Effectiveness of Transcranial Direct Current Stimulation in Chronic Daily Headaches: An Experimental Single Case Report with a Novel Protocol

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Keywords
Chronic daily headaches · Depression · Anxiety · Stress · Transcranial direct current stimulation-intervention

Abstract
Chronic daily headaches are often refractory to prescribed or non-prescribed medications. Transcranial direct current stimulation (tDCS) is a new technological-based intervention with various modes of applicability. Therefore, we aimed to study the effectiveness of tDCS in an individual with symptoms of chronic daily headaches and the associated comorbidities like depression, anxiety, stress, and RLS or sleepiness, numbness, a sensation of fullness, or ringing in the ears. Based on DASS-21 and Epworth questionnaires, headache diary, and semi-structured interviews, we used repeated measures for assessing the symptoms such as frequency, duration, intensity, or severity of chronic daily headaches and associated comorbidities at baseline, after tDCS-intervention, and at a 12-month follow-up. The results showed that tDCS-intervention reduced the frequency, duration, intensity, or severity of chronic daily headaches and associated symptoms after tDCS-intervention and at a 12-month follow-up.

Chronic daily headaches (CDHs) are transitional [1] and a cumbersome disease with primary brain dysfunction and obvious electrophysiological dysresponsiveness in mechanism to nonnoxious endogenous and exogenous stimuli [2]. Restless legs syndrome (RLS) and atypical neuropathic numbness at the back of the head and in the fingers or atypical sensation of fullness or ringing in the ears are the symptoms that further complicate this type...
of dysresponsiveness [3]. In addition, daily stressors, anxiety, and depression worsen daily headaches and negatively affect patients’ tolerance to pain. In this situation, patients will not be able to deal appropriately with such a condition, which will negatively affect the exacerbation of their headaches [4, 5].

Due to this type of pathologic dysregulation or altered functional connectivity, e.g., atypical rhythmic feedback oscillations, there are currently no satisfactory therapeutic prescribed or non-prescribed medication-related interventions for patients with the symptoms of primary headache disorders [2]. Accordingly and informed by the view that transcranial direct current stimulation (tDCS) is a modality of transcranial electrical stimulation (tES) that targets pathologic processes [2], we hypothesized that using tDCS over the central and prefrontal cortices can enhance these types of oscillations or can decrease pain and related symptoms in a brain with chronic daily headaches [2].

In the present study, we have investigated the effectiveness of tDCS in a patient with refractory and chronic daily headaches with intermittent RLS and neuropathic numbness. The patient experienced numbness in the left-foot toe, left-hand fingers (except the thumb), and back of the head. She had also reported a sensation of fullness or ringing in both ears. Therefore, we suggest that tDCS, by an adapted method, improves cumulative feedforward and feedback corticocortical responses between several areas of frontal cortices in a brain with chronic daily headaches that are refractory to common pharmacological interventions [6].

**Methods**

**Case Report**

GR is a 67-year-old, illiterate woman with a 50-year history of migraine and a 20-year history of RLS (i.e., an average score = 18 [7]) with a middle-class social and low economic status. Headache with a duration between 4 and 72 h, intensity between 5 and 7 visual analogue scale, or frequency with more than 24 attacks per month in the last 3 months was reported by her [8–11]. The general level of her daytime sleepiness score was >15 in the last month [12]. She has experienced negative emotion symptoms (i.e., depression = 25; anxiety = 17; stress = 23) on a four-point severity or frequency scale over the last 4 weeks [13]. She was assessed over several lines of neurological, neurophysiological, and neuroimaging examinations within a month before the present study, which showed no known complete or partial physiological, structural, or sensory abnormalities. While she did not have any other neurological diseases or psychiatric disorders and no history of hospitalizations or emergency visits due to such a complication, she has reported a history of splenectomy (≈10-year ago) and chronic right kidney disease, which was treated successfully by hemodialysis (≈20-year ago). Her vital signs, including body temperature, blood pressure, heart rate (pulse), and respiratory rate, remained regular before and during the present study.

She has almost had the experience of using all available over-the-counter drugs, NSAIDs (e.g., ibuprofen, diclofenac, or naproxen), sedatives, selective serotonin reuptake inhibitors (i.e., fluoxetine), serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants (i.e., imipramine), β-blockers (i.e., propranolol), migraine- and epileptic-specific medications, e.g., valproate sodium and topiramate with various doses. She adds that almost all these medications add to the complication of headache attacks and their associated comorbidities, e.g., RLS (severe = 26 [7]) and neuropathic numbness, with undesirable side effects such as dizziness and lethargy or depression.

**Inclusion and Exclusion Criteria**

The experience of brain stimulation, history of other neurological diseases, and metal implants in the head or neck were criteria of exclusion. Having a diagnosis of concomitant
secondary headache disorders was also excluded. Concomitant use of neurologic- and psychiatric-related prescribed or non-prescribed medications was also a criterion of exclusion. In the present study, chronic daily headaches, restless legs syndrome, anxiety, stress, and depression were the inclusion criteria.

**Design**

The experimental single case report involves repeated measures and the application of tDCS-intervention. Headache frequency, duration, and intensity; severity of anxiety, stress, depression, or frequency of sleepiness; and RLS were assessed before, after tDCS-intervention, and at a 12-month follow-up. She also reported atypical numbness at the back of the head and fingers or an atypical sensation of fullness or ringing in the ears.

**Transcranial Direct Current Stimulation**

A pair of wired carbon electrodes (cathodal size = 3 × 3 [9 cm2]; anodal size = 3 × 3 [9 cm2]), covered by sponges (soaked in 0.9% saline), was used to transfer electricity from a battery-driven current stimulator (Neurostim2 Brain Stimulation Device™; MedinaTeb Co.) to modulate target areas (i.e., F 8 – FC5 ∼ T7 & C 4 – FCz [6]) in a participant that showed the symptoms of chronic daily headaches. The device has a smart scan monitoring system that presents live digital information regarding connection quality and current.

**Electrode Montage**

In the present experimental case report, tDCS was used with a novel protocol at the right ventrolateral prefrontal cortices or F 8, the left dorsomedial and superior frontal gyrus or FC5 ∼ T7, the right primary motor area or C 4, and the medial crosstalk of hemispheres cortices or FCz [6] in a patient with the symptom of chronic daily headaches and the associated comorbidities like depression, anxiety, stress, RLS, sleepiness, atypical numbness at the back of the head and in the fingers, or atypical sensation of fullness or ringing in the ears.

The patient received twenty-four sessions of tDCS for ten consecutive weeks. Each session consisted of two consecutive montages. In the first montage, she received 30 min of anodal direct current (i.e., 2,000 μA) at the right ventrolateral prefrontal cortices and cathode at the left dorsomedial and superior frontal gyrus. In the second montage, she received 20 min of anodal direct current (i.e., 2,000 μA) at the right primary motor area and cathodal at the medial crosstalk of the hemispheres.

She received five daily sessions in the first week, from Saturday to Wednesday. From second to fifth, she received sessions every other day, on Saturdays, Mondays, and Wednesdays. The sixth and seventh weeks settled with two sessions on Saturdays and Thursdays. From eighth to tenth, she received one session per week on Mondays.

However, the frequency, duration, and intensity of chronic daily headaches and the symptoms of comorbidities like RLS, depression, anxiety, stress, and sleepiness were assessed at baseline, after tDCS-intervention, and at a 12-month follow-up on a 4-week basis. The research assistant had weekly and monthly surveillance to record and see how the symptoms do with the participant during the 10-week tDCS-intervention (i.e., weekly) and the 12-month follow-up period (i.e., monthly).

**Measures**

**Headache diary**

The patient was screened for frequency, duration, and intensity of attack in the past 4 weeks at baseline, over 10 weeks of tDCS-intervention, and a 12-month follow-up [8].
In the present patient with the symptoms of chronic daily headache, to assess the symptoms of comorbidities associated with chronic daily headaches (CDHs) like depression, anxiety, and stress, we used the DASS-21 questionnaire, with three subscales, each has seven questions. In this questionnaire, the subthreshold scale of depression is 0–9, anxiety is 0–7, and stress is 0–14. The mild scale is 10–13 for depression, 8–9 for anxiety, and 15–18 for stress. Moderate symptoms of depression also range from 14 to 20, anxiety from 10 to 14, and stress from 19 to 25. In this regard, severe symptoms of depression are 21–27, anxiety from 15 to 19, and stress from 26 to 33. Finally, it has a high-intensity score of 28 for depression, a score of 20 for anxiety, and a score of 23 for stress.

Meanwhile, the Epworth Scale (ESS) was used to assess the present patient’s sleepiness symptoms. This questionnaire has nine questions with a scoring range of 0–3. The score on this scale is 0 (without any signs of sleepiness) to 24 (high sleepiness). A score from 0 to 8 is a sign of a normal state, a score of 9–12 is a sign of mild sleepiness, a score of 13–16 is a sign of moderate sleepiness, and a score above 16 is a sign of severe sleepiness (19). That is, the DAAS and ESS questionnaires were taken from the patient at baseline, after tDCS-intervention, and at a 12-month follow-up.

To assess or report ringing in the ears or tinnitus symptoms, the researcher’s assistant had weekly semi-structured interviews about the ringing frequency in the last 4 weeks. Although the interviews were held weekly during the tDCS-intervention, they were held monthly during the 12-month follow-up.

### Intervention and Outcomes

Table 1 shows the frequency, duration, and intensity of chronic daily headaches at baseline, after tDCS-intervention, and a 12-month follow-up. After twenty-four sessions of tDCS-intervention and a 12-month follow-up, the patient reported a substantial decline in frequency, duration, intensity, and the comorbidities associated with chronic daily headaches.

The results also showed that after tDCS-intervention and at a 12-month follow-up, the frequency had declined from 24 to 4 and 3 attacks after tDCS-intervention and follow-up. The duration decreased from 72 h to 5 after tDCS-intervention and follow-up. The intensity decreased from 7–5 to 3 after tDCS-intervention and at a 12-month follow-up (Fig. 1a).

Table 2 shows the reduction in the severity of depression, sleepiness, anxiety, stress, and RLS after tDCS-intervention and at a 12-month follow-up. The severity of anxiety has changed from 17 to 6 and 5; depression from 25 to 8 and 7; stress from 23 to 4 and 5; sleepiness has changed from 15 to 6 and 4; and RLS from 19 to 0. She reports no change in ringing in the ears. Figure 1 shows changes in the associated symptoms of chronic daily headaches like anxiety (Fig. 1b), depression (Fig. 1c), stress (Fig. 1d), sleepiness (Fig. 1e), and restless legs syndrome (Fig. 1f) at baseline, after the tDCS-intervention, and at a 12-month follow-up.

In addition, after the first week of tDCS-intervention over to the 12-month follow-up, she reported no further numbness at the back of the head, the left-foot toe, left-hand fingers, or a
Fig. 1. Symptoms of chronic daily headache attacks (a: the duration decreased from 72 h to 5 after tDCS-intervention and follow-up; the intensity decreased from 7–5 to 3 after tDCS-intervention and at a 12-month follow-up) and the associated symptoms like anxiety (b: the intensity has remarkably dropped from 17 to 6 after tDCS-intervention and 5 at a 12-month follow-up); depression (c: the severity was 25 at baseline, 8 after tDCS-intervention, and 7 in the follow-up); stress (d: the intensity fell from 23 to 4 after tDCS-intervention and 5 at a 12-month follow-up); sleepiness (e: at baseline, the severity was 15, after the tDCS-intervention dropped to 6, at 12-month follow-up fell to 4); and RLS (f: the intensity of RLS plunged from 18 to 0 after tDCS-intervention and at a 12-month follow-up).
sense of fullness in her ears. In addition, the results showed no change in the frequency of ringing, or tinnitus after tDCS-intervention and at a 12-month follow-up. Therefore, further analysis was considered unnecessary. Except for an intermittent sense of tingling under the cathodal or anodal electrode, the investigator or the research assistant reported no other discomfort or undesirable side effects of tDCS-intervention with the participant.

**Discussion**

The present study aimed to assess the effectiveness of tDCS-intervention in a woman with chronic daily headaches and the associated comorbidities like depression, anxiety, stress, RLS, sleepiness, numbness, and a sensation of fullness or ringing in the ears. The results showed that tDCS-intervention could significantly reduce the frequency, duration, and intensity of chronic daily headaches and the associated comorbidities like depression, anxiety, stress, RLS, sleepiness, numbness, the sensation of fullness, or ringing in the ears (Tables 1, 2). The anterior and central cortices and the common core of neuropsychiatric disorders (i.e., headache disorders, depression, and anxiety) form converging crosstalk within the brain’s functional connectome [6].

That is, motivational demands or wiring constraints associated with the symptoms of chronic daily headaches, depression, and anxiety coupled with circadian and somatosensory-related symptoms like RLS, sleepiness, numbness, or sensation of fullness and ringing in the ears appear to correlate to disorders of wires or wiring within several and overlapping intrinsic networks, including salient or anterior-insula-network, default-mode-network, somatomotor, and limbic network. In general, co-activation, coordination, and correlation of these intrinsic networks correspond with the co-occurrence of the symptoms of chronic daily headaches and the associated comorbidities such as depression, anxiety, stress, and RLS or sleepiness, numbness, a sensation of fullness or ringing in the ears [6].

| Symptoms | Time | Severity |
|----------|------|----------|
| Depression | Pretest | 25 |
| Sleepiness | Pretest | 15 |
| Anxiety | Pretest | 17 |
| Stress | Pretest | 23 |
| RLS | Pretest | 18 |

| | Time | Severity |
|---|------|----------|
| Depression | Posttest | 8 |
| Sleepiness | Posttest | 6 |
| Anxiety | Posttest | 6 |
| Stress | Posttest | 4 |
| RLS | Posttest | 0 |

| | Follow-up | |
|---|-----------|------|
| Depression | Follow-up | 7 |
| Sleepiness | Follow-up | 4 |
| Anxiety | Follow-up | 5 |
| Stress | Follow-up | 5 |
| RLS | Follow-up | 0 |

CDHs, chronic daily headaches; Baseline, pretest; after tDCS-intervention, posttest; and at a 12-month follow-up, follow-up.
Therefore, we adapted a polarization stability-based protocol with two consecutive montages. In the first montage, the anode electrode was positioned at the right ventrolateral prefrontal cortex and the cathode at the left dorsomedial and superior frontal gyrus. In the second montage, an anode electrode was positioned at the right primary motor area and a cathode at the medial crosstalk of hemispheres. However, this type of electrode positioning appears to boost the polarization stability of the brain with intrinsic and core-based psycho-architecture-related disease and disorders like chronic daily headaches and the associated comorbidities [6].

The present single case is the first study that reports positive outcomes of tDCS-intervention in an individual with symptoms of chronic daily headaches and the associated comorbidities. Using electrophysiological and imaging methods like EEG or fMRI, future studies are recommended to replicate the protocol or method of the present work with a suitable sample of individuals with the symptoms of chronic daily headaches and the associated comorbidities. In such a single case study, according to Kratochwill et al. [14] (2010), it would be better to have a minimum of five observations in each phase. One of our limitations is that we could not follow such a procedure. Therefore, future single case studies are recommended to see such a procedure. Furthermore, the results of the present study are not conclusive.

Acknowledgment

We thank the participant who took part in the present study.

Statement of Ethics

Seeing the Helsinki Declaration, the present study protocol was reviewed and approved by the Ethics Committee of the Mashhad University of Medical Sciences: Ir.mums.fm.rec.1396.362. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare. We also show that the author of the present study has no personal relationship with other people or organizations that could inappropriately influence this work.

Funding Sources

It is worth noting that the present study did not receive any full or partial financial support.

Author Contributions

Mohammad Dawood Rahimi: conceptualization, method, data curation, investigation, administration, editing, reviewing, and writing – original draft; Hedieh Zargani: formal analysis; and Karim Nikkhah: supervision and resources.
Data Availability Statement

The manuscript holds all reports or analyzed data. Datasets used in the present study could be given by the corresponding author upon practical demand. In addition, further inquiries can be directed to the corresponding author.

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