Neuropathologic-Epidemiological Study of Metallomics and Alzheimers Disease

https://neurodegenerationresearch.eu/survey/neuropathologic-epidemiological-study-of-metallomics-and-alzheimers-disease/

Principal Investigators

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Institution

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Contact information of lead PI
Country

USA

Title of project or programme

Neuropathologic-Epidemiological Study of Metallomics and Alzheimers Disease

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 2,593,814.68

Start date of award

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... Clinical Research... Clinical Research - Extramural... Dementia... Epidemiology And Longitudinal Studies... Neurodegenerative... Neurosciences... Nutrition

Research Abstract

Principal Investigator/Program Director (Last, First, Middle): Morris, Martha Clare This R01 application, entitled “Epidemiological Neuropathologic Study of Metallomics and Alzheimer’s Disease” is a new submission in response to PAR-15-356. By the year 2050 it is projected that there will be 13.5 million Americans with AD at a cost of $1.1 trillion. Recent large-scale phase III clinical trials of drugs targeting known pathways involved in AD have either failed to benefit patients, or indicated very limited efficacy. Whereas beta amyloid (A?) may be a principal driver of the disease, multiple failed clinical trials of drugs targeting this peptide suggest that A? is a poor therapeutic target for AD. Iron accumulates in the affected brain regions in AD, and has the potential to drive disease progression by causing oxidative stress and the aggregation of A? and tau, and is thus an alternate therapeutic target. In previous studies we showed that the iron burden of the brain (as reflected in CSF ferritin levels) has an effect on multiple longitudinal outcomes of AD comparable in magnitude to more established factors in the disease: tau and A?. We have preliminary data showing a strong positive association between brain iron levels and neurofibrillary tangle pathology, particularly in APOE-?4 carriers. There has not been a systematic, well powered, and detailed exploration of brain iron levels in AD. Here, we propose to use a large, well-characterized post mortem cohort study, the Rush Memory and Aging Project, to investigate brain iron concentrations in AD of 680 autopsied brains using advanced techniques. We will investigate the impact of the iron load of the brain on AD neuropathology and cognitive clinical history; investigate potential causes of iron accumulation in AD including diet, and genetic factors; and explore neurochemical mechanisms of iron elevation using advanced proteomics and metalloproteomics. This foundational study has the potential to (1) establish whether iron concentrations are related to the disease, (2) validate iron as a therapeutic target for AD, (3) discover new molecular targets for lowering iron, (4) identify whether diet influences brain iron levels and AD risk, and (6) determine whether genetic factors, including APOE allele variation, impacts on iron in AD. PHS 398/2590 (Rev. 09/04, Reissued 4/2006) Page Continuation Format Page

Lay Summary

Program Director/Principal Investigator (Last, First, Middle): Morris, Martha Clare Large-scale phase III clinical trials of drugs targeting known pathways involved in AD have demonstrated limited efficacy. Previous studies indicate that iron may be an alternate therapeutic target. This application proposes to use a large, well-characterized post mortem cohort study, the Rush Memory and Aging Project, to investigate brain iron concentrations in AD of 680 autopsied brains using advanced metallomics and metalloproteomic techniques. PHS 398/2590 (Rev. 06/09) Page Continuation Format Page

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