Re-visiting Methods for MCI Diagnosis to Improve Biomarker and Trial Findings

https://www.neurodegenerationresearch.eu/survey/re-visiting-methods-for-mci-diagnosis-to-improve-biomarker-and-trial-findings/

Principal Investigators

BONDI, MARK W

Institution

UNIVERSITY OF CALIFORNIA SAN DIEGO

Contact information of lead PI
Country

USA

Title of project or programme

Re-visiting Methods for MCI Diagnosis to Improve Biomarker and Trial Findings

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 3,413,115.60

Start date of award

15/03/2016

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)... Behavioral and Social Science... Brain Disorders... Dementia... Neurodegenerative... Neurosciences... Prevention

Research Abstract

? DESCRIPTION (provided by applicant): In Response to PA-13-168 (Secondary Analyses of Existing Data Sets and Stored Biospecimens To Address Clinical Aging Research Questions (R01)). Despite increasing sophistication in the application of biomarkers to the study of mild forms of cognitive impairment (MCI), sophistication in profiling cognition has not been commensurate. Criteria for MCI diagnosis in many large-scale studies rely on a single cognitive test score, screening measures, rating scales and clinical judgment, resulting in coarse characterizations of the types or severity of MCI being studied despite the availability of rich neuropsychological data from such studies. We propose to apply our novel actuarial neuropsychological and statistical methods to more accurately diagnose MCI and predict its progression. Applying these methods to large-scale existing open source (ADCS donepezil trial, ADNI, NACC/UDS) and institutional (FHS, MCSA, WHICAP) datasets will uncover stronger relationships between biomarkers, cognition, pathology, and progression rates, and will result in stronger treatment effects in clinical trials aimed at MCI. Our methods will improve effect sizes that inform power analyses for clinical trials and reduce the number of patients needed for such trials. Finally, our methods will be implemented to improve the NIA-AA operational definition of 'subtle cognitive decline' in Preclinical AD. These improvements will have important impacts on prospective design of future biomarker and clinical trial studies. Specific aims: Aim 1. Actuarial neuropsychological criteria for MCI diagnosis will better specify cognitive phenotypes as well as identify possible diagnostic errors from conventional criteria; removal of the resultant false positive (i.e., cognitively normal via neuropsychological criteria) cases and addition of false negative (i.e., `missed') cases will strengthen biomarker and trial findings from several large-scale studies. Aim 2. Empirically derived MCI diagnostic criteria will result in more efficient tril and study designs (i.e., studies that need fewer subjects) compared to conventional MCI criteria. Aim 3. An operational definition of subtle cognitive decline based on extensions of the above neuropsychological MCI criteria will improve characterization of NIA-AA criteria for ""Preclinical"" AD. Aim 4. In exploratory analyses, we will use novel computational tools to harmonize and combine 1) cognitive and 2) multi-marker profiles predictive of progression/pathology across multiple datasets. Demonstrations of improvement in diagnostic precision in MCI and Preclinical AD will have an important impact on prospective design of future studies of genetics, biomarkers, treatments and ultimately prevention. If successful, we will be able to more clearly model effects of biomarkers changes and neurodegeneration, together with factors such as age and comorbidities, on specific profiles and trajectories of cognitive decline.

Lay Summary

PUBLIC HEALTH RELEVANCE: We are entering a new era of research and clinical activity that will increasingly focus on the role of biomarkers in dementia detection, diagnosis, and clinical outcome. We seek to improve Mild Cognitive Impairment (MCI) diagnosis, characterization of its subtypes, and appraise operational definitions of the subtle cognitive decline of Preclinical AD. Demonstrations of improvement in diagnostic precision in MCI and Preclinical AD will have important impacts on prospective design of future studies of genetics, biomarkers, treatments and ultimately prevention.

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