Angiogenesis and Alzheimer’s Disease

https://www.neurodegenerationresearch.eu/survey/angiogenesis-and-alzheimer%c2%92s-disease/

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Country

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Title of project or programme

Angiogenesis and Alzheimer’s Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

402436.6972

Start date of award

15/05/2016

Total duration of award in years

1

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... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention... Stem Cell Research... Stem Cell Research - Nonembryonic - Human... Vascular Cognitive Impairment/Dementia

Research Abstract

? DESCRIPTION (provided by applicant): This proposal seeks support for an exploratory and developmental research project. Microvascular disease and chronic cerebral hypoperfusion may play a larger role in the cause of Alzheimer disease (AD) than previously understood.

Angiogenesis triggered by cerebral hypoperfusion may play an initial moderating and inciting role in the development of AD. A peripheral marker of angiogenesis could serve as an early biomarker of pre-AD pathology. We have demonstrated that relative levels of angiogenesis activity can be identified through the measurement of two phenotypically and functionally distinct sub-populations of circulating hematopoietic stem and progenitor cells (CHSPCs) in the peripheral blood. We hypothesize that cerebral hypoperfusion results in early and appropriate angiogenesis but over time this process becomes an aberrant or pathological angiogenesis eventually leading to AD. This R21 has three specific aims: Aim 1: Measure the levels of CHSPCs in a well-characterized sample of 40 older adults from the following four groups (10 each): a) cognitively normal, b) subjective cognitive decline, c) amnestic mild cognitive impairment (MCI); and d) mild severity late onset AD. Hypothesis 1: The pCHSPC:nCHSPC ratio: 1a) will be elevated among those with subjective cognitive decline and MCI; 1b) will be decreased in the context of a clinical diagnosis of AD compared with normal subjects. Aim 2: Test the relationship between CPSPC levels and quantitative MRI-based measures of cerebrovascular integrity including a) microvascular pathology on fluid-attenuated inversion recovery (FLAIR) and b) regional cerebral blood flow (rCBF) using 3D pseudo-continuous arterial spin labeling (3D pCASL) perfusion measurement. Hypothesis 2: The pCHSPC:nCHSPC ratio will predict 2a) white matter hyperintensity (WMHI) burden on FLAIR and 2b) lobar rCBF on 3D pCASL MRI. Aim 3: Test the association of CPSPC levels with established risk factors or biomarkers of AD including: (a) APOE epsilon 4 carrier status; (b) hippocampal volume and temporal lobe atrophy; and c) amyloid burden on [18F]florbetapir PET. Hypothesis 3: The pCHSPC:nCHSPC ratio will be significantly associated with existing AD biomarkers but with stronger correlation at earlier stages (i.e., subjective cognitive decline>MCI>AD). This study represents a first step toward establishing the pCHSPC:nCHSPC ratio as a pre-symptomatic or early prodromal marker of the cerebrovascular dysregulation that may precede AD.

Further information available at:

Types:
Investments < €500k

Member States:
United States of America

Diseases:
N/A

Years:
2016

Database Categories:
N/A

Database Tags:
N/A