Neurodegeneration in Aging Down Syndrome (NiAD): A Longitudinal Study of Cognition and Biomarkers of Alzheimers Disease

https://neurodegenerationresearch.eu/survey/neurodegeneration-in-aging-down-syndrome-niad-a-longitudinal-study-of-cognition-and-biomarkers-of-alzheimers-disease/

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Country

USA

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Neurodegeneration in Aging Down Syndrome (NiAD): A Longitudinal Study of Cognition and Biomarkers of Alzheimers Disease

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NIH (NIA)

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30/09/2015

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2

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)... Behavioral and Social Science... Brain

Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Down Syndrome... Epidemiology And Longitudinal Studies... Intellectual and Developmental Disabilities (IDD)... Neurodegenerative... Neurosciences... Prevention

Research Abstract
? DESCRIPTION (provided by applicant): Individuals with Down syndrome (DS) have been largely neglected in therapeutic and biomarker studies of Alzheimer's disease (AD). Adults with DS are uniformly affected by AD pathology by their 30's and have a 70-80% chance of clinical dementia by their 60's. In 95% of cases, DS is associated with three copies of chromosome 21, each containing of copy of the Amyloid-beta (A?) Precursor Protein gene (leading to a 1.5-fold increase in A? protein). Yet, nowhere is it clearer than in DS that A? deposition is not sufficiet to produce dementia, as individuals harbor this pathology for over a decade before cognitive decline is apparent. DS can be seen as a setting of amplified sensitivity to risk and protective factors that moderate the relationship between A?, neurodegeneration and clinical dementia. Understanding the factors that moderate this relationship in DS and biomarkers for those factors is critically important in the design of therapeutic trials for AD in DS and in general. Thus, this longitudinal study of Neurodegeneration in Aging DS (NiAD) and its relationship to cognition has the potential to: 1) identify critical factors that link A? deposition to neurodegeneration and, ultimately, dementia; 2) define biomarkers for these factors; and, most importantly, 3) set a foundation for an efficient transition from this biomarker study to a therapeutic trial to combat A in DS augmented by biomarker outcomes. For the past 5 years, the three independent research groups included in this application have been studying the course of A? deposition and other imaging biomarkers and their impact on cognitive/functional measures in adults with DS [(a) the combined Pittsburgh/Madison study; (b) the Banner Alzheimer's Institute study; and (c) the Cambridge study]. In their ongoing work, 140 adults with DS (including 23 with DS/AD-dementia) have undergone magnetic resonance imaging (MRI) and amyloid-positron emission tomography (PET) scans and neuropsychological/ functional assessments. These three research groups now propose to combine resources and harmonize all protocols in response to the request from NIA/NICHD to develop a large AD biomarker study in DS. This study will be further strengthened by aligning NiAD with the three largest ongoing longitudinal studies of AD biomarkers in the general population: the Alzheimer Disease Neuroimaging Initiative (ADNI), the Dominantly Inherited Alzheimer Network (DIAN) and the Alzheimer Prevention Initiative (API). All data will be made available in an open-access format using a model similar to ADNI. The established DS cohort is a significant advantage that will shorten the recruitment phase, maximize longitudinal data that can be acquired and allow for addition of new biomarkers to be compared to longitudinal clinical and imaging measures. The proposed 5-year longitudinal study will examine progression of AD related biomarkers (A?-, tau- and fluorodeoxyglucose-PET, structural and functional MRI, cerebrospinal fluid A? and tau, plasma A? and proteomics, genetics, neuropathology) and cognitive/functional measures in 180 adults with DS (>25 yrs. of age) and 40 biomarker-controls. Subjects will be re-evaluated every 15 months to assess changes in cognition/adaptive functioning and every 30 months to detect biomarker changes.

Lay Summary
PUBLIC HEALTH RELEVANCE: Adults with Down syndrome (DS) are at an extremely high risk for developing Alzheimer's disease (AD), with most individuals over age 40 evidencing neurofibrillary tangles and neuritic plaques (which are thought to be associated with the eventual appearance of AD symptoms). The goal of the current application is to recruit and follow 180 adults with DS and 40 biomarker controls to enable the identification of the

longitudinal progression of AD in adults with DS using clinical, cognitive, imaging and genetic and biochemical biomarkers. This data is not only necessary to deepen our understanding of the pathophysiology of AD in DS, but may also offer information that will prove useful in the design of treatment trials to slow or prevent AD in DS.

Further information available at:

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Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

Database Categories:
N/A

Database Tags:
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