# Visual and motor evoked potentials in experimental autoimmune encephalomyelitis

Elena Rossi[1], Silvia Marenna[1], Valerio Castoldi[1], Su-Chun Huang[1], Giancarlo Comi[2,3], Letizia Leocani[1,2]

[1]Experimental Neurophysiology Unit, Institute of Experimental Neurology (INSPE), Scientific Institute Hospital San Raffaele, Milan, Italy.
[2]Vita-Salute San Raffaele University, Milan, Italy.
[3]Casa di Cura del Policlinico, Milan, Italy.

## Introduction

**Background:** Mice with experimental autoimmune encephalomyelitis (EAE) develop visual and motor dysfunction that recapitulate some of the most prominent symptoms of multiple sclerosis[1]. Whilst visual[2] and motor[3] function in EAE have been explored independently, functional characterization of these systems in parallel is lacking. Understanding the timing of onset and the development of visual and motor abnormalities in preclinical models is pivotal to develop diagnostic and neuroprotective strategies.

**Objective:** to characterize visual and motor system involvement in C57BL/6 mice immunized with myelin oligodendrocyte glycoprotein (MOG 35-55).

## Methods

Thirty mice with EAE (10 sacrificed at each timepoint) and 10 healthy controls (in follow up) underwent visual evoked potentials (VEP) and optical coherence tomography (OCT) to assess optic nerve function and neuroretinal damage. Motor evoked potentials (MEP) were employed to characterize motor function involvement. All assessments were performed at 7, 14, and 31 days post immunization (dpi).

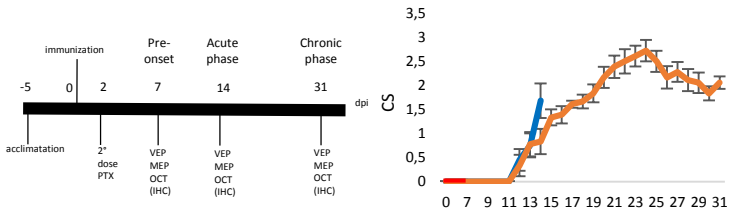


***Fig. 1.*** *Experimental timeline and EAE clinical score.*

## Results

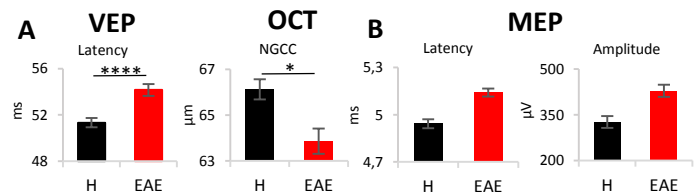


***Fig. 2. VEP, OCT,MEP at 7 dpi****. A) Optic nerve and retina showed functional and morphological alteration by VEP and OCT respectively. B) MEP showed no evident corticospinal dysfunction. EAE (n=20 eyes/hindlimbs) vs controls (n=18 eyes, 20 hindlimbs). *p<.05,****p <.0001.*

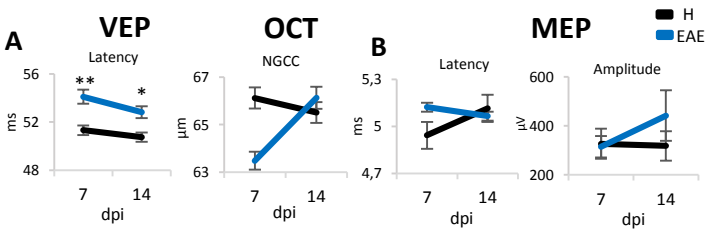


***Fig. 3. VEP, OCT,MEP at 14 dpi****. A) VEPs showed persistent functional damage in the optic nerve, but no significant alterations for MEP parameters despite clinical motor onset EAE (n=20 eyes/hindlimbs) vs controls (n=18 eyes, 20 hindlimbs).* *p<.05,** p <.01.

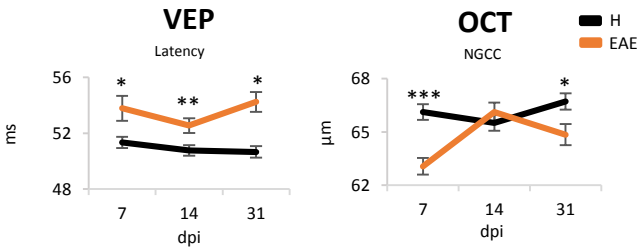


***Fig. 4. VEP and OCT at 31 dpi****. VEPs showed latency delay in EAE consistently at 7, 14, and 31 dpi. OCT revealed reduced NGCC in EAE at 7 and 31 dpi. EAE (n=18 eyes/hindlimbs) vs controls (n=18 eyes/hindlimbs).*
*p<.05, **p<.01, *** p<.001.

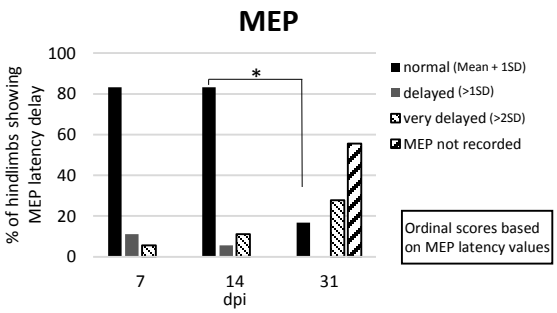


***Fig. 5. MEP at 31 dpi****. MEPs at 7 and 14 dpi showed no differences between controls and EAE (data not shown).* The number of hindlimbs with normal MEP latency significantly decreased from14 to 31 dpi. At 31 dpi several hindlimbs failed to show a MEP response. *EAE (n=18 eyes/hindlimbs) vs controls (n=18 eyes/hindlimbs).* *p<.05.

***Table 1.*** *Quantification of abnormal VEP and MEP based on cutoff values – data for eyes and hindlimbs*

| | **7 dpi** (60 eyes/hindlimbs) | **14 dpi** (40 eyes/hindlimbs) | **31 dpi** (18 eyes/hindlimbs) |
|---|---|---|---|
| Abnormal VEP | 56,7 % (34)*** | 35,0 % (14)* | 55,6 % (10) |
| Abnormal MEP | 6,7 % (4) | 10,0 % (4) | 83,3 % (15) |

McNemar test statistics for matched pairs.
*p<.05,***p<.00001 = differences with MEP at respective timepoints

## Conclusions

VEPs indicate optic nerve dysfunction earlier in the disease course at both 7 (56.7% eyes) and 14 dpi (35% eyes); however MEP alterations became predominant (83.3%) at 31 dpi.
Corticospinal functional abnormalities are detected later in time compared with visual system dysfunction and neuroretinal damage.

## Fundings

Institute of Experimental Neurology (INSPE).

**References:** [1] Constantinescu, Cris S et al. "Experimental autoimmune encephalomyelitis (EAE) as a model for multiple sclerosis (MS)." British journal of pharmacology vol. 164,4 (2011): 1079-106. doi:10.1111/j.1476-5381.2011.01302.x, [2] Marenna, S. et al. "Functional evolution of visual involvement in experimental autoimmune encephalomyelitis. " Multiple Sclerosis Journal–Experimental, Translational and Clinical, *6*(4), 2055217320963474, [3] Amadio, Stefano et al. "Motor evoked potentials in a mouse model of chronic multiple sclerosis." Muscle & nerve vol. 33,2 (2006): 265-73. doi:10.1002/mus.20463