

Particulate Air Pollutants, Cognitive Impairment, and Neuropathology in Elderly Women

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Background/Rationale

- Every 70 seconds, there is a new case of Alzheimer's disease in the US (Alzheimer's Association 2009).
- Neuroepidemiologic and pathological data: cardiovascular disease (CVD)/risk factors → cognitive impairment/dementia/Alzheimer's disease
- Long-term PM exposure increases CVD risk and mortality.
- Accumulating data on PM neurotoxicity:
 - neurotoxicity on the hippocampus; histopathological lesions of dementia (e.g., plaques formation, β -amyloid accumulation, and neurofibrillary tangles), and neurobiological changes associated with cognitive aging (e.g., neuroinflammation, central oxidative stress, and activation of stress axis)
- Lack of convincing cohort data linking neurocognitive disorders with PM exposure

Research Questions / *Hypotheses*

Q1: Does PM exposure increase the risk of cognitive impairments?

- *H1: Residing in places with high levels of particulate air pollutants is associated with increased risks for all-cause dementia and mild cognitive impairment, after adjustment for potential confounders.*

Q2: What is the possible neuropathology linking cognitive impairment with long-term PM exposure?

- *H2: Exposure to high levels of particulate air pollutants is associated with MRI-measured larger ischemic lesion volumes and lower regional volumes in hippocampus and frontal lobe.*

Study Design/Methods

- **A longitudinal cohort study on a geographically-diverse and susceptible population (1996-2007)**
 - 38-centers (in 22 states) Women's Health Initiative Memory Study (WHIMS): N=7479; aged 71.0 ± 3.8 years
 - WHIMS-MRI Study: n=1403
- **Ascertainment of outcomes**
 - 4-phase protocols: dementia/mild cognitive impairment
 - MRI-measured ischemic lesions and region-specific volumes
- **Estimation of PM exposure**
 - PM_{2.5}: nearest-neighborhood averaging + spatiotemporal modeling to estimate residence-specific annual exposure
 - Diesel PM: ASPEN Dispersion Model (NATA, EPA)
- **Statistical Data Analyses**
 - Cox proportional hazards and multilevel mixed-effect models adjusting for multiple potential confounders