

Cell-to-cell communication within the neurovascular unit (NVU) in a model of cerebral cortex demyelination

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The concept of neurovascular unit (NVU) emphasizes the critical role of cell-to-cell interaction and communication between glial, neuronal, and vascular cell components during blood-brain barrier (BBB) development, and in adult normal and pathological conditions. In this study we have analysed the involvement of the nerve glial antigen 2, NG2, a chondroitin sulphate proteoglycan, highly expressed in developing and adult CNS, in cell cross-talk within the NVU. During CNS development NG2 is expressed by activated pericyte and appears downregulated as these cells undergo terminal differentiation. NG2 has also been identified on the surface of oligodendrocyte precursor cells, OPCs, evenly distributed throughout the CNS already by the end of the first postnatal week in mice and throughout adulthood. In a previous study on cerebral cortex experimental autoimmune encephalomyelitis (EAE) in mice, we firstly observed and described the glia-limitans-like position of NG2-bearing OPCs that during neuroinflammation extend processes to the pial surface and acquire a perivascular arrangement, coming in contact with the wall of EAE cortex microvessels. With the aim of understanding if a subset of OPCs specifically contributes to the cell composition of the NVU during EAE, we have explored, by morphometric analyses applied to laser confocal microscopy, OPCs distribution and vascular relationships in the cerebral cortex of WT controls and naïve NG2KO and in EAE WT and EAE NG2KO mice, at both early (20 dpi) and late (40 dpi) disease stages. In EAE WT mice, juxtavascular (JV) and perivascular (PV) OPCs were identified in a higher number compared to healthy mice. On the contrary, absence of NG2 in EAE NG2 KO mice seemed to affect the proliferative response of OPCs, specifically inhibiting the emergence of the JV and PV OPC subsets. The results indicate that in WT mice during EAE, the NVU microenvironment, classically formed by perivascular astrocytes, receives the insertion of OPCs as a specific vascular subset and suggest NG2 as the molecule involved in the observed NVU damage.