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Microvascular pericytes involvement in experimental autoimmune encephalomyelitis

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In the CNS, pericytes are microvessel wall-encircling cells that, together with endothelial cells, perivascular glial endfeet and basement membrane, form the blood-brain barrier (BBB). Dysfunction of the BBB and migration of autoreactive T lymphocytes into the CNS are histopathological hallmarks of both Multiple Sclerosis (MS), a chronic demyelinating disease, and experimental autoimmune encephalomyelitis (EAE), a widely used MS animal model. The proteoglycan NG2, which has been described to accumulate within MS plaques and at spinal cord (SC) injury sites, is a primary component of pericytes, engaged in pericyte/endothelial cell interaction, proliferation and migration. To explore the role of NG2-expressing pericytes during neuroinflammation and BBB dysfunction, pericyte coverage (pericyte number/vessel length) and density (pericyte number/tissue volume) ratios were studied in brain microvessels by immunohistochemistry and laser confocal microscopy using specific pericyte markers, NG2, RGS5, and CD13. The observations were made in mice affected by MOG-induced chronic EAE with two different genetic C57BL/6 backgrounds: wild type (WT) and homozygous NG2 null (NG2-/-). In literature, NG2-/- mice did not exhibit gross phenotypic or vascular alterations, whereas our results demonstrated an unaltered pericyte density associated with slightly decreased pericyte coverage index and pericyte/endothelial cell ratio. These observations were confirmed in NG2-/- EAE-affected mice, that showed an attenuated disease severity and demyelination, and a milder BBB leakage and leukocyte infiltration, as compared with EAE WT. Taken together these results lend support to the idea of a direct involvement of NG2 proteoglycan in pericyte-endothelial cell interactions essential for the preservation of a proper BBB function.

Keywords: experimental autoimmune encephalomyelitis, NG2 null mice, pericyte, blood-brain barrier, confocal microscopy.