Antecedent Biomarker Changes in AD: Ordering, Stages, and Implications for Trials

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Country

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Title of project or programme

Antecedent Biomarker Changes in AD: Ordering, Stages, and Implications for Trials

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NIH (NIA)

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€ 3,134,276.15

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01/09/2016

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... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention

Research Abstract

Accumulating research suggests that the neurodegenerative processes associated with Alzheimer's disease (AD) begin years prior to the symptomatic onset when the disease is clinically at the early prodromal stage or a latent stage. These observations, coupled with the fact that there are currently no pharmaceutical treatments that reverse the pathological processes of AD, have led to a major paradigm shift in the search of efficacious treatments of AD, that is, the focus of modern AD clinical trials now is on individuals at the preclinical stage prior to the substantial development of clinical symptoms as these may be the groups of individuals in which targeted therapies may have the greatest chance of preserving brain function. Because of lack of clinical symptoms at the preclinical stage of AD, designing clinical trials for early intervention is only possible if biomarkers can help both identify at-risk individuals and classify them into different levels of risk for developing clinical symptoms during a given period by distinguishing the cascade of preclinical changes across multiple modalities of biomarkers. We are proposing to integrate the databases from 4 major biomarker studies of aging and AD across the world (Washington University (WU) Adult Children Study (ACS) enriched by data from WU Alzheimer Disease Research Center (ADRC) and the PPG titled 'Healthy Aging and Senile Dementia' (HASD), the Australian Imaging, Biomarkers and Lifestyle (AIBL) flagship study of aging, Johns Hopkins University Biomarkers for Older Controls in Risk for Dementia (BIOCARD) study, and the Wisconsin Registry for Alzheimer's Prevention (WRAP)) to provide the most comprehensive and up-to-date characterization of changes in cerebrospinal fluid (CSF) biomarkers and neuroimaging biomarkers (positron emission tomography (PET) amyloid imaging, magnetic resonance imaging (MRI)-based brain volumes, and PET fludeoxyglucose (FDG)) as well as their cognitive correlates among 3649 individuals across a wide age span starting ~45y from healthy aging to early AD. We also propose to study the contribution of vascular lesions to biomarker and cognitive changes, and validate the findings both neuropathologically by uniformly assessing brain tissues from 50 autopsied brains and in the WU Dominantly Inherited Alzheimer Network (DIAN) consisting of 343 individuals who were members of a pedigree with a known causative mutation for autosomal dominant AD (ADAD) in the amyloid precursor protein, presenilin 1, or presenilin 2 (PSEN2) genes. We have assembled an extraordinary interdisciplinary team with outstanding expertise from all major AD biomarkers(Drs. Fagan for CSF, Benzinger/Johnson for neuroimaging, Masters for trials) & clinical/cognitive characterization of AD (Drs. Morris, Albert) to analyze one of the world's largest biomarker databases with a crucial age window (~45 y to 65 y) that will capture the initiation of all major changes prior to the symptomatic onset of AD. Our study is highly significant because understanding very early biomarkers/cognitive changes will allow therapeutic interventions to be administered well before dementia symptoms are fully developed.

Lay Summary

This project proposes to analyze one of the world's largest biomarker database with a crucial age window (~40 y to 65 y) that will capture the very initiation of major changes prior to the symptom onset of AD so that therapeutic interventions can be tested and allowed well before dementia symptoms are fully developed.

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