Community based assessments regarding vascular contributions to Alzheimers Disease in M2OVE AD consortium

https://neurodegenerationresearch.eu/survey/community-based-assessments-regarding-vascular-contributions-to-alzheimers-disease-in-m2ove-ad-consortium/

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Country

USA

Title of project or programme

Community based assessments regarding vascular contributions to Alzheimers Disease in M2OVE AD consortium

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 5,258,883.49

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 including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Cardiovascular...

Dementia... Neurodegenerative... Neurosciences

Research Abstract

? DESCRIPTION (provided by applicant): Despite advances in our knowledge of Alzheimer's disease (AD) course, our understanding of the pathogenesis of this devastating illness is lagging behind. This application, in response to RFA-AG-15-010, aims to identify the contribution of vascular dysfunction and its associated molecular mechanisms related to the endothelium and angiotensin pathways in AD. We propose to assess systemic and cerebral vascular functions and identify their molecular regulators in prodromal AD and use experimental models to define the precise contribution of these pathways and potential therapeutic interventions. We leverage existing cohorts (Emory Cardiovascular Biobank and Predictive Health Studies); excellent infrastructure for molecular and translational vascular phenotyping; ongoing NIH funded projects (Emory ADRC) at our institution; and a strong interdisciplinary team with expertise in cardiology, vascular biology, cognitive aging, neurosciences, neuroimaging, metabolomics and bioinformatics. To achieve this goal of studying the role of vascular function in AD, we will study 100 individuals with prodromal AD (MCI with AD-signature cerebrospinal fluid (CSF) profile, MCI-AD) and 100 matched cognitively normal individuals for 2 years and use a novel AD rat model (TgF344) that exhibits changes in both amyloid and tau also followed for 2 years. Our Aims are to investigate the role of vascular function and regenerative capacity in MCI-AD (AIM1); Identify CSF and plasma markers in vascular other metabolic pathways using explorative unbiased metabolomic profiling in MCI-AD (AIM2); and use a rat AD animal model to establish the chronological order between vascular dysfunction and AD trajectory and study the impact of modifying vascular dysfunction via angiotensin II blockade on AD trajectory (AIM3). Our preliminary work suggests that (i) systemic and cerebral vascular dysfunction contribute to cognitive impairments, and that (ii) molecular/cellular modulators of vascular function (oxidative stress (OS), renin angiotensin aldosterone system, endothelial activity and vascular regeneration) are related to cognitive function and neuropathological indicators of AD. We intend to build on this prior work and will leverage ongoing studies to ensure recruitment of the proposed sample (n=200). We incorporate a set of parallel measures in the human and rat studies enhancing 2-way translational capabilities: object location cognitive paradigm, A?/tau levels, and comparable measures of vascular. To uncover underlying known and unknown molecular regulators, we have a cutting edge metabolomic facility and use novel “”metabolomic analysis of CSF and plasma of our participants. We validate the role of significant metabolite in AD in (i) our AD rats using gene expression and (ii) in an independent CSF sample (N=800). Our infrastructure of a strong vascular phenotyping program and a highly accomplished interdisciplinary team put us in a unique place to achieve the goals of this RFA: identify novel vascular biomarkers and provide new vascular-targeted therapies in early AD.

Lay Summary

PUBLIC HEALTH RELEVANCE: Although great advances have been made in understanding Alzheimer's disease (AD), underlying vascular mechanisms are still not fully described. This study investigates the vascular effects and mechanisms in early stages of AD. This project would offer new targets for future therapeutic interventions.

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