Study Analysis Plan – December 13, 2023

Effect of Noninvasive Electrical Brain Stimulation on Memory Performance at Different Times of Day in Younger and Older Adults

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Analysis Plan

PRIMARY ANALYSES

Set 1 (1a, 1b, 1c). The first set of primary analyses will estimate the effect of tDCS to left dlPFC on cognitive performance and the extent to which different aspects of the cognitive task will be impacted. These analyses will be done separately for episodic and working memory.

1.a This analysis will be done on younger adults only. We shall use a linear mixed (i.e., random participant-level intercepts) model with memory performance (defined as memory accuracy computed by subtracting false alarms from target hits) as the dependent variable and stimulation condition (stimulation vs. sham), session Time of Day (AM, PM), and task manipulations (stimulus format and difficulty) as within-subjects predictors along with session order as a covariate (session 1, session 2). Interaction terms between stimulation condition and both task manipulation and time of day will be used to examine the impact of these variables on the stimulation effect.

1.b This analysis will use the same model as in 1a (above), but including data from both younger and older adults and a corresponding age-group factor in the model. Interaction terms between age group, stimulation condition, and time-of-day will be used to determine whether the overall stimulation effect is the same for older as for younger adults, and if not, whether the difference varies by time of day.

1.c This analysis will assess the impact of preferred time of day on tDCS effects, using wrist-worn (minimum 7-days, max 12-days) accelerometry to measure preferred time of day (i.e. “Owl” vs “Lark”), and validation using the subjective Morningness-Eveningness Questionnaire (MEQ). For this analysis, accelerometry-derived variables capturing preferred time of days (eg, including wake time, rise time and midpoint of sleep) will be added as covariates to the model in 1.b., and interactions between these, time of day and stimulation effects will be evaluated.

Set 2. The second set of primary analyses will focus on dlPFC vs parietal vs sham effects in younger adults only. For these analyses, similar models to those described above will be used (e.g., 1a, 1c, 2), except we will include 3 levels for tDCS (dlPFC, parietal, sham). We will test the relative fit of three models: (1) a model in which parietal has the same effect as sham, (2) a model in which parietal has the same effect as dlPFC, and (3) a model in which the effect of parietal differs from the other two conditions.

All analyses will initially be performed without using the baseline performance measures. We shall then repeat each analysis adjusting for the baseline value of the cognitive measure being analyzed. To the extent that the cognitive measures are highly correlated across timepoints, the latter analyses will provide additional power.

STATISTICAL SIGNIFICANCE

A two-sided p-value cutoff of 0.05 will be used for all null-hypothesis significance testing. In addition, point estimates for all first order and interaction effects will be reported, together with 95% confidence intervals. Between-individual contrasts (e.g., overall treatment effects) will be standardized (i.e., equivalent to Cohen’s d). Results of all analyses performed will be reported (not just those that meet the 0.05 cutoff). Since Hypotheses 1-4 are distinct, we shall not make any adjustment for multiple testing across the corresponding analyses. Within each analysis, we shall use a hierarchical approach in which we

begin with an overall test of the null hypothesis at the coarsest level, separately for episodic and working memory, and only if that is statistically significant will we conduct further testing among subgroups.

Although the primary analyses will utilize the frequentist approach to estimating and testing, we will complement this with a secondary Bayesian analysis using the same model. For parameters capturing treatment effects or between-group differences in treatment effects (i.e., interaction terms), we shall use a weakly informative prior (e.g., Normal(0, 1-10)). The primary value of this analysis will be to provide more interpretable (i.e., probability) statements about the magnitude of the effects of tDCS and about the amount of information contained in the data.