PHARMACOLOGICAL MODULATION OF FUNCTION AND VIABILITY OF ASTROCYTES AS A NOVEL NEUROPROTECTIVE STRATEGY IN STROKE

Summary

Neuron-astrocyte interactions are critical for signalling, energy metabolism, extracellular ion and glutamate homeostasis, volume regulation and neuroprotection in the central nervous system. Glutamate uptake by astrocytes may prevent excitotoxic glutamate elevation and determine neuronal survival. However, activation of astrogliosis and brain inflammation during cerebral ischemia exacerbates primary brain damage, resulting in upregulation of cytotoxic/infammatory cytokines and mediators, that alter blood flow and increase vascular permeability, thus leading to secondary damage and accumulation of immune cells in the brain. Although, astrocytes are more resistant than neurons to ischemic injury, astrocyte death have been demonstrated in animal models of brain ischemia. Exposure of cultured cortical astrocytes to glutamate induces apoptotic cell death and similar events can be detected in ischemic brain. FK506, an inhibitor of calcineurin and immunosuppressive drug, is neuroprotective in animal models of neurologic diseases, including focal and global ischemia. FK506 exerts a complex action on many processes ongoing in pathological brain: it directly protects neurons from glutamate-induced neuronal cell death, reduces gliosis and brain inflammation in animal models of stroke, and inhibits Glu-induced apoptosis of astrocytes *in vitro* and in ischemic brain. Altogether, recent findings suggest that modulation of astrocyte functions and astrocytic survival/cell death in neurodegeneration may be a novel therapeutic strategy in neurological disorders.