

Effect of tDCS on Cognition, Symptoms in Chronic Schizophrenia  
Patients With Tardive Dyskinesia

NCT03497013

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# Study Protocol and Statistical Analysis Plan

## 1.Objective

The aim of the study was to evaluate the efficacy, safety, and cognitive function of transcranial direct current stimulation (tDCS) in chronic schizophrenia patients with tardive dyskinesia (TD).

## 2.Methods

### 2.1. Subjects

Between July 2017 and August 2020, 64 schizophrenic inpatients with TD were recruited from four different psychiatric hospitals, in mainland China. All of the subjects satisfied the following inclusion criteria: (1) aged from 18 to 70 years old; (2) clinical diagnosis of schizophrenia according to the criteria of Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition (DSM-IV) and had been receiving antipsychotic drugs for at least 12 months; (3) diagnosis of TD based on the Schooler-Kane criteria, that is, at least one AIMS item rated (moderate) or at least two AIMS items rated  $\geq 2$  (mild), confirmed independently by 2 trained psychiatrists; (4) right-handed; (5) all patients volunteered to participate in this study. The exclusion criteria included (1) organic disorder that could cause movement disorders, mental retardation, and a history of substance dependence (except nicotine); (2) with serious physical illness (e.g. severe cardiovascular diseases); (3) with color blindness/weakness, stuttering, deafness.

The patients were screened and given a complete clinical evaluation, including medical and neurologic examinations and laboratory tests, before they were included in the study. The study was approved by the Institute Review Board Committees. Written informed consent was obtained from the subjects prior to entry after they had been provided with a detailed explanation of the study. The trial was registered with ClinicalTrials.gov (NCT03497013).

### 2.2. Procedures

#### 2.2.1. Overall design

This study is a randomized, double-blind, sham-controlled clinical trial. Patients with TD were randomly allocated to active or sham tDCS groups by computer software based on a simple randomization method. All patients received 15 tDCS sessions. The participants would not know the tDCS status. The assessors for clinical outcomes would be blinded to the randomization status. The person who perform the intervention would not know the assessment results.

#### 2.2.2. transcranial Direct Current Stimulation (tDCS)

tDCS is a Transcranial Electrical Stimulation (tES) technique that delivered by Soterix Medical 1×1 Low-Intensity Transcranial Electrical Stimulator (tES) Model 2001. It sends a small current across the scalp to modulate brain function. All patients received 2-mA anodal left dorsolateral prefrontal cortex/cathode right contralateral supraorbital area tDCS treatment (fifteen 30-minutes sessions: Monday to Friday once daily, every other week to do a group of treatment). Electrodes are encased with 5×7 cm sponges and moistened with saline (0.9% NaCl). For sham stimulation, the current will stop after 30 seconds from the start of stimulation. In this way, the patients would experience the same initial sensation of slight tingling and it is a blinding method considered reliable for several previous studies.

### 2.2.3. Primary outcomes

The primary outcome measure was the severity of TD symptoms, which was measured by the Abnormal Involuntary Movements Scale (AIMS) and Tardive Dyskinesia Rating Scale (TDRS). All evaluations were scored at baseline, the end of 3rd weeks, 5th weeks, and 7th weeks.

### 2.2.4. Other clinical assessments

Side effects of tDCS were assessed with an experimenter-administered open-ended questionnaire during the whole experiment. The questionnaire contained rating scales regarding the presence and severity of headache, difficulties in concentrating, acute mood changes, visual perceptual changes and any discomforting sensation like pain, tingling, itching or burning under the electrodes.

Each patient was given a series of computerized tests from the Cambridge Neuropsychological Test Automated Battery. The language-independent tests and touch screen technology deliver rapid and non-invasive cognitive assessment. Executive and memory function were assessed with the following three tasks: The Pattern Recognition Memory (PRM), Intra/Extradimensional Set Shift (IED), and Spatial Working Memory.

Negative symptoms were assessed with the scale for assessment of Negative Symptoms (SANS) and Psychopathology was measured by the Positive and Negative symptom scale (PANSS). These assessments were performed at baseline, the end of 3rd weeks, 5th weeks, and 7th weeks.

## 2.3. Statistical analysis

The entire statistical analysis was performed using the Statistical Package for Social Sciences (SPSS), version 23.0. The Kolmogorov-Smirnov nonparametric test was used to test the normality

of continuous variables. The continuous variables were described using summary statistics, such as the means and standard deviations. The categorical variables were described using frequencies and percentages. The baseline characteristics of each group were compared using a t test for the continuous variables and the  $\chi^2$  test for the categorical variables. Repeated-measures analysis of variance (ANOVA) was used to analysis the repeated measurement data.  $P < 0.05$  was considered statistically significant.