CHOLESTEROL METABOLISM IN THE AGING BRAIN-INFLUENCE OF DIETARY RESTRICTION

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Introduction: Aging is leading risk factor for AD. Cholesterol, a main component of cell membranes and a key determinant of its fluidity, is essential for proper proteolysis of APP. The brain contains 25% of total body cholesterol and regulates its content independently of periphery by de novo in situ synthesis.

Aims: This study was aimed to define the influence of long term dietary restriction on age-related changes in the cholesterol metabolism in two brain regions critical for AD pathology, cortex and hippocampus.

Methods: The experiments were performed on 3-, 12-, and 24-month-old male Wistar rats fed ad libitum (AL) or exposed to long term DR (100% EOD) starting from 3 months of age. Levels of cholesterol, its precursors (lanosterol, lathosterol and desmosterol) and its brain specific metabolite (24S-hydroxycholesterol) were determined in the cortex and hippocampus using gas chromatography-mass spectrometry (GC-MS).

Results: The levels of cholesterol and 24S-hydroxycholesterol remained unchanged during aging and under DR in both cortex and hippocampus. However, following DR decreased levels of lanosterol in 12-month-old cortex and hippocampus and of lathosterol in 12-month-old hippocampus were detected. Our results also demonstrated ~3 times higher levels of the desmosterol in the hippocampus compared to cortex, indicating that hippocampal cholesterol synthesis is accomplished predominantly via Bloch pathway. DR influenced desmosterol content in 24-month-old rats.

Conclusions: Our data showed region specific response to long term DR at the level of cholesterol precursors. The overall cholesterol content remained unchanged under both aging and DR, indicating the importance of maintaining brain cholesterol homeostasis.