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Moving to accelerated protocols of tDCS in schizophrenia: A case report



Dear Editor,

In recent years, transcranial direct current stimulation (tDCS) has been increasingly used to reduce symptoms in patients with schizophrenia with good outcomes, particularly for auditory hallucinations [1] and negative symptoms [2]. tDCS protocols for schizophrenia typically include ten 20-min sessions of tDCS at 2 mA applied with a frontotemporal montage, *i.e.*, with the anode over the left prefrontal cortex and the cathode over the left temporoparietal junction. The tDCS sessions were mostly delivered at a rate of 2 sessions per day over 5 consecutive days with an interval of at least 2 hours between consecutive sessions. However, the optimal interval between sessions remains unknown and has received little consideration in studies investigating the clinical interest of tDCS. Some studies in animal models and healthy human populations suggested that the duration of this interval critically influences the effects of tDCS [3]. For instance, Monte-Silva *et al.* reported that spacing two tDCS sessions by short intervals of 3 and 20 minutes resulted in long-lasting effects of tDCS on motor cortical excitability with a greater magnitude of effects for the 20-min interval [4], whereas longer intervals, such as 3 or 24 hours, abolished the long-lasting effects of tDCS [4,5]. Thus, the use of short intervals between sessions (<30 min) has been proposed to prolong the effect of tDCS [6]. The clinical potential of such protocols, which can be referred to as “accelerated” or “intensive”, is increasingly being investigated with other forms of noninvasive brain stimulation. For instance, accelerated repetitive transcranial magnetic stimulation has been reported to produce a rapid and meaningful clinical response in patients with treatment-resistant depression [7]. Such accelerated protocols propose delivering a greater number of sessions in a shorter period of time to reduce the financial and time burdens associated with standard protocols, which can last up to 6 weeks or longer. No studies have yet applied accelerated tDCS in patients with schizophrenia. Here, we propose to administer an accelerated tDCS protocol consisting of the delivery of 5 tDCS sessions per day with short (20 min) intervals between sessions on 2 consecutive days in a patient with treatment-resistant schizophrenia and evaluate its feasibility and safety.

Case report

We report the case of a 56-year-old man who presented with 30 years of diagnosed schizophrenia according to DSM 5 criteria. The patient presented with severe refractory symptoms, including delusions, persistent multimodal hallucinations primarily in the olfactory and auditory modalities, somatic concerns, difficulties in

abstract thinking and unusual thought content, despite being on stable doses of paliperidone long-acting injection (100 mg every 28 days), loxapine (300 mg per day), and valproate (2000 mg per day). In addition, due to continuous olfactory hallucinations, the patient declared having the feeling of releasing a bad smell, which subsequently triggered a long history of washing hands compulsions (all day long from wake up to bedtime with boiling water) and compulsive water drinking (estimated at approximately 15 L per day). In the past, several different classes of antipsychotics, including clozapine, and several drug combinations have been proposed without major clinical benefits. The patient showed no evidence for a depressive episode (score of 5 at the Calgary Depression Scale for Schizophrenia at baseline). Two clinical evaluations separated by one month were performed to assess the stability of schizophrenic symptoms at baseline (Table 1). The evaluation includes the Positive And Negative Syndrome Scale (PANSS) and the Psycho-Sensory hallucinations Scale (PSAS) [8].

A total of 10 tDCS sessions were delivered over two consecutive days using a NeuroConn device (Ilmeneau, GmbH) with two 7 × 5 cm saline-soaked sponge electrodes. The anode was placed over the left prefrontal cortex (midpoint of F3-FP1 according to the 10/20 EEG electrode placement system), and the cathode was placed over the left temporoparietal junction (midpoint of T3-P3). Twenty minutes of 2-mA stimulation (ramp up/down 30 s) was administered five times a day spaced by a 20-min interval. The electrode montage was kept consistent across repeated sessions. The impedance measures range from 2.3 to 5.2 kΩ. Tolerability and safety were monitored after each session using a standardized checklist, including itching, pain, skin reactions, etc. [9].

After the completion of accelerated tDCS treatment, the patient showed global clinical improvement with a 17% reduction in the PANSS total score (Table 1). This improvement was maintained one month after the intervention. Clinical changes were mostly observed in the negative (−16% after tDCS, −29% at follow-up) and general psychopathology subscales (−21% after tDCS, −15% at follow-up), whereas no significant changes were noted in the positive subscale. PANSS subscore analysis according to Lindenmayer *et al.*'s five dimensions (negative, positive, excitement, cognitive, and depression/anxiety) [10] revealed an acute effect on both negative and depressive dimensions (−27% and −30% from baseline to post-tDCS assessment) that was maintained and even increased at the one-month follow-up for the negative dimension (−34%) but not for the depressive dimension (−14%). The patient reported a moderate reduction in hallucinations (PSAS total scores reduced from 56 to 40), which was maintained at the one-month follow-up (PSAS score of 43). This reduction was mostly driven by a

Table 1
Clinical outcomes.

	Baseline-1	Baseline-2	Post-tDCS	Follow-up
PANSS total score	127	126	105	108
Positive	34	33	30	33
Negative	32	31	26	22
General psychopathology	61	62	49	53
PANSS dimension scores ^a				
Negative	25	24	18	16
Positive	22	22	20	21
Excitement	14	12	12	14
Cognitive	21	23	22	23
Depression/anxiety	17	20	13	16
PSAS total score		56	40	43
Auditory hallucinations		23	20	22
Visual hallucinations		10	0	0
Olfactory/Gustatory hallucinations		23	20	21
Cenesthetic hallucinations		0	0	0

PANSS: Positive and Negative Syndrome Scale; PSAS: Psychosensory hAllucinations Scale.

^a PANSS dimension scores were computed according to Lindenmayer et al., 1994.

complete suppression of visual hallucinations (PSAS visual hallucination subscore reduced from 10 to 0). While no objective measurements were made, the patient's family described a moderate reduction in compulsive water drinking after treatment. The accelerated tDCS protocol was well tolerated, and no severe adverse effects were reported. Only mild and transient skin redness was observed under the anode at the end of each day of stimulation, which resolved shortly after cessation of stimulation.

The present case provides evidence for the feasibility, tolerability and safety of accelerated tDCS in a patient with schizophrenia. The observed reduction in total PANSS scores as well as negative and general symptom subscores seems comparable to that reported in previous clinical trials [1,2]. However, the effect on hallucinations was mild and restricted to the visual modality, whereas the patient's complaints mainly concerned auditory and olfactory hallucinations. Future studies are needed to directly compare the clinical effects of accelerated tDCS to more standard tDCS protocols in patients with schizophrenia in terms of amplitude and duration. Accelerating tDCS protocols by reducing intervals between sessions decreases the number of separate days that patients must visit the clinical unit and thus has the advantage of being less time-consuming and easier to organize logistically. This alternative type of tDCS protocol could be particularly suitable for patients who refuse or are hostile to engage in protocols requiring many visits and appointments as well as for patients who present cognitive and clinical symptoms too severe to be able to commit to standard protocols.

Declaration of competing interest

The authors declare that they have no conflicts of interest.

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References

- [1] Brunelin J, Mondino M, Gassab L, Haesebaert F, Gaha L, Suaud-Chagny M-F, et al. Examining transcranial direct-current stimulation (tDCS) as a treatment for hallucinations in schizophrenia. *Am J Psychiatr* 2012;169:719–24. <https://doi.org/10.1176/appi.ajp.2012.11071091>.
- [2] Valiengo L da CL, Goerigk S, Gordon PC, Padberg F, Serpa MH, Koebe S, et al. Efficacy and safety of transcranial direct current stimulation for treating

negative symptoms in schizophrenia. *JAMA Psychiatr*. 2020;77:121–9. <https://doi.org/10.1001/jamapsychiatry.2019.3199>.

- [3] Goldsworthy MR, Pitcher JB, Ridding MC. Spaced noninvasive brain stimulation: prospects for inducing long-lasting human cortical plasticity. *Neurorehabilitation Neural Repair* 2015;29:714–21. <https://doi.org/10.1177/1545968314562649>.
- [4] Monte-Silva K, Kuo MF, Liebetanz D, Paulus W, Nitsche MA. Shaping the optimal repetition interval for cathodal transcranial direct current stimulation (tDCS). *J Neurophysiol* 2010;103:1735–40. <https://doi.org/10.1152/jn.00924.2009>.
- [5] Monte-Silva K, Kuo M-F, Hessenthaler S, Fresnoza S, Liebetanz D, Paulus W, et al. Induction of late LTP-like plasticity in the human motor cortex by repeated non-invasive brain stimulation. *Brain Stimulat* 2013;6:424–32. <https://doi.org/10.1016/j.brs.2012.04.011>.
- [6] Bystad M, Storø B, Gundersen N, Wiik IL, Nordvang L, Grønli O, et al. Can accelerated transcranial direct current stimulation improve memory functions? An experimental, placebo-controlled study. *Heliyon* 2020;6:e05132. <https://doi.org/10.1016/j.heliyon.2020.e05132>.
- [7] Baeken C, Vanderhasselt M-A, Remue J, Herremans S, Vanderbruggen N, Zeeuws D, et al. Intensive HF-rTMS treatment in refractory medication-resistant unipolar depressed patients. *J Affect Disord* 2013;151:625–31. <https://doi.org/10.1016/j.jad.2013.07.008>.
- [8] de Chazeron I, Pereira B, Chereau-Boudet I, Brousse G, Misdrachi D, Fénelon G, et al. Validation of a Psycho-Sensory hAllucinations Scale (PSAS) in schizophrenia and Parkinson's disease. *Schizophr Res* 2015;161:269–76. <https://doi.org/10.1016/j.schres.2014.11.010>.
- [9] Antal A, Alekseiuk I, Bikson M, Brockmüller J, Brunoni AR, Chen R, et al. Low intensity transcranial electric stimulation: safety, ethical, legal regulatory and application guidelines. *Clin Neurophysiol Off J Int Fed Clin Neurophysiol* 2017;128:1774–809. <https://doi.org/10.1016/j.clinph.2017.06.001>.
- [10] Lindenmayer J-P, Bernstein-Hyman R, Grochowski S. A new five factor model of schizophrenia. *Psychiatr Q* 1994;65:299–322. <https://doi.org/10.1007/BF02354306>.

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