

Modulation of synaptic transmission by a novel activity-dependent regulatory mechanism of astrocytic gap junction coupling

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Project description:

It is known that gap junction coupling between astrocytes is regulated by neuronal activity. Such modification of gap junction coupling will modify the operation of synapses by different processes, such as modulation of spatial buffering, transmitter up-take, and release of modulatory factors. Recently, we were able to show that the interaction of drebrin with connexin 43 (Cx43) stabilizes gap junction coupling in astrocytes. As demonstrated in neurons, drebrin might also serve as a signal transduction mechanism in astrocytes, which signals to other components of the sub-membrane cytoskeleton as well as to Cx43. This might be responsible for regulation of cell-cell coupling. It remains to be investigated, however, how drebrin-mediated changes of Cx43-function and gap junction coupling in astrocytes modulate on-going synaptic activity. The proposed project is aiming to analyze the functional significance of the activity-dependent regulation of synaptic transmission. In the new DFG program we will aim to prove the following hypothesis. (1) Neuronal activity modulates coupling of adjacent astrocytes by modifying Drebrin-Cx43 interaction. (2) This Drebrin-Cx43 interaction provides a novel activitydependent mechanism for sensing and adjusting synaptic transmission. To answer these questions, we will use different experimental model systems, including cell culture, in which transfection of siRNA against drebrin allows specific down-regulation of cellcell communication in astrocytes and parallel electrophysiological analysis of synaptic activity. Additionally, this novel interaction will be analyzed in acute brain slices, in which we will inject siRNA into a population of identified astrocytes from Tgn(GFAP-EGFP) mice. This will allow us to investigate the Drebrin-Cx43 mediated modulation of synaptic transmission in a functional environment.

Quelle:

<https://gepris.dfg.de/gepris/projekt/5430344?language=en>