Regional Neurotoxicity & Early Biomarkers of Air Pollution Effects on Brain Aging

https://neurodegenerationresearch.eu/survey/regional-neurotoxicity-early-biomarkers-of-air-pollution-effects-on-brain-aging/

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USA

Title of project or programme

Regional Neurotoxicity & Early Biomarkers of Air Pollution Effects on Brain Aging

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

410111.0092

Start date of award

01/09/2015

Total duration of award in years

2

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Climate-Related Exposures and Conditions... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Epidemiology And Longitudinal Studies... Networking and Information Technology R&D... Neurodegenerative... Neurosciences... Prevention... Women's Health for IC Use

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer's disease (AD) affects more women than

men and burdens millions of aging Americans and their families. While our knowledge of modifiable risk factors for AD remains limited, there is growing evidence that exposure to ambient air pollutants, including particulate matter (PM) and ozone, accelerates brain aging. Built on our collaborative work on neurotoxic effects of ambient air pollution and cognitive aging in Women's Health Initiative Study (WHIMS), this application will address two critical knowledge gaps in this promising area of air pollution-neuroepidemiology: (1) It is unclear whether brain region- and/or site-specific neurotoxicity occurs from ambient air pollution exposure; and (2) Strong epidemiologic evidence linking ambient air pollution to increased AD risk are still lacking. These knowledge gaps reflect limitations of previous research with conventional analyses of neuroimaging data and insufficient power in linking AD risk with exposures. This application will overcome these challenges by combing three unique data sources (WHIMS air pollution exposure; WHIMS MRI; and the Alzheimer's Disease Neuroimaging Initiative [ADNI]). Leveraging the longitudinal brain structure data from WHIMS MRI (gathered in 2005-6; 2010-2011) plus air pollution exposure estimates generated for WHIMS (gathered in 1993-2010), we will apply high-dimensional computational methods to conduct voxel-based analyses with a systematic and agnostic approach to examining the brain region-specific neurotoxicity of air pollution. This exploratory R21 application will also test the hypothesized adverse effect of ambient air pollution on the pattern of brain structure predictive of increased AD risk in an optimal population context, where ambient air pollutants affected the cognitive aging in older women. ADNI provides a well-characterized clinical database of cognitive normal and AD phenotypes, enabling our development/validation of novel AD risk metrics based on neuroimaging data applicable to WHIMS MRI. Thus, our Specific Aims are: Aim 1) Using structural brain MRI and air pollution data from the WHIMS-MRI cohort, to examine whether spatial patterns of grey matter/white matter atrophy at baseline and their changes over time are associated with air pollutant exposures; and Aim 2) Using novel metrics of AD risk to conduct a quantitative assessment linking AD risk with ambient air pollution. We have assembled a multidisciplinary team with complementary expertise in high-dimensional machining learning for neuroimaging data analyses, cognitive aging, and air pollution neurotoxicology/epidemiology. Our study will advance the field of environmental epidemiology of aging by using advanced analytical tools to link air pollution exposures to spatial patterns of brain structure and the predicted risk of AD.

Further information available at:

Types:

Investments < €500k

Member States:

United States of America

Diseases:

N/A

Years:

2016

Database Categories:

N/A

Database Tags:

N/A