doi: 10.4085/1062-6050-0728.24

# Transcranial Direct Current Stimulation over the Motor or Frontal Cortex in Patients with Chronic Ankle Instability

Alan R. Needle, Ph.D., ATC, CSCS, FNATA [a, b]

Jared W. Skinner, Ph.D. [a]

Mabry G. Watson, BS [a]

Shawn E. Roberts, MS [c]

Samuel A. Grattan, MS [d]

Jennifer S. Howard, Ph.D., ATC [b]

[a] Department of Public Health & Exercise Science, Appalachian State University, Boone, NC

[b] Department of Rehabilitation Sciences, Appalachian State University, Boone, NC

[c] Children's Hospital Los Angeles, Los Angeles, CA

[d] School of Health Sciences & Human Performance, Ithaca College, Ithaca, NY

Corresponding Author:

Alan R. Needle, Ph.D., ATC, CSCS, FNATA

Department of Public Health & Exercise Science

Department of Rehabilitation Sciences

ASU Box 32071

Appalachian State University

Boone, NC 28608

828-262-4039

needlear@appstate.edu

**ACKNOWLEDGMENTS**

Funding for this study was provided by the NATA Foundation. The authors thank the statistical consultants in Research Design & Analysis, part of the Office of Research & Innovation at Appalachian State University."

## ABSTRACT

Objective: Growing evidence has suggested clinical efficacy for the use of anodal transcranial direct current stimulation (atDCS) when combined with motor interventions in patients with chronic ankle instability (CAI). However, no studies have compared multiple approaches for improving motor function with atDCS in patients with CAI. We therefore aimed to determine the efficacy of atDCS over the motor or frontal cortex when combined with a four-week motor planning intervention on neural function, performance, and patient-reported outcomes in patients with CAI.

Design: Double-blind, sham-controlled, parallel randomized control trial.

Methods: Participants (n=44, 15 males, 29 females, 23.6±6.1 yrs) were assessed for outcome measures of cortical and reflexive excitability; performance measures of dynamic balance, muscle activation, reaction times, and cognitive performance on a dual-task balance test; and patient-reported outcome measures at baseline, mid-training (week 2), post-training (week 4), and retention (week 6). After baseline testing, participants were randomized to receive atDCS over the motor cortex, frontal cortex, or a sham current during rehabilitation exercises over four weeks. Participants reported for eight training sessions where they were instrumented for atDCS while performing obstacle walking, dual-task balance, and agility exercises. Analyses between groups and time points were performed with mixed linear models (α=0.05).

Results: Forty-six individuals were recruited & randomized with 37 completing the investigation (motor=14, frontal=11, sham=12). No differences across groups or times were observed in neural excitability or muscle activation variables (P>0.05). Significant improvements in dynamic postural stability indices were observed from baseline across all groups (P<0.05). Improvements were observed for foot & ankle function, perceived disablement, and the Global Rating of Change at post-training and retention (p<0.001).

Conclusions: Improvements in patient function were observed across all groups, suggesting the motor planning intervention improved function, regardless of atDCS application. Observing benefits from atDCS may be dependent on proper pairing of rehabilitation exercise with electrode location.

Key Words: ankle sprain, neuromodulation, dual-tasking, rehabilitation

Word count: 4459

**KEY POINTS:**

Patient-reported function, functional performance, and balance improved following a 4-week rehabilitation intervention emphasizing motor planning in patients with chronic ankle instability.

Participants received transcranial direct current stimulation over the motor or frontal cortex or a sham current; however, improvements were not tied to whether participants received an active brain stimulation current.

Rehabilitation emphasizing motor planning may be beneficial for individuals with limited participation restrictions; however, further research is needed to understand mechanistic changes.

## INTRODUCTION

Ankle sprains are an often-confounding injury to clinicians due to high reinjury rates.[1] Re-injury rates up to 70 percent are reported, with recurrent sensations of rolling termed chronic ankle instability (CAI) developing in approximately half of these patients.[2] Patients with CAI report impairments that include decreased balance, diminished neuromuscular control and altered reaction times.[3] Collectively, these impairments lead to decreased health-related quality of life and physical activity across the lifespan, contributing to increased risk of long-term health complications.[4-6] This negative symptom progression originating from an ankle sprain suggests that current rehabilitation protocols that emphasize the minimization of impairment may need to be reconsidered to better address underlying factors contributing to decreased function.

In patients with ligamentous pathology at the knee and ankle, emerging evidence supports the presence of maladaptive neuroplasticity that may undermine rehabilitation efforts.[7,8] Current models suggest that both acute and chronic sensory changes contribute to inhibition at the cortical and segmental levels, yielding decreased neural excitability. While these inhibitory changes can hinder the activation of stabilizing musculature and potentially leave the joint vulnerable, muscle function is often regained through increased neural activation from extraneous areas, such as the cerebellum, contralateral motor cortex, somatosensory cortex, and the frontal cortex as observed in individuals with CAI.[9,10] Therefore, muscle function appears largely restored following the injury rehabilitation process, but is being achieved with less efficient neural activation that can lead to degraded movement strategies when placed in complex and unconstrained environments.[11] These models suggest the need to consciously address maladaptive neuroplasticity throughout rehabilitation efforts for CAI and other ligament pathologies in order to adequately restore patient function.[12]

Many common clinical therapies have neuromodulatory effects that may positively affect neuroplasticity in patients with musculoskeletal injury.[13] Recently, transcranial direct current

stimulation (tDCS) has been implemented in patients with chronic & acute ligament pathology to directly address neuroplasticity.[7,13,14] tDCS implements a direct current across the brain to modify synaptic plasticity.[15] In most rehabilitation research contexts, anodal tDCS (atDCS) has been implemented to facilitate the primary motor cortex (M1) while individuals perform exercises emphasizing muscle strength. In patients with CAI and following ACL reconstruction, this protocol has been tied to improved postural control, neural excitability, and health-related quality of life following a 2 to 4 week intervention.[16-18] However, these improvements are compared to a sham current rather than alternate cortical targets. The dorsolateral prefrontal cortex (DLPFC) has been targeted with atDCS in individuals with neurological pathologies (e.g., stroke, Parkinson's disease) and healthy adults to evoke improvements in motor planning and affect motor cortex activity and performance.[19,20] Given the recruitment of extraneous cortical areas in patients with CAI, such an intervention may be effective in this population.

The current study aimed to investigate the comparative effects of rehabilitative exercises when combined with atDCS over M1, atDCS over the DLPFC, and sham tDCS on neural excitability, dynamic balance, neuromuscular control, and patient-reported function in patients with CAI. We hypothesized that stimulation over M1 would yield the greatest improvements in neural excitability and muscle activation, whereas stimulation over the DLPFC would yield the greatest improvements in reaction times and dynamic balance indicating enhanced motor planning.[21,22] We further hypothesized that both groups receiving tDCS would improve patient-reported function to a greater degree than those receiving sham stimulation and maintain those changes following cessation of the rehabilitation program.

## METHODS

*Study Design*

The present study implemented a double-blind parallel randomized, controlled trial. Participants performed a 4-week intervention consisting of eight rehabilitation sessions that emphasized muscle activation and motor planning. Participants were tested for outcome measures at week 0 (baseline), week 2 (mid-training), week 4 (post-training), and week 6 (retention). Independent variables included group (Motor, Frontal, Sham) and time (baseline, mid-training, post-training, retention). Dependent variables included measures of neural excitability; dynamic postural control, lower-leg muscle activation and reaction times during a reactive hop test; and patient-reported outcome measures (modified disablement in the physically active scale, mDPAS; foot and ankle ability measure, FAAM; Tampa scale for kinesiophobia, TSK; and global rating of change, GROC). Participants were masked to group allocation, and both therapists and assessors were masked to whether participants received an active or sham current, although were aware of electrode location (motor or frontal). This clinical trial was registered on clinicaltrials.gov (NCTXXX).

*Participants*

Forty-six individuals with CAI were recruited for the present study. Classification with CAI followed guidelines from the International Ankle Consortium,[23] including experiencing their first ankle sprain more than 1 year prior to study enrollment, and scoring above a 10 on the identification of functional ankle instability (IdFAI) instrument.[24] Participants had no history of foot, ankle, or lower leg fractures or surgery, or injuries restricting physical activity in the 3 months prior to study enrollment and reported no red-green color vision deficiency. Additionally, participants met criteria for the safe practice of transcranial magnetic stimulation (TMS) and tDCS , including no personal or immediate family history of seizure or epilepsy, metallic implants or medication infusion devices, skull abnormalities, frequent headaches or migraines, concussion withing 6 months, or on medications that raise the risk of seizure.[25-27] Sample size was based on preliminary data,[17] which reported effect sizes of $\eta_p^2$ between 0.07 to 0.14. To

achieve statistical power (1-β) of 0.95 with the previously observed effect (f=0.27) and a level of significance (α) at 0.05, 11 participants were required per group. To account for potential attrition of up to 25 percent, we aimed to recruit 45 total participants. All participants provided informed consent as approved by the XXX Institutional Review Board (XXX).

*Outcome Measures*

Neural excitability was assessed using the Hoffmann (H)-reflex and TMS for segmental and corticospinal excitability, respectively. For these measurements, participants were instrumented with electromyography (EMG) electrodes over the tibialis anterior (TA), peroneus longus (PL), and soleus (SOL). The area over each muscle was palpated, shaved if necessary, cleaned with isopropyl alcohol, abraded, and an active electrode connected to an amplifier (B&L Engineering, Santa Ana, CA) was placed along the muscle.[28] The H-reflex was assessed first with the patient in a prone position. A bar electrode connected to a constant current stimulator (DS7R, Digitimer LTD, Hertfordshire, England) set to 300V was placed in the popliteal fossa. In order to assess H-reflex across all target muscles, the location of the sciatic nerve prior to its bifurcation was identified using 10mA pulses and used for subsequent testing.[29] Pulses (1ms duration) were applied every 10 seconds beginning at a stimulation of 0 and increasing by 2mA each pulse until a plateau response was noted across all recorded muscles. The ratio of the maximal reflexive response ($H_{max}$), occurring 40-80ms from stimulus, was compared to the maximal motor response ($M_{max}$), occurring from 10-30ms from stimulus to derive $H_{max}$:$M_{max}$ for each muscle.[29]

Following H-reflex assessment, cortical excitability was assessed simultaneously across all muscles using TMS. Participants were seated and familiarized with TMS prior to locating M1 by providing submaximal pulses and observing the location yielding the largest response in TA.[30] The TA was selected due to its greater cortical representation relative to the PL and SOL.[31,32] Following these procedures, 40-50 stimuli, ranging from below the previously noted motor

threshold to above a maximal response would be expected from each muscle were applied to obtain a stimulus-response curve from each muscle.[33] The stimulus-response curve was used to estimate the RMT and $MEP_{max}$ (normalized to $M_{max}$) for each muscle.[30] All neural outcomes were assessed in an electromagnetically-shielded laboratory.

Dynamic balance, muscle activation, and reaction times were assessed using a reactive hop. Participants were re-instrumented with EMG as described above using a system that allowed for free movement (Bagnoli-4, Delsys Inc., Boston, MA, USA). Participants were positioned in unipedal stance in the middle of three in-ground force plates (60x90cm, Bertec, Columbus, OH, USA), with a 5cm vertical hurdle placed between each force plate. Three reactive lights (ROXProX, A-Champs, Barcelona, Spain) were placed on tripods surrounding the participant, with one 10-feet directly in front of the participant (memory light), and the other 2 placed at the front outside corners of the adjacent force plates (trigger lights). Participants were familiarized with the task, consisting of monitoring the memory light, which flashed one of four colors every 2 seconds, as participants were instructed to recall the previous 3 colors in order. At a random time in a 15-second interval, the trigger lights illuminated, and participants were instructed to hop towards the green-lit light. When participants were within 50 cm of the trigger light, it would deactivate and send a reaction time (i.e. time between trigger light illumination and deactivation) to the linked software via Bluetooth connection (ROXPro Android application, A-Champs, Barcelona, Spain). Participants were instructed to land on the affected side, regain balance for 15-seconds, and recite the 3 colors that occurred before the trigger light. To offset fatigue, participants did three consecutive trials and then were provided a 1–2-minute rest period. Three trials were provided for familiarization and practice, and then a minimum of 5-hops to each side were collected. If participants did not successfully complete the task (e.g. did not clear the hurdle, touched opposite limb down within 15s, hopped in the wrong direction), an error was recorded on the data collection sheet and the trial was not include in the five that needed to be

completed to each side. This method provided strong reliability for reaction time and color memory across multiple trials (ICC[1,k] between 0.707 to 0.828). Force plate and EMG data were collected in custom LabVIEW software (National Instruments, Austin, TX) at 1000 Hz.

Dynamic balance was quantified from force plate data using dynamic postural stability indices (DPSIs), including anteroposterior (APSI), mediolateral (MLSI), and vertical (VSI) components.[21] EMG data were bandpass filtered (20-400 Hz), rectified, and low-pass filtered (10-Hz) to create a complete linear envelope, and normalized to peak activation across all trials. Average activation for each muscle was extracted in the 500ms before and after landing on each force plate. Reaction times were recorded from the reactive lights using the ROXPro Android application and color memory was written down noting the number of correct colors out of the three displayed. Trials were further stratified into medial and lateral hops, relative to the test leg.

Patient-reported outcome measures were collected in the Research Electronic Data Capture (REDCap) tools hosted by XXX.[34] Foot & ankle function was assessed using the FAAM, including ADL and Sport subscales.[35] Health-related quality of life was assessed using the mDPAS.[36] Kinesiophobia related to sport activity was assessed using the TSK 17-item scale.[37] Lastly, global changes from baseline were assessed at mid-training, post-training, and retention using the GROC, which consists of a 15-point scale where a 0 indicated no change (“About the same”) from baseline, a 7 indicated “A very great deal better” and a -7 indicated “A very great deal worse”.[38] As a performance-based metric of patient function, participants were also tested for a side-hop test, consisting of 10 side-to-side hops over two parallel lines placed 30cm apart.[39] Participants were provided a full practice trial, and the time to complete a single trial was extracted. To test fidelity of masking efforts, at the conclusion of the retention visit, participants were asked whether they felt they received the real or sham current.

*Intervention*

Following the baseline test session, participants were randomized into either Motor, Frontal, or Sham groups using a block-randomization scheme (randomized block sizes of 3 to 9). To maintain masking, individuals were assigned a 6-digit code that was entered into a stimulator (1x1-CT, Soterix, New York, NY) that corresponded with an active current (1.8mA provided over 20 minutes) or a sham current to mimic some sensation while maintaining participant blinding (1.8mA provided over 1 minute).[17,20] The codes were accompanied by a stimulus location, instructing researchers where to place electrodes (frontal or motor locations). This allowed for participants in the sham group to be near-equally allocated to have electrodes placed at motor or frontal locations.

Participants reported to a separate laboratory and were instrumented with tDCS. For participants receiving the "motor" location, a 5x3 anode (EASYPad, Soterix Inc., New York, NY) was placed at the C3/C4 location of the international 10:20 system, corresponding with the hemisphere contralateral to the test ankle, and the same sized cathode was placed at the opposite supraorbital area (ipsilateral to the test ankle).[17] For participants receiving the "frontal" location, a 5x7 EASYPad anode was placed over the F3/F4 location of the International 10:20 system, corresponding with the hemisphere contralateral to the injured ankle, and the same sized cathode was placed at the opposite F3/F4 location.[19] Electrodes were saturated with 6-8mL of saline prior to placement on the individual, and electrodes were secured using an elastic fastener set provided by the manufacturer. Good electrode impedance was assured prior to beginning the stimulation. Participants were instructed to sit for 2 minutes after beginning stimulation, and then proceed through the exercise protocol.

Full details of the rehabilitation progression, including stages of progressions achieved by each group, are included in *Supplementary Materials*. First, participants performed hurdle walking, performed laterally and at oblique angles. Second, participants performed a unipedal stand-and-reach task with a go/no-go component, in which participants balanced on the test side and

reached with the non-test side towards a light trigger placed at 50% of leg length in front of the participant. Lastly, participants performed 6 agility ladder exercises consisting of 3 rounds of lateral stepping, and 3 rounds of a shuffle step (Figure 1). Treatment sessions were designed to take 18-20 minutes, aligning with the duration of tDCS administration. In all cases, tDCS remained through the entire 20-minute timer.

*Data Analysis*

All data were assessed using linear mixed models, to account for the nested nature of the data and allow for the inclusion of partial data in an intention to treat analysis. Descriptives were examined and baseline characteristics were compared for a group effect. Each variable was assessed for fixed effects of group (motor vs. frontal vs. sham), time (baseline, mid-training, post-training, and retention), and the group-by-time interaction effect. In the case of a significant effect on omnibus tests for fixed effects, we reported the marginal ($R^2_M$) and conditional ($R^2_C$) $R^2$ values to estimate the contribution of fixed and random effects on the linear mixed models.[40] Further, for significant fixed effects parameter estimates were examined post hoc to assess the source of significant differences. To allow for understanding the magnitude of the observed changes, 95% confidence intervals were reported surrounding mean differences. An a priori level of significance ($\alpha$) was set at 0.05.

## RESULTS

*Demographics*

Forty-six individuals were recruited for this study, with 37 completing all testing sessions and considered compliant (≥6 out of 8 training sessions completed) (Figure 2). There were no significant differences in attrition across groups ($\chi^2[2]=1.342$, $p=0.511$), with only the frontal group having retention below 80%. Demographic information for all groups is presented in Table 1. No significant differences were observed between groups for sex ($\chi^2[2]=5.004$, $p=0.082$), age

(F[2,41]=0.658, p=0.523), height (F[2,41]=0.963, p=0.392), mass (F[2,41]=0.254, p=0.777), or IdFAI scores (F[2,41]=0.880, p=0.422). A chi-squared analysis was conducted to explore whether individuals in each group perceived themselves to receive an active or sham current. In motor, frontal, and sham groups, 72.7, 75.0, and 72.7 percent of participants thought they received an active current, respectively ($\chi^2$[2]=0.015, p=0.992).

*Neural excitability*

Means, standard deviations, and omnibus effects for $H_{max}$:$M_{max}$, RMT, and $MEP_{max}$ are presented in Table 2. No significant main effects of time, group, or group-by-time interactions were observed for neural excitability variables within any muscle.

*Dynamic Postural Control and Muscle Activation*

Means, standard deviations, and omnibus effects for APSI, APSI, MLSI, and VSI during medial and lateral hops are presented in Table 3. No significant group or group-by-time interaction effects were noted for any dynamic postural control variables. Significant main effects of time were observed for DPSI and VSI on the lateral hops (DPSI: F[3,100.2]=4.389, p=0.006, $R_M^2$=0.120, $R_C^2$=0.559; VSI: F[3,100.2]=4.225, p=0.007, $R_M^2$=0.118, $R_C^2$=0.555). Significant improvements in postural stability from baseline were noted at mid-training (DPSI: MD=-0.04, 95%CI: [-0.06, -0.02], p<0.001; VSI: MD=-0.04, 95%CI: [-0.06, -0.02], p<0.001), post-training (DPSI: MD=-0.03, 95%CI: [-0.05, 0.00], p=0.020; VSI: MD=-0.03, 95%CI: [-0.05, -0.00], p=0.023), and retention (DPSI: MD=-0.03, 95%CI: [-0.06, -0.01], p=0.014; VSI: MD=-0.03, 95%CI: [-0.05, -0.01], p=0.017) for lateral hops.

Means, standard deviations, and omnibus effects for muscle activation during medial and lateral hops are presented in Table 4. No significant main effects of time, group, or group-by-time interaction effects were observed for average activation within any muscle before or after landing.

*Reaction Times and Cognitive Performance*

Reaction times and cognitive performance are presented in Table 4. No significant changes in reaction times on medial or lateral hops were observed for the main effects of group, time, or group-by-time interaction effect. Improvements were observed for the number of colors correctly recalled over time (F[3,108.0]=9.83, p<0.001, $R_M^2$=0.146, $R_C^2$=0.478), with significant differences from baseline noted at mid-training (MD: 0.2, 95%CI: [0.1,0.3], p<0.001), post-training (MD: 0.2, 95%CI: [0.1,0.4], p<0.001), and retention (MD: 0.3, 95%CI: [0.2,0.4], p<0.001).

*Side Hop Test*

Significant improvements were observed in side-hop test performance over time (F[3,104.5]=11.004, p<0.001, $R_M^2$=0.096, $R_C^2$=0.674), while no group or group-by-time interaction effect was observed (Table 4). Significant differences from baseline indicating improvement performance were noted at mid-training (MD: -3.2, 95%CI: [-4.7,-1.6], p<0.001), post-training (MD: -3.9, 95%CI: [-5.5,-2.3], p<0.001), and retention (MD: -4.2, 95%CI: [-5.9,-2.6], p<0.001).

*Patient-reported outcomes*

Means, standard deviations, and omnibus test effects are presented in Table 5. The FAAM ADL revealed no significant group or group-by-time interaction effects, but the time effect was significant (F[3,105.7]=6.775, p<0.001, $R_M^2$=0.036, $R_C^2$=0.846). Parameter estimates were significant at post-training (MD=3.3, 95%CI: [1.3, 5.3], p=0.002) and retention (MD=4.36, 95%CI: [2.3, 6.4], p<0.001), but not at mid-training (MD=1.7, 95%CI: [-0.3, 3.7], p=0.091). The FAAM Sport revealed no significant group or group-by-time interaction effects, but the time effect was significant (F[3,106.5]=13.58, p<0.001, $R_M^2$=0.062, $R_C^2$=0.830). Parameter estimates were significant at mid-training (MD=3.8, 95%CI: [0.7, 6.9], p=0.019), post-training (MD=8.1, 95%CI: [4.9, 11.3], p<0.001) and retention (MD=9.35, 95%CI: [6.1, 12.6], p<0.001). Both scales followed the same pattern of increased perceived function over time.

The mDPAS Physical subscale revealed no significant group or group-by-time interaction effect, but a significant effect of time was observed (F[3,106.9]=8.049, p<0.001, $R_M^2$=0.045, $R_C^2$=0.791). Parameter estimates showed significant differences from baseline at post-training (MD=-3.8, 95%CI: [-4.8, -1.8], p<0.001) and retention (MD=-4.7, 95%CI: [-5.7, -2.6], p<0.001), but not at mid-training (MD=-1.8, 95%CI: [-3.8, 0.2], p=0.083). The mDPAS Mental subscale also demonstrated no significant group or group-by-time interaction effect, but a significant effect of time (F[3, 107.5]=3.43, p=0.020, $R_M^2$=0.045, $R_C^2$=0.791. Parameter estimates showed significant differences at post-training (MD=-0.8, 95%CI: [-1.5, -0.1], p=0.034) and retention (MD=-0.9, 95%CI: [-1.6, -0.2], p=0.014), but not at mid-training (MD=-0.0, 95%CI: [-0.7, 0.6], p=0.919). A similar pattern was observed for the TSK, as there was no significant group or group-by-time interaction effect, but a significant effect of time was observed (F[3,107.7]=2.719, p=0.048, $R_M^2$=0.040, $R_C^2$=0.772). However, post hoc parameter estimates revealed no significant differences at any given time for the TSK.

The GroC followed a similar trend, demonstrating no significant group or group-by-time interaction effect, but a significant effect of time was observed (F[2,69.6]=20.046, p<0.001, $R_M^2$=0.129, $R_C^2$=0.747). Parameter estimates showed significant differences at post-training (MD=1.3, 95%CI: [0.7, 1.8], p<0.001) and retention (MD=1.6, 95%CI: [1.1, 2.1], p<0.001).

## DISCUSSION

This study aimed to explore whether tDCS over the motor or frontal cortex improved patient function when combined with rehabilitative exercises emphasizing motor planning. While patients demonstrated improvements in patient-reported function and some performance measures over the course of the intervention, changes were not tied to the use of tDCS at either location. These data potentially highlight the effectiveness of motor planning interventions, while

suggesting caution in the implementation of tDCS to augment rehabilitation efforts in patients with musculoskeletal injury.

*Functional Improvements following the Intervention*

Across all groups, participants displayed improvements in patient-reported outcome measures, side-hop test performance, and dynamic balance during lateral hops. These improvements were observed following the 4-week intervention, regardless of tDCS application, suggesting improvements were tied to the exercises performed. The exercises in the rehabilitation intervention – consisting of stepping over obstacles, reactive semi-dynamic balance exercises, and agility – were selected to demand activation of motor execution areas of the cortex while simultaneously challenging planning areas, which may be less efficient in individuals with CAI.[12] Implementing motor learning strategies and dual-task focused interventions has recently grown in patients with musculoskeletal injury,[41,42] with improvements generally observed in balance performance.[43] Given deficits in motor planning in patients with CAI, it is possible that incorporating motor planning-focused exercises into rehabilitation was sufficient to improve patient-reported function, supporting the implementation of these exercises in rehabilitation efforts for CAI.[41]

Although the observed improvements in patient-reported function were statistically significant, caution should be exercised when interpreting the clinical significance of these data. Many of the outcome measures did not exceed published minimum clinically-important differences (MCIDs). Improvements did not exceed the MCID for the FAAM-ADL (MCID=8)[44], TSK (MCID=4)[45], and mDPAS (MCID=9)[36], with only the FAAM-Sport (MCID=9)[44] having confidence intervals that exceeded this threshold. For the GROC, indicating participants' perceived improvement from the intervention, scores observed were in line with the MCID of 2; however a score of 5 that has been recommended to gauge the success of an intervention.[46] While we observed improvements from our intervention, it would be important to compare an intervention

emphasizing motor planning to a more typical rehabilitation protocol that may emphasize balance and strength training.[47]

Participants were recruited from a general population rather than those specifically seeking care for CAI. As such, while similar across groups, these individuals may have had higher baseline function, limiting the magnitude of potential improvements. However, the observed increases in patient-reported function represents a potentially meaningful change. Clinically, this suggests that bringing patients who exhibit impairments with few participation restrictions through continued rehabilitation emphasizing motor planning and dual-tasking may improve function. The responsiveness to the intervention seen across groups may be evidence of unfulfilled potential in traditional rehabilitation, where patients often resume activity and discontinue care for a variety of reasons before advanced, dynamic rehabilitation strategies can be implemented. However, the observed small effect sizes for these clinical improvements may be due to a lack of concurrent neural changes. That is, while individuals gained confidence in their ankle over the course of the intervention, the absence of neural changes (e.g. improvements in neural excitability) potentially limited the magnitude of these effects and may reflect a lack of durability to these changes. Overall, these results suggest a degree of effectiveness to the intervention, but a failure to optimally restore patient function.

*Efficacy of tDCS*

Our a priori hypotheses were that the implementation of tDCS would enhance rehabilitation by driving mechanistic changes that would subsequently improve function. However, nearly all measures tied to mechanistic changes in individuals with CAI did not demonstrate improvements over the course of the intervention. Notably, improvements in segmental or corticospinal excitability – a consistent finding in tDCS-related research[48] – were not observed in this study. Similarly, no improvements were observed in muscle activation or reaction times during the reactive hop task.

These data are in contrast to previous studies implementing tDCS in individuals with musculoskeletal injuries.[16,17,49] In individuals with CAI, tDCS has been implemented with eccentric strengthening exercises,[17] foot intrinsic muscle strengthening,[16] and balance training[49] yielding improvements in neural excitability, muscle activation, dynamic balance outcomes, as well as patient function when compared to a similar sham group.[16,17] While no evidence exists for the use of DLPFC stimulation in individuals with musculoskeletal injury, improvements have been seen in motor performance of complex walking in healthy individuals.[50] Alternately, stimulation over the supplementary motor area, similarly used to improve motor planning, has not demonstrated improvements on motor planning outcomes in individuals with CAI.[51] A key difference between the current investigation and these previous studies is the intervention paired with tDCS. Here, the intervention was selected to create both motor execution and planning demands, allowing for all participants to do the same exercise sets despite the intention of their tDCS application (motor execution versus planning). However, our results and prior investigations suggests that the exercise selection may be of utmost importance in the treatment of joint instability. tDCS over M1 may need to be implemented with direct strengthening exercises that have disinhibitory effects (e.g. eccentric exercise, plyometrics); whereas frontal cortex stimulation may require interventions that more intentionally create demand on the DLPFC, such as motor imagery or action-observation interventions.[12]

While early evidence supports the use of M1 stimulation in patients with CAI,[16,17] the use of DLPFC stimulation has been less explored. The aim of frontal cortex stimulation would be to improve neural efficiency in feed-forward motor planning by improving the brain's ability to anticipate outcomes; however, patients with CAI may have increased dependence on these frontal areas and facilitation here may not be warranted.[10]

*Limitations*

Certain limitations in study design limit our ability to draw finite conclusions based on our intervention. All participants received exercises for CAI, potentially generating biases to improve scores on patient-reported outcome measures, reflecting a potential Hawthorne effect.[52] A true control group receiving no intervention could have alleviated this concern. Similarly, physical and cognitive performance improvements, such as that on the SHT, VSI, or cognitive correct letters, may have been tied to learning effects that may explain some of the improvements we observed. Alternately, as approximately 75% of participants across all groups felt they received an active tDCS current, a placebo effect may have aided outcome scores. Inclusion of longer follow-up may have provided a better indication of whether the improvements in patient-reported outcomes were durable beyond 2-weeks after cessation of training. While efforts were made to control for as many variables at baseline, there is of course a great deal of variability among the deficits observed in patients with CAI that could have been mitigated by controlling for factors such as sex and baseline function prior to randomization; however, doing so often limits the clinical applicability of the data observed.

*Clinical and Research Implications*

Recent findings related to the use of brain stimulation in treating musculoskeletal injuries reflect the need for neuromodulatory interventions in the treatment of joint instability. While it is unclear whether the increase in brain stimulation research in sports medicine has yielded its increased use in clinical practice, the results of this study provide some pause towards tDCS implementation. Placing this investigation in the context of the existing evidence, it appears that the impacts of tDCS are optimized when motor cortex stimulation is combined with direct motor interventions such as eccentric strengthening or foot intrinsic strengthening.[12,16] Conversely, the evidence does not support the use of tDCS over motor planning areas in these patients.

Our rehabilitation intervention, emphasizing motor planning and dual-tasking components did yield improvements in function. This emphasizes the need to incorporate these components into

rehab, especially in continuing rehabilitation for individuals with few participation restrictions. These findings can be further enhanced by considering individualized changes to mechanical, sensorimotor, and psychological function, reflecting the varied clinical presentation of CAI.[3]

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## LIST OF FIGURES

570 Table 1. Participant characteristics. Abbreviations: SD, standard deviation; IdFAI, Identification
571 of Functional Ankle Instability Instrument.

| | Motor | Frontal | Sham | p-value |
|---|---|---|---|---|
| **Number recruited (M/F)** | 15 (3/12) | 14 (8/6) | 15 (4/11) | 0.082 |
| **Age (yrs) (SD)** | 22.6 (2.7) | 22.9 (5.6) | 25.2 (8.7) | 0.523 |
| **Height (cm) (SD)** | 169.1 (12.9) | 175.3 (12.6) | 180.4 (9.1) | 0.392 |
| **Mass (kg) (SD)** | 69.3 (14.0) | 73.2 (12.5) | 72.4 (16.6) | 0.777 |
| **IdFAI Score (SD)** | 22.9 (5.5) | 20.2 (5.8) | 20.9 (5.8) | 0.422 |
| **Number completing study (%)** | 14 (93.3) | 11 (78.5%) | 12 (80.0) | 0.511 |

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Table 2. Neural excitability means (standard deviations) across groups and timepoints and F-values for the main effect of time and the group-by-time interaction effect for each variable. Abbreviations: $H_{max}$:$M_{max}$, ratio of maximum reflexive response to maximum motor response; $MEP_{max}$:$M_{max}$, ratio of maximum motor evoked potential to maximum motor response.

| | | | Week 0 | Week 2 | Week 4 | Week 6 | Time Effect (P-value) | Interaction Effect (P-value) |
|---|---|---|---|---|---|---|---|---|
| **Tibialis Anterior** | $H_{max}$:$M_{max}$ | Motor | 0.227 (0.169) | 0.168 (0.082) | 0.199 (0.125) | 0.215 (0.152) | 1.39 (0.249) | 1.41 (0.216) |
| | | Frontal | 0.170 (0.115) | 0.156 (0.078) | 0.305 (0.254) | 0.242 (0.263) | | |
| | | Sham | 0.157 (0.073) | 0.198 (0.147) | 0.170 (0.102) | 0.192 (0.134) | | |
| | Motor Threshold (%2T) | Motor | 33.5 (9.0) | 27.6 (12.2) | 33.8 (10.4) | 28.3 (8.4) | 2.22 (0.091) | 0.45 (0.845) |
| | | Frontal | 32.3 (9.6) | 32.9 (10.1) | 34.4 (12.6) | 29.2 (13.4) | | |
| | | Sham | 35.7 (12.5) | 36.8 (12.6) | 39.9 (12.5) | 34.3 (15.9) | | |
| | $MEP_{max}$:$M_{max}$ | Motor | 0.165 (0.140) | 0.202 (0.168) | 0.139 (0.064) | 0.162 (0.145) | 3.83 (0.012) | 1.23 (0.298) |
| | | Frontal | 0.141 (0.116) | 0.117 (0.084) | 0.092 (0.064) | 0.165 (0.140) | | |
| | | Sham | 0.121 (0.090) | 0.144 (0.101) | 0.096 (0.058) | 0.124 (0.104) | | |
| **Peroneus Longus** | $H_{max}$:$M_{max}$ | Motor | 0.251 (0.165) | 0.258 (0.133) | 0.290 (0.141) | 0.259 (0.169) | 0.77 (0.515) | 0.95 (0.466) |
| | | Frontal | 0.382 (0.230) | 0.326 (0.194) | 0.303 (0.169) | 0.269 (0.184) | | |
| | | Sham | 0.307 (0.147) | 0.296 (0.188) | 0.314 (0.195) | 0.286 (0.203) | | |
| | Motor Threshold (%2T) | Motor | 29.9 (11.6) | 28.4 (11.2) | 31.8 (10.8) | 30.8 (13.8) | 0.24 (0.867) | 0.28 (0.947) |
| | | Frontal | 32.5 (11.4) | 34.2 (13.1) | 35.8 (13.8) | 34.7 (17.7) | | |
| | | Sham | 36.8 (9.8) | 35.4 (14.2) | 39.3 (10.2) | 38.3 (16.1) | | |
| | $MEP_{max}$:$M_{max}$ | Motor | 0.078 (0.067) | 0.058 (0.032) | 0.078 (0.055) | 0.047 (0.031) | 0.48 (0.699) | 1.56 (0.167) |
| | | Frontal | 0.065 (0.060) | 0.077 (0.076) | 0.042 (0.043) | 0.092 (0.092) | | |
| | | Sham | 0.071 (0.089) | 0.077 (0.051) | 0.050 (0.043) | 0.059 (0.052) | | |
| **Soleus** | $H_{max}$:$M_{max}$ | Motor | 0.552 (0.185) | 0.505 (0.210) | 0.442 (0.176) | 0.427 (0.132) | 1.35 (0.264) | 1.13 (0.351) |
| | | Frontal | 0.560 (0.213) | 0.542 (0.220) | 0.491 (0.191) | 0.558 (0.193) | | |
| | | Sham | 0.516 (0.212) | 0.473 (0.193) | 0.505 (0.215) | 0.507 (0.216) | | |
| | Motor Threshold (%2T) | Motor | 27.6 (11.0) | 29.4 (10.3) | 27.3 (17.1) | 31.2 (6.5) | 0.32 (0.812) | 0.51 (0.802) |
| | | Frontal | 34.1 (12.1) | 35.4 (13.0) | 36.3 (15.0) | 33.2 (12.6) | | |
| | | Sham | 35.5 (12.1) | 37.7 (13.8) | 37.8 (11.4) | 34.6 (17.6) | | |
| | $MEP_{max}$:$M_{max}$ | Motor | 0.026 (0.018) | 0.026 (0.019) | 0.023 (0.017) | 0.023 (0.020) | 0.69 (0.562) | 0.08 (0.998) |
| | | Frontal | 0.017 (0.012) | 0.029 (0.029) | 0.023 (0.026) | 0.019 (0.016) | | |
| | | Sham | 0.027 (0.017) | 0.029 (0.023) | 0.022 (0.016) | 0.025 (0.016) | | |

Table 3. Means (standard deviations) for balance variables on medial and lateral hops across groups and timepoints and F-values for the main effect of time and the group-by-time interaction effect for each variable. Abbreviations: DPSI, dynamic postural stability index; APSI, anteroposterior stability index; MLSI, mediolateral stability index; VSI, vertical stability index. [a] significant at 0.05 level.

| | | Week 0 | Week 2 | Week 4 | Week 6 | Time Effect (P-value) | Interaction Effect (P-value) |
|---|---|---|---|---|---|---|---|
| **Medial DPSI** | Motor | 0.329 (0.072) | 0.342 (0.068) | 0.335 (0.065) | 0.340 (0.085) | 2.38 (0.074) | 0.66 (0.68) |
| | Frontal | 0.324 (0.069) | 0.276 (0.033) | 0.283 (0.044) | 0.326 (0.068) | | |
| | Sham | 0.332 (0.113) | 0.281 (0.058) | 0.282 (0.063) | 0.313 (0.102) | | |
| **Medial APSI** | Motor | 0.074 (0.009) | 0.072 (0.009) | 0.070 (0.009) | 0.070 (0.008) | 0.92 (0.437) | 0.63 (0.703) |
| | Frontal | 0.069 (0.009) | 0.072 (0.005) | 0.069 (0.006) | 0.069 (0.008) | | |
| | Sham | 0.068 (0.008) | 0.067 (0.007) | 0.066 (0.007) | 0.066 (0.006) | | |
| **Medial MLSI** | Motor | 0.037 (0.011) | 0.038 (0.008) | 0.036 (0.008) | 0.038 (0.007) | 0.64 (0.591) | 1.09 (0.371) |
| | Frontal | 0.036 (0.009) | 0.033 (0.007) | 0.033 (0.007) | 0.038 (0.008) | | |
| | Sham | 0.035 (0.010) | 0.033 (0.008) | 0.032 (0.007) | 0.031 (0.007) | | |
| **Medial VSI** | Motor | 0.317 (0.074) | 0.331 (0.070) | 0.324 (0.066) | 0.329 (0.088) | 2.38 (0.074) | 0.66 (0.679) |
| | Frontal | 0.314 (0.069) | 0.263 (0.034) | 0.272 (0.045) | 0.315 (0.069) | | |
| | Sham | 0.321 (0.115) | 0.270 (0.059) | 0.264 (0.065) | 0.303 (0.104) | | |
| **Lateral DPSI** | Motor | 0.363 (0.077) | 0.319 (0.046) | 0.333 (0.083) | 0.307 (0.054) | 4.39 (0.006)[a] | 1.00 (0.431) |
| | Frontal | 0.312 (0.059) | 0.275 (0.042) | 0.268 (0.045) | 0.291 (0.056) | | |
| | Sham | 0.311 | 0.270 | 0.291 | 0.288 | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | (0.096) | (0.043) | (0.068) | (0.093) | | |
| **Lateral APSI** | Motor | 0.066 (0.007) | 0.067 (0.006) | 0.067 (0.007) | 0.066 (0.006) | 2.26 (0.086) | 0.96 (0.456) |
| | Frontal | 0.068 (0.007) | 0.065 (0.004) | 0.065 (0.005) | 0.062 (0.004) | | |
| | Sham | 0.066 (0.006) | 0.064 (0.008) | 0.062 (0.005) | 0.064 (0.006) | | |
| **Lateral MLSI** | Motor | 0.037 (0.009) | 0.037 (0.005) | 0.038 (0.009) | 0.039 (0.006) | 0.71 (0.550) | 0.89 (0.508) |
| | Frontal | 0.036 (0.006) | 0.030 (0.006) | 0.032 (0.006) | 0.031 (0.004) | | |
| | Sham | 0.034 (0.009) | 0.034 (0.007) | 0.032 (0.003) | 0.034 (0.008) | | |
| **Lateral VSI** | Motor | 0.354 (0.079) | 0.309 (0.047) | 0.322 (0.085) | 0.297 (0.055) | 4.23 (0.007)[a] | 1.01 (0.424) |
| | Frontal | 0.301 (0.060) | 0.265 (0.042) | 0.258 (0.045) | 0.282 (0.057) | | |
| | Sham | 0.301 (0.098) | 0.259 (0.043) | 0.282 (0.069) | 0.278 (0.095) | | |

Table 4. Means (standard deviations) for electromyography variables on medial and lateral hops across groups and timepoints and F-values for the main effect of time and the group-by-time interaction effect for each variable. All units are percentage of ensemble peak.

| | | | | **Week 0** | **Week 2** | **Week 4** | **Week 6** | **Time Effect (P-value)** | **Interaction Effect (P-value)** |
|---|---|---|---|---|---|---|---|---|---|
| **Medial Hops** | *Tibialis Anterior* | Pre-Landing | Motor | 0.402 (0.117) | 0.367 (0.106) | 0.422 (0.121) | 0.337 (0.125) | 0.366 (0.778) | 1.980 (0.074) |
| | | | Frontal | 0.381 (0.126) | 0.418 (0.137) | 0.408 (0.132) | 0.405 (0.126) | | |
| | | | Sham | 0.463 (0.139) | 0.386 (0.126) | 0.344 (0.114) | 0.411 (0.141) | | |
| | | Post-Landing | Motor | 0.481 (0.098) | 0.433 (0.069) | 0.530 (0.194) | 0.447 (0.156) | 1.574 (0.200) | 10.109 (0.361) |
| | | | Frontal | 0.473 (0.099) | 0.521 (0.075) | 0.548 (0.115) | 0.474 (0.104) | | |
| | | | Sham | 0.528 (0.139) | 0.478 (0.075) | 0.474 (0.076) | 0.478 (0.142) | | |

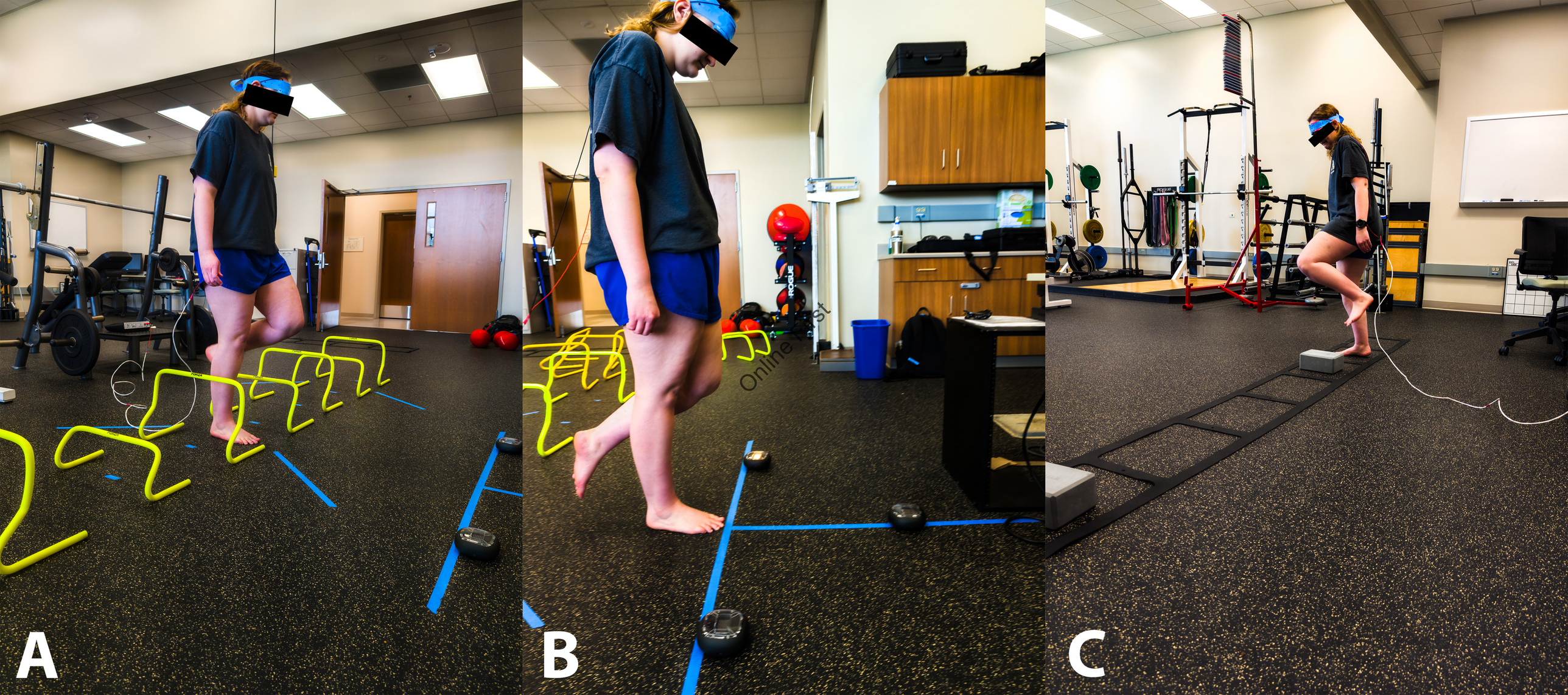
| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | *Peroneus Longus* | Pre-Landing | Motor | 0.510 (0.078) | 0.482 (0.103) | 0.575 (0.183) | 0.559 (0.134) | 1.051 (0.373) | 0.720 (0.634) |
| | | | Frontal | 0.510 (0.102) | 0.483 (0.095) | 0.533 (0.094) | 0.517 (0.171) | | |
| | | | Sham | 0.554 (0.162) | 0.533 (0.107) | 0.509 (0.129) | 0.562 (0.140) | | |
| | | Post-Landing | Motor | 0.486 (0.120) | 0.450 (0.141) | 0.498 (0.236) | 0.540 (0.215) | 1.735 (0.164) | 0.562 (0.760) |
| | | | Frontal | 0.475 (0.069) | 0.423 (0.067) | 0.483 (0.093) | 0.459 (0.150) | | |
| | | | Sham | 0.463 (0.119) | 0.423 (0.109) | 0.425 (0.086) | 0.473 (0.110) | | |
| | *Soleus* | Pre-Landing | Motor | 0.373 (0.044) | 0.385 (0.104) | 0.419 (0.136) | 0.465 (0.166) | 1.895 (0.135) | 0.997 (0.431) |
| | | | Frontal | 0.382 (0.097) | 0.349 (0.072) | 0.369 (0.127) | 0.476 (0.209) | | |
| | | | Sham | 0.415 (0.159) | 0.449 (0.174) | 0.383 (0.087) | 0.416 (0.150) | | |
| | | Post-Landing | Motor | 0.295 (0.074) | 0.296 (0.076) | 0.318 (0.146) | 0.376 (0.156) | 2.119 (0.102) | 0.800 (0.572) |
| | | | Frontal | 0.300 (0.083) | 0.270 (0.057) | 0.279 (0.093) | 0.356 (0.142) | | |
| | | | Sham | 0.310 (0.125) | 0.299 (0.106) | 0.326 (0.088) | 0.303 (0.101) | | |
| **Lateral Hops** | *Tibialis Anterior* | Pre-Landing | Motor | 0.398 (0.155) | 0.426 (0.114) | 0.411 (0.157) | 0.422 (0.125) | 1.185 (0.319) | 0.267 (0.951) |
| | | | Frontal | 0.443 (0.083) | 0.437 (0.155) | 0.411 (0.123) | 0.396 (0.114) | | |
| | | | Sham | 0.461 (0.117) | 0.441 (0.076) | 0.375 (0.094) | 0.420 (0.132) | | |
| | | Post-Landing | Motor | 0.484 (0.164) | 0.544 (0.123) | 0.525 (0.155) | 0.500 (0.145) | 0.498 (0.685) | 0.410 (0.871) |
| | | | Frontal | 0.532 (0.116) | 0.521 (0.070) | 0.500 (0.082) | 0.526 (0.099) | | |
| | | | Sham | 0.528 (0.103) | 0.521 (0.105) | 0.505 (0.074) | 0.488 (0.116) | | |
| | *Peroneus Longus* | Pre-Landing | Motor | 0.515 (0.128) | 0.477 (0.114) | 0.565 (0.222) | 0.523 (0.110) | 0.228 (0.877) | 1.263 (0.280) |
| | | | Frontal | 0.502 (0.098) | 0.562 (0.103) | 0.524 (0.103) | 0.507 (0.090) | | |
| | | | Sham | 0.518 (0.116) | 0.461 (0.121) | 0.476 (0.092) | 0.494 (0.092) | | |
| | | Post-Landing | Motor | 0.429 (0.135) | 0.430 (0.163) | 0.481 (0.238) | 0.457 (0.164) | 0.591 (0.622) | 1.125 (0.352) |
| | | | Frontal | 0.455 (0.082) | 0.439 (0.089) | 0.399 (0.09) | 0.448 (0.141) | | |
| | | | Sham | 0.455 (0.135) | 0.377 (0.115) | 0.437 (0.073) | 0.401 (0.116) | | |
| | *Soleus* | Pre-Landing | Motor | 0.452 (0.140) | 0.363 (0.066) | 0.447 (0.173) | 0.382 (0.066) | 1.243 (0.298) | 1.854 (0.095) |
| | | | Frontal | 0.396 (0.104) | 0.399 (0.067) | 0.351 (0.071) | 0.465 (0.130) | | |
| | | | Sham | 0.401 (0.138) | 0.398 (0.091) | 0.427 (0.119) | 0.461 (0.151) | | |
| | | Post-Landing | Motor | 0.339 (0.719) | 0.274 (0.437) | 0.309 (0.484) | 0.307 (0.536) | 2.400 (0.072) | 0.970 (0.449) |
| | | | Frontal | 0.304 (0.487) | 0.291 (0.447) | 0.257 (0.318) | 0.340 (0.509) | | |
| | | | Sham | 0.337 (0.760) | 0.285 (0.435) | 0.330 (0.492) | 0.329 (0.510) | | |

Table 5. Means (standard deviations) for side hop test, choice reaction time, and cognitive performance. F-values for the main effect of time and the group-by-time interaction effect for each variable. [a] significant at 0.05 level.

| | | Week 0 | Week 2 | Week 4 | Week 6 | Time Effect (P-value) | Interaction Effect (P-value) |
|---|---|---|---|---|---|---|---|
| **Side Hop Test (s)** | Motor | 17.0 (8.4) | 15.1 (8.9) | 15.0 (9.8) | 15.1 (11.6) | 11.00 (<0.001)[a] | 0.49 (0.812) |
| | Frontal | 16.1 (4.8) | 12.6 (3.4) | 11.8 (3.9) | 11.5 (3.8) | | |
| | Sham | 16.8 (10.5) | 12.2 (3.8) | 11.2 (2.3) | 10.8 (3.1) | | |
| **Medial Reaction Time (s)** | Motor | 1.95 (0.45) | 1.92 (0.54) | 1.98 (0.63) | 1.84 (0.50) | 0.46 (0.714) | 1.20 (0.310) |
| | Frontal | 2.00 (0.38) | 1.73 (0.37) | 1.88 (0.26) | 1.79 (0.24) | | |
| | Sham | 1.83 (0.55) | 1.96 (0.62) | 1.81 (0.45) | 1.86 (0.35) | | |
| **Lateral Reaction Time (s)** | Motor | 1.73 (0.330 | 1.80 (0.66) | 1.91 (0.94) | 2.11 (0.90) | 0.56 (0.645) | 1.40 (0.220) |
| | Frontal | 1.68 (0.38) | 1.58 (0.31) | 1.72 (0.38) | 1.62 (0.21) | | |
| | Sham | 1.72 (0.39) | 1.93 (0.68) | 1.82 (0.49) | 1.77 (0.43) | | |
| **Colors Correct (n)** | Motor | 2.3 (0.6) | 2.6 (0.3) | 2.7 (0.3) | 2.7 (0.4) | 9.82 (<0.001)[a] | 0.92 (0.484) |
| | Frontal | 2.5 (0.4) | 2.7 (0.3) | 2.7 (0.2) | 2.8 (0.2) | | |
| | Sham | 2.6 (0.4) | 2.7 (0.2) | 2.7 (0.3) | 2.8 (0.3) | | |

Table 6. Means (standard deviations) for patient-reported outcome measures. F-values for the main effect of time and the group-by-time interaction effect for each variable. Abbreviations: FAAM, foot and ankle ability measure; mDPAS, modified disablement in the physically active scale. [a] significant at 0.05 level.

| | | Week 0 | Week 2 | Week 4 | Week 6 | Time Effect | Interaction Effect |
|---|---|---|---|---|---|---|---|
| **Global Rating of Change** | Motor | | 1.36 (1.60) | 3.00 (1.96) | 3.36 (1.99) | 20.05 (<0.001)[a] | 0.759 (0.555) |
| | Frontal | | 0.77 (1.96) | 2.33 (2.27) | 2.45 (2.62) | | |
| | Sham | | 1.15 (2.54) | 1.83 (2.25) | 2.42 (2.39) | | |
| **FAAM: ADL Subscale** | Motor | 86.9 (14.2) | 87.4 (12.0) | 90.7 (10.7) | 92.5 (9.7) | 6.77 (<0.001)[a] | 1.95 (0.080) |
| | Frontal | 90.7 (9.5) | 90.4 (12.9) | 90.3 (14.2) | 90.4 (14.0) | | |
| | Sham | 85.6 (11.9) | 92.0 (6.5) | 93.5 (7.3) | 94.3 (6.9) | | |
| **FAAM: Sport Subscale** | Motor | 75.3 (18.6) | 77.8 (15.2) | 83.9 (13.4) | 82.4 (14.7) | 13.58 (<0.001 [a] | 0.50 (0.808) |
| | Frontal | 75.5 (20.8) | 77.8 (21.4) | 81.3 (18.9) | 81.8 (16.8) | | |
| | Sham | 68.7 (17.4) | 76.5 (17.7) | 80.7 (12.2) | 83.0 (12.8) | | |
| **mDPAS: Physical Subscale** | Motor | 12.7 (12.1) | 12.1 (10.3) | 9.7 (9.7) | 8.5 (8.7) | 8.05 (<0.001)[a] | 1.03 (0.409) |
| | Frontal | 12.1 (12.3) | 11.0 (10.7) | 9.8 (11.3) | 11.1 (12.0) | | |
| | Sham | 15.8 (6.7) | 10.8 (8.1) | 8.4 (7.5) | 6.6 (7.0) | | |
| **mDPAS: Mental Subscale** | Motor | 3.3 (3.1) | 3.5 (5.0) | 2.5 (3.4) | 1.9 (2.8) | 3.43 (0.020) | 0.73 (0.624) |
| | Frontal | 3.0 (3.7) | 2.6 (4.1) | 2.0 (2.9) | 1.8 (3.0) | | |
| | Sham | 1.9 (2.4) | 1.8 (2.5) | 1.3 (2.6) | 1.6 (2.9) | | |
| **Tampa Scale for Kinesiophobia** | Motor | 35.5 (6.1) | 35.9 (7.8) | 35.2 (7.4) | 34.6 (7.4) | 2.72 (0.048)[a] | 0.24 (0.96) |
| | Frontal | 32.6 (3.9) | 33.9 (5.1) | 33.0 (7.1) | 32.3 (5.9) | | |
| | Sham | 34.1 (6.1) | 36.0 (9.4) | 33.8 (6.4) | 33.1 (6.3) | | |


A
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ROGUE
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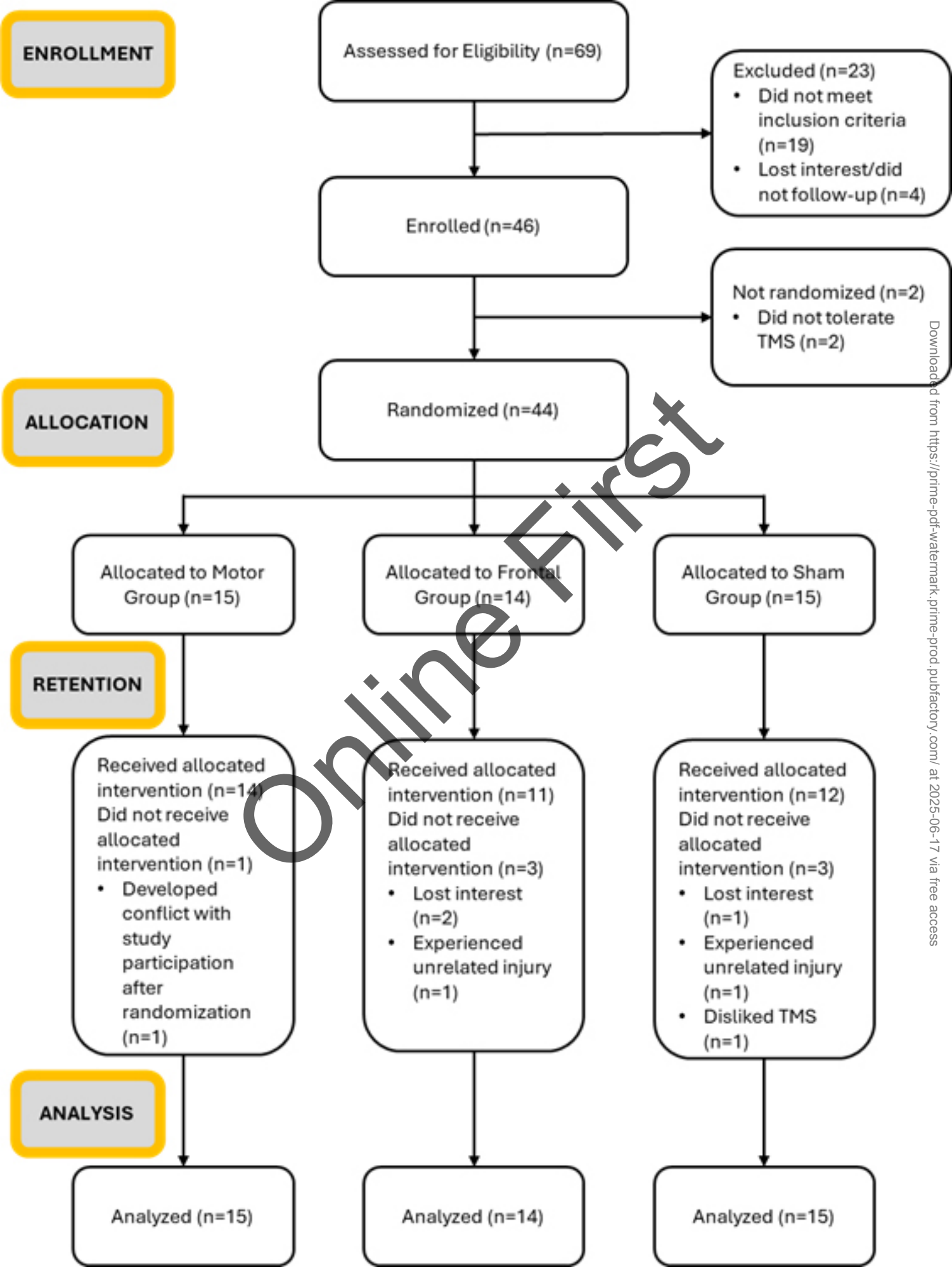


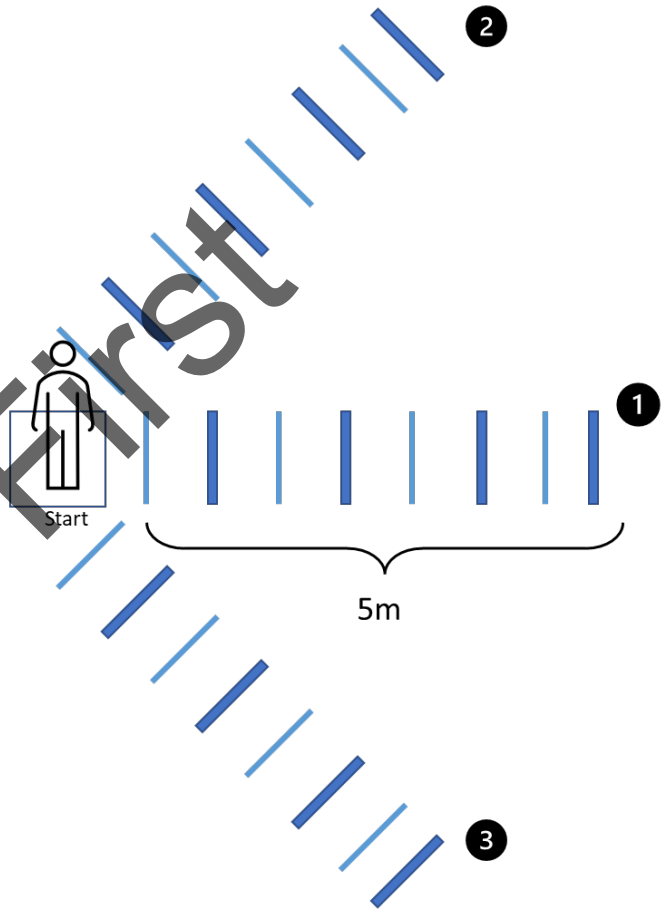
**Supplementary Material: Rehabilitation Protocol**

Each treatment session consisted of three exercises performed in sequence, with each individually progressed based on specified criteria:

A. Hurdle walking
B. Reactive balance:
C. Ladder agility

**A. Hurdle Walking**

Description: Participants stepped through a 5m course of hurdles walking first laterally (1), diagonally (2) forward, and diagonally backwards (3). Each was performed out-and-back, and the sequence of three was performed twice (6 total out-and-backs). Time-to-completion and errors (knocked hurdles) were recorded.



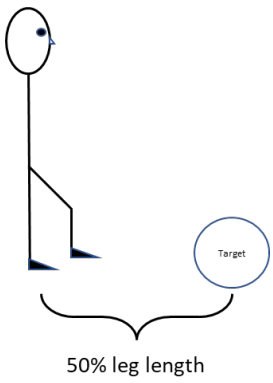

Progression:

1. Hurdles spaced 18 cm apart and alternated between heights of 15cm and 30cm
2. Hurdles spaced evenly, but height is randomized
3. Up to 2 hurdles replaced by yoga blocks (23cm x 14cm x 9cm) to force wide steps
4. Dribbling goggles added to progression #2
5. Obstacle distances randomized between 10 and 32 cm apart

Criteria to progress: Participants complete all 6 repetitions in under 4 minutes without knocking an obstacle.

**B. Reactive Balance**

Description: Participants maintained unipedal balance on the involved limb while monitoring one or more reactive lights, with instructions to respond to a specific cue. Participants performed 5 sets of 30 seconds, with 30s rest between trials. Average reaction time and errors (missed light, incorrect response, or loss of unipedal balance) were recorded.




Progression:

1. Single reactive light placed at a distance of 50% of leg length in front of the participant. Colors of red, green, blue, and yellow randomly shown in an interval of 2s, with participants instructed to step on green lights.

2. Participants instructed to hold 2 additional lights set to “balance” mode. These lights would provide vibratory feedback if they did not remain level. An error would be indicated if this was not corrected within 1s.
3. Same as number 1, but with 2 additional lights added lateral and medial to the involved side at a distance of 50% leg length from the participant.
4. Participants instructed to hold 2 additional lights set to “balance” mode as in #2, with 3 lights.
5. Balance mode was increased in sensitivity to cause an error.
6. Dribbling goggles were added to limit direct downward vision.

Criteria for progression: No errors (loss of unipedal stance, missing lights, reacting to wrong color, or balance light error) and average reaction time less than 1.5 seconds.

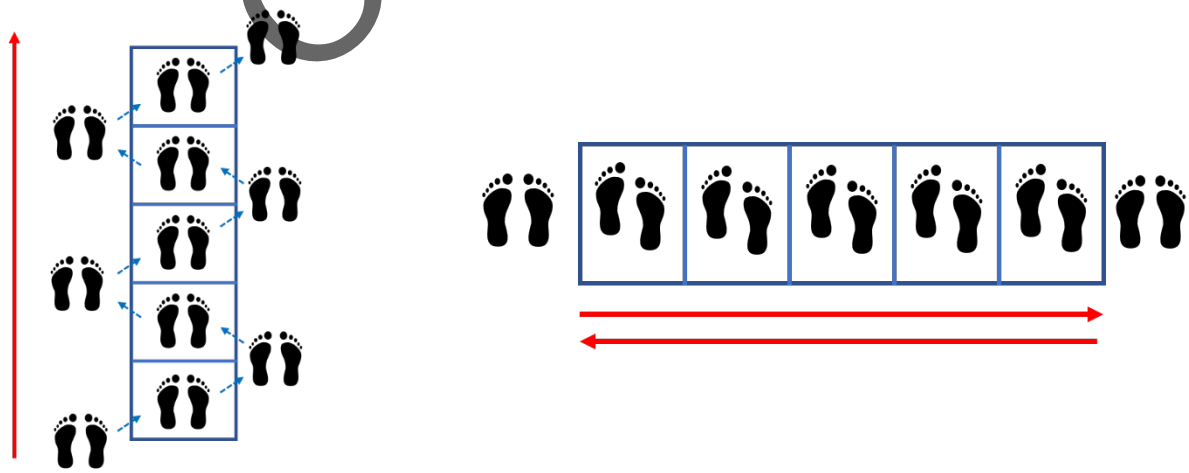
**C. Ladder Agility**

Description: Participants performed 6 out-and-back movements on a 3.65m agility ladder. In this, participants alternated a forward shuffle step (“in, in, out, out”) and a lateral shuffle step (“in, in, next square”). Participants were allotted 1 minute for each repetition, where any remaining time was provided as rest. Time to complete each repetition and errors (missing a square or tripping) were recorded.

Progression:

1. Participants completed repetitions with no obstacles.
2. Two yoga blocks were added into randomized squares of the ladder. Participants were instructed to skip a box with a block in it.
3. In addition to #2, 2 hurdles were added at randomized rungs for participants to step over.
4. Two additional blocks added.
5. Two additional hurdles added.

Criteria for progression: Participants able to complete each repetition in less than 20 seconds without errors.



Supplementary Table: Completion statistics for training protocol, including the total number of training sessions completed by participants within each group, the time between training sessions, and the highest progression reached on each exercise.

| | Motor | Frontal | Sham |
|---|---|---|---|
| **Total training sessions completed (n)** | 6.7 (2.1) | 6.8 (1.9) | 6.5 (2.4) |
| **Time between training sessions (days)** | 4.4 (1.8 | 3.9 (1.4) | 3.5 (1.3) |
| **Highest progression on agility walk** | 1.9 (1.4) | 1.6 (1.3) | 1.9 (1.2) |
| **Highest progression on reactive balance** | 3.5 (1.1) | 3.1 (1.4) | 3.5 (1.6) |
| **Highest progression on ladder agility** | 3.3 (1.5) | 2.9 (1.4) | 2.7 (1.3) |