TDCS to prevent optic nerve damage and to promote remyelination in EAE mouse model

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Altered nerve conduction can be modulated by transcranial direct current stimulation (tDCS) which is a non-invasive brain stimulation that has promising clinical outcomes, Multiple Sclerosis. TDCS induces polarity-dependent changes in membrane excitability by anodal tDCS, depolarizing, and cathodal tDCS, hyperpolarizing, in neurons of the stimulated areas. However, the neurobiological mechanisms underlying tDCS remain poorly understood, impeding its implementation into clinical routine. For this reason, tDCS application on animal models appears fundamental to understand and validate its treatment efficiency. Chronic Experimental Autoimmune Encephalomyelitis (EAE) disease is characterized by optic nerve abnormalities, consisting in demyelination/axonal loss, and retina thinning. Our aim was to test multisession tDCS to modulate myelin alteration in different EAE disease phases. Optic nerve and retinal functional alterations can be detectable using non-invasive methods, visual evoked potentials (VEPs), and photopic electroretinogram (pERG), while optical coherence tomography (OCT) was involved to detect morphological retinal changes. In preventive EAE phase, cathodal stimulation significantly decreased the latency delay compared to EAE-Sham and EAE-Anodal groups. Immunohistochemistry on optic nerves, showed significant decreased in microglia/macrophage cells and axonal loss in cathodal tDCS mice compared to EAE-Anodal, while demyelination area was compared between EAE groups. On the other hand, immunofluorescence suggested a significant effect of the anodal stimulation that induced an increased of paranodal and gap/paranodal length. Moving on acute EAE phase, both active stimulations restored the optic nerve functionality, while only cathodal tDCS partially protected from retinal structural damage. Interesting results were found on the clinical score and disease incidence because cathodal tDCS decreased the motor disability and the disease severity. To conclude, the tDCS effects seem dependent on the disease phase. We need to investigate more physiopathological aspects to understand better their respective effects in the acute and post-acute phases of EAE.