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Protective mechanism of FTY720 in ischemic stroke

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The contribution of neuroinflammation is increasingly recognized as a substantial pathophysiological mechanism after stroke. FTY720 is a potent treatment for primary neuroinflammatory diseases by inhibiting lymphocyte circulation and brain immigration. Infiltrating monocytes and leukocytes are considered major producer of tumor necrosis factor (TNF) TNF can have a neuroprotective role but also has been described as a mediator of brain inflammation. Previous studies using transient focal ischemia models showed a protective effect of FTY720 but did only partially characterize the involved pathways. FTY720 treatment resulted in substantial reduction of circulating lymphocytes while monocyte counts were significantly increased. After temporary middle cerebral artery occlusion (tMCAO), the number of flow cytometrically analyzed brain invading macrophages significantly increased where as T- and B-lymphocytes were significantly reduced in FTY720 treated mice. Particularly, the number of TNF positive inflammatory macrophage increased in FTY720 treated mice. There was a significant decrease in infarct volume and behavioral dysfunction on 3d after tMCAO between treated and untreated mice. In the present study, we were able to detect increased monocyte population and reduction of lymphocyte brain invasion after cerebral ischemia following FTY720 treatment. The neuroprotection with effective inclination in the TNF positive macrophages and decreased lymphocyte invasion might attribute to a divergent impact of FTY720 in the brain ischemia. We could identify a new mechanism of FTY720, which is attributable to an increase in monocyte, and microglia derived TNF in cerebral ischemia.

Biography

I am Priyadharshini Arunachalam M.Sc., ASMB (M.S.), doing my PhD in University Hamburg (Universitätsklinikum Hamburg-Eppendorf) in medical faculty under Department of Neurology. I work as junior scientist in same department. I have published 5 papers as a co-author and my main first author paper is in process. I have expertise in neuroimmunology research for past 4 years, working in cerebral ischemic disease models.

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