

Tight junction protein changes in experimental autoimmune encephalomyelitis models

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Experimental autoimmune encephalomyelitis (EAE), an animal model of human multiple sclerosis (MS), is characterized by vascular changes, particularly endothelial tight junction (TJ) protein (claudin-5 and occludin) alterations. During blood-brain barrier function, the vascular wall components, endothelial cells, pericytes and perivascular astrocytes, engage in crosstalks through cell-associated molecules and soluble factors. Pericyte-associated NG2 is a large transmembrane proteoglycan participating in these interactions, as well as in the control of pericyte proliferation and migration. We have analyzed the role of NG2 on endothelial TJ arrangement in two groups of mice, wild type (WT) and homozygous NG2 null (NG2^{-/-}), affected by MOG-induced EAE. Expression and distribution of the TJ transmembrane proteins claudin-5 and occludin were analyzed in the cerebral cortex microvessels by immunohistochemistry and laser confocal microscopy. In NG2^{-/-} mice, most cortex vessels showed an altered, chain-like claudin-5 staining pattern with aggregates distributed irregularly along the junctional membranes. Unlike the claudin-5 changes, the occludin staining pattern appeared continuous and linear and only a few cortex microvessels showed protein clustering. These TJ protein expression results in NG2^{-/-} mice affected by EAE were compared with our previous results on WT EAE mice sacrificed at 39 days post immunization. In WT EAE both claudin-5 and occludin appeared severely damaged but occludin changes were related to more severe disease stages. Interestingly, in NG2^{-/-} EAE-affected mice, claudin-5 and occludin formed an apparently unaffected linear and continuous junctional staining, suggesting a compensation of TJ damage, with cerebral cortex microvessels showing a restored claudin-5 and occludin junctional pattern. Overall, these observations suggest that absence of NG2 in the brain microvessels of naïve NG2 null mice may affect the normal arrangement of TJ proteins, whereas under inflammatory stimuli these effects seem to be partly reversed.

Keywords: EAE, NG2 null mice, BBB, TJ, confocal microscopy