Title

Transcorneal retinal neuromodulation: preclinical proof of concept

Short title

Transcorneal retinal neuromodulation in mice

Authors

Valerio Castoldi[a], Elena Rossi[a], Su-Chun Huang[a], Silvia Marenna[a], Giancarlo Comi[b,c], Letizia Leocani[a,b]

[a] *Experimental Neurophysiology Unit, INSPE - Institute of Experimental Neurology, San Raffaele Scientific Institute, via Olgettina 60, 20132 Milan, Italy*

[b] *Vita-Salute San Raffaele University, via Olgettina 58, 20132 Milan, Italy*

[c] *Casa di Cura del Policlinico, via Giuseppe Dezza, 48, 20144 Milan, Italy*

Abstract

Background

Electrical eye stimulation may be a promising therapy for preserving or restoring vision in retinal and optic nerve diseases. Retinal and optic nerve degeneration are involved in Multiple Sclerosis (MS) and its animal model, Experimental Autoimmune Encephalomyelitis (EAE). We tested Transcorneal Electrical Stimulation (TES) on naïve mice to evaluate its neuromodulatory effect on retina and optic nerve through visual evoked potential (VEP) and electroretinogram (ERG).

Methods

VEP or ERG were acquired before (baseline), immediately (t0), after 5 (t5) and 10 (t10) minutes of sham or TES applied on anaesthetised C57/BL6 mice. Different types of stimulation were tested (anodal, cathodal and sinusoidal) to determine the most effective waveform able to modulate electrophysiological responses. Then, sinusoidal stimulation was applied on an additional batch of mice to confirm VEP and ERG amplitude changes. Finally, sham and sinusoidal stimulation were delivered to two independent groups of mice and ERG was recorded at baseline, t0, t5 and t10.

Results

TES affected neuronal activity, since changes in VEP and ERG amplitude were detected in TES mice compared with sham-stimulated controls. Sinusoidal current seemed to cause a more stable increase in VEP and ERG amplitude than anodal and cathodal stimulations. ERG amplitude increase persisted after 10 minutes from stimulation**,** whereas VEP change tended to return to baseline.

Conclusion

This proof-of-concept demonstrated the neuromodulatory effect of TES. Sinusoidal stimulation increased VEP and ERG amplitude, influencing optic nerve and retinal function. TES seemed to be more effective in modulating retinal than optic nerve responses, since ERG amplitude increase lasted over time. This might depend on the stimulation site that is closer to the retina; however, further experiments could clarify the effect of TES on optic nerve. Amplitude increase induced by TES could enhance neuronal electrical activity that may ameliorate retina and optic nerve function in EAE and MS.