Pathophysiology of reactive astroglia and microglia

There are two types of cells in the CNS, namely neurons and the glial cells. These last support neurons in their function of communication within the CNS. Among glial cells, astroglial and microglia cells subtypes are involved in most, if not all, pathologies of the brain. Microglia have resulted in the definition of two specific phenotypes: M1 (proinflammatory) and M2 (immunosuppressive), also termed states of “classical activation” and “alternative activation and acquired deactivation”. Depending on the phenotypes activated, microglia can produce either cytotoxic or neuroprotective effects. Classical activation is associated with the production and secretion of proinflammatory cytokines such as TNF-α, IL-1β, superoxide, NO and reactive oxygen species (ROS). Alternative activation and acquired deactivation are associated with the production of anti-inflammatory cytokines such as IL-10 and TGF-β. M1/M2 paradigm has been studied in several neurodegenerative diseases in attempt to uncover the mechanisms of immunopathogenesis. Likewise, reactive astrocytes can be divided in two phenotypes named A1 and A2, with the induction of A1 proinflammatory phenotype due to brain or CNS damages/lesions. A1 reactive astrocytes, that can secrete neurotoxins which in turn induce rapid death of neurons, are induced by activated microglia. Conversely, A2 astrocytes, which are induced by ischemia, strongly promote neuronal survival and tissue repair.

One of the most striking hallmarks shared by various neurodegenerative diseases including AD, HD, PD, ALS and MS is the microglial and astroglial activation in the CNS. Therefore, a better understanding of the signaling mechanisms that occur between microglia, glia and neurons is an important step toward the development of pharmacological strategies that would allow the manipulation of metabolic pathways in order to control and harness reactive astrocytes to promote repair in CNS diseases.

References:


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