Introduction

Background: Multiple sclerosis (MS) is a disease of the central nervous system in which the interplay between inflammatory and neurodegenerative processes typically results in intermittent neurological disorders followed by progressive accumulation of disability. About 10 to 30% of MS patients have a clinical presentation that starts with an attack of optic neuritis (ON). ON is an acute inflammatory disorder that causes demyelination of the optic nerve, thinning of the retinal nerve fiber layer (RNFL), and death of retinal ganglion cells (RGCs). These clinical symptoms can be observed and studied in the experimental autoimmune encephalomyelitis (EAE) model induced through myelin oligodendrocyte glycoprotein (MOG) injection. Immune-mediated CSF/RBCs mice develop chronic EAE. For what concerns the visual system, EAE is characterized by optic nerve abnormalities, consisting in demyelination and/or axonal loss, and retina damage detectable with visual evoked potentials (VEPs) and optical coherence tomography (OCT) respectively.

Objective: The present study aimed to investigate the usefulness of non-invasive visual evoked potential (VEP), optical coherence tomography (OCT) histology and the correlations to detect optic nerve involvement in the EAE model.

Results

Clinical score, VEP, OCT and histology

EAE mice were divided in two groups, with optic neuritis (ON, 70%) and without optic neuritis (W/O, 30%), based on cutoff for both latency and amplitude (latency cutoff: 8.12 µs; amplitude cutoff: 36%). In both EAE groups, NGCC reductions were not found. While histology showed a significant demyelination (p<0.003) and axonal loss (p<0.001) in EAE compared to HEALTHY but was not found in EAE W/O. Pearson’s correlation was significant between latency and demyelination and between axonal loss and NGCC reduction. Concerning clinical score, EAE mice were divided in 3 groups: binocular ON (BO), monocular ON (MO), W/O. EAE BO showed no significant difference compared to healthy. On the other hand, EAE W/O and MO both showed a significant increase of clinical score compared to HEALTHY. Interestingly, EAE MO presented a higher motor disability compared to EAE BO (p=0.002).

Discussion

- VEP latencies in EAE mice with ON increased at 7 dpi until 37 dpi. Amplitude decreased only in chronic phase at 23 dpi despite partial variability compared to the latency.
- NGCC reduction was not significant comparing groups at 37 dpi. The correlation between axonal loss (%) and NGCC thickness was significant.
- Demyelination correlated with VEP delay while axonal loss did not correlate with amplitude. Moreover, positive correlation was found between inflammation and latency.
- Non-invasive VEPs can be used to detect optic neuritis and to discriminate between clinical profiles with different degrees of motor disability.
- These findings suggest that VEPs can be used as an early biomarker of demyelination in EAE to test new remyelinating treatments, while OCT is suitable for monitoring subsequent neuroaxonal loss for testing neuroprotective strategies.

Literature


Conflict of interest

The authors declare no competing financial interest.

Acknowledgements

Part of this work was financially supported by Mercia and VASCOMAR.