Early Preclinical Changes in Hippocampal CREB-Binding Protein Expression in a Mouse Model of Familial Alzheimer?s Disease

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The molecular basis of memory loss in Alzheimer?s disease (AD), the main cause of senile dementia, is under investigation. In the present study, we have focused on the early hippocampal memory-related changes in APPswe/PS1dE9 (APP/PS1) mice, a well-established mouse model of familial AD. It is well known that molecules like cAMP response element binding (CREB) and binding protein (CBP) play a crucial role in memory consolidation. We analyzed CBP on its transcriptional activity and protein levels, finding a significant downregulation of both of them at 3-month-old mice. In addition, the downregulation of this molecule was associated with a decrease on acetylation levels of histone H3 in the hippocampus of APP/PS1 mice. Moreover, the p-CREB levels, which are important for memory acquisition at 3 months in APP/PS1 mice, were downregulated. Furthermore, we suggest that early neuroinflammation, especially due to the Tnf? gene increased expression,

could also be responsible to this process of memory loss. Given all the previously mentioned results, we propose that an early suitable treatment to prevent the evolution of the disease should include a combination of drugs, including anti-inflammatories, which may decrease glial activation and Tnf? levels, and phosphodiesterase inhibitors that increase cAMP levels.

Alzheimer disease

APPSwe/PS1dE9

CBP

CREB

Hippocampus

ADAM10 endopeptidase

beta secretase 1

brain derived neurotrophic factor

calcium calmodulin dependent protein kinase

cyclic AMP dependent protein kinase

cyclic AMP responsive element binding protein binding protein

histone H3

messenger RNA

mitogen activated protein kinase 1

mitogen activated protein kinase 3

n methyl dextro aspartic acid receptor

n methyl dextro aspartic acid receptor 1

n methyl dextro aspartic acid receptor 2

protein kinase B

protein kinase C

tumor necrosis factor

unclassified drug

amyloid precursor protein

cyclic AMP responsive element binding protein

cyclic AMP responsive element binding protein binding protein

histone

presenilin 1

Alzheimer disease

animal experiment

animal model

animal tissue

Article

BDNF gene

CBP gene

down regulation

gene expression

gene expression regulation

hippocampus

histone acetylation

male

memory consolidation

mouse

mouse model

nervous system inflammation

nonhuman

protein expression

protein phosphorylation

TNF alpha gene

Western blotting

wild type

acetylation

Alzheimer disease

animal

disease model

genetics

hippocampus

memory disorder

metabolism

transgenic mouse

Acetylation

Alzheimer Disease

Amyloid beta-Protein Precursor

Animals

CREB-Binding Protein

Cyclic AMP Response Element-Binding Protein

Disease Models, Animal

Hippocampus

Histones

Memory Disorders

Mice

Mice, Transgenic

Presenilin-1