Journal of Advances in Medicine and Medical Research

24(3): 1-8, 2017; Article no.JAMMR.36905
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

The Effect of Simultaneous Transcranial Direct Current Stimulation and Speech Therapy Treatment in Stroke Patients with Aphasia

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Authors' contributions

This work was carried out in collaboration between the two authors. Author KP designed the study, performed the statistical analysis, wrote the protocol and the first draft of the manuscript. Author VG managed the statistical analyses of the study and the literature searches in collaboration with author KP. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2017/36905
Editor(s):
(1) Thomas I. Nathaniel, University of South Carolina, School of Medicine-Greenville, Greenville, USA.
Reviewers:
(1) Badr E. Mostafa, Ain-Shams University, Egypt.
(2) Eliton da Silva Vasconcelos, Federal University of São Carlos – UFSCar, Brazil.
Complete Peer review History: http://www.sciencedomain.org/review-history/21516

Original Research Article

Received 22nd September 2017
Accepted 17th October 2017
Published 23rd October 2017

ABSTRACT

Transcranial direct current stimulation (tDCS) is a neuromodulating technique for the treatment of speech disorders after stroke in patients with aphasia. In the current study we examined the effect of tDCS over inferior frontal gyrus area in twelve aphasic male patients. We evaluated the accuracy of picture naming before and after the completion of anodal tDCS (2 mA, 20 min) stimulation during speech therapy, compared to tDCS and speech therapy taking place at different times and to the control group that only followed speech therapy. The post-treatment values of picture naming (14.96 ± 2.41) after simultaneous treatment with tDCS and speech therapy in the same therapeutic session, were statistically improved compared to the double treatment at different times (12.81 ± 2.12, p=0.04) and to speech therapy group (10.98±1.76, p=0.03), however, no statistical significance was recorded in post-treatment values between double treatment at different time group and speech therapy group (12.81 ± 2.12 vs 10.98±1.76 respectively, p=0.06). Simultaneous therapeutic session with tDCS and speech therapy can be used as a safe and effective interventional method, in place of the conventional speech-language therapy, for the treatment of aphasic patients following a stroke.

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Keywords: Transcranial direct current stimulation; aphasia; stroke; rehabilitation.

1. INTRODUCTION

Transcranial Direct Current Stimulation (tDCS) is a a neuromodulating technique for therapeutic use, that changes spontaneous neuronal activity through a weak - in intensity - direct current delivered on the scalp by superficial electrodes, inducing immediate and prolonged functional effects in the brain [1]. The stimulating electrode is placed over the area of interest and the reference electrode can be placed on the scalp or on a different body part, usually the right arm [2,3]. The scientific community considers tDCS safe, inducing no major adverse effects [4-6].

The physiological mechanisms during stimulation are probably different from those responsible for long-lasting effects [7-15]. The tDCS effect during stimulation is induced by modulation of the resting membrane potential, while the long-lasting effects can be explained by multiple mechanisms, primarily the induction of long-term potentiation and depression [16-20]. Pharmacological studies show that using a NMDA-receptor antagonist, the long-lasting effects of tDCS are abolished and that other drugs acting on neuronal transmitters (such as GABAergic, dopaminergic, cholinergic) modificate the tDCS effect [21]. Direct current electrical stimulation could also change the protein synthesis [22] the calcium neuronal influx [23,24], the shape of cytoskeleton [25], the blood flow [26], the level of brain oxygenation [26] and locally the pH [27].

Some of the advantages of tDCS compared to Transcranial Magnetic Stimulation (TMS) are the lower cost, ease of use, and the presence of portable systems [28,29]. The low focality of tDCS can represent a further advantage over TMS, because larger brain areas are targeted when tDCS is applied for therapeutic purposes without using expensive and time-consuming targeting procedures required for TMS (neuronavigation). Finally, since the electrodes can be easily secured to the scalp and leave the patient free to move, tDCS can be delivered while patients engage in a task or during rehabilitation procedures [29] (for example speech therapy as used in the current study).

Aphasia is a combination of speech and language disorder caused by damage to the brain [30,31]. Approximately 21% to 38% of acute stroke patients suffer from aphasia, which is typically associated with high mortality, significant motor impairment, and severe limitations in social participation [32,33]. The traditional speech and language therapy (SLT) for aphasia is predominately based on compensatory strategies or training for lost functions [31].

The aim of the current study is to assess the effect of simultaneous treatment of tDCS and speech/language therapy in the same therapeutic session, compared to the effect of the same interventions undergone in different therapeutic sessions, in patients with chronic post-stroke aphasia. The direct current stimulation was applied over the damaged left inferior frontal gyrus areas in right handed patients with chronic post-stroke aphasia. For the evaluation of the intervention, was used a computer-controlled picture naming task before and after anodal tDCS and speech/language therapy. Additionally, control patients were evaluated in the same task, before and after the intervention of speech/language therapy.

2. MATERIALS AND METHODS

2.1 Participants

Twelve chronic stroke patients (aged 63.47±5.81 years, range 57-68 years, all males) with aphasia participated in the current study. Seven of the twelve patients had non-fluent aphasia, while the remaining five had fluent aphasia. All participants were enrolled at least 6 months after the onset of aphasia due to a stroke. The inclusion criteria for the study were the following: native Greek speakers, right handed before the stroke, single first-ever left hemispheric stroke, and primarily clinically diagnosed with aphasia. Prior to the final participation in the study, all patients were evaluated by the same professional speech therapist to determine the type and the severity of aphasia. The exclusion criteria included history of seizure and implanted metal object, as these are main contraindications relevant to tDCS [34]. We also excluded patients who had severely impaired auditory-verbal comprehension or other neurological diseases such as dementia, and those who were uncooperative with speech therapy. The study was conducted between April 2016 and May 2017 at Filoktitis Rehabilitation Center (Koropi-Attica, Greece), where the participants underwent a complete neuropsychological evaluation, including a shorter version of Token Test [35] and a

standard language examination currently used at the neurological rehabilitation unit of the center. Participants with severely impaired auditory verbal comprehension (Token Test < 8) [36], were excluded. Table 1 summarizes the patients' stroke characteristics. In a double-blind manner, patients were randomized and divided into 3 groups. Besides the study coordinator (first author) who performed the tDCS treatments, the speech therapist and all patients were blinded to the randomization process and the experimental procedure. The study was designed as a randomized, double-blind cross-over study.

2.2 Picture Naming Task

For every picture naming session, participants were asked to name pictures presented on a computer screen from one out of six lists (A-F). For the accuracy of naming (the number of picture correctly named in a 20-items list), was given score 1 for a correct response and 0 for an incorrect, ranging between 1-20. The items lists were homogeneous for difficulties and were controlled for frequency of use, familiarity, visual complexity, grammatical class and syllable length. Each participant was examined in different lists before and after the completion of the treatment protocol.

2.3 tDCS Treatment

tDCS (2 mA, 20 min) was delivered by a constant current electrical stimulator (Soterix Medical NY, USA) connected to a pair of using saline-soaked sponge electrodes (5 cm^2). The active anodal electrode was placed over the left inferior frontal gyrus areas. For the purpose of the current study, the international 10-20 electroencephalogram (EEG) system was used to locate the inferior frontal gyrus area. According to the 10-20 EEG system, the left inferior frontal gyrus area is defined as F7 [37] and the reference electrode was placed on the right shoulder of the patients. Participants underwent a total of five daily sessions, and were evaluated before and immediately after the completion of the treatment. All tDCS sessions, in all patients, were performed by the same, well experienced, medical specialist (K.P.).

2.4 Speech-language Therapy

During the study, each patient underwent speech-language therapy for 20 minutes per day, 5 times per week, and it was conducted one on one by the same speech therapist. The speech-language program was formulated based on each patient's aphasic severity, which was evaluated after stroke at his admission to the rehabilitation center and included free talk, corrections of mistakes in pronunciation, and the phonetic annotation of Greek characters.

2.5 Group 1

Patients were assigned randomly to group 1 (4 participants) and underwent anodal tDCS over the left inferior frontal gyrus area simultaneously with language/speech therapy in the same therapeutic session (total time duration 20 minutes). The participants and the speech therapist were blinded regarding the type of electrical stimulation and the aim of the study. For each naming session the accuracy in naming 20 pictures from one list, randomly selected out of six homogeneous lists, before and after double treatment, was measured. Each participant did not receive the same list twice during the study.

2.6 Group 2

Patients were assigned randomly to group 2 (4 participants) and underwent anodal tDCS over the left inferior frontal gyrus area and language-speech therapy in different therapeutic sessions during the same day. The first session to take place was speech therapy (20 minutes duration) and after an interval of 60 minutes, patients underwent the tDCS treatment (20 minutes duration). The participants and the speech therapist were blinded regarding the type of electrical stimulation and the aim of the study. Similarly to the first group, for each naming session the accuracy in naming 20 pictures from one list, randomly selected out of six homogeneous lists, before and after treatment was measured. Each participant did not receive the same list twice during the study.

2.7 Control Group

Patients were assigned randomly to control group (4 participants) and underwent only language/speech therapy for a total of 5 therapeutic sessions (20 minutes duration for each single session). The participants and the speech therapist were blinded regarding the aim of the study. Similarly to the previous 2 groups, for each naming session the accuracy in naming 20 pictures from one list, randomly selected out of six homogeneous lists, before and after treatment was measured. Each participant did not receive the same list twice during the study.

Table 1. Patients' stroke characteristics

Patient	Gender (M:male)	Duration of aphasia (months)	Brain lesion	Type of aphasia
1	M	7	left middle cerebral artery infarction	Broca
2	M	6	left basal ganglia infarction	Broca
3	M	8	left middle cerebral artery infarction	Anomic
4	M	6	left basal ganglia infarction	Transcortical motor
5	M	9	left basal ganglia intracerebral hemorrhage	Broca
6	M	7	left basal ganglia infarction	Anomic
7	M	8	left middle cerebral artery infarction	Anomic
8	M	6	left basal ganglia infarction	Broca
9	M	6	left basal ganglia intracerebral hemorrhage	Transcortical motor
10	M	7	left basal ganglia intracerebral hemorrhage	Broca
11	M	7	left middle cerebral artery infarction	Anomic
12	M	6	left middle cerebral artery infarction	Anomic

2.8 Ethical Approval

The protocol approval was obtained from the clinical human research and ethical review committee at the Kapodestrian University of Athens, School of Medicine (Athens, Greece). The purpose of the current study, potential benefits and/or risks, inconveniences, and the participants' rights and responsibilities were explained in detail to the patients and their family members. After reading the consent form to the participants and family members, a written informed consent (in accordance with the current revision of the Declaration of Helsinki) was obtained from every participant.

2.9 Data Analysis

All analyses were performed using the software package SPSS version 20.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test revealed that the data were not normally distributed in the present study. For this reason, Wilcoxon signed-rank tests were used to evaluate the differences between accuracy naming before and after therapeutic intervention for each experimental group. Baseline values of all groups were analyzed using the Mann-Whitney U test. Statistical significance was considered to be at a level of p=.05.

3. RESULTS

None of the participants reported severe adverse effects during or after the electrical stimulation, and they all tolerated the tDCS without interrupting the procedure.

Before the treatment (baseline values) there was no statistical difference between the groups in terms of age (1st group 61.12 years, 2nd group 64.32 years and control group 62.18 years, p=0.06) and time of the onset of aphasia (1st group 6.28 months vs 2nd group 7.12 months vs control group 6.17 months, p=0.07).

Baseline values (before treatment) in all three groups did not differ statistically (1st group 11.08±2.13, 2nd group 10.92±1.85, control group 10.67±2.04, p=0.75). Statistical analysis indicated a statistically significant difference between the baseline and post treatment values in groups 1 and 2, where group 1 (baseline 11.08±2.13, post 14.96 ± 2.41, p=0.03) and group 2 (baseline 10.92±1.85, post 12.81 ± 2.12, p=0.04). The statistical analysis in the control group indicated a non statistical significance in pre and post-treatment values in the accuracy in naming (before 10.67±2.04, after 10.98± 1.76, p=0.99). The post-treatment values of picture naming (14.96 ± 2.41) in the first group were statistically improved compared to the second

group (12.81 ± 2.12, p=0.04) and to the control group (10.98±1.76, p=0.03), meanwhile there was not recorded any statistical significance in post-treatment values between group 2 and the control group (12.81 ± 2.12 vs 10.98±1.76 respectively, p=0.06).

4. DISCUSSION

The current study confirmed the positive effect of tDCS on the treatment of stroke patients with aphasia, where the simultaneous therapeutic session with tDCS and speech therapy cause the biggest improvement in naming accuracy of the patients. In accordance with previous studies [38-43], the tDCS provoked a statistically significant improvement in language recovery, without presence of severe adverse effects. For the purpose of the current research, we used an extracephalic (arm) reference electrode, avoiding confusion regarding the source of the observed effect [44]. We investigated the effect of the simultaneous therapeutic procedure of anodal tDCS over the left inferior frontal gyrus area and speech/language therapy in post stroke aphasic patients and compared the results with those of anodal tDCS combined, at different time on the same day, with daily speech/language therapy, and those participants who underwent only speech/language therapy. Our results demonstrated that the naming accuracy scores were significantly higher after the simultaneous therapeutic procedure with tDCS and speech/language therapy, compared to the other experimental procedures. In both groups 1 and 2, the post-treatment naming accuracy was improved within a short time of 5 therapeutic days, indicating the significant role of transcranial direct current stimulation in aphasia's rehabilitation. The current consensus is that two main mechanisms are involved in the recovery from aphasia [45,46]. First, in patients with relatively small lesions in the left hemisphere, the recruitment of perilesional cortical neuronal elements plays a critical role in the recovery from aphasia after stroke. Various functional magnetic resonance imaging studies [47,48] have previously demonstrated that greater activation in the left hemisphere is associated with a better outcome for language recovery [45-48]. Thus, the enhancement of the excitability of the left language-related cortical regions by non-invasive brain stimulation may improve recovery from aphasia [42].

In the current study, both simultaneous tDCS/speech therapy sessions (group 1) and tDCS intervention combined with speech therapy sessions at different time (group 2) provoked an improvement in naming accuracy with no severe adverse effects, which suggests that both methods can be used as effective therapeutic tools to enhance language function in patients with chronic post-stroke aphasia. However, the simultaneous tDCS/speech therapy (group 1) brought about greater improvement in naming accuracy than the rest 2 groups. Therefore, the simultaneous tDCS/speech therapy contributed to a greater activation in the left hemisphere, in association with a better outcome in language recovery.

The patients included in the current study varied with respect to the subtypes of aphasia, lesion location, and the extent of brain damage. Regardless of the type of aphasia, the role of the left frontal cortex in its recovery has been demonstrated as in previous studies [47,48]. A previous functional magnetic resonance imaging study revealed that the activation of the left frontal cortex was correlated with the naming accuracy in stroke patients with aphasia [49]. Furthermore, increasing the excitability of the left frontal cortex using tDCS improved naming accuracy, irrespective of the subtype of the aphasia, and the extent of the stroke lesion [7]. The results from our study are consistent with previous reports and confirm that the activation of the left frontal cortex, particularly the left inferior frontal gyrus area, improves naming ability in various types of aphasia [47,48]. The traditional speech and language therapy for aphasia is predominately based on compensatory strategies or training for lost functions [49]. However, the results did not demonstrate any significant change in the naming accuracy after speech therapy. The short experimental period of 5 days could be a reasonable answer for the relative stability in the naming accuracy progress. It seems that the simultaneous activation, via transcranial direct current stimulation and speech therapy, of the corresponding speech areas provokes better results in the rehabilitation of the stroke patients with aphasia.

The current study has several limitations, however. First, the excitability of the stimulated cortical area was not examined directly (for example, via functional imaging techniques). Second, the population was relatively small and heterogeneous, and thus, it was not possible to evaluate the effects relative to specific brain lesions or subtypes of aphasia. Third, we did not

consider the type of sham activation in the experimental protocol, because of the already existing complexity of the procedure. Finally, the long-term effect (follow-up) of the experimental interventions was not examined, in order to evaluate additional positive effects in speech recovery. Further studies on the cumulative and long-term effects of simultaneous tDCS/speech therapy sessions are required for appropriate daily clinical application.

5. CONCLUSION

In conclusion, we consider that simultaneous therapeutic session with tDCS and speech therapy can be used as a safe and effective interventional method, in place of the conventional speech-language therapy, for the treatment of aphasic patients following a stroke, in absence of contraindications for tDCS use.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

ACKNOWLEDGEMENTS

The current study was funded by the State Scholarships Foundation (IKY) Fellowships of Excellence for PostDoc Studies in Greece–Siemens Program, in the framework of the Hellenic Republic–Siemens Settlement Agreement.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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