Psychiatria Danubina, 2021; Vol. 33, No. 3, pp 366-367 https://doi.org/10.24869/psyd.2021.366 *Case report*

THE UTILITY OF HD-TDCS AS ADD ON TREATMENT FOR NEGATIVE SYMPTOMS IN SCHIZOPHRENIA: A CASE REPORT

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received: 14.3.2021; revised: 19.5.2021; accepted: 1.6.2021

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INTRODUCTION

The 'negative symptoms' in schizophrenia present an etiological conundrum and a management challenge (Mitra et al. 2016). Transcranial direct current stimulation (tDCS) is being used for the management of these symptoms with mixed results (Aleman et al. 2018). A review of the evidence suggests that most studies have used the conventional 1x1 tDCS, target the dominant dorsolateral prefrontal cortex (DLPFC) (usually F3 as per the 10-20 system) which is anodally 'stimulated', and have used a variable number of sessions. There is some evidence to suggest that benefit is related to a greater number of sessions/time that stimulation is received (Kim et al. 2019). High-definition tDCS (HD-tDCS) involves the use of more than two electrodes unlike conventional tDCS and results in more focal stimulation of the target cortical area. The 4x1 ring setup is frequently used (Turski et al. 2017). HD-tDCS has been safely used for persistent auditory hallucinations in schizophrenia (Bose et al. 2017; Sreeraj et al. 2018). Hence, HD-tDCS may be useful and safe in the management of negative symptoms of schizophrenia. We present a case report of a patient with predominant negative symptom schizophrenia in which add-on HD-tDCS was tried.

CASE REPORT

A 30-year-old right-handed, unemployed male presented to the outpatient clinic in December 2019. He was 2nd in birth order, with an unremarkable developmental and family history. He presented with illness characterized by insidious onset, continuous and progressive course from 18 years of age (around 2007). The symptoms were initially characterized by gradually decreased attention and academic decline, irritability, insomnia, delusion of reference, hallucinatory behavior in the form of talking and smiling to self, decline in self-care, anhedonia, avolition, social withdrawal, three attempts of self-harm and aggression towards self and family members. After 5-6 years the symptoms of anhedonia, avolition and social withdrawal became more prominent. He started to receive treatment after 6 years of symptoms and had received adequate trials of clozapine, olanzapine, amisulpiride, quetiapine and aripiprazole but with minimal improvement. There was a doubtful episode of an epileptic seizure 3 years back for which he had been started on adequate doses of sodium valproate and oxcarbazepine with no recurrence. Following his presentation at our clinic the patient underwent routine investigations, a CT scan of the brain and electroencephalogram all of which were reported normal. Hence, we gradually tapered and stopped all medications except 200 mg of clozapine per day. He was admitted in March 2020 for further management. At admission, the patient was rated P20 N31 G38 on Positive and Negative Syndrome Scale (PANSS), Scale for the Assessment of Negative Symptoms (SANS) score was 71 (affective flattening-18, alogia-15, avolition-15, anhedonia-13, attention-10) and Global Assessment of Functioning (GAF) score of 40. On clinical assessment and by using standardized scales, the patient was not found to be depressed and other conditions that would explain his negative symptoms were ruled out. The patient could not tolerate an increase in dose of clozapine due to sedation and also in view of his past seizure further dose escalation was not done. In view of recalcitrant negative symptoms, we offered a trial of HD-tDCS. Written informed consent was obtained. Using transcranial magnetic stimulation, we identified the dominant motor hotspot (contralateral abductor pollicis brevis) and used the 5 cm rule to identify the area on the scalp overlying the DLPFC (F3). HD-tDCS was delivered through a 4×1 Soterix device with the anode overlying F3 and cathodes overlying F1, AF3, F5 and FC3 as per usual protocol (*4x1 – Soterix Medical*, n.d.). Time to ramp up and ramp down was 30 seconds. A single 20-minute session per day using 2mA current was delivered. The patient received one session each day on 4 consecutive days and no side effects were observed. The patient had to be discharged from the ward owing to the COVID-19 outbreak and subsequent lockdown as per the wishes of the patient's family even though more sessions were planned (*High-Definition Transcranial Direct Current Stimulation as a Treatment of Negative Symptoms of Schizophrenia - Full Text View - ClinicalTrials.Gov*, n.d.). We followed up the patient and communicated with the family through telepsychiatry services as the patient was unable to follow-up in person. By the 2nd week after the last session of HD-tDCS, we noticed an improvement in the patient's symptomatology over video conferencing which was corroborated by family members. The patient also did not report any side effects and continued his medications regularly. On follow up at 6 weeks following the last session, he rated P16 N24 G31 on PANSS, 48

(affective flattening-9, alogia-11, avolition-6, anhedonia-13, attention-9) on SANS, and the GAF score was 50. On subsequent regular follow up, the same improvement was also sustained at 12 weeks following the last session.

DISCUSSION

HD-tDCS makes use of a greater number of electrodes than conventional tDCS thus enabling more precise cortical targeting and less diffusion of electric current and may translate into more reliable physiological changes. This may lead to greater clinical benefit (Lefebvre et al. 2019). Negative symptoms are associated with hypofunction in the prefrontal cortex. Hence anodal (activating) stimulation via conventional (1x1) tDCS of this area has been reported to be useful (Aleman et al. 2018). We found that HD-tDCS for negative symptom schizophrenia is safe and well tolerated. Despite the history of an unconfirmed epileptic episode, the patient tolerated the sessions well and no adverse effects were seen. Serendipitously, we also found that as few as 4 sessions delivered as a single session/day may be useful. At 6 weeks, there was 22.5% improvement in PANSS factor score for negative symptoms (PANSS FSNS), 33.8% improvement in SANS score and 25% improvement in GAF score compared to baseline and the effects were found to be sustained. HD-tDCS may require fewer sessions than conventional tDCS thus making treatment easier and more cost effective. This may be due to the differential effects of HD-tDCS as compared to conventional tDCS (Kuo et al. 2013). We believe that patient ratings on video conferencing are an accurate representation of his clinical state.

CONCLUSION

HD-tDCS is seen to be more effective, faster acting and equally safe as conventional tDCS. It may be useful as an add-on treatment option in negative symptom schizophrenia. There is need for randomized controlled trials to establish the same.

Acknowledgements: None.

Conflict of interest: None to declare.

Contribution of individual authors:

Sanjana Kathiravan: concept, design, literature search, experimental study, data acquisition, data analysis, statistical analysis, manuscript preparation, editing and review.

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Shivanee Kumari: definition of intellectual content, data acquisition, manuscript preparation.

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