Transcranial Direct Current Stimulation Effect on Demented Patients

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Abstract

Background: Elderly individuals with dementia are susceptible to a decline in physical functioning and activities of daily living that leads to a decline in their mobility and participation in life.

Aim of Study: To investigate the effectiveness of transcranial Direct Current Stimulation (tDCS) on improving mobility in patients with dementia.

Material and Methods: A double-blinded, randomized, sham-controlled trial was conducted and approved by the Institutional Review Board of the Faculty of Physical Therapy, Cairo University, Egypt. The study setting was the outpatient clinic of dementia, Kasr Al-Ainy Hospital, Faculty of Medicine, Cairo University, Cairo, Egypt. Participants were 29 demented patients randomly divided into two groups; intervention (n=16; mean age 62.98 ± 10.11 years) and sham (n=13, mean age 60.23 ± 7.57 years) groups.

Intervention was one 20 minutes session of active or sham tDCS. Patients in the intervention group received active tDCS for 20 minutes by applying an intensity of (2mA) using a montage with the cathode over site Pz and the anode over site AF4. Patients in the sham group received a sham tDCS for 20 minutes as well; however, the current was ramped up to 1mA and remain constant for 30 seconds before ramping down. Outcome measures used were the Timed Up and Go test (TUG) and the 10 Meter Walk Test (10MWT). Outcome measures were recorded before (pre-stimulation) and after interventions (post-stimulation) for all participants in both groups.

Results: Post-stimulation, a statistically significant change in both of the TUG and 10MWT (p<0.05) was detected only in the intervention group. No serious adverse effects were reported in either group.

Conclusion: The transcranial direct current stimulation can enhance motor function in demented patients. Because the transcranial direct current stimulation is a non-invasive therapeutic method, it can be suggested as a useful tool to improve locomotor performance in patients with dementia.

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Key Words: Non-invasive brain stimulation – Transcranial direct current stimulation – Dementia – Mobility.

Introduction

DEMENTIA is used to describe a collection of symptoms including memory loss, problems with reasoning and communication, and a reduction in a person's ability to carry out daily activities [1]. Impairments of cognitive function and mobility are commonly found in aging [2]. More than 47 million people worldwide were affected by dementia in 2015. By the year 2030, people living with dementia is estimated to be more than 75 million [3]. In Egypt, dementia prevalence ranged from 2.01% to 5.07% [4].

People with dementia may experience difficulties in interacting with their physical and social environments [5]. Multifactorial causes of mobility decline in dementia might include but are not limited to; cerebrovascular disease, neurodegenerative changes, and age-related musculoskeletal and/or sensory changes. Other factors contributing to mobility deficits in this population include cognitive changes and behavioral symptoms associated with dementia [6]. Because pharmacologic treatments may increase the risk of adverse effects, research is increasingly becoming interested in non-pharmacologic interventions that target central nervous system pain processing [7].

Mild Cognitive Impairment (MCI) is defined as the stage between normal and dementia-type pathological aging [8]. In MCI, cognitive change is greater than expected for age but independence in the community, and activities of daily living are preserved [9]. People with MCI have a high risk of progression to dementia [10].
Modulating the activity of the brain network with transcranial Direct Current Stimulation (tDCS) appears to be one of the potential treatment approaches for improving cognitive symptoms in Mild Cognitive Impairment (MCI) and dementia [11]. tDCS is a safe, non-invasive, and portable brain stimulation technique capable of altering the excitability of targeted brain areas through changing neuronal membrane potentials according to the polarity of the current transmitted through the scalp by using sponge electrodes [12]. tDCS uses sub-threshold electrical currents and ground their potential on the capability of shifting intrinsic neuronal excitability rather than eliciting neuronal firing [13]. Anodal (positive) stimulation increases cortical excitability in the stimulated brain area while cathodal (negative) stimulation decreases it.

It was reported that one session of tDCS improves mobility in young and old adults, [14] and reduces the dual-task costs to gait and postural control if tested immediately following stimulation [15]. Up to our knowledge, limited studies are investigating the influence of tDCS on mobility in demented people. Therefore, this study was conducted to investigate the effectiveness of transcranial Direct Current Stimulation (tDCS) on improving mobility in patients with dementia. Based on the study of Hampstead BM et al. 2014, [16] their study suggested that the tDCS application using Pz-F4+ montage may be preferable in patients with MCI and mild dementia. Therefore, this study was designed to investigate the effectiveness of tDCS on improving mobility in patients with dementia.

Patients and Methods

Study design:

A prospective, randomized, double-blinded, sham-controlled Pre-post Clinical Trial (RCT) was conducted at the outpatient clinic of Dementia, Kasr Al-Ainy, Cairo University, Cairo, Egypt between the period of February 2018 to February 2020. The study was approved by the Ethics Committee of the Faculty of Physical Therapy, Cairo University (P.T.REC/012/001892), and conform to the principles of the Declaration of Helsinki.

Participants:

119 patients were screened for study eligibility Fig. (1). Only 29 patients (intervention group n=16, sham group n=13) with dementia, from both genders, fulfilled the inclusion criteria and randomly assigned into two groups and completed the study. All participants were diagnosed and referred by a neurologist. Patients were recruited from the out

patient clinic of Dementia in Kasr Al-Aini Hospital, Faculty of Medicine, Cairo University.

The selection of patients was based on careful history taking and neurological examination conducted by a neurologist. Patients who had the following criteria were included in the study; diagnosed as dementia or mild cognitive impairment, age more than 40 years of age, right-handed individual, independently ambulant, medically stable, have not participated in a previous tDCS experiment, able to follow instructions in Arabic. Patients were excluded if they had any of the following; a history of major neurological conditions or mental illness, patients with moderate to severe pain when walking, severe hearing and/or vision impairment, learning or attentional disorder, drugs and/or alcohol abuse.

Randomization:

Patients were informed by the aim and the procedure of this study with signed informed consent, obtained before their enrollment in the study.
The patients were randomly assigned using excel random number formula into two groups; the intervention group (n=16) who received active tDCS stimulation and the sham group (n=13) who received sham tDCS stimulation Fig. (1).

Blinding:
Double blinding was applied in this work. To ensure blinding of the study team, an expert neurologist, who was blinded to group assignment, administered, and scored the mental status testing. One experienced physical therapist applied the tDCS, navigation tests, and mobility tests throughout the whole study. Further, participants remained blinded to their stimulation group throughout the study.

Assessment procedure:
Patients were evaluated and referred by an expert neurologist. On the baseline, all patients underwent a full battery of evaluation including general clinical assessment: History taking, general medical examination, neurological examination, neurological physical therapy evaluation. Clinical Evaluation of Dementia was done using Montreal Cognitive Assessment (MoCA) and Dementia Rating Scale (DRS).

Outcome measures:
In this work, the pre-stimulation evaluation included patient mobility functions, evaluated by using the Timed Up and Go (TUG) test and the 10 Meter Walk Test (10MWT). The TUG was administered with the patient sitting in a chair with his/her back against the chair back. At the start of the test, the patient rose from the chair, walked a distance of 3 meters at a comfortable speed with or without an assistive device, then turned, and walked back to the chair, and sat down. The timing of the test started at the command “go” and stopped when the patient sat. The scores were recorded in seconds as the time between the command till the buttocks touch the chair. The patient had one practice trial that was not included in the score [17].

In the 10 Meter Walk Test (10MWT) the patient was instructed to walk 10 meters with marks on the ground. Time is measured while the patient walked the set distance. The distance walked is divided by the time in seconds it took the patient to walk that distance. Three trials were collected and the average of the three trials was calculated. The test was performed at the preferred walking speed [18].

The post-stimulation evaluation was performed to each patient in the two groups by the same examiner immediately after completion of the session. The assessment was performed using the same pre-stimulation measures also the patients completed a brief questionnaire about the nature and severity of any adverse effects [19].

Intervention procedures:
All patients in both groups were treated for one-hour of assessment and stimulation in one tDCS session. tDCS stimulation which was performed using a battery-powered constant current stimulator (model #Combi 400V; Gymna Uniphy, Belgium), calibrated direct current stimulation before using in the study. Two 7cm X 5cm rubber electrodes were placed within saline-soaked sponge pads and centered over the target locations using Velcro straps.

Using the 10/20 Electroencephalogram (EEG) system, the cathode electrode over the point (Pz) was placed perpendicular to the midline while the anode electrode over (AF4) was placed parallel to the midline [16]. For the active group stimulation was performed at an intensity of 2mA for 20 minutes, which has been found to modulate cognitive functioning in previous studies [20]. For the sham group however, patients received a sham tDCS as the intervention group except the current was ramped up to 1mA and remained constant for 30s before ramping down and session time lasted also for 20 minutes.

Statistical analysis:
Descriptive statistics and unpaired t-test were conducted for comparison of subject characteristics between both groups. Mann-Whitney U-test was conducted for comparison of DRS between groups Chi-squared test was used for comparison of categorical data between groups. The normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to ensure the homogeneity between groups. Unpaired t-test was conducted to compare the mean values of 10MWT and TUG between groups. Paired t-test was conducted for comparison between pre-and post-stimulation in each group. The level of significance for all statistical tests was set at \( p<0.05 \). All statistical analysis was conducted through the Statistical Package for Social Studies (SPSS) version 22 for windows (IBM SPSS, Chicago, IL, USA).

Results

Subject characteristics:
Table (1) showed the subject characteristics of both the intervention and sham groups. There was
no significant difference between groups in age, MOCA, walking speed, and DRS ($p>0.05$). Also, there was no significant difference in the distribution of sex, diagnosis, and education between groups ($p>0.05$).

**Results of the 10MWT and TUG:**

- **Within-group comparison:** There was a significant increase in 10MWT and a significant decrease in TUG of the intervention group post-treatment ($p<0.01$). However, there was no significant change in 10MWT and TUG in the sham group ($p>0.05$) (Table 2).

- **Between groups comparison:** There was no significant difference in the 10MWT and TUG between both groups pre-treatment ($p>0.05$). A comparison between both intervention and sham groups post-treatment revealed a non-significant difference in 10MWT and TUG ($p>0.05$) (Table 2).

<table>
<thead>
<tr>
<th>Table (1): Comparison of subject characteristics between the intervention group and Sham group.</th>
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<tbody>
<tr>
<td><strong>X ± SD</strong></td>
</tr>
<tr>
<td>---------</td>
</tr>
<tr>
<td><strong>Intervention group</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>MOCA</td>
</tr>
<tr>
<td>Walking speed (m/sec)</td>
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<tr>
<td>DRS, median</td>
</tr>
<tr>
<td>Sex:</td>
</tr>
<tr>
<td>Males</td>
</tr>
<tr>
<td>Females</td>
</tr>
<tr>
<td>Diagnosis, N (%):</td>
</tr>
<tr>
<td>Frontotemporal Dementia (FTD)</td>
</tr>
<tr>
<td>Posterior Cortical Atrophy</td>
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<tr>
<td>Vascular Dementia</td>
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<tr>
<td>Parkinson's Disease</td>
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<tr>
<td>Alzheimer Disease</td>
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<tr>
<td>Others</td>
</tr>
<tr>
<td>Education:</td>
</tr>
<tr>
<td>Illiterate</td>
</tr>
<tr>
<td>Primary</td>
</tr>
<tr>
<td>Preparatory</td>
</tr>
<tr>
<td>Secondary</td>
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<td>University</td>
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</table>

**Table (2): Mean 10MWT and TUG pre-and post-treatment of the intervention and sham groups.**

<table>
<thead>
<tr>
<th>X ± SD</th>
<th>MD</th>
<th>t-value</th>
<th>p-value</th>
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<tbody>
<tr>
<td><strong>10MWT (m/sec):</strong></td>
<td></td>
<td></td>
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<tr>
<td>Pre-treatment</td>
<td>0.9±0.23</td>
<td></td>
<td></td>
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<tr>
<td>Post-treatment</td>
<td>0.98±0.28</td>
<td>1.01±0.</td>
<td>-0.11</td>
</tr>
<tr>
<td>MD</td>
<td>-0.08</td>
<td>1.03±0.</td>
<td></td>
</tr>
<tr>
<td>% of change</td>
<td>8.88</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>t-value</td>
<td>-2.66</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td>p=0.01</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>TUG (sec):</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-treatment</td>
<td>14.46±8.94</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-treatment</td>
<td>14.77±6.8</td>
<td>1.24</td>
<td>-0.84</td>
</tr>
<tr>
<td>MD</td>
<td>12.93</td>
<td>2.14</td>
<td></td>
</tr>
<tr>
<td>% of change</td>
<td>3.84</td>
<td>2.14</td>
<td></td>
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<tr>
<td>t-value</td>
<td></td>
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<td></td>
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<tr>
<td>p=0.002</td>
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</table>

Discussion

This study shows that one session of active tDCS with cathode over Pz and anode over AF4 in MCI and mildly demented subjects had a significant effect on improving mobility functions through the 10MWT and the TUG test with no major adverse effects. Mobility is usually measured by performance on tests such as the 10MWT or the TUG test and can be used as an early marker of a decline in physical activity [21].

The results of improved mobility in this work came in agreement with the findings of Benjamin M. Hampstead et al. 2014. [16] Suggesting tDCS, with the P-F+ montage being most effective in causing polarity-specific neurophysiological effects on the brain regions underlying spatial navigation and thus mobility.

In contrast, Brad Manor et al., 2014 reported tDCS intervention did not induce significant changes in walking speed or TUG performance [22]. This discrepancy in results could be related to the different stimulation parameters (anode placed over the left dorsolateral prefrontal cortex and cathode over the right supraorbital region), small sample size, or including only adults aged ≥65 years which may have caused age-related changes in brain anatomy [22,23].

Improvement of mobility measures of the active tDCS group in this study can be attributed to anodal stimulation over the prefrontal cortex facilitating hippocampal activation and specifically engaging the more posterior regions of the hippocampus that are preserved early in MCI and early dementia patients [16].

Although it is now established that Non-Alzheimer’s (AD) dementia disorders in general, may be associated with a faster decline in physical function compared to both AD and normal cognition [24]. Our population had more FTD per diagnosis subjects in the active (11, 68.8%) than the sham subjects (3, 23.1%). Yet, we were able to have greater increases in the 10MWT distance (0.98±0.28m/sec) than the sham group (1.03±0.4m/sec). While the active tDCS group in the TUG test had a significant decrease (13.93±3.45m/sec) with that pre-treatment (16±5.13m/sec).

After stimulation, participants completed a brief questionnaire about the nature and severity of any adverse effects as recommended by Brunoni et al. [19].

Some limitations were found in the current study. Our study was limited by the small sample size. Trials with larger samples and longer follow-ups are needed to confirm the observed effects of tDCS on mobility functions. Furthermore, difficulty in accurately placing electrodes to improve the localization of tDCS suggests the need to use High Definition (HD) tDCS where a small central electrode positioned over the target is surrounded by 4 return electrodes [25]. Finally, patient compliance and the psychological aspect of the patients and motivation while applying the assessment could also influence the results. Further studies with different dementia levels, variable tDCS montage, intervention duration, and frequency can be recommended.

Conclusion:

Because of the findings of this study, it could be concluded that tDCS in MCI and demented subjects have a significant effect on improving mobility functioning. Further studies with larger samples and longer-term follow-up are needed.

Competing interests: The authors have no competing interests relevant to this article.

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Transcranial Direct Current Stimulation Effect on Demented Patients


تأثير التنبيه الدماغي الغير التداخلي على مرضى الخرف

الخلفية: كبار السن المصابون بالخرف عرضة لانخفاض الاداء البيني والأنشطة اليومية مما يؤدي إلى إخفاض في الحركة والمشاركة.

أهداف الدراسة: دراسة فعالية التنبيه الدماغي الغير التداخلي على تحسن الحركة لدى مرضى الخرف.

المكان: المباني الخارجية للأماكن الخالية بالذكرى والخرف، القصر العيني، جامعة القاهرة، مصر.

المشاركين: 26 مريضاً يعانون من الخرف، تم تقسيمهم بشكل عشوائي إلى مجموعتين: مجموعة علاج نشط (عدد=12) ومجموعة علاج صوري (عدد=14).

الطريقة: تم علاج المرضى في مجموعة العلاج الحقيقي باستخدام التنبيه الدماغي الغير التداخلي لمدة 20 دقيقة باستخدام شدة (2.4 ملي أمبير) باستخدام أسلوب السبل نوع نقطة PZ والموجة فوق نقطة AF4. بينما تلقى المرضى في مجموعة العلاج الصوري التنبيه الدماغي من التدوير كمجموعة تدخل باستخدام التيار المتردد، تصميمه لتمكني المرضى من تطبيقها إلى 1 ملي أمبير وتبديلها تدريجياً لمدة 20 ثانية قبل التوقف وقت الجلسة الذي يستمر أيضاً لمدة 20 دقيقة.

نتائج الدراسة: بعد جلسة واحدة، كانت مجموعة التنبيه الدماغي الفرد التداخلي النشطة لديها زيادة في إختبار مسافة العشرة أمثال من المجموعة الصورية. بينما شهدت مجموعة التنبيه الدماغي الفرد التداخلي النشطة في اختبار الوقوف والجلس إنخفاضاً كبيرًا مع المجموعة الصورية.

الملاحظات: تظهر نتائجنا أن التنبيه الدماغي الفرد التداخلي في ضعف الإدراك المعتدل مرضى الخرف له تأثير كبير على تحسين أداء النتائج. هناك حاجة إلى مزيد من الدراسات مع عينات أكبر ومتتابعة طويلة الأجل.