White matter degeneration: biomarkers in preclinical Alzheimers Disease

https://neurodegenerationresearch.eu/survey/white-matter-degeneration-biomarkers-in-preclinical-alzheimers-disease/

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Country

USA

Title of project or programme

White matter degeneration: biomarkers in preclinical Alzheimers Disease

Source of funding information

NIH (NIA)

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5

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... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention

Research Abstract

DESCRIPTION (provided by applicant): Brain white matter (WM) is substantially altered in Alzheimer's disease (AD), and in people who are at increased risk for AD due to mild cognitive impairment (MCI), genotype (APOE4), and parental family history of AD. New data suggest that WM alterations can be measured preclinically with diffusion tensor imaging (DTI), in the absence of gray matter alterations measured with T1-weighted MRI. WM is primarily composed of myelin and axons; however, the component of WM affected preclinically is still unknown, as are the mechanisms underlying this phenomenon. Also unknown is the extent to which early WM alterations signal additional future brain degeneration. The objective of the proposed project is to determine, in vivo, the nature of WM alterations in preclinical AD, the temporal pattern of early brain change, and the extent to which known AD mechanisms impact preclinical WM health. The central hypothesis is that WM alterations are related to tau pathology, accumulation of beta-amyloid, and neuroinflammation, and precede degeneration of gray matter. The central hypothesis will be tested by pursuing two specific aims: Aim 1: Determine the temporal time course of white matter alteration and gray matter alteration in the development of AD pathology. This will be accomplished by performing longitudinal MRI and cerebrospinal fluid (CSF) collection in people with parental family history of AD and matched controls to obtain WM measures (fractional anisotropy, radial diffusion and axial diffusion from DTI, myelin water fraction maps from mcDESPOT MRI, and myelin basic protein, anti- myelin antibody, and neurofilament light protein from CSF). These measures will be used to account for change in gray matter measures (volume and cortical thickness) from baseline to 2-year and 4-year follow-up. Aim 2: Establish the extent to which pathological mechanisms implicated in AD are related to preclinical white matter alterations in AD-vulnerable brain regions. This will be accomplished by collecting longitudinal MRI and CSF in people with parental family history of AD and controls where CSF biomarkers of AD will be used to predict longitudinal changes in WM integrity indexed by MRI & CSF. We expect the results of this project to provide new knowledge concerning early WM alterations in AD, provide information leading to earlier diagnosis of AD, and contribute to the development of new prevention and treatment strategies, which in turn is expected to reduce the prevalence of this devastating disease. White matter markers have received less attention in the study of preclinical AD, and WM markers in preclinical AD remain relatively unexplored. This project will address this gap in knowledge, in addition to providing novel data that links WM alterations to hypothesized mechanisms of degeneration. The project has a high likelihood of success because the PI's team of basic and clinical science investigators is well-versed in both basic and clinical research methods, is expert in analyzing and interpreting MRI and CSF data, is focusing on a unique preclinical population at risk for AD, and is equipped with exceptional resources provided by the Wisconsin ADRC.

Lay Summary

Without intervention, Alzheimer's disease (AD) will exert a devastating human toll. Clarifying the earliest brain changes in AD is expected to lead to earlier diagnosis, and contribute positively to the development of prevention strategies and treatments that in turn would decrease the incidence of AD.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

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Alzheimer's disease & other dementias

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2016

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