Using TMS to Increase Executive Function in Older Adults

NCT02767323

Statistical Plan

Date of Approval:
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Data Analysis & Statistical Considerations

fMRI data*:*
All image pre-processing will be implemented using the FSL program (https://fsl.fmrib.ox.ac.uk/fsl/fslwiki).Event-related fMRI data will be extracted by time-series modeling using rectangular time windows for the memory encoding and probe phases of the task, one modeling a brief (400 ms) neural response at the beginning of the task phase, and another modeling a neural response lasting for the entire 3000 ms phase. A single rectangular function of 7000 ms will be used for the retention phase. Group data will then be analyzed using ordinal trends model (OrT: a newly-developed multivariate covariance analysis). Any fMRI network related to performance in the WM task from previous fMRI research using the WM task in young and elderly subjects will be prospectively applied to the fMRI data of the subjects. Specifically, the imaging data from the pre- and post-MRI sessions will be log transformed and subtracted from each other at each site in each subject. The global mean across sites will be subtracted from each log-transformed regional value, producing regional values normalized to each subject's global mean activity. In a second normalization, the mean for each site across subjects will be subtracted from each regional value. The result of these two normalizations is a subject x region matrix with the mean activity within and across subjects removed. This will be cross-correlated with the patterns previously found in order to quantify pattern expression for individual subjects in the present group. These individual subject pattern expressions will be entered into regressions predicting WM performance in order to verify that the patterns predict performance in new group. In addition, pattern expression will be used to predict rTMS effects on WM performance (for example, differences in RT with active and sham rTMS).

TMS data:

Aim 1a: rTMS applied over the DLPFC either before the encoding or during the delay period of the Delayed Response Alphabetization Task (DRAT, a workin memory task in which participants were asked to maintain and reorganize in alphabetical order an array of letter) will be performed by young and older healthy adults with three difficulty levels , during 4 rTMS visits. Since it is expected that Valid (trials in which the number matches the position of the letter in the reorganized alphabetical order) and Invalid (trials in which the number does not match the position of the letter) trials will lead to strong differences in accuracy, two ANOVAs will be performed separately on each trial condition, for reaction time and accuracy. The two ANOVAs will be conducted with Group (Younger or Older adults), as the between-subject factor; and Visit (Visit 3, Visit 4, Visit 5 and Visit 6), Difficulty (Easy, Medium, and Hard), Stimulation Timing (Pre and Post) and Stimulation Type (Active and Sham) as the within-subject factor. If no difference are found between the two groups, they will be collapsed and the ANOVA will be performed on the larger sample.

Aim 1b: rTMS applied over the PC during the delay period of the DRAT performed with two difficulty levels in older adults, comparing the effect of two stimulation intensities defined with electric field modeling (E-field). A repeated measure ANOVA will be performed with Task Condition (Valid and Invalid), Stimulation Type (Active and Sham), Stimulation Amplitude (80% and 100% Eref), and Task Difficulty (Easy and Hard).

Aim 1c: rTMS applied over the DLPFC and the PC in younger adults performing the DRAT and the Delayed Response Maintenance Task (DRMT, an additional WM task added to the design and involving only the maintenance of the array of letter). rTMS will be applied before the encoding period of the WM tasks, performed with either one difficulty level (Hard) or two difficulty levels (Easy and Hard) in younger adults. A repeated ANOVA will be conducted with Task Condition (Valid and Invalid), Difficulty levels (only for subjects who performed the task with Easy and Hard difficulty levels), WM task (DRAT and DRMT), Stimulation Site (DLPFC and PC) , and Stimulation Type (Active and Sham).