Onset of Optic Neuritis Precedes Motor disability in a Preclinical model of Multiple Sclerosis

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BACKGROUND

Experimental autoimmune encephalomyelitis(EAE) is the mostly used preclinical model for multiple sclerosis(MS). Neurodegeneration in retina of rats can be measured as thinning of retinal nerve fiber layer(RNFL) and ganglion cell layer/inner plexiform layer(GCL-IPL) by optical coherence tomography(OCT), while prolonged latency of visual evoked potential(VEP) indicates inflammation or demyelination. Here we employed OCT and VEP to detect the temporal relationship between visual and motor symptom during disease evolution of EAE.

MATERIALS AND METHODS

Ten dark Agouti female rats with EAE induced through myelin oligodendrocyte glycoprotein(MOG) immunization were compared to twelve healthy controls. They all underwent bilateral circular peripapillary OCT scans and flash VEP recording at baseline, 7, 14, and 21 days post immunization(dpi). RNFL and GCL-IPL thickness were segmented from OCT images and latency of N1 peak was measured from VEP. Histology of retina and optic nerve were collected at 21 dpi.

RESULTS AND DISCUSSIONS

Five EAE rats did not develop any motor symptoms(w/o), the other five had motor symptom onset from 13 dpi(w/). Mixed ANOVA showed thicker RNFL in w/ group compared with healthy at 7 dpi, probably due to edema. Main effects for both time and group was found in GCL-IPL thickness, both EAE groups showed thinning of GCL-IPL at 14 dpi compared with healthy. Compared with healthy, delayed VEP was also found from 7dpi in w/ group, and from 14dpi in w/o group. No demyelination nor axonal loss was found in histology. However, significantly higher infiltration of microglia/macrophage and RGC loss were found in w/ group compared with w/o group.

Our results showed that in MOG-EAE, ON can appear regardless of motor symptom, also, the onset of ON precedes appearance of motor symptoms. Our data also supports that instead of secondary to inflammatory demyelination, neurodegeneration exists from the onset of EAE, mainly driven by inflammation.