BBB-endothelial tight junction response to mesenchymal stem cells in a model of MOG EAE

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Experimental autoimmune encephalomyelitis (EAE), an induced autoimmune disease of the central nervous system, simulates the main histopathological and clinical aspects of multiple sclerosis including the impairment of the blood-brain barrier (BBB). In several experimental models of human neurodegenerative diseases, the intravenous (iv) injection of bone marrow-derived mesenchymal stem cells (MSCs) ameliorates clinical symptoms and histopathological features [1,2]. On the basis of these data, we have analyzed the status of BBB tight junctions (TJs) of cerebral cortex microvessels in a model of MOG-EAE with iv injection of MSCs (EAE-MSC). The observations were carried out on EAE-MSC mice sacrificed at 6-24 hrs and 10 days after MSCs iv injection. The expression of endothelial TJ proteins, claudin-5 and occludin, was analyzed in healthy, EAE, and EAE-MSC mice by immunofluorescence confocal microscopy, together with the evaluation of barrier function by FITC-Dextran, as an exogenous permeability tracer. The results demonstrate that unlike EAE animals, characterized by an interrupted junctional staining and a barrier leakage, EAE-MSC mice show together with attenuate disease symptoms, a continuous, control-like claudin-5 and occludin junctional pattern and a functionally recovered barrier efficiency. Overall, these findings suggest that during EAE, the neuroprotective effect of the injected MSCs includes a reparative BBB response that in turn may contribute to the reduction of the inflammatory infiltrates and to the significant amelioration of the disease.

References


Keywords

Experimental autoimmune encephalomyelitis; Mesenchymal stem cells; Blood-brain barrier; Tight junctions; Claudin-5; Occludin.