Commentary

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Effects of Blood Exposure, Increased Catecholamine Levels and Inflammatory Mediators on Brain Microvascular Endothelial Cell Integrity in Vitro

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Abstract

Introduction: Recent studies have suggested the impact of increased catecholamine levels CAT and inflammatory mediators INF on blood on the integrity of the blood brain barrier (BBB), especially when occurring in combination with hemorrhagic stroke, a situation frequently observed in Taktosubo syndrome TTS. We investigated the possible effects of these stressors on the brain microvascular endothelium in vitro.

Methods: As an in vitro model of the BBB we used an immortalized murine microvascular endothelial cell line from the cerebral cortex (cEND). The cEND were treated with medium or patient blood containing supraphysiological concentrations of stress factors such as catecholamines, TNF-α and Interleukin-6 as characteristically elevated in patient blood suffering from acute takotsubo syndrome TTS. We investigated the impact on monolayer integrity and cellular morphology by light microscopy and immunofluorescence staining. Furthermore, alterations of representative tight and adherence junction proteins as well as integrins were determined by RT-PCR and/or Western Blot.

Results: After stress factor/ patient blood treatment, reduced viability of brain capillary endothelial cells in vitro was observed. This was concomitant with a disruption of cellular monolayer integrity and changed localisation of BBB-forming tight junction proteins as determined by real-time RT-PCR (qPCR), western blot and immunofluorescence labeling. Monolayer integrity was moreover determined by measurement of transendothelial electrical resistance.

Conclusion: Cellular monolayer integrity and the expression of proteins forming the BBB are clearly affected by exposure to patient blood, catecholamines CAT and inflammatory mediators INF, respectively. Most of barrier proteins are downregulated, so a negative impact on brain endothelial cells forming the blood-brain barrier can be assumed

Biography

Carola Förster, Professor of Molecular Medicine, Academic director for basic research at Clinics of Anesthesia and critical care, Würzburg university hospital. Diploma in Biochemistry, PhD in Biochemistry, Institute of Biotechnology, Research Centre Jülich/ Institute of Biochemistry, University of Cologne, Germany. Post doc fellow 1999-00 Department of Biochemistry and Molecular Biology Upstate Medical University, Syracuse, NY, and 2000-03, Department of Medical Nutrition, Karolinska Institute. 2007 lecture qualification for subject: Histology and Cell Biology. Present position: 2008- Associate professorship for Molecular Medicine, University hospital Würzburg, Würzburg, Germany. This position is devoted to lead and develop research in the field of molecular medicine. Her position as university professor includes supervision of MD and PhD-students and postdocs as well as teaching undergraduate, graduate and post-graduate level in the subjects of molecular medicine and molecular neurophysiology and cell biology. CF´s research has been mainly focused in studying cell physiology of the cerebral blood vessels and with a special emphasis on its permeability regulation at the level of transport processes and cellular adhesion molecules in physiology and disorders like Neuroinflammation, Ischemic brain injury, brain cancer, comorbidities of heart failure. CF is moreover devoted to characterization of the related neurovascular barriers in the eye and inner ear.

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