SPP 1757

Heterogeneity of neuron-NG2 glia synapses matches glial response to regionally diverse neuronal firing behavior.

Speaker:

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Project description:

Radial glial cells (RGCs) are multipotent precursor cells and serve as guiding structures for migrating neurons. Previous work from this group has shown that the extracellular matrix protein Reelin is important for the establishment of the secondary radial glial scaffold in the dentate gyrus. In reeler mutants and mice deficient in the Reelin receptors ApoER2 and VLDLR, the formation of the dentate radial glial scaffold is severely altered and adult gliogenesis is increased at the expense of neurogenesis. In the present project we aim to understand how Reelin signalling contributes to the formation of the radial glial scaffold and to cell fate decisions in the dentate gyrus. 1) As a first step, we aim to localize the two Reelin receptors on RGCs using high-pressure freezing and immunogold labeling for electron microscopy. We will study differential functions of ApoER2 and VLDLR in glial cells and neurons by transfecting single cells in hippocampal slice cultures from receptor double knockout mice with one of the two receptors. 2) Next, we will visualize the interactions of RGCs and granule cells (RGC-guided granule cell migration) using real-time microscopy in slice cultures from transgenic mice in which immature granule cells express eGFP (POMCeGFP), while glial cells express RFP (hGFAP RFP). 3) Finally, we aim to find out whether decreased adult neurogenesis in the reeler mutant is a direct effect of Reelin, which in the postnatal period is synthesized by interneurons in the hilus and subgranular layer, the stem cell niche of the dentate gyrus. We will take advantage of our recently produced conditional Reelin knockout mice and switch off Reelin expression in adult animals that were allowed to undergo normal development of the dentate gyrus. These studies will show whether the malformation of the dentate gyrus in the reeler mutant or direct effects of Reelin on RGCs affect cell fate decisions in the adult dentate gyrus. In this context we will focus on Notch signaling since we recently found an interaction of Reelin and Notch in the dentate gyrus. Notch signaling is generally known to be important for the maintenance of precursor cells. We expect that these studies will contribute to our understanding of Reelin`s effects on radial glial cells and the stem cell niche in the dentate gyrus, respectively.

Quelle:
https://gepris.dfg.de/gepris/projekt/254852455?language=en