

**Astrocytes in the critical period regulate synapse-scaling microglia**

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Glial cells play essential roles for the modulation of synaptic connections and healthy development of brain networks. They control the excitatory/inhibitory synaptic balance and assemble neural circuitry by synapse-formation through synaptogenic factors or by synapse-elimination through phagocytosis. We have recently demonstrated that astrocytes form excitatory synapses in the adult injured brain, for which mGluR5 has an essential role. However, astrocytic mGluR5 is, in health brain, limitedly expressed in the early developmental stage (critical period). Thus, we surveyed how astrocytic mGluR5 in the critical period destines the subsequent synapse scaling using astrocyte-specific mGluR5 KO mice (cKO). Astrocytes in cKO were slightly reactive in the critical period. Unexpectedly, inhibitory synapses changed significantly more than excitatory synapses in cKO, and number of inhibitory synapses was significantly decreased in cKO throughout ages. This was mainly due to phagocytic microglia that frequently engulfed inhibitory synaptic elements in the critical period in cKO. Taken together, we conclude that astrocytic mGluR5 controls inhibitory synapses more significantly than excitatory synapses in the critical period, and its dysfunction results in decrease in inhibitory synapses throughout life, for which microglia has a pivotal role. We would like to emphasize that astrocytes in the critical period fate a lifelong inhibitory network by controlling microglia.