Characterizing novel hippocampal drugs for Alzheimers disease

https://www.neurodegenerationresearch.eu/survey/characterizing-novel-hippocampal-drugs-for-alzheimers-disease/

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Country

USA

Title of project or programme

Characterizing novel hippocampal drugs for Alzheimers disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,777,522.94

Start date of award

01/05/2016

Total duration of award in years

1

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Translational Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is the most common human neurodegenerative disorder of the CNS and one of the most common signs of AD is memory loss. Despite intense investigations, no effective therapy is available to improve memory in AD. Peroxisome proliferator-activated receptor (PPAR) ? is a transcription factor that regulates genes involved in fatty acid catabolism. Although hippocampus does not metabolize fat, recently we have demonstrated that PPAR? is constitutively expressed in nuclei of hippocampal neurons and surprisingly controls calcium influx and the expression of various plasticity-related genes via direct transcriptional regulation of CREB. Being a nuclear hormone receptor, PPAR? needs ligand(s) for translocation into the nucleus. Because PPAR? is constitutively present in nuclei of hippocampal neurons, ligands must be constitutively present in the hippocampal neurons as well. Interestingly, we have identified three novel ligands (Hexadecanamide, Octadecenamide and 3-hydroxy, 2, 2-dimethyl butyrate) from hippocampal extracts of normal mice. Here, we would like to examine functions of these novel ligands in the hippocampus, compare levels of these ligands and their receptor PPAR? in the hippocampus of patients with AD, mild cognitive impairment (MCI) and age-matched controls with no cognitive impairment, and delineate whether these ligands improve memory and learning in an animal model of AD via PPAR?. A positive outcome of this grant proposal will highlight the discovery of novel hippocampal ligands of PPAR?, allowing us to develop hippocampus-based drugs to enhance synaptic plasticity and protect memory and learning in cognitive disorders including AD.

Lay Summary
PUBLIC HEALTH RELEVANCE: Despite intense investigations, no effective therapy is available to improve memory in patients with Alzheimer’s disease (AD). We have identified three novel ligands of PPAR? from the hippocampus and here, we would like to examine functions of these novel ligands in the hippocampus and delineate whether these ligands improve memory and learning in an animal model of AD via PPAR?. A positive outcome of this grant proposal may highlight the discovery of novel hippocampus-based drugs to enhance synaptic plasticity and protect memory and learning in AD.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
N/A