Microglial phagocytosis

Microglia are brain professional phagocytes mainly finalized to clearance of apoptotic or necrotic cells [1].

Stroke, including ischemic stroke and hemorrhagic stroke, can cause massive neuronal death and disruption of the brain structure, which is followed by secondary inflammatory injury initiated by pro-inflammatory molecules and cellular debris. Phagocytic clearance of cellular debris by microglia, the brain's scavenger cells, is pivotal for neuroinflammation resolution and neurorestoration. However, microglia can also exacerbate neuronal loss by phagocytosing stressed-but-viable neurons in the penumbra, thereby expanding the injury area and hindering neurofunctional recovery. Microglia constantly patrol the central nervous system using their processes to scour the cellular environment and start or cease the phagocytosis progress depending on the “eat me” or “don't eat me'' signals on the cellular surface. An optimal immune response requires a delicate balance between different phenotypic states to regulate neuroinflammation and facilitate reconstruction after stroke [2].

Zhao et al. demonstrated that elevated mTOR signaling in mouse microglia leads to phenotypic changes, including an amoeboid-like morphology, increased proliferation, and robust phagocytosis activity, but without a significant induction of pro-inflammatory cytokines. We further provide evidence that these noninflammatory changes in microglia disrupt homeostasis of the CNS, leading to reduced synapse density, marked microglial infiltration into hippocampal pyramidal layers, moderate neuronal degeneration, and massive proliferation of astrocytes. Moreover, the mice thus affected develop severe early-onset spontaneous recurrent seizures (SRSs). Therefore, we have revealed an epileptogenic mechanism that is independent of the microglial inflammatory response. Our data suggest that microglia could be an opportune target for epilepsy prevention [3].

1)
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