INFLUENCE OF TRANSCRANIAL DIRECT CURRENT STIMULATION ON DEPRESSION IN STROKE PATIENT

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Abstract

Background: The aim of this work was to investigate the influence of transcranial direct current stimulation (TDCS) on improving depression in stroke patients. **Subjects and Methods:** forty hemiparetic stroke patients from both sexes represent the sample of this study. The patients' ages ranged from 45 to 60 years with a mean value of 55.475 ± 4.01 years. Patients were assigned randomly into two groups equal in number; the study group A and the control group B. The study group A treated by the prescribed medications for depression as the control group B in addition to transcranial direct current stimulation for 30 minutes, three times per week for one month in addition to physical therapy program. The control group B treated by the prescribed medication only and sham transcranial direct current stimulation in addition to physical therapy program. Depression was evaluated by Hamilton Depression scale pre and post treatment in both groups and quality of life was evaluated by The Stroke Specific Quality Of Life scale. **Results:** results of this study revealed a significant improvement in all different parameters in study group A $P \leq 0.05$; over the control group B. Comparison of post treatment results of both groups showed that transcranial direct current stimulation used in study group A showed significant improvement in post stroke depression and Stroke Specific Quality Of Life than group B. **Conclusion:** transcranial direct current stimulation has significant effect on treatment of depression and Stroke Specific Quality Of Life in stroke patients.

Key words*:* Depression, Quality Of Life, Stroke, Transcranial direct current stimulation.

INTRODUCTION

Stroke patients experience many mental and functional problems. depression is the most frequent psychiatric disorder following ischemic stroke due to long-term disability and loss of motor and cognitive functions caused by brain damage. Depression negatively affects survivals' functional outcome, response to rehabilitation and quality of life. Approximately, one-third of Stroke patients manifested post-stroke depression (PSD), making it a serious social and public health problem. However, a

two-way association between depression and stroke has been also established: stroke increases the risk of PSD, but depression is an independent risk factor for stroke **(1).**

Major depression is a common psychiatric disease with a lifetime prevalence of about 15% and a 12-month prevalence of about 7% **(2)** that generates a large socio-economic burden. Although antidepressant drug treatment has improved during the last decades, symptoms in about 20% of the patients are not in remission two years after initiation of pharmacological intervention A review based on 10 prospective longitudinal studies, observed a biphasic pattern, with a rise in depressive symptoms within the first six months, a slight drop at about one year and a new increase within the second year after stroke **(3).**

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation modality that has been increasingly used for major depressive disorder (MDD) treatment **(4)**. It is a painless corticomotor modulator technique with no or minimal side effects and it can be applied by an inexpensive battery-operated device **(5 - 6).**

Non-invasive brain stimulation methods, including transcranial direct current stimulation (tDCS), have emerged as promising new interventions for the treatment of neuropsychiatric disorders and enhancement of cognitive functions. TDCS involves the application of a small direct electrical current to the brain usually through two electrodes that are placed upon the scalp. TDCS antidepressant effects were first observed in controlled trials conducted in the 1960s and 1970s **(7).**

Several characteristics (such as noninvasiveness, absence of pharmacokinetics interactions, safety, tolerability, and low-cost) make tDCS an interesting tool to be used in the treatment of psychiatric disorders **(8)**.

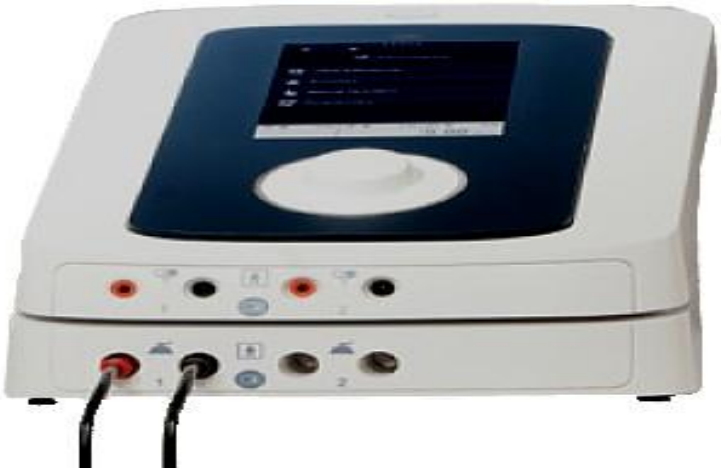
SUBJECTS AND METHODS

Study design: Patients were selected from outpatient clinic of Faculty of Physical Therapy, Cairo University in the period between November 2017 to September 2018. Patients ages ranged from 45 to 60 years old. Patients were medically stable, oriented and follow commands. All patients diagnosed as having a stroke based on careful clinical assessment by neurologist and radiological investigations including computed tomography and / or magnetic resonance imaging of the brain. Also patients diagnosed with having depression based on examination by Psychiatrist.

The patients were divided randomly by closed envelop method into two groups equal in number (20 each); (Group A) was the study group that was treated by Traditional physical therapy in addition to Transcranial direct current stimulation and (Group B) was the control group that was treated by the traditional physical therapy with sham transcranial direct current stimulation.

Participants; The patients recruited to this study were diagnosed by computed tomography (CT) or magnetic resonance imaging (MRI), and were admitted to the rehabilitation center for department of Neuromuscular disorders and its surgery in faculty of physical therapy Cairo University for four weeks between November 2017 to September 2018. Subjects were excluded for any of the following criteria: Blindness, sickness or language defects that may impair patient`s cooperation, Epilepsy or abnormal electroencephalography (E.E.G), Previous brain surgery, Skin irritation and Metallic implanted within the brain. This study was approved by the faculty of physical therapy Cairo University Institutional Review Board. The final group of participants consisted of patients who were confirmed to be depressed, understood the purpose of our study, and provided their written consent. The 40

patients selected based on these criteria were divided into two groups (containing 20 patients each): an experimental group that would receive conventional physical therapy and tDCS, and a control group that would receive conventional physical therapy and sham tDCS. The participants were divided according to the closed envelop method, The tDCS protocol involved generating a direct current using FDA-approved batteries (Phoresor® PM 850 (Phoresor® II Auto Model No. PM 850, IOMED,Inc.,SaltLake City, USA)).



Measurements procedures: The Hamilton Depression scale (HDS); This observer-rating scale was designed in 1957 and a preliminary report published 3 years later. The primary outcome measure for depression evaluation was Hamilton depression scale. Participants were evaluated at base line, and one month after trial completion. Each participant was rated by psychiatrist throughout the study using the Hamilton depression scale. This study targeted patients with severe depression.

The Stroke-Specific Quality of Life (SS-QOL) developed by Williams et al. **(9)** was used to investigate QOL.

Treatment procedures: According to the International 10–20 system, the anode was wrapped in straps and attached to the left dorsolateral prefrontal cortex (DLPFC), while the cathode was attached in the same manner to the right DLPFC.

The experimental group received tDCS applied at 2 mA 12 times over the course of four weeks (three times a week), for 30 minutes during each session based on the stability study by **Bueno et al., (10).** In the control group, the anode and cathode positions were the same as in the experimental group; however, the stimulation was stopped 30 seconds after the application without letting the participants know until 30 minutes elapsed.

Data analysis: The mean and standard deviation of all scores in the two groups were calculated using descriptive statistics. The difference between scores measured before and after treatment was determined using a paired t-test. The statistical significance level (α) was set at 0.05. All statistical tests were performed using SPSS v22.0.

RESULTS

Table 1. The general characteristics of the subjects (N=40)

Categories	Items	Experimental group		Control group	
		N	%	N	%
Gender	Male	15	75	16	80
	Female	5	25	4	20
Paretic side	Left	13	65.0	13	65.0
	Right	7	35.0	7	35.0
Cause of disease	Cerebral infarction	12	60	13	65.0
	Cerebral hemorrhage	8	40	7	35.0
Time since stroke (month)		14.5 ± 5.3		14.6 ± 5.1	
Age (years)		54.60 ±4.06		56.35 ± 3.87	

The mean values of Hamilton Depression scale in experimental group (GA) pre treatment was 15.3± 3.82 and post treatment it decreased significantly to 11.9 ± 4.87, t-value was 6.24 and p value was 0.000. The mean values of Hamilton Depression scale in control group (GB) pre-treatment was 15.45± 2.70 and post treatment it improved non significantly to 15.25 ±3.32, t-value was 0.44 and p value was 0.66.

The mean values of Stroke Specific Quality of Life Scale in experimental group (GA) pre-treatment was 123.50 ±18.98 and post treatment it improved significantly to 144.70 ±27.77, t-value was 5.33 and p value was 0.000. The mean values of Stroke Specific Quality of Life Scale in control group (GB) pre-treatment

was 121.05 ±16.21 and post treatment it improved non-significantly to 124.05 ±18.44, t-value was 1.21 and p value was 0.243.

***Table (2)**: Comparison of the mean values of Hamilton Depression scale in both groups before and after treatment*

Descriptive results	Hamilton Depression scale			
	G1		G2	
	Pre treatment	Post treatment	Pre treatment	Post treatment
Mean ± SD	**15.3 ± 3.82**	**11.9 ±4.87**	**15.45 ±2.70**	**15.25 ±3.32**
t-value	**6.24**		**0.44**	
p value	**.000****		**.66**	

SD: standard deviation P > 0.05 = Non-significant

P ≤ 0.05 = significant* P ≤ 0.01 = highly significant**

***Table (3):** Comparison of mean values of Stroke Specific Quality of Life Scale in both groups' before and after treatment:*

Descriptive results	Stroke Specific Quality of Life Scale			
	G1		G2	
	Pre treatment	Post treatment	Pre treatment	Post treatment
Mean ± SD	**123.50 ±18.98**	**144.70 ±27.77**	**121.05 ±16.21**	**124.05 ±18.44**
t-value	**5.33**		**1.21**	
p value	**.000****		**.243**	

SD: standard deviation | P > 0.05 = Non-significant

P ≤ 0.05 = significant* | P ≤ 0.01 = highly significant**

DISCUSSION

The current study aimed at evaluating the effectiveness of transcranial direct current stimulation (tDCS) used to reduce symptoms in stroke patients with depressive disorders. Researchers gradually try to invent methods that did not need systemic convulsions, but only stimulate focal points in the cortex and thus treat depression.

The current study results revealed that tDCS intervention caused a significant decrease in depression levels in the experimental group. The anode stimulation is known to increase the excitability of cerebral cortex and enhance awareness, while the cathode stimulation is known to suppress the excitability of the cerebral cortex and make the subject quieter and passive **(11)**. Based on these observations, it can be assumed that the decrease in depression levels was caused by the enhancement of awareness resulting from the increase in brain activity in patients with stroke. The current study findings are in line with those observed by **(2),** who used 10 applications of tDCS to the DLPFC of 23 stroke survivors with aphasia and found that their depressive symptoms decreased after four weeks.

In addition to the improvement in depression symptoms, the current study found a significant increase in the QOL of the experimental group. This result is similar to that of the study by **Viana et al. (12)** in which an experimental group (n=10) received virtual reality therapy (VRT) as well as tDCS, while the control group (n=10) received VRT and false tDCS. The authors reported significant improvement in the QOL as well as upper limb function in the experimental group.

The current study is significant as it confirms that tDCS, a method to increase brain plasticity in patients with decreased QOL, improves depression and QOL in stroke survivors with depression. Moreover, the current study results indicate that tDCS can be effectively applied in the patients' depression treatment in order to improve their QOL.

All methodology in the present study was based on the same relatively simple administration of the tDCS electrode montage (see methodology) **(13)**. The previous electrode montage was based on the experiments in Göttingen, Germany (Nitsche and Paulus) in the early 2000's that physiologically established the excitatory and inhibitory effects of anodal and cathodal tDCS. Presently, this arrangement with two relatively large electrodes can be considered prototypical **(14),** and modeling has shown that the resulting distribution of electric field in the brain is not focal **(15).** However, low focality is not necessarily a problem for application in clinical syndromes, where modulation of altered excitability in larger regions might be preferable, or where the intended effects are thought to originate from an interaction of task - and stimulation- generated activity alternations **(16).** While the simplicity and subsequently low focality of the stimulation can be criticized, the simplicity can also be regarded as advantageous. The most appealing points of tDCS are the relative ease of administration and thereby low administration costs **(17, 18),** high safety **(19),** and the potential for effects that endure for some time after the stimulation **(20, 21).** While working towards improving the method through more focal stimulation, more accurate targeting and more sophisticated stimulation devices, these aspects should be preserved if possible. For example, evidence from computational models suggests that individual differences in anatomy may affect the distribution of electric field in the

brain, and that a uniform dose for all patients may not be the most efficient procedure **(22).**

The current study results came in agreement with the results of **(23)** who announced that repeated sessions of active tDCS do not result in cognitive impairment compared to placebo tDCS in patients with depression; on the contrary, they appear able to improve one aspect of cognitive function working memory. This cognitive enhancement was not observed after sham tDCS and was not correlated with mood effects. This is in line with a previous study that showed an enhancement of working memory after a single session of tDCS of the left DLPFC in healthy subjects**.** In addition, they showed no correlation between mood improvement and cognitive improvement, suggesting that independent mechanisms were responsible for cognitive and mood changes **(23).**

The current study has two limitations: 1) the results are difficult to generalize due to the small sample size, and 2) other factors influencing QOL have not been investigated. Therefore, future studies should investigate a larger number patient in order to allow generalization of the results and conduct continuous research on depression and improvement in QOL in patients with stroke.

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المستخلص

أجريت هذه الدراسة بهدف معرفة تاثير التنبيه بالتيار الكهربي المباشر عبر الجمجمه في علاج الاكتئاب بمرضي السكته الدماغيه لدى اربعون مريضا من مرضى الشلل النصفى التقلصى متوسط اعمارهم ٥٥.٤٧٥ ± ٤.٠١ عاما.وقد اختيروا وقسموا عشواءيا إلى مجموعتين متساويتين في العدد (مجموعة دراسة ومجموعة ضابطة وقد تم تقييمهم قبل وبعد العلاج عن طريق تقييم الاكتئاب بمقياس استبيان هاميلتون للإكتئاب وكذلك تقييم معدل التحسن في كفاءة الحياة باستبيان تحسن كفاءة الحياة لمرضى السكته الدماغيه. وقد تلقت المجموعتين العلاج الدوائي الخاص بعلاج الاكتئاب. وقد تلقت مجموعة الدراسة بالإضافة للعلاج الدوائي الخاص بعلاج الاكتئاب تنبيها بجهاز التنبيه بالتيار الكهربي المباشر عبر الجمجمه بالاضافه الي برنامج علاج طبيعي مختار بينما تلقت المجموعه الضابطه نفس العلاج الدوائي و برنامج العلاج الطبيعي المختار مع جهاز التنبيه الكهربي المباشر عبر الجمجمه بدون عمل . واستمر علاج المجموعتين مدة شهر واحد بمعدل ثلاث جلسات أسبوعيا. وقد أوضحت نتائج الدراسة وجود تحسن اكلينيكى ملحوظ فى مجموعة الدراسة مع وجود فارق ذو دلالة احصائية فى مجموعة الدراسة عن المجموعة الضابطة. وقد استنتج من هذه الدراسة أنه يمكن استخدام التنبيه بالتيار الكهربي المباشر عبر الجمجمه في علاج الاكتئاب بمرضي السكته الدماغيه كعلاج مباشر لعلاج الاكتئاب حيث أنه يساعد على تحسن كفاءة الحياة لمرضى السكته الدماغيه.

الكلمات الدالة: السكته الدماغيه –التنبيه بالتيار الكهربي عبر الجمجمه – الاكتئاب – كفاءة الحياة.