Statistical Analysis Plan

NCT04102228

Repetitive Transcranial Magnetic Stimulation and Multi-modality Aphasia Therapy for Post-stroke Non-fluent Aphasia (REMAP)

Finalized September 25, 2023.
Uploaded to Clinicaltrials.gov on October 5, 2023, after completion of data collection and prior to outcome data analysis.

Sample Size Determination

The trial will consist of two parallel cohorts (sub-acute and chronic stroke) with identical study interventions and procedures. The sample size is based upon a minimal clinical important difference of 5 points on the Western Aphasia Battery, a standard deviation of 15 and a correlation between pre- and post- measurements of 0.9. These estimates are concordant with the psychometric properties of the Western Aphasia Battery. Therefore, with 23 patients per intervention or sham group and therefore 46 patients in each cohort (N=92 in total), the study will have 85% power within each cohort (sub-acute and chronic). The sample will be inflated to 100 to account for any loss to follow-up.

General statistical methods

Data related to baseline measures and participant demographics will be compared between groups using t-tests or Fisher's exact tests. If a baseline factor is found to differ between groups, it will be considered for inclusion as a covariate during hypothesis testing. Our primary analysis will follow intent-to-treat methods and any missing data will be handled with the restricted maximum likelihood method, assuming that data are missing at random. We will first assess for heterogeneity of treatment effect with all patients (n=100) and include stroke cohort (sub-acute and chronic) and a treatment-by-cohort interaction term. If there is evidence of heterogeneity, we will present a cohort-specific analysis assessing for treatment effect.

Hypothesis testing

To test our primary hypothesis that compared with 10 days of sham stimulation and multi-modality aphasia therapy, 10 days of 1Hz rTMS combined with multi-modality aphasia therapy will elicit significantly greater improvement in Western Aphasia Battery Aphasia Quotient scores, we will use a linear mixed-effects model. In this model, we will use fixed effects for group (rTMS, Sham), time (Pre-treatment, Post-treatment, 3-months), a group by time interaction, baseline WAB AQ scores, age at intervention and sex, with an unstructured covariance matrix.

Secondary outcomes will be tested separately using the same model. The Benjamini-Hochberg procedure will be used to account for multiple comparisons among secondary outcomes, which include trained and untrained nouns and verbs, the scenario test, the communication effectiveness index, Stroke Aphasic Depression Questionnaire, Stroke and Aphasia Quality of Life scale, and measures of descriptive discourse (number of words per minute and correct information units per minute during connected speech samples).