Astrocytes have multiple functions in the central nervous system (CNS), e.g. control of the formation, function and removal of neuronal synapses, control of blood flow, and they play a role in brain responses to neurotrauma and stroke. In CNS injury, stroke, or in neurodegenerative diseases, astrocytes upregulate the expression of intermediate filament (nanofilament) proteins glial fibrillary acidic protein (GFAP) and vimentin as one of the hallmarks of astrocyte activation and reactive gliosis. Reactive gliosis is attenuated in mice lacking GFAP and vimentin (GFAP<sup>−/−</sup>-Vim<sup>−/−</sup>) and we previously demonstrated that this genetic attenuation of reactive gliosis leads to improved synaptic and axonal regeneration after neurotrauma, better integration of neural grafts, and enhanced neurogenesis and astrogenesis from transplanted neural stem cells. On the other hand, genetic attenuation of reactive gliosis leads to increased synaptic loss and neuronal degeneration in the acute stage of brain injury, increased loss of brain tissue in ischemic stroke and facilitates progression of Batten disease and Alzheimer’s disease. In a mouse model of Alzheimer’s disease, genetic attenuation of reactive gliosis leads to more pronounced amyloid deposits, enhanced neurite dystrophy and an altered response of microglia. Thus, astrocyte activation and reactive gliosis seem to be beneficial in acute stages of CNS injuries and in some neurodegenerative diseases, however reactive astrocytes seem to limit regenerative responses later on. Our results suggest that astrocyte activation is disease-specific and that reactive astrocytes should be considered as an attractive target for novel therapeutic interventions.