APP Regulates Brain and Adipose Changes in Obesity

https://neurodegenerationresearch.eu/survey/app-regulates-brain-and-adipose-changes-in-obesity/

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Country

USA

Title of project or programme

APP Regulates Brain and Adipose Changes in Obesity

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,268,426.61

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01/08/2012

Total duration of award in years

5

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... Nutrition... Obesity

Research Abstract

DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is estimated to affect over 5

million Americans. A significant risk factor for AD is particularly mid-life obesity. In itself, obsity also represents a tremendous health concern for the U.S. with its suggested epidemic levels. Therefore, any strategy to ameliorate either or both conditions is extremely attractive therapeutically. We propose that the relationship between AD and obesity is not correlative but that there may be a common pathophysiology. It is well known that mutations in the gene coding for amyloid precursor protein, APP, are responsible for autosomal dominant forms of AD. However, our preliminary data indicates that APP is critically required for weight gain and the associated brain and adipose changes that occur in a murine model of high fat diet-induced obesity. APP expression is actually required for efficient uptake of fatty acids into cells. Therefore, we hypothesize that APP regulates diverse cellular differentiation involving, in particular, changes in lipid metabolism that regulates adipocytes, neurons, and macrophage/microglia during diet-induced obesity. Dysregulation or alteration of this biology by mutant APP will have ramifications during obesity but, more importantly, during AD. We will first test this hypothesis quantifying the ability of wild type and mutant APP and any associated signaling or processing to regulate adipocyte, macrophage/microglia, and neuron phenotype in vitro. We will then define a role for APP in tissue specific changes during diet-induced obesity in vivo using wild type and mutant APP expressing mice compared to APP-/- mice. By defining the role of normal and mutant forms of APP in regulating cellular phenotype in adipose tissue depots and brain we will explain how APP contributes directly to diet-induced obesity and possibly to progression of AD. This not only offers a common mechanistic pathophysiology of these two diseases but also targets APP and its associated signaling response for therapeutic intervention.

Lay Summary
This study will validate a novel mechanism by which amyloid precursor protein regulates the ability of cells to metabolize and utilize fatty acids. This biolog is particularly important for the changes that occur in adipose tissue but also in the brain and immune cells during the condition of diet-induced obesity. Because expression of mutant forms of amyloid precursor protein produces Alzheimer’s disease, we speculate that the role of amyloid precursor protein in regulating lipid metabolism is also related to mechanisms of Alzheimer’s disease. Defining the function of amyloid precursor protein in diet-induced obesity will not only offer insight into the pathophysiology of obesity but also that of Alzheimer’s diseas.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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