



The Effect of transcranial Direct Current Stimulation (tDCS) on the Reduction of Negative Symptoms in Schizophrenic Patients in Ahvaz Golestan Hospital

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Abstract

Background: Schizophrenia is one of the chronic psychiatric disorders that positive and negative symptoms, particularly negative ones, causes reducing performance in personal, social, and family performances. The aim of this study was to evaluate the effect of transcranial direct current stimulation (tDCS) on reducing the negative symptoms of patients with schizophrenia.

Methods: In this double-blind clinical trial study, 30 patients with schizophrenia were admitted according to the DSM-V criteria and divided into two equal groups. On the first group (case), two mill amperes of transcranial direct current stimulation were applied bilaterally in weeks 0, 4 and 8 for 20 minutes in each session. The second group (control) was stimulated by sham. Then, after 4 and 8 weeks, the two groups were compared in terms of negative symptoms and the overall score of the Positive and Negative Syndrome Scale (PANSS).

Results: After 4 and 8 weeks, the negative symptom score in the control group did not change significantly, while in the control group, these changes clearly indicated an improvement in the patient's condition.

Conclusion: Based on results it can be said that Trans cranial Direct Current Stimulation in combination with pharmacotherapy can be effective in reducing negative symptoms of schizophrenic patients.

Keywords: Schizophrenia, transcranial direct current stimulation (tDCS), Negative symptoms, PANSS.

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Introduction

Psychiatric disorders have been raised as one of the major problems in the world. Better treatment management, finding new pharmacological and non-pharmacological methods and increasing the quality of life of these patients have become especially important[1, 2]. One of the most common psychiatric disorders is schizophrenia[3]. Schizophrenia (SCZ) affects approximately 1% of the population and can be considered the most disabling neuropsychiatric disorder[4].

Schizophrenia is a mental disorder characterized by disabilities of mental processes and severe emotional damage. The disease, which is the most serious of the major psychological illnesses,

usually presents as auditory hallucinations, insane or bizarre hallucinations, or disturbed speech and thinking, and is associated with significant social or occupational dysfunction that symptoms usually begin in adolescence [5, 6]

Symptoms of schizophrenia are of two types: positive and negative symptoms [7, 8]. Positive symptoms include hallucinations, delusions, disturbed speech, disturbed behavior, and thought disorder[9]. Negative symptoms in schizophrenia are less known than positive symptoms, but it can be argued that negative symptoms are the most important symptoms in schizophrenia, because these symptoms are the best predictor of schizophrenia patient's disability in the future[4, 10]. These symptoms include



superficial emotion, lack of pleasure, apathy, and social withdrawal[11]. In schizophrenia, negative symptoms are frequent; up to 60% of individuals may have clinically meaningful negative symptoms that require treatment. Although negative symptoms are the most prevalent first indication of schizophrenia, they can appear at any time during the illness[7].

Neuroimaging findings about the negative symptoms of schizophrenia are still contradictory. However, an association is often found between negative symptoms and gray matter reductions in the prefrontal cortex[12]. In addition, even at rest, hypoactivity of the prefrontal cortex, especially of the left dorsolateral, and of the anterior cingulate regions, has been associated negative symptoms[13]. The negative and positive symptoms of the illness are also linked to striatal dopaminergic hyperactivity[14]. Treatments that target these areas of the brain would be a valuable and promising treatment approach for schizophrenia's negative symptoms[15].

Transcranial direct current stimulation (tDCS), a neuromodulatory and noninvasive brain stimulation technology, has been studied in a variety of various neuropsychiatric disorders[16]. tDCS is used as a technique to induce weak electrical currents through two electrodes on the scalp[17-19]. Therefore, we aimed to conduct a study to evaluate the effectiveness of transcranial direct current stimulation (tDCS) on negative symptoms in schizophrenia patients in Golestan Hospital, Ahvaz.

Method and materials:

This double blind clinical trial study was performed on 30 patients with schizophrenia with negative symptoms admitted to the psychiatric ward or referred to the psychiatric clinic of the Golestan Hospital in Ahvaz in 2021. Schizophrenia was diagnosed by two psychiatrist based on DSM-5 clinical interview or Structured Clinical Interview for DSM (SCID). The semi-structured diagnostic interview at SCID begins with questions about demographic information, mood and psychotic disorders, substance abuse, physical, eating and adjustment disorders[20].

Significant negative symptoms (score more than 15 negative in PANSS and more than 50 in PANSS), no liver disease (based on patient history

and test), no ECT treatment in six months before enrollment, duration of illness more than one year and age over 18 years were the inclusion criteria. Depression (clinical interview based on DSM-5), mental retardation, schizoaffective, bipolar disorder, history of allergies or serious side effects with the drugs in the study, pregnant or lactating women, use of antidepressants or lithium for any reason, neurological disease, suicidal ideation and active suicide, patient reluctance to continue in this project, patients with cardiovascular problems, patient with closed angle glaucoma, history of urinary obstruction, Presence of ADHD in the individual were the 2498 exclusion criteria.

In this study, PANSS test was used to measure the severity of positive and negative symptoms in schizophrenic patients. PANSS questionnaire has been widely used in the study of antipsychotic therapies[21]. This test is designed to evaluate the dimensions and typology of schizophrenia and has 30 questions that assess the positive and negative symptoms of the patient based on a semi-structured clinical interview. Each question is answered on a seven-point Likert scale from no sign to excessive intensity. The validity and reliability of this questionnaire has been studied in our country and its validity is 0.89 according to Cronbach's alpha coefficient[22]. After explaining the plan to the patients and considering the inclusion and exclusion criteria, the two groups of 15 people were divided into case and control groups. In the case group, two mill amperes of direct transcranial electrical stimulation using 7*5 cm electrodes with the center of the anode placed over the left prefrontal cortex (F3) and the cathode over the left temporoparietal junction (between T3 and P3) [17] were applied bilaterally in sessions 0, 4 and 8 for each session of 20 minutes. The control group was stimulated by sham. Sham stimulation is like active stimulation, except that there was a current and the device would turn off after one minute. The PANSS questionnaires were completed at the end of sessions zero, four and eight. Then, after 4 and 8 sessions, the two groups were compared in terms of negative symptoms and the overall score of the scale. In the present study, physicians and patients were blind to the type of group. It should be noted that tDCS intervention was performed as adjunctive therapy along with drug treatment of patients. The study was approved by the Ethics Committee of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran (Ethics number:



Table1. Characteristics and negative symptom scores in schizophrenia patients treatment and control groups

Variables	Case	Control	P-value
Age	38.93 ± 12.10	42.13 ± 9.72	0.43
Sex (Male: Female)	7: 8 (46%: 53.3%)	9: 6 (60%: 40%)	0.46
Negative symptoms			
Bassline	29.53 ± 4.42	28.66 ± 4.93	0.001
Fourth session	27.60 ± 3.64	28.53 ± 4.79	
Eighth session	23.46 ± 3.64	27.80 ± 4.63	

Matching was performed for the two groups in terms of demographic

IR.AJUMS.HGOLESTAN.REC.1399.149), and this trial was registered in the Iranian Clinical Trial system with the patented number of IRCT20100520003979N10. Written informed consents were obtained from all subjects.

Statistical analysis

Statistical analysis was performed by SPSS software Version 22 (IBM, Chicago, USA). The Quantitative and qualitative variables were indicated as mean±SD and number (percentage), respectively. Kolmogorov–Smirnov and Shapiro–Wilk tests were used to test for the distribution. Differences were compared by using Mann–Whitney U test. For the test of significances, chi-square test was calculated to compare the frequencies among groups. P-value <0.05 was considered statistically significant.

Results

In this study, the effect of direct transcranial electrical stimulation on reducing the negative symptoms of 30 patients with schizophrenia was investigated. 15 patients were selected as the control group and 15 patients as the case group.

raphic information (age and sex). Sex distribution in the two groups showed that 7 (46%) in the control group were female and 8 (53.3%) were male. Also in the case group, 9 (60%) were female and 6 (40%) were male. Another variable studied in these patients was the level of education. Based on the evaluation, it was found that the majority in both groups were undergraduates. Only one person in the case group had a bachelor's degree. According to the Chi-square test, there was no significant difference between the two groups regarding education. The trend of negative symptom score changes between the two groups was examined based on the repeated measures test. The results of this test showed that the score of negative symptoms in the case group decreased significantly, while in the control group there were no significant changes. This indicated the positive effects of transcranial electrical stimulation. **Table1** shows the characteristics and negative symptom scores in schizophrenia patients' treatment and control groups.

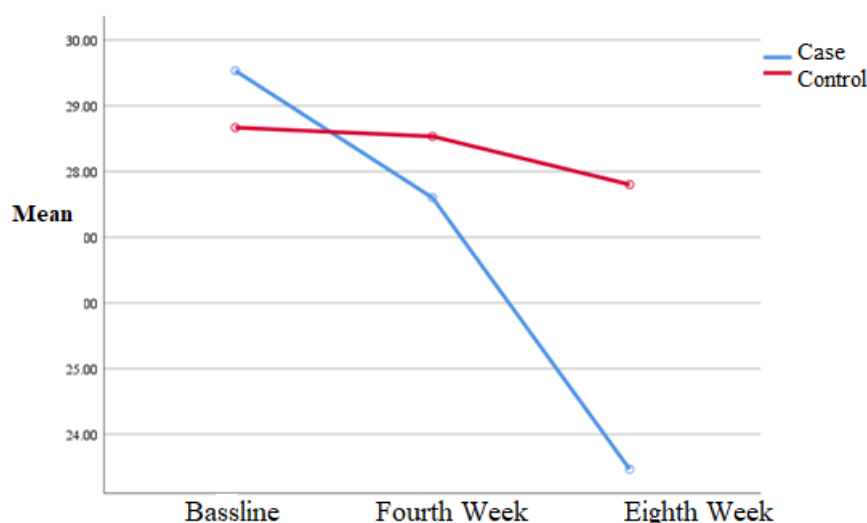


Figure1. Comparison of patients' negative symptom score trends

Discussion:

Schizophrenia is a mental disorder characterized by disabilities of mental processes and severe emotional damage. Negative symptoms in schizophrenia are less known than positive symptoms, but it can be argued that negative symptoms are the most important symptoms in schizophrenia[4]. The aim of this study was to evaluate the effect of direct transcranial electrical stimulation (tDCS) in reducing the negative symptoms of patients with schizophrenia in Golestan Hospital in Ahvaz.

Our findings showed that the direct transcranial electrical stimulation (tDCS) led to a decrease in patients' negative symptom scores.

Omranifard et al.'s study also showed that transcranial electrical stimulation has a significant effect on reducing the negative symptoms of patients with schizophrenia[23].

The result of this study is similar to the current study in terms of its effect on reducing negative symptoms. Verbal Poverty and Poverty of the patient's verbal content is due to impaired flow and content of thought which is one of the main symptoms of schizophrenia. According to the glutamate hypothesis, hypotension in the glutamate system causes positive and negative symptoms of schizophrenia, especially thought disorder and negative symptoms. Therefore, it is likely that transcranial electrical stimulation by regulating the activity of mGLUR2 receptors not only improves glutamate function but also improves negative symptoms and thinking disorders in patients[24].

Similar to the results of our study, the results of Lane Valiengo et al., Dharani et al. and Ulrich et al. showed that transcranial stimulation of the brain with tDCS has a significant effect on reducing the negative symptoms of chronic schizophrenia [6, 25, 26].

Explaining the results of this hypothesis, it can be said that transcranial stimulation of the brain by tDCS, changes the message transmission process through the neuroplasticity of the brain, and since the forehead is responsible for high-level actions such as mobility, speech, motivation, judgment; transcranial stimulation of the brain by direct anodic current to the posterior lateral cortex of the left forehead can be effective in

reducing negative symptoms such as poor speech, poor emotions and inattention[27].

On the other hand, studies have reported that patients with schizophrenia have reduced activity in the prefrontal cortex, basal ganglia, and temporal cortex, called the social brain system, based on the present finding, it can be concluded that direct stimulation of the frontal and posterior lateral regions is effective in reducing negative symptoms such as emotion, problems in emotional relationships and verbal poverty in patients with schizophrenia[28]. The results of a study by Puntillo et al. Showed that negative symptoms in schizophrenia could be treated with tDCS, but the results were influenced by several factors such as electrode assembly, concomitant drug use, sample homogeneity, and severity of tDCS therapy[4].

Also in the study of Gomes et al., The results showed the therapeutic effects of tDCS in the treatment of refractory symptoms in schizophrenia by reducing the negative symptoms[29]. The results of this study were consistent with the findings of our study

Fitzgerald and colleagues conducted a study entitled negative study of two-dimensional daily transcranial direct stimulation in schizophrenia. In this study, two randomized controlled studies with the same method were performed on 24 patients. The only difference was that in one study the tDCS was unilateral and in another it was bilateral. The results of the study showed that daily use of tDCS did not have a significant effect on reducing negative symptoms [30]. The result of this study is inconsistent with the result of the current study. This difference may be due to differences in sample size.

Conclusion:

In general, it can be said that direct transcranial electrical stimulation with tDCS had a significant effect on reducing the negative symptoms of patients with schizophrenia and this method can be used in psychiatric hospitals, rehabilitation centers along with medication. The present study had several limitations. First, the sample size was small. The second limitation was that the follow-up to the current study was relatively short. It is recommended that further studies be performed with larger sample size and more tDCS sessions.

Conflicts of interest:

The authors declare that they have no competing interests.

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