

# Interdisciplinary Research to Understand the Interplay of Diabetes, Cerebrovascular disease and Alzheimers disease

<https://neurodegenerationresearch.eu/survey/interdisciplinary-research-to-understand-the-interplay-of-diabetes-cerebrovascular-disease-and-alzheimers-disease/>

## Principal Investigators

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## Contact information of lead PI

### Country

USA

## Title of project or programme

Interdisciplinary Research to Understand the Interplay of Diabetes, Cerebrovascular disease and Alzheimers disease

## Source of funding information

NIH (NIA)

## Total sum awarded (Euro)

€ 5,314,577.06

## Start date of award

30/09/2015

## 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 Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias

(AD/ADRD)... Brain Disorders... Cerebrovascular... Dementia... Diabetes... Endocrine System... Neurodegenerative... Neurosciences... Vascular Cognitive Impairment/Dementia

### **Research Abstract**

? DESCRIPTION (provided by applicant): The main goal of this proposal is to study the interplay of diabetes, cerebrovascular disease (CVD), and Alzheimer's disease (AD) in response to RFA-AG-15-010 "Interdisciplinary Research to Understand the Vascular Contributions to Alzheimer's Disease (R01)". Type 2 diabetes and pre-diabetes affect one third of United States adults, and the majority of persons aged 60 years and older, who are most susceptible to AD. Diabetes is a strong risk factor for CVD and for vascular cognitive impairment. Diabetes is also associated with a higher risk of the clinical manifestations of AD including dementia and amnesic mild cognitive impairment, but it is unclear whether AD, CVD, or both, mediate this association, and whether this association is causal. We hypothesize that diabetes causes AD in addition to CVD, and that the coexistence of AD and CVD mediate the association of diabetes with memory impairment, the earliest manifestation of AD. We will test these hypotheses in human and mouse studies. Our primary aim is to examine the association of diabetes with the interplay of AD and CVD in humans and mice. We will conduct a brain imaging study with 2 waves in a cohort of 200 persons with a mean age of 62 years followed at 2-year intervals in order to examine the cross-sectional and longitudinal association of diabetes with AD. We will categorize diabetes as pre-diabetes, diabetes, and normal glucose tolerance (NGT), and examine glycemia continuously using HbA1C. We will ascertain AD with amyloid ? (A?) imaging using Positron Emission Tomography with 18F-Florbetaben. We will characterize CVD with brain magnetic resonance imaging (MRI) as white matter hyperintensities (WMH) and infarcts. We will also explore the coexistence of aggregate and regional CVD, AD, and cerebral amyloid angiopathy (CAA, ascertained as microbleeds on MRI) in relation to diabetes. We will explore if AD mediates the association of diabetes with memory impairment, and whether CVD modifies this association. We will compare among diabetic, AD (J20), AD/diabetic mice, and appropriate controls the distribution and load of AD neuropathology (phosphorylated tau, soluble A? peptides, and plaques) in three ages (2, 5 and 14 months) with and without transient occlusion of the middle cerebral artery (MCA). We will also compare cognitive performance in these groups. Our secondary aim is to examine if diabetes is related with AD-like brain functional correlates in humans and mice. Our exploratory aims are to explore in humans whether AD predicts incident pre-diabetes and diabetes and increasing glycemia among persons with NGT, whether AD mice are more likely to develop hyperglycemia, explore the plasma lipidomic and proteomic profile predictive of clinical, pathologic, and physiologic outcomes, and explore the association of correlates of diabetes, such as adiposity, dyslipidemia, inflammation, hypertension, insulin resistance, with AD.

### **Lay Summary**

**PUBLIC HEALTH RELEVANCE:** Our multidisciplinary research project is responsive to the goal of the National Alzheimer's Project Act to prevent and effectively treat AD by 2025 by understanding how pre-diabetes and diabetes, which affect a majority of the population at risk for dementia, are related to the interplay of Alzheimer's disease and cerebrovascular disease.

**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