Functional and structural in vivo assessment of demyelination and axonal loss in experimental autoimmune encephalomyelitis mouse model

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Experimental autoimmune encephalomyelitis (EAE) is a common animal model to study multiple sclerosis (MS), an autoimmune and demyelinating disease of the central nervous system. In 30% of MS patients clinical presentation starts with optic neuritis (ON). In this work, C57BL/6 mice (n=41) immunized with myelin oligodendrocyte glycoprotein peptide exhibited a chronic disease course, together with ON. We aimed at investigating ON with two follow up studies, using visual evoked potentials (VEPs), electroretinograms (ERG), optic coherence tomography (OCT) and optic nerve histology. Clinical score was measured daily. In the first study, eyes of EAE mice were divided in "EAE eyes with latency delay (EAE W LD)" and "EAE eyes without latency delay (EAE W/O LD). EAE W LD showed a significant VEP latency increase at 7 dpi compared to baseline ($p<0.0001$), while the b-wave component of ERG showed a significant amplitude decrease in EAE W/O LD ($p=0.008$). Despite these results, any difference was detected by OCT, while histology showed significant increase of $Iba1^+$ cells in both EAE groups, axonal loss only in EAE W/O LD and demyelination in EAE W LD. In the second study, eyes of EAE mice were divided in "EAE eyes with delay before clinical onset (EAE BCO)" and "EAE eyes with delay after clinical onset (EAE ACO)". Interestingly in EAE BCO, a dysfunction seems focused only in the optic nerve. In EAE ACO, ERG b-wave decreased before clinical onset and OCT detected a decrease in thickness of neuronal ganglion cell complex ($p=0.005$). However, optic nerve histology at 37 dpi showed no differences between EAE groups. To conclude, our non-invasive methods can be applied to characterize the visual pathway alterations in order to develop more effective treatments.