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| Unique Protocol ID: | STUDY22070009 |
| Brief Title: | Auditory Control Enhancement (ACE) in Schizophrenia (ACES) |
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Statistical Analysis Plan

Aim 1: H1. We will use General Linear Model (GLM) in SPM12 to assess the parametric modulation of 2nd -echo phase and magnitude data with the applied tDCS current as a regressor (as in Jog, Wang, et al., 2020). Phase data provide maps of tDCS-induced current tangential to the static (Bz) magnetic field of the MRI. Magnitude data provide BOLD response. We will test spatial correlation between the measured magnetic field and tDCS current modeled by SIMNIBS to assess overlap with target areas in rVLPFC and left TPJ.

Aim 2: H1. we will calculate retention, blinding, and acceptability scores with benchmarks of success being >80% study completion, high-moderate acceptability rating, and no-greater-than-chance ability to identify study condition. Additionally, t-tests will be used to compare acceptability between ACE and sham sessions.

Aim3: H1. Motion correction will be performed by realignment of the control and label image series to the M0 image. A structural correlation-based outlier rejection method will be applied to remove artifacts arising from outlier control-label pairs in ASL data. The perfusion-weighted maps will be calculated voxel by voxel from the average of signal differences between labeling and control images. The CBF will be quantified by $(6000 \cdot \lambda \cdot \Delta S \cdot \exp(-PLD/T1, \text{blood})) / (2 \cdot \alpha \cdot T1, \text{blood} \cdot SPD \cdot (1 - \exp(-\tau/T1, \text{blood})))$, where λ is the brain/blood partition coefficient in mL/g, ΔS is perfusion-weighted signal, $T1, \text{blood}$ is the longitudinal relaxation time of blood in seconds, α is the labeling efficiency, SPD is the signal intensity of a proton density-weighted image, and τ is the label duration. pcASL images will be registered to the T1-weighted anatomical image and normalized to MNI space. The CBF maps will be normalized by mean CBF value of GM and a 3D Gaussian filter will be applied. Comparisons will be restricted to rVLPFC and left TPJ ROIs, where 5000 permutations will be generated to identify statistically significant voxels pre- vs post-tDCS, controlling family-wise error rate ($p < 0.05$). H2. Data analysis will focus on (1) behavior assessed by reaction time and accuracy (d') measures from the AX-CPT, and on (2) attend-ignore difference in gamma-band oscillatory power measured from frontocentral electrodes in scalp-recorded ASSR (100-500 ms post-stimulus) as well as during the "preparation" window from 500-1000 ms following "B" trials of the AX-CPT. Spectral power will be measured using Morlet wavelet transforms with minimum width of 5 cycles, will be applied to elongated epochs at logarithmic steps from 4 to 80 Hz across the epoch. Maps of spectral measures will be baseline-corrected using a pre-stimulus baseline adjusted for >3 cycles per frequency to avoid edge effects. Four wavelet measures will be derived: Evoked power, the squared amplitude of oscillations that are phase-locked to stimulus onset; Total power, the average of power on each trial, which includes both evoked and "induced" (non-stimulus locked) responses; Induced power, calculated by removing

evoked from total power; and phase locking, the degree to which signals are in phase from trial to trial. We are most interested in total power in the AX-CPT, and evoked power ASSR; however, we will examine each of these measures as appropriate. Change scores will be calculated for each dependent variable as the difference between measures taken before and after each arm of the study (Active and Sham). We will compare these difference scores between active and sham arms of the study using repeated measures MANOVA with follow-up univariate RM-ANOVA and paired t-tests as appropriate. H3. Data analysis for H3 will follow the same procedures as H2; however, ASSR in the ignore condition will be the primary dependent variable in this analysis.