



The effect of transcranial direct current stimulation on social cognition in schizophrenia: A preliminary study



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ABSTRACT

In this preliminary study, we examined the effect of transcranial direct current stimulation (tDCS) on social cognition in 36 individuals with schizophrenia. Participants received a baseline assessment and one week later received either anodal, cathodal, or sham tDCS, with 12 participants randomized to each condition. A single 20-minute session tDCS was administered bilaterally over the dorsolateral prefrontal cortex (centered at positions Fp1 and Fp2) at 2 mA. Among the 4 social cognitive tasks, participants showed a significant improvement on one of them, emotion identification, following anodal stimulation. Findings demonstrate the safety of this procedure and suggest potential therapeutic effects on one aspect of social cognition in schizophrenia.

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1. Introduction

Impairment in social functioning has been extensively documented in schizophrenia and recognized as one of the hallmarks of the disorder (Brunet-Gouet and Decety, 2006; Thakkar et al., 2014). Over the last decade, considerable research has focused on social cognition, which is the ability to construct mental representations about others, oneself, and relations between others and oneself (Adolphs, 2001). Social cognition is thought to facilitate social interactions and is considered a determinant of social dysfunction among people with schizophrenia (Fett et al., 2011; Green et al., 2012).

This preliminary study examined the effects of transcranial direct current stimulation (tDCS), a non-invasive neurostimulation technique, on social cognitive deficits in schizophrenia. Unlike other non-invasive brain stimulation techniques, such as transcranial magnetic stimulation, tDCS does not induce neuronal firing by suprathreshold neuronal membrane depolarization, but rather modulates spontaneous neuronal network activity (Priori et al., 2009). Studies suggest that anodal-tDCS, or flow from anode to

cathode, generally enhances cortical activity and excitability, whereas cathodal-tDCS, or flow from the cathode to anode, has the opposite effect (Nitsche and Paulus, 2000), although other factors, such as outcome measures and assessment procedures, influence the net effect of tDCS on neural networks (Brunoni et al., 2014). Various studies demonstrated the beneficial therapeutic effects of tDCS in reducing epileptiform discharges in refractory epilepsy (Fregni et al., 2006), improving aphasic symptoms in post-stroke patients (Baker et al., 2010), diminishing depressive symptoms in mood disorder (Brunoni et al., 2011), reducing auditory hallucinations (Brunelin et al., 2012), and improving working memory (Hoy et al., 2014) and association learning (Vercammen et al., 2011) performance in schizophrenia.

To explore the effect of tDCS on several social cognitive functions, we applied anodal and cathodal tDCS bilaterally over the dorsolateral prefrontal cortex (DLPFC) in 36 individuals with schizophrenia. Patients were randomly divided into three groups who received anodal tDCS, cathodal tDCS, and sham tDCS. Performance data on several standardized measures of social cognition were collected immediately following stimulation. A standardized neuropsychological battery was also administered. As this was the first study to examine the effect of this procedure on social cognition in schizophrenia, no directional hypotheses were made.

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2. Methods

2.1. Participants

Participants were recruited through outpatient clinics at the UCLA and the VA Greater Los Angeles Healthcare System and through presentations in the community. All patients were administered the Structured Clinical Interview for DSM-IV (SCID-P) (First et al., 1997) and met the DSM-IV diagnostic criteria for Schizophrenia (American Psychiatric Association, 1994). All interviewers were trained by the Treatment Unit of the Mental Illness Research, Education, and Clinical Center (MIRECC). Patients were excluded if they had an identifiable neurological condition, psychiatric inpatient hospitalization in the last three months, substantial changes in their antipsychotic medications during the previous 6 weeks (as determined by the clinical psychiatrists during case reviews), $IQ < 70$ based on reading ability, or substance dependence in the last six months.

The present study included 36 individuals with schizophrenia (67% males), all receiving antipsychotic medications (84% atypical). Mean age was 45.1 years ($SD = 9.86$), and mean education was 12.8 years ($SD = 2.16$). Patients' mean illness chronicity was 20.4 years ($SD = 11.7$). Mean symptom rating on the Brief Psychiatric Rating Scale (BPRS) was 41.3 ($SD = 12.8$) and on the Scale for the Assessment of Negative Symptoms (SANS) was 42.3 ($SD = 14.4$). All participants gave written informed consent after receiving a full explanation of the research according to procedures approved by the Institutional Review Boards.

2.2. Assessments

Symptom ratings were collected using the expanded BPRS (Ventura et al., 1993) and SANS (Andreasen, 1984). Social cognition assessments included measures of social cognition used previously in schizophrenia research (Green et al., 2005). The Mayer–Salovey–Caruso Emotional Intelligence Test (MSCEIT) (Mayer et al., 2002) assesses four components of emotional processing. In this study, the Managing Emotions branch was administered. Facial Emotion Identification Test (FEIT) is a test of identification of facial emotion based on photographs from software developed by Ekman (Ekman, 2004). Profile of Nonverbal Sensitivity (PONS) is used to assess social perception (Rosenthal et al., 1979; Ambady et al., 1995) using scenes that contain facial expressions, voice intonations, and/or bodily gestures. The Awareness of Social Inference Test (TASIT) (McDonald et al., 2002) is a videotape test of theory of mind (ToM) in various social contexts. We also administered the MATRICS Consensus Cognitive Battery (MCCB), to obtain the non-social Neurocognitive Composite score (Green et al., 2004; Kern et al., 2008). Participants were also interviewed regarding the most common side effects typically reported following tDCS using a structured interview with symptom severity ratings (0 = none, 1 = mild, 2 = moderate, 3 = considerable, 4 = severe).

2.3. Equipment

The tDCS was delivered by an Activa Dose II Iontophoresis Delivery Unit, using a pair of saline-soaked sponge electrodes held in place by elastic bands. The two 5×7 cm tDCS active electrodes (anodal or cathodal) were placed bilaterally over the DLPFC, centered at positions Fp1 and Fp2 of the 10/20 International System (Koenigs et al., 2009). The current intensity was set 2 mA with a current density of 0.028 mA/cm^2 at the skin. A variable resistor was included in series with each active electrode, which allowed for continuous monitoring of current delivered and ensured that equivalent intensity balanced at 1 mA per active electrode. The reference electrode (also 5×7 cm) was placed on the upper right arm. In the sham condition, the current was turned on for 30 s and then ramped down to 0 mA. In this way,

the participants experience the same initial sensation of mild tingling, thus preserving the sham manipulation (Poreisz et al., 2007).

2.4. Procedures

Participants made two visits. During the first visit, they completed the diagnostic interviews and baseline social cognitive and neurocognitive measures. In the second session, which took place 1–2 weeks later, participants were randomly assigned to one of three conditions (12 per group): 1) anodal tDCS, 2) cathodal tDCS, and 3) sham stimulation. The research assistants administering the tDCS procedures were not blinded to the type of condition. Participants received a 20-minute stimulation session, following which they completed the social cognitive and neurocognitive measures. The order of administration of the social cognitive and neurocognitive measures was randomized across participants within each group.

2.5. Statistical analyses

Analyses of variance (ANOVA) with repeated measures were conducted to examine the effects of tDCS on patients' social cognitive and neurocognitive performance. The stimulation condition (anodal, cathodal, and sham) was the between-subjects factor. The primary interest was in the time (baseline vs. post-stimulation) by condition interaction effects. Given the small sample size and preliminary nature of the study, no corrections for multiple analyses were made.

3. Results

The three groups (anodal vs. cathodal vs. sham) did not differ on any demographic variables, illness chronicity, or symptom ratings. The tDCS procedure was well tolerated by all participants, with no dropouts associated with the procedure. The most common side effects reported by the participants were itchiness, followed by warmth and burning sensations. These reported side effects did not differ across the three experimental conditions (see Table 1).

For the performance-based tasks, none of the measures showed any main effects for condition or for time. Repeated measures ANOVA revealed a significant condition by time interaction only for the FEIT. No significant condition by time interactions was found for any of the other social cognitive measures. Also, no significant differences were noted for the Neurocognitive Composite score, or for any individual neurocognitive domains. Table 2 presents the descriptive and inferential statistics for these analyses. (Given the primary focus on social cognitive outcome measures in this study and the lack of statistical significance for any of the neurocognitive measures, only the Neurocognitive Composite score is presented in the table.) We further explored the interaction by conducting post-hoc contrasts of the simple main effects to evaluate the change over time within each of the three conditions. We found that there was a significant change from baseline to post-tDCS in the anodal condition ($F(1,10) = 11.8$, $p < 0.01$, p (Bonferroni corrected) = 0.02), but not in either the cathodal condition ($F(1,11) = 0.7$, $p = 0.41$, p (Bonferroni corrected) > 1.0) or in the sham condition ($F(1,11) = 0.01$, $p = 0.93$, p (Bonferroni corrected) > 1.0).

4. Discussion

Considerable efforts have been made to find ways to enhance cognition in schizophrenia (Green et al., 2004; Marder and Fenton, 2004; Buchanan et al., 2005), but neurostimulation has received little attention so far. This pilot study was the first to examine the effect of single tDCS administration on several components of social cognition in schizophrenia. Among the 4 social cognitive tasks administered, assessing different aspects of social cognition (managing emotions, identification of facial emotion, social perception, and ToM), participants showed a significant improvement on

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