Epidemiologic Study of Neural Reserve and Neurobiology of Aging

https://neurodegenerationresearch.eu/survey/epidemiologic-study-of-neural-reserve-and-neurobiology-of-aging/

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Country

USA

Title of project or programme

Epidemiologic Study of Neural Reserve and Neurobiology of Aging

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 9,340,165.14

Start date of award

01/03/2000

Total duration of award in years

13

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... Prevention

Research Abstract

DESCRIPTION (provided by applicant): The prevention of cognitive decline and dementia is a major public health priority. The Memory and Aging Project (MAP) has made considerable progress elucidating the complex relationships between risk factors, common neuropathologies and resilience markers that increase or decrease the rate of cognitive decline, and risk of dementia. In nearly 200 peer-reviewed manuscripts, we reported genetic, medical, experiential, and psychological factors associated with increased or decreased rates of cognitive decline and dementia risk. We reported that Alzheimer's, vascular, and Lewy body pathologies (AD, CVD, LBD) explain about 40% of the variation of cognitive decline, and that resilience markers (e.g., cortical presynaptic proteins and locus coeruleus neurons) were associated with a slower rate of decline accounting for 8% of the variation, and that many risk factors with little direct relation o pathologies or resilience markers accounted for >10% of the variation of decline, controlling for pathologies. Additional factors related to cognitive decline await discovery. The overall goal of the planned continuation of MAP is to discover additional proteins associated with the slope of cognitive decline, after accounting for the effects of common pathologies. We use the term ""residual cognitive decline"" to describe this innovative primary study outcome. Methods to interrogate the genome, and therefore, the proteome, have improved markedly over the past decade, making the discovery of proteins that underlie cognitive decline both timely and feasible. We plan to continue collecting clinical and post-mortem data on MAP participants. Aim 1, Discovery and Verification Phase, will combine ""omics-wide"" association studies with innovative integrative pathway analyses on genomic, epigenomic, and transcriptomic data from human brain from 500 MAP participants to discover proteins associated with residual cognitive decline; it will select 200 proteins for quantitation in human brain to verify that protein level i associated with residual cognitive decline. Aim 2, Validation Phase, will quantify the 200 proteins selected and verified in Aim 1 with a new sample of 350 brains from MAP participants that will accrue by the end the funding period, followed by a joint statistical analysis to increas power (n=850). Aim 3 will link the validated proteins to the wealth of available risk factor data t discover novel biologic pathways linking risk factors to cognitive decline and dementia. Our plan is supported by extensive and compelling new preliminary data that demonstrate its high likelihood of success and demonstrate that the study is innovative, high yield and low risk. The continuation of MAP will discover additional proteins associated with cognitive decline and novel biologic pathways linking risk factors to cognitive decline. These proteins will represent either unknown pathologies that increase rates of cognitive decline or resilience markers that decrease rates of cognitive decline. Both sets of proteins will offer new therapeutic targets for the prevention and treatment of cognitive decline and dementia. Thus, the study has the potential to have a high and sustained impact on aging and dementia research.

Lay Summary

PUBLIC HEALTH RELEVANCE: The prevention of cognitive decline, MCI and dementia is a major public health priority. The proposed continuation of MAP will discover additional proteins associated with cognitive decline and novel biologic pathways linking risk factors to cognitive decline, MCI and dementia. These proteins, representing unknown pathologies and resilience markers associated with faster and slower rates of cognitive decline, will offer new therapeutic targets for the prevention and treatment of cognitive decline, MCI and dementia.

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