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Transcranial alternating current stimulation reduces symptoms in intractable idiopathic cervical dystonia: A case study

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HIGHLIGHTS

- The patient reported unprecedented symptom reduction in head rotation.
- Part of this effect was experienced by the patient for several days.
- She was free of pain most of the time.
- These effects were present at one month follow up.
- The first report to demonstrate a significant therapeutic effect of tACS in ICD.

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ABSTRACT

Idiopathic cervical dystonia (ICD) is a movement disorder often resulting in profound disability and pain. Treatment options include oral medications or other invasive procedures, whereas intractable ICD has been shown to respond to invasive (deep) brain stimulation. In the present blinded, placebo-controlled case study, transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) has been applied to a 54-year old patient with intractable ICD. Results showed that 15 Hz tACS had both immediate and cumulative effects in dystonic symptom reduction, with a 54% reduction in the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) total score, and a 75% in the TWSTRS Pain Scale. These effects were persistent at 30-days follow-up. This is the first report to demonstrate a significant and lasting therapeutic effect of non-invasive electrical brain stimulation in dystonia.

1. Introduction

Idiopathic cervical dystonia (ICD, also spasmodic torticollis) is the most common form of primary dystonia, often resulting in cervical pain, disability, and impairment of postural control [9]. Treatment options for ICD include oral medications, botulinum toxin, intrathecal baclofen, denervation procedures and deep brain stimulation (DBS). Positron emission tomography (PET) of the brain showed that symptom relief with sensory tricks in ICD decreased activity of the supplementary motor area (SMA) and primary sensory-motor cortex (SMC) contralaterally to the head turn, as well as increased activation of the superior and inferior parietal cortex (ipsilaterally to the head turn) and bilateral occipital cortex [7]. The present controlled case study investigated the effects of transcranial direct current stimulation (tDCS) and transcranial alternating current stimulation (tACS) in intractable ICD. Both these methods have been shown to modulate the excitability of the cerebral cortex [3,8,12,15]. With tDCS, the anodal pole (electrode) has excitatory effects and the cathodal pole has inhibitory effects on the underlying cortex [8], whereas with tACS both poles have equivalent effects on the cortex, and these effects are dependent on the AC frequency [3,15]. So far, one prior study has reported no benefit from tDCS in focal dystonia (writer's cramp) [10].

In the present case study, 15 Hz tACS was used as a possible therapeutic stimulation frequency, whereas 5 Hz tACS was used as control stimulation frequency. Our rationale for selecting 15 Hz was based on early EEG studies showing cortical rhythms of 12–15 Hz being associated with behavioral inhibition [13]. Zaghi et al. [15] have recently suggested that 20 min of 15 Hz tACS over the primary SMC (C3–C4) inhibited cortical excitability, reflected by the diminished amplitude of motor evoked potentials. As a control frequency,

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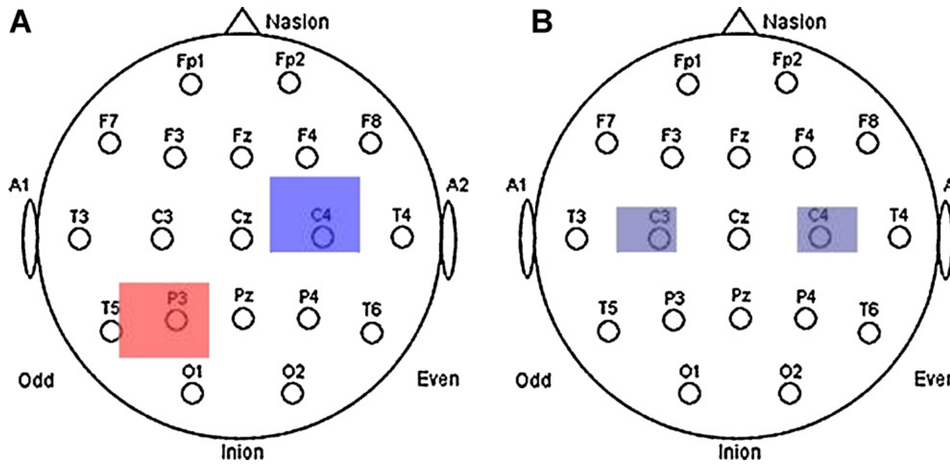

Fig. 1. Electrode Placement: (A) Sponge electrode placement for real and sham tDCS. (B) Sponge electrode placement for 15 Hz and 5 Hz tACS.

5 Hz was selected for three reasons: (i) because it is not a neighboring frequency to 15 Hz, since the alpha rhythm (8–12 Hz) lies in between, and therefore there is no overlap between the two rhythms (5 Hz and 15 Hz); (ii) because the behavioral or cognitive correlates of EEG rhythms in these frequencies (theta: 4–8 Hz, low beta or SMR: 12–15 Hz) are often quite different or even opposite, as shown in epilepsy [14] or attention deficit hyperactivity disorder (ADHD) [5]; and (iii) because 5 Hz stimulation with repeated transcranial magnetic stimulation (rTMS) shows excitatory effects over the motor cortex [6].

2. Methods

2.1. Participant

The study subject was a 54-year-old woman with a five-year history of severe, intractable ICD with left head turn, referred to our department for DBS treatment. Her previous treatment modalities included oral medications (trihexyphenidyl, clonazepam, baclofen, gabapentin, pregabalin, venlafaxine and levetiracetam) and more than five sessions of botulinum toxin injections. Most of the above treatment modalities proved unfruitful (except for some temporary improvement reported after one of the botulinum toxin injections).

2.2. Procedure

2.2.1. Experiment 1

The patient received (a) five consecutive daily sessions of tDCS (15 min of 1.5 mA, 35 cm^2 sponge electrodes, cathode at C4, anode at P3, according to the international 10/20 EEG electrode system), and (b) five consecutive daily sessions of sham tDCS (as in (a), but stimulation was turned off after 30 s) starting two days after real tDCS completion. The rationale for electrode positions in tDCS was based on PET findings of sensory tricks in ICD [7].

2.2.2. Experiment 2

First, tACS was piloted in two sessions, 5 and 17 days following completion of experiment 1. Each session applied tACS (sinusoidal AC, 1.5 mA, 25 cm^2 sponge electrodes at C3–C4), in an ABA order (6 min at 15 Hz, 3 min at 5 Hz, and 6 min at 15 Hz). Then, five consecutive daily sessions of tACS were administered (20 min at 15 Hz, 1.5 mA, 25 cm^2 sponge electrodes at C3–C4), starting 35 days after the last tACS session. Electrode position was selected to target the primary SMC, as in the study by Zaghi et al. [15]. A Magstim-Eldith DC Stimulator Plus (The Magstim Company Ltd.) was used.

2.3. Assessment

Assessment was performed at baseline (pre-treatment), at the end of each treatment protocol (five real tDCS sessions, five sham tDCS sessions, single pilot tACS sessions, and five consecutive tACS sessions), and one month post-treatment. Dystonic symptoms were assessed with the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) [1], including all of its subscales: Torticollis Severity Scale (TSS), Disability Scale (DS), and Pain Scale (PS), scored by a neurologist blind to the treatment conditions. Moreover, self-ratings of symptoms were provided by the patient, also blind to the treatment conditions. Eventually, brain effects of 15-Hz tACS were evaluated with fMRI, comparing 15 Hz with 5 Hz tACS. The patient received tACS in the MRI scanner in the following order: (1.a) 5 min tACS – 15 Hz; (2.a) 5 min rest; (3.a) 5 min tACS – 5 Hz; (4.a) 5 min rest; (1.b) 5 min tACS – 15 Hz; (2.b) 5 min rest; (3.b) 5 min tACS – 5 Hz; (4.b) 5 min rest. Data analysis compared the post-tACS resting periods between 15 Hz and 5 Hz (2.a + 2.b vs. 4.a + 4.b).

All procedures were approved by the "Evangelismos" hospital IRB and the patient provided informed consent for participation and publication of identifying data.

2.4. Electric field calculation

A realistically shaped head model was created from MR images with a voxel size of 1 mm × 1 mm × 1 mm, available from http://www.bic.mni.mcgill.ca/brainweb/, and was used to calculate the electric field in the brain. The images were segmented into five different tissues: scalp, skull, cerebrospinal fluid (CSF), gray matter (GM) and white matter (WM). Particular attention was paid to an accurate representation of the CSF–GM interface, as well as that of all other surfaces. The positions defined in the 10/10 International System were identified on the model's scalp to allow reproducible placement of the center of the stimulation electrodes. Two models were implemented, corresponding to the two electrode montages used in this study (P3–C4 and C3–C4). The electric field was calculated using the finite element method, as described by Salvador and associates [11]. The current intensity was set to 1.5 mA for tDCS and the amplitude was also set to 1.5 mA for tACS.