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Letters to the Editor

Treatment of major depression with transcranial direct current stimulation

To the Editor:

Various forms of brain stimulation appear to be effective in the treatment of depression. Eletroconvulsive therapy (ECT) is the most effective treatment of depression available, but it is associated with anesthetic risks, adverse cognitive effects, and social burden. The advent of repetitive transcranial magnetic stimulation (rTMS) offers a less invasive option for depression treatment. However, rTMS is still expensive and the results are heterogeneous (1). Deep brain stimulation and vagal nerve stimulation are being studied as potentially promising depression treatments, but both are invasive. In recent years, a brain stimulation technique that seemed long forgotten has received renewed attention: the transcranial stimulation with weak direct currents (transcranical direct current stimulation). There are few past reports of tDCS to treat depression (2). However, at the time of those trials much less was known about methodological aspects and physiologic effects of tDCS and the results were quite variable. It is now clear that the efficacy of tDCS depends critically on parameters like electrode position and current strength (3). Furthermore, important advances in the understanding of depression pathophysiology, such as neuroimaging studies showing a focal frontal dysfunction in brain activity, suggest that a focal technique of brain stimulation might be helpful for the treatment of depression (4). Therefore, based on these recent evidences, studies re-evaluating the effects of tDCS on depressed patients are warranted.

In this randomized, controlled and double-blind trial, we investigate the effects of 5 days of anodal stimulation of the left dorsolateral prefrontal cortex in 10 patients with major depression (42.7 ± 10 years). Patients were randomly assigned into one of two groups: active or sham tDCS. All patients were evaluated by the same rater, who remained blinded to the results of the study group assignment. tDCS was applied through a saline-soaked pair of surface sponge electrodes (35 cm^2). The anode electrode was placed over F3 (10–20 International EEG System) of each subject. The cathode was placed over the contralateral supraorbital area. A constant current of 1 mA strength was applied for 20 min/day (administered for five alternated days). For sham stimulation, the stimulator was turned off after a few seconds.

All patients tolerated tDCS without complications. At the end of treatment, there were four treatment responders in the active group versus no responders in the sham group. The patients that received active stimulation had a significant decrease in the Hamilton Depression Rating Scale and Beck Depression Inventory scores when compared with baseline that was not observed in patients that received sham stimulation (Fig. 1).

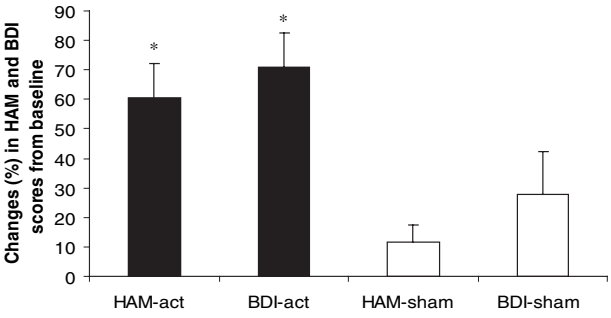

Fig. 1. Mean scores changes (%) after treatment in Hamilton (HAM) and Beck Depression Inventory (BDI) of patients treated with active tDCS (black column) and sham tDCS (white column). There was a significant improvement in depression scores measured by HAM and BDI after treatment only in the active tDCS group. Error bars are standard errors. Significance level (*) assessed by paired Student's *t*-test (comparison of HAM and BDI scores between baseline and post-treatment for both groups). Statistical significance refers to a two-tailed p-value < 0.05.

The authors of this paper do not have any commercial associations that might pose a conflict of interest in connection with this manuscript.

The importance of this study lies in the fact that this treatment is inexpensive, easy to administer, non-invasive and painless (3). Previous animal studies suggest that cathodal tDCS reduces spontaneous firing of cortical neurons, most likely by hyperpolarization of cell body, while anodal stimulation results in a reversed effect (5). Therefore, we speculate that the antidepressant effect in our patients was due to neuronal depolarization and subsequent prolonged enhanced excitability of the left dorsolateral prefrontal cortex. This may have increased the pathologically reduced activity of this cortical region revealed by neuroimaging studies in major depression (6). However, it is possible that right prefrontal reduction in excitability through cathodal stimulation may have contributed to the results as right prefrontal hyperactivity may be associated with depressive states.

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References

1. Hasey G. Transcranial magnetic stimulation in the treatment of mood disorder: a review and comparison with electroconvulsive therapy. Can J Psychiatry 2001; 46: 720–727.
2. Lolas F. Brain polarization: behavioral and therapeutic effects. Biol Psychiatry 1977; 12: 37–47.
3. Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, Paulus W. Modulation of cortical excitability by weak direct current stimulation – technical, safety and functional aspects. Suppl Clin Neurophysiol 2003; 56: 255–276.
4. Nitsche MA. Transcranial direct current stimulation: a new treatment for depression? Bipolar Disord 2002; 4 (Suppl. 1): 98–99.
5. Bindman LJ, Lippold OC, Redfearn JW. The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. J Physiol 1964; 172: 369–382.
6. Bench CJ, Frackowiak RS, Dolan RJ. Changes in regional cerebral blood flow on recovery from depression. Psychol Med 1995; 25: 247–261.

Key words: brain polarization – major depression – transcranial direct current stimulation

Ephedrine-induced emergence of bipolar symptoms

To the Editor:

Ephedrine is an amphetamine stimulant with mixed-action sympathomimetic properties used in over-the-counter dietary supplements (*Ephedra sinica*, or Ma Huang). Recently, the cardiovascular dangers of ephedrine prompted the U.S. Food and Drug Administration (FDA) to ban sales of these supplements (1, 2).

Medline search yielded several cases of ephedrine-induced psychosis/mania (3). Most resulted from ingestion of large quantities (>400 mg) and resolved quickly after ephedrine withdrawal (4). We present a case of ephedrine-induced mania over a 3-month period in a patient who consumed the 'recommended' dose of a dietary supplement.

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