CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION (TDCS) IN DRUG-RESISTAN EPILEPSY

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Background: Transcranial direct current stimulation (tDCS) is an emerging non-invasive and well tolerated neuromodulation technique, its use in epilepsy bases on the hypotesis that extrinsic stimulation can reduce hyperexcitability or interfere with the discharges of epileptogenic networks. Preliminary results states its safety and efficacy on seizures and EEG modulation but target and stimulation parameters have not been yet established, particularly for multifocal or generalized epilepsies. Animal model and studies about deep brain stimulation suggest that cerebellum can be a good target for neuromodulation in these patients.

Methods: 10 patients with drug resistant focal or generalized epilepsy, seizure frequency >4 per month underwent to a daily session of cerebellar cathodal tDCS (2 mA, 20 min, stimulation electrode applied 1-2 cm below the inion with its lateral borders about 1 cm medially to the mastoid apophysis) for 5 consecutive days. Patients were asked to report on a diary every seizure occurred during the 30 days before and after treatment. Basal EEG was recorded before stimulation on day 1, at the end of the last session on day 5 and after 30 days. Interictal epileptic activity was manually detected and quantified. Frequency analysis of the EEG trace recorded before and after tDCS was performed, when technically possible.

***Results*:** we recruited 6 F and 4 M, aged 22-55, 5 with focal epilepsy (4 focal cryptogenic, 1 bilateral lesion) and 5 generalized epilepsy (2 Lennox-Gastaut Syndrome, 1 genetic –ring 20-, 2 generalized of unknown origin).
5 patients were cognitively normal, while 2 had borderline I.Q., one mild cognitive delay and 2 severe intellectual disability. Four patients reported focal seizures, 6 generalized seizure (absences, tonic seizures, GCTS, polymorphic seizures were reported by 3 pt), 2 patients reported recurrence of non convulsive epileptic status. Pre-treatment seizure rate ranged from 4 to 72 per month. EEG and MRI findings are reported in figures 1 and 2.
All patients completed the study protocol, referred side effects were short lasting hitching and redness on site of stimulation (8/10), transient somnolence during the stimulation (2/10) and excessive daytime somnolence during the treatment week (3/10). No serious adverse event was reported. Seizure diary was available for 8 patients.
No statistically significant changes were observed in seizure frequency at 7, 15 and 30 day after stimulation (Figure 3), however 5 patients reported a subjective short lasting benefit on seizure frequencies and intensity, mainly during the treatment week and the following days. EEG abnormalities rate was highly variable between patients (ranging from no paroxysmal abnormalities to almost continuous sharp-waves discharge) and varied within subsequent EEG recordings but no significant differences emerged in pre/post TDCS traces (Figure 4). Frequency analysis of pre vs post tDCS EEG didn't reveal any relevant effect of cerebrellar tDCS on bands power and distribution (Figure 5).

Fig. 1 - EEG abnormalities

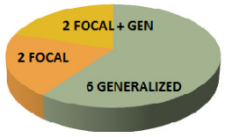


Fig. 2 - MRI findings

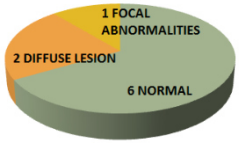


Fig. 3

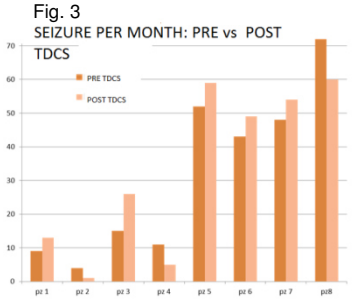


Fig. 4

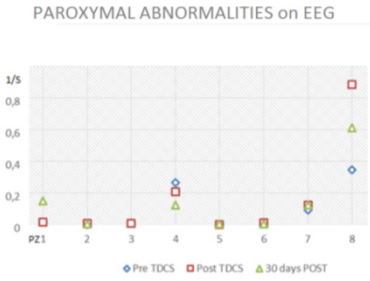
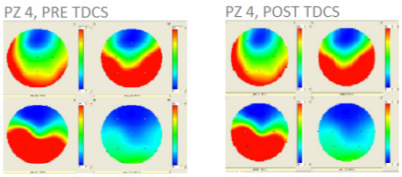


Fig. 5



Conclusions: our study confirm the safety and good tolerability of tDCS in drug resistant epilepsy, also in patients with severe intellectual disability. No relevant side effects seem related to the cerebellar stimulation. We weren't able to detect any significant change in seizure frequency, however half of the patients and caregivers reported a short-term benficial effect of the treatment. This discrepancy could be partially related to the difficulty in assessing the frequency of seizures without a clear motor component, particularly in highly disabled patients. Moreover some patient's referred a benefit on seizure "intensity" that is difficult to quantify. Moreover is possible that better results could be obtained with different stimulation parameters (i.e. higher stimulus intesity).

REFERENCES

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