Vulnerability of calbindin, calretinin and parvalbumin in a transgenic/knock-in APPswe/PS1dE9 mouse model of Alzheimer disease together with disruption of hippocampal neurogenesis

Verdaguer E.

Brox S.

Petrov D.

Olloquequi J.

Romero R.

de Lemos M.L.

Camins A.

Auladell C.

The pathogenesis of Alzheimer disease (AD) is characterized by accumulation of ?-amyloid protein in the brain (in both soluble and insoluble forms) and by the presence of intracellular neurofibrillary tangles (NFTs), leading to neurotoxicity. The exact mechanisms whereby A? triggers brain alterations are unclear. However, accumulating evidence suggests that a deregulation of Ca2+ signaling may play a major role in disease progression. Calcium-buffering proteins, including calbindin-D28K (CB), calretinin (CR) and parvalbumin (PV), may offer neuroprotection by maintaining calcium homeostasis. Although marked reductions in these proteins have been observed in the brains of mice and humans with AD, their contribution to AD pathology remains unclear. The aim of the present study was to analyze distribution patterns of CB+, CR+ and PV+ interneurons in different areas of the hippocampus, a brain region that is severely affected in AD. A transgenic knock-in APPswe/PS1dE9 mouse model of familial AD was used. The data were obtained from the brains of 3- and 12-month-old animals. These ages roughly correspond to an early mature adult (prior to clinical manifestations) and a late middle-age (clinical symptoms readily detectable) phase in human AD patients. Immunostaining revealed increases in CB and PV immunoreactivity (IR) in the hippocampus of 3-month-old transgenic mice, compared to wild-type

animals. Possibly, these proteins are upregulated in an attempt to control cellular homeostasis and synaptic plasticity. However, the pattern of CB-IR was reversed in 12-month-old animals, potentially indicating a loss of cellular capacity to respond to pathophysiological processes. In addition, at this age, a noticeable increase in PV-IR was observed, suggesting the presence of hippocampal network hyperactivity in older AD-like mice. Our results indicate that CaBP+ neuronal subpopulations play a role in adult neurogenesis and in AD pathology, particularly at early disease stages, suggesting that these neurons may serve as potential predictors of future AD in non-demented individuals.

Alzheimer disease

APPswe/PS1dE9 mouse

Calbindin

Calretinin

Hippocampus

Parvalbumin

calbindin

calretinin

doublecortin

neuron specific nuclear protein

parvalbumin

calbindin

calretinin

parvalbumin

Alzheimer disease

animal experiment

animal model

animal tissue

APPswe mouse

Article

brain tissue

cell metabolism

cellular distribution

clinical feature

controlled study

dentate gyrus

hippocampal CA1 region

hippocampal CA3 region

hippocampus

immunohistochemistry

immunoreactivity

interneuron

male

mouse

mouse strain

nerve cell network

nerve cell plasticity

nervous system development

neuropathology

nonhuman

pathophysiology

priority journal

protein expression

PS1dE9 mouse

transgenic mouse

upregulation

wild type mouse

Alzheimer disease

animal

disease course

disease model

metabolism

nerve conduction

nervous system development

neurofibrillary tangle

pathology

physiology

Alzheimer Disease

Animals

Calbindin 2

Calbindins

Disease Models, Animal

Disease Progression

Hippocampus

Mice

Mice, Transgenic

Neural Conduction

Neurofibrillary Tangles

Neurogenesis

Neuronal Plasticity

Parvalbumins