Comparing the Effectiveness of Neurofeedback and Transcranial Direct Current Stimulation (tDCS) in Reducing Symptoms of Women with Migraine

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ABSTRACT

Background & Objective: Migraine is a neurological syndrome that involves one-way or two-way recurrent headaches with a moderate to severe severity and lasts from 2 to 72 hours. Chronic migraines occur about 3 months and at least 15 days or more per month, with a global incidence of 1.4 to 2.2 percent. The aim of this study was to compare the effectiveness of neurofeedback and transcranial direct current stimulation (tDCS) in reducing symptoms of women with migraine.

Materials & Methods: This is a quasi-experimental study with pre-test, post-test, and follow-up for 2 months. The sample consisted of 20 migraine patients aged 15-55 years. Initial evaluation (entrance examination and exit), implementation of the Ahvaz Migraine Questionnaire (AMQ), and Blanchard Headache Diary (BHD) were performed. Patients were randomly assigned to the neurofeedback treatment group (N=10) and tDCS (N=10). Subjects of each group were evaluated 4 times consisting before intervention. The data were analyzed using SPSS 23 software.

Results: The results of Mann-Whitney U test indicated that there was no significant difference between the two treatments during the stages of evaluation in the severity, duration, and number of pain attacks per month. The results of Friedman test showed that there was a significant difference between the severity of headaches and the number of pain attacks in one month in the treatment groups during the stages of evaluation, but the duration of pain relief in each group in the evaluation steps did not differ significantly.

Conclusion: Neurofeedback and tDCS treatments reduce the symptoms of migraine disease, but there is no significant difference between the two treatments in terms of headache symptoms improvement.

Keywords: Migraine, Neurofeedback, Transcranial direct current stimulation

Introduction

Headache disorders are the most prevalent medical disorders worldwide (1). Accordingly, the incidence of headaches in the general population is 90 percent over a year and about 99 percent in life. Today, 20% of women and 6% of men suffer from it. The disease is often debilitating and nearly 57% of people with this condition suffer from moderate to severe disability (2). Chronic migraines occur for about 3 months and at least 15 days or more per month, with a global prevalence of 1.4-2.2% and in women 3 times that of men (3). Migraine headaches that are often severe, pulsating, and more unilateral, from a few hours to a few days (4), have symptoms such as nausea, vomiting, intolerance of the light and sound, neck pain, and muscle tension (5). Research shows that migraine is associated with physical illnesses such as asthma, heart disease, gastric ulcer, arthritis, and psychiatric disorders such as anxiety, bipolar disorder, depression, and chronic pain (6). Headache attacks may begin with stressful changes in life including puberty, changing spatial and social situations, and the like or happen by numerous special events or experiences (2). Poor sleep quality is considered as one of the predictors of headache attacks (7). This disease reduces the individual's efficiency in the occupational affairs (8). Research studies show that the reduction in the threshold of efficacy of these people is 2 to 3 times more than healthy people, and the family activity of these patients is more difficult than healthy ones (9). The purpose of the treatment of migraine patients is to reduce the severity and frequency of their migraine attacks, so as they have the highest efficacy and the
At least complications. However, about one-third of people are not satisfied with the therapeutic results of taking medications. Side effects of medicines and their use restrictions for pregnant women and those with high blood pressure and heart disease have limited their usage (9,10). It also has high social and medical costs for the community (11). Therefore, in a safe and effective way, fewer side effects are needed (12).

Therefore, if there is an effective and non-side-effect therapeutic approach, it will help the economy of patients, families, and communities. Some non-therapeutic interventions have high efficacy for migraines. Therefore, behavioral interventions are used instead of drug interventions (11). Neurofeedback is one of the non-pharmacological treatments that have these characteristics. Neurofeedback causes the growth and alteration of the cellular level of the brain and can be used instead of drugs (13). Considering the short-term treatment, lack of any side effect, and its effects on brain waves and relationships, neurofeedback has various advantages compared to most interventions such as pharmacologic interventions. Neurofeedback is a complex therapeutic system and a safe and noninvasive method which improves brain cell growth and change (14).

During the neurofeedback, electrodes can be attached to the individual's scalp using a special adhesive according to the international 10-20 system; in this way, electrical changes from the brain's surface are continuously recorded. The person in front of the computer sees the animation and recording of the waves. When the brain waves of a person approach the conditions of the protocol, animation moves and the person takes points. Thus, certain waves are suppressed or amplified. In fact, the person learns to remain in the proper state and does not have the waveform that causes the symptoms of the disease. Thus, the symptoms of the disease disappear and the patient gets into his normal state of health (15).

Another treatment is transcranial direct current stimulation (tDCS). Indirect irritation in the cortical regions plays a major role in the pathogenesis of migraine. The tDCS is a non-invasive and pain-free method of stimulating the brain and can alter cortical irritability by modulating the resting potential of the neuronal membrane. In the past decade, direct brain electrical stimulation has also been extensively investigated. Electric stimulation works by changing the resting potential of cortical neurons. This is a safe and non-invasive technique and an appropriate alternative to medical treatment (16,17). The tDCS causes a very weak electrical current (1 to 3 mA) on the scalp. As it flows directly with discrete momentum, it polarizes and does not stimulate, so its activity does not directly affect the action potential of the cortical neurons. This treatment is perhaps one of the easiest ways to stimulate the brain (18).

Considering the high prevalence of migraine and limiting drug treatment and given the lack of any study to compare the effectiveness of neurofeedback and tDCS in reducing symptoms of migraine in women, the present study was conducted. Therefore, limiting drug treatment and determining the efficient and effective treatment is one of the priorities. Accordingly, the following assumptions are addressed:

Hypothesis 1: There is a significant difference between neurofeedback and tDCS in reducing the pain intensity of migraine patients.

Hypothesis 2: There is a significant difference between neurofeedback and tDCS in reducing the duration of pain relief in migraine patients.

Hypothesis 3: There is a significant difference between neurofeedback treatment and tDCS in reducing the number of pain attacks in patients with migraine.

Materials and Methods
This is a clinical trial with the ethics code of ZUMS.REC.1396.152. Also, the clinical trial code of the study is (IRCT) IRCT20171023036952N: (IRCT).

The statistical population included all patients with migraine in Zanjan city. For the purpose of this study, 20 patients with migraine were selected by purposive sampling and randomly assigned to two groups.

Inclusion Criteria
The inclusion criteria are: presence of migraine diagnostic proprietors according to the International Classification of Headache Disorders (ICHD) criteria, the diagnostic interview, the student's scores on the scale of the 25 questions of the Ahvaz Migraine Questionnaire (AMQ), the minimum level of secondary education, the age range of 15 to 55 years, signing a written consent, not having received treatment for behavioral therapies (biofeedback, neurofeedback, tDCS) in the month before entering the research.

Exclusion Criteria
The exclusion criteria are: absence of physical illness (syositis, diabetes, history of epilepsy, brain damage), and mental illness associated with migraine headaches, alcohol and drug abuse, pregnancy, consumption of hormones and oral contraceptives, the occurrence of psychotic disorders based on diagnostic interviews, the presence of metal devices or other electrical devices in the head, scarring or scratching in the scalp.

Measurement Tools
In this research, the following questionnaires were used for data collection:

Ahvaz Migraine Questionnaire (AMQ): This tool was created and validated by Najjarian in 1997. The reliability of this test was calculated in two ways. The
reliability of this questionnaire was 0.8 and the Cronbach's alpha coefficient was 0.91. Also, Azizi et al. (2015) evaluated the validity of this tool using Cronbach's alpha coefficient of 0.72 (19).

Blanchard Headache Diary (BHD): The validity of the migraine headache questionnaire was used to determine the content validity method. The questionnaire contains 18 questions about the age of the onset of the headache, the age of the diagnosis of migraine, the frequency, severity and duration of headache attacks, headache area, early symptoms, etc.

The severity of headache was measured by visual analogue scale (VAS) of 0 to 10 (0 without pain and 10 severe pain) and the score of this questionnaire was given as the number of headache indicators (1-2-....). In order to measure the reliability of the instrument, a test-retest method was used, which was confirmed with a reliability of r=0.95 (20).

Methods
Research samples were selected from the patients referring to the psychiatric clinic of Shahid Beheshti Medical Center and Neurologist Clinic in Zanjan based on diagnosis (ICHD); the patients were referred by a psychiatrist and neurologist and entered the study after initial evaluation of migraine. Along with drug therapy, patients entered one of the groups of neurofeedback or tDCS as a simple imaging. The treatment was performed as follows:

Neurofeedback Treatment
The first stage:
Diagnostic interviews of migraine were performed by a psychiatrist and neurologist and an appropriate therapeutic relationship between the researcher and the referrals. Then, the AMQ and BHD were filled out and consent letters were presented to the patients with explanations related to treatment and research.

The second stage:
The treatment and prevention of migraine attacks and neurofeedback treatment were explained and the patient became familiar with the logic of treatment. From this session, patients were treated with neurofeedback for 20 sessions. In addition to drug therapy, these patients also received neurofeedback treatment. Each session was 45 minutes. During the neurofeedback, electrodes were attached to the individual's scalp using a special adhesive according to the international 10-20 system and the electrical changes from the brain's surface were continuously recorded. The person in front of the computer could see the animation and recording of the waves. In this method, when the brain waves of a person approach the conditions of the protocol, animation moves and the person takes points. Thus, certain waves are suppressed or amplified. In fact, the person learns to remain in the proper state and does not have the waveform that causes the symptoms of the disease. Thus, the symptoms of the disease disappear and the patient gets into his/her normal state of health (15).

Neurofeedback protocol in migraine is theta suppression (4-8) Hz and suppression (21-30) Hz and amplification of sensory-motor wave (12-15) SMR in T4, T3 region during 20 sessions and every 45 minutes (21).

The final stage: BHD was used as a post-test. To evaluate the efficacy of the treatment, follow-ups of 1 and 2 months were also carried out.

TDCS treatment process
Patients were treated with tDCS for 10 sessions. After evaluation, the method of implementation of this method was taught to patients. Each session lasted for 20 minutes at 2 mA-treated patients with a 9-volt battery. An anode of tDCS on the CZ and a cathode was placed for inhibition in the OZ region (22).

In tDCS, the direct current is transferred from the electrodes covered with serum-soaked sponge and the size of the electrodes was 4 at 4.5 centimeters square.

Data analysis method
For data analysis, descriptive methods such as mean, percentage points, and inferential statistics methods of U Mann-Whitney, Friedman, and Wilcoxon tests were used. The data were analyzed by SPSS 23 (SPSS Inc., Chicago, Illinois, USA).

Results
Demographic characteristics of the subjects are provided in Table 1.

As shown in Table 1, all the subjects were female. The Chi-square (Fisher) test was used to compare the results of pretest regarding marital status and occupation in both neurofeedback and tDCS groups. Further, the Kolmogorov-Smirnov and independent t-tests were employed to compare the age and homogeneity of variance based on Levine's test for both groups. Based on the results of the Chi-square test, no significant difference was observed between the two groups with respect to gender, marital status, and occupation. The mean (SD) ages of these patients were 30.3 (2.6) and 33.2 (2.69) in the neurofeedback and tDCS groups, respectively. Comparing the mean age of the subjects using the independent t-test revealed that there was no significant difference between the groups, and they were homogeneous in terms of this variable.

Testing hypotheses
To test the hypothesis, the U Mann-Whitney was used because of the rank of the variables studied. As shown in Table 2, the severity of pain, the duration of pain, the numbers of pain attacks per month in the groups were not significant. Therefore, there was no significant difference between severity of pain, duration, and number of pain attacks in patients.
undergoing post-test, first, and second follow-up periods in the two groups.

As shown in Table 3, Friedman test was used to examine changes in headache variables in each group. The severity of the pain and the number of attacks during one month in both groups were significantly different during the evaluation. Thus, it can be concluded that the severity of pain and the number of headache attacks in each group decreased significantly.

As shown in Table 4, the Wilcoxon test was used to examine changes in headache variables in each group. The severity of the pain and the number of headache attacks during one month in both groups were significantly different. Therefore, it can be concluded that the severity of pain and the number of headache attacks in each group during the evaluation process from the pre-test to post-test and first and second follow-up sessions in each group decreased significantly.

Table 1. Demographic Characteristics of the Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>Chi-square Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neurofeedback</td>
<td>tDCS</td>
</tr>
<tr>
<td>N (%)</td>
<td>N (%)</td>
<td>P-value</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>6 (60)</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Married</td>
<td>4 (40)</td>
<td>7 (70)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Housewife</td>
<td>4 (40)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Employed</td>
<td>3 (30)</td>
<td>4 (40)</td>
</tr>
<tr>
<td>Student</td>
<td>3 (30)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Note. The tDCS: transcranial direct current stimulation. P<0.05.

Table 2. Mann-Whitney U test results in neurofeedback and tDCS groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Test stages</th>
<th>Z amount</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>The severity of the attacks</td>
<td>Post test</td>
<td>-.04</td>
<td>.968</td>
</tr>
<tr>
<td></td>
<td>First follow-up</td>
<td>-1/268</td>
<td>.205</td>
</tr>
<tr>
<td></td>
<td>Second follow-up</td>
<td>-1/268</td>
<td>.205</td>
</tr>
<tr>
<td>Duration of the attacks</td>
<td>Post test</td>
<td>-1/371</td>
<td>.17</td>
</tr>
<tr>
<td></td>
<td>First follow-up</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Second follow-up</td>
<td>-1/438</td>
<td>.661</td>
</tr>
<tr>
<td>Number of customs in the month</td>
<td>Post test</td>
<td>-.281</td>
<td>.779</td>
</tr>
<tr>
<td></td>
<td>First follow-up</td>
<td>-1/169</td>
<td>.243</td>
</tr>
<tr>
<td></td>
<td>Second follow-up</td>
<td>-1/508</td>
<td>.132</td>
</tr>
</tbody>
</table>

Table 3. Friedman test for research variables

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Variable</th>
<th>Chi Square amount</th>
<th>Degree of freedom</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurofeedback</td>
<td>Severity of the attacks</td>
<td>15/436</td>
<td>3</td>
<td>.001</td>
</tr>
<tr>
<td>Neurofeedback</td>
<td>Duration of the attacks</td>
<td>2/2</td>
<td>3</td>
<td>.532</td>
</tr>
<tr>
<td>Neurofeedback</td>
<td>Frequency of the attacks</td>
<td>12/482</td>
<td>3</td>
<td>.006</td>
</tr>
<tr>
<td>tDCS</td>
<td>Severity of the attacks</td>
<td>17/133</td>
<td>3</td>
<td>.001</td>
</tr>
<tr>
<td>tDCS</td>
<td>Duration of the attacks</td>
<td>2/57</td>
<td>3</td>
<td>.463</td>
</tr>
<tr>
<td>tDCS</td>
<td>Frequency of the attacks</td>
<td>13/673</td>
<td>3</td>
<td>.003</td>
</tr>
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</table>
### Table 4: Wilcoxon Test for Variables in Each Group

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Test stages</th>
<th>Z amount</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Severity of the attacks</strong></td>
<td>Neurofeedback</td>
<td>Pre-test</td>
<td>Post test</td>
<td>-2/33</td>
</tr>
<tr>
<td></td>
<td>Neurofeedback</td>
<td>Pre-test</td>
<td>First follow-up</td>
<td>-2/46</td>
</tr>
<tr>
<td></td>
<td>Neurofeedback</td>
<td>Pre-test</td>
<td>Second follow-up</td>
<td>-2/46</td>
</tr>
<tr>
<td></td>
<td>tDCS</td>
<td>Pre-test</td>
<td>Post test</td>
<td>-2/251</td>
</tr>
<tr>
<td></td>
<td>tDCS</td>
<td>Pre-test</td>
<td>First follow-up</td>
<td>-2/271</td>
</tr>
<tr>
<td></td>
<td>tDCS</td>
<td>Pre-test</td>
<td>Second follow-up</td>
<td>-2/271</td>
</tr>
<tr>
<td><strong>Frequency of the attacks per month</strong></td>
<td>Neurofeedback</td>
<td>Pre-test</td>
<td>Post test</td>
<td>-2/07</td>
</tr>
<tr>
<td></td>
<td>tDCS</td>
<td>Pre-test</td>
<td>First follow-up</td>
<td>-2/251</td>
</tr>
<tr>
<td></td>
<td>tDCS</td>
<td>Pre-test</td>
<td>Second follow-up</td>
<td>-2/428</td>
</tr>
</tbody>
</table>

### Discussion

The results of this study indicated that neurofeedback and tDCS treatments are effective in reducing the severity of chronic stress-related headache attacks and adding it to standard medication which can add to the efficacy of drug therapy.

In this study, neurofeedback treatment significantly reduced the severity of pain in these patients. The results of Farahani et al. (20) also indicated that neurofeedback treatment significantly reduced the severity of pain in these patients. Besides, Rahmati et al. (2013) showed that neurofeedback treatment is associated with a reduction severity of pain in migraine symptoms. Therefore, our research results are consistent with this study (12).

In the research of Antal et al. (2011), tDCS treatment on migraine patients after intervention severely decreased pain in intervention group compared to control group (22). Our research results are also consistent with this study.

Neurofeedback and tDCS treatment did not have a significant effect on the duration of headache in the three patients with short duration of headache in the post test. Sepehri et al. (2014) investigated the effectiveness of neurofeedback and relaxation on people with migraine. Their study was performed on 2 subjects. The intervention took 24 sessions. The instrument used in this study was a distance. The duration of the attacks was significantly reduced (23).

It seems that the single treatment method, the large number of samples, the difference in the scale used, and the number of lesson sessions in this study has led to this inconsistency.

Antal et al. (2011) examined the effect of tDCS on migraine patients. After the pre-test, 13 patients in the treatment group and 13 subjects in the control group participated in 15 sessions which lasted for 6 weeks. In this treatment, the cathode and anode electrodes were placed on OZ and CZ, respectively. Then, the subjects took the post-test. The results showed that after intervention, the intervention group had less pain intensity than the control group (22). It seems that the lower number of samples and meetings in this study has led to this 6. In the neurofeedback group, the process of reducing the frequency of attacks continued from pre-test to post-test and the first follow-up. As a result, the effect of treatment in reducing the number of headache attacks over the course of the month was stable in this group and this decrease in the number of attacks in the neurofeedback group was significant.

The present investigation is in line with the results of Azizi et al. (2017), Dobrushina et al. (2017), Rocha et al. (2015), Walker (2011), and Siniatchkin (2000) (19, 24-27).
The results showed that there is no significant difference between the two groups in reducing the number of headache attacks in the post-test and the two follow-ups.

Neurofeedback behavior therapy is rooted in the belief that a psychiatric disorder headache is a physiological disorder influenced by environmental and psychosocial stressors. Therapeutic approaches, such as neurofeedback, focus on physiologically relevant headache responses. Neurofeedback is used to obtain information about electrical activities of the brain. In this method, based on the frequency of brain waves, it uses electrical activities of the brain to inform the patient. In this context and out of curiosity, patients use information from the electrical activities of their brain and gradually learn how to modify and improve these activities. Therefore, neurofeedback interventions can affect the electrical activity of the brain and are useful for these patients. Early studies of neurofeedback are suitable for treating a number of cognitive, emotional, and physical disorders.

Scientific research has shown that there are abnormalities in brain waves of migraine, such as theta increase. Neurofeedback treatment also increases the ability of the individual to control the physiological responses associated with the headache; and by controlling these responses, the headache is decreased (20). The neurofeedback is used to assess the alterations of the brain states and modifies, strengthens, and enhances the efficiency of the brain cells. As a result, sleep pattern alteration and regulation are among the first changes that the patients typically observe after initiating the neurofeedback treatment (28).

The tDCS is another therapeutic method that is applied by the electrodes on the scalp, and it is believed that the cortical irritability is altered by altering the potential of the cell membrane due to the anodal (cathodal effect) effect. In patients with migraine, the irritability of the cortex was higher than the control group (29).

In the explanation of the decrease in the severity of the attacks, it seems that reducing cortical irritability in these individuals reduces the individual’s sensitivity to triggers causing headaches and thus reduces pain intensity. As far as the researchers investigated, no similar research has been done in this regard so far. Therefore, there is no possibility of comparison in terms of alignment and inconsistency with previous studies. From this point of view, this research is important and can be promising for future research.

It should also be noted that, in the interpretation of the results, attention should be paid to the limited sampling of the Zanjan Shahid Beheshti Medical Center, the size of the samples, and the difference in years of illness. The implementation of similar studies and considering more examples can increase the power of generalizing these findings. It is also recommended that the protocol for tDCS and neurofeedback be based on the brain map of each individual patient according to quantitative electroencephalography (qEEG) in order to identify and treat the exact brain regions involved.

**Conclusion**

The findings of this study should be interpreted with caution. Although the researchers attempted to manage the situation in the best way possible, it is difficult to control all human subjects, including psychological treatment. Overall, it can be concluded that both neurofeedback and tDCS treatments along with drug therapy have been able to significantly reduce the symptoms of migraine from pre-test to post-test along with first and second follow-ups.

Due to the fact that both treatments were effective, it is suggested that this treatment be used to reduce the symptoms of migraine along with drug therapy for the treatment of patients. It is also suggested that further studies be conducted considering the suggestions and limitations of this study.

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**Conflict of Interest**

Authors declared no conflict of interests.

**References**


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