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The Effects of Cathodal Transcranial Direct Current Stimulation in a Patient with Drug-Resistant Temporal Lobe Epilepsy (Case Study)

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Letter to the Editor

The Effects of Cathodal Transcranial Direct Current Stimulation in a Patient with Drug-Resistant Temporal Lobe Epilepsy (Case Study)

Dear Editor:

Temporal lobe epilepsy is often resistant to anti-epileptic drugs [1], and epilepsy surgery cannot be performed in many of these cases. Even for those in whom surgery is possible, 30–50% of patients are not free of seizures after surgery [2]. Approximately 73% of patients undergoing epilepsy surgery have temporal lobe epilepsy [1].

Transcranial direct current stimulation (tDCS) is a well-established cortical stimulation method used to modulate neuronal excitability [3]. TDCS is a non-invasive and painless technique that uses low intensity currents (1–2 mA) and modulates brain excitability via membrane polarisation: cathodal stimulation (c-tDCS) hyperpolarises, while anodal stimulation (a-tDCS) depolarises the resting membrane potentials [4]. Modification of dysfunctional electrical brain activity by tDCS is a potentially valuable non-invasive alternative for seizure management in patients. Here we present a case study of the use of tDCS in a patient with drug resistant epilepsy.

Case description

A 48-year-old female was admitted as a surgical candidate for 5 days to the Video-EEG Monitoring Unit at the Royal Melbourne Hospital. She was diagnosed with a Grade 2 right fronto-temporal pleomorphic astrocytoma 10 years earlier. She reported having 5–10 seizures per day at the time of admission. The seizures were focal sensory seizures with left hemi-sensory changes (tingling sensation in face > leg, lasting 15–30 sec), occasionally associated with eye and hand twitching and sometimes with a metallic taste in mouth. Her medications were levetiracetam (1500 mg BD), carbamazepine CR (600 mg BD) and zonisamide (300 mg daily). Twenty-three typical epileptic seizures were captured with video-EEG recordings during her 5-day admission. Written informed consent was obtained for participation in this study. All procedures used conformed with the Declaration of Helsinki, and the protocol was approved by the Human Research Ethics Committees at The University of Melbourne and Melbourne Health.

Intervention

Two sessions of c-tDCS (9–20–9 protocol) were applied in the last two days of the patient's admission. The protocol involved a total of 18 minutes c-tDCS, with 20 minutes rest after the first 9 minutes. A DC-stimulator (Chattanooga Intelect® Advanced Combo) was used to deliver a 1 mA continuous galvanic current to the brain via two surface electrodes with surrounding saline-soaked sponges (0.9% NaCl). The active surface electrode (cathode, 3×4 cm) was placed over the right temporal lobe, and the return electrode [5] (anode, 5×7 cm) was placed over the left supraorbital area.

Assessment

The patient was asked to keep a record of her seizures in a daily seizure diary for 4 weeks. Paired-pulse transcranial magnetic stimulation (TMS) (Magstim Bistim^2) was used to assess GABAergic intracortical inhibitory circuits (ICI) before and after each intervention. In this method, TMS that is subthreshold for a motor response activates ICI circuits and reduces the size of the motor evoked potential (MEP) elicited by a supra-threshold test TMS pulse delivered up to 5 ms later [6]. The participant was seated with her head and neck supported by a headrest. MEPs were recorded from the left first dorsal interosseous (FDI) muscle before and after each intervention. TMS thresholds were assessed for FDI at rest (resting threshold, RT). MEP threshold was tested in steps of 2% maximum stimulator output, and defined as the lowest intensity for which three of five successive MEPs exceed 50 μV (rest) peak-to-peak amplitude. Test TMS intensity was adjusted to produce a test MEP in FDI at rest of about 1 mV amplitude. Conditioning TMS intensity was adjusted to $0.8 \times$ RT with 3 ms inter stimulus interval. Single or paired-pulse TMS was delivered in blocks of 20 stimuli (10 s interval between stimuli) at rest (40 trials at each session).

The areas of the conditioned and unconditioned MEPs were measured from the averaged rectified MEPs obtained in each trial by using a custom designed macro in PowerLab 8/30 software. The size of the conditioned MEPs was expressed as a percentage of the unconditioned test MEPs in order to assess the effectiveness of ICI.

Results

The c-tDCS intervention was well tolerated, with no adverse effects. ICI increased from 57% at baseline to 67% after the second treatment session (Fig. 1).

Seizures reduced from 6–10 per day to 0–3 seizures per day. Seizure diaries showed that seizure rates remained as low as 0–3 per day for 4 months and then started to increase again.

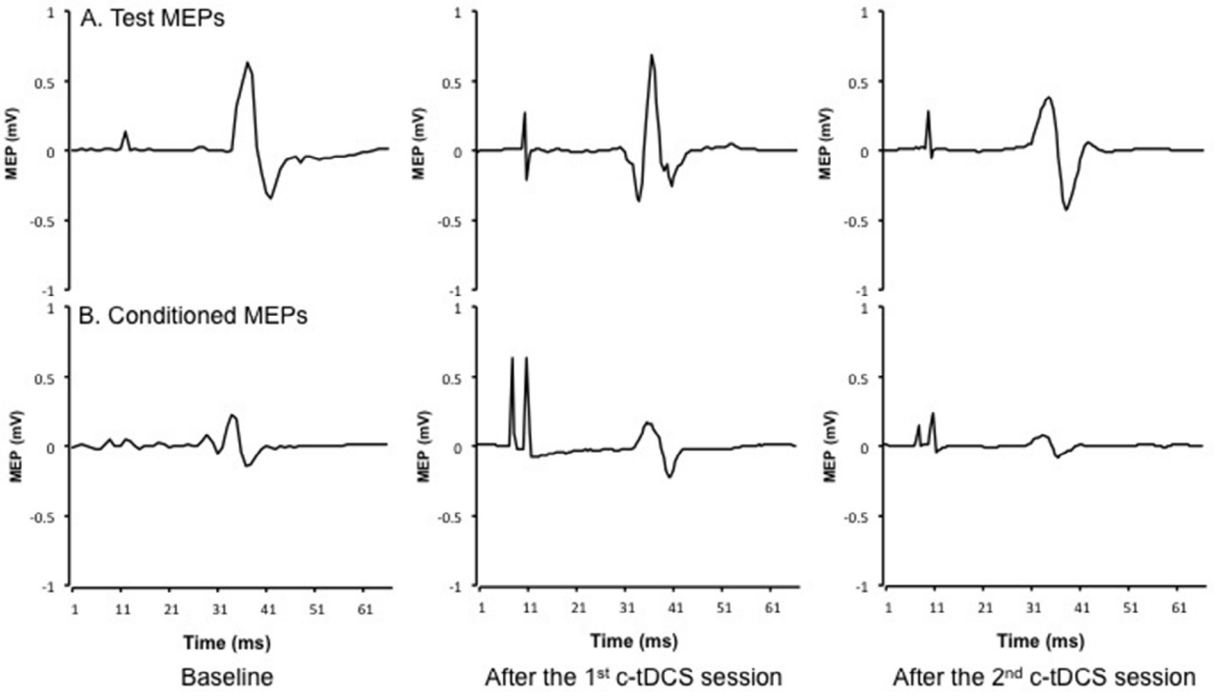

Figure 1. Test and conditioned MEPs from the left FDI after the 1st and the 2nd c-tDCS interventions. The top traces are test MEPs and the bottom ones are conditioned MEPs. Test TMS intensity was adjusted to produce a test MEP in FDI at rest of about 1 mV amplitude. Conditioning TMS intensity was adjusted to 0.8 × RT with 3 ms inter stimulus interval. The size of the conditioned MEPs was expressed as a percentage of the unconditioned test MEPs in order to assess the effectiveness of ICI. The left traces are MEPs at baseline. The ICI was 57% at baseline. The middle traces are MEPs after the 1st c-tDCS intervention. The ICI was 58% after the 1st c-tDCS intervention. The right side traces are MEPs after the 2nd c-tDCS intervention. The ICI was 67% after the 2nd c-tDCS intervention. These data suggest that c-tDCS could have a cumulative effect over time. MEP: motor evoked potential; TMS: transcranial magnetic stimulation; c-tDCS: cathodal transcranial direct current stimulation; RT: resting threshold.

Discussion

The anti-epileptic effects of c-tDCS can be explained due to the fact that c-tDCS decreases cortical excitability by hyperpolarising the membrane potentials and subsequently altering synaptic efficacy [7]. Our results in this case study are consistent with those of Yook et al. [8], who applied c-tDCS application (20 min, 2 mA, 5 days/week for 2 weeks) over the area of the abnormal EEG wave in an 11-year-old female with focal cortical dysplasia. Over the two-month monitoring period the frequency of seizures reduced from 8 per month to 3 per month with a reduction in seizure duration. The protocol was re-applied for another two weeks and the patient only reported one seizure attack in the following two months.

The effects of tDCS are strongly dependent on electrode montage and parameters of stimulation. It has been shown that the induced excitability changes and the length of the lasting effect depend on two parameters of direct currents: *intensity* and *duration of application* [9]. It is a general goal to keep current exposure as low as possible. High-intensity stimulation cannot only be painful [10], but can also affect different neuronal populations compared with low intensity stimulation. By increasing the intensity, the current may reach deeper sites that might not be the intended target.

One way to prolong the after-effects of tDCS might be the repetition of tDCS sessions. Monte-Silva et al. showed that application of c-tDCS for 18 minutes with a 20 minute break after the first 9 minutes will increase the inhibitory effects of this technique (9–20–9 protocol) [11]. The number of seizures in the present case decreased from 6–10 seizures per day to 0–3 for 4 months.

This case study demonstrates promising effects of this novel and non-invasive technique and should be further explored in a double blind randomised control trial. This non-pharmacological treatment approach may be appropriate for routine clinical use, and may provide a safe and effective therapy for patients with drug resistant epilepsy, minimising adverse drug reactions, clinic appointments, and hospital admissions. This, in turn, will improve quality of life, and reduce the financial burden placed on them and the health care system.

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