Official title Cerebellar Transcranial Direct Current Stimulation in Parkinson's Disease

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Prospective subjects will include 10 adults with mild-moderate PD that will be recruited to complete five randomly ordered cerebellar stimulation sessions (SHAM, unilateral 2 mA, unilateral 4 mA, bilateral 2 mA, and bilateral 4 mA), separated by at least 5 days. Each session will involve one visit to the Integrative Neurophysiology Laboratory (INPL) and will last for approximately one hour. We expect data collection to last 4-6 months. Cerebellar tDCS will be performed during all of the gait and balance tests. All five sessions will be the same, except for changes in tDCS stimulation. First, the Movement Disorder Society-Unified Parkinson's Disease Rating Scale Motor Section (MDSUPDRSIII) will be completed. Then tDCS will be donned and the stimulation period will begin. After 5 minutes of pre-activity stimulation, gait and balance testing will be performed in randomly-ordered blocks of randomized tests (i.e., block order randomized; each test randomized within the block; see below). The gait and balance blocks are expected to take approximately 20 minutes to complete, accounting for rest periods between the activities. Once all of the tests have been completed, and the stimulation period has ended (25 minutes), the tDCS device will be removed and the MDS-UPDRS III will be repeated to check for any acute changes in disease symptoms.

Gait block: 1) the fast 30-meter walk test (30mWT; walk 30 meters as fast as safely possible; walking characteristics and time taken to complete the task are the primary outcomes), 2) a 6-minute walk test (6MWT; walk continuously between two markers spaced 30 meters apart for 6 minutes at a brisk pace; total distance walked and walking characteristics are the primary outcomes), 3) two trials of the Timed Up and Go test (TUG; stand from a seated position, walk 5 meters, turn around, sit back down in the chair; time to complete the test is the primary outcome). Subjects will wear six motion sensors (OPAL inertial motion units) on the top of both shoes/feet, at both wrists, on the lower back (5th lumbar spine), and on the chest/sternum during the 30mWT and the 6MWT. The subjects will perform these walks in a cordoned-off hallway adjacent to the laboratory.

Balance block: 1) stand on a firm surface (directly on a force platform) for 1 minute with eyes open (balance characteristics [95% confidence interval of the total 2D area explored, center of pressure movement velocity in forward/backward and left/right directions] are the primary outcomes), 2) stand on a foam surface (6 cm foam pad placed on top of force platform) for 1 minute with eyes open (the same balance characteristics as above are the primary outcomes).

Subjects will be carefully watched and guarded against falling during all of the testing procedures. Study personnel will always be within arm's reach to help the subject recover their balance, when necessary.

Active cerebellar tDCS protocol: A tDCS device (Soterix) will deliver either 2 mA or 4 mA of direct current through two sponge surface electrodes (5cm × 7cm, soaked with 15 mM NaCl). Unilateral cerebellar tDCS will have the anode (positive electrode) placed 3 cm lateral to the inion, on the side ipsilateral to the most PD-affected side. The cathode (negative electrode) will be placed on the ipsilateral buccinator muscle (cheek). Bilateral cerebellar tDCS will have both electrodes placed 3 cm to either side of the inion, with the anode assigned to the most PD-affected side and the cathode assigned to the less PD-affected side. Total simulation time will be 25 minutes.

SHAM cerebellar tDCS session: Electrode placement for SHAM will be the same as the unilateral cerebellar montage in 50% of subjects (5 subjects) and the bilateral cerebellar montage in the other 50% of subjects (5subjects). During SHAM, the tDCS device automatically performs a ramp-up and ramp-down (gradual increase/decrease in intensity) during the first 30

seconds and the last 30 seconds of the SHAM condition. During the intervening time (0:30 - 24:30), the stimulation is set to 0 mA.

The stimulation device will be placed in a backpack worn by the subjects during testing gait and balance testing. Both subjects and study personnel (except the PI) will be blinded to the stimulation condition; the PI will be the only one that knows the stimulation condition and will be the only one to operate the tDCS device. All other study personnel who help administer the gait and balance tests will be blind to the stimulation condition. The subjects will be asked to guess their stimulation condition at the end of each session. However, they will not be informed of the accuracy of their guesses until they have fully completed study participation (i.e., after the last session). We will also ask subjects to report any stimulation-related sensations (e.g., itching, burning, tingling, headache, etc.), and their magnitude (10- point Likert scale), they experienced during the session. These will be recorded on the demographic/data collection form (see attached).

There will be no long-term follow up.

STATISTICAL ANALYSIS

Performance on the gait and balance tests will be analyzed using a one-way repeated measures ANOVA with five conditions (SHAM, unilateral 2 mA, unilateral 4 mA, bilateral 2 mA, bilateral 4 mA) followed by Tukey adjusted pairwise comparisons.

The primary gait outcome measures will be time to complete the 30mWT, distance walked in the 6MWT, and the average time to complete the TUG test. Because we hypothesize that tDCS will improve the negative effects of gait, standard gait metrics during the two walk tests, including gait speed, cadence, stride length and time, step length and time, will be assessed with the OPAL motion sensor system.

The primary balance outcome measures will be 95% confidence interval ellipse (an ellipse that contains 95% of the 2D trace of the center of pressure [COP] movement during the balance tests) and COP velocity in the forward/backward and left/right directions.