Journal of Medicine and Life Science

eISSN: 2671-4922

Journal of Medicine and Life Science Vol. 19, No. 3, 134-136, December 2022
https://doi.org/10.22730/jmls.2022.19.3.134

Letter

Transcranial direct current stimulation of the cerebellum in essential tremor patients: an open-label study

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Key words: Cerebellum, Essential tremor, Transcranial direct current stimulation

Received: December 9, 2022
Revised: December 16, 2022
Accepted: December 21, 2022

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Essential tremor (ET) is characterized by bilateral upper extremity action tremor and is among the most common movement disorders in adults. It has been suggested that ET behaves as a neurodegenerative disorder and many studies support the ability of cerebellar transcranial direct current stimulation (tDCS) to modulate motor and non-motor function.[1] We investigate the efficacy of cerebellar tDCS in patients with ET in an open-label design.

Ten patients (three males, seven females; mean age 63.5 years) who met the definite ET criteria by the Movement Disorders Society Committee were included in the study. Patients with epileptic disorders, stroke, Parkinson disease, Parkinson-plus syndrome, or dementia were excluded. All patients had received medical treatment for at least 4 months. 1 week before the initiation of study, all medications for ET were stopped. Each patient was interviewed about the

Table 1. Mean values of the TCRS and the ADL score in 10 patients at baseline, after 10 days of treatment, and 30 days after the last tDCS session

Variable	Day 1	Day 10	Day 30	*P*-value
TCRS	34.3±13.9	35.1±11.2	34.8±10.4	0.42
ADL	45.5±10.2	46.1±13.7	46.2±11.1	0.55
Disability	48.3±13.4	47.7±10.4	47.2±10.3	0.46

Data are given as mean ± standard deviation.
TCRS: tremor clinical rating scale, ADL: activities of daily living, tDCS: transcranial direct current stimulation, Disability: self-reported disability scale.

duration of their disease and associated medical diseases. The tremor clinical rating scale (TCRS) and the activities of daily living (ADL) scale for ET were performed. tDCS was delivered through two rectangular sponge electrodes (measuring 5×5 cm, area 25 cm^2) embedded in a saline-soaked solution. The cathodal stimulation (2 mA) was delivered on the both cerebellar hemispheres (3 cm lateral to the inion) for 20 min. Two anodal electrodes were placed on bilateral prefrontal areas (Fp [frontopolar] 1 and Fp2 electoencephalography leads position). We performed tDCS in 10 consecutive sessions. We compared results of TCRS and ADL between day 1 (before treatment), day 10 (5 min after last tDCS session) and day 30 (20 days after last tDCS session). Descriptive statistical methods applied to evaluate the data. The Friedman test was used to assess the entirety of the time course and the Wilcoxon test for paired comparisons. Values are presented as mean ± standard deviation and $P<0.05$ was considered statistically significant. Analyses were performed using SPSS 22.00 (SPSS Inc., Chicago, IL, USA). This study protocol was approved by the Institution Review Board of the Jeju National University Hospital. The mean age was 63.5 years (range 54-71 years) and the mean disease duration was 7.4 years (range 4-11 years). No adverse effects were reported. Table 1 shows the data of the main variables. Clinical scores showed no significant changes in motor task performance ADL, or the patients' subjective assessment between baseline, day 10 and day 30 (20 days after the last tDCS session). No significant differences were observed in the analysis of the patients' subjective assessment and the disability scale.

Data from neuroimaging and neurophysiological studies have put into evidence the existence of a cerebello-thalamo-cortical and inferior olivocerebellar network for ET. It has been suggested that cerebellar tDCS is more likely to produce effects by polarizing Purkinje cells and intensify the inhibitory effect of the dentate-thalamo-cortical pathway.[2,3] The effects of cerebellar tDCS on behaviors, cognitive and motor function are attributed to different cerebellar neural substrates. It is hypothesized that cerebellar tDCS might be able to have an effect on processing of sensory signals. Therefore, cerebellar tDCS has modulating effects in the excitability of neural structures involved in cerebellar brain inhibition. The extensive evidence suggests that tDCS can be applied to modulate the excitability of cerebellum and has a value of hopeful tool as disease-modifying treatments in the area of cerebellar disorders.[4,5]

In this preliminary study in patients with ET, cathodal tDCS of the cerebellum did not show any beneficial effect. We infer from the negative results of our study that the electrical field strength in tDCS, although applying bilateral stimulation, is too low to create beneficial effects. Besides the small number of patients included, further limitations of the study should be pointed out. The first of these is the intrinsic difficulty in assessing tremor in clinical trials. We did not perform tremor evaluation by accelerometry. Also, it is not clear whether it is possible to stimulate the human cerebellum through the intact scalp using tDCS.

There is a wide scope evidence that cerebellum plays a pivotal role in ET. Therefore, neuromodulation of the cerebellum using tDCS is an exciting new development that has potential as a therapeutic strategy. As the pathophysiology of ET is still unclear in many areas, there is augmenting interest in the use of noninvasive brain stimulation technique as research tools to evaluate the pathophysiology of tremor. In conclusion, this study did not show an effect of tDCS of the cerebellum in ET.

ACKNOWLEDGEMENT

This work was supported by the 2022 education, research and student guidance grant funded by Jeju National University.

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