SPP 1757

Heterogeneity in astrocyte sodium signalling: Functional consequences

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Earlier work performed in juvenile mouse hippocampus and cerebellum has established that astrocytes respond to excitatory synaptic activity with transient increases in their sodium concentration, which are mainly generated by high-affinity glutamate uptake. Changes in astrocyte sodium are functionally highly relevant because they alter the activity of sodium-dependent transporters such as the sodium/calcium exchanger (NCX) and serve an important role in neuro-metabolic coupling. In the first funding period of the SPP, we revealed the existence of developmental, subcellular and inter-regional heterogeneity in astrocyte sodium signalling in the mouse brain. In this context, we uncovered marked differences in the magnitude and pathways of sodium signals between neocortex and hippocampal CA1 region. Cortical astrocytes not only respond with much larger sodium transients to glutamate and to activation of glutamatergic afferents, they also experience strong NMDA-receptor-mediated sodium influx, a component, which hippocampal astrocytes lack. In the second funding period, we now aim to address the possible functional consequences of this heterogeneity. Employing high-resolution, fluorescence-based imaging of ion transients in combination with whole-cell patch-clamp and genetically-encoded nanosensors for metabolites, we will test the hypothesis that activity-induced astrocyte sodium transients are coupled to intracellular calcium homeostasis and signalling through NCX. Furthermore, we propose that they directly influence glial metabolism. The striking difference in the magnitude of activity-related astrocyte sodium signals between hippocampus and neocortex suggests functional differences between both brain regions. We hypothesize that this inter-regional functional heterogeneity of astrocytes mainly relates to the heterogeneity in sodium influx through NMDA receptors. Finally, we propose that differential sodium signalling -as mediated by NMDA receptors- amplifies sodium-related calcium signalling and augments neuro-metabolic coupling in neocortical as compared to hippocampal networks.

Quelle:
https://gepris.dfg.de/gepris/projekt/254538139?language=en