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Title: Stimulating the Brain to Improve Self-Awareness

NCT Number: NCT03370341

Document Date: 9/19/2017

Objectives

The overall goal is to determine whether we can improve Introspective Accuracy (IA), defined as one's ability to correctly evaluate their own skills and abilities, in individuals with schizophrenia by stimulating the rostrolateral prefrontal cortex via transcranial Direct Current Stimulation (tDCS). Participants will undergo two brain stimulation sessions (one active and one sham) approximately one week apart and, after each session, will complete cognitive and social cognitive assessments along with real-time assessments of their performance (i.e., IA). We hypothesize that individuals will more accurately assess their performance immediately following the active brain stimulation session as compared to immediately following the sham session.

Design

The study will utilize a double-blind, crossover design wherein participants will receive both active and sham stimulation in a counterbalanced order.

Methods and Procedures

This study will involve two sessions, completed approximately one week apart. The sessions will be identical except that the first session will include clinical interviews for the purposes of confirming diagnosis and one session will involve active neurostimulation while the other will involve sham stimulation. We will use a double-blind, cross-over procedure so that across participants the sham session will be equally likely to have occurred first or second and so that both participants and experimenters will be unaware of which session includes the active simulation.

After providing written informed consent, participants will complete clinical measures to confirm diagnosis and to assess current symptomatology. These include:

1. Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998). The MINI will be administered by trained study personnel. The MINI was designed to assess Axis I disorders as listed in the DSM-IV-TR. This interview will provide a more nuanced evaluation of the participant's clinical history.

2. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I- P) (First, Spitzer, Gibbon, & Williams, 2002). The SCID-I-P will be administered by trained study personnel. The SCID-I-P was designed as a structured interviewing tool to assess Axis I disorders as listed in the DSM-IV-TR. The SCID-I-P is considered to be the gold-standard instrument for DSM-IV diagnosis.

3. Positive and Negative Syndrome Scale (PANSS) (Kay et al., 2009). The PANSS will be administered by study staff, who will be trained to gold standard reliability, to assess the severity of positive and negative symptoms in individuals with schizophrenia. The PANSS has good psychometric properties, which include internal consistency reliabilities of .72 for the Positive Scale, .81 for the Negative scale, and .77 for the General Psychopathology Scale. The PANSS demonstrates good construct validity and criterion- related validity. In a study of 51 patients with chronic schizophrenia, the PANSS Positive scale was significantly correlated

(r=.77, p<.001) to the Scale for Assessing Positive Symptoms (SAPS) and the PANSS negative scale was significantly correlated (r=.77, p<.001) with the Scale for Assessing Negative Symptoms (SANS) (Kay et al., 2009).

Participants will then begin the neurostimulation portion of the session, which will last for 20 minutes. The participant will be set up with the tDCS material that will start real or sham stimulation, and participants will be informed that they may read or otherwise entertain themselves during this portion of the study. The two electrodes of the tDCS will be placed over the left and right rostrolateral prefrontal cortex. For active stimulation the electrical current will be initially increased in a ramp-like fashion over several seconds (5 seconds) until reaching 1.5mA, and stimulation will be maintained for 20 minutes until it ramps down (5 seconds). For sham stimulation, the electrical current will be increased in a ramp- like fashion over several seconds (5 seconds) until reaching 1.5mA to mimic the sensation present during the first 5 seconds of real stimulation, and then stimulation will be stopped without the participant knowing. The total duration of the sham tDCS will be identical to the active condition in order to appropriately blind the procedure.

Following the neurostimulation portion, the participant will be asked to sit quietly for 30 minutes. After that time has elapsed, the participant will complete the following behavioral measures in a random order:

1. Wisconsin Card Sorting Task (WSCT) (Heaton, Chelune, Talley, Kay & Curtiss, 1993). The WCST is a widely used measure of executive function that requires participants to match a presented card to one of four stimulus cards. There are several ways in which the card could be successfully sorted but participants are not informed of the criterion they should use to match the card. Instead, feedback is given after each sort (i.e. correct or incorrect), and participants must use this information to adjust their responses. 10 minutes.

2. Emotion Recognition 40, Degraded Stimuli (ER-40D; Kohler, Turner, Bilker, Brinsinger, Siegel, Kanes… Gur, 2003). The ER-40 is a standardized, computer administered measure of facial affect recognition ability. It includes 40 color photographs of faces expressing 4 basic emotions (i.e. happiness, sadness, anger or fear) and neutral expressions. Participants view one face at a time and are asked to choose the correct emotion for each face. For this version, facial stimuli are be digitally blurred in order to make the expressions more difficult to identify. 3 minutes

3. MATRICS Consensus Cognitive Battery - Brief (MCCB-B; Nuechterlein et al., 2008). Trained study staff will administer the MCCB-B to all participants to obtain an estimate of level of cognitive functioning. The MCCB is considered the gold standard cognitive assessment in schizophrenia research and assesses the following domains: Speed of processing, working memory, and verbal learning. 15 minutes.

4. Emotion Recognition Signal Detection Task (ER-SDT; Tsoi et al., 2008). The ER-SDT is a task of emotion recognition that utilizes a signal detection framework. Participants will view 5 different series, or blocks, of 60 emotional faces. For each block, a target emotion (i.e. happy, sad, anger, fear or neutral) will be identified, and participants will be asked to view each face and determine if that face is or is not displaying the target emotion. Following each decision, participants will rate their confidence in the accuracy of that decision on a 4-point scale from "probably wrong" to "probably right." 20 minutes

IA procedure: For all behavioral tasks, participants will self-evaluate their performance in order to obtain estimates of IA. For the WCST, ratings of confidence in correctness are performed after each sort in the 64-card WCST. For the ER-40D, ratings will be performed after each of the 40 trials. For our cognitive assessment battery, the MCCB, performance will be rated after each of the 5 tests. As noted, for the ER- SDT task, participants will self-evaluate their correctness after each item.

At the end of the session, we will ask participants to report which session they believed they just received. This will allow us to assess the success of our blinding procedure.

Statistical Analysis Plan

Repeated Measures ANOVAs will be used to compare indices of neurocognitive and social cognitive IA between stimulation conditions.