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In vivo responses in CNS glia to peripheral metabolic changes

Speaker:

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Project description:

Integrity of the complex brain functions relies on import, utilization and excretion of appropriate metabolites. While glucose maintains neural metabolism under physiological conditions in the adult animal, 60-70% of the brain energy demand can be met by ketone bodies (KB) in case of starvation, dietary intervention with ketogenic diets (fat is main energy source) or during the suckling period of mammals as a natural condition of ketosis. During ketosis, the liver catabolizes fat to produce KB, predominantly beta-hydroxybutyrate and acetoacetate. Monocarboxylate transporter 1 (MCT1) which is abundantly expressed in endothelial cells of the blood-brain barrier during the first weeks of postnatal development, facilitates the entry of KB into the brain. When mice are weaned, glucose becomes the major energy source for brain cells concomitantly with a change in expression of respective transporters; MCT1 is downregulated, while the glucose transporter GLUT1 is upregulated. Also brain metabolism switches, downregulating ketone body utilization and upregulating glucose utilizing enzymes. While these global changes have been characterized in considerable detail, it is unknown how brain cells, especially astrocytes and oligodendroglial cells adapt to the metabolic switch to facilitate brain development. What is the cell type specific metabolic specialization? What is the metabolic crosstalk between these glial cells and neurons in the developing brain? In this proposal we compare mice that are reared on ketogenic diet with normally reared mice. We aim at integrating cell type specific profiling data obtained by in vivo sampling of non-diseased CNS glia. We anticipate that our findings will contribute to the understanding of the metabolic heterogeneity of glial subtypes and shed light on the metabolic coupling between neural cells to maintain functional integrity which might open new roads for managing neurodegenerative pathologies.

Quelle:
https://gepris.dfg.de/gepris/projekt/254941457