

Regional und subregional heterogeneity of astrocytes as determinants for viscoelastic tissue properties, neuronal function, and aging

Speaker:

Professorin Dr. Daniela C. Dieterich
Otto-von-Guericke-Universität Magdeburg
Institut für Pharmakologie und Toxikologie

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Project description:

In the recent years, astrocytes unravel more and more diverse and individual characteristics but in how far these heterogeneous phenotypes contribute to specific functions and particularly to a fine-tuning of neuronal activity throughout all stages of life and cognition is largely unknown. In this proposal, we aim to extend our previous work on the investigation of molecular, cellular and regional astroglial heterogeneity by performing cell type-selective proteomic profiling of astrocytes in cocultures, acute slices and in living transgenic mice using the recently developed techniques BONCAT, FUNCAT and GINCAT. We will address the consequences of astroglial heterogeneity for synaptic plasticity at different ages in mice as well as in selected culture systems mimicking the aging brain with a special emphasis on protein translation regulation and modulation of mechanical stiffness properties by astrocytes. Furthermore, we will investigate regulation of astroglial protein synthesis as well as protein turnover depending on mechanosensitive modulation, being one candidate that might promote changes in the aging brain. For this we will use agonists and inhibitors of mechanosensitive cation channels (MSC) with a special focus on the spatial organization of protein synthesis, as well as protein turnover and local stability in astroglial microdomains with regards to astrocytic heterogeneity. Finally, we will address the effect of known rejuvenators of brain function on astrocytes and their heterogeneity in the hippocampus. Ultimately, this work shall help to understand the underpinnings of cognitive function in general as well as cognitive decline in particular.

Quelle:

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