Dexibuprofen prevents neurodegeneration and cognitive decline in APPswe/PS1dE9 through multiple signaling pathways

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The aim of the present study is to elucidate the neuronal pathways associated to NSAIDs causing a reduction of the risk and progression of Alzheimer's disease. The research was developed administering the active enantiomer of ibuprofen, dexibuprofen (DXI), in order to reduce associated gastric toxicity. DXI was administered from three to six-month-old female APPswe/PS1dE9 mice as a model of familial Alzheimer's disease. DXI treatment reduced the activation of glial cells and the cytokine release involved in the neurodegenerative process, especially TNF?. Moreover, DXI reduced soluble ?-amyloid (A?1-42) plaque deposition by decreasing APP, BACE1 and facilitating A? degradation by enhancing insulin-degrading enzyme. DXI also decreased TAU hyperphosphorylation inhibiting c-Abl/CABLES/p-CDK5 activation signal pathway and prevented spatial learning and memory impairment in transgenic mice. Therefore, chronic DXI treatment could constitute a potential AD-modifying drug, both restoring cognitive functions and reversing multiple brain neuropathological hallmarks. © 2017 The Authors

Alzheimer's disease

APPSwe/PS1dE9

Dexibuprofen

Hippocampus

Insulin receptor

Memory impairment

Mitochondria

TAU

Abelson kinase

amyloid beta protein[1-42]

beta secretase 1

cyclin dependent kinase 5

dexibuprofen

tau protein

Abelson kinase

amyloid precursor protein

aspartic proteinase

Bace1 protein, mouse

Cables1 protein, mouse

carrier protein

Cdk5 protein, mouse

cyclin dependent kinase 5

cycline

dexibuprofen

ibuprofen

neuroprotective agent

phosphoprotein

presenilin 1

secretase

tau protein

tumor necrosis factor

Alzheimer disease

animal cell

animal experiment

animal model

animal tissue

Article

cell activation

cognition assessment

controlled study

disease course

enzyme linked immunosorbent assay

female

glia cell

immunofluorescence

male

memory disorder

mental deterioration

mouse

nerve degeneration

nonhuman

priority journal

protein degradation

protein phosphorylation

real time polymerase chain reaction

signal transduction

spatial learning

treatment outcome

treatment response

Western blotting

Alzheimer disease

analogs and derivatives

animal

brain

C57BL mouse

cognition

drug effects

genetics

metabolism

signal transduction

Alzheimer Disease

Amyloid beta-Protein Precursor

Amyloid Precursor Protein Secretases

Animals

Aspartic Acid Endopeptidases

Brain

Carrier Proteins

Cognition

Cyclin-Dependent Kinase 5

Cyclins

Female

Ibuprofen

Mice

Mice, Inbred C57BL

Neuroprotective Agents

Phosphoproteins

Presenilin-1

Proto-Oncogene Proteins c-abl

Signal Transduction

tau Proteins

Tumor Necrosis Factor-alpha