DATA ANALYSIS PLAN

Computer Training and Transcranial Direct Current Stimulation for Cognition in HIV

Identifier: NCT03440840

National Institute on Aging grant: R21AG056256

Date: 12/2/2020

DATA ANALYSIS PLAN

A mixed models approach to repeated measures analysis will be used to test core study hypotheses. Potential confounders found important in the pilot study will be examined via correlations and included in analyses as indicated. Based on our pilot study, these variables are likely to include age, gender, race, education, mood, and immune status markers.

Power analysis. Power analyses were completed using the mixed models simulation routine in PASS 11[125] and with estimates of effect size based on results of our pilot study and 1,000 simulation runs. A sample size of 30 per group provides a power of 0.88 (95th %ile confidence interval 0.87 – 0.91) to detect the interaction of group membership over assessments for cognitive and self-report measures.

Data preparation and preliminary analyses. Statistical tests for skew and kurtosis will be obtained, as well as visual inspections of the empirical distributions. Any significant deviations from normality will be addressed through transformations of the data and if transformations are not possible, non-parametric approaches to the planned analyses will be employed. Reliability estimates of the internal consistency of measures (Cronbach's alpha) will also be examined. Statistical tests of between-group baseline differences on key variables will also be conducted to ensure effectiveness of the randomization procedure.

Missing data. Although we will make every effort to minimize loss to follow-up, we recognize some attrition is likely over time. Multiple imputation (MI) will be employed to address missing data. MI creates plausible values for missing data while preserving the underlying data distribution's characteristics.[126] MI is based on the assumption of missing-at-random (MAR), which is plausible in a closely-controlled study such as this. Whereas mixed models are robust to MAR data without the use of MI, MI has also been shown to improve performance when data is missing not at random and an inclusive strategy, as we plan to use, is followed.[127]

Test of hypotheses. We will evaluate hypothesis 1 in SPSS, and evaluate hypothesis 2 treatment effects in intent to treat analyses in mixed models evaluated in the MPlus statistical software.[128]

Hypothesis 1: A game-based cognitive training intervention combined with tDCS will be acceptable to older persons with HIV infection. We will test this hypothesis based on participant ratings of the intervention on the Usability scale of our questionnaire based on the Technology Acceptance Model. Using a single sample *t* test, we will assess whether ratings are significantly greater than the midpoint of the scale.

Hypothesis 2: Action game based cognitive training will be superior to strategy game based training, while action game training with tDCS will be superior to training alone (control + sham < training + sham < training + tDCS) on objective measures of reaction time, attention, and psychomotor speed. Outcome measures will be CalCap (reaction time), Digit and Spatial Span (attention) and Grooved Pegboard and Trail Making Test Part B (psychomotor speed).

Sex as a biological variable. As discussed above, we will work to ensure that substantial numbers of women participate in this study. Given data suggesting that HIV infection may differentially affect cognition in women compared to men,[72;75] we will evaluate sex as a covariate in analyses and explore the possibility of sex differences in cognitive function and response to training.