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Long-term response to cathodal transcranial direct current stimulation of temporoparietal junction in a patient with refractory auditory hallucinations of schizophrenia

Braz J Psychiatry. 2019 May-Jun;41(3):271–272
 | doi:10.1590/1516-4446-2018-0330

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that alters the neuronal membrane resting potential by sending a continuous electric current between two electrodes (cathode and anode) placed over the scalp, leading to changes in motor-cortical excitability.[1] Given the neuromodulatory effects of tDCS, the applicability of this technique has been tested for different clinical entities, such as ultra-treatment resistant hallucinations in schizophrenia.[2,3]

The main mechanisms of tDCS modulation have been linked to the action of N-methyl-D-aspartate (NMDA) receptors, especially with regard to post-stimulation effects, which may also be influenced by neuromodulators such as serotonin, dopamine, adrenaline, GABA, and acetylcholine. Furthermore, it is believed that the NMDA receptor plays a central role in the induction of neuroplasticity, and that NMDA modulation by tDCS produces remission of long-term symptoms.[4]

In our research, we search for a long-term effect of tDCS on auditory hallucinations, which if confirmed could suggest long-term modulation of NMDA receptors. Thus, the present case report describes the use of a stimulation protocol as adjuvant treatment for an ultra-treatment resistant schizophrenic patient.

A 28-year-old white man with a 22-year DSM-V diagnosis of schizophrenia was admitted to a psychiatric inpatient unit with auditory hallucinations, persecutory delusions, and severe psychomotor agitation. The initial prescription included haloperidol tapered up to 20 mg/day, and up to 6 mg/day of risperidone in multiple daily doses (twice in a day). Unfortunately, the use of both medications led to neuroleptic malignant syndrome. After recovery from this clinical condition, the patient was switched to clozapine up to 400 mg/day. Because the auditory hallucinations persisted, a course of 12 electroconvulsive sessions was indicated, with no response.

Because the residual symptoms of auditory hallucinations strongly impacted the patient's overall functioning, he made the decision to try an off-label tDCS protocol. The protocol consisted of two 20-minute stimulation

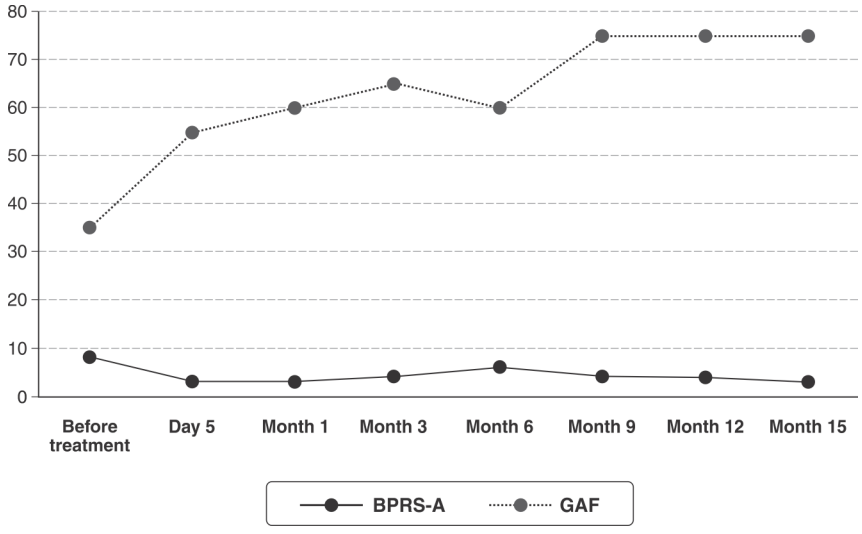

Figure 1 Clinical progress measured by BPRS-A and evaluation of overall functioning measured by GAF. Note the robust post-intervention response in both psychometric scales; the effect was maintained during the 15 months of follow-up. BPRS-A = Brief Psychiatric Rating Scale-Anchored; GAF = Global Assessment of Functioning.

sessions per day performed 1 hour apart, for 5 consecutive days. A 2mA current was used, with the anode placed on the left temporal-parietal junction and the cathode on the left dorsolateral pre-frontal cortex. The choice for this setup was based on a systematic review showing this as the most usual montage in schizophrenia, because it covers areas associated with both positive and negative symptoms. In addition, the precise places being stimulated can be mapped through computer modeling analysis or a neuronavigation system.[5]

After signing an informed consent form, the patient was started on the protocol. Clinical evaluations were performed on eight occasions using the Brief Psychiatric Rating Scale-Anchored (BPRS-A) and the Global Assessment of Functioning (GAF) scales: before the stimulation protocol, on the last day of the protocol and at months 1, 3, 6, 9, 12, and 15 after the end of stimulation. Also, medications remained stable along the 15 follow-up months. Figure 1 shows a robust reduction in overall BPRS-A and GAF scores during the 15 month-follow-up, during which no new tDCS sessions were applied. The BPRS-A score assessing auditory hallucinations had the highest reduction (ranging from 5 to 1). In the 9th month, the patient resumed work and was able to be alone in public places.

The synergistic effect between tDCS and psychotropic drugs has been recognized. According to the neuroplasticity hypothesis of tDCS, this technique may induce the release of neurotransmitters that increase the sensitivity of postsynaptic receptors, inducing subsequent cortical reorganization over time. This sustained effect over a prolonged period is more frequent in patients with short duration of disease, higher educational level, and absence of substance abuse, as seen in this case report. It is postulated that the associated mechanism of action involves the correction of inhibition deficit mediated by GABA receptors.[6]

Despite the limited level of evidence, the present case does support the notion of a direct, positive tDCS impact, as shown by 1) rapid response, which had not yet occurred with use of antipsychotics only; 2) clinical response measured by BPRS-A, suggesting an impact of tDCS over time (Figure 1). Given the characteristics of this case, this approach requires further investigation before it can be used in different mental disorders. For that, prospective studies, different tDCS protocols and adequate follow-up evaluations must be designed.

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Submitted Oct 22 2018, accepted Mar 16 2019.

Acknowledgements

This study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Fundo de Incentivo à Pesquisa – Hospital de Clínicas de Porto Alegre (FIPE-HCPA).

Disclosure

The authors report no conflicts of interest.

How to cite this article: Janovik N, Cordova VH, Chwal B, Ogliari C, Belmonte-de-Abreu P. Long-term response to cathodal transcranial direct current stimulation of temporoparietal junction in a patient with refractory auditory hallucinations of schizophrenia. Braz J Psychiatry. 2019;41:271-272. http://dx.doi.org/10.1590/1516-4446-2018-0330

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First psychotic episode in an adult with Becker muscular dystrophy

Braz J Psychiatry. 2019 May-Jun;41(3):272–273
 | doi:10.1590/1516-4446-2018-0350

In the present report, I describe the case of a 50-year-old male diagnosed with Becker muscular dystrophy (BMD) six years earlier, prior heart transplant and progressive motor impairment, treated with everolimus and mycophenolate mofetil, and no previous psychiatric history. The patient was admitted to a psychiatric emergency room with persecutory and prejudice delusions, as well as ideas of reference; these symptoms had worsened over the past months. Secondarily, he developed depressive mood, initial and intermediate insomnia, anorexia, passive death wishes, and decreased cognitive performance. He denied alcohol or recreational drug consumption. Both his brother and cousin had BMD and similar psychiatric symptoms.

No relevant changes had been detected on previous brain imaging. Laboratory and electrocardiographic evaluation