Alzheimers Disease Connectome Project

https://neurodegenerationresearch.eu/survey/alzheimers-disease-connectome-project/

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Country

USA

Title of project or programme

Alzheimers Disease Connectome Project

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 5,064,228.44

Start date of award

01/04/2016

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

Research Abstract

? DESCRIPTION (provided by applicant): The long-term goal of this proposal is to apply the Human Connectome Project (HCP) data collection protocol and develop robust technology to accurately stage Alzheimer’s disease (AD) across the full spectrum of its progression on an

individual subject basis. The onset of AD is insidious, and significant irreversible brain damage is already present by the time clinical symptoms appear. One difficulty in the field of AD research is that we have not yet established firm links between the appearance of any specific biomarker in asymptomatic individuals and the subsequent emergence of clinical symptoms. In this proposed study, we will utilize the HCP approach to determine when, where, and how the dysfunctional networks occur during disease development, and establish links by integrating HCP connectome biomarkers with well-studied molecular, genetic, and cognitive biomarkers to stage preclinical AD risks and subsequent AD progression. The success of the proposed project will open a crucial window of opportunity to intervene with disease-modifying therapy. Specifically, we hypothesize that HCP connectome biomarkers can predict and stage the full spectrum of AD dementia from the preclinical phase to dementia onset using a novel event-based probabilistic model on an individual subject basis. To test this hypothesis, we will conduct the following four aims. Aim 1. HCP compatibility. We will implement the HCP LifeSpan protocols with additional anatomical, functional, and positron emission tomography (PET) sequences tailored for aging and AD. Aim 2. Aberrant connectivity in AD. We will acquire and quantitatively characterize the connectome biomarkers in the AD connectome project (ADCP) cohort and determine their individual stages in AD progression. Aim 3. We will measure longitudinal changes in brain connectome, diseases stage development, and cognitive changes in the ADCP cohort and prospectively validate the probability distribution of biomarker-based AD stages on an individual subject basis using Markov chain estimation. Aim 4. Determine the extent to which connectome biomarkers are predicted by amyloid (A?) and tau pathologies. The completion of this Aim 4 will shed light on the molecular neurobiology of connectivity dysfunction and clarify the pathophysiology of AD development. This study will have significant impact to transform AD research paradigms in three ways. It will 1) allow for selection of individuals at high risk in order to enrich clinical trials, 2) identify the earliest preclinical disease stage atthe individual subject level, and 3) be a critical step toward the goal of developing personalized medicine for AD prevention and treatment.

Lay Summary
PUBLIC HEALTH RELEVANCE: Alzheimer’s disease (AD) is a progressive, neurodegenerative disease. In order to facilitate AD prevention and early treatment to halt, or at least slow, diseas progression, we must be able to mark its preclinical stage, before the brain damage becomes irreversible. Our goal is to identify structural and functional network abnormalities early in the disease process, as well as their network trajectories in the different AD stages in order to develop neural biomarkers for AD. We will implement and optimize Human Connectome Project protocols to longitudinally collect the detailed structural and functional neuroimaging and disease-related information with large and well-defined study samples at the different AD phases (300 human study subjects). We will also conduct amyloid PET (PIB) and tau PET (THK-1157) measurements to shed light on the molecular neurobiology of connectivity dysfunction and clarify the pathophysiology of AD development. The collected datasets will be released to the Connectome Coordination Facility at Washington University.

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