

Environmental Determinants of Pathological Brain Aging in WHI Memory Studies

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Contact information of lead PI Country

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Environmental Determinants of Pathological Brain Aging in WHI Memory Studies

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4

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Alzheimer's disease & other dementias

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aging brain, Women's Health, ambient air pollution, Air Pollution, Dementia

Research Abstract

Dementia, including Alzheimer's disease (AD), burdens more women than men and affect millions of aging Americans and their families. While the search for effective prevention

continues, scientific evidence on modifiable risk factors for dementia remains uncertain. In the last two decades, compelling data have documented significant neurotoxicity in animals and humans exposed to ambient air pollutants. Toxicopathological studies show evidence of accelerated brain aging (e.g., β -amyloid accumulation) and possible neurodegeneration (e.g., neuro-fibrillary tangles). Although epidemiologic data also support that ambient air pollutants may represent a novel and modifiable environmental determinant of pathological brain aging, the proposed longitudinal study will address the following critical knowledge gaps. First, convincing prospective cohort data linking ambient air pollution to increased dementia risks are still lacking. Second, most published air pollution-neuroepidemiologic studies were studying late-life (aged > 65) exposures; whether/how exposures before late life shape the profile of neuropsychological functions and determine the subsequent risk for dementia has not been studied. Third, mechanistic mediators underlying the adverse effects and human brain structures perturbed by air pollutants remain elusive. Fourth, very little is known about the PM exposure sources/compositions affecting brain aging. Specifically, this application is built on two well-characterized and geographically-diverse cohorts of postmenopausal and older women participating in Women's Health Initiative (WHI) Memory Study (WHIMS;1995-2007; n=7479, aged 65-80) and WHIMS of Younger Women (WHIMS-Y; n=1326, aged 50-55) since 1996. Supported by the preliminary results and drawing on the extended follow-up of WHIMS+ WHIMS-Y, we will update the neurocognitive outcome database (dementia subtype; annual neuropsychological assessment; structural brain MRI) until 2016. This application also leverages recent advances in spatiotemporal modeling to enrich the residential exposure database for NO₂/ozone/PM₁₀ (1993- 2016 monthly) and PM_{2.5} (1993-1999 yearly; 1999-2016 monthly). In Aim 1, we will determine the impact of long-term exposures on dementia/AD incidence. Aim 2 will examine the adverse effects of air pollution on latent trajectories of internally validated neuropsychological biomarkers, putatively associated with estimated exposures starting at age of 50-55 and continuing into later life. In Aim 3, we will use structural equation models to evaluate the hypothesized mediation by emotional disturbance, reduced limbic brain volume, and increased neurovascular damages underling the neurotoxic effects of air pollution. In Aim 4, we will explore the associations between PM exposure sources/compositions and brain aging. We have assembled a multidisciplinary team working together on this emerging field of environmental neurosciences in brain aging. Expected new knowledge gained from this R01 will greatly improve our understanding of the role of air pollution in contributing to neuropsychological processes and mechanisms of dementia/AD in late life.

Lay Summary

Relevance to Public Health In search of modifiable environmental factors to help develop new strategies for preventing dementia including Alzheimer's disease, scientists at the University of Southern California and the University of Washington have teamed up in this large epidemiologic study to examine the link of residential environment and risk of dementia & Alzheimer's disease in older women. They will investigate: (1) whether long-term exposure to ambient air pollutants make older people more likely to develop dementia and Alzheimer's disease; (2) whether individuals could show earlier signs of declining cognitive functions several years before the dementia and Alzheimer's if they were exposed to higher levels of ambient air pollutants before and/or during late life; and (3) what may be happening in the brains that link exposures to ambient air pollution with increased risk for dementia and Alzheimer's disease. This project holds the promise to generate new knowledge about modifiable environmental

factors that may contribute new approaches to developing effective prevention modalities, a national goal set in the National Plan to Address Alzheimer's Disease by 2025.

Further information available at:

Types:

Investments > €500k

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United States of America

Diseases:

Alzheimer's disease & other dementias

Years:

2016

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N/A

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