

Transcranial direct current stimulation applied in Experimental Autoimmune Encephalomyelitis mouse model

Silvia Marenga¹, Su-Chun Huang¹, Valerio Castoldi¹, Rossi Elena¹, Giancarlo Comi^{2,3}, Letizia Leocani^{1,2}

¹*Experimental Neurophysiology Unit, Institute of Experimental Neurology (INSPE) - IRCCS-Scientific Institute San Raffaele, Milan;* ²*Università Vita-Salute San Raffaele, Milan;* ³*Casa di Cura del Policlinico, Milan, Italy.*

Transcranial direct current stimulation (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 possible 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 acute EAE disease phase. Optic nerve and retinal functional alterations can be detectable using non-invasive methods, visual evoked potentials (VEPs), and electroretinogram (ERG), while optical coherence tomography (OCT) was involved to detect morphological retinal changes. 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. In vivo results were confirmed by myelin and neurofilament staining that showed recovery in optic nerve of both EAE-Anodal and EAE-Cathodal while in EAE-Sham myelin was significantly decreased compared to Healthy. About Iba 1 staining, cells density was significantly reduced in EAE-Cathodal compared to EAE-Sham and EAE-Anodal, which presented a significant infiltration compared to Healthy. Moving to coronal spinal cord sections, myelin and neurofilament stainings showed significant myelin loss in EAE-Sham and EAE-Anodal compared to Healthy. While density of microglia/macrophage cells was significantly higher in all EAE groups compared to Healthy. To conclude, cathodal tDCS recovered functional and structural optic nerve and spinal cord damages with more effect compared to anodal stimulation. However, anodal tDCS recovered optic nerve function and seems to have effect during the second week of treatment. Studies on tDCS effects in chronic phase are under investigation.