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Effectiveness of Transcranial Direct Current Stimulation for the Reduction of Symptoms in Patients with Major Depressive Disorder Admitted to Public, Educational, and Private Hospitals in Ilam, Iran

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Abstract

Objectives: The current study aimed at analyzing the effect of transcranial direct current stimulation (TDCS) on reduction of depression symptoms in patients admitted to public, educational, and private hospitals in Ilam, Iran.
Methods: In the current clinical trial, pre-tests and post-tests were used to analyze data. The study population consisted of patients diagnosed with depression admitted to public, educational, and private hospitals of Ilam. After explaining the study objectives, 40 patients agreed to cooperate. The convenience sampling method was used in the current study through which patients were selected randomly and allocated into 2 groups of 10 and 20 stimulation sessions, respectively. The Beck depression inventory was used to collect data. The t test and Pearson correlation test were used in hypothesis assessment procedure.
Results: The results of the current study revealed that TDCS reduced depression in the studied patients.
Conclusions: The duration of electrical current pulses to the brain is associated with the reduction of depression symptoms in patients with depression. No study demonstrated compatibility and incompatibility with this hypothesis. The counselling centers, institutes, university and other institutions can benefit from the results of the current and other similar ones.

Keywords: Depression Symptoms, Depressed Patients, Hospitals

1. Background

Depression is one of the most important neuropsychological disorders. The risk of being affected by depression is 17% for every individual and currently 10% of the global population is in need for serious medical services for this disorder. The prevalence of the disease in the United States is estimated 0.4% - 2.5% in adolescents and 4% - 8% in teenagers. The disorder approximately affects 14% of the American population currently aged 15 - 18 years at different degrees during their lifetime. Depression is the most prevalent disorder amongst mental and physical diseases that more affects females within the age range of 15 to 45 years (1) than their male counterparts.

Depression may be treated by pharmacotherapy, psychotherapy, and also shock therapy. However, these methods are ineffective to half of the patients, and do not resolve any of the symptoms. Estimates show that about 23% of the patients show minimal response and many more show no response to the therapeutic methods. Antidepressant drugs are considered as the first line treatment in many mood disorders, especially depression, and shock therapy is only used in patients unresponsive to pharmacotherapy or cannot take medicine. Even though shock therapy was an efficient treatment method, researchers gradually started developing methods that did not require systemic convulsions, but only stimulate focal points in the cortex and thus treat depression (2). The current study aimed at evaluating the effectiveness of transcranial direct current stimulation (TDCS) used to reduce symptoms in patients with major depressive disorders admitted to public, educational, and private hospitals in Ilam, Iran.

2. Methods

2.1. Study Design

Transcranial direct signal stimulation is a non-invasive method in which a direct current of 1 to 4 mA is conducted through the scalp. This procedure causes long-term

changes in the polarity of the cerebral cortex by affecting depolarization and hyperpolarisation of neural cells and neural receptors. In other words, in this method focal points of the cortex are subjected to direct current transduction (3). The procedure relies on placing 2 electrodes, 1 positive and the 1 negative, on the scalp using spongy pads soaked in conductive solution. The applied current passes through skin and bone and reaches the cerebral cortex, polarizes cortical neurons, and then, changes the activity and performance of that region. Due to certain complications, these parameters should be defined prior to performing the procedure: amperage, duration and direction of the flow, the location of either of the electrodes, size of the sponge pads, and number of the required sessions (4).

Flow amperage: It has a direct correlation with the density of flow passing through the brain. The increased amperage is followed by increased and much deeper effects. Electricity flows from the positive electrode (anode) to the negative electrode (cathode).

Shape and size of the electrodes: It has an inverted correlation with the flow density. It may be concluded that flow density is considerably more important than flow amperage. Flow density is the flow amperage conducted through 1 cm of surface. The average flow density used in most studies is 0.029 to 0.08 mA/cm^2. Therefore, the shape and size of the employed electrodes are important. In most of the performed studies, 25 - 35-cm^2 electrodes were employed. In order to provide desired contact between the pads and skin, the pads are soaked in water or saline (required concentration: 15 - 140 mM). Special gels or creams may be used and some manufacturers introduced electrodes that eliminate the need of conductive media between skin and the electrodes.

Placement of electrodes: In accordance with the size of the employed electrodes and the principles of TDCS technology, highly accurate electrode placement cannot be anticipated. However, it can determine the regional effectivities including motor regions in the left or right hemisphere or prefrontal cortex. Research revealed that the anode increases regional neural activity, while the cathode reduces such qualities. Although such effects are reversed in the deeper regions of the cerebrum, it can be concluded that TDCS increases the activity of one region and at the same time reduces that of another. Under such circumstances that only 1 cerebrum- e g, motor cortex of the left cerebrum- is studied, 1 cathode should be placed on the selected region and the other on a different section. By referring to the second electrode as the reference electrode or simply by not acknowledging its presence, the effects of the desired electrode on the selected region can be studied. However, if the reference electrode causes interference by affecting the underneath regions, selecting bigger electrodes and reducing flow density or relocating the reference electrode to a point outside the cranium, such as the neck, may reduce and remove such interferences. In some studies the combined effects of electrodes are analyzed; simultaneous stimulation of the left prefrontal cortex and right prefrontal cortex via anode and cathode, respectively, and studying the combined effects on the behavior of the patient may be an example of such studies.

Duration of electrical current flow: It is evident that increased current flow duration or amperage yields more prominent results in TDCS. However, since increased amperage also increases the size of affected regions and the number of neurons, causing uncontrollable and immeasurable effects and increasing the current flow duration are preferred to increasing flow amperage. When contact is achieved, the effect of a flow limited to mere seconds fades directly subsequent to disconnection. However, if the flow is maintained for about 10 minutes (throughout most studies this duration ranges from 9 to 13 minutes), said effects last for about an hour.

Studies reveal that TDCS is a non-invasive method, which is also devoid of serious complications (5). Other positive properties that increase the clinical potential of this method include: simplicity of employment and movement of equipment (6, 7) appropriate for home use (8), significant results (based on results gathered from clinical trials), rapidly achievable results (mainly up to 1.5 week subsequent to treatment), and painlessness as well as lack of interference with other clinical methods. Due to the mentioned serious side effects, TDCS is considered a safe therapeutic method with minimal side effects and complications. No known complication or side effects are reported yet. Insignificant reported side effects include slight burn around the electrodes locations, lethargy, and insomnia, which are resolved in 72 hours following the procedure. As already mentioned, most patients did not experience any side effects. Some studies in Iran evaluated the possible application of TDCS in cases of brain strokes, verbal memory, aesthetic, and moral judgment (9, 10). However, to the authors' best knowledge, the effects of TDCS on patients with depression are not assessed. Therefore, the current study aimed at investigating the effectiveness of TDCS on reducing depression.

2.2. Study Population

The current study employed the convenience sampling method. Due to the limited size of the study population, the entire available samples were selected; 40 patients were randomly allocated into 2 groups of 20; one group received 10 sessions of TDCS and the other 20.

Beck depression inventory: Depression has various manifestations, prohibiting its simple diagnosis. This dis-

order is accompanied by a vast range of symptoms such as headache, constipation, anorexia, backache, or chronic lethargy. The inventory is designed to aid the diagnosis. This questionnaire consists of 21 questions, each containing 4 statements. Each of these statements describes a state which may/may not be observed in the subject. The test is specifically designed for subjects over 16 years old. The interpretation of the obtained scores is as follows: 1 - 10 normal depression; 11 - 16 mild depression; 17 - 20 need for psychiatric consultation; 21 - 30 moderate depression; 31 - 40 heavy depression; and > 40 indicates excessive depression.

TDCS technique: Cerebral stimulation through the cranium using direct currents is an old method recently rediscovered and used in various cerebral disorders. The TDCS treatment device used in the current study was the ActivaDose® Iontophoresis (ActiveTek Inc., Salt Lake City, Utah). The energy source of this device consists of an 8-V battery, which provides a maximum flow, and voltage of 4 mA and 82 V through a direct current.

2.3. Data Collection

Subsequent to obtaining referral letters from Islamic Azad University and permission to use the TDCS device belonging to the Faculty of Medical Sciences, the clinical trial was commenced with the help of technicians as well as a neuropsychologist (the study supervisor). Patients were primarily interviewed and assessed for depression through the Beck depression inventory. TDCS treatment was initiated; one group received 10 sessions and the other 20 sessions of TDCS. Patients' information was confidential and the method used in the study had no side effects on patients and no cost was imposed to them.

2.4. Data Analysis

Descriptive analytical methods such as frequency, percentage of frequency, and standard deviation (SD), as well as inferential tests such as t test, regression, and the Pearson correlation test, were employed in the statistical analysis of attributes of demographic values with SPSS software version 20.

3. Results

Table 1 shows the frequency of participants based on gender, level of education, and age. According to Table 1, the groups were matched by gender.

Table 1 shows that 30% (majority) of the participants aged 26 - 30 years, while the age range of 10% (minority) was 36 - 40 years.

The participants' occupational status analysis showed that 22% (majority) of the subjects were unemployed and7.5% (minority) self-employed.

Table 1. Frequency of Participants Based on Demographic Variables

Variable	Subcategory	N	Percentage
Gender	Female	20	50
	Male	20	50
	Total	40	100
Age, y	Under 20	7	17.5
	21 - 25	6	15
	26 - 30	12	30
	31 - 35	7	17.5
	36 - 40	4	10
	Above 40	4	10
Education	Illiterate	6	15
	high school student (studying)	5	12.5
	Primary school	4	10
	High school diploma	8	20
	Associate degree	3	7.5
	Bachelor's degree	7	17.5
	Master's degree	1	2.5
	Bachelor's degree (studying)	5	12.5
	Medical student	1	2.5
	Total	40	100

As it is shown in Table 1, 20% of the patients had high school diploma (majority), while 2.5% either had a Master's degree or were the medical student (minority).

Table 2 presents the mean ± SD of depression before and after receiving the treatment; it is evident that treatment was effective and levels of depression reduced.

Table 2. Mean and Standard Deviation of Depression Before and After the Treatment

Gender	Dependent Value	SD	Mean
Female	Depression (before treatment)	1.157	23.150
	Depression (after treatment)	1.028	23.850
Male	Depression (before treatment)	1.157	33.150
	Depression (after treatment)	1.028	22.00

First hypothesis in the Table 3: electrical stimulation of the brain has a significant impact on reducing depression symptoms in patients with depression.

The results of Table 4 showed a statistically significant relationship between depression and the onset of electrical stimulation, given that significant level achieved be-

Table 3. The Effect of Electric Current Duration on Depression Levels Before and After the Treatment, Based on Gender

Gender	Session	Value	Depression (Before Treatment)	Depression (After Treatment)
Female	10	Mean	30.96	23.38
		SD	3.56802	4.99230
	20	Mean	37.7143	24.7143
		SD	6.42169	4.92322
	Total	Mean	33.1500	23.8500
		SD	5.73333	4.88041
Male	10	Mean	29.1429	20.2857
		SD	3.33809	2.13809
	20	Mean	35.3077	22.9231
		SD	3.56802	4.92378
	Total	Mean	33.1500	22.0000
		SD	4.54539	4.29198
Total	10	Mean	30.1500	22.3000
		SD	3.48342	4.41409
	20	Mean	36.1500	23.5500
		SD	4.73814	4.87178
	Total	Mean	33.1500	22.9250
		SD	5.10681	4.63204

tween depression score before treatment and the effect of electrical stimulation($P = 0.000$) was smaller than the error level ($P = 0.05$); as a result, a significant statistical relationship was observed. In other words, the effect of electrical stimulation was effective in both applied methods. Also, there was no significant difference in the 2 different periods of depression scores after treatment and the effect of electrical stimulation.

Second hypothesis: there was a significant relationship between the duration of electrical stimulation session and reduced depression symptom in patients with depression by gender.

The results of Table 5 showed a correlation between the occurrence of electrical stimulation and decrease of depression symptoms by gender; given that the achieved significance level ($P = 0.000$) was smaller than the error level ($\alpha = 0.05$), as a result, there was a statistically significant relationship between the effect of electrical stimulation and reduction of depressive symptoms after the treatment. In other words, the current electrical stimulation in males and females dropped after the application of electrical stimulation and indicated that electrical stimulation was effective on reducing depression symptoms.

Third hypothesis: there is a significant relationship between the duration of electrical stimulation session and reduced depression symptoms.

Electrical stimulation to reduce depression symptoms in terms of the time showed the interaction between the duration of the sessions and decreased depression symptoms. There was no significant difference between the duration of sessions and reduced depression score ($P > 0.192$).

Fourth hypothesis: there was a significant relationship between depression and age in the study subjects.

The current study results showed a relationship between depression and age; given that the value of $r = 0.32$, $P = 0.778$ showed the level of $\alpha = 0.05$, there was no significant relationship between depression and age.

3.1. Inferential Statistics

According to Table 6, the duration of treatment course had no significant effect on the reduction of depression score ($P > 0.05$).

4. Discussion and Conclusion

First hypothesis: electrical stimulation of the brain has a significant impact on reducing depression symptoms in patients with depression.

According to Table 6, electrical stimulation can reduce depression in patients with depression. The results of the

Table 4. The Mean Depression Score of Electrical Stimulation[a]

Treatment Duration	No.	Group	Mean	SD	F	T	P Value
10 sessions	20	Depression (before treatment)	30.15	3.48	3.37	4.69	0.000
10 sessions	20	Depression (after treatment)	22.30	4.41			
20 sessions	20	Depression (before treatment)	36.16	4.73	0.312	9.89	0.000
20 sessions	20	Depression (after treatment)	23.55	4.87			

[a] t test.

Table 5. The Effect of Electrical Stimulation Duration on Depression Symptoms, Based on Gender

Gender	Duration	Group	Mean	F	T	P Value
Female	10 Sessions	Depression (before treatment)	30.69	9.13	-2.67	0.028
		Depression (after treatment)	23.38			
	20 Sessions	Depression (before treatment)	37.71	0.247	-0.571	0.577
		Depression (after treatment)	24.71			
Male	10 Sessions	Depression (before treatment)	19.14	0.090	-3.84	0.002
		Depression (after treatment)	20.28			
	20 Sessions	Depression (before treatment)	35.30	3.12	-1.62	0.114
		Depression (after treatment)	22.92			

Table 6. The Effect of Electrical Stimulation Duration on Depression Symptoms, Based on Gender

Age	Total	Average	SD	F	P Value	Results
10	Under 20	27.0000	4.94413	0.540	0.745	No Difference
	21 - 25	30.0000	2.91548			
	26 - 30	27.1538	6.09434			
	31 - 35	25.4286	4.15761			
	36 - 40	27.5000	9.19239			
	Above 40	24.6667	7.50555			
	Total	27.0000	5.26235			
20	Under 20	32.5000	5.97216	0.893	0.497	No Difference
	21 - 25	29.2857	10.27480			
	26 - 30	26.8182	9.94805			
	31 - 35	25.8571	5.66947			
	36 - 40	30.0000	7.21110			
	Above 40	34.4000	8.26438			
	Total	29.0750	8.44101			

current study were consistent with those of the other studies. The researchers concluded in their study that stimulation of the left DLPFC anode led to experience more positive emotions in people with depression and it also corresponded to the results of the study by arvel-anandum (11). The study on 73 patients with major depression reported a significant decrease in depression symptoms after the anode stimulation of the left frontal areas. The researchers concluded that anode stimulation of the dorsolateral prefrontal for 23 minutes in 13 sessions significantly

decreased depression symptoms (12); these effects lasted up to 4 weeks after the treatment and the results were in agreement with those of the current study showing that the effect of the brain TDCS to treat depression was similar to that of fluoxetine (the increased cognitive function and pain relief is compatible with that of TDCS) (12). Anodic stimulation of the left lateral prefrontal cortex (of the same area triggered to treat depression) indicated that reinforcing the effectiveness of cognitive-behavioral correlation over a number of tasks, take advantage of higher-level cognitive functions, including working memory, verbal influence, and ability to plan. Other studies also showed certain improvement in language learning and reading, after TDCS. Apart from these studies that checked a single period of TDCS, a study referred to successive courses of provocations that may be useful and beneficial to cognitive and motor learning aid, which was consistent with the results of the current study. The primary stimulation in the frontal prescribed to treat depression may also have other clinical effects.

Second hypothesis: There is a significant relationship between the duration of electrical stimulation course and reduced depression symptoms in patients with depression, based on gender.

According to Table 6, there was a significant relationship between the duration of electrical stimulation sessions and reduced depression symptoms in patients with depression, based on gender. And the results of the current study indicated that stimulation was more effective on females than males (13).

Third hypothesis: There is a significant relationship between the duration of electrical stimulation course and reduced depression symptoms in patients with depression.

According to Table 6, there was a significant relationship between the duration of electrical current flow and depression symptoms in patients with depression and it was consistent with the results of the current study (14); the frequency and intensity of stimulation were greater in patients with depression and had similar effects on depression relief.

Fourth hypothesis: There was a significant relationship between depression symptoms and age.

According to Table 6, the duration of electrical current flow in the brain was associated with the reduction of depression symptoms based on age. No study demonstrated compatibility and incompatibility with the hypothesis.

4.1. Limitations

In most TDCS studies, at least 72 hours were considered between the sessions. The current study fixed the minimum time, but failed to control the maximum intervals between meetings in all subjects.

Given that the current study was on people with depression in Ilam, the generalizability of the results to other cities should be done cautiously.

Inappropriate responses of the subjects and limitations of the Likert scale, including the tendency to respond some items, were noted in some studies.

An attitude toward the tests that researchers used honest operation, commitment to their interest, and fully implementation of them in learning were out of the authors' will and control.

The time limit was less than 6 months.

4.2. Suggestions

Future studies should be conducted on the role of some other methods to treat patients with depression.

It was suggested that similar studies with larger sample sizes be conducted to facilitate the generalization of more comprehensive and reliable results.

It was suggested that future studies be conducted in the other cities of Ilam Province and results of different cities compared, and the effect of environmental factors introduced.

It was suggested that the results of the current study be provided to counselling centers, institutes, universities, and other institutions dealing with family affairs for the practical application.

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