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Glia-mediated control of extracellular GABA/glutamate balance in the developing cortex

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Projekt Beschreibung:

The principal inhibitory neurotransmitters of the brain, GABA and glycine, operate before synapses are formed. Extracellular GABA concentration ([GABA]_e) is regulated via GABA transporters (GATs). Different GAT isoforms show a cell typespecific distribution: GAT-1 was mainly found in neurons, whereas GAT-3 was mainly observed in glia. Our preliminary data shows that the strength and development of GABAergic synaptic transmission (GST) in the immature visual cortex is regulated by the level of extracellular inhibitory amino acids:i) GST at Cajal-Retzius cells, a class of pioneer neurons, was weakened by pharmacological GAT-1 block, whereas GAT-3 inhibition enhanced GABA release,ii) Cortical neurons overexpressing a high-affinity form of the glycine receptor demonstrated reduced GABAergic synaptogenesis.We intend to address the following questions:a) How are the main sources of GABA (vesicular and GATs) spatially arranged in the marginal zone of the developing visual cortex?b) How does GABAergic synaptic activity affect the signaling of nearby astrocytes?c) How do astrocytes modulate GST in the immature cortex?d) What is the role of glial GAT-3 in synapse development?

Quelle:

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