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Prolonged seizure duration of electroconvulsive therapy in a patient pre-stimulated with transcranial direct current stimulation

To the editor,

We were presented with a 26 year old male with no history of epileptic seizures suffering from amotivational symptoms induced by 4-methyl methcathinone (mephedrone). He used mephedrone eleven months ago during at least five months, with approximately 5g per day. The patient was initially hospitalized for 3 months because of a first episode of drug-induced psychosis, treated with intramuscular paliperidone 100mg. Since, the patient experienced a general lack of motivation, blunted emotions and drive, disinterest, anhedonia, passivity, and apathy. Differential diagnoses were depression, psychosis and amotivational syndrome, for which antidepressants (duloxetine, bupropion), antipsychotics (aripiprazole, paliperidone) and methylphenidate were subsequently used. None of these showed sufficient clinical improvement and the patient was referred to our centre for transcranial Direct Current Stimulation (tDCS) treatment.

The stimulation protocol consisted of 30 sessions (once daily, with exception on weekends) using a battery driven Soterix 1 × 1, stimulated at 2.0 mA for 20 minutes daily. The anode was placed over the left dorsolateral prefrontal cortex using the BeamF3 method [1]. The cathode was placed over the right supraorbital area. We used 4 × 4cm electrodes with 5 × 7cm Easypads soaked in saline solution. Depressive symptoms were assessed with the Hamilton Depression Rating Scale (HDRS) with a total baseline score of 16, indicating moderate depressive symptoms. The HDRS was scored weekly and showed minor but no clinically relevant improvements, respectively 17, 15, 16 and 14 throughout the stimulation period. The amotivation scale was filled out at baseline and at the end of treatment, scoring respectively 29 and 23 on a total of 48. The Positive and Negative Syndrome Scale (PANSS) showed a score of 27 at the beginning and 28 at the end of tDCS treatment on the negative scale. After 30 tDCS sessions, it was decided to start with bilateral electroconvulsive therapy (ECT). This ECT session took place 22 hours after the last tDCS session. The ECT parameters were 1 ms (pulse width), 60 Hz (frequency), 3 s (stimulation time), 0.8 A (current) and 288 mC (total charge). Unexpectedly, the patient experienced a prolonged seizure of 3 minutes and 23 seconds monitored by the electroencephalogram, despite receiving 10mg of diazepam intravenously at 2 minutes and 3 seconds. Because of the unexpected prolonged seizure to this first ECT session, it was decided to postpone the second session to decrease the excitability. The second session with identical parameters took place ten days after. Here, the patient objectively convulsed for 54 s, considered as a normal seizure duration during ECT [2]. The patient received 9 ECT sessions in total within a time span of one month. The range of seizure times was 49 seconds to 1 minute and 30 seconds. According to the patient, his mood improved, although this was not observed clinically.

This report is the first to present the case of a prolonged seizure duration during ECT after intensive pre-treatment with tDCS. A prolonged seizure duration, defined as more or equal to 3 minutes, can occur for other reasons, difficult to disentangle in complex clinical cases as this one. One hypothesis is that the seizure duration was prolonged because of the electrical stimulus being applied close to the stimulus threshold, which has been described also due to medication interactions [3]. At the start of ECT, the patient was still under treatment with methylphenidate 54mg OROS and trazodone 100mg. In earlier reports, no differences in excitability have been reported when combining tDCS and methylphenidate [4], although this is contested by another study showing alterations in excitability upon combining tDCS and methylphenidate until the morning after the procedure [5]. Besides, it has been shown that mephedrone has the ability to induce seizures depending on the dose [6]. However, animal studies suggest that multiple tDCS sessions could provoke seizures [7], where reduced seizure thresholds could occur due to the cumulative action of electric stimulation [7]. It has been reported that cathodal tDCS does not enhance the duration of seizures in epileptic patients, but rather results in a decreased amount of seizures [8]. An earlier case report described a paediatric patient experiencing a seizure after being treated with daily tDCS sessions. The event occurred four hours after the third session. After discontinuation of the treatment, no seizure activity was witnessed [9]. Using ultra-brief (0,3 ms) pulse width right unilateral ECT, Mayur et al. demonstrated that concomitant use of tDCS is feasible and safe albeit a higher need for tDCS restimulation in comparison with sham tDCS [10]. However, to our knowledge, no prior literature is available on the effect of multiple sessions of tDCS treatment immediately prior to ECT.

This N-of-1 trial presents a prolonged seizure duration during ECT upon intensive (30 sessions) pre-stimulation with tDCS, while showing a normal seizure duration when no prior tDCS stimulation was given, highlighting a potential relationship between repeated tDCS treatment prior to ECT and prolonged seizure duration. While more research is warranted, we propose a dosage titration or a 'washout' period after the last tDCS session and the first ECT session.

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

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We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed.

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