Astrocyte-synapse interaction in health and diseases

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Glial cells are very sensitive to environmental changes such as infections, inflammation, neurodegenerative diseases and even psychiatric diseases, and then, change their phenotypes into very different ones. Such a phenotypical change in glial cells is one of the most important and also problematic characteristic features of glia. As for astrocytes, they become 'reactive astrocytes' and contribute to both beneficial and hazardous brain functions. Here, I talk about reactive astrocyte-mediated network in the somatosensory cortex (S1) and striatum. Peripheral neuropathic pain that includes mechanical allodynia remains poorly treated. While glial activation and altered nociceptive transmission within the spinal cord is associated with the pathogenesis of mechanical allodynia, changes in cortical circuits also accompanies peripheral nerve injury and may represent additional therapeutic targets. Dendritic spine plasticity in the S1 cortex appears within days following peripheral nerve injury, however, its causal relationship to allodynia and the underlying cellular mechanisms remain unsolved. Furthermore, whether glial activation occurs within the S1 cortex following injury and how it contributes to this S1 synaptic plasticity is unknown. Using *in vivo* two-photon imaging with genetic and pharmacological manipulations, we show that sciatic nerve ligation induces a re-emergence of immature mGluR5 signaling in S1 reactive astrocytes, which elicits spontaneous somatic Ca^{2+} transients, synaptogenic TSP-1 release and synapse formation. Such S1 astrocyte reactivation was evident only during the first week post-injury, correlating with the temporal changes in S1 extracellular glutamate levels and dendritic spine turnover. Blocking this astrocytic signaling pathway suppressed mechanical allodynia, while activating this pathway in the absence of any peripheral injury induced long-lasting (over 1 month) allodynia. We conclude that reactive astrocytes are a key trigger for S1 circuit rewiring and contribute to neuropathic mechanical allodynia. In addition to these, reactive astrocytes cause remodeling of the neuronal network of the ischemic penumbra in the striatum. In this case, astrocytes become rather phagocytic and contribute to the rewiring. We will talk the beneficial roles of reactive astrocytes.