Statistical Analysis Plan

Protocol ID: 5715-FEX

Wearable Gait Interventions for Augmenting Paretic Propulsion: Towards Personalized Post-Stroke Gait Rehabilitation

Clinical Trial Number: NCT07212608

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Objective

The primary objective of this study was to understand whether certain post-stroke patient subsets, identified from clinical, biomechanical, and neuromuscular characteristics, preferentially respond to different walking rehabilitation interventions that augment paretic limb propulsion (e.g., soft robotic exosuits or electrical stimulation neuroprostheses). This work could enhance post-stroke gait recovery trajectories by informing clinical decision-making to better match patients with rehabilitation devices tailored to their specific gait characteristics.

Study Participants

Twenty-two people in the chronic phase of stroke recovery completed this study (3 female; 58 ± 11 years old; 6 ± 4 years post-stroke). Inclusion criteria consisted of age at least 18 years, diagnosis of a stroke greater than 6 months prior to study participation, ability to walk independently with or without an assistive device for at least 30 meters, and passive range of motion of the paretic ankle reaching neutral (90 degree angle). Participants were excluded if they had history of lower extremity joint replacement, metal implants beneath neurostimulation sites, and/or inability to communicate with the study team. All study procedures were approved by the Institutional Review Board at Boston University (Protocol 5715). Prior to participation in the study, all study participants provided written informed consent, and medical clearance was obtained for from their healthcare providers.

Study Design

This study was designed to evaluate clinical, biomechanical, and neuromuscular characteristics associated with improved walking speed after one session of gait training with a propulsion-augmenting technology (i.e., neuroprosthesis or soft robotic exosuit).

Each participant completed three study visits on separate days: a Baseline Evaluation, a Neuroprosthesis Training Day, and an Exosuit Training Day. There was at least one day between the Baseline Evaluation and the first training visit, and the training visits were conducted in a randomized order with at least two days in between. All study visits occurred within six weeks. The Baseline Evaluation assessed comfortable and fast walking speeds using the Ten-Meter Walk Test (10mWT), Six-Minute Walk Test (6MWT) distance, and central drive of the plantarflexor muscles. At each training visit, pre-session and post-session overground fast walking speed was assessed during two laps around a 26.6-meter track, and forward propulsion metrics and energy expenditure were assessed during a 3-minute treadmill walk at a speed that was matched pre and post session. The rehabilitation device (i.e., neuroprosthesis or exosuit) was tuned for each

participant prior to a 30-minute overground training walk with intermittent assistance from the rehabilitation device (90 seconds active / 30 seconds off). Participants were cued to maintain a training speed based on the 6MWT from their baseline visit and were prompted to take a break if they did not meet this speed, if their heartrate exceeded 80% of their heart rate reserve, or if they asked to take a rest. Total walking time and total rest time were recorded and matched across training visits. For safety during all walking, participants were guarded by a physical therapist and wore a lightweight harness that did not provide bodyweight support.

Kinetic data were collected at 2000 Hz using an instrumented split-belt treadmill and six floor-embedded force platforms (Bertec Corp., Columbus, Ohio). Propulsion peak was computed as the maximum anteriorly directed ground reaction force (AGRF). Propulsion symmetry was computed as the percent contribution of the paretic propulsion impulse (i.e., the positive integral of the AGRF) to the total propulsion impulse from both limbs, such that 50% indicates symmetrical gait. Energy expenditure was collected on a breath-by-breath basis using indirect calorimetry (K5, COSMED, Rome, Italy). The energy cost of walking was computed as the net volume of oxygen, compared to standing rest, consumed per meter walked and normalized by bodyweight. Kinematic data were collected at 200 Hz using optical motion capture cameras (Oqus, Qualisys, Gothenburg, Sweden). Inertial data were collected at 100 Hz using inertial sensors (MTi, Xsens, Movella Inc., Henderson, Nevada). Electromyography data were collected from the tibialis anterior and gastrocnemius muscles (Trigno Quattro, Delsys Inc., Natick, Massachusetts). Strength capacity was computed as the torque generated by the plantarflexors during a maximum voluntary contraction (MVC). Central drive was computed as the percentage of strength capacity to the maximum force-generating ability of the plantarflexors (i.e., MVC with a supramaximal electrical stimulation burst). Strength symmetry was computed using the same method as propulsion symmetry.

Data Processing and Analysis

Gait data were processed using a biomechanics software (Visual3D, HAS-Motion, Kingston, Ontario, Canada) and a computing platform (MATLAB, The MathWorks Inc., Natick, MA). Kinetic and kinematic data were filtered using a fourth-order Butterworth lowpass filter with a cutoff frequency at 10 Hz. A force threshold of 15 N was used to remove noise in the vertical ground reaction force on the treadmill. Timeseries gait data were segmented into strides by the heel strike (HS) gait event and normalized as a percentage of the gait cycle. Timeseries outcomes were obtained by averaging across strides. Energy expenditure was averaged across the last minute of a 3-minute treadmill walk with outliers exceeding 2 standard deviations of the mean excluded.

Statistical analyses were conducted in a commercial statistical software (SPSS, Version 28, IBM Corp.). The sample size of 22 participants with an alpha of 0.5 was powered to detect an effect size of 0.63 with 80% power. Pre-to-post session changes were assessed using paired t-tests. Linear regression analysis was used to assess baseline predictors for pre-to-post session changes in walking speed at the training visit. Characteristics assessed at baseline were reported as mean ± standard deviation (SD). Outcomes compared pre-to-post training day or across training days were reported as mean ± standard error (SE) with standardized effect sizes computed using Cohen's d. Percent changes (%Δ) are reported as medians.