

Alzheimers Disease & Related Dementias: Geography, Environments, and Mechanisms

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Alzheimers Disease & Related Dementias: Geography, Environments, and Mechanisms

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1

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Alzheimer's disease & other dementias

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Research Abstract

Post-menopausal and older women are a vulnerable population in the research on Alzheimer's disease (AD) and related dementias (ADRD). ADRD affects more women than men, and increasing evidence indicates different risk factors by sex. While the search for effective prevention continues, we only have limited knowledge about environmental risk factors, especially those modifiable in late life. In the US, there are well- documented regional differences in both prevalence and mortality of dementia, but no studies have provided useful insights for modifiable environmental factors. Although an important step towards identifying modifiable environmental factors, investigating within-country geographic differences in ADRD risks remains a great challenge, as it requires substantial investment to follow a prospective cohort and employ identical, well- validated protocols to ascertain incident dementia in multi-site populations. In a nationwide cohort of older women from the Women's Health Initiative Memory Study (WHIMS), we recently reported the first evidence of geographic disparities in AD incidence. Our preliminary data also indicate that exposure to regional air pollutants is a novel neurotoxin associated with increased ADRD risks, but the ADRD geo-disparities were not explained by cardiovascular disease and other conventional risk factors. These findings highlight the critical need to examine other environmental-social determinants and further elucidate the mechanistic mediators. To address these knowledge gaps cost-efficiently, we propose to study the well-characterized and geographically- diverse cohorts of postmenopausal and older women in WHIMS (n=7479, aged 65-80) and WHIMS of Younger Women (WHIMS-Y; n=1336, aged 50-54), both followed annually since 1996. We will capitalize on extant data on hypothesized environmental determinants (ambient air pollutants; psychosocial factors; dietary patterns and fatty acids) and update outcomes (dementia subtype; annual neuropsychological assessment; longitudinal structural brain MRI) through 2016. In Aim 1, we will define the cognitive endophenotypes (CEP) predictive of ADRD, and examine how indicators of residential geography affect CEP and its progression. In Aim 2, we will construct multivariate structural equation models (SEMs) and test whether the hypothesized environmental factors contribute to the geo-disparities in CEP and ADRD risks. In Aim 3, we will use SEMs to evaluate brain structural correlates (prefrontal cortex; hippocampal-amygdalar complex; white matter) and small-vessel ischemia, putatively mediating the geo-environmental disparities in CEP. In Aim 4, we will explore the environmental interactions in shaping the geo-disparities in CEP and ADRD risks. A multidisciplinary team has been assembled to work together on this emerging field of environmental-social neurosciences on health disparities in population brain aging. Expected new knowledge gained from this R01 will help identify both adverse exposures and protective processes amenable to intervention, towards developing evidence-based, mechanistically-informed prevention strategies to reduce the geographical disparities in ADRD risks.

Lay Summary

Relevance to Public Health Places matter when counting the number of US older adults affected by or dying from Alzheimer's disease and related dementias (ADRD), and increasing epidemiologic data suggest that where people live in late-life may determine the individual's probability to develop ADRD. Hoping to better understand such geographic disparities in ADRD, the investigative team will study: (1) whether individuals could show earlier signs of declining cognitive functions several years before ADRD; (2) what environmental factors could possibly explain the difference in ADRD risks that depend on where people live; and (3) which parts of the human brains may be affected by where people live and how they differ in these possible environmental contributors. This project holds the promise to generate new knowledge about

environmental risk factors in late life that are amenable to intervention, and better understanding why places matter in ADRD risks 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:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

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