particularly during dual-task conditions (Udina et al., 2020) and when the difficulty of the balance task is low (St George et al., 2021). Increased automaticity would present as lower PFC activation at the post-intervention visit compared to pre-intervention, as fewer neural resources in the attention network would be required to carry out the same balance task (Lacour et al., 2008). Based on neurovascular coupling and the hemodynamic response, activation of the PFC would show positive oxy-hemoglobin ~~HBO~~ values as fresh blood is brought to the cortical sight and negative ~~HBR~~ deoxy-hemoglobin values as used blood is taken away (Scholkmann et al., 2014). PFC activation would increase from single- to dual-task, as the cognitive task increases attentional demand (Lacour et al., 2008; St George et al., 2021). We expected reduced PFC oxy-hemoglobin ~~HBO~~ and PFC ~~HBR~~ deoxy-hemoglobin values after the intervention, represented by smaller t-statistic magnitudes. However, the data does not support this hypothesis. While the averages

of PFC oxy-hemoglobin ~~HBO~~ and PFC ~~HBR~~ deoxy-hemoglobin for both hemispheres are positive and negative, respectively, implying that the PFC activity increased during the dual-task, we do not see any significant intervention-related changes in either intervention group. ~~Although, the pre- to post-intervention changes in the Standard+ group suggest that participants had a trend towards a decrease in PFC HBR. The standard deviations are quite large obscuring statistical significance, limiting our ability to make a strong conclusion.~~ It is important to note that brain activity responses are likely quite task dependent. The frontal parietal cortex has been shown to exhibit decreased activity during a balance task while performing a spatial working memory task but not with a nonspatial working memory task (Chen et al., 2018). A different study of standing and cognition dual-task experiments in older adults found that hemodynamic responses of the PFC were more influenced by changes in postural task than by addition of a serial subtraction cognitive task (Marusic et al., 2019), which could explain why we did not see any strong changes. The cognitive task may not inherently alter PFC activation enough for changes to be noticeable.

There are some important limitations to mention. The intervention and mobility assessment tasks were optimized for gait and not standing balance. The standing balance tasks were the control conditions for the mobility protocol. The balance tasks performed are perhaps too simple and subject to ceiling effects. One review of postural control interventions suggests that standing balance with eyes open is not likely to be impacted by exercise-based interventions (Low et al., 2017). Instead, they suggest that standing balance with eyes closed should be used to evaluate postural control improvements from exercise interventions. The rationale is that

neuromuscular and sensorimotor systems are ~~the~~ modifiable systems that exercise interventions can target; yet standing balance with eyes open relies heavily on visual input. When vision is removed, only neuromuscular and sensorimotor feedback remain (Low et al., 2017). In addition, the small sample size in this study likely affected this analysis. With only 34 participants in the whole sample and 18 and 16 participants in the Standard and Standard+ treatment groups, respectively, the possibility that conclusions of no change/difference are due to lack of statistical power rather than a true similarity cannot be ruled out. This study also lacked a non-exercise therapy control group, all participants received some sort of exercise intervention therapy. The lack of a non-exercise control group obscures a potential outcome where the exercise groups maintained and the non-exercise group declined over the 12 weeks. Additionally, we have a very high percentage of White participants, and the sample was also relatively well educated. The lack of diversity limits the generalizability of our research; it remains unknown how individuals from different demographic backgrounds that were not present in this sample may respond to this intervention. Lastly, instances of poor signal quality resulted in some unusable data. The accelerometry data often had flat traces when the sensors detected low levels of activity. An “idle sleep mode” default setting on the accelerometers was discovered and subsequently turned off; however, most participants had already been tested. Signals with more than 2 seconds of flat traces were removed from analysis. The accelerometry frequency variables may have been affected by the relatively short accelerometry signal lengths (1200 to 1700 data points), and vocalizations from the verbal cognitive task (St George et al., 2021).

This study does boast several strengths. Firstly, mobility interventions usually focus mostly on the physical treatment and omit tactics to improve neuronal processes involved in mobility. The treatment arm of the "Program to Improve Mobility in Aging" intervention incorporated both of those components (Brach et al., 2020). Additionally, few interventions have evaluated postural control using accelerometers, a low cost and easy to use technology. Force plates or clinical balance assessments are more often used for quantifying changes in postural control over the course of an intervention (Low et al., 2017). The features extracted from accelerometry signals can quantify center of mass balance characteristics across a variety of domains that force plates and common clinical assessments cannot (e.g., entropy rate, wavelet entropy). fNIRS has also not previously been used to monitor PFC activation changes during standing balance over course of a mobility intervention, providing insight on longitudinal comparisons of attentional demand. Furthermore, both accelerometry and fNIRS are portable, non-invasive technologies that can be leveraged to expand healthcare access, particularly to the increasing population of older adults that have mobility deficits.

4.1 Conclusion

Exercise interventions did not have an impact on standing balance performance nor on PFC activation during dual-task standing. Small sample size may limit our findings, underestimating differences that may be present. Future studies may want to consider including combined interventions for both walking and standing balance that employ more challenging balance tasks.

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6 Figures

Figure 1: Flowchart outlining participant recruitment and data availability. PRIMA = program to improve mobility in aging, ACC = accelerometry, fNIRS = functional near-infrared spectroscopy

Figure 2: Approximate placement of the 2 detectors (filled circles, center of each 'X') and 8 sources (unfilled circles, ends of each 'X' arm) from the functional near-infrared spectroscopy system.

7 Tables

Table 1. Baseline characteristics of older adults enrolled in a randomized clinical trial of a timing and coordination physical therapy intervention.

Table 2: Intervention-induced changes in the Standard+ and Standard groups and adjusted comparisons between the groups.

Table 3: Intervention-induced changes in the whole sample.

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9 Declaration of Interest

Declarations of interest: none.

10 Author Contributions

K.B. and A.L.R. worked on project conceptualization and methods development. K.B., E.S., and E.M.B. wrote software. S.P. and K.B. performed formal analysis. K.B. curated data and wrote the original manuscript draft. A.L.R. was involved in investigation, providing resources and project administration. E.S. and A.L.R. acquired funding for this research and provided supervision. K.B., S.P., E.M.B., M.S.R., P.J.S, E.S., and A.L.R. all reviewed and edited the manuscript. All authors have read and agreed to the published version of this manuscript.

11 Data Availability

Data is available upon request.

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Table 1. Baseline characteristics of older adults enrolled in a randomized clinical trial of a timing and coordination physical therapy intervention.

Characteristic	Full Sample (*n*=34) Mean (SD) or *n* (%)	Standard+ (*n*=16) Mean (SD) or *n* (%)	Standard (*n*=18) Mean (SD) or *n* (%)
Age	76.0 (6.4)	74.5 (8.1)	77.3 (4.3)
Gender			
Female	20 (58.8%)	11 (68.8%)	9 (50.0%)
Male	14 (41.2%)	5 (31.3%)	9 (50.0%)
Race			
Black	5 (14.7%)	1 (6.3%)	4 (22.2%)
White	29 (85.3%)	15 (93.8%)	14 (77.8%)
Education			
Grade 9-12	5 (14.7%)	0 (0.0%)	5 (27.8%)
College	16 (47.1%)	10 (62.5%)	6 (33.3%)
Post-graduate	13 (38.2%)	6 (37.5%)	7 (38.9%)
Duke comorbidity index	3.1 (1.3)	2.9 (1.2)	3.3 (1.4)
3MS	96.1 (3.7)	95.9 (4.6)	96.3 (2.7)
Trails A (~~second~~s)	31.9 (11.1)	28.2 (10.0)	35.2 (11.2)
Trails B (~~second~~s)	72.9 (32.4)	63.5 (34.3)	82.4 (28.4)
Height (~~m~~inches)	1.70~~66.8~~ (0~~3~~.10~~8~~)	1.67~~65.8~~ (0~~3~~.09~~7~~)	1.72~~67.6~~ (0~~3~~.10~~8~~)
Weight (kg~~pounds~~)	~~1~~82.~~8~~1 (15~~33~~.1~~+~~)	~~1~~83.5~~7~~ (17~~37~~.1~~6~~)	~~1~~82~~0~~.2~~8~~ (~~2~~13~~9~~.5~~7~~)
Body-mass index	28.7 (3.9)	29.8 (4.8)	27.7 (2.5)
Fear of falling	16 (47.1%)	7 (43.8%)	9 (50.0%)
Fall prior year	8 (23.5%)	5 (31.3%)	3 (16.7%)
Short Physical Performance Battery	9.9 (1.7)	10.2 (1.4)	9.6 (1.9)

Gait speed (m/s)	0.96 (0.15)	0.97 (0.14)	0.95 (0.15)
Alphabet performance (letters/s)*	0.63 (0.13)	0.68 (0.11)	0.59 (0.14)
Accelerometry	**Full Sample (*n*=27)**	**Standard+ (*n*=13)**	**Standard (*n*=14)**
Single-Task Features			
RMS ML (G/s)	0.012 (0.010)	0.011 (0.011)	0.014 (0.010)
RMS AP (G/s)	0.034 (0.016)	0.031 (0.017)	0.037 (0.016)
CFR AP (Hz)	0.315 (0.058)	0.325 (0.059)	0.307 (0.058)
BND ML (Hz)	0.926 (0.337)	1.040 (0.366)	0.821 (0.280)
ENTR AP	0.884 (0.010)	0.885 (0.011)	0.884 (0.009)
WE ML	0.443 (0.242)	0.428 (0.259)	0.458 (0.234)
CORR ML-AP	0.407 (0.091)	0.431 (0.094)	0.384 (0.084)
Dual-Task Features			
RMS ML (G/s)	0.013 (0.012)	0.013 (0.016)	0.012 (0.006)
RMS AP (G/s)	0.030 (0.022)	0.030 (0.029)	0.031 (0.014)
CFR AP (Hz)	0.311 (0.064)	0.316 (0.062)	0.307 (0.068)
BND ML (Hz)	0.835 (0.344)	0.832 (0.440)	0.838 (0.240)
ENTR AP	0.910 (0.011)	0.910 (0.012)	0.910 (0.011)
WE ML	0.419 (0.202)	0.388 (0.195)	0.448 (0.212)
CORR ML-AP	0.386 (0.106)	0.371 (0.102)	0.400 (0.112)
fNIRS t-Statistics	**Full Sample (*n*=33)**	**Standard+ (*n*=16)**	**Standard (*n*=17)**
Left PFC HBO	~~0.92 (2.23)~~1.00 (2.06)	~~1.40~~0.59 (2.35~~27~~)	1.38~~0.48~~ (1~~2~~.72~~17~~)
Right PFC HBO	1.22 (2.32)	0.96 (1.90)	1.48 (2.70)
Left PFC HBR	-1.~~84~~52 (2.704)	-1~~2~~.6044 (2.78~~55~~)	-1.45~~26~~ (2.71~~87~~)
Right PFC HBR	-1.55 (2.52)	-1.91 (2.23)	-1.21 (2.80)

*: values were significantly different between treatment groups ($p < 0.05$);

Abbreviations: SD = standard deviation; ML = medial-lateral; AP = anterior-posterior; RMS = root-mean-square; CFR = centroid frequency; BND = bandwidth; ENTR = entropy rate; WE = wavelet entropy; CORR = cross correlation; PFC = prefrontal cortex; fNIRS = functional near-infrared spectroscopy; HBO = oxy-hemoglobin; HBR = deoxy-hemoglobin, GLM = generalized linear model

Table 2: Intervention-induced changes in the Standard+ and Standard groups and adjusted comparisons between the groups.

Measure	**Standard+ Pre- to Post-Intervention Change Mean (SD)**	**Standard Pre- to Post-Intervention Change Mean (SD)**	**Standard Plus vs Standard Adjusted Difference**	
			Estimate (SE)	**p-Value**
Gait speed (m/s)	0.056 (0.094)*	0.045 (0.110)	0.015 (0.035)	0.7
Alphabet performance (letters/s)	-0.003 (0.169)	0.029 (0.134)	0.013 (0.051)	0.8
Accelerometry (*n* = 27)				
Single-Task Features				
RMS ML (G/s)	0.001 (0.005)	0.000 (0.011)	0.000 (0.003)	0.1
RMS AP (G/s)	-0.002 (0.019)	-0.001 (0.040)	-0.008 (0.010)	0.4
CFR AP (Hz)	-0.022 (0.098)	0.005 (0.080)	-0.015 (0.031)	0.6
BND ML (Hz)	-0.073 (0.420)	0.158 (0.433)	-0.068 (0.147)	0.6
ENTR AP	0.003 (0.016)	-0.003 (0.010)	0.006 (0.004)	0.1
WE ML	-0.064 (0.310)	0.065 (0.238)	-0.148 (0.087)	0.1
CORR ML-AP	0.034 (0.100)	0.025 (0.064)	0.029 (0.030)	0.3

Dual-Task Features				
RMS ML (G/s)	0.000 (0.003)	-0.001 (0.005)	0.002 (0.002)	0.2
RMS AP (G/s)	-0.002 (0.024)	-0.011 (0.016)*	0.008 (0.004)	0.09
CFR AP (Hz)	-0.032 (0.078)	-0.015 (0.142)	-0.005 (0.030)	0.9
BND ML (Hz)	-0.101 (0.364)	0.241 (0.589)	-0.346 (0.171)	0.05
ENTR AP	0.000 (0.011)	0.001 (0.018)	-0.001 (0.005)	0.9
WE ML	0.247 (0.432)	-0.032 (0.311)	0.264 (0.147)	0.09
CORR ML-AP	0.043 (0.169)	0.004 (0.085)	0.016 (0.040)	0.7
fNIRS t-Statistics (*n* = 33)				
Left PFC HBO	-0.080.525 (2.830486)	-0.3140.473 (2.3202.921)	-0.153579 (0.858914)	0.95
Right PFC HBO	0.221 (3.029)	-0.733 (2.321)	0.728 (0.887)	0.4
Left PFC HBR	0.557 1.001 (42.058135)	-0.210889 (33.952.279)	01.613304 (10.007884)	0.52
Right PFC HBR	0.465 (3.589)	-0.691 (3.326)	0.501 (0.897)	0.6

* p<0.05

Abbreviations: SD = standard deviation; ML = medial-lateral; AP = anterior-posterior; RMS = root-mean-square; CFR = centroid frequency; BND = bandwidth; ENTR = entropy rate; WE = wavelet entropy; CORR = cross correlation; PFC = prefrontal cortex; fNIRS = functional near-infrared spectroscopy; HBO = oxy-hemoglobin; HBR = deoxy-hemoglobin, GLM = generalized linear model

Table 3: Intervention-induced changes in the whole sample.

Measure	Pre- to Post-Intervention Change Mean (SD)	p-Value
Gait speed (m/s)	0.050 (0.102)*	0.007*
Alphabet performance (letters/s)	0.014 (0.150)	0.6
Accelerometry (*n* = 27)		
Single-Task Features		
RMS ML (G/s)	0.001 (0.009)	0.7
RMS AP (G/s)	-0.001 (0.031)	0.8
CFR AP (Hz)	-0.008 (0.089)	0.6
BND ML (Hz)	0.047 (0.435)	0.6
ENTR AP	-0.000 (0.013)	1
WE ML	0.003 (0.277)	1
CORR ML-AP	0.029 (0.082)	0.07
Dual-Task Features		
RMS ML (G/s)	-0.001 (0.004)	0.5
RMS AP (G/s)	-0.007 (0.021)	0.1
CFR AP (Hz)	-0.023 (0.114)	0.3
BND ML (Hz)	0.076 (0.514)	0.4
ENTR AP	0.001 (0.015)	0.8
WE ML	0.102 (0.393)	0.2
CORR ML-AP	0.023 (0.131)	0.4
fNIRS t-Statistics (*n* = 33)		
Left PFC HBO~~PFC HBO~~	-0.201~~011~~ (2.5472~~4~~)	0.7~~1~~
Right PFC HBO	-0.271 (2.689)	0.6
Left PFC HBR~~PFC HBR~~	0.162~~027~~ (~~2.904~~3.960)	0.8~~1~~
Right PFC HBR	-0.131 (3.451)	0.8

* $p<0.05$

Abbreviations: SD = standard deviation; ML = medial-lateral; AP = anterior-posterior; RMS = root-mean-square; CFR = centroid frequency; BND = bandwidth; ENTR = entropy rate; WE = wavelet entropy; CORR = cross correlation; PFC = prefrontal cortex; fNIRS = functional near-infrared spectroscopy; HBO = oxy-hemoglobin; HBR = deoxy-hemoglobin, GLM = generalized linear model