Study Protocol & Statistical Analysis Plan

Title: At-home Transcranial Alternating Current Stimulation During Multitasking
NCT#: NCT04231825
Last Updated: 08/11/21

Participants. In this preregistered study (ClinicalTrials.gov identifier: NCT04231825), 40 younger adult participants (Mean age: 25.2, standard deviation (SD): 4.38, 25 females) completed the baseline, home-training, and follow-up sessions of this study over the course of one-week. All participants provided informed consent as approved by the University of California, San Francisco Institutional Review Board and were compensated $20 per hour for participation with a $50 bonus for completion of the study. Participants had no history of neurological or psychiatric disease, were not currently on medications that modulate neural excitability, and had corrected-to-normal vision. All participants were native English speakers. Participants were randomly assigned to one of two stimulation frequency groups, which received 20 minutes of 6 Hz (Mean age: 25.8, SD: 4.56, 12 females) or 1 Hz tACS (Mean age: 24.55, SD: 4.21, 13 females) over five consecutive days. The participants, researchers, and outcomes assessor were all blinded to the tACS conditions.

Neurostimulation. The tACS was delivered through a Starstim device (Neuroelectrics, Spain) with NG Pistim electrodes (contact area: 3.14 cm^2) placed over the PFC at 1 mA (baseline to peak; 2mA peak-to-peak) with a 180-degree phase offset. Participants applied the electrodes themselves within a neoprene EEG head cap where the only two holes corresponded to the electrode locations F3 and F4. Participants were given instructions to self-apply conductive gel within the Pistim electrodes, which screw open for easy access to the scalp underneath. Following self-monitored impedance check, the participants were able to begin the stimulation through a secondary tablet (Windows Surface 3) that had wireless Bluetooth connectivity to the tACS device, which was Velcro-attached on the back of the head cap. The current was ramped up and down over the course of 10 seconds at the beginning and end of 20 minutes of stimulation, respectively. Participants began the stimulation then immediately began the training task on five consecutive days. Researchers were able to remotely monitor adherence to the tACS sessions as well as any reported side effects in real time.

Baseline & follow-up session. To measure multitasking performance, participants were assessed in the laboratory with NeuroRacer, a gamified task where they must continuously perform visuomotor tracking (driving a car) while simultaneously performing visual discrimination (detect a target sign) with a button press (for details see: Anguera et al., 2013). On both in-lab sessions (baseline and follow-up), participants first completed thresholding of the visual discrimination (sign) and visuomotor tracking (drive) tasks, to establish a difficulty level where participants scored ~80% accuracy. Target signs appeared every 2-3 seconds and lasted for 400 ms. Next, in a counterbalanced order, participants completed two runs of only the NeuroRacer sign task, two runs of only the NeuroRacer drive task, and three multitasking runs of the NeuroRacer sign and drive task together. Furthermore, participants had to respond within their individual reaction time window as determined by single task thresholding during the baseline session to be counted as correct (participant range: 320 - 490 ms). Perceptual discrimination performance was measured during each multitasking run using a metric of discrimination (d'), which was estimated for each participant by comparing hit (correct responses to target signs) rates and false alarm (responses to non-targets) rates and calculated as d' = Z(hits)–Z(false alarms). Finally, we calculated multitasking cost by measuring the difference in d' between sign only and multitask runs within each session ((multitask d'/sign only d')-1). The total number of signs to respond to on both the sign only and multitask tasks portions totaled 216 trials with 33% target trials.

Following the NeuroRacer tasks, participants completed a computerized continuous performance task (CPT) that tests sustained attention performance. The CPT was a well-validated modified version of the Test of Variables of Attention (TOVA; Greenberg and Waldmant, 1993), which tests sustained attention by measuring reaction time (RT) and reaction time variability (RTV) to stimuli (white squares) which appear on a black background on either the top or bottom half of the screen. Participants were instructed to press the space bar as quickly as possible when the white square appeared on the top half, but not the bottom half of the screen. The ratio of targets to non-targets was 25% (1 target for every 4 non-targets). Participants completed two blocks of 125 trials with 25 targets per block, resulting in 50 total target trials. This version of the CPT has been previously employed in multiple studies from our

research group[1,3–6]. Lastly, participants were trained on how to apply the neurostimulation for use on the following at-home sessions.

Training sessions. On five consecutive days participants began the self-applied tACS and immediately began the training task, *AKL-T01* (Akili Interactive Labs, Inc). AKL-T01 is a proprietary system based on the NeuroRacer paradigm that challenges cognitive control by requiring multitasking performance (for more details see: [7]. During the intervention, participants must guide a character down a path by tilting the iPad similar to a steering wheel (visuospatial tracking). At the same time, participants are engaged in a feature discrimination task, where they must tap on the screen during target items (e.g., green fish) and ignore all distractors (e.g., blue fish). AKL-T01 is developed on the iPad with high-quality graphics and rewards designed to be more engaging than standard laboratory cognitive tasks. Importantly, AKL-T01 employs algorithms that continuously adapts to individual drive and target performance in real time with feedback provided. Participants completed five missions per day, which last roughly the same length as the 20-minute tACS protocol. Participants were instructed to administer the tACS and play AKL-T01 at the same time of day during all five training sessions. Researchers were able to remotely monitor adherence to the training sessions as data is uploaded online during each session. Given the adaptive nature of AKL-T01, which maintains accuracy as participants improve, we did not analyze performance between groups.

Statistical analyses.
Outcome measures (d', d' cost, RT, RTV) during the follow-up session were each separately submitted to an analysis of covariance (ANCOVA) as the dependent variable and group as a fixed factor (6Hz, 1Hz). Furthermore, we included baseline performance as a covariate to test for the main effects of tACS condition and to control for baseline variability.

References

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