Intranasal Insulin in a Mouse Model of Alzheimers Disease

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Principal Investigators

BANKS, WILLIAM A

Institution

SEATTLE INST FOR BIOMEDICAL/CLINICAL RES

Contact information of lead PI
Country

USA

Title of project or programme

Intranasal Insulin in a Mouse Model of Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,156,355.96

Start date of award

01/09/2014

Total duration of award in years

3

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... Endocrine System... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): Although several clinical studies from two different

groups have shown that insulin when given by the intranasal (INL) route results in an almost immediate improvement in cognition in Alzheimer’s disease (AD) patients that is sustainable to at least 4 mo, there is very little work examining how INL insulin works. Our preliminary results show that radioactive insulin (I-Ins) reaches the hippocampus after INL administration in mice through a saturable mechanism and that INL insulin improves both learning and memory in an AD mouse model (the aged SAMP8 mouse) at doses that do not affect peripheral metabolism. The cognitive effect of INL insulin is evident in the SAMP8 within 24 h, but new preliminary results submitted in this A1 show further improvement in cognition when INL insulin is repeatedly administered for 2 weeks. In this application, we will examine in the aged SAMP8 mouse three critical aspects that are important to understanding how INL acts in AD, testing the widely held hypothesis that AD is a state in which CNS insulin action is deficient. In SA1, we will determine the pharmacokinetics and brain distribution of transport of INL administered insulin in the SAMP8. In SA2, we will determine the status of hippocampal insulin receptor expression and function, determining if the aged SAMP8 has CNS insulin resistance. In SA3, we will determine the effects of INL insulin on the AD phenotype as expressed by the aged SAMP8 [increased brain amyloid beta load and vasculopathy , tauopathy, BBB dysfunctions (decreased bulk flow of CSF; P-gp and LRP-1 efflux deficits), cholinergic defect, and oxidative stress], determine the types of cognitive deficits remediable by INL insulin, and determine the effects of INL insulin on gene expression, and hippocampal cell death , synaptogenesis, and neurogenesis. We will also compare the effects of immediate (24 h after treatment) and sustained (2 weeks of treatment) INL insulin administration on key aspects of the phenotype. Overall, these studies will for the first time define how INL insulin works in an AD model.

Lay Summary
PUBLIC HEALTH RELEVANCE: These studies will determine how intranasal insulin, a treatment that produces rapid memory improvement in AD patients, works; this, in turn, will aid in designing approaches to improve its effectiveness.

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

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