Validating the New Criteria for Preclinical Alzheimers disease

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Country

USA

Title of project or programme

Validating the New Criteria for Preclinical Alzheimers disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,431,889.91

Start date of award

01/04/2012

Total duration of award in years

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... Neurodegenerative... Neurosciences

Research Abstract

DESCRIPTION (provided by applicant): In 2010, the Alzheimer’s Association (AA), National

Institute on Aging (NIA) and National Institute of Neurological Disorders and Stroke formed three workgroups to revise diagnostic guidelines for Alzheimer's disease (AD) that had been employed since 1984. The preclinical workgroup devised guidelines for a stage of the disease that had not yet been formally defined. Most in the field believe that successful disease modifying treatment of AD will require that treatment begin prior to onset of dementia and perhaps prior to overt clinical symptoms (i.e. MCI). Thus, validation of the new preclinical AD criteria is a major new investigational frontier. The preclinical phase of AD is defined by abnormal AD biomarker studies with no, or only subtle, cognitive deficits. At present, there are five major AD biomarkers which fall into two classes: 1) biomarkers of brain Ab amyloidosis and 2) biomarkers of neuronal injury. The preclinical criteria describe three stages of preclinical AD that represent incrementally more advanced disease: Stage 1 – Asymptomatic cerebral amyloidosis. Stage 2 – Amyloid positivity plus evidence of synaptic dysfunction and/or early neurodegeneration. Stage 3 – Amyloid positivity plus evidence of neurodegeneration plus subtle cognitive symptoms. While formulation of the new criteria alone represents an advance, there were many issues left unaddressed, the major one being: “”Are the criteria valid?””.In addition, many issues necessary for operationalization of the criteria were not specified. Our overall goal in this grant proposal is to assess the validity of the new NIA-AA preclinical AD criteria. A necessary first step in operationalizing and assessing the validity of the criteria is to develop ct-points or thresholds for different biomarkers and cognitive tests to identify cognitively normal elderly subjects with abnormal biomarker values or subtle cognitive deficits. We have five Specific Aims: Aim 1: To create a cohort of AD subjects (1a) and cognitively normal subjects (1b) who have all 5 biomarkers. Aim 2: To develop cut-points for each biomarker (Aim 2a), evaluate the agreement between biomarkers of the same class (Aim 2b) and develop cut-points for subtle cognitive change (Aim 2c). Aim 3: To use the findings from Aim 2 to estimate the distribution of subjects that fall into preclinical stages in an elderly population-based cohort. Am 4: To determine how well the stages of the new criteria for Preclinical AD predict progression to mild cognitive impairment or dementia (Aim 4a) and to determine the association of the stages of Preclinical AD with decline on serial cognitive testing (Aim 4b). Aim 5: To revise cut-points and re-estimate the distribution of subjects that fall into preclinical stages based on clinical follow-up and longitudinal cognitive testing and compare these with cross-sectionally derived cut-points from Aim 2 and the population distribution of Preclinical AD stages from Aim 3.

Lay Summary
Recently a workgroup of Alzheimer's Association (AA), National Institute on Aging (NIA) and National Institute of Neurological Disorders and Stroke devised new guidelines for a preclinical stage of Alzheimer's disease. While formulation of criteria for the previously undefined phase of AD represents an advance, there were many issues left unaddressed. Our overall goal in this grant proposal is to assess the validity of the new NIA-AA preclinical AD criteria.

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