

Publication

Basic fibroblast growth factor modulates density of blood vessels and preserves tight junctions in organotypic cortical cultures of mice : a new in vitro model of the blood-brain barrier

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This study was performed to examine the maintenance of blood vessels in vitro in cortical organotypic slice cultures of mice with special emphasis on basic fibroblast growth factor (FGF-2), which is known to promote angiogenesis and to preserve the integrity of the blood-brain barrier. Slices of neonatal day 3 or 4 mouse brain were maintained for 3, 7, or 10 d in vitro (DIV) under standard culture conditions or in the presence of FGF-2. Immunohistochemistry for factor VIII-related antigen or laminin revealed a relative low number of blood vessels under standard conditions. In contrast, moderate FGF-2 concentrations increased the number of vessels: with 0.5 ng/ml FGF-2 it was 1.4-fold higher after DIV 3 or 1.5-fold after DIV 7 compared with controls; with 5 ng/ml it was almost doubled in both cases. With an excess of 50 ng/ml, FGF-2 vessels were reduced after DIV 3 or similar to controls after DIV 7. FGF receptor 1 was preferentially found on endothelial cells; its immunolabeling was reduced in the presence of the ligand. Cell death detected by an ethidium bromide analog or the apoptosis marker caspase-3 was barely detectable during the 10 d culture period. Immunolabeling of the tight junction proteins ZO-1 (zonula occludens protein 1), occludin, claudin-5, and claudin-3 revealed evidence for structural integrity of the blood-brain barrier in the presence of moderate FGF-2 concentrations. In conclusion, FGF-2 maintains blood vessels in vitro and preserves the composition of the tight junction. Hence, we propose FGF-2-treated organotypic cortical slices as a new tool for mechanistic studies of the blood-brain barrier.

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