Diabetes Status and Brain Amyloid in Middle Aged Hispanics

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Country

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Title of project or programme

Diabetes Status and Brain Amyloid in Middle Aged Hispanics

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 5,084,326.61

Start date of award

01/09/2015

Total duration of award in years

2

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... Cerebrovascular... Clinical Research... Clinical Research - Extramural... Dementia... Diabetes... Diagnostic Radiology... Endocrine System... Minority Health for IC Use... Neurodegenerative... Neurosciences

Research Abstract

This revision application is submitted in response to PA-13-302, Research Project Grant (Parent R01). The purpose of this revision application is to add tau positron emission tomography (PET) imaging to grant 1R01AG050440-01A1 entitled Diabetes and Brain Amyloid in Middle Aged Hispanics", using the Tau ligand 18F-THK-5351, for in-vivo neuroimaging of paired helical filament tau aggregates. The parent R01 already funds brain magnetic resonance imaging (MRI) and amyloid ? (A?) PET. The funded period for the parent grant is 09/01/15 to 06/30/20. The funding period of the proposed revision application is 10/01/16 to 05/31/20, overlapping with the funded project in its last 4 years of funding. The main goal of this revision proposal is to study whether diabetes status (type 2 diabetes [referred to as diabetes] and pre-diabetes, compared with normal glucose tolerance [NGT]), is associated with increased tau accumulation in the brain, one of the culprits of Alzheimer's disease (AD), in a community-based sample of middle aged Caribbean-Hispanics with a mean age of 63 years. In this application we refer to tau imaging as imaging of paired helical filament tau aggregates, not normal cytoskeletal tau. We propose to add tau PET imaging with the ligand 18F-THK-5351 taking advantage of the ongoing funded parent R01 of A? PET imaging with 18F-Florbetaben PET in 150 middle aged Hispanics with concurrent brain magnetic resonance imaging (MRI), and assessment of cognition and diabetes status, at 2 time points, 24 months apart. Our primary hypothesis is that diabetes and pre-diabetes are related to accumulation of brain tau aggregates as compared with NGT. Our secondary hypotheses are that brain tau aggregates mediate the association of diabetes and pre-diabetes with memory impairment, and brain A? and CVD interact with tau aggregates in causing memory impairment. Our primary aim is to compare the amount of tau accumulation, measured with 18F-THK-5351, in medial temporal and inferior temporal cortex, cross- sectionally and longitudinally (with an interval of 2 years) between participants with diabetes (n=50), pre- diabetes (n=50), and NGT (n = 50). We will also examine glycemia continuously using Hemoglobin A1c (HbA1c) as an exposure. Secondary aim 1 is to explore whether differences in tau in medial temporal and inferior temporal cortex among participants with diabetes, pre-diabetes, and NGT, mediate the association of diabetes and pre-diabetes with worse memory performance. Secondary aim 2 is to explore the interaction of tau in medial temporal and inferior temporal cortex with (a) brain fibrillar A? and (b) CVD in mediating the association of diabetes and pre-diabetes with memory impairment. These aims are our main focus. However, we will be able to explore effect modification by APOE-?4, other correlates of diabetes as exposures (insulin, components of the metabolic syndrome), other regions of interest for tau accumulation, and the temporal relation of the accumulation of brain tau aggregates and A?.

Lay Summary

Our revision application will address the increasing interest in tau as a mechanism driving the clinical consequences of Alzheimer's disease (AD) in the context of disappointing result for Amyloid ? based therapies. Our project is in line with the goals of the National Alzheimer's Project Act (NAPA) in that it may inform the prevention and treatment of cognitive impairment by clarifying the mechanisms relating diabetes status to clinical manifestation of AD, and by providing information that may explain the high burden of AD manifestations among minorities, which we have found may be significantly explained by diabetes compared with Non-Hispanic Whites.

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