Title

Air pollution and traffic noise interact to affect cognitive health in older Mexican Americans

Authors

Yu, Yu
Su, Jason
Jerrett, Michael
et al.

Publication Date

2023-03-01

DOI

10.1016/j.envint.2023.107810

Peer reviewed

HHS Public Access

Author manuscript

Environ Int. Author manuscript; available in PMC 2024 May 24.

Published in final edited form as:

Environ Int. 2023 March ; 173: 107810. doi:10.1016/j.envint.2023.107810.

Air pollution and traffic noise interact to affect cognitive health in older Mexican Americans

Yu Yu[a,b], **Jason Su**[c], **Michael Jerrett**[b], **Kimberly C. Paul**[d], **Eunice Lee**[c], **I-Fan Shih**[e], **Mary Haan**[f], **Beate Ritz**[b,d,e,*]

[a]Center for Health Policy Research, University of California Los Angeles, California, USA

[b]Department of Environmental Health Sciences, Fielding School of Public Health, University of California Los Angeles, California, USA

[c]Division of Environmental Health Sciences, School of Public Health, University of California Berkeley, California, USA

[d]Department of Neurology, David Geffen School of Medicine, University of California Los Angeles, California, USA

[e]Department of Epidemiology, Fielding School of Public Health, University of California Los Angeles, California, USA

[f]Department of Epidemiology & Biostatistics, University of California San Francisco, California, USA

Abstract

Background: Both air pollution and noise exposures have separately been shown to affect cognitive impairment. Here, we examine how air pollution and noise exposures interact to influence the development of incident dementia or cognitive impairment without dementia (CIND).

Methods: We used 1,612 Mexican American participants from the Sacramento Area Latino Study on Aging conducted from 1998 to 2007. Air pollution (nitrogen dioxides, particulate matter, ozone) and noise exposure levels were modeled with a land-use regression and via the SoundPLAN software package implemented with the Traffic Noise Model applied to the greater

*Corresponding author at: Department of Epidemiology, Fielding School of Public Health, University of California at Los Angeles, 650 Charles E. Young Drive South, Los Angeles, CA 90095-1772, USA., britz@ucla.edu (B. Ritz).

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Yu Yu: Conceptualization, Methodology, Formal analysis, Writing – original draft. **Jason Su:** Conceptualization, Resources, Methodology, Writing – review & editing. **Michael Jerrett:** Conceptualization, Methodology, Writing – review & editing. **Kimberly C. Paul:** Methodology, Writing – review & editing. **Eunice Lee:** Resources, Writing – review & editing. **I-Fan Shih:** Formal analysis, Writing – review & editing. **Mary Haan:** Investigation, Resources, Funding acquisition, Writing – review & editing. **Beate Ritz:** Conceptualization, Methodology, Formal analysis, Funding acquisition, Writing – review & editing, Supervision.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2023.107810.

Sacramento area, respectively. Using Cox proportional hazard models, we estimated the hazard of incident dementia or CIND from air pollution exposure at the residence up to 5-years prior to diagnosis for the members of each risk set at event time. Further, we investigated whether noise exposure modified the association between air pollution exposure and dementia or CIND.

Results: In total, 104 incident dementia and 159 incident dementia/CIND cases were identified during the 10 years of follow-up. For each ~2 μg/m^3 increase in time-varying 1- and 5-year average $PM_{2.5}$ exposure, the hazard of dementia increased 33% (HR = 1.33, 95%CI: 1.00, 1.76). The hazard ratios for NO_2-related dementia/CIND and $PM_{2.5}$-related dementia were stronger in high-noise (≥65 dB) exposed than low-noise (<65 dB) exposed participants.

Conclusion: Our study indicates that $PM_{2.5}$ and NO_2 air pollution adversely affect cognition in elderly Mexican Americans. Our findings also suggest that air pollutants may interact with traffic-related noise exposure to affect cognitive function in vulnerable populations.

Keywords

Air pollution; Nitrogen dioxide; Particulate matter; Ozone; Noise; Dementia; Cognitive impairment

1. Introduction

Alzheimer's disease and related dementias (ADRD) are a major public health challenge in societies with aging populations (Ritz and Yu, 2021), due in part to the health care burden associated with these disorders (Livingston et al., 2020). In the United States, the number of people with ADRD is expected to increase by at least 6.7% from 2020 to 2025, and the annual number of new cases of Alzheimer's and other dementias is projected to double by 2050 (Alzheimers Dementia, 2021). Therefore, identifying modifiable risk factors for dementia is urgently needed to address and combat this costly and growing global health crisis (Ritz and Yu, 2021).

Ambient air pollution has been linked to various adverse health outcomes (Paul et al., 2019). Evidence has been emerging that air pollutants – both short- and long-term exposure to nitrogen dioxides (NO_2), particulate matter ($PM_{2.5}$), and ozone (O_3) – increase the incidence of dementia (Paul et al., 2019; Yuchi et al., 2020; Andersson et al., 2018; Paul et al., 2020; Andersen et al., 2022), although some studies did not find associations between these air pollutants and incident dementia of the Alzheimer's type (Trevenen et al., 2022). The Betula study (Oudin et al., 2016) and the Women's Health Initiative Memory Study (Cacciottolo et al., 2017) have estimated that the population attributable fraction of ambient air pollution exposure to dementia is about 16–21%. Even in places with comparatively low air pollution, association with dementia have been observed. Recently, the Swedish National Study on Aging and Care in Kungsholmen (SNAC-K) reported a 75% increase in the hazard ratios for incident CIND per 1 μg/m^3 increase in 3-year moving average $PM_{2.5}$ exposure and increases of 8% per 1 μg/m^3 increase in PM_{10} and 18% per 10 μg/m^3 NOx respectively (Wu et al., 2022). In the same cohort, air pollution also increased the risk for conversion from CIND to dementia (Grande et al., 2020). An Australian cohort study of 11,243 men aged 65 years or older, however, found no association between air pollutants and incident dementia

or Alzheimer's disease, but $PM_{2.5}$ increased risk of vascular dementia (per 5 μg/m^3 $PM_{2.5}$ increase HR = 1.39, 95% CI 0.93, 2.08) (Trevenen et al., 2022).

The evidence for an involvement of noise in cognitive impairment is also growing (Yu et al., 2020; Cantuaria et al., 2021). The World Health Organization has reported that traffic noise alone is responsible for the annual loss of more than one million healthy life years in Western Europe as a result of noise-related disability and disease, including cognitive impairment (World Health Organization, 2011). Noise can disturb sleep and influence its quality (Minakawa et al., 2019; Irwin and Vitiello, 2019), and it may also induce stress pathways, activate the autonomic nervous system and the endocrine system, and affect physiological function through the release of stress hormones (Babisch, 2002; Selander et al., 2009).

Air pollution and ambient noise often co-occur as they are generated by the same sources such as traffic. Few studies, however, have investigated whether air pollution and noise exposures may amplify each other's adverse health effects. Thus, the objective of this study was to examine whether air pollution and noise exposures interact to influence the development of dementia in a cohort of older Mexican Americans followed over almost a decade for cognitive decline.

2. Method

2.1. Study population

Study participants were enrolled in the Sacramento Area Latino Study on Aging (SALSA), a longitudinal cohort of older Mexican Americans residing in the Sacramento Valley area from 1998 to 2007. Participants were recruited from the Sacramento metropolitan area and surrounding suburban and rural counties via mail, telephone, and door-to-door neighborhood enumeration (Haan et al., 2003). Participants who (a) were 60 years or older; (b) lived in the six counties of the Sacramento Valley; (c) self-identifying as Latino, Mexican, Central American, or Mexican American; (d) were Spanish or English speakers; and (e) were living in a noninstitutionalized setting were eligible to be enrolled (Mungas et al., 2018). The participation rate was 83.5% among those eligible and contacted, and 1,789 participants in total were recruited at baseline. Participants were interviewed at home for both baseline interview and follow-up visits. Follow-up visits were conducted every 12–15 months with a maximum of seven follow-up visits. The average annual attrition rate from mortality and loss to follow-up was 2.6% and 2.3%, respectively. Between home visits, a 10-minute phone call every 6 months was performed to update participants' contact information, health status, and medication information (Haan et al., 2003). We excluded those who (1) did not participate in the interview at baseline (n = 3); (2) lived too far from traffic sources to generate air pollution and noise exposure measures (n = 3); (3) only had a baseline visit (n = 57); and (4) already had dementia/CIND (n = 114) at baseline, leaving 1,612 in total for the analysis (Fig. 1).

All procedures described here were approved by the Institutional Review Boards of the Universities of California, San Francisco, Los Angeles, and Davis; the University of

North Carolina; and the University of Michigan. All participants provided written informed consent.

2.2. Exposure Assessment

Details of how we generated NO_2, $PM_{2.5}$, O_3 and traffic-related noise estimates have been described elsewhere (Yu et al., 2020; Su et al., 2020; Yu et al., 2021). Briefly, NO_2 and O_3 concentrations were estimated based on a land use regression (LUR) model. To build this model, we conducted two air pollution monitoring campaigns in the Sacramento metro area for NO_2 at 69 sites and O_3 at 49 sites respectively, one in late spring (5/20/2016 – 6/3/2016) and one in winter (12/2/2016–12/16/2016). The mean (±standard deviation [SD]) of the measured NO_2 and O_3 concentrations were 6.1 ppb (SD = 1.4 ppb) and 21.5 ppb (SD = 4.7 ppb) respectively. For the LUR modeling, we applied the Deletion/Substitution/Addition (D/S/A) algorithm to generate an annual exposure prediction model (Su et al., 2020; Beckerman et al., 2013). More details can be found elsewhere (Su et al., 2020). The LUR model was developed specifically for the Sacramento area based on the monitoring data we collected in 2016, with the input of both buffered (i.e., land cover and traffic) and non-buffered data sources (i.e., distance to coast and roadways). A NO_2 concentration surface throughout the Sacramento area was generated at a spatial resolution of 30 × 30 m (Fig. 2A). The O_3 surface was first generated at a spatial resolution of 30 × 30 m and then averaged within a 1-km radius using zonal statistics through the mean function to account for regional impacts due to temperature effects (Fig. 2B). The final LUR model for NO_2 and O_3 had an adjusted prediction power (adjusted R^2) of 60% and 76% respectively (Miles, 2014).

Fine particulate matter with a diameter <2.5 μm ($PM_{2.5}$) estimates were also derived from a LUR model applying the D/S/A LUR modeling technique based on the measurements at 110 unique governmental monitoring stations located throughout California in 2004. The mean (±SD) for the measured $PM_{2.5}$ concentration was 10.7 (±3.9) $\mu g/m^3$. Similar predictors we used for the NO_2 LUR model were also used for the annual $PM_{2.5}$ modeling, with an adjusted prediction power of 64%. The annual average $PM_{2.5}$ concentration surface was also generated at a spatial resolution of 30 × 30 m and was used as a reference layer to derive annual residential level $PM_{2.5}$ exposures for the SALSA participants (Fig. 2C).

Each residential address was first assigned the pollutant concentrations for NO_2 or O_3 modeled in the reference year 2016, and for $PM_{2.5}$ modeled in the reference year 2004. To generate annual exposures for the years 1998–2007 at each residential address, we used the nearest EPA air quality monitoring data with an effective annual measurement (at least 75% completeness in each quarter of a year) for a specific year (Environmental Protection Agency 2006) to annualize the modeled air pollution (i.e. temporally calibrate the surface generated for the year 2004). The nearest distance from one regulatory monitor to another monitor ranged between 3.3–25.5 km, with a mean distance of 14.4 km. For a residential address in location i and year t with reference year d, the exposure value $E^j_{i,d,t}$ for pollutant j (here $j = NO_2, PM_{2.5}, O_3$) was calculated as:

$$E^{j}_{i,d,t} = C^{j}_{d,i} \times \frac{C^{j}_{m,t}}{c^{j}_{m,d}}$$

where $C^{j}_{d,i}$ is the modeled concentration of pollutant j at location i in reference year d; $C^{j}_{m,t}$ is the measured concentration of pollutant j at the EPA monitor m that is closest to location i in year t; $c^{j}_{m,d}$ is the concentration of pollutant j at the nearest EPA monitor m in reference year d. For the residential exposures to NO_2, O_3 and $PM_{2.5,\ we}$ used the same equation to estimate the annual exposures for years 1998–2007.

Traffic-related noise exposure was estimated using the SoundPLAN software package (Version 8.0, NAVCON, Fullerton, CA, USA), which is implemented with a noise prediction model-the Federal Highway Administration Traffic Noise Model that uses annual average daily traffic (AADT) data from Metropolitan Planning Organizations (MPO). The Traffic Noise Model estimated the noise levels with average vehicle speed, counts of different types of vehicles, ground classification (soft vs. hard ground), and distance from receptor points to the roadway (USDOT, 1998, 2002). We used hourly traffic counts obtained from the State Department of Transportation in 2002 to calculate average diurnal traffic patterns and used these to adjust the MPO AADT values to generate hour-of-day specific traffic counts at each subject's geocoded residential address at baseline, which was treated as the receptor point. We estimated the A-weighted measure – the most common weighting applied to noise measurements accounting for differences in sensitivity of human sound perception at specific frequencies (International Electrotechnical Commission) – daily average (Ldn) sound levels for each participant's residence. Roadway traffic was the only source of noise assessed in our study; we only used counts of FHWA classified as light- and heavy-duty vehicles and assumed that the average vehicle speed was 55 miles per hour to generate noise estimates. More details can be found elsewhere. (USDOT, 1998, 2002).

2.3. Outcome measurement

Two cognitive screening tests – the Modified Mini–Mental State Examination (3MSE) and a delayed word recall trial from the Spanish English Verbal Learning Test (SEVLT) – were performed with each participant at baseline and follow-up visits. A geriatrician referred the participants for a neuropsychological test battery and a standard neuropsychological examination (Informant Questionnaire on Cognitive Decline in the Elderly) if their scores (1) were below the 20th percentile at baseline on the 3MSE or SEVLT, or (2) had decreased ≥ 8 points on the 3MSE or ≥ 3 points on the SEVLT between baseline and follow-up. The cases were reviewed by a team of neurologists and neuropsychologist and given a diagnosis of "cognitively normal", "cognitively impaired but not dementia (CIND)," or "dementia" according to standard diagnostic criteria. Those diagnosed with dementia or CIND were also referred for a magnetic resonance imaging (MRI) examination (American Psychiatric Association, 2000). Detailed procedures for dementia and CIND screening and classification are described elsewhere (Haan et al., 2003). In this study, we used (1) dementia and (2) a combined outcome which included incident dementia or CIND cases and those who were CIND at baseline and converted to dementia during the follow-up to capture both cognitive decline prior to dementia and dementia incidence to improve our statistical power.

Mortality data was collected through interviews with family members when we did not reach participants for annual follow-up visits or during the interim 6-months phone calls, by reviewing online death notices, checking the Social Security Death Index, the National Death Index and California state vital statistics data.

2.4. Covariates

Demographic information including age, sex, years of education, and longest held occupation during the lifetime were collected at baseline. At each interview, participants also reported household income, marital status, smoking, general health status, and medication use. We evaluated physical activity level according to time spent performing 18 different activities that older adults commonly engage in during a regular week (Shih et al., 2018). Activities of daily living (ADL) was derived on a self-reported multi-format scale referring to six activities including bathing, dressing, eating, transferring, toileting and continence (Inoue et al., 2020). Urban or rural residential location was generated as an indicator according to Census tract 2000 information (United States Department of Agriculture Economic Research Service, 2019). Neighborhood socioeconomic status (NSES) is represented as a score ranging from 1 to 5 (low–high NSES) depending on six census (2000) estimates (Yost et al., 2001): percentage of (1) individuals aged 25+ years without a high school diploma, (2) individuals below the poverty limit, (3) individuals aged 16+ who had been in the workforce at one time but are unemployed, (4) households owning their home, (5) vacant housing units, and (6) median number of rooms in a household.

2.5. Statistical methods

Cox proportional hazards regression models with a calendar time scale were used to estimate the impact of NO_2, $PM_{2.5}$ and O_3 exposures on incident dementia/CIND or dementia, respectively. Participants were censored at their last date of contact if they did not return for a follow-up visit or at the time of death before the end of 2007. Time-varying NO_2, $PM_{2.5}$ and O_3 exposures were calculated as the three air pollutant levels averaged over 1-, 3- and 5-calendar years prior to the onset of an event for everyone in the risk set at the event time and were treated as continuous variables scaled by their inter-quartile ranges (IQRs). To examine the impact of NO_2, $PM_{2.5}$ and O_3 exposures on cognitive impairment, covariates were selected based on the prior literature for air pollution and dementia for adjustment (Andersson et al., 2018; Paul et al., 2020). We first estimated effects using a model that only adjusted for baseline age, sex and years of education. We then added longest held occupation and household income, outdoor physical activity and smoking status which are major risk factors for cardio-metabolic diseases, as well as a NSES indicator, considering that air pollutants vary spatially. We additionally adjusted for marital status and ADL considering these factors might influence lifestyle or where participants live and, thus, act as potential confounders. We also co-adjusted for the two other air pollutants in separate models to address the potential confounding by other air pollutants.

We then examined associations between air pollution and cognitive impairment after stratifying by traffic-related noise exposure levels and also including an interaction term between noise and NO_2, $PM_{2.5}$ or O_3 exposure, respectively. The air pollution exposures were treated as continuous variables; the baseline annual average 24-hour noise exposure

calculated using 2002 annual average daily traffic data as the input was used as a binary modifier variable with a cut-point of <65 vs. ≥65 dB, which was based on previous studies in the United States and European countries (Lee et al., 2014; Seong et al., 2011).

In sensitivity analyses, we also repeated analyses using 70 dB as cut-points to assess higher noise exposure levels. Furthermore, we repeated analyses by calculating the time-varying exposures as the three air pollutants levels averaged over 2- and 4-calendar years prior to the onset of an event for everyone in the risk set at the event time. Additionally, 5-year average NO_2, $PM_{2.5}$ and O_3 exposure prior to the baseline year only were used as time invariant exposure variables when examining the relationship between air pollution and dementia. Finally, we applied the $PM_{2.5}$ estimates generated by the GEOS-Chem chemical transport model developed by Atmospheric Composition Analysis Group at Washington University in St. Louis (https://sites.wustl.edu/acag/datasets/surface-pm2-5/). We conducted these sensitivity analyses for comparison purposes because our own $PM_{2.5}$ estimates were generated from a statewide LUR model, rather than one specific for the Sacramento area as done for NO_2 and O_3.

Statistical analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, NC).

3. Results

The average age of participants at baseline was 70 years and ~ 60% were women. About 78% of the participants resided in Sacramento County and 87% in urban areas. Around 60% of participants held a manual job during most of their lifetime, 12% were current smokers, and ~ 20% were physically active at baseline. Those who developed incident dementia/CIND were older, less educated, had a lower household income and needed more assistance to perform daily activities at baseline. The average annual concentration of NO_2, $PM_{2.5}$, O_3 and 24-hour noise exposure during the baseline year were ~ 29 ppb, 13 $\mu g/m^3$, 47 ppb, 69 dB respectively (Table 1). Pearson's correlation coefficients for the three air pollutants and noise exposure at baseline ranged from −0.23 (for NO_2 and O_3) to 0.23 (for NO_2 and 24-hour noise exposure) (Table S1).

A total of 104 incident dementia and 159 incident dementia/CIND cases were identified during the 10 years of follow-up. Each participant on average completed about 5 follow-up visits. The average length of follow-up was 6.5 years, with a maximum of 10 years. Generally, increasing air pollution levels were almost linearly associated with incident dementia or CIND in most cases (Figure S1). Overall, higher level of noise exposure was positively associated with the incidence of dementia or CIND (Table 2). In single air pollutant models, we found for each IQR increase in time-varying 1-, 3- and 5-year average $PM_{2.5}$ exposure a ~30% elevated hazard for dementia (HR = 1.33, 95% CI: 1.00, 1.76 5-year average). While $PM_{2.5}$ exposure was also positively related to dementia/CIND, this association was weaker and did not reach statistically significance (Table 2). For each IQR increase in time-varying 1-year average NO_2 exposure, the hazard ratio of incident dementia/CIND was 1.22 (95% CI: 0.99, 1.51), but the hazard ratio for dementia alone was smaller and the 95% CI included the null value (HR = 1.14,95% CI: 0.86, 1.49); 5-year averages showed a similar pattern (Table 2). No association was found between O_3

exposure either with dementia/CIND or dementia alone (Table 2). The effect estimates for NO_2, $PM_{2.5}$, and O_3 from single exposure models were very similar to those from models adjusted for the other two pollutants or noise exposure (Table S2–S4). When using the $PM_{2.5}$ estimates derived from the Atmospheric Composition Analysis Group's GEOS-Chem chemical transport model, the estimated effects sizes were quite similar, but the confidence intervals were wider and crossed null (Table S5). Using non-time-varying 5-year average NO_2, $PM_{2.5}$ and O_3 exposure prior to baseline year, the HRs for dementia/CIND or dementia only were generally attenuated or null (Table S6).

Finally, we modeled interactions between traffic-related noise (<65 vs. ≥ 65 dB) exposure and each of the three air pollutants, respectively. For NO_2, the hazard ratio of developing dementia/CIND was 1.28 (95% CI: 0.97, 1.69, p for interaction term = 0.02) for those also experiencing higher noise exposure, while there was no increased hazard observed among those with lower traffic noise exposure. Similarly, for $PM_{2.5}$, the hazard ratio of incident dementia alone was 1.57 (95% CI: 1.11, 2.21) among those whose noise exposure level was higher than 65 dB (p-values for interaction term = 0.03) (Table 3). For those with even higher noise exposure (≥70 dB), the hazard of developing incident dementia/CIND associated with NO_2 exposure also increased by 29% but had wider confidence intervals (Table S7). The hazard of $PM_{2.5}$-related incident dementia increased 72% (HR = 1.72, 95% CI: 1.15, 2.57, p for interaction term = 0.04) at this very high noise level. A smaller increase in the hazard ratio for O_3 exposure associated with dementia only outcomes at the highest-noise exposure level also emerged, but the 95% CI included the null (HR = 1.25, 95% CI: 0.93, 1.66) (Table S7).

4. Discussion

In this cohort of older Mexican American individuals, we found increased hazard ratios for incident dementia and dementia/CIND with 1- to 5-year average NO_2 and $PM_{2.5}$ exposures respectively, but not with O_3 exposure. The effect estimates were highest among study participants not only exposed to NO_2 or $PM_{2.5}$ but also exposed to high traffic-related noise levels, suggesting a synergism for the two exposures.

Previous studies reported similar results for air pollution and cognitive outcomes in older populations. For example, a retrospective cohort study of 130,978 adults aged 50–79 years living in London observed risk increases of ~16% and 7% for dementia diagnoses derived from primary care records for each IQR increase in NO_2 (IQR = 7.47 $\mu g/m^3$) and $PM_{2.5}$ (0.95 $\mu g/m^3$) exposure (1-year average prior to baseline) respectively and also found no associations with O_3 exposure (Carey et al., 2018). In the Adult Changes in Thought (ACT) population-based cohort study in Seattle that enrolled 4,166 participants, the researchers linked spatiotemporal model-based $PM_{2.5}$ exposures to the participants' addresses and observed that for each 1 $\mu g/m^3$ increase in time-varying 10-year average $PM_{2.5}$, the hazard of developing all-cause dementia increased by 16% (HR = 1.16, 95% CI: 1.03, 1.31) (Shaffer et al., 2021). In a population-based cohort study in Canada with ~2.1 million individuals, researchers observed for incident dementia recorded in health administrative databases positive associations with both $PM_{2.5}$ and NO_2 but no associations with O_3 exposures generated with LUR models (Chen et al., 2017). Recently, in a cohort of

Puerto Ricans (n = 1,255) living in Greater Boston researchers showed that while $PM_{2.5}$ was associated with decreased recognition (−0.35; 95% CI = − 0.57, −0.12) only, black carbon as a tracer of traffic pollution was associated with decreased verbal memory (−0.38; 95% CI: −0.46, −0.30), recognition (−0.35; 95% CI:−0.46, −0.25), mental processing (−1.14; 95% CI: −1.55, −0.74), and executive function (−0.94; 95% CI: −1.31, −0.56) (Wurth et al., 2018). The Chinese Longitudinal Healthy Longevity Survey (2005–2018) cohort study that recruited 9,544 Chinese older adults (65 years and over), observed a 10.4% increased hazard ratio in cognitive impairment assessed using the Chinese version of the Mini-Mental State Examination for O_3 exposure (HR = 1.104, 95% CI: 1.041, 1.172 for each 10-μg/m^3 increase in annual mean O_3) (Gao et al., 2022).

In this study, 1- to 5-year time-varying $PM_{2.5}$ exposures were associated with dementia while for NO_2 the increased hazard ratio we observed for dementia/CIND with a 1-year average was attenuated and not formally statistically significant for the 3- or 5-year NO_2 exposure averages. Generally, $PM_{2.5}$ captures both local and regional pollution sources for fine particles, while NO_2 has finer-scale variability that represents traffic-related air pollution generated from local sources of combustion such as traffic exhaust (HEI 2010). For O_3 we found no associations and this is a secondary pollutant generated from traffic pollutants by atmospheric chemistry that is generally distributed more homogenously across a region (Crouse et al., 2015). In addition, in our study as well as more generally, O_3 correlates negatively with other modelled traffic-related air pollutants as atmospheric chemistry predicts O_3 to be lower near sources of NO and NO_2 and higher away for these sources. Thus, when such local patterns are captured by a model, we expect to see reverse directions for association of these pollutants with health outcomes.

Air pollution can induce oxidative stress and systemic inflammatory responses. It can also disrupt the blood–brain barrier (BBB), precipitating β-amyloid and activating microglia (Genc et al., 2012; Calderón-Garcidueñas et al., 2008; Levesque et al., 2011). Air pollutants may reach the brain through different routes (Lucchini et al., 2012). Very small particulate pollutants, specifically ultrafine particles, might travel to the brain through the olfactory system which provides a direct anatomic connection from the nose to the brain (Oberdörster et al., 2004; Eren and Ozturk, 2022). In experiments that exposed the olfactory system of animals to an aerosol of uranium tetroxide particles, researchers observed an anteroposterior gradient from the olfactory bulb to the brain with cerebral uranium accumulation (Ibanez et al., 2019). Small particles may also reach the brain via the autonomous nervous system or they may reach the brain via the blood (Eren and Ozturk, 2022). Generally, an increased AD risk due to $PM_{2.5}$ exposure may be related to inflammatory responses in the brain (Näslund et al., 2000) and the subsequent dysfunction of blood–brain barrier, neural degeneration and apoptosis, and cerebrovascular pathology (Calderón-Garcidueñas L and Maronpot, 2004).

In this study, we found that dementia/CIND was mainly associated with 1-year average NO_2 exposure. Compared to $PM_{2.5}$, NO_2 captures a smaller scale variability of traffic-related pollution. The assumption that study participants are homebound and exposed to fresh traffic exhaust might be more accurate when participants become less mobile during dementia development. For spatially highly variable NO_2 exposures, shorter term exposure averages

close to diagnosis might be less affected by exposure misclassification due to participants' mobility.

Different from all previous studies, we investigated traffic-related noise co-exposures and found that the hazard of developing dementia and CIND were strongest among those exposed to NO_2 or $PM_{2.5}$ when there was co-exposure to high traffic-related noise. Although both the air pollution and the noise models used traffic data, due to their physical properties these two types of exposures are expected to vary considerably with distance from traffic sources owing to the different effects that buildings, land cover and meteorological influences have on the dispersion behavior of air pollution and noise (Fecht et al., 2016). Consequently, we observed relatively weak correlations between our air pollutant and noise metrics. Nevertheless, it may still be possible that noise acts as a surrogate for more toxic traffic sources of the air pollutant mixture.

Health effects from noise exposure are a growing concern for public health especially for neuro-degenerative diseases (Ritz and Yu, 2021; Cantuaria et al., 2021; Fuks et al., 2019; Tzivian et al., 2016). Experimental studies have shown that noise can act as a stressor influencing brain structures such as reducing cortical thickness in the hippocampus and amygdala area, which are essential parts of the neural circuitry mediating stress responses (Czeh et al., 2007; Jafari et al., 2018)]. Noise can also cause the amygdala to activate stress pathways in the hypothalamus and brainstem, increasing the release of the neurotransmitters noradrenaline and dopamine and resulting in dysregulation of the prefrontal cortex responsible for cognition related to executive function (Arnsten and Goldman-Rakic, 1998; Arnsten, 2009; Jafari et al., 2019). Further, similar to air pollution, noise exposure might also increase oxidative stress. In a controlled random sequence study in Denmark consisting of 18 healthy participants (9 males and 9 females, non-smoking, and 40–66 years of age), peripheral blood samples were collected after exposure to noise higher than 75 dB for 3 h at 4 time points- (Hemmingsen et al., 2015). The researchers found that exposure to high levels of traffic noise was associated with an increase of 0.11 lesions per 10^6 basepairs (95% CI: 0.03, 0.21) in the level of 8-oxoguanine DNA glycosylase (hOGG1)-sensitive sites, suggesting that exposure to noise might cause oxidative damage to the DNA. Generally, traffic-related noise and air pollution are moderately correlated (Stansfeld, 2015), as their dispersion patterns from the source differ, i.e. air pollution dispersion is influenced more by meteorological conditions, while noise is affected more by intervening barriers and building. In a cross-sectional study conducted in Germany (4,086 participants aged 50–80 years), researchers reported that the risk of mild cognitive impairment (MCI) and amnestic MCI increased by 40% (odds ratio [OR] = 1.4, 95% CI: 1.0, 1.9) and 50% (OR = 1.5, 95% CI: 1.1, 2.2) respectively for each 10 A-weighted decibel [dB(A)] increase in traffic noise estimated at the participants' residence (Tzivian et al., 2016). In a previous study in the SALSA cohort, we found the hazard of developing dementia or CIND to be increased by 20% (HR = 1.2, 95% CI: 1.0, 1.5) per 11.6 dB increase in 24-hour noise, and the hazard of developing dementia/CIND to be elevated when 24-hour noise was higher than 75 dB (Yu et al., 2020). Here, we further observed that the increase in the hazard ratio of developing dementia/CIND reached 50 or even 70% when noise exposure was high (≥65 dB or 70 dB) for co-exposure with traffic-related air pollution. This suggests both independent and combined (synergistic) associations between noise exposure and traffic-related air pollution

and cognitive impairment. A few previous studies, however, did not find associations with noise or interactions with air pollution. The Betula study in Northern Sweden (n = 1,721) found that residing in areas with the two highest quartiles of NOx exposure was associated with a 38–47% increased risk of dementia compared to the lowest quartile of NOx exposure (<9 μg/m^3), while the exposure to high noise levels (>55 dB) was not associated with dementia, and there was no statistically significant interaction between NOx and road traffic noise on dementia (Andersson et al., 2018). A cohort study in Canada assembled an administrative health database of 45–84 years old residents in Vancouver (n = 678,000) and observed associations between $PM_{2.5}$ and NO_2 exposures and non-Alzheimer's dementia but not Alzheimer's dementia. Noise exposure was not associated with these outcomes and the effect estimates for air pollution were not modified by noise (Yuchi et al., 2020). This inconsistency in results might be related to differences in the methods used to identify the outcomes and in assessing noise exposure or sources and levels of traffic noise in these cities.

The SALSA study has several strengths. It is one of few population-based longitudinal cohort studies focusing on effects of air pollution and noise exposures on cognitive function among older Mexican Americans, one of the most highly environmentally exposed population subgroup in California (OEHHA 2018). Instead of relying on health administrative records that may miss the onset of ADRD, we used repeated cognitive function testing and further confirmed diagnoses by imaging examination (MRI), leading to a high accuracy for the dementia or CIND diagnosis and its timing in SALSA. Both air pollution and noise exposures were estimated based on participants' residential addresses which were geocoded by global positioning system readings during home visits, ensuring high geo-location quality. We built and employed LUR models to generate the air pollution estimates with the input of land use and meteorological data as well as data from air pollution monitoring campaigns in the study area. We captured important air pollution sources such as traffic and modeled variations in pollutants on a small spatial scale. In addition, the noise model has been validated in several urban settings across the United States (Lee et al., 2014).

Some limitations also merit mentioning. This study focused on elderly Mexican American participants living in the Sacramento Valley area which may limit the generalizability of our results to other age and ethnic groups. We lacked lifetime residential history and assessed the air pollution and noise exposures based on the participants' geocoded addresses recorded at baseline. Additionally, we did not have information related to potential protective measures such as window soundproofing, bedroom orientation, window insulation or habits of opening windows or using protective measures. Furthermore, prediction power for the LUR models ranged from 60 to 76% and we would expect exposure misclassification to be greater for the entire study period than for the modeled concentrations in the years 2004 or 2016. In the SALSA cohort, the average age of the participants was 70 years or older at baseline and most were already retired and consequently are expected to be at home regularly during the day. The spatial pollution pattern likely remained consistent throughout the study years given the relative stable land use (Kang et al., 2012), nevertheless, land use changes may have introduced some exposure misclassification. Additionally, the average length that participants reported having lived at their baseline residences was 22 years,

and 90% remained in California throughout the study period. Thus, the exposure estimates based on the baseline addresses likely serve as a good indicator to characterize long-term spatial air pollution and noise exposures around each participants' residence before and throughout the study period. There were only eight Environmental Protection Agency air quality monitoring sites for O_3 in total in the Sacramento area, and we only conducted monitoring campaigns in spring and winter, thus the absolute annual average concentrations were possibly underestimated due to lack of summer measurements (Yu et al., 2021). For noise estimates, we only accounted for continuous major roadway traffic as the source of residential noise exposures not including stop-and-go traffic, noise from the airport or railways, or occupational noise exposure before retirement, and we applied the same speed (55 miles/hour) for all roads and did not take into account screening from buildings, terrain and barriers, and reflections in the noise estimate. Thus, we likely underestimated total noise exposure but expect this misclassification to be non-differential. Further, we did not conduct a field measurement campaign for ambient noise to estimate the predictive performance of the model for the Sacramento area. While this model has performed well in other locations, (Lee et al., 2014; Seto et al., 2007) we cannot rule out the possibility that model predictive accuracies vary by location such that the exposure misclassification for noise in this study is greater than previously reported. Individuals with cognitive impairment tend to be less likely to be retained as study participants during follow-up. For selection bias due to loss of follow-up to occur, however, continued participation has to depend on exposure history being differential by disease status. We do not see how traffic related air pollution or noise would have contributed to differential loss of participants who developed cognitive impairment or dementia.

5. Conclusion

This study provides further evidence for the impact of air pollution on cognitive impairment among older Mexican Americans and suggests synergistic effects between air pollutants and traffic-related noise exposures. Mexican Americans are among the most highly exposed population groups in California. Potential synergisms among multiple environmental exposures represent a key concern for communities facing a high environmental exposure burden. Our findings suggest that such synergisms likely exist and should be considered in policies designed to protect public health. New regulations, land use planning approaches, and technological innovations are needed to reduce these pervasive environmental risk factors and the risk of ADRD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

This work was supported by grants R01ES023451 and F32ES028087 from National Institute of Environmental Health Sciences, AG012975 and AG033751 from National Institute on Aging, and DK060753 from National Institute of Diabetes and Digestive and Kidney Diseases.

Data availability

Data will be made available on request.

References

Alzheimers Dementia. 2021. Alzheimer's disease facts and figures. 2021 Mar;17(3):327–406. doi: 10.1002/alz.12328. Epub 2021 Mar 23.

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Washington, DC: American Psychiatric Association; 2000.

Andersen ZJ, Zhang J, Jørgensen JT, et al. , 2022. Long-term exposure to air pollution and mortality from dementia, psychiatric disorders, and suicide in a large pooled European cohort: ELAPSE study. Environ. Int. 170. 10.1016/j.envint.2022.107581.

Andersson J, Oudin A, Sundstrom A, Forsberg B, Adolfsson R, Nordin M, 2018. Road traffic noise, air pollution, and risk of dementia - results from the Betula project. Environ Res. 166, 334–339. 10.1016/j.envres.2018.06.008166. [PubMed: 29909174]

Arnsten AFT, Goldman-Rakic PS, 1998. Noise Stress Impairs Prefrontal Cortical Cognitive Function in Monkeys: Evidence for a Hyperdopaminergic Mechanism. JAMA Psychiat. 55 (4), 362–368. 10.1001/archpsyc.55.4.362.

Arnsten AF, 2009. Stress signalling pathways that impair prefrontal cortex structure and function. Nat. Rev. Neurosci. 10 (6), 410–422. 10.1038/nrn2648. [PubMed: 19455173]

Babisch W, 2002. The noise/stress concept, risk assessment and research needs. Noise Health. 4 (16), 1.

Beckerman BS, Jerrett M, Martin RV, van Donkelaar A, Ross Z, Burnett RT, 2013. Application of the deletion/substitution/addition algorithm to selecting land use regression models for interpolating air pollution measurements in California. Atmosph. Environ. 77 (172–177) 10.1016/j.atmosenv.2013.04.024.

Cacciottolo M, Wang X, Driscoll I, et al. , 2017. Particulate air pollutants, APOE alleles and their contributions to cognitive impairment in older women and to amyloidogenesis in experimental models. Translational psychiatry. 7 (1), e1022. [PubMed: 28140404]

Calderón-Garcidueñas L, Mora-Tiscareño A, Ontiveros E, et al. , 2008. Air pollution, cognitive deficits and brain abnormalities: a pilot study with children and dogs. Brain Cogn. 68 (2), 117–127. 10.1016/j.bandc.2008.04.008. [PubMed: 18550243]

Calderón-Garcidueñas L, Reed W., Maronpot RR, et al. , 2004. Brain inflammation and Alzheimer's-like pathology in individuals exposed to severe air pollution. Toxicol. Pathol. 32 (6), 650–658. 10.1080/01926230490520232. [PubMed: 15513908]

California EPA Office of Environmental Health Hazard Assessment (OEHHA). Analysis of Race/Ethnicity, Age, and CalEnviroScreen 3.0 Scores. 2018.

Cantuaria ML, Waldorff FB, Wermuth L, et al. , 2021. Residential exposure to transportation noise in Denmark and incidence of dementia: national cohort study. BMJ 374 (1954).

Carey IM, Anderson HR, Atkinson RW, et al. , 2018. Are noise and air pollution related to the incidence of dementia? A cohort study in London, England. BMJ Open 8 (9), e022404.

Chen H, Kwong JC, Copes R, et al. , 2017. Exposure to ambient air pollution and the incidence of dementia: A population-based cohort study. Environ Int. 108 (271–277).

Crouse DL, Peters PA, Hystad P, et al. , 2015. Ambient PM2.5, O3, and NO2 Exposures and Associations with Mortality over 16 Years of Follow-Up in the Canadian Census Health and Environment Cohort (CanCHEC). Environmental Health Perspectives 123 (11), 1180–1186. 10.1289/ehp.1409276. [PubMed: 26528712]

Czeh B, Muller-Keuker JI, Rygula R, et al. , 2007. Chronic social stress inhibits cell proliferation in the adult medial prefrontal cortex: hemispheric asymmetry and reversal by fluoxetine treatment. Neuropsychopharmacology 32 (7), 1490–1503. 10.1038/sj.npp.1301275. [PubMed: 17164819]

Eren F, Ozturk S, 2022. Evaluation of the Effect of Air Pollution on Cognitive Functions, Cognitive Decline, and Dementia. Ann Indian Acad. Neurol. 25 (Suppl 1), S9–S14. 10.4103/aian.aian_453_22. [PubMed: 36213096]

Fecht D, Hansell AL, Morley D, et al. , 2016. Spatial and temporal associations of road traffic noise and air pollution in London: Implications for epidemiological studies. Environ Int. 88, 235–242. 10.1016/j.envint.2015.12.001. [PubMed: 26773394]

Fuks KB, Wigmann C, Altug H, Schikowski T, 2019. Road traffic noise at the residence, annoyance, and cognitive function in elderly women. Int. J. Environ. Res. Public Health. 16 (10) 10.3390/ijerph16101790.

Gao Q, Zang E, Bi J, et al. , 2022. Long-term ozone exposure and cognitive impairment among Chinese older adults: A cohort study. Environ. Int. 160, 107072 10.1016/j.envint.2021.107072. [PubMed: 34979350]

Genc S, Zadeoglulari Z, Fuss SH, Genc K, 2012. The adverse effects of air pollution on the nervous system. J Toxicol. 2012, 782462 10.1155/2012/782462. [PubMed: 22523490]

Grande G, Ljungman PLS, Eneroth K, Bellander T, Rizzuto D, 2020. Association Between Cardiovascular Disease and Long-term Exposure to Air Pollution With the Risk of Dementia. JAMA Neurol. 77 (7), 801–809. 10.1001/jamaneurol.2019.4914. [PubMed: 32227140]

Haan MN, Mungas DM, Gonzalez HM, Ortiz TA, Acharya A, Jagust WJ, 2003. Prevalence of dementia in older latinos: the influence of type 2 diabetes mellitus, stroke and genetic factors. J. Am. Geriatr. Soc. 51 (2), 169–177. 10.1046/j.1532-5415.2003.51054.x. [PubMed: 12558712]

Health Effects Institute. Traffic-related air pollution: a critical review of the literature on emissions, exposures, and health effects. HEI Special Report 17. 2010. Available at: https://www.healtheffects.org/system/files/SR17TrafficReview.pdf (Access on 1/21/2022).

Hemmingsen JG, Moller P, Jantzen K, et al. , 2015. Controlled exposure to diesel exhaust and traffic noise–Effects on oxidative stress and activation in mononuclear blood cells. Mutat. Res. 775, 66–71. 10.1016/j.mrfmmm.2015.03.009. [PubMed: 25898780]

Ibanez C, Suhard D, Elie C, et al. , 2019. Evaluation of the Nose-to-Brain Transport of Different Physicochemical Forms of Uranium after Exposure via Inhalation of a UO4 Aerosol in the Rat. Environ. Health Perspect. 127 (9), 97010. 10.1289/EHP4927. [PubMed: 31566443]

Inoue K, Mayeda ER, Paul KC, et al. , 2020. The Association of Physical Activity with Cardiovascular Events and Mortality Mediated by Diabetes in Older Mexican Americans. Am. J. Epidemiol. 189 (10), 1124–1133. 10.1093/aje/kwaa068. [PubMed: 32383448]

International Electrotechnical Commission Glossary A-weighting sound pressure level; A-weighted sound pressure level. http://stdiecch/terms/termsnsf/3385f156e728849bc1256e8c00278ad2/f2cdfd3b716912c9c12579eb004f55f6?OpenDocument (Accessed on July 17, 2020).

Irwin MR, Vitiello MV, 2019. Implications of sleep disturbance and inflammation for Alzheimer's disease dementia. The Lancet Neurol. 18 (3), 296–306. 10.1016/s1474-4422(18)30450-2. [PubMed: 30661858]

Jafari Z, Kolb BE, Mohajerani MH, 2018. Chronic traffic noise stress accelerates brain impairment and cognitive decline in mice. Exp Neurol. 308, 1–12. 10.1016/j.expneurol.2018.06.011. [PubMed: 29936225]

Jafari Z, Kolb BE, Mohajerani MH, 2019. Noise Exposure Accelerates the Risk of Cognitive Impairment and Alzheimer's Disease: Adulthood, Gestational, and Prenatal Mechanistic Evidence from Animal Studies. Neurosci. Biobehav. Rev. 10.1016/j.neubiorev.2019.04.001.

Kang S, Spiller M, Jang K, Bigham JM, Seo J, 2012. Spatiotemporal analysis of macroscopic patterns of urbanization and traffic safety: case study in Sacramento County, California. Transport. Res. Record. 2318 (1), 45–51. 10.3141/2318-06.

Lee EY, Jerrett M, Ross Z, Coogan PF, Seto EY, 2014. Assessment of traffic-related noise in three cities in the United States. Environ Res. 132, 182–189. 10.1016/j.envres.2014.03.005. [PubMed: 24792415]

Levesque S, Taetzsch T, Lull ME, et al. , 2011. Diesel exhaust activates and primes microglia: air pollution, neuroinflammation, and regulation of dopaminergic neurotoxicity. Environ. Health Perspect. 119 (8), 1149–1155. 10.1289/ehp.1002986. [PubMed: 21561831]

Livingston G, Huntley J, Sommerlad A, et al. , 2020. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet 396 (10248), 413–446. 10.1016/s0140-6736(20)30367-6. [PubMed: 32738937]

Lucchini RG, Dorman DC, Elder A, Veronesi B, 2012. Neurological impacts from inhalation of pollutants and the nose-brain connection. Neurotoxicology 33 (4), 838–841. 10.1016/j.neuro.2011.12.001. [PubMed: 22178536]

Miles J R squared, adjusted R squared. Wiley StatsRef: Statistics Reference Online. 2014.

Minakawa EN, Wada K, Nagai Y, 2019. Sleep Disturbance as a Potential Modifiable Risk Factor for Alzheimer's Disease. Int J Mol Sci. 20 (4) 10.3390/ijms20040803.

Mungas D, Early DR, Glymour MM, Zeki Al Hazzouri A, Haan MN, 2018. Education, bilingualism, and cognitive trajectories: Sacramento Area Latino Aging Study (SALSA). Neuropsychology 32 (1), 77. 10.1037/neu0000356. [PubMed: 28967765]

Näslund J, Haroutunian V, Mohs R, et al. , 2000. Correlation between elevated levels of amyloid β-peptide in the brain and cognitive decline. JAMA 283 (12), 1571–1577. [PubMed: 10735393]

Oberdörster G, Sharp Z, Atudorei V, et al. , 2004. Translocation of inhaled ultrafine particles to the brain. Inhal Toxicol. 16 (6–7), 437–445. 10.1080/08958370490439597. [PubMed: 15204759]

Oudin A, Forsberg B, Adolfsson AN, et al. , 2016. Traffic-Related Air Pollution and Dementia Incidence in Northern Sweden: A Longitudinal Study. Environ Health Perspect. 124 (3), 306–312. 10.1289/ehp.1408322. [PubMed: 26305859]

Paul KC, Haan M, Mayeda ER, Ritz BR, 2019. Ambient Air Pollution, Noise, and Late-Life Cognitive Decline and Dementia Risk. Annu. Rev. Public Health. 40, 203–220. 10.1146/annurev-publhealth-040218-044058. [PubMed: 30935305]

Paul KC, Haan M, Yu Y, et al. , 2020. Traffic-related air pollution and incident dementia: direct and indirect pathways through metabolic dysfunction. J. Alzheimers Dis. 76 (4), 1477–1491. 10.3233/JAD-200320. [PubMed: 32651321]

Ritz B, Yu Y, 2021. Invited Perspective: Air Pollution and Dementia: Challenges and Opportunities. Environmental Health Perspectives. 129 (8), 081301 10.1289/EHP9605. [PubMed: 34347532]

Ritz B, Yu Y, 2021. Noise exposure and dementia: a rising concern in ageing populations. BMJ. 374, n2120 10.1136/bmj.n2120. [PubMed: 34497051]

Selander J, Bluhm G, Theorell T, et al. , 2009. Saliva cortisol and exposure to aircraft noise in six European countries. Environ. Health Perspect. 117 (11), 1713–1717. 10.1289/ehp.0900933. [PubMed: 20049122]

Seong JC, Park TH, Ko JH, et al. , 2011. Modeling of road traffic noise and estimated human exposure in Fulton County, Georgia, USA. Environ Int. 37 (8), 1336–1341. 10.1016/j.envint.2011.05.019. [PubMed: 21704376]

Seto EY, Holt A, et al. , 2007. Spatial distribution of traffic induced noise exposures in a US city: an analytic tool for assessing the health impacts of urban planning decisions. Int J Health Geogr. 6 (24), 1–16. 10.10.1186/1476-072X-6-24. [PubMed: 17214903]

Shaffer RM, Blanco MN, Li G, et al. , 2021. Fine Particulate Matter and Dementia Incidence in the Adult Changes in Thought Study. Environ Health Perspect. 129 (8), 87001. 10.1289/EHP9018. [PubMed: 34347531]

Shih IF, Paul K, Haan M, Yu Y, Ritz B, 2018. Physical activity modifies the influence of apolipoprotein E epsilon4 allele and type 2 diabetes on dementia and cognitive impairment among older Mexican Americans. Alzheimers Dement. 14 (1), 1–9. 10.1016/j.jalz.2017.05.005. [PubMed: 28692819]

Stansfeld SA, 2015. Noise Effects on Health in the Context of Air Pollution Exposure. Int. J. Environ. Res. Public Health. 12 (10), 12735–12760. 10.3390/ijerph121012735. [PubMed: 26473905]

Su JG, Meng Y-Y, Chen X, Molitor J, Yue D, Jerrett M, 2020. Predicting differential improvements in annual pollutant concentrations and exposures for regulatory policy assessment. Environ. Int. 143.

Trevenen ML, Heyworth J, Almeida OP, et al. , 2022. Ambient air pollution and risk of incident dementia in older men living in a region with relatively low concentrations of pollutants: The Health in Men Study. Environ Res. 215 (Pt 2), 114349. 10.1016/j.envres.2022.114349. [PubMed: 36116491]

Tzivian L, Dlugaj M, Winkler A, et al. , 2016. Long-Term Air Pollution and Traffic Noise Exposures and Mild Cognitive Impairment in Older Adults: A Cross-Sectional Analysis of the Heinz Nixdorf Recall Study. Environ Health Perspect. 124 (9), 1361–1368. 10.1289/ehp.1509824. [PubMed: 26863687]

United States Department of Agriculture Economic Research Service. Rural-Urban Commuting Area Codes. https://www.ers.usda.gov/data-products/rural-urban-commuting-area-codes/.

USDOT, 1998. FHWA Traffic Noise Model (FHWA TNM) Technical Manual. Federal Highway Administration, FHWA-PD-96–010, DOTVNTSC-FHWA-98–2. http://www.fhwa.dot.gov/environment/noise/tnm/ver10tm/tnm10techmanual.pdf.

USDOT, 2002. Validation of FHWA's Traffic Noise Model (TNM): Phase 1. Federal Highway Administration, U.S. Department of Transportation, DOT-VNTSC-FHWA-02–01. http://www.fhwa.dot.gov/environment/noise/traffic_noise_model/model_validation/phase_one/tnmph1va.pdf.

World Health Organization. Burden of disease from environmental noise: Quantification of healthy life years lost in Europe. World Health Organization. Regional Office for Europe; 2011.

Wu J, Grande G, Stafoggia M, et al. , 2022. Air pollution as a risk factor for Cognitive Impairment no Dementia (CIND) and its progression to dementia: A longitudinal study. Environ Int. 160, 107067. 10.1016/j.envint.2021.107067. [PubMed: 35032863]

Wurth R, Kioumourtzoglou MA, Tucker KL, Griffith J, Manjourides J, Suh H, 2018. Fine Particle Sources and Cognitive Function in An Older Puerto Rican Cohort in Greater Boston. Environ Epidemiol. 2 (3) 10.1097/EE9.0000000000000022.

Yost K, Perkins C, Cohen R, Morris C, Wright W, 2001. Socioeconomic status and breast cancer incidence in California for different race/ethnic groups. Cancer Causes Control. 12 (8), 703–711. 10.1023/a:1011240019516. [PubMed: 11562110]

Yu Y, Mayeda ER, Paul KC, et al. , 2020. Traffic-related Noise Exposure and Late-life Dementia and Cognitive Impairment in Mexican-Americans. Epidemiology 31 (6), 771–778. 10.1097/EDE.0000000000001249. [PubMed: 33555809]

Yu Y, Jerrett M, Paul KC, et al. , 2021. Ozone Exposure, Outdoor Physical Activity, and Incident Type 2 Diabetes in the SALSA Cohort of Older Mexican Americans. Environ Health Perspect. 129 (9), 97004. 10.1289/EHP8620. [PubMed: 34494856]

Yuchi W, Sbihi H, Davies H, Tamburic L, Brauer M, 2020. Road proximity, air pollution, noise, green space and neurologic disease incidence: a population-based cohort study. Environ Health. 19 (1), 8. 10.1186/s12940-020-0565-4. [PubMed: 31964412]

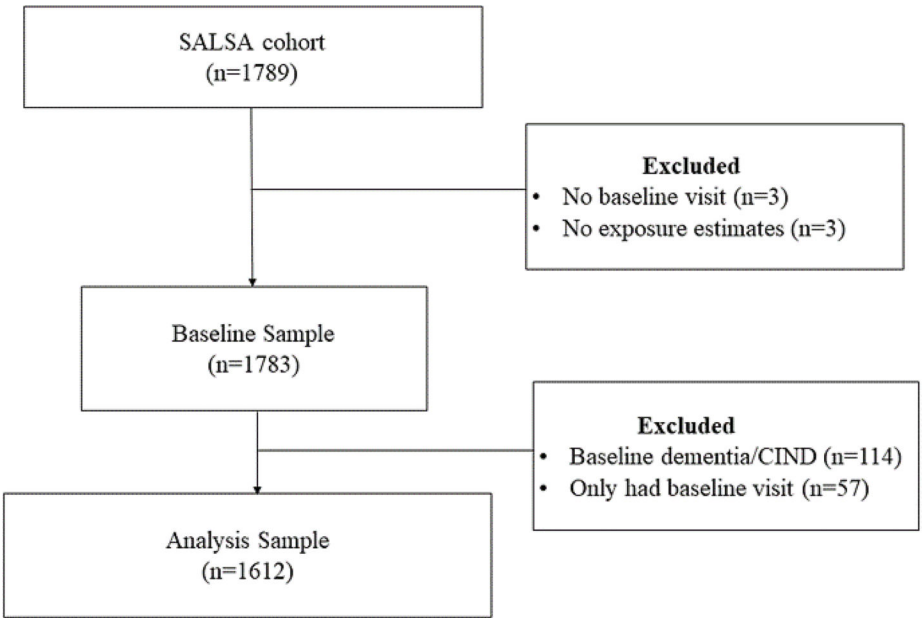
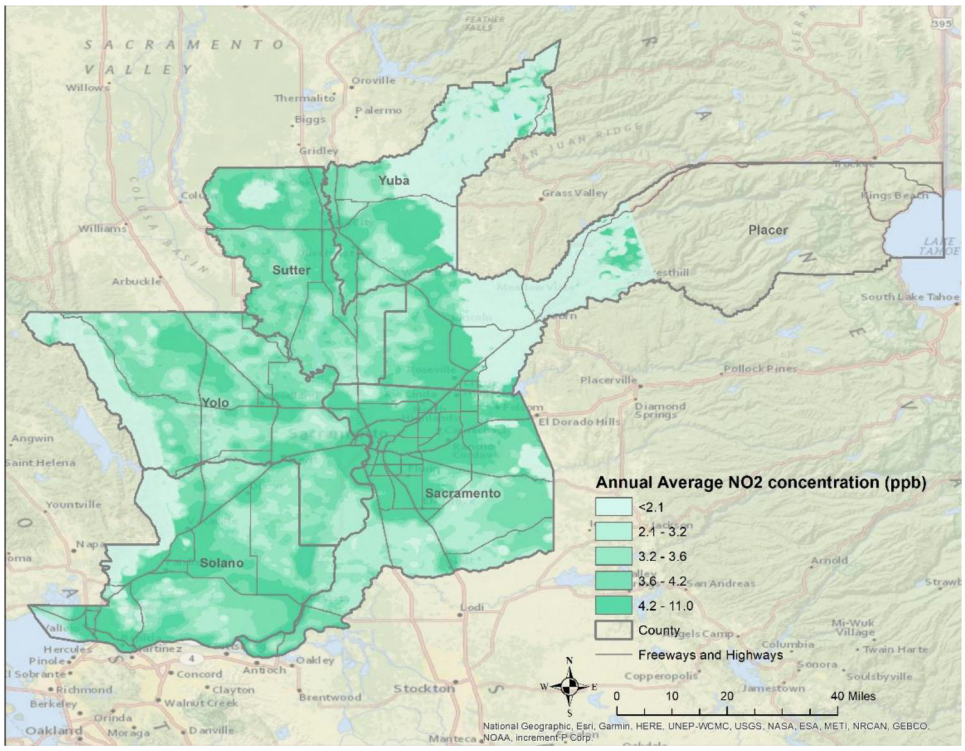


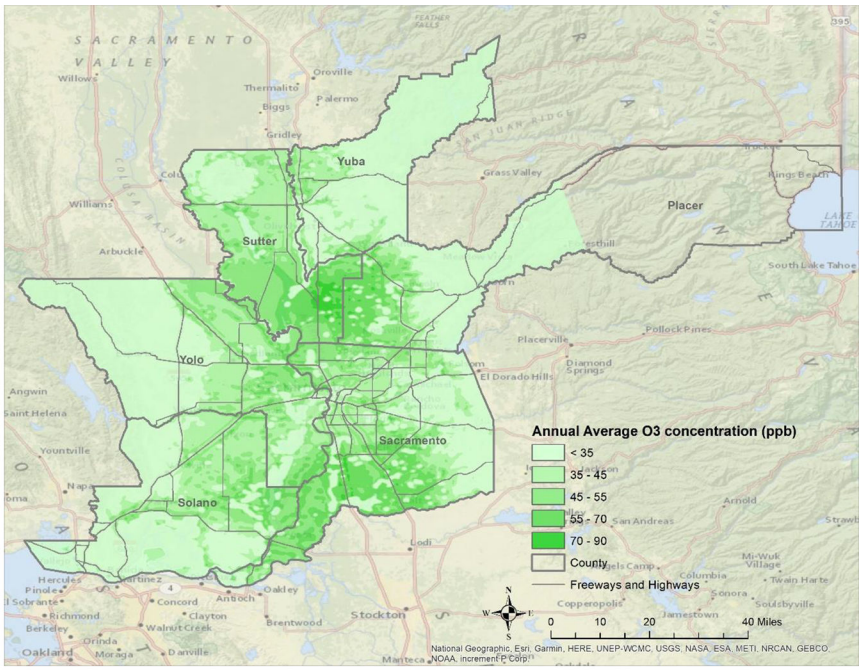
Fig. 1.

Flow chart of study population, Sacramento Area Latino Study on Aging (SALSA), 1998–2007. Note: CIND, cognitive impaired without dementia.

A.



B



C.

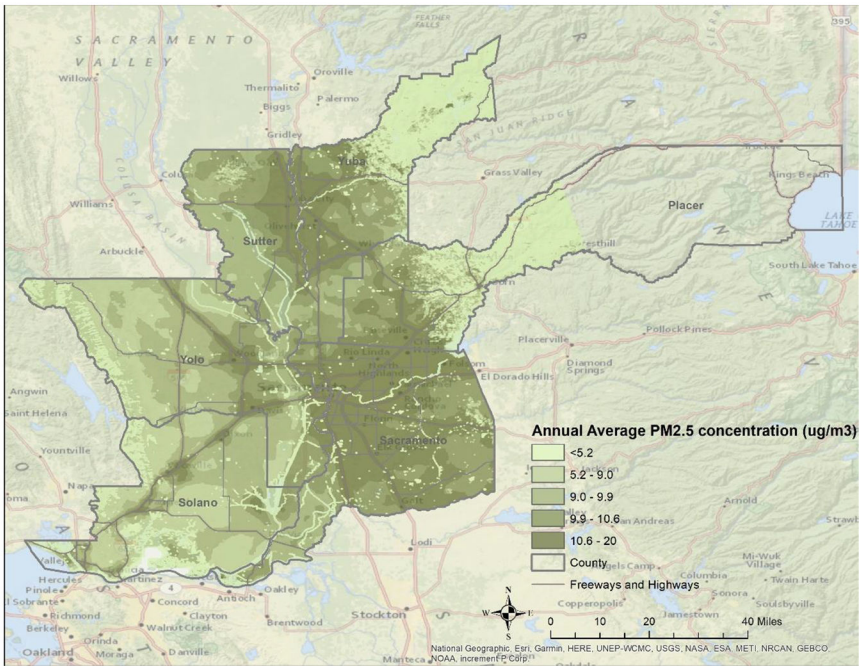


Fig. 2.

Estimated annual average NO_2, O_3 and $PM_{2.5}$ concentration surface in the Sacramento area, Sacramento Area Latino Study on Aging (SALSA, 1998–2007). (A) Estimated annual average NO_2 concentration surface in the Sacramento area in 2016 with a spatial resolution of 30 × 30 m. (B) Estimated annual average O_3 concentration surface in the Sacramento area in 2016 with a spatial resolution of 1 × 1 km. (C) Estimated annual average $PM_{2.5}$ concentration surface in the Sacramento area in 2004 with a spatial resolution of 30 × 30 m. The base map was developed by National Geographic and ESRI and reflects the distinctive

National Geographic cartographic style in a multiscale reference map of the world. The map was authored using data from a variety of leading data providers, including Garmin, HERE Technologies, the United Nations Environment Programme's World Conservation Monitoring Centre, the National Aeronautics and Space Administration, the European Space Agency, and the U.S. Geological Survey, and others. County boundary data was taken from the California Open Data Portal (https://data.ca.gov/dataset/ca-geographic-boundaries).

Table 1

Summary of characteristics of the participants at baseline used for incidence analyses, Sacramento Area Latino Study of Aging, 1998–2007.

Characteristics, Mean ± SD / N (%)	Total (n = 1612)	*DEMENTIA/CIND*			*DEMENTIA*		
		Event (n = 159)	Non-event (n = 1453)	*P-value*	Event (n = 104)	Non-event (n = 1508)	*P-value*
Baseline Age (Years, mean ± SD)	70.2 (±6.8)	75.3 (±7.8)	69.7 (±6.5)	< 0.01	76.5 (±7.6)	69.8 (±6.5)	<0.01
Male	680 (42.2)	58 (36.5)	622 (42.8)	0.12	36 (34.6)	644 (42.7)	0.11
Years of Education (Years, mean ± SD)	7.4 (±5.3)	5.8 (±5.2)	7.6 (±5.3)	<0.01	5.6 (±4.4)	7.5 (±5.4)	<0.01
Sacramento County Residence	1255 (77.9)	118 (74.2)	1137 (78.3)	0.24	80 (76.9)	1175 (77.9)	0.81
Urban Residence	1400 (86.9)	136 (85.5)	1264 (87.0)	0.61	90 (86.5)	1310 (86.9)	0.92
Occupation held during most of the lifetime				<0.01			<0.01
Non-Manual	346 (21.8)	14 (9.0)	332 (23.2)		8 (7.9)	338 (22.7)	
Manual	960 (60.5)	104 (66.7)	856 (59.8)		69 (68.3)	891 (59.9)	
Other (Housewives and Unemployed)	282 (17.8)	38 (24.4)	244 (17.0)		24 (23.8)	258 (17.4)	
Marriage status				<0.01			<0.01
Single/Never married	47 (2.9)	6 (3.8)	41 (2.8)		3 (2.9)	44 (2.9)	
Married	946 (59.0)	82 (51.9)	864 (59.8)		54 (52.4)	892 (59.4)	
Widowed	379 (23.6)	58 (36.7)	321 (22.2)		41 (39.8)	338 (22.5)	
Divorced	171 (10.7)	9 (0.6)	162 (11.2)		4 (3.9)	167 (11.1)	
Separated	47 (2.9)	1 (0.6)	46 (3.2)		1 (1.0)	46 (3.1)	
Living with someone as a spouse	14 (0.9)	2 (1.3)	12 (0.8)		0 (0.0)	14 (0.9)	
Household Income ($/month):				0.06			0.06
Less than 1000	691 (43.7)	81 (51.6)	610 (42.8)		55 (52.9)	636 (43.0)	
1000 TO 1499	321 (20.3)	35 (22.3)	286 (20.1)		25 (24.0)	296 (20.0)	
1500 TO 1999	184 (11.6)	17 (10.8)	167 (11.7)		10 (9.6)	174 (11.8)	
2000 TO 2499	154 (9.7)	9 (5.7)	145 (10.2)		6 (5.8)	148 (10.0)	
2500 or more	233 (14.7)	15 (9.6)	218 (15.3)		8 (7.7)	225 (15.2)	
Neighborhood Socio-Economic Status (NSES)				0.18			0.06
Low NSES = 1	544 (33.8)	64 (40.3)	480 (33.0)		46 (44.2)	498 (33.0)	
Low-Middle/Middle NSES = 2,3	912 (56.6)	80 (50.3)	832 (57.3)		49 (47.1)	863 (57.2)	
Middle-High/High NSES = 4,5	156 (9.7)	15 (9.4)	141 (9.7)		9 (8.7)	147 (9.8)	
Baseline Smoking Status				0.83			0.97

Characteristics, Mean ± SD / N (%)	Total (n = 1612)	*DEMENTIA/CIND*			*DEMENTIA*		
		Event (n = 159)	Non-event (n = 1453)	*P-value*	Event (n = 104)	Non-event (n = 1508)	*P-value*
Never/Non-Smoker	735 (45.8)	75 (47.2)	660 (45.6)		47 (45.2)	688 (45.8)	
Former Smoker	681 (42.4)	64 (40.3)	617 (42.7)		44 (42.3)	637 (42.4)	
Current Smoker	189 (11.8)	20 (12.6)	169 (11.7)		13 (12.5)	176 (11.7)	
Baseline High Outdoor Physical Activity	341 (21.2)	27 (17.0)	314 (21.6)	0.17	15 (14.4)	326 (21.6)	0.08
Baseline ADL summary score (mean ± SD)	0.6 (±2.3)	1.9 (±4.0)	0.5 (±2.0)	<0.01	2.4 (±4.4)	0.5 (±2.1)	<0.01
NO_2 exposure at baseline (ppb, mean ± SD)	28.6 (±6.0)	29.2 (±5.6)	28.5 (±6.1)	0.19	28.5 (±6.0)	28.6 (±6.0)	0.84
$PM_{2.5}$ exposure at baseline ($\mu g/m^3$, mean ± SD)	12.8 (±1.4)	12.7 (±1.4)	12.8 (±1.4)	0.39	12.8 (±1.3)	12.8 (±1.4)	0.84
O_3 exposure at baseline (ppb, mean ± SD)	46.6 (±11.0)	45.6 (±10.2)	46.7 (±11.1)	0.26	45.9 (±8.8)	46.6 (±11.1)	0.50
24-hour noise at baseline (dB, mean ± SD)	68.5 (±8.9)	69.5 (±8.9)	68.3 (±8.9)	0.11	69.1 (±8.7)	68.5 (±8.9)	0.41

Note: SD, standard deviation; ADL, activities of daily living; NSES, neighborhood socioeconomic status; NO_2, nitrogen dioxide; $PM_{2.5}$, fine particulate matter (diameter small than 2.5 μm); O_3, ozone; ppb, parts per billion; dB, decibel.

Table 2

Effect estimates (and 95%CIs) from Cox models[a] for time-varying air pollution exposures on incident dementia or CIND.

Air pollutant	Exposure period (years)	IQR	Dementia/CIND	Dementia
			HR (95% CI)	*HR (95% CI)*
NO_2	1	6.99 ppb	1.22 (0.99, 1.51)	1.14 (0.86, 1.49)
	3	6.74 ppb	1.10 (0.86, 1.41)	0.99 (0.71, 1.34)
	5	6.45 ppb	1.13 (0.89, 1.44)	1.05 (0.77, 1.43)
$PM_{2.5}$	1	2.02 μg/m^3	1.08 (0.87, 1.34)	1.33 (1.00, 1.76)
	3	1.66 μg/m^3	1.06 (0.86, 1.30)	1.27 (0.97, 1.65)
	5	1.61 μg/m^3	1.06 (0.85, 1.32)	1.33 (1.00, 1.77)
O_3	1	10.56 ppb	1.03 (0.87, 1.23)	1.07 (0.86, 1.34)
	3	9.77 ppb	1.02 (0.86, 1.20)	1.05 (0.85, 1.30)
	5	10.04 ppb	1.01 (0.87, 1.16)	1.03 (0.86, 1.24)
24-hour noise	Baseline yearly average	11.6 dB	1.25 (1.01, 1.53)	1.19 (0.92, 1.53)
		<65 vs. ≥ 65 dB	1.39 (0.99, 1.96)	1.25 (0.82, 1.89)

Note: CIND, cognitive impairment without dementia; NO_2, nitrogen dioxide; $PM_{2.5}$, fine particulate matter with diameter < 2.5 μm; O_3, ozone; ppb, parts per billion; HR, hazard ratio; 95% CI, 95% confidence interval.

[a]Model was adjusted for age, sex, education, longest held occupation, NSES, living county, outdoor physical activity, smoking status, household income at baseline.

Table 3

Effect estimates (and 95%CIs) from Cox models[a] for time-varying air pollution exposures on incident dementia or CIND, stratified by 24-hour noise exposure level (< 65 vs. ≥ 65 dB).

Air pollutant	Exposure period (year)		Dementia/CIND			Dementia		
		IQR	*24-hour noise < 65 dB*	*24-hour noise ≥ 65 dB*	*P for interaction*	*24-hour noise < 65 dB*	*24-hour noise ≥ 65 dB*	*p for interaction*
			HR (95% CI)	*HR (95% CI)*		*HR (95% CI)*	*HR (95% CI)*	
NO_2	1	6.99 ppb	0.92 (0.65, 1.31)	1.31 (1.03, 1.68)	0.09	1.01 (0.65, 1.58)	1.15 (0.83, 1.60)	0.62
	3	6.74 ppb	0.73 (0.49, 1.09)	1.24 (0.93, 1.64)	0.02	0.74 (0.45, 1.22)	1.06 (0.72, 1.55)	0.24
	5	6.45 ppb	0.76 (0.52, 1.11)	1.28 (0.97, 1.69)	0.02	0.80 (0.50, 1.29)	1.15 (0.79, 1.67)	0.21
$PM_{2.5}$	1	2.02 ug/m3	0.99 (0.72, 1.36)	1.06 (0.82, 1.37)	0.73	1.07 (0.73, 1.59)	1.37 (0.98, 1.92)	0.32
	3	1.66 ug/m3	0.92 (0.71, 1.20)	1.10 (0.86, 1.41)	0.31	0.94 (0.68, 1.29)	1.47 (1.07, 2.03)	0.04
	5	1.61 ug/m3	0.94 (0.71, 1.23)	1.10 (0.84, 1.44)	0.38	0.96 (0.69, 1.33)	1.57 (1.11, 2.21)	0.03
O_3	1	10.56 ppb	1.07 (0.81, 1.41)	1.02 (0.83, 1.25)	0.78	0.99 (0.69, 1.43)	1.13 (0.86, 1.47)	0.57
	3	9.77 ppb	1.04 (0.79, 1.36)	1.01 (0.83, 1.22)	0.86	0.91 (0.64, 1.31)	1.13 (0.88, 1.46)	0.31
	5	10.04 ppb	1.02 (0.83, 1.26)	1.00 (0.83, 1.21)	0.92	0.93 (0.69, 1.25)	1.13 (0.89, 1.43)	0.30

Note: CIND, cognitive impairment without dementia; NO_2, nitrogen dioxide; $PM_{2.5}$, fine particulate matter with diameter < 2.5 μm; O_3, ozone; ppb, parts per billion; HR, hazard ratio; 95% CI, 95% confidence interval.

[a]Model was adjusted for age, sex, education, longest held occupation, NSES, county of residence, outdoor physical activity, smoking status, household income at baseline.