Research Article

Adverse Effects of Transcranial Direct Current Stimulation (TDCS) in a Group of Psychiatric Patients

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Abstract: Transcranial direct current stimulation (TDCS) is a promising neuromodulatory treatment option in neuropsychiatry. However, such a novel neuromodulation application also brings challenges regarding safety. In this paper, we aimed to provide a retrospective evaluation of adverse effects related to TDCS implementation in a group of psychiatric patients. Twenty-nine patients who were on TDCS with different psychiatric diagnosis were evaluated retrospectively. Occurrence and severity of adverse events monitored with a questionnaire. No subjects experienced seizures or other adverse effects requiring medical intervention. During TDCS an itching sensation was the most common reported adverse effect (48%, n=12) whereas after TDCS fatigue occurred in 32% of cases (n=8). Also one patient reported mild nausea during the first 3 sessions and one patient reported numbness in the electrode area. Transient redness at the site of stimulation was reported by 3 (12%) of patients. None of the reported side effects were marked as severe. Results suggest that TDCS applied according to the present TDCS safety guidelines, is associated with relatively minor adverse effects in psychiatric population. Our findings encourage further prospective studies to explore the effect of TDCS in psychiatric diseases.

Keywords: Adverse effect, Psychiatry, Transcranial direct current stimulation.

INTRODUCTION

Transcranial direct stimulation (TDCS) is a noninvasive brain stimulation method. It induces plasticity via generation of a sub threshold, stimulation polarity dependent alteration of membrane potentials modifying spontaneous discharge rates. Depolarization and increase in spontaneous neuronal activity in the cell membrane occurs by anodal stimulation; decrease in neuronal activity occurs by cathode stimulation [1].

Current studies suggest that TDCS is a promising technique that helps to improve rehabilitation after stroke, to enhance cognitive deficiencies, to reduce depression and to relieve chronic pain [2]. Moreover, it is a safe, simple and cheap device that could be easily integrated in a rehabilitation program [3].

In this study, side effects of TDCS performed in a psychiatric hospital were evaluated retrospectively.

METHODOLOGY

In this study we retrospectively evaluated 29 patients who were on TDCS with different psychiatric diagnosis during 2011-2013. Uskudar University Institutional Review Board approved the retrospectively designed study protocol. Direct current was transferred by a saline-soaked pair of surface sponge electrodes (35 cm²) and delivered by TDCS equipment (Medelec Ltd, Surrey, UK). While in 23 patients, anode was applied over the left prefrontal cortex (PFC) and the cathode was applied over the right PFC, in 6 of cases anode was placed over the right PFC and cathode was placed over the left PFC.

We monitored adverse events by asking patients, after each session of stimulation, whether they had experienced any adverse event and the relationship of these events to treatment with TDCS with a questionnaire. The questionnaire contained categorical rating scales (from 0-none, 1- very mildly, 2-mildly, 3-moderate, 4-severe, 5- very severe) for occurrence of 13 symptoms during or after TDCS. Psychiatric symptoms were also assessed with the Brief Psychiatric Rating Scale (BPRS).

RESULTS

Total of 29 patients received TDCS treatment. 23 patients were hospitalized patients and 6 were outpatients. The mean age of the patients was 45.7 years. 14 of the cases were males (48.3%) and 15 were (51.7%) females. The mean duration of disease history was 7.8 years. Diagnostic distribution was as...
follows; MDD (n=9 cases); dementia comorbid with MDD (n=5); bipolar disorder (n=8); panic disorder (n=4); obsessive compulsive disorder (n=2); alcohol addiction (n=1).

Of these 29 patients, 4 withdrew from the TDCS treatment. Reason for withdrawal was unwillingness to come to the hospital repeatedly on a daily basis in an 26 years-old outpatient with MDD. Another 30 years-old outpatient with MDD who had already received 7 sessions of repeated transcranial magnetic stimulation (rTMS) was switched to TDCS because of a suspected convulsion triggered by rTMS. However after detailed assessment of the patient epileptic seizure diagnosis was not confirmed and the patient was switched back to rTMS after two sessions of TDCS. A 64 years-old patient on rTMS was agitated which prevented the patient from complying with rTMS. 5 sessions of TDCS in this patient resulted in clinical settlement and the patient easily complied with rTMS. Similarly, TDCS treatment was planned for a 78 years old male patient who had not been compatible with rTMS due to his dementia and agitation and rTMS treatment was reinitiated after 2 sessions of TDCS.

Total number of TDCS sessions in each patient is not the same for the cases completing the treatment regimen, giving a mean of 20 sessions. Response to treatment with TDCS was evaluated with BPRS in all patients except those aforementioned 4 cases who had received less than 10 sessions. A paired-samples t-test was performed to evaluate the effectiveness of TDCS yielding a significant decrease in post treatment BPRS scores (p=0.001).

During TDCS an itching sensation was the most common reported adverse effect (48%, n=12) whereas after TDCS fatigue occurred in 32% of cases (n=8). Also one patient reported mild nausea during the first 3 sessions (4%) and one patient reported numbness in the electrode area (4%). Transient redness at the site of stimulation was reported by 3 (12%) of patients. The severity of side effects was generally low, with a median of severity index of 1 (mild or none at all) for all side effect questions except for numbness at stimulation site, burning at stimulation site and fatigue. None of the reported side effects were marked as having a severity of 4 or 5. The occurrence and severity of side effects are summarized in Table 1.

### Table 1: Side effects and severity ratings during and after TDCS

<table>
<thead>
<tr>
<th>Side Effect</th>
<th>n (%)</th>
<th>Severity median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbness at stimulation site</td>
<td>1 (4%)</td>
<td>2(2)</td>
</tr>
<tr>
<td>Redness at stimulation site</td>
<td>3 (12%)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Itching at stimulation site</td>
<td>12 (48%)</td>
<td>1 (1–3)</td>
</tr>
<tr>
<td>Burning at stimulation site</td>
<td>4 (16%)</td>
<td>3 (1–2)</td>
</tr>
<tr>
<td>Pain at stimulation site</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (4%)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>8 (32%)</td>
<td>1 (1–3)</td>
</tr>
<tr>
<td>Nervousness</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Insomnia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Difficulty in concentrating</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Acutemoodchanges</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Changes in visual perception</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

**DISCUSSION**

A number of recent studies suggest that TDCS is safe and may be efficacious in the treatment of a variety of psychiatric and neurological disorders, including mania, psychosis, substance addiction and fibromyalgia[4,5]. Generally, TDCS is considered an option in cases in whom additional brain stimulation treatments such as rTMS or electroconvulsive therapy is needed but at the same time risky for the patient or in cases unresponsive to these therapies. In light of several guideline studies concerning the methodology and areas of application of TDCS, Gottingen protocol was created. According to this protocol electrode sizes of 25 – 35 cm², applied current of 1 – 2 mA and duration of stimulation of 20 minutes were reported to be safe[6].

The size of electrodes we used were compatible with literature. In MDD patients placement of the electrodes were left PFC for anode and right PFC for cathode which was compatible with the literature[7]. In those cases of psychotic and bipolar hypomania, anode was placed on right PFC and cathode was placed on left PFC. In a study conducted with 30 patients with schizophrenia, 20 minutes of 2mA and twice daily stimulation for 5 days with anode on left PFC and cathode on right temporal-parietal cortex, a decrease in auditory hallucinations compared to placebo was reported[5].

TDCS was beneficial in our 64 year-old patient with MD and 78 year-old patient with dementia who were agitated and therefore who were not compliant
with rTMS. 2-5 sessions of TDCS was enough to provide a decrease in agitation to comply with rTMS respectively. It might be suggested that, ease of application of TDCS may offer an advantage particularly for elderly patients with agitation. Thus, it may be preferred since it is a noninvasive method and easy to apply.

Till date, only a few studies on the safety of TDCS have been published[8,9]. In a review article TDCS related studies between the years 1998 and 2010 were screened, 209 studies were found and when compared to sham TDCS, itching, tingling, headache and discomfort were reported as side effects [10]. Also psychotic mania was reported following 5 sessions of TDCS (2mA/30 minutes) in a 60 years old patient taking sertraline 50 mg with MDD [11]. Again in a 33 years old patient with bipolar disorder depressive episode on mood stabilizer, development of manic symptoms were reported after 2 sessions of TDCS (2mA/30 minutes)[12]. Anandam et al. reported a 57-year-old man who experienced an episode of hypomania while participating in a clinical trial of TDCS for the treatment of major depressive disorder[13].

In our study group only TDCS related very mild to moderateside-effects were observed. During TDCS an itching sensation was the most common reported adverse effect (48 %, n=12), followed by fatigue, burning, numbness and redness in the electrode area and mild nausea. All the reported adverse effects associated with TDCS were short lived. The severity of reported side effects was generally low, with a median of severity index of 1 (very mild) for all side effect questions except for nausea and numbness at stimulation site. Only one patient reported nausea and another reported numbness at stimulation site, both with a severity of 2 (mild). None of the reported side effects were marked as having a severity of 4 or 5. Other side effects such as, insomnia, nervousness, visual perceptual changes, difficulties in concentrating, headache, acute mood changes and pain, which were previously reported in the literature, were not observed in our study group.

However, a number of methodological limitations warrant caution in generalizing from this study. The most important limitations are the small sample size, retrospective design and lack of the control group for this study. The possibility remains that subjects reporting side effects may have experienced the adverse effects of psychotropic medications. However, the majority of subjects who were taking a medication had been on stable doses of medication for longer than 4 weeks. Another limitation is the lack of a systematic monitoring of the duration of the adverse effects. In a recent study which assesses post-acute effects of TDCS in the mid-term, in a sample of MDD, it was reported that the antidepressant effects of acute TDCS persisted over 3 months in almost half of the sample and no post-acute side effects emerged during the follow-up observation [14].

TDCS has a wide range of potential applications and can be used to explore the basic aspects of neurosciences as well as for the treatment of neuropsychiatric disorders. It is an easily applied, portable, non-invasive technique with a low cost and lacking pharmacokinetics interaction. These features make TDCS a promising neuromodulatory treatment option in neuropsychiatry. However, such a novel neuromodulation application also brings challenges regarding safety. In this paper, we aimed to provide a retrospective evaluation of adverse effects related to TDCS implementation in a group of psychiatric patients. Sensory side effects are common but mild and transient. None of the patients drop-out due to adverse effects. Our results suggest that TDCS applied to non-motor areas according to the present TDCS safety guidelines, is associated with relatively minor adverse effects in psychiatric population. Our findings encourage further prospective studies to explore the effect of TDCS in psychiatric diseases.

REFERENCES

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