Insulin Resistance and Accelerated Cognitive Aging

https://neurodegenerationresearch.eu/survey/insulin-resistance-and-accelerated-cognitive-aging/

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Country

USA

Title of project or programme

Insulin Resistance and Accelerated Cognitive Aging

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,142,403.67

Start date of award

01/09/2016

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)... Basic Behavioral and Social Science... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diabetes... Endocrine System... Neurodegenerative... Neurosciences... Obesity... Prevention

Research Abstract

Insulin resistance (IR) is the modifiable metabolic state underlying type 2 diabetes mellitus (DM2), cardiovascular disease (CVD), and Alzheimer's disease. Studies to date have shown significantly increased risk for Mild Cognitive Impairment and Alzheimer's disease in the presence of DM2, as well as overt cognitive, morphological and functional brain abnormalities in cognitively-normal male and female individuals with IR. While DM2 can be modified with pharmacological and/or behavioral interventions, IR (a precursor to DM2), is a reversible condition. Of notable concern is that rates of IR, and pre-diabetes, are ever increasing; as of 2007, the CDC estimated 57 million (26%) of American adults have it. Further mechanistic studies on the deleterious effects of IR on Alzheimer's disease risk are needed. Better, more effective and early detection of Alzheimer's disease risk will strongly depend on disentangling the effects of non-modifiable genetic biomarkers, such as APOE4 and familial risk, from modifiable biomarkers, such as IR. This proposal aims to advance our understanding of the mechanisms of insulin action in the living human brain, before overt neurodegeneration has begun, thus identifying the earliest signs of Alzheimer's disease. It's not known whether IR can predict cognitive decline in individuals younger than age 50 without overt mental illness. We propose to use an innovative accelerated longitudinal design (ALD) to characterize trajectories of cognitive and neural biomarkers and to: 1) describe baseline cognitive and neural biomarkers of brain function across the spectrum of IR in persons ages 25-50; 2) assess how the baseline IR and change in IR at a younger age affects the pattern of decline in cognitive and neural biomarkers and 3) explore the effects of baseline IR on changes in cognitive and neural variables of interest as moderated by non-modifiable risk factors for Alzheimer's disease (gender, and APOE4/family history). Utilizing an accelerated longitudinal design (ALD) we will recruit overweight/obese individuals (total N=135) aged 25-50. Based on semi-longitudinal data, this design will allow us to examine outcome development over 25 years between ages 25-50 after 3-year follow-up. All subjects will undergo baseline qualitative measure of IR, cognitive assessments and multimodal magnetic resonance imaging (MMRI). Neuropsychological evaluation will focus on cognitive flexibility/set shifting tests reflecting hippocampal connectivity to the medial prefrontal region. MMRI will include memory-related hippocampal function and connectivity (measured with task- and resting-state fMRI) and hippocampal volumes. This project will help to identify adults at risk for Alzheimer's disease and afford a unique opportunity to assess whether IR mediates cognitive and correlating neural processes decades before the age-related cognitive impairment, Mild Cognitive Impairment or Alzheimer's disease become apparent.

Lay Summary

PUBLIC HEALTH RELEVANCE: Premature and accelerated brain aging trajectories have been observed among people with metabolic dysfunction, but mechanisms of these altered trajectories are not understood; insulin resistance (IR) is known to change with age, affect cognition in older and elderly adults as well as in patients with mood disorders. The main purpose of the study is to describe the developmental trajectory of cognitive and neural biomarkers across the spectrum of metabolic dysfunction in overweight/obese adults younger than 50 years of age. The innovative study design will allow us to examine cognitive outcome development over 25 year span without an investment into the longitudinal observation of changes in cognition and neural function.

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