THE EFFECTS OF DIETARY RESTRICTION ON EXPRESSION PATTERN OF PROTEINS INVOLVED IN CHOLESTEROL METABOLISM IN THE BRAIN DURING AGING

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Introduction: Neurodegenerative diseases such as AD are associated with disturbances of cholesterol homeostasis in the brain. Enzyme 3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGR) is involved in cholesterol biosynthesis. Cholesterol synthesis in the brain is strongly balanced with cholesterol excretion. Enzyme responsible for cholesterol excretion from the brain is cholesterol 24S-hydroxylase (Cyp46). Under normal conditions, the cholesterol is recycled in the brain by a very efficient apolipoprotein-dependent process involving apolipoprotein E (ApoE).

Aims: The aim of this study was to analyze the expression patterns of HMGR, Cyp46 and ApoE in rat brain, as a function of aging and in response to long-term dietary restriction (DR).

Methods: The experiments were performed on 3-, 12-, and 24-month-old male Wistar rats fed ad libitum (AL), or exposed to long term dietary restriction (100% EOD) starting from 3 months of age. The expression patterns HMGR, Cyp46 and ApoE in rat cortex and hippocampus were determined using Western blot analysis.

Results: Obtained results revealed specific changes in expression profiles of examined proteins. In cortex, DR increased HMGR level in 12-month-old animals. However, DR decreased the level of HMGR expression only in hippocampus of 24-month-old rats. Regarding Cyp46, DR had no influence on its expression. DR affected ApoE expression in cortex and hippocampus in different manner: decreased its level in 12-month-old cortex, and increased it in 24-month-old hippocampus.

Conclusions: Maintaining the cholesterol homeostasis in the brain is accomplished by a series of interdependent processes that include synthesis, transport and removal of cholesterol excess in region specific manner.