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The Application of Theta Burst Stimulation in Negative Symptoms of Patients with Schizophrenia

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Abstract

***Background*:** The aim of this research is study of theta burst stimulation on left dorsolateral prefrontal cortex in remission of negative symptoms in patients with schizophrenia.

***Materials and Methods*:** In a placebo, double blind and randomized study, 10 patients with schizophrenia assigned in experimental and control group. The experimental group received 20 sessions of TBS with 50 Hz frequency, but control group were treated just with sham coil. All the patients were appraised before, the 10th sessions and after the treatment. The treatment efficacy was calculated with ANOVA.

***Results*:** The results indicated that the experimental group had statistical difference to control group in negative symptoms (p>0.007) and social functioning (p>0.01). But there weren't any significant difference in quality of life and depression between two groups.

***Conclusion*:** Theta burst stimulation can be mentioned as an efficacious treatment for people with schizophrenia.

Introduction

Repetitive transcranial magnetic stimulation (rTMS) is a method which through it the electrical activity of cortex is influenced by magnetic fields. The magnetic fields pass from the scalp through the pulses currents which are induced by a figure eight coil. This coil which its coating is plastic is placed on the head directly and thereby the magnetic fields can stimulate some areas of the cortex [1]. The objectives of the first researches about schizophrenia were reduction of auditory hallucination and many studies have reported similar and notable efficacy in reduction of these symptoms. In these researches rTMS was applied with 1 Hz on tempo parietal region [2, 3].

These results were caused that the researchers examined the effectiveness of this treatment on negative symptoms of schizophrenia. Being chronic and medication resistant nature of these symptoms have direct effects on quality of life and prognosis of these patients. With due to the important of this matter, the first study was performed in 1997. Two of ten patients with schizophrenia were better temporarily [4].

In addition to traditional rTMS protocols which are included to high and low frequency, a new protocol has recently emerged which is called theta burst stimulation; TBS. The studies have shown that TBS can induce longer changes than traditional protocols in cortical excitability. The aim of this research is the study of TBS efficacy on negative symptoms of patients with schizophrenia.

Materials and Methods

This research was performed in Atieh comprehensive mind and psyche nerve center by method of double blind clinical trial with placebo group. After the ethic committee approval of University of Social welfare and Rehabilitation Sciences, the patients were entered to study with a complete justification and acquiring the informed consent by their legal guardians. The inclusion criteria were the rang of ages between 18-50, having schizophrenia diagnosis based on DSM-IV-TR by a psychiatrist, having the scores of 15 or more in positive and negative syndrome scale: PANSS subscale, having under supervision of a psychiatrist, the patients whose symptoms were stable and there was no need to change their medications during 4 weeks and their medications could be stable during the study and the patients who were able to participate to this research by considered timetable. The exclusion criteria were having the previous treatment with rTMS for each disorder, intracranial implants or every metal things near the skull which can't peak than out, the risk of seizure because of intracranial blood pressure increasing, the history of head trauma and loss of consciousness, peacemaker, medications pump, acute disease, having personality disorder in axis II, drug abuse, having the risk of suicide, significantly positive symptoms, pregnant and breast feeding and women who were applied the birth control methods. Before entering to

the study, informed consent was received from the legal guardians of the patients.

Ten patients were assigned to two groups of experimental (5 patients) and control (5 patients) randomly. Theta burst stimulation was performed by Rapid 2 magstim device. Our coil was 8 figure type and we could stimulate the target locally. The coil had a cooling setting which through it we can apply our protocols by our desirable time. In the first session the resting motor threshold of all patients was recorded. The motor threshold is the minimum intensity for inducing a movement in abductor pollicis brevis (APB) at least in six trials which either can observe this movement visually or cause to induce 50 micro volts in EMG. The site of stimulation was left dorsolateral prefrontal cortex (LDLPFC). For the site determination, we placed the coil in region which was 5 cm anterior the motor threshold area. The theta burst protocol was 80% MT, 3 pulses in 50 ^{Hz} frequency which was repeated during 2 seconds in every 200 milliseconds, the intertrain of stimulation was 8 seconds, the duration was 190 seconds in every session and the total session were 20.

We performed this protocol in control group similarity except this group has sham coil and any pulses weren't delivered to the patients. The positive and negative of PANASS scale was performed for negative symptoms examination. Negative and positive symptoms scale is a 33 items questionnaire. There are many studies about the reliability of this scale and their results indicate high reliability of that [5]. Calgary depression scale for schizophrenia was applied for the examination of depression. The Calgary depression scale is a semi structural interview which has 9 questions and each question is included 4 items and its validity and reliability has been reported high [6].

Schizophrenia quality of life scale (SQLS) was applied of the examination of life quality. This questionnaire has 30 questions and assesses 3 dimensions of the patients with schizophrenia quality of life.The Persian version reliability of this test 0.89 [7].The social and occupational functional assessment scale (SOFAS) assessed the social and occupational function of patients. This scale which has been adapted by global assessment of scale (GAS) has the high validity and reliability [8]. All the patients were assessed at the first of study, the 10th and the end of treatment. The data analyzing was performed by one way ANOVA with SPSS-18 software. The significantly level was determined at p >0.05.

Results

The demographic characteristics of two groups have been shown in table 1. The factors that could be efficacious in the results of treatment were the numbers of hospitalization and numbers of illness episodes. So all the patients matched in both items. The results of one way analysis of variance in the PANSS scores in experimental and control group in the 10th and 20th of treatment are respectively p=0.38 and p=0.007. Hence, we conclude there are significant differences between two groups in the end of treatment. The ANOVA results in CDSS scores were p=0.86 and p=0.54 in the 10th and 20th sessions, so we can conclude because of having no statistical differences between groups, theta burst doesn't have any effects in this variable.

The ANOVA in SOFAS were p=0.02 and p=0.01 in the 10th and the end of treatment, so this variable has a significantly difference between both. SQLS ANOVA results are p=0.67 and p=0.12 and it shows a statistical differences between two groups in this variable.

Discussion

The result of research indicates that theta burst stimulation can affect negative symptoms and social function of patients with schizophrenia. But, we didn't see any significant changes in depression and quality of life. Although there was a good remission in negative symptoms but depression didn't affect by theta burst stimulation. This could be shown the different brain mechanism involving in these patients who have had depression. In other words, the depression symptoms are separate from negative symptoms and theta burst stimulation can only affect apathy, abulia and loss of individual hygiene. Quality of life scale focuses on side effects, energy, motivation and social and psychological function. Because of our patients were consuming antipsychotics for a long time, there's no changing in this scale. Theta burst stimulation effects in quality of life need to control of positive symptoms and medications interruptions. The results of our study are similar to the only study [9] which has been performed. Traditional TMS protocols [10-12] have had significant efficacy on negative symptoms. The common point of all studies was using high frequency. In spite of applying TBS protocol with 50 Hz frequency, there wasn't any seizure in the patients In 1996, a workshop was established for the study of TMS safety and researcher concluded that high frequency can be cause the seizure. But nowadays we see that with consider of some implications, neither there is no problem for patients nor high frequency can increase the effects of treatment with comparison to traditional protocols. In addition to applying high frequency, the number of sessions can be considering as an important factor in our experiment. Previous studies [13, 14] which have indicated that TMS doesn't induce any positive therapeutic effects have delivered less sessions (10 sessions).

Table 1. Demographic information of test and control group

Groups	Age (yr)	Age at the first episode	Number episodes of illness	Number of hospitalization	Duration of affliction (yr)
Experimental (Mean±SD)	26.6±4.66	19.40±2.30	3±1	2±1	3.6±1.94
Control (Mean±SD)	27.6±2.50	24.2±2.16	3.6±1.81	2.6±1.81	4.6±2.07

The numbers of subjects were few in our study and this lead us to have a conservative conclusion. Theta burst stimulation can have efficacy only in two fields (negative symptoms and social function). It is hoped that with continued researches in these fields, the deficiencies has been identified and corrected.

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Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

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