SPP 1757

Metabolic heterogeneity of astrocytes in grey and white matter of the brain

Speaker:

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Funding period:

since 2017

Project description:

Astrocytes crucially contribute to brain energy metabolism. However, the environment and therefore the requirements for these cells are very different in grey and white matter. Astrocytes in grey matter mainly contact synapses, blood vessels and other astrocytes, while white matter astrocytes mainly contact axons (at the node of Ranvier), oligodendrocytes and their myelin. Functionally, the major task for neurons within grey matter is transmission and computation of information at synapses; white matter tracts are specialized to allow reliable axon potential propagation along axons for long distances. We hypothesize that these diverse environments and requirements result in metabolic heterogeneity of astrocytes in respect to different basal as well as stimulated energy metabolism including regulation by different signals. In addition, we hypothesize that metabolic feedback to signaling is different in these cells. Therefore, this project aims at unraveling the discriminative metabolic events in astrocytes of grey and white matter, the underlying regulatory principles as well as their physiological relevance for brain function. These objectives will be addressed using state-of-the-art methodology including imaging of metabolites employing genetically encoded fluorescent sensors and calcium imaging in acutely isolated brain slices from mice comparing cortex and corpus callosum. Mechanisms underlying metabolic differences between astrocytes in grey and white matter will be established using cell transplantations between different brain regions as well as by correlation of metabolic phenotypes with gene expression profiles. We expect to identify differences between astrocytes in grey and white matter in basal energy metabolism as well as in the main regulatory mechanisms affecting astrocytic energy metabolism, but also providing feedback from metabolism to signaling events. In addition, we expect obtaining insights on how the astrocytic metabolic phenotype is specified in different areas of the brain. In summary, the proposed project aims at establishing a comprehensive picture of astrocytic metabolism, its regulation, and heterogeneity in different but also within brain regions. These insights will allow a deeper understanding of how brain energy metabolism is embedded in brain physiology to enable brain function.

Quelle:
https://gepris.dfg.de/gepris/projekt/387283613