Received: 10 August 2021 | Accepted: 10 August 2021

DOI: 10.1002/alz.12471

Alzheimer's & Dementia®
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION

LETTER

Recently decreased association of air pollution with cognitive impairment in a population-based aging cohort and in a mouse model

Particulate matter air pollution is an environmental risk factor for poor cognitive function in the elderly,[1–3] together with accelerated cognitive loss,[4,5,6] increased risk of dementia,[5,7,8] loss of brain grey and white matter,[9,10] and small vessel disease.[11] Rodent models document the neurotoxicity of air pollution components for cognitive impairments,[12,13] oxidative damage and increased brain amyloid,[5,14,15] and impaired adult neurogenesis.[12,16] Our labs have independently reported indications of recent decreases in the neurotoxicity of air pollution components in human populations[17] and rodent models.[18]

In the US-wide Health and Retirement Study (HRS), Ailshire showed a strong association of cognitive deficits with air pollution for cohorts with lower education in 2004: a 12% higher risk of incident cognitive impairment per 5 $\mu g/m^3$ increase in PM2.5 among adults ages 65 and older with ≤8 years of education.[17] However, by 2014 there was no such association for the corresponding HRS cohort.

Among possibilities for the lack of association in 2014, a likely factor is the reduction in PM2.5 from 2004 to 2014. The mean annual ambient PM2.5 in neighborhoods of HRS respondents was 9.2 $\mu g/m^3$ (SD = 1.7) in 2014, 25% below the 2004 level of 12.4 $\mu g/m^3$ (SD = 2.8).[17] Importantly, in 2014 very few HRS respondents lived in places with an annual average PM2.5 level above the EPA standard of 12.0 $\mu g/m^3$, suggesting a decline in exposure to high pollution among older adults.

Rodent models indicate diminished neurotoxicity of air pollution from urban sites. A nanoscale subfraction of PM2.5 (nPM) from Los Angeles showed sharp declines after 2017 in neurotoxicity for nine parameters, including spatial learning and oxidative damage.[18] These experiments exposed the same mouse genotype (B6) to nPM collected at the same urban site and for the same levels of nPM and duration.

The composition of air pollution was also changing during these observations. The levels of PM2.5 declined US-wide by 50% (from 13 $\mu g/m^3$ in 2000 to 8 $\mu g/m^3$ in 2019), while the Los Angeles urban PM2.5 level declined slightly, from 13 $\mu g/m^3$ in 2009 to 12 $\mu g/m^3$ in 2019.[18] Although US-wide ozone levels continued to decrease,[19] Los Angeles County ozone reversed the prior trends by increasing after 2015.[20] Chemical analysis of Los Angeles nPM did not identify changes attributable to the lower neurotoxicity per μg.[18,21]

The findings of the HRS cohort are consistent with the lower dementia risk by advancing birth year in other population-based studies.[22–24] The protective role of increased education for dementia risk from air pollution[17] could be a factor in these prior findings, because higher education was increasingly available in the 20th century to both women and men.[25] Nonetheless, air pollution must be considered among environmental factors in the AD-Exposome[26,27] over the lifespan because of the present evidence for recent changes in level and neurotoxicity.

We emphasize that our findings cannot evaluate potential benefits of air pollution improvements to the risk of cognitive decline and dementia. Although PM2.5 levels did decline nationally from 2009 to 2016, the year-over-year increases that have been observed since 2017[20,27] show that improvements in air quality can be reversed. Our findings underscore the importance of efforts to improve air quality in the ambient and indoor environments and the continued importance of parallel demographic and experimental evaluation of air pollution neurotoxicity.

Jennifer A. Ailshire
Caleb E Finch

Leonard Davis School of Gerontology, University of Southern California, Los Angeles, California, USA

Correspondence
Caleb E Finch, Leonard Davis School of Gerontology, University of Southern California, Los Angeles, CA, USA.
Email: cefinch@usc.edu

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