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FROM THE ALZHEIMER'S ASSOCIATION INTERNATIONAL CONFERENCE 2025

DECADES-OLD LEAD POLLUTION LINKED TO MEMORY PROBLEMS IN OLDER ADULTS, STUDY FINDS

Key Takeaways

- **A study of more than 600,000 adults links early-life environmental lead exposure to memory problems later in life.**
- **People who grew up in areas with moderate to extremely high atmospheric lead levels from 1960-1974 were 20% more likely to report memory problems as adults 50 years later.**
- **Lead exposure may leave a lasting molecular imprint on the brain, making it more vulnerable to age-related diseases, including Alzheimer's.**

TORONTO, July 27, 2025 — Historic lead levels from the era of leaded gasoline may be contributing to cognitive issues 50 years later, suggests research reported for the first time at the Alzheimer's Association International Conference® 2025 (AAIC®), in Toronto and online.

Americans are about 20% more likely to experience memory problems if they lived in areas with high levels of atmospheric lead between 1960 and 1974, according to the analysis of more than 600,000 adults 65 and older.

"Research suggests half the U.S. population — more than 170 million people — were exposed to high lead levels in early childhood. This research sheds more light on the toxicity of lead related to brain health in older adults today," said Maria C. Carrillo, Ph.D., Alzheimer's Association chief science officer and medical affairs lead. "Other studies reported at AAIC 2025 suggest that (a) lead exposure at any point in life may cause cognitive problems, (b) it may be more likely to affect certain populations and reflect disparities, and (c) there is a biological connection between lead exposure and Alzheimer's."

Historic levels of lead air pollution are associated with memory problems 50 years later

In a first-of-its-kind study, researchers examined how exposure to airborne lead from 1960-1974 — when leaded gasoline use was at its highest — may affect brain health later in life. They determined that older adults who grew up in areas with moderate to extremely high historical atmospheric lead levels (HALL) were about 20% more likely to report memory problems as adults 50 years later.

The researchers calculated the average HALL by area and linked it to self-reported memory problems from the American Community Survey from 2012-2017 (368,208 people) and 2018-2021 (276,476 people). They didn't analyze the source of the lead but believe that the higher the density of automobile traffic, such as in urban areas, the higher the atmospheric lead. Factoring in both time periods, the researchers determined that 17-22% of people living in areas with moderate, high or extremely high atmospheric lead reported memory issues.

"Our study may help us understand the pathways that contribute to some people developing dementia and Alzheimer's disease," said Eric Brown, M.D., MSc, FRCPC, lead author of the study, associate scientist and associate chief of geriatric psychiatry at the Centre for Addiction and Mental Health, Toronto.

Lead was originally added to gasoline to increase performance until researchers determined it posed serious risks to health and the environment. The more than 20-year-long phase-out of leaded gas began in 1975 when all new cars sold in the U.S. were required to have catalytic converters.

“When I was a child in 1976, our blood carried 15 times more lead than children’s blood today,” said Esme Fuller-Thomson, Ph.D., senior author of the study and a professor at the University of Toronto’s Factor-Ientash Faculty of Social Work and director of the Institute for Life Course and Aging. “An astonishing 88% of us had levels higher than 10 micrograms per deciliter, which are now considered dangerously high.”

While the risk of atmospheric lead has decreased, other sources of exposure remain, such as old lead paint and pipes. Those who have been exposed to atmospheric lead should focus on reducing other risk factors for dementia, including high blood pressure, smoking and social isolation, said Brown.

Living near lead-polluting sites may affect memory

Another study reported at AAIC found that older adults who live about three miles from a lead-releasing facility — such as glass, ready-mixed concrete or computer and electronics manufacturers — are more likely to have memory and thinking problems than those who live farther away. This research, which focused on a racially and ethnically diverse group of older adults, reinforces concerns about the long-term cognitive impact of environmental lead exposure, especially in communities already facing health disparities.

Researchers assessed 2,379 patients (average age ~74 years) from two studies: the Kaiser Health Aging and Diverse Life Experienced study (KHANDLE, 1,638 patients) of a diverse group of Kaiser Permanente insurance plan members who live in northern California, and the Study of Healthy Aging in African Americans (STAR, 741 patients) study of Black adults age 50 and older who live in the San Francisco and Sacramento areas. They evaluated the participants’ proximity to the nearest lead-releasing facility and compared the distance to participants’ Neuropsychological Assessment Scales results at baseline and two years later.

Compared to two years earlier, the KHANDLE participants who lived within 5 km (just over three miles) of a lead-releasing facility scored 0.15 times lower on verbal episodic memory tests (recall of personal experiences), and 0.07 times lower on overall cognitive ability compared to those living farther away. Every 5 km farther a participant lived from a lead-releasing facility was associated with 5% higher memory scores two years later. Among STAR group participants living within 5 km of a lead-releasing facility, researchers observed a 0.20 times lower score on semantic memory (general knowledge) two years later, compared to those who lived farther away.

“Our results indicate that lead exposure in adulthood could contribute to worse cognitive performance within a few years,” said Kathryn Conlon, Ph.D., MPH, senior author and associate professor of environmental epidemiology, School of Medicine, University of California, Davis. “Despite tremendous progress on lead abatement, studies have shown there is no safe level of exposure, and half of U.S. children have detectable levels of lead in their blood. Additionally, there are regions and neighborhoods that have more exposure.”

According to Conlon, there were 7,507 lead-releasing facilities in the U.S. in 2023. To reduce exposure, Conlon said people living near lead-producing facilities should keep their homes clean to avoid the accumulation of lead-contaminated dust, remove their shoes when coming inside, and place dust mats inside and outside to avoid tracking lead-contaminated dust indoors. Use the Environmental Protection Agency's TRI Toxics Tracker to identify lead-releasing facilities near you.

Study reveals how lead exposure may set the stage for Alzheimer's

Even low levels of lead exposure can create permanent changes in brain cells, including increased buildup of abnormal tau and amyloid beta, which are proteins associated with Alzheimer's, suggests a third study reported at AAIC 2025.

The researchers exposed human brain cells to lead concentrations of zero, 15 and 50 parts per billion (ppb), simulating the kind of lead exposure people might experience through contaminated water or air. The EPA's action level for lead in drinking water is 15 ppb.

They ran molecular, genetic, biochemical and functional tests on the cells and determined that (a) the 15-ppb and 50-ppb lead-exposed neurons were more electrically active (suggesting early dysfunction) than those that had no exposure, (b) energy-producing cells were damaged, and (c) there was an increase in tau and amyloid beta. Even after the lead was removed, the cells remained primed for damage, responding more severely to additional stressors such as tau.

"These findings help explain how lead exposure, especially in early life or from occupational and environmental sources, might leave a lasting molecular imprint on the brain making it more vulnerable to age-related diseases like Alzheimer's," said Junkai Xie, Ph.D., lead author of the study and post-doctoral research associate in chemical engineering at Purdue University. "Our results show that lead exposure isn't just a short-term concern; it may set the stage for cognitive problems decades later."

About the Alzheimer's Association International Conference® (AAIC®)
The Alzheimer's Association International Conference (AAIC) is the world's largest gathering of researchers from around the world focused on Alzheimer's and other dementias. As a part of the Alzheimer's Association's research program, AAIC serves as a catalyst for generating new knowledge about dementia and fostering a vital, collegial research community.
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- Eric Brown, M.D., MSc, et al. Historical atmospheric lead concentrations (1960-1974) and memory problems half a century later: Findings from two large, independent representative sample**s**
- Kathryn C. Conlon, Ph.D., MPH, et al. Residential proximity to a lead-releasing facility is associated with cognition in KHANDLE and STAR cohorts (Funding: *NIA/NIH R01 AG074347*
- Junkai Xie, Ph.D., et al. Persistent vulnerabilities in neurons following lead (Pb) exposure and implications for Alzheimer's Disease (Funding: NIH: R01NS130722, U01AG088662, R01AG080917)

***** AAIC 2025 news releases may contain updated data that does not match what is reported in the following abstracts.**

Proposal ID: 101687
Poster: Monday, July 28, 2025: 7:30 A.M.-4:15 P.M. EDT
Slot: P2-135: Public Health: Epidemiology

Historical atmospheric lead concentrations (1960-1974) and memory problems half a century later: Findings from two large, independent representative samples

Background: Lead exposure has adverse impacts on cognition and dementia risk factors such as hypertension. A major historical source of lead exposure was via atmospheric pollution due to leaded gasoline.

Method: We mapped historical atmospheric lead levels (HALL) in the contiguous US using measurements obtained by the US EPA from 1960 to 1974, a period of high leaded gasoline combustion. We extrapolated HALL by kriging and calculated mean HALL for each public use microdata area (PUMA). Our analyses include only PUMAs which contained at least one lead measurement in 1960-74. We obtained individual-level data of self-reported memory problems, from the American Community Survey (ACS) in two time periods, 2012-2017 (n=368,208) and 2018-2021 (n=276,476). The samples were restricted to respondents aged 65 and older living in their natal state.

We calculated odds ratios using HALL as the exposure variable and self-reported memory problems as the outcome, controlling for respondents' age, sex, race/ethnicity, and education. We used individuals in PUMAs with the lowest HALL (< 0.4 $\mu g/m^3$) as reference in comparison to those in PUMAs with moderate (0.4-.79 $\mu g/m^3$), high (0.8-1.19 $\mu g/m^3$) and extremely high HALL (>=1.2 $\mu g/m^3$).

Result: In the 2012-2017 ACS, in comparison to older adults living in PUMAs with the lowest HALL, the odds of reported memory impairment were higher in those in PUMAs with moderate (Odds ratio (OR)=1.21; 95% CI=1.17-1.25), high (OR=1.21; 95% CI=1.17-1.25) and extremely high HALL levels (OR=1.19; 95% CI=1.13-1.25). We replicated the study using 2018-2021 ACS data and found comparable outcomes for older adults living in PUMAs with moderate (OR= 1.17; 95% CI=1.12-1.21), high (OR=1.20; 95% CI=1.16-1.25) and very high HALL (OR=1.22; 95% CI=1.15-1.29).

Conclusion: We observed in two very large (n>250,000) independent representative samples that older adults had approximately 20% higher odds of reporting memory problems if they lived in PUMAs that had HALL > 0.4 $\mu g/m^3$ compared to <0.4 $\mu g/m^3$. This adds to the evidence implicating lasting health outcomes, including cognition, due to earlier life lead exposure from air pollution. The precipitous decline in atmospheric lead exposure in the last quarter of the 20th century may help to explain the declining incidence of dementia in the US.

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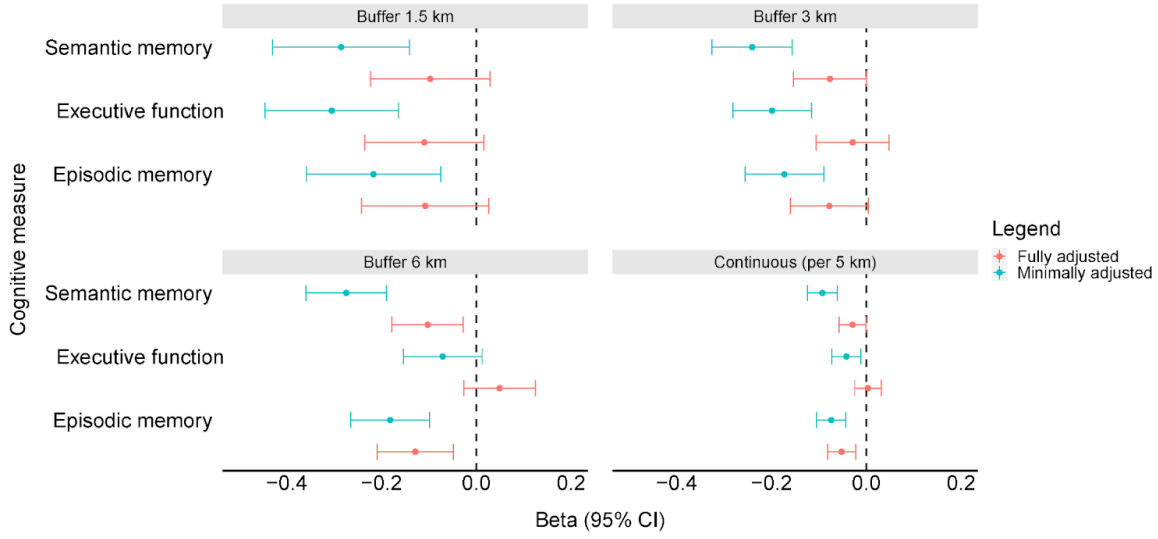
Proposal ID: 103527
Poster Sunday, July 27, 2025: 7:30 A.M.-4:15 P.M. EDT
Slot P1-15 Public Health Epidemiology

Residential proximity to a lead-releasing facility is associated with cognition in KHANDLE and STAR cohorts

Background: Environmental chemical exposures are potentially modifiable risk factors for dementia. While lead is a well-documented early life neurotoxicant, pertinent time periods for exposures and their contribution to cognition in later life requires further investigation, particularly for diverse cohorts.
Method: In a multi-ethnic sample of participants from two harmonized cohorts (Kaiser Health Aging and Diverse Life Experiences (KHANDLE), Study of Healthy Aging in African Americans (STAR); n= 2,409), we assessed the relationships between residential proximity to a lead releasing facility, measured through the Toxics Release Inventory, with domain-specific baseline cognition. Executive function, verbal episodic memory, and semantic memory were measured using the Spanish and English Neuropsychological Assessment Scales. We evaluated distance to the nearest lead releasing facility as a continuous measure as well as categorically (buffers with radii of 1.5 km, 3km, 6km) two years before cognitive testing. Linear regression models were adjusted for age at cognitive testing and cohort (minimally adjusted) and further adjusted for sex, race/ethnicity, income, education, and marital status (fully adjusted).
Result: Average age at cognitive assessment was 74 years (SD=8), 62% were female, 48% identified as Black, 17% as Asian, 14% as LatinX, and 20% as Non-Hispanic White. The average distance between residence and lead releasing facility was 6.6 km (SD=6.3). Every 5km decrease in residential distance from a lead releasing facility was associated with -0.07 lower verbal episodic memory (95% CI: -0.04, -0.10) and -0.09 lower semantic memory (95% CI: -0.06, -0.12) scores two years later. Living within a 6km buffer of a lead releasing facility was associated with -0.18 lower episodic memory (95% CI: -0.27, -0.10) and -0.27 lower semantic memory (95% CI: -0.36, -0.19) two years later. Point estimates were attenuated in fully adjusted models (Figure 1).
Conclusion: Residential proximity to a lead releasing facility may be associated with poorer cognition among older adults in a diverse cohort, and comprehensive understanding of environmental factors related to dementia is a critical step to advance disease prevention.

Figure 1. Forest plot of effect estimates for residential proximity to lead releasing facility and baseline cognition two years before cognitive testing. Continuous distance measure interpreted for every 5km increase in distance.



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Proposal ID: 107301
Poster: Monday, July 28, 2025: 7:30 A.M.-4:15 P.M. EDT
Slot: P2-05: Basic Science and Pathogenesis: Molecular and Cell Biology

Persistent vulnerabilities in neurons following lead (pb) exposure and implications for Alzheimer's disease

Background: Exposure to environmental neurotoxicants such as lead (Pb) during critical developmental periods and adulthood has been linked to persistent neurological deficits and pathological features resembling Alzheimer's disease (AD). Epidemiological studies have reported associations between Pb exposure and an increased risk of AD later in life, a link further supported by animal models. However, the molecular mechanisms underlying this association remain poorly understood.
Method: In this study, we utilized hiPSC-derived cortical neurons to investigate the impact of Pb exposure at different life stages on the onset of AD-like pathogenesis. We selected environmentally relevant Pb concentrations (0, 15, and 50 ppb) and assessed both immediate and persistent neurological effects using immunofluorescence, Western blotting, RNA sequencing, enzyme-linked immunosorbent assay (ELISA), microelectrode array (MEA) and a "secondary hit" model.
Result: Although neurite morphology remained largely intact, Pb-exposed neurons displayed significant hyperactivity and mitochondrial dysfunction. Transcriptomic profiling identified differentially expressed genes enriched in oxidative phosphorylation and AD-related pathways. Furthermore, Pb exposure led to an increase in phosphorylated Tau, Tau aggregates, and Aβ42/40 ratios—hallmarks of AD pathology. Notably, Pb-exposed neurons exhibited increased susceptibility to AD-relevant secondary stressors, including PHF-Tau and the mitochondrial toxin MPP+, with these vulnerabilities persisting even after Pb withdrawal.
Conclusion: These findings provide mechanistic insight into how Pb exposure may contribute to AD pathogenesis, highlighting potential molecular pathways that could mediate the increased AD risk observed in Pb-exposed populations.

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