Transcranial Direct Current Stimulation for Post-stroke Gait Rehab

NCT03666533

July 13, 2023

Simultaneous transcranial direct current stimulation and gait training for chronic stroke NCT 03666533

Abbreviated Protocol (from last IRB approved version- 07/2023)

SPECIFIC AIMS Gait deficits following stroke are prevalent and frequently persistent after stroke. Current rehabilitation methods fail to restore normal gait for many stroke survivors. Those who have persistent gait deficits following stroke even after intensive rehabilitation efforts tend to be more dependent on caregivers for assistance with ADLs, demonstrate limitations in household and/or community ambulation, are at higher risk for falls, and report poor quality of life (QOL). One promising treatment method that warrants further investigation is transcranial Direct Current Stimulation (tDCS), a form of non-invasive brain stimulation (NIBS). If found to be effective, tDCS is readily deployable into the neurorehabilitation clinical setting because of its safety, ease of set-up and ability to be paired with other established and effective gait rehabilitation methods. The purpose of this current study is to develop treatment methods that improve gait for those with persistent deficits following stroke. In the proposed study, we will compare the response to active tDCS+gait training versus sham tDCS +gait training. Gait training will be provided within a virtual reality (VR) gait training system and overground and will ensure a consistent, repeated motor learning-based pattern of practice. AIM 1: Determine whether the combination of simultaneous tDCS and gait training produces superior improvement in gait performance than gait training alone. Hypothesis 1: There is an additive advantage in combining tDCS and gait training in improving gait performance in chronic stroke survivors. AIM 2: Characterize the neuroplastic brain changes in response to bihemispheric tDCS combined with gait training. Hypothesis 2: The combination of gait training and tDCS results in a greater increase in corticospinal excitability and strengthened functional connectivity compared with gait training alone. AIM 3: Identify factors that predict gait improvement in response to tDCS with gait training. Hypothesis 3a: Greater gait improvement in response to bihemispheric tDCS with gait training is related to the following combination of baseline factors 1) corticospinal tract (CST) lesion load; 2) greater motor abilities of the affected lower extremity; 3) greater corticospinal excitability; 4) greater functional connectivity; 5) higher integrity of the stroke-affected corticospinal tract; and, 6) lesion type (cortical, subcortical, brain stem). Hypothesis 3b: Greater gait improvement in response to bihemispheric tDCS is dependent on the tDCS-induced electrical current density at the targeted cortical areas in the primary motor cortex for lower extremities.

Study design overview This study is testing the efficacy of utilizing tDCS during gait training for individuals with chronic stroke (>6 mo post-stroke) who demonstrate an abnormal gait pattern. This is a randomized controlled multi-session study to test the potential benefit of combining tDCS and gait training for individuals with chronic gait deficits after stroke. The key exclusion criteria will be more than one stroke, contraindications for transcranial magnetic stimulation, and presence of implanted medical devices such as cardiac pacemaker or vagus nerve stimulator. .

Study intervention Subjects participated in 10 treatment sessions, a baseline testing (includes MRI), a mid-treatment testing session, a testing session after the 10th treatment session (includes MRI) and a 6-week follow-up testing visit. Clinical outcome measures were collected by a trained study staff who is not involved in therapy and blinded to group allocation. Subjects will be randomly allocated to either Treatment Group 1) active tDCS+gait training or Treatment Group 2) sham tDCS+gait training. Each VR gait training session lasted 30 minutes and tDCS will be "on" for the first 15 minutes while the subject simultaneously participates in gait training with guidance of a study physical therapist. Immediately after VR+tDCS training,

subjects participated in 30 minutes of overground training guided by a physical therapist. Home exercises were assigned to be completed on non-training days and reinforced in-person therapy training. Both, the subject and the study staff who is delivering therapy were blinded to group allocation.

Aims 1 and 2 analysis: We directly compare pre to post changes for gait speed and paretic single limb stance duration between the two groups. Similarly, secondary outcome measure changes are being compared between the study groups. We compare trajectories of changes in primary and secondary outcome measures afforded by longitudinal measurement through the course of study participation, using mixed models and the analysis of Treatment Group by time interaction effects. Time is considered as a categorical variable as well as modeled with random slope parameters. Two-sample comparisons of change values are conducted with t-tests or nonparametric methods such as Mann-Whitney U tests.

Aim3 analysis: We correlate change in clinical gait performance measures in response to intervention with baseline variables describing the structural integrity of the corticospinal tracts, functional brain connectivity and lower limb motor abilities. We also explore regression analyses where changes in gait measures is modeled as a dependent variable, and include predictors such as baseline TMS measures (MEP-rc), DTI measures, functional connectivity, motor ability measure and electrical field estimate values.

Inclusion and Exclusion Criteria

Inclusion criteria

- Medically stable and at least 6 months after first ever stroke
- Cognition sufficiently intact to give valid informed consent
- Ability to follow two stage commands.
- Sufficient endurance to participate in the study.
- Age >18
- Observable stance gait deficit while walking on level surface.

Exclusion Criteria

- Acute or progressive cardiac, renal, respiratory, neurological disorders or malignancy.
- Any psychiatric diagnosis or active psychological condition
- More than one ischemic stroke or stroke affecting both sides
- Lower motor neuron damage or radiculopathy
- No observable gait deficit during ambulation
- Presence of implanted medical devices such as cardiac pacemakers and defibrillators, intrathecal drug delivery pumps, or spinal cord, vagus nerve or similar stimulators, or cochlear implants
- Presence of metallic hardware in close contact with the TMS coil such as intracranial implants, aneurysm clips, plates, electrodes
- Past history of seizures or unexplained loss of consciousness
- Family history of medication refractory epilepsy
- History of substance abuse within the last 6 months

- Chronic sleep deprivation, ongoing untreated sleep disorder
- Pregnancy or pregnancy planning during the study period
- Inability to understand English.
- Activity tolerance insufficient to complete VR treadmill training.