Protective role of reactive astrocytes in brain injuries: A double edge sword

For decades, astrocytes have been considered to be non-excitable support cells that are relatively resistant to brain injury. This view has changed radically during the past twenty years. Multiple essential functions are performed by astrocytes in normal brain. Astrocytes are dynamically involved in synaptic transmission, metabolic and ionic homeostasis, and inflammatory maintenance of the blood-brain barrier. Advances in our understanding of astrocytes include new observations about their structure, organization, and function. Astrocytes play an active and important role in the pathophysiology of brain damage. Brain injury impairs mitochondrial function and this is accompanied by increased oxidative stress, leading to prominent astrogliosis, which involves changes in gene expression and morphology, and therefore glial scar formation. Recent works have demonstrated a protective role of reactive astrocytes after brain injury. Nevertheless, others have pointed to an inhibitory role of astrocytes in axonal regeneration after injury. Reactive astrogliosis is a complex phenomenon that includes a mixture of positive and negative responses for neuronal survival and regeneration. Reactive astrogliosis maintains the integrity of the blood-brain barrier and the survival of the perilesional tissue, but may prevent axonal and damaged tissue regeneration. Neuroprotective strategies aiming at reducing gliosis and enhance brain plasticity are of potential interest for translational neuroscience research in brain injuries. In this context, neurosteroids and mesenchymal stem cells have shown to be promising strategies to protect brain against injury, as their effects may rely on reducing gliosis, brain inflammation and potentially modulating recovery from brain injury by engaging mechanisms of neural plasticity. Altogether, these findings indicate how potential therapeutic strategies may control astrogliosis and therefore improve neuronal survival, focusing particularly on the two-sided role of reactive astrocytes, which is an experimental paradigm helpful in discriminating destructive from protective mechanisms after brain injury.

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