Coversheet

Protocol

Spinal excitation to enhance mobility in elderly adults

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Protocol

1. Project Title

Spinal Excitation to Enhance Mobility in Elderly Adults: “The Charge Study”

2. Investigator(s):

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3. Abstract:

It is well known that age-related impairments of the brain and peripheral nerves contribute to a decline in walking function. Age-related impairment of the spinal cord is also a likely contributing factor, as the literature describes a variety of changes in spinal cord structure and function with aging. Specifically, the elderly spinal cord is less excitable, conducts signals more slowly, and is subject to neural noise. Therefore, we are initiating a new line of research with the goal of enhancing walking function in older adults by intervening on age-related neural impairment of the spinal cord. The objective of the proposed study is to establish the feasibility, preliminary efficacy, and variance of response for using transcutaneous spinal direct current stimulation (tsDCS) and textured shoe insoles to excite spinal locomotor circuits and enhance practice-related performance and retention on an obstacle walking task. Enhanced practice and retention effects will support future efforts to translate this approach into a longer term rehabilitation intervention.

Excitatory tsDCS is a non-invasive neuromodulation approach in which a relatively weak electrical current is delivered to the desired region of the spinal cord via electrodes placed on the skin. The electrical current does not cause discharge of action potentials, but rather is designed to bring neurons closer to their discharge threshold by inducing a sub-threshold depolarization of membrane potentials. When combined with a behavioral task, tsDCS has the potential to upregulate neural circuits in a task-specific manner and promote Hebbian neuroplasticity (‘fire together, wire together’). We will use a previously established electrode montage to deliver excitatory tsDCS to the lumbosacral spinal cord during practice of a complex obstacle walking task.

We also propose to combine the use of textured shoe insoles with tsDCS. This combinatorial approach may be a potent strategy for simultaneously optimizing spinal responsiveness to input from both descending and ascending excitatory signals to spinal centers of locomotor control. One anticipated benefit of increasing the excitation of spinal locomotor circuits is a reduction in the executive demand of walking, as measured by prefrontal cortical activation. Our research shows that elderly adults rely heavily on compensatory executive control while walking. This is widely considered to be a risk factor for adverse outcomes including falls.

We propose a parallel groups study design in which 40 older adults who have walking deficits and who demonstrate a compensatory executive locomotor control strategy will be randomized into one of four groups: 1) active tsDCS with smooth insoles (active/smooth); 2) sham tsDCS with smooth insoles (sham/smooth); 3) active tsDCS with textured insoles (active/textured); and 4) sham tsDCS with textured insole (sham/textured). Participants will be blinded to group assignment. While receiving stimulation for up to 30 minutes, participants will engage in walking practice over a standardized obstacle course. Practice-related gains in performance will be quantified by walking speed and other biomechanical metrics. Retention of performance gains will also be assessed at a separate visit 2 days later. tsDCS-induced changes in spinal excitability will be assessed by measuring soleus H-reflex. Executive demand of walking will be assessed as prefrontal cortical activation, measured with functional near infrared spectroscopy (fNIRS). Intervening on age-related impairment of the spinal cord to improve walking function is

a promising but untapped area of research. The proposed intervention techniques are low cost and translatable to real-world settings, which enhances the potential long term impact of this work on the well-being of older adults.

4. Background:

People with walking deficits have higher rates of morbidity and mortality, more hospitalizations, poorer quality of life, and are less likely to remain independent in the community.[1-10] Preserving walking function has become a major public health priority as it would drastically reduce health care costs and improve quality of life for many older Americans and their families.[11] Data from the American Community Survey (Profile of Veterans: 2011) shows that over 65% of Veterans are age 55 or older. The median age of male Veterans is 64. Therefore, a very large proportion of the Veteran population is currently or will soon be at risk for the well-known decline of walking function that occurs with aging. Preserving walking function is therefore crucial to the personal well-being of aging Veterans and has considerable fiscal and pragmatic implications for the VA Health Care System.

The spinal cord has a critical role in the control of walking. The lumbar spinal cord contains complex circuits called central pattern generators (CGPs) that contribute to patterned muscle activation needed for intra- and inter-limb coordination of walking.[12,13] During complex walking tasks such as obstacle crossing, the spinal cord must transmit descending motor commands from the brain that are needed to adapt the stepping pattern in order to meet environmental demands or task objectives (e.g., clearing the obstacle). These descending signals are integrated with ongoing activity of the CPGs, and this process is critical to successful stepping adaptations.[14] The spinal cord is also crucial for receiving and transmitting somatosensory information from the periphery, which is an important source of excitation to CPGs[15-17] and also important for eliciting reflex responses to unexpected perturbations (e.g., striking an obstacle).[18,19] Somatosensory information is also a crucial source of feedback for motor learning.[20,21] In the proposed project we seek to upregulate these spinal control mechanisms using tsDCS[22-25] in order to enhance performance and retention of walking on a complex obstacle course. The obstacle course task was selected because it engages all of the aforementioned roles that the spinal cord serves during walking.

Accumulating evidence has demonstrated that with old age the spinal cord is less excitable, conducts signals more slowly, and is subject to neural noise that obscures meaningful sensorimotor information. This may reduce the effectiveness of the pattern generating circuitry of the spinal cord that is crucial to control of walking. Spinal motor neurons, sensory neurons, inter- and projection neurons, axonal pathways, and glial cells are vulnerable to aging.[26] Notable findings in animal or human research include reduced concentrations of key neurotransmitters[27], abnormal metabolite levels (consistent with neurodegeneration)[28], and decline in spinal white matter (myelin) integrity.[29-31] There is also a dramatic decrease in the number of central terminals at the spinal cord from myelinated primary afferent neurons.[32]

Given the importance of the spinal cord to control of walking as well as the prominent age-related changes in spinal cord structure and function reported in the literature, we hypothesize that interventions targeting the spinal cord are likely to improve walking ability in older adults. We propose to test this hypothesis by using tsDCS to enhance practice-related performance and retention of an obstacle walking task. tsDCS is a neuromodulatory approach that delivers mild non-invasive electrical current via surface electrodes. Evidence suggests that tsDCS acts through both synaptic and axonal mechanisms.[33] Prior literature indicates that tsDCS can induce immediate and lasting changes in spinal cord excitability[34-37] and can alter reflexive[36,38,39] and voluntary[25] behaviors in humans and rodents.[40] During locomotion, tsDCS has been shown to modulate both alpha and gamma motor neuron activity and improve rhythmic motor output.[40] Human data indicate that tsDCS modulates spinal reflexes including H-

reflex[21,22], increases corticospinal excitability[24], and increases motor unit recruitment.[41] We propose to deliver tsDCS using an electrode montage that targets lumbar spinal excitability, and has been validated by modeling of electrical current flow[42] and by gains in lower extremity motor performance.[25] The objective with tsDCS is to bring spinal neurons closer to their discharge threshold. When applied during walking, this increased excitability of spinal neurons contributes to a physiological environment that is more responsive to task-specific activation by descending/motor and afferent/sensory pathways.[22] The proposed study is designed to provide evidence of short term effects of tsDCS on task practice, which can be translated to longer rehabilitation interventions in the future.

5. Specific Aims:

Specific Aim 1: Acquire preliminary data to assess whether active tsDCS and/or textured shoe insoles improve practice-related gains in performance and retention for a complex obstacle walking task.

Hypothesis 1a: Within-session, effect sizes will support the following group differences for improved walking speed and reduced prefrontal activity after the practice period:
[active/textured**] > [**active/smooth = sham/textured**] > [**sham/smooth**]**

Hypothesis 1b: At the 2-day retention test, effect sizes will support the same findings described for Hyp 1a.

Specific Aim 2: Establish evidence of increased spinal excitability following tsDCS.

Hypothesis 2: Spinal excitability post-stimulation (measured by H-reflex) will be significantly elevated above pre-stimulation baseline for active tsDCS but not sham tsDCS.

6. Research Plan:

Study Overview

All study procedures will be conducted at the Brain Rehabilitation Research Center within the Malcom Randall VA Medical Center. Up to forty older men and women will be enrolled in the intervention component of this study. A larger number will be enrolled for onsite screening, because some will fail the screening tests and not proceed to the study intervention. Participants will undergo the following sequence of events:

- *Telephone Screening*: Volunteers will be screened by telephone to determine if they meet basic enrollment criteria including age and general health status.
- *Informed Consent and Onsite Screening Visit*: Volunteers who pass the phone screen will be invited to participate in on-site screening. Informed consent will be obtained. Mobility function, cognitive screening, and somatosensory screening will be conducted. This visit will last approximately 3 hours.
- *Study Intervention Visit(s):* Qualifying participants will be invited to participate in the full study. They will attend either one or two intervention sessions (randomly determined to study dosage effects) in which they will practice a “locomotor learning” task comprised of a 10m walking course with obstacles and transitions between hard and soft floor surfaces. During this task they will receive either active or sham transcutaneous spinal direct current stimulation. They will also wear either smooth or textured shoe insoles. Biomechanical and neural control of walking will be assessed with various non-invasive

modalities. Participants will also undergo H-reflex assessment. This visit will last approximately 3 hours.

- *Follow up Visit*: 2 days following the study intervention visit, participants will return to perform the "locomotor learning" task again so that we can assess retention of learning. This visit will last approximately 2 hours.

Telephone Screening

Participants will be screened by telephone to determine if they meet the following criteria:

Inclusion criteria

- Age 65 years or older
- Willingness to be randomized to either intervention and to participate in all aspects of study assessment and intervention

Exclusion criteria

- Diagnosed neurological disorder or injury of the central nervous system, or observation of symptoms consistent with such a condition (spinal cord injury, Alzheimer's, Parkinson's, stroke, etc.)
- Contraindications to non-invasive spinal stimulation including any prior spinal surgical procedure
- Chronic lower back pain
- Obesity, defined as Body Mass Index exceeding 30. This is due to the potential influence of body fat on the amplitude of electrical current flow to the spinal cord.
- Use of medications affecting the central nervous system including, but not limited to, benzodiazepines, anti-cholinergic medication and GABAergic medication.
- severe arthritis, such as awaiting joint replacement
- current cardiovascular, lung or renal disease; diabetes; terminal illness
- myocardial infarction or major heart surgery in the previous year
- cancer treatment in the past year, except for nonmelanoma skin cancers and cancers having an excellent prognosis (e.g., early stage breast or prostate cancer)
- current diagnosis of schizophrenia, other psychotic disorders, or bipolar disorder
- difficulty communicating with study personnel (including people who cannot speak English)
- uncontrolled hypertension at rest (systolic > 180 mmHg and/or diastolic > 100 mmHg)
- bone fracture or joint replacement in the previous six months
- current participation in physical therapy for lower extremity function or cardiopulmonary rehabilitation
- current enrollment in any clinical trial
- clinical judgment of investigative team

Informed Consent and Onsite Screening Visit

Upon arriving to the research site, participants will undergo informed consent for screening and functional assessments. As part of screening, we will explain in the detail the full study protocol including transcutaneous spinal direct current stimulation.
All questions from the phone screening will be repeated, and additional health/medical screening criteria will be evaluated. This will include:

- Resting blood pressure
- Basic visual examination with Snellen eye chart
- preferred 10m walking speed (inclusion criterion is speed < 1.0 m/s)
- Height, weight, age, sex

- Obtain list of medications that the participant is currently using
- abdominal skinfold thickness
- walking speed during performance of a cognitive task (i.e., dual tasking)
- Somatosensory assessments of the foot, including two-point discrimination, vibratory perception, and tactile pressure sensation.
- Activities Specific Balance Confidence Scale: 16-item questionnaire that gauges confidence (on a scale of 0-100%) on various balance and walking tasks relevant to household and community ambulation.
- Berg Balance Scale: 14-item assessment of balance task performance to assess balance ability and fall risk.
- Movement-specific Reinvestment Scale: questionnaire that asked about the extent to which a person directs conscious attention to control of movement.
- Trailmaking Test – paper based test where the person must "connect the dots" between numbers or between alternating letters and numbers.
- Digit Span Test – paper based test to determine the longest list of numbers that a person can remember.
- Cognitive Assessment Battery from Cambridge Brain Sciences, which includes up to 12 cognitive tests. All are short, simple, computer-based assessment that assess domains of cognitive such as spatial working memory, response inhibition, and reasoning. A specific example is the visuospatial working memory test, in which participants are asked to remember the sequence and location of shapes that appear and disappear from the screen.

Following the screening visit, study staff will evaluate performance/responses relative to the study enrollment inclusion/exclusion criteria. Medical records may be examined to verify absence of exclusion diagnoses, and to obtain complete/accurate medication lists. Individuals who meet all criteria will be invited to enroll in the full study.

At the discretion of the Principal Investigator, any individual may be deemed ineligible for further participation in this study if there are concerns about the individual's capability to perform study procedures or if it may be unsafe for the volunteer to participate in the study. Furthermore, minor exceptions to the inclusion/exclusion criteria may be permitted at the discretion of the Principal Investigator if those exceptions do not influence participant safety. For example, small deviations from the target range of walking speed or somatosensory function. This is important to ensure that individuals are not excluded for insignificant reasons and to facilitate meeting enrollment benchmarks.

Walking Practice Visit(s)

Walking practice protocol

Walking practice will consist of 10-20 passes over a 10-meter complex walking course consisting of foam obstacles of various heights and widths, as well as transitioning between hard (bare floor) and soft surfaces (exercise mats). Each pass will be separated by a short rest period of approximately one minute. Participants will be instructed to walk as fast as safely possible.

For most participants, the walking practice protocol will be completed in a single visit. However, a subset of participants (up to 20) will perform the walking practice protocol twice so that we can study dosage effects (i.e., one session versus two sessions). This subset will be selected randomly.

During the walking practice protocol, participants will receive either active or sham transcutaneous spinal direct current stimulation (tsDCS) and will wear either smooth or textures shoes insoles. Specifically, participants will be randomized to one of four groups: active tsDCS with smooth insoles (*active/smooth group*); 2) sham tsDCS with smooth insoles (*sham/smooth group*); 3) active tsDCS with textured insoles (*active/textured group*); and 4) sham tsDCS with textured insole (*sham/textured group*). More detail about tsDCS and insoles are given below.

Transcutaneous spinal direct current stimulation (tsDCS) during walking practice protocol
tsDCS will be delivered to the posterior lumbar region of the spinal cord during walking using a commercially available direct current stimulation unit (Soterix Medical Inc). Each tsDCS electrode is comprised of a carbon rubber electrode encased in a saline-soaked sponge. The anode electrode will be placed on the skin over the 11th and 12th thoracic vertebrae, and the cathode electrode will be placed over the umbilicus. This electrode configuration has been shown to appropriately target the lumbosacral spinal cord, as validated by modeling of electrical current flow[42] and by gains in lower extremity motor performance.[25] A standard dosage of up to 30 continous minutes of 2.5 mA stimulus will be used. This dosage (or similar) has been used in numerous prior studies and has been shown to be well-tolerated and to produce measurable changes in reflex activity and/or lower extremity motor performance.[23-25,38,39,43,44] An identical electrode arrangement will be used for the sham condition, except the stimulation will be delivered in a brief ramp-like manner for just a few seconds at the beginning and end of the stimulation period. This sham approach is widely used in the field of direct current stimulation, and has been reported to be indistinguishable from active stimulation.[39,45] This is because participants quickly habituate to the sensation of active stimulation.

Textured Shoe Insoles during walking practice protocol
Each participant will be tested using smooth insoles and textured insoles. Both insole types will be created with 3D printing technology (SolidWorks software and Makerbot Replicator 2 printer). The insole material is a thin flexible plastic called Acrylonitrile Butadiene Styrene. This base material is extremely thin (about 1.5 millimeters) and does not substantially alter the fit or feel of the shoe. The smooth insole will consist of only this base material. The textured insole will use the same base material, but with firm raised cylindrical bumps (approximately 2.5mm height and 2.0mm diameter) spaced in a grid pattern. The grid of bumps will be located under the big toe, the head of the first metatarsal, the heads of 2nd-5th metatarsals, and the heel. On average, the typical insole will have 30-50 bumps depending on the size of the individual's foot. All insoles will be custom-sized to fit the participants' feet. All participants will wear socks (new out of package) and appropriately sized sandals (sanitized between study visits) that we provide. The sandals will be "walking sandals" with adjustable padded straps across the forefoot and heel.

Dual Task Walking Protocol
We will also ask participants to perform dual-task walking tests with a verbal phonemic fluency task and/or with a serial-7 subtraction task. Dual-task cost will be quantified as decrements in performance on either walking (e.g., slowing of walking speed) or cognitive task (e.g., fewer correct responses). Participant responses will be captured with a voice recorder and quantified as rate of word generation (after accounting for incorrect or repeated words). Participants will be instructed to focus equally on both the walking task and the cognitive task, in order to ensure divided attention.

Assessments of walking performance and neural control
Various assessments of walking performance and neural control will be made during the walking practice protocol, or during separate periods of walking, or while at rest.

Biomechanics and movement data
Performance on walking tests will be assessed using motion analysis instrumentation such as force plates, motion capture camera, and/or an electronic walkway. When motion capture cameras are used, we will tape small reflective markers to the participant's body which are visible to the camera and allow offline calculation of joint movements.

fNIRS prefrontal activation
Prefrontal brain activity may be measured with fNIRS during walking and cognitive assessments. fNIRS is a safe non-invasive technology for indirectly assessing cortical activation based on changes in blood flow and oxygenation. Sensors are placed on the forehead, and produce infrared light that is able to pass through the skull and is absorbed or reflected by blood and other tissues in the head. Infrared light is considered safe and there is no sensation association with this procedure. Calculations made from the relative amount of light absorption/reflection provide an estimate of the metabolic activity level of underlying cortical tissue. We will use a commercially available fNIRS monitor (Octamon by Artinis Medical Systems).

Muscle activity with surface electromyography (EMG)
EMG is a non-invasive approach to measuring the timing and amplitude of neuromuscular activity by placing recording sensors over the muscles. We may record EMG during walking assessments from up to 8 muscles per leg. Adhesives will be used to secure the electrodes to the legs. Prior to electrode placement, the recording site will be shaved and cleaned to ensure good quality contact.

H-reflex of the soleus muscle to assess spinal excitability
H-reflex testing involves delivering an electrical stimulus to the peripheral nerve and measuring the resultant muscle activity using surface electromyography. H-reflex assessment of the soleus muscle may be conducted immediately preceding tsDCS, as well as immediately post-tsDCS and at 30 minutes post-tsDCS. H-reflex may also be recorded while the participant rests in a semi-reclined positioned with the foot supported in slight ankle dorsiflexion (10 degrees) and the knee in 30 degrees of flexion. H-reflex may also be recorded while the participant is walking on a treadmill or overground. Stimulation will be delivered via a cathode placed in the popliteal fossa and an anode placed above the patella. Electromyography (EMG) will be recorded from the soleus with bipolar surface electrodes place 3 cm apart. Electrode placement will be along the mid-dorsal line of the leg, 4cm below where the gastrocnemius joins the Achilles tendon.

Sympathetic nervous system activity measured by skin conductance
Participants may be asked to wear sensors on their fingers that measure skin conductivity, which is a measure of sympathetic nervous system arousal. Adhesive electrodes are placed on the index and ring fingers. We will use a commercially available data acquisition unit (Flexcomp Infiniti by Though Technologies Inc).

Video, photos, and voice recordings
During this study, videos and/or photos may be taken during to document the functional abilities of participants, and for possible use in research presentations or education. We may also use voice recordings to capture performance on cognitive assessments such as verbal fluency or serial-7 subtraction tests. At the time of consent, participants will choose what their videos/photos/recordings can be used for. We will avoid capturing images of the participants' faces, and will obscure or delete any such images.

Follow Up Visit

Approximately 2 days after the intervention visit, participants will return to the lab and perform several more walking trials on the same course that was used for practice, so that we can evaluate retention of walking performance.
The dual-task walking assessment will also be repeated.

Possible Discomforts and Risks:

As with all physical activity, there is a risk of falling while we test or train walking ability. Falls can lead to injuries ranging from minor to serious. When participants are asked to walk on a treadmill (e.g., during the H-reflex test described above), they will wear a safety harness so that they cannot fall of the treadmill. The harness will catch the participant, but might still cause injury (scrapes or bruises) if there is forceful contact with the straps. It is also possible that participants could experience musculoskeletal injury such as an ankle sprain. It is possible that the participant may experience fatigue, soreness, and discomfort due to physical activity associated with this study. These are unlikely to be worse than what he/she would experience due to increased physical activity outside of our study. These are normal responses to exercise and most discomfort would generally disappear within a matter of days. In general, walking exercise is strongly recommended for all adults, including elderly adults with medical conditions. Transcutaneous spinal direct current stimulation is considered safe but some people might experience some side effects. The most common side effects are itching and tingling or mild discomfort at the area of stimulation. Whenever an electrical stimulation is applied to the body, it could possibly have unexpected consequences. tsDCS will be applied and operated by research personnel listed in myIRB (with all required training in human subjects research) who have been thoroughly trained in the use and safety of tsDCS by the investigative team. Furthermore, we will carefully document any potential adverse reactions. We will closely monitor any potential discomfort, irritation, redness, muscle spasms, altered sensation, or changes in autonomic function due to tsDCS with questionnaires conducted at each session and also with a follow-up phone call.

Textured insoles are generally safe, although we will impose exclusion criteria related to foot health including prior history of foot ulcer, present signs of broken skin or blisters, and/or structural deformity causing major pressure points on the sole of the foot. If necessary, the textured insoles can be trimmed or particular regions can be sanded down to avoid irritating sensitive areas on the sole of the foot. The participants' feet will be visually examined prior to and following the assessment, and the participant will be interviewed about any potential discomfort. Any noteworthy issues will be recorded.

fNIRS is considered safe. The infrared light used in assessment is not known to cause any harm or to alter the brain in any way. The sensors are secured to the participant's head using adhesive tape, which may cause minor skin irritation in some people, particularly those who are sensitive/allergic to adhesives. We will check with participants about any known sensitivities to adhesives.

There is a risk that participants may find cognitive and functional tests challenging or uncomfortable if they have difficulty succeeding with the tasks. Participants may skip any question that they do not wish to respond do.

8. Possible Benefits:

There is no direct benefit to the participant.

9. Conflict of Interest:

None.

Data and Safety Monitoring Plan

Adverse Event Reporting

Adverse events (including expected, unexpected, serious and non-serious) will be tracked in a cumulative table. Adverse events will be reported according to the guidelines of the University of Florida Institutional Review. Specifically, adverse events that are serious and unexpected (see definitions below) will be reported to the UF IRB within 5 working days of when study personnel learned about it. Reports of adverse events that are not serious or that are expected (e.g., muscle soreness) will be added to the cumulative adverse event table and reported to the UF IRB annually.

A *serious adverse event* is any adverse event that results in any of the following outcomes:

- death,
- a life-threatening adverse event,
- inpatient hospitalization or prolonging existing hospitalization,
- a persistent or significant disability/incapacity,
- or a congenital anomaly/birth defect.

Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered a serious adverse event when the event may jeopardize the patient or subject and/or may require medical or surgical intervention to prevent one of the outcomes listed in the definition above.
An *unexpected adverse event* is any adverse event that is not consistent with the current investigator brochure, protocol, consent form, or is not part of the normal disease progression. In addition, known adverse events may occur more frequently than expected. If so, then this meets the definition of “unexpected” and must be reported to the IRB.

Protection Against Risk

Staff training: All personnel will be thoroughly trained in the study procedures by the Principal Investigator or other appropriate member of the research team, and will complete all required trainings concerning human subjects research at the University of Florida.

Health monitoring and medical response: Volunteers at risk of health problems due to recent history of medical conditions (e.g., serious cardiac or pulmonary conditions) will be excluded, as noted above in the inclusion/exclusion criteria. Any adverse events will be recorded and monitored as required by our University of Florida Institutional Review Board. In the event o fa medical emergency at the VA Hospital (our study site) we will call the hospital emergency response line, 6-9-1-1 and alter them to a code blue (medical emergency). Subjects will be able to terminate a study session at their request at any time without prejudice. Minimization of risk during neurorehabilitation and assessments will be accomplished by monitoring vital signs, with prescribed criteria for termination of the testing session. Vital signs will be monitored before, during and after assessment. Contraindications for participation will include resting heart rate >100 bpm or <50 bpm, resting systolic blood pressure >180 mmHg or <100 mm Hg or resting diastolic blood pressure >100 mmHg. Indications to terminate physical activity will include heart

rate that exceeds age-predicted maximum (220-age), sudden drop in heart rate exceeding 15 bpm, systolic blood pressure >220 mmHg or <100 mmHg, or diastolic blood pressure >110 mmHg. Other criteria for termination include subject complaints of shortness of breath, light-headedness, dizziness, confusion, severe headache, dyspnea or onset of angina. Should the session be halted, the subject will be asked to rest while BP and HR are monitored and will resume only if BP and HR return to acceptable values. If any of these conditions persist after rest, the patient's primary physician will be called and patient referred for evaluation. If the patient complains of angina at rest, loss of consciousness occurs, or cardiac arrest, emergency medical services through 911 will be called immediately. Portable defibrillators are available.

Confidentiality: Data will be used only in aggregate and no identifying characteristics of individuals will be published or presented. Confidentiality of data will be maintained by using research identification numbers that uniquely identify each individual. Safeguards will be established to ensure the security and privacy of participants' study records. Appropriate measures will be taken to prevent unauthorized use of study information. Data other than demographic information will not use names as an identifier. The research ID number will be used. The research records will be kept in a locked room in the study site. The files matching participants' names and demographic information with research ID numbers will be kept in a locked file that uses a different key from that of all other files. Only trained and certified study personnel will have access to these files, and they will be asked to sign a document that they agree to maintain the confidentiality of the information. Electronic records will be stored on password protected network server maintained by the university information technology department. In compliance with the Health Insurance Portability and Accountability Act (HIPAA) and the Standards for Privacy of Individually Identifiable Health Information of the Department of Health and Human Services, we access personal health information and medical records only after receiving signed informed consent.

Safety during walking: The intensity and duration of walking activity will be carefully monitored to ensure that it is appropriate to the participant's capabilities. Participants will wear a gait belt during walking, which will better enable the therapist and/or assistants to provide support in the event of a loss of balance. Falls will be tracked on the therapy log and reported to the PI and IRB even if there is no injury associated.

tsDCS Safety: Our protocol uses stimulation parameters that are considered standard practice, and have been used safely in prior research. The most common side effects of tsDCS are slight itching, tingling, and reddening of the skin under the electrode. Participants typically habituate to itching or tingling sensations within 60 seconds of stimulation. To minimize risk associated with tsDCS, participants will be monitored throughout stimulation sessions and asked to report any discomfort. If stimulation sensation is uncomfortable, the stimulation levels will be decreased to a comfortable level or will be stopped.

fNIRS Safety: fNIRS poses no safety risk. Infrared light from the fNIRS device is not harmful and elicits no sensation. Sensors may be secured to the skin using adhesive tape, which could lead to mild skin irritation in those who are sensitive to adhesives. If a person indicates or displays such a sensitivity, we will avoid using adhesive tape and instead use elastic fabric or straps to secure the sensors.

Questionnaire administration: Questionnaire data are collected in secure spaces where the interview cannot be overheard. Participants will be informed that they are not required to answer questions that they do not wish to answer.

Statistical Analysis Plan: Effect sizes for between-group differences will be calculated for *improved* walking speed after the practice period. For Hypothesis 1b, an analogous comparison

will be made for the 2-day retention test. We do not claim that this study is powered to conduct statistically significant tests of group differences, although we will examine our data for evidence of directional effects:

[active/textured**] > [**active/smooth = sham/textured**] > [**sham/smooth**].**

Rather, our goal is to calculate effect sizes and variance of response in order to provide data needed for powering a future full scale trial. This study will also provide information on the feasibility of our protocol including safety and recruitment.

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