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Environmental Research 279 (2025) 121830

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

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A R T I C L E I N F O

Keywords:
Air pollution
Road traffic noise
Neighborhood socioeconomic position
Correlated exposure
Self organized maps
Principal component analysis
Neighborhood socioeconomic factors

A B S T R A C T

Background: Modifiable physical and social environments are believed to influence cognitive health in older age.
Objectives: To employ cutting-edge methods to analyze the impact of correlated environmental and socioeconomic neighborhood factors on cognitive function in German older participants.
Methods: In the German Heinz Nixdorf Recall cohort study, participants underwent neuropsychological testing at the first follow-up examination (2006–2008) to derive a global cognitive score (GCS). Long-term exposure to air pollution was estimated by the land-use regression and chemistry transport models. Road traffic noise was assessed as outdoor weighted 24h and nighttime means. Seven neighborhood-level socioeconomic position (nSEP) characteristics were linked from administrative data. The joint effects of exposure combinations on GCS were estimated using two dimensionality reduction techniques: principal component (PC) analysis (PCA) and self-organizing maps (SOM).
Results: Overall, 3748 individuals were included (median age 65 years; 50.7 % female). In single-exposure linear regression analysis, higher particle matter with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) and nitrogen oxides exposure, higher proportion of welfare recipients, and lower living area per resident were negatively associated with GCS. In the PCA, the first principal component (PC), the direction of maximum variance, was positively correlated with all disadvantageous nSEP factors and higher concentrations of all environmental exposures except ozone. This PC was associated with lower GCS. SOM revealed associations with lower GCS for 3 of 6 exposure clusters. These clusters were characterized by low nSEP (Cluster 1), high environmental exposure (Cluster 4) and high concentration of accumulation mode particle number concentration (Cluster 5).
Discussion: We identified associations between distinct combinations of intercorrelated air pollution, road traffic noise, and nSEP disadvantages with poorer cognitive function, using two different dimensionality reduction methods. Our findings highlight the importance of considering combined environmental and social exposures to systematically assess the potential benefits of multimodal urban interventions aimed at mitigating these risk factors.

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https://doi.org/10.1016/j.envres.2025.121830
Received 14 January 2025; Received in revised form 25 April 2025; Accepted 10 May 2025
Available online 12 May 2025

Abbreviations

BMI = Body mass index
CI = Confidence interval
CMT = Chemistry transport model
DAG = Directed acyclic graph
dB(A) = A-weighted decibels
ESCAPE = European Study of Cohorts for Air Pollution Effects
EURAD = EURopean Air pollution Dispersion
GCS = Global cognitive score
HNR = Heinz Nixdorf Recall Study
IQR = Interquartile range
ISCED-9 = International Standard Classification of Education, 9th Edition
L_{den} = Day-evening-night noise/outdoor 24h traffic noise
L_{night} = Nighttime noise/outdoor nighttime traffic noise
LUR = Land-use regression model
NO_2 = Nitrogen dioxide; NO_x = Nitrogen oxides
O_3 = Ozone
PC = Principal component; PC1, PC2, PC3 etc. = first, second, third etc. principal components
PCA = Principal component analysis
PM = Particle matter; PM_{10} = Particle matter with aerodynamic diameter ≤10 μm; $PM_{2.5}$ = Particle matter with aerodynamic diameter ≤2.5 μm; $PM_{2.5abs}$ = $PM_{2.5}$ absorbance
PN_{acc} = Accumulation mode particle number concentration
SEP = Socioeconomic position; iSEP = Individual SEP; nSEP = Neighborhood SEP
SOM = Self-organizing maps
T_0 = Baseline examination in the Heinz Nixdorf Recall study (2000–2003)
T_1 = First follow-up examination

1. Introduction

Genetic and lifestyle factors, as well as physical and social environments, are known to influence cognitive health in older age (Besser et al., 2017; Bloomberg et al., 2024; Song et al., 2024; Wimo et al., 2023; Wu et al., 2015). Cognitive impairment or dementia in older ages holds substantial societal importance by straining healthcare systems and leading to higher costs for families and societies (Jönsson, 2022; Nandi et al., 2024). Addressing its risk factors, many of which are modifiable, is crucial for public health. A promising approach to prevent impaired cognitive health on the population level is a joint improvement of environmental and socioeconomic conditions. Both domains are systematically related to each other: adverse characteristics commonly co-occur, are highly correlated, partly mediated one another, and may have synergistic effects (Abo Hamza et al., 2024). However, the current interventions for protecting cognitive health tend to focus on individual risk factors, neglecting a more comprehensive, system-wide approach (Castellani et al., 2022).

Regarding environmental factors, long-term air pollution and noise exposure are known to be key risk factors for neurocognitive health issues. Air pollution, for instance, is linked to a higher risk of cognitive decline, cognitive impairment, dementia, and stroke (Chen et al., 2020; Delgado-Saborit et al., 2021; Health Effects Institute, 2022; Zare Sakhvidi et al., 2022). Systematic reviews emphasize the association between greater exposure to specific pollutants (particularly particle matters (PM) with aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) and nitrogen oxides (NO_x)) and an increased risk of dementia (Peters et al., 2019; Weuve et al., 2021a; Wilker et al., 2023). Regarding chronic noise, a recent systematic review provided high quality evidence for an association between ambient environmental noise (e.g., road traffic noise, aircraft noise etc.) and cognitive impairment in middle aged-to-older adults (Thompson et al., 2022). Because air pollution and noise share many sources, there is potential for noise to confound studies of air pollution and neurocognitive function, and vice versa, or for complex interactions to occur (Thompson et al., 2023).

Socioeconomic position (SEP) can be measured individually and at an "area level", representing the social position and economic prosperity of the surrounding neighborhood or community. Typically, neighborhood SEP (nSEP) encompasses indicators such as mean income, education, and employment, wealth or measures of deprivation. It has been demonstrated that low nSEP, independently of environmental factors or individual SEP (iSEP), is associated with lower cognitive function in older adults (Besser et al., 2017; Zhao et al., 2021). Moreover, modest evidence was also found for associations between neighborhood demographics (e.g., population density), urban design (e.g., intersection density, presence of sidewalks), and social destination accessibility (e.g., distance to nearest store) and cognition (Besser et al., 2017).

At the same time, nSEP, air pollution and noise are highly correlated and may jointly contribute to health outcome disparities (Bowe et al., 2019). Lower nSEP neighborhoods are more likely to have higher levels of air pollution and noise (Dreger et al., 2019; Hajat et al., 2015) that may be explained by lower housing prices in areas near industrial plants, sites emitting hazardous waste, construction areas, transport corridors or higher traffic density. In Europe, this relationship is not consistent: nonlinear neighborhood associations between air pollution concentrations and deprivation are observed, and both direction and magnitude of associations vary by study area, country and pollutant (Fecht et al., 2015). Furthermore, in some Western city agglomerations, such as Paris (Padilla et al., 2014) or Madrid (Iungman et al., 2021), the least deprived neighborhoods are exposed to higher mean concentrations of NO_2 and noise. In such situations, failure to consider neighborhood-level confounding may result in severely biased associations (Chaix et al., 2010).

Environmental and socioeconomic contextual, i.e. defined at the ecological (or neighborhood) level, factors may interact with each other, with a possible effect modification. For instance, low nSEP areas and neighborhoods with higher prevalence of social stressors, like as poverty and disorder, show significant associations of exposure to carbon monoxide, NO_x, and $PM_{2.5}$ with cognitive function, particularly among older adults (Li et al., 2022; Wang et al., 2020), as well as associations of exposure to noise with higher odds of Alzheimer's and poorer cognition (Weuve et al., 2021b); and these associations are weaker or even non-significant in wealthy neighborhoods. However, evidence on potential interaction between exposure to air pollution or noise and indicators of area-level social deprivation and their synergism or antagonism on neurocognitive outcomes is scarce (Christensen et al., 2022; Ilango et al., 2023). Moreover, testing their interdependent effects requires controlled experiments often unachievable in observational studies (Mauderly and Samet, 2009).

The lack of evidence could be a result of methodological challenges in performing respective investigations. In case of confounding, the high correlation of exposures may lead to multicollinearity that decreases the interpretability of regression coefficients by inflating standard errors and making the coefficients vary greatly from one sample to the next (Allen, 1997).

Using advanced environmental mixture methods (Hamra and Buckley, 2018), especially developed to investigate effects of highly correlated exposure variables, allows to examine the relationships between exposure to multiple environmental and neighborhood socioeconomic factors with health outcomes from different perspectives. Specifically, it enables the investigation of a mixture or a combination instead of individual components. Some of the methods use dimensionality reduction techniques to transform correlated exposures into a low-dimensional representation of a mixture as well as to discoverer patterns and relationships in the mixture (Astel et al., 2007). The different methods, each based on distinct principles, typically yield comparable but not identical results, which may be subject to varying interpretations (Choy et al., 2019; Das et al., 2016). Advanced approaches in environmental epidemiology often combine several techniques to provide more robust results in complex environmental systems. Recently, such an approach was used to quantify the complex relationship between air pollution and nSEP on cognitive decline in the USA, in a municipalities level analysis (Christensen et al., 2022); however, noise as an important co-exposure and independent hazardous factor was not included into this analysis. Furthermore, there were limitations to the generalizability of the results, particularly to Europe where social, geographic, and regulatory factors differ significantly.

Previously, we studied the association of air pollution and road traffic noise with cognitive function and cognitive decline, controlled by nSEP, in a German cohort of middle-aged to older adults. The analysis examined the effects of air pollution and traffic noise exposure both individually and in two-exposure models to assess potential interaction effects (Ogurtsova et al., 2023; Tzivian et al., 2016b, 2017). However, mixture effects of multipollutant combinations including nSEP-related factors were not assessed.

In this study, we aimed to investigate the joint association of air pollution, road traffic noise, and nSEP with cognitive function among the middle-aged to older adults in Heinz Nixdorf Recall cohort study. We analyzed environmental and socioeconomic factors of neighborhood as a mixture, and the association of this mixture with cognitive function to gain a broader understanding of the joint exposure patterns. We hypothesize an adverse joint association of exposure profiles that consists of higher air pollution, higher road traffic noise and lower nSEP, with cognition. We used two complementary dimensionality reduction methods to overcome the challenge of highly correlated multiple exposures: principal component (PC) analysis (PCA) (Christensen et al., 2023) and self-organizing maps (SOM) to find patterns of multipollutant combinations jointly affecting cognitive health (Amariglio et al., 2015; Pearce et al., 2014).

2. Methods

2.1. Data sources

We analyzed data from the first follow-up examination of the German prospective population-based Heinz Nixdorf Recall cohort study (HNR), located in three adjacent cities (Bochum, Essen, and Mulheim an der Ruhr) in the highly urbanized Ruhr Area. The study design was described elsewhere (Schmermund et al., 2002). At baseline (2000–2003), 4814 individuals 45–75 years old were enrolled (baseline response proportion: 55.8 %) (Stang et al., 2005). The first follow-up examination (T_1) was performed with a response rate of 90.2 % in 2006–2008 leading to enrolment of 4157 participants (reassessment rate: 86.4 %). The HNR study was approved by the ethics committee of the University Hospital Essen. All participants gave written informed consent.

This analysis was focused on mild cognitive changes. We therefore excluded participants (22 of 4,157, 0.05 %) with a physician's diagnosis of dementia or Alzheimer's disease, with intake of cholinesterase inhibitors (anatomic-therapeutic-chemical classification issued by the World Health Organization is N06DA) or other dementia medications (N06DX), or fulfilling the Diagnostic and Statistical Manual of Mental Disorders, 4th edition dementia diagnosis.

Several covariates were assessed in the study population for this analysis. Height and weight were measured per standard protocols. Alcohol intake was categorized into sex-specific quartiles. Smoking status included current, former (>1 year since quitting), or never-smoker. Cumulative smoking exposure (pack-years) was assessed for former and current smokers, accounting for non-smoking periods. Exposure to environmental tobacco smoke (Yes/No) was defined as regular passive exposure. Diet quality was evaluated using a nutrition pattern index created by incorporating consumption frequency of 13 food items (Winkler and Döring, 1998). This index ranging from 0 to 26, with 26 representing an ideal diet, was divided by tertile formation of the study population into three groups (<12, 12–14, >14) and classified as "Unfavorable Diet," "Normal Diet," and "Favorable Diet". Physical activity was determined by regular sport activities (Yes/No). All variables for analysis were collected at T_1, except for environmental tobacco smoke and cumulative smoking exposure, assessed at baseline (Ogurtsova et al., 2023).

2.2. Long-term environmental exposure assessment

Exposures were assessed for years 2006–2008, the first follow-up, and represented the long-term exposure to environmental factors.

The study area included about 600 km^2. Particular matter of varying aerodynamic diameter (PM_{10}: ≤10 μm, and $PM_{2.5}$), $PM_{2.5}$ absorbance ($PM_{2.5abs}$), and nitrogen oxide concentrations (NO_x and NO_2) were estimated using the land-use regression model (LUR) of European Study of Cohorts for Air Pollution Effects (ESCAPE) (Beelen et al., 2013; Eeftens et al., 2012). For building the ESCAPE-LUR model, we used annual averages of the measured pollutant concentrations from background and traffic-specific monitoring sites as well as predictor variables from Europe-wide and local Geographic Information System databases. The model was validated for each pollutant using the goodness of fit criteria and in the leave-one-out cross-validation (Hennig et al., 2016). We estimated the 2006–2008 average concentrations for the participants' residential addresses at T_1 (Hennig et al., 2016).

Accumulation mode particle number concentration (PN_{acc}, mean aerodynamic diameter of 0.07 μm, 67 % of particles ranged between 0.035 and 0.14 μm), a measure of quasi-ultrafine particles, and ozone (O_3) were estimated for each participant using the validated, spatio-temporal, three-dimensional EURopean Air pollution Dispersion (EURAD) chemistry transport model (CTM) (Memmesheimer et al., 2004). PN_{acc} estimates from the EURAD-CTM have been validated against measurements obtained between January 2011 and December 2014 (Birmili et al., 2016). Participants were assigned the 2006–2008 average PN_{acc} and O_3 concentrations from the 1-km^2 grid cell in which they resided at T_1 (Nonnemacher et al., 2014).

Long-term outdoor road traffic noise exposure in A-weighted decibels (dB(A)) was modelled in 2006 according to the 2002/49/EC Directive (EC 2002): we obtained averaged weighted day-evening-night noise (L_{den}; 24 h) and average levels of nighttime noise (L_{night}; 22:00–06:00 h) (European Parliament and the Council, 2002). The road traffic noise was modelled with consideration of the following determinants: small-scale topography of the area, dimensions of buildings, noise barriers, street axis, vehicle type specific traffic density, speed limit, and type of street surface. Models were performed on behalf of the cities for road traffic noise, industrial noise, and aircraft noise, and were supplied as source-specific facade values from local city administrations (Ohlwein et al., 2019). We assigned the most exposed facade values estimated at the residential addresses to each participant. As an indicator for traffic-related exposure, we used the total traffic load at major roads (roads with >5000 vehicles/day) in a 100-m buffer (vehicles × meters/day) that was obtained from local traffic intensity data in 2006–2008.

2.3. Neighborhood socioeconomic position (nSEP)

The selection of neighborhood SEP characteristics was based on data availability and the clarity of their direction and magnitude in terms of interpreting social deprivation.

Neighborhood SEP data representing administrative units was retrieved from the municipal statistical departments. The three cities included in the study consist of 106 rural and urban districts, the lowest level of official territorial division in Germany, with a median size of 11,263 inhabitants (IQR 7875–16,022). These municipal districts were used as proxies for neighborhoods. Socioeconomic characteristics of each neighborhood were obtained for different years at or shortly after study baseline examinations of the HNR study. The characteristics reflecting nSEP were unemployment rate (%, 2001), proportion of welfare recipients (%, 2001), mean per-capita income (Euro, 2004), motor vehicles per resident (%, 2001), living area per resident (m^2, 2001), proportion of inhabitants with migration background (%, 2001), and residential (in-)stability (%, 2000) in the area of residence. Unemployment rate was calculated by dividing the number of unemployed by the economically active population (employed and unemployed) below retirement age in the neighborhood. Proportion of welfare recipients per resident was calculated as the number of residents receiving financial support from the welfare authorities of the city or community divided by the total number of residents. Proportion of inhabitants with migration background was calculated as the number of residents without German citizenship divided by all residents in the area. Residential (in-)stability was calculated as the sum of people that moved in the area and people moved out of the area and divided by the number of residents. Neighborhood information, representing municipal districts and thus serving as contextual data, was assigned to the participants by address linkage. Per-capita income, percent of motor vehicles per resident, and living area per resident were multiplied by -1 (reverse-coded), meaning that an increasing value indicates lower nSEP. The overview of all exposure factors was given in Supplementary Table 1.

2.4. *Cognitive assessment*

Cognitive function was assessed during the first follow-up examination in 2006–2008, and represented the result of long-term slow changes during the previous years.

The assessment of cognitive function has been previously described in detail (Dlugaj et al., 2010; Wege et al., 2011). Briefly, it consisted of established neuropsychological tests to measure verbal fluency (semantic category "animals", number of words within 1 min), problem solving/speed of processing (Labyrinth Test, time in seconds needed to complete the task), immediate and delayed verbal memory (Verbal Memory Test, eight-word list, performance measured as a number of words recalled immediately and at the end of the interview), and abstraction/visual-spatial organization (Clock-Drawing Test, performance was rated from 1 "perfect clock" to 6 "poor performance"). The raw data for each subtest were z-transformed (mean = 0, standard deviation = 1) according to three age groups (50–59, 60–69, and 70–80 years old) and within every age group according to three education groups ($\leq$10, 11–13, and $\geq$14 years of formal education). Technically, we calculated the relative deviations from the mean within each subgroup to represent how much an individual value deviated from the expected value. Before transformation, scores of Labyrinth and Clock-Drawing tests were reverse-coded, so the higher score refers to better performance. The global cognitive score (GCS) was calculated additively using all five age- and education-specific z-scores of individual cognitive subtests. The GCS score was used as a primary outcome in the analysis.

2.5. *Statistical analysis*

The analysis was based on cross-sectional examinations. Only observations with complete data were analyzed. The list of potential covariates was selected based on knowledge from previous studies (Tzivian et al., 2017). Confounder adjustment was based on a directed acyclic graph (DAG) (Greenland et al., 1999) (Supplementary Fig. 1), complemented with a suggested minimal sufficient adjustment sets and covariate extensions. Correlations between continuous exposures were checked using the Spearman correlation test.

We adjusted the models for individual characteristics (age, sex, educational level as an indicator of iSEP), physiological factors and lifestyle factors (body mass index (BMI), smoking habits, alcohol consumption, physical activity, and diet).

2.5.1. *Individual exposure associations*

We constructed multivariate linear regression models for each air pollutant, road traffic noise, and nSEP characteristic to reveal their associations with GCS.

Additionally, to account for other types of exposures, we derived the PCs of the co-exposure mixtures using PCA (Jolliffe, 2002). In the analysis of individual exposure associations, this method was used to control for confounding, reduce overfitting of a model and eliminate multicollinearity of multi-component and highly mutual-correlated mixtures. In adjusting models for associations between air pollution and GCS, we considered the best set of PCs based on an exposure combination involving nSEP and road traffic noise. The best set of PCs was taken by the variable selection in a linear regression with the help of F-test (Hill et al., 2007). Similarly, for road traffic noise associations, adjustments, in addition to personal and lifestyle related covariates, were made for the best set of PCs of air pollution and nSEP, and for nSEP associations, adjustments considered the best set of PCs based on air pollution and road traffic noise. The loading scores of PCs are given in Supplementary Table 3. The best sets of PCs, to adjust each exposure type in the individual exposure analysis, and the variance they explained are given in Supplementary Table 4.

2.5.2. *Joint exposure associations*

To model joint effects of air pollution and road traffic noise exposures as well as nSEP, two multiple exposure mixture modelling techniques were used.

First, we used a PCA, a linear unsupervised dimensionality reduction technique that transforms correlated variables into uncorrelated PCs where each component accounts for a certain percentage of the total variance in the data. Data points are projected then onto the new coordinate system defined by the principal components. The dimension of the data is reduced by switching from multiple exposures to a few principal components (Abdi and Williams, 2010). We applied a PCA to the full mixture of exposures (air pollutants, road traffic noise, and nSEP characteristics) and subsequently regressed the leading PCs on the GCS. We constrained the selection of PCs to only those accounting for at least 10 % variance within the mixture. Crude and full linear regression models were estimated. The crude models contained only selected PCs as independent variables. The full models were additionally adjusted for personal and lifestyle related covariates.

Second, we used SOM, a special type of neural network belonging to unsupervised dimensionality reduction algorithms. It is a classification method, creating a low dimensional projection of a higher dimensional data set by grouping observations with similar exposure profiles. SOM defines clusters of profiles that are homogenous within clusters and heterogeneous between clusters. These clusters can be visualized as a two-dimensional "map" such that profiles in proximal clusters have more similar values than profiles in distal clusters (Kohonen, 2013). In contrast to PCA, SOM can capture non-linear relationships in the data. We used the full mixture of exposures (air pollution, road traffic noise and nSEP) for clustering. First, we identified the clusters with specific exposure profiles using the SOM algorithm. The number of clusters was determined by identifying group structure using within cluster and between cluster sum of squares statistics, as well as visual inspection of resulting exposure profiles (Kohonen, 2001; Vesanto and Alhoniemi, 2000). The cluster determination procedure is explained in the Supplementary Materials. Each participant belonged to one of the clusters. Then, we analyzed whether belonging to a cluster was associated with GCS. In this step, crude and fully adjusted linear regression models were built using the “least disadvantageous” profile (the lowest level of air pollution concentrations and road traffic noise, and the advantageous nSEP) as the reference category. When there was no clear choice for the reference cluster, a sensitivity analysis was conducted to assess the robustness of the results.

The associations were estimated per interquartile range (IQR) increase for air pollutants, for per-capita income, for living area per resident, for residential (in-)stability, and per 10 dB increase for road traffic noise. The unemployment rate, welfare recipients per resident, percent of motor vehicles per resident, and percent of persons with migrational background per resident were estimated per 10 % increase. The associations were presented alongside 95 % confidence intervals.

Statistical software R (version 4.2.2) was used for the analysis and processing of all data. The following key packages were used: “sandwich” and “sommix” available at https://github.com/johnlpearce/sommix.

3. Results

After removing participants with diagnosis of dementia and with missing covariates, 3748 of 4157 (90.2 %) individuals participating in the first follow-up examination were included in the analysis. The flow diagram of the sample selection is shown in Supplementary Fig. 2. Median age was 65 years (range 50–80 years), 1902 (50.7 %) participants were female, 362 (9.7 %) had equal to or less than 10 years and 1275 (34.0 %) had equal to or more than 14 years of education (Table 1). The mean BMI was 28.3 kg/m^2, and 650 (17.3 %) participants were current smokers (Table 1). Supplementary Table 2 compared individuals included and excluded from the analysis. Included individuals were more likely to have higher education, smoke less during life, and exercise more.

The mean annual concentrations of PM_{10} (27.7 μg/m^3), $PM_{2.5}$ (18.4 μg/m^3) and NO_2 (30.1 μg/m^3) were higher than long-term concentration levels recommended by World Health Organization (15, 5, 10 μg/m^3 correspondingly) (World Health Organization and Organization, W.H., 2021) but lower than the current European Union standards (40, 25 and 40 μg/m^3 accordingly) (European Parliament and Council of the European Union, 2008) (Table 2).

The neighborhood characteristics varied substantially: the unemployment rate ranged between 4.5 % and 23.8 %, the highest per-capita income level was almost 4 times higher than the smallest one.

Table 1
Demographic and lifestyle characteristics of the participants included in the analysis at the first follow-up of the Heinz Nixdorf Recall Study, unless explicitly stated otherwise.

Individual Characteristics (N = 3748)	Mean (SD) n (%)[a]	Median (Min, Max)	IQR (Q1, Q3)
Age (years)	64.3 (7.66)	65.0 (50.0, 80.0)	12.0 (58.0, 70.0)
Sex (male)	1846 (49.3)		
Education by ISCED-9			
≤10 (years)	362 (9.7)		
11–13 Years	2111 (56.3)		
≥14 Years	1275 (34.0)		
BMI (kg/m^2)	28.3 (4.9)	27.7 (16.6, 62.6)	5.7 (25.0, 30.7)
Alcohol consumption (Quartiles, assessed by sex)			
No alcohol	1108 (29.6)		
1st Quartile	717 (19.1)		
2nd Quartile	659 (17.6)		
3rd Quartile	599 (16.0)		
4th Quartile	665 (17.7)		
Smoking status			
Never smoker	1596 (42.6)		
Ex-smoker	1502 (40.1)		
Current smoker	650 (17.3)		
Environmental tobacco smoke, all sources			
No	2811 (75.0)		
Yes	937 (25.0)		
Cumulative Smoking, at T_0 (Packs/year)	15.6 (24.4)	3.9 (0, 400)	24.2 (0, 24.2)
Nutrition Pattern Index			
Unfavorable consumption frequency	1307 (34.9)		
Normal consumption frequency	1317 (35.1)		
Favorable consumption frequency	1124 (30.0)		
Physical inactivity			
No Sports	1605 (42.8)		
Sports	2143 (57.2)		

Abbreviations: BMI, body mass index; ISCED-9, International Standard Classification of Education, 9th Edition; T_0, baseline examination in the Heinz Nixdorf Recall study (2000–2003); SD, standard deviation; IQR, interquartile range; Q1, the value below which 25 % of the distribution lies; Q3, the value below which 75 % of the distribution lies.

[a] mean for continuous variables, % for categorical variables.

Table 2
Description of long-term air pollution, road traffic noise exposure levels and neighborhood socioeconomic factors at residential addresses of the participants included in the analysis at the first follow-up of the Heinz Nixdorf Recall Study.

Exposure factors (N = 3748)	Mean (SD) n (%)[a]	Median (Min, Max)	IQR (Q1, Q3)
Environmental			
PM_{10} (μg/m^3)	27.7 (1.8)	27.4 (23.9, 34.7)	2.1 (26.5, 28.6)
$PM_{2.5}$ (μg/m^3)	18.4 (1.1)	18.3 (16.0, 21.4)	1.4 (17.6, 19.1)
$PM_{2.5abs}$ (0.0001/m)	1.6 (0.3)	1.5 (1.0, 3.4)	0.3 (1.4, 1.7)
NO_2 (μg/m^3)	30.1 (4.8)	29.4 (19.8, 62.4)	6.1 (26.8, 32.9)
NO_x (μg/m^3)	50.4 (11.6)	49.1 (24.3, 127.0)	15.7 (42.0, 57.6)
O_3 (μg/m^3)	37.0 (1.5)	37.1 (32.5, 40.1)	2.1 (36.1, 38.2)
PN_{acc} (1M/m^3)	3230 (363)	3210 (2450, 4710)	513 (2960, 3480)
L_{den} (dB(A))	53.8 (9.2)	52.1 (25.9, 84.6)	14.2 (46.7, 60.9)
L_{night} (dB(A))	44.9 (9.0)	43.5 (16.8, 76.3)	13.6 (38.1, 51.7)
L_{den} > 55 dB(A)	1103 (29.4 %)		
L_{night} > 50 dB(A)	1496 (39.9 %)		
Total traffic load (100m) (10^6 vehicle[a]meter/day)	1.0 (2.2)	0.0 (0.0, 26.8)	1.4 (0.0, 1.4)
Socioeconomic			
Unemployment rate, 2001 (%)	12.4 (3.4)	12.0 (4.5, 23.8)	4.3 (10.0, 14.3)
Welfare recipients per resident, 2001 (%)	4.5 (2.6)	4.4 (0.2, 13.5)	3.3 (2.7, 6.0)
Per-capita income, 2004 (Euro)	25400 (8190)	22700 (13400, 49200)	11900 (18600, 30500)
Percent of motor vehicles per resident, 2001 (%)	55.1 (17.9)	55.6 (21.8, 177)	15.6 (46.5, 62.1)
Living area per resident, 2001 (m^2)	39.0 (4.6)	38.2 (30.5, 69.0)	6.6 (35.6, 42.2)
Percent of persons with migrational background per resident, 2001 (%)	7.9 (5.0)	6.7 (1.2, 38.0)	5.2 (4.4, 9.6)
Residential (in-)stability, 2000 (%)	176 (46.3)	168 (102, 530)	49.4 (144, 193)

Abbreviations: dB(A), A-weighted decibels; L_{night}, outdoor nighttime traffic noise; L_{den}, outdoor 24h traffic noise; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; O_3, ozone; PM_{10}, particulate matter with diameter ≤10 μm; $PM_{2.5}$, particulate matter with diameter ≤2.5 μm; $PM_{2.5abs}$, $PM_{2.5}$ absorbance; PN_{acc}, accumulation mode particle number concentration; SD, standard deviation; IQR, interquartile range; Q1, the value below which 25 % of the distribution lies; Q3, the value below which 75 % of the distribution lies.

[a] mean for continuous variables, % for categorical variables.

Road traffic noise also showed relatively high levels and a wide range of values: the day-evening-night average (L_{den}) was 53.8 dB and the night average (L_{night}) was 44.9 dB, slightly below the European standards of 55 dB and 50 dB respectively. The maximum values reached 84.6 for L_{den} and 76.3 for L_{night}.

Air pollutants (PM_{10}, $PM_{2.5}$, NO_x, NO_2, $PM_{2.5abs}$, PN_{acc}), road traffic noise (L_{night}, L_{den}), and nSEP characteristics were positively correlated with one another within their groups, except for O_3, which had a negative correlation with other air pollutants (Fig. 1 and Supplementary Table 5). Furthermore, O_3 was negatively correlated with road traffic noise and mostly all nSEP characteristics except per-capita income (reverse-coded) and living area per resident.

The performances for the different cognitive tests were not or moderately correlated (Supplementary Tables 6 and 7).

3.1. Individual exposure associations

Air pollution estimates were calculated per IQR increase of 2.1 μg/m^3 for PM_{10}, of 1.4 μg/m^3 for $PM_{2.5}$, of 0.35 × 10−5/m for $PM_{2.5abs}$, of 513 1M/m^3 for PN_{acc}, of 6.1 μg/m^3 for NO_2, of 15.7 μg/m^3 for NO_x. Income per capita, living area per resident, and residential (in-)stability estimates were calculated per IQR increase of 11,900 Euro, of 6.6 m^2, and 49.4 % accordingly.

Higher exposure to $PM_{2.5}$ and NO_x was negatively significantly associated with GCS in the fully adjusted models (−0.18, 95 % Confidence Interval (CI) [−0.35, −0.01], and −0.18, 95 %CI [−0.33, −0.03], accordingly) (Fig. 2). The associations with other air pollution and traffic noise were null in the adjusted models (Supplementary Table 8).

Regarding nSEP, negative associations of higher proportion of welfare recipients per resident (−0.45, 95 %CI [−0.89, −0.01]) and lower living area per resident (−0.22, 95 %CI [−0.39, −0.05]) with GCS were observed in the fully adjusted models. Overall, the effect size estimated in the crude and adjusted models were very similar (Supplementary Table 8).

3.2. Joint exposure associations

In the PCA analysis, we selected the first three PCs accounting together for 81.5 % of total variance within the mixture. PC1, explaining 39.2 % of variance, was positively correlated with all exposure components in the mixture, except for O_3, and was labelled as “High exposures” (Fig. 3B and Supplementary Table 9). PC2, explaining 16,0 % of

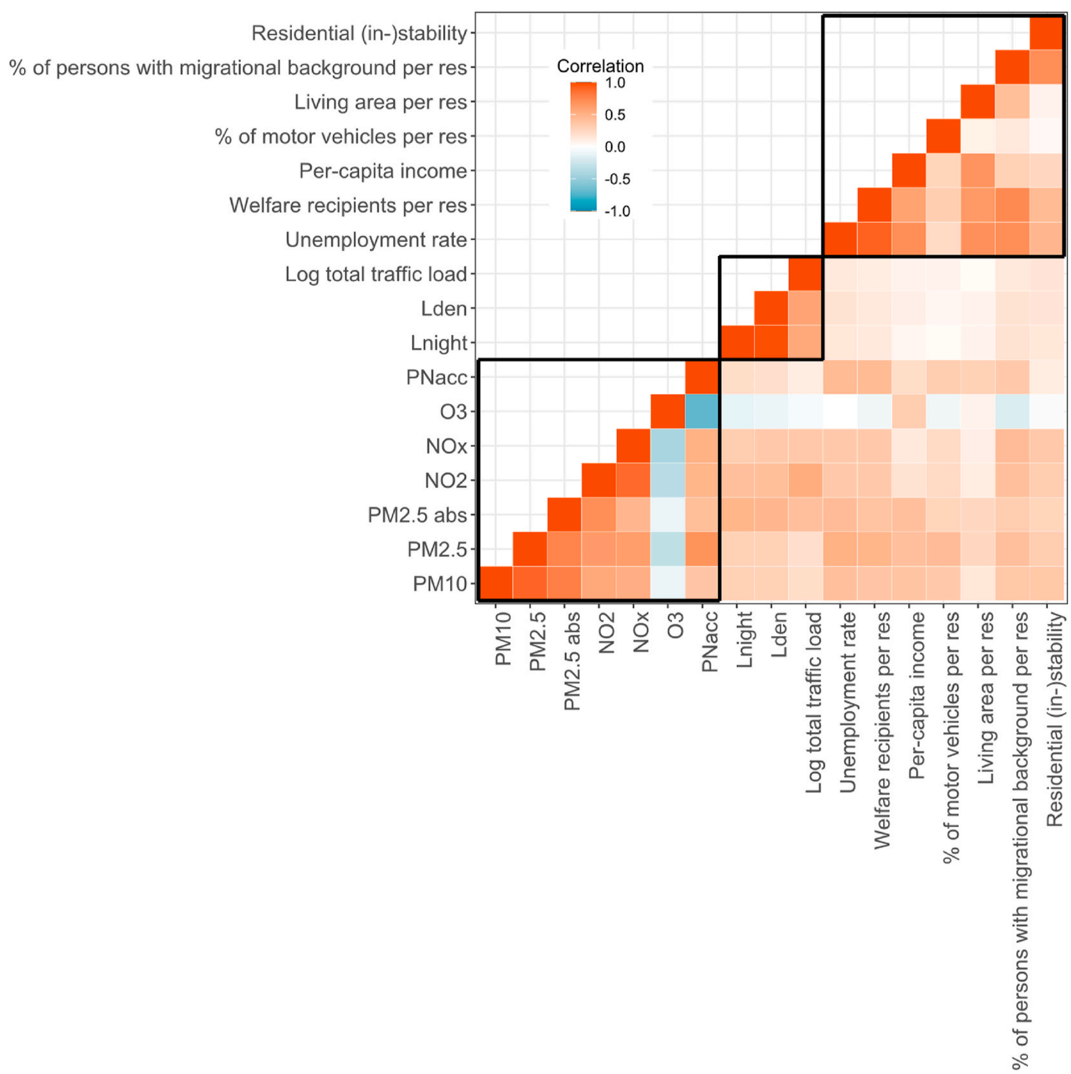

Fig. 1. Correlation matrix of all exposures (air pollution, noise and nSEP) at residential addresses of the participants included in the analysis at the first follow-up of the Heinz Nixdorf Recall Study. **Notes:** Per-capita income, percent of motor vehicles per resident, living area per resident are reverse-coded. The figure corresponds to Supplementary Table 5. **Abbreviations:** L_{night}, outdoor nighttime traffic noise; L_{den}, outdoor 24h traffic noise; nSEP, neighborhood socioeconomic position; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; O_3, ozone; PM_{10}, particulate matter with diameter ≤10 μm; $PM_{2.5}$, particulate matter with diameter ≤2.5 μm; $PM_{2.5abs}$, $PM_{2.5}$ absorbance; PN_{acc}, accumulation mode particle number concentration; per res, per resident.

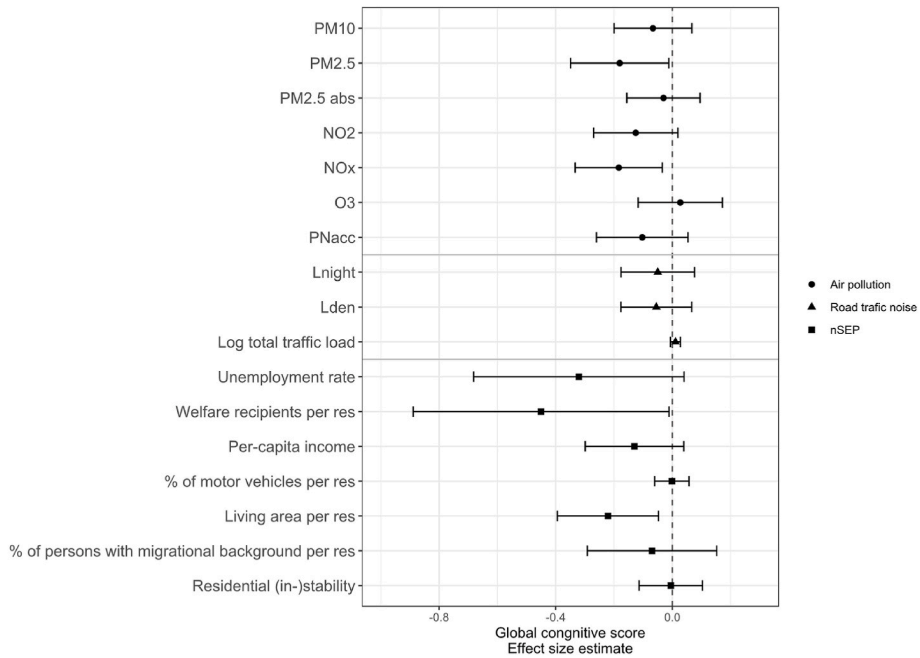

Fig. 2. The point estimates and 95 % confidence intervals of a regression analysis on the association between individual exposure factors (air pollution, road traffic noise, nSEP) with global cognitive score of the participants included in the analysis at the first follow-up of the Heinz Nixdorf Recall Study. **Notes:** the models are adjusted to individual level confounders (age, sex, iSEP, BMI, smoking status, cumulative smoking exposure, exposure to environment tobacco smoke, alcohol consumption, physical activity, diet) and PCs of other exposure types. Air pollution estimates were calculated per IQR increase of 2.1 μg/m^3 for PM_{10}, of 1.4 μg/m^3 for $PM_{2.5}$, of 0.35 × 10−5/m for $PM_{2.5abs}$, of 513 1M/m^3 for PN_{acc}, of 6.1 μg/m^3 for NO_2, of 15.7 μg/m^3 for NO_x. Noise estimates were calculated per 10 dB increase. Welfare recipients per residents, percent of motor vehicles per resident, percent of persons with migrational background per resident, and unemployment rate estimates were calculated per 10 % increase. Income per capita, living area per resident, and residential (in-)stability estimates were calculated per IQR increase of 11,900 Euro, of 6.6 m^2, and 49.4 % accordingly. Per-capita income, percent of motor vehicles per resident, living area per resident are reverse-coded. The figure corresponds to Supplementary Table 8. **Abbreviations:** AP, air pollution; BMI, body mass index; iSEP, individual socioeconomic position; nSEP, neighborhood socioeconomic position; L_{night}, outdoor nighttime traffic noise; L_{den}, outdoor 24h traffic noise; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; O_3, ozone; PM_{10}, particulate matter with diameter ≤10 μm; $PM_{2.5}$, particulate matter with diameter ≤2.5 μm; $PM_{2.5abs}$, $PM_{2.5}$ absorbance; PN_{acc}, accumulation mode particle number concentration; per res, per resident.

variance in the mixture of exposures, was positively correlated with air pollution, except O_3, and road traffic noise exposures, and negatively correlated with disadvantageous nSEP characteristics; thus, higher values of PC2 refer to high environmental exposures and least disadvantageous neighborhood socioeconomic conditions. It was labelled as “High air pollution and High nSEP”. PC3 was negatively correlated with road traffic noise exposures and explained 11 % of variance. We labelled it as “Low noise”. The PCA-loading plots to report the eigenvalues (loadings) of each parameter in the mixture in the first three PCs are shown in Supplementary Table 10 and Supplementary Fig. 3.

In fully adjusted regression models, PC1, “High exposures”, was significantly associated with lower GCS (−0.07, 95 %CI [−0.10, −0.04]). PC2, “High air pollution and High nSEP”, was positively but non-significantly associated with GCS (0.05, 95 %CI [−0.01, 0.10]). The association of PC3, “Low noise”, with GCS was null (−0.01, 95 %CI [−0.07, 0.06]) (Fig. 3A and Supplementary Table 11).

In the SOM analysis we identified six clusters (Fig. 4A). The choice of six was based on optimizing of several parameters: variance explained, group cohesion, and cluster sizes. The six clusters explained 48 % of variance in the data. The biggest cluster (Cluster 5) contained 966 (25.8 %) participants, the smallest cluster (Cluster 1) 178 (4.7 %) individuals (Supplementary Table 12). Cluster 1 (“Low nSEP”) was characterized by higher residential instability, higher proportion of persons with a migration background and welfare recipients per resident, higher unemployment rate, smaller living area per resident, and lower per-capita income. The air pollution and road traffic noise levels were average. Cluster 2 (“High ozone”) contained individuals experiencing high exposure to ozone and living in areas with average per-capita income and living area per resident. The air pollution and road traffic noise levels were very low in this cluster. In Cluster 3 (“Low exposures”), all exposures (air pollution, road traffic noise and nSEP) were low except for average PN_{acc}, NO_x and NO_2 exposure. Cluster 4 (“High air pollution and noise”) was characterized by high air pollution and road traffic noise exposure, lower number of vehicles per resident, and average levels of other nSEP factors. In Cluster 5 (“High PN_{acc}”), the majority of exposure levels were average with an exception of high PN_{acc}. Cluster 6 (“High noise”) had high road traffic noise exposure and traffic load, average air pollution exposure and low to average levels of nSEP factors. Also, Cluster 6 included the highest proportion of individuals living in the areas with the traffic noise levels exceeding EU thresholds. The detailed description of the clusters is given in Supplementary Table 13. Both Cluster 2 “High ozone” and Cluster 3 “Low exposures” had lower exposures compared with other clusters (see in Supplementary Table 13) and could be considered being the least disadvantageous clusters. We used Cluster 3 as a reference in the main analysis, and Cluster 2 - in the sensitivity analysis. In the radar plot (Supplementary Fig. 7), Cluster 3 had smaller “spikes”, while Cluster 2 exhibits higher “spike” levels (particularly in O_3, living area per resident and per capita income).

In the fully adjusted linear regression analysis with SOM-defined clusters as independent variables and in comparison to the reference Cluster 3 (“Low exposures”), Clusters 1 (“Low nSEP”), 4 (“High air pollution and noise”) and 5 (“High PN_{acc}”) were associated with lower GCS (−0.72, 95 %CI [1.17, −0.27]; −0.45, 95 %CI [−0.77, −0.13]; −0.51, 95 %CI [−0.79, −0.23], respectively) (Fig. 4B and Supplementary Table 11). Cluster 2 (“High Ozone”) and Cluster 6 (“High noise”) were also negatively but non-significantly associated with GCS, compared to the reference cluster.

When the Cluster 2 (“High Ozone”) was used as a reference cluster in

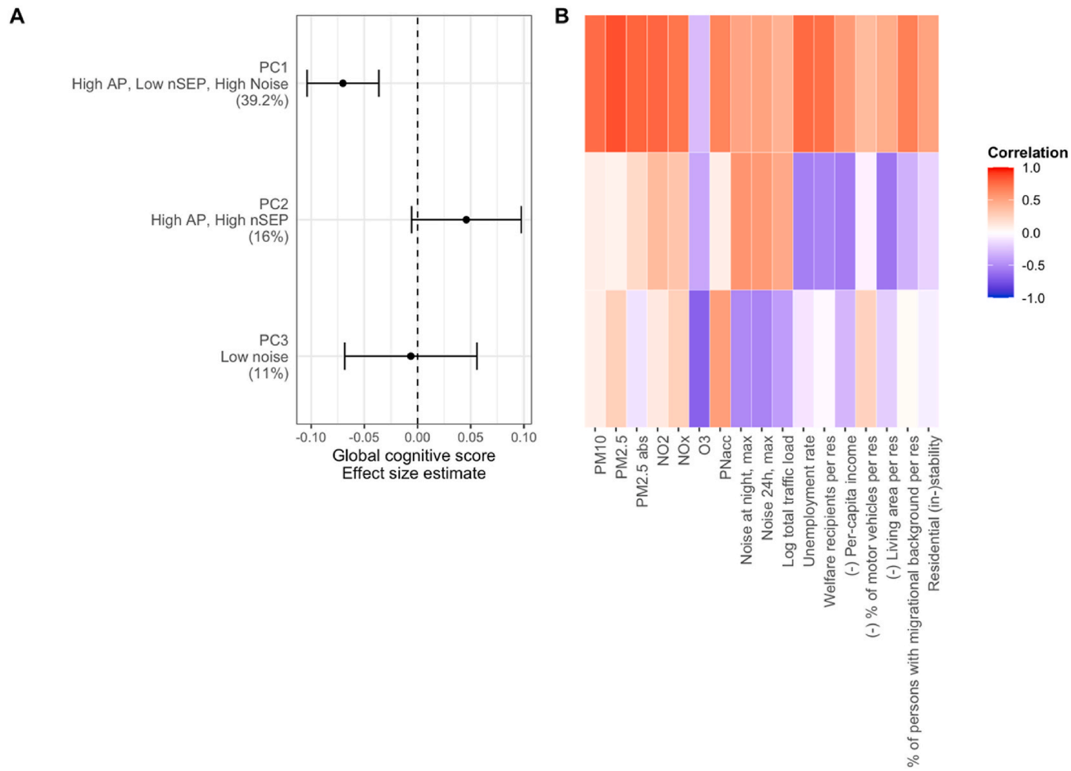

Fig. 3. **A:** The point estimates and 95 % confidence intervals of the regression analysis on the association between the first three principal components (PCs) of exposure mixture with global cognitive score of the participants included in the analysis at the first follow-up of the Heinz Nixdorf Recall Study. **B:** A correlation matrix between exposure factors and the first three principal components of exposure mixture. **Notes:** the models are adjusted to individual level confounders (age, sex, iSEP, BMI, smoking status, cumulative smoking exposure, exposure to environment tobacco smoke, alcohol consumption, physical activity, diet). The variance explained by principal components are given in brackets. Per-capita income, percent of motor vehicles per resident, living area per resident are reverse-coded. The figure corresponds to Supplementary Tables 9 and 11. **Abbreviations:** BMI, body mass index; iSEP, individual socioeconomic position; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; O_3, ozone; PM_{10}, particulate matter with diameter ≤10 μm; $PM_{2.5}$, particulate matter with diameter ≤2.5 μm; $PM_{2.5abs}$, $PM_{2.5}$ absorbance; PN_{acc}, accumulation mode particle number concentration; per res, per resident; PC, principal component.

the sensitivity analysis, the negative associations with GCS were closer to zero but still significant for Clusters 1 ("Low nSEP") and 5 ("High PN_{acc}"), and non-significant for Cluster 4 ("High air pollution and noise") (Supplementary Fig. 8). At the same time, Cluster 3 "Low exposures" was positively but non-significantly associated with GCS.

Supplementary Figs. 4 and 5 illustrate the similarities between SOM clusters and PCs. Observations from different SOM clusters are represented along the axes of PC scores. Specifically, Clusters 1, 4, and 5, which were significantly associated with lower GCS scores, were predominantly located in the right half of the coordinate space along PC1 axis, which was also inversely associated with GCS. Additionally, SOM Cluster 6 ("High Noise") and PC3 ("Low Noise") showed a negative correlation (the observations located in the left half of the coordinate space along PC3). The reference Cluster 3 ("Low exposures") was located in the positive half along PC2 ("High air pollution and High nSEP").

Also, we located clusters on the map of the region (Supplementary Fig. 6). Clusters 4, 5 and 6 were prevalent on the north where the major transport arteries are located. In contrast, Cluster 2 with high exposure to ozone was prevalent on the south, further from the traffic lines. The reference Cluster 3 with most advantageous profile was concentrated near the city of Mulheim an der Ruhr, known as a higher middle-class area.

4. Discussion

We investigated the joint association of highly correlated air pollution, road traffic noise, and nSEP on cognitive function in an elderly population from a German population-based cohort study. Through the application of various statistical methods, we showed, using two different clustering methods, robust associations of distinct combinations of disadvantageous environmental and neighborhood socioeconomic exposures with poorer cognitive function.

In our previous analysis, we observed associations of air pollution with cognitive decline (Ogurtsova et al., 2023), associations of long-term exposures to road traffic noise with decreased cognitive function (Tzivian et al., 2016b), and found suggestive evidence for an interaction of air pollution and noise (Tzivian et al., 2017). There we adjusted the single exposure models for nSEP, namely unemployment rate (Glaubitz et al., 2022; Lucht et al., 2022; Ogurtsova et al., 2023), whereas in the current analysis we assessed for the first time the combined effect of distinct patterns of intercorrelated environmental and neighborhood socioeconomic exposures to sched the light on the interplay between them.

4.1. Exposure patterns

Previous research, which demonstrated a harmful association between various combinations of air pollution and nSEP, both assigned based on residential census tract, with cognitive decline, was performed in the USA (Christensen et al., 2022). The authors conducted the study in Metro Atlanta, a racially and socioeconomically diverse region with intensive car traffic. The authors employed individual exposure linear regression and Least Absolute Shrinkage and Selection Operator (LASSO) models to explore individual exposure effects. Environmental mixture modelling methods including SOM, Bayesian kernel machine regression, and quantile-based G-computation explored joint effects and effect modification between air pollutants and nSEP characteristics on cognitive decline (Christensen et al., 2022).

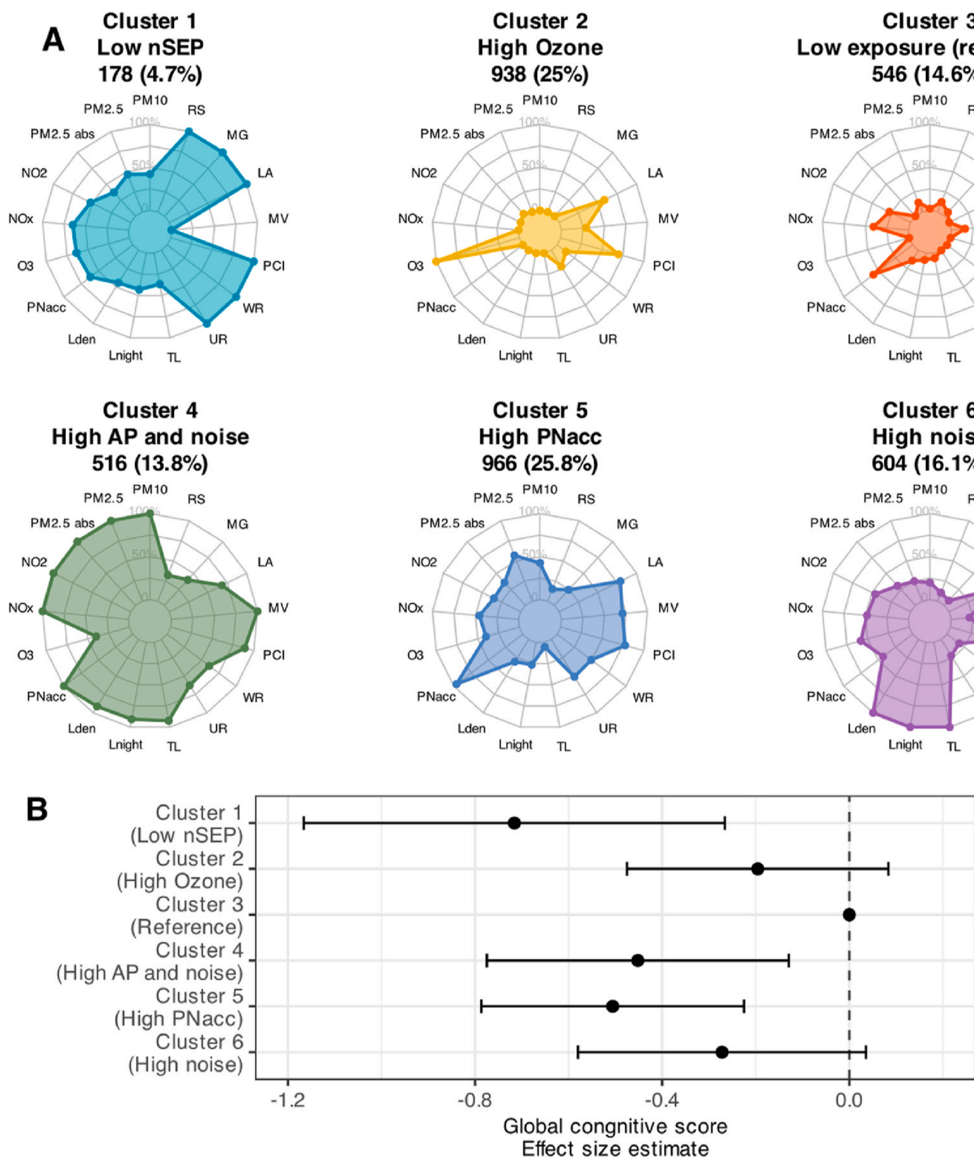

Fig. 4. **A**: SOM clusters and **B:** the point estimates and 95 % confidence intervals of the regression analysis on the association between SOM clusters and global cognitive score of the participants included in the analysis at the first follow-up of the Heinz Nixdorf Recall Study. **Notes**: **A:** slices represent a relative scale from minimum to maximum values of a mixture component, each circle is one SOM cluster. Per-capita income, percent of motor vehicles per resident, living area per resident are reverse-coded. The axes indicate the percentage in the range from minimum to maximum value of an exposure component. **B:** The models are adjusted to individual level confounders (age, sex, iSEP, BMI, smoking status, cumulative smoking exposure, exposure to environment tobacco smoke, alcohol consumption, physical activity, diet). Cluster 3, the least disadvantageous cluster, is a reference. The figure corresponds to Supplementary Table 12. **Abbreviations:** AP, air pollution; BMI, body mass index; iSEP, individual socioeconomic position; nSEP, neighborhood socioeconomic position; L_{night}, outdoor nighttime traffic noise; L_{den}, outdoor 24h traffic noise; NO_2, nitrogen dioxide; NO_x, nitrogen oxides; O_3, ozone; PM_{10}, particulate matter with diameter $\leq$10 µm; $PM_{2.5}$, particulate matter with diameter $\leq$2.5 µm; $PM_{2.5abs}$, $PM_{2.5}$ absorbance; PN_{acc}, accumulation mode particle number concentration; TL, traffic load; UR, unemployment rate; WR, welfare recipients per resident; PCI, per-capita income; SOM, self-organized maps; MV, percent of motor vehicles per resident; LA, living area per resident; MG, percent of persons with migrational background per resident; RS, residential (in-)stability.

In both the Metro Atlanta study and our research, a cluster characterized by the lowest air pollution levels and the highest nSEP was identified and used as a reference group in the linear regression analysis. However, the patterns observed in other clusters differed. In the Metro Atlanta study, two clusters (2 and 3) exhibited the highest air pollution concentrations and the lowest nSEP. Instead, we identified SOM clusters dominated by either high air pollution (Cluster 4) or low nSEP (Cluster 1). At the same time, in our study the first principal component in PCA was similar to Clusters 2 and 3 in Metro Atlanta study, was highly correlated to all exposures except O_3, and was significantly associated with lower GCS. Also, Cluster 5 ("High PN_{acc}") in our analysis exhibited average exposure levels across all exposure groups and high PN_{acc}, similar to cluster 6 in the Metro Atlanta Study. Despite these differences, all these clusters (1, 4 and 5) in our study were negatively associated with cognitive function, consistent with findings from the Metro Atlanta study. Furthermore, we visually demonstrated that, in our study, SOM clusters were well-separated in the two-dimensional space of PC1 and PC2, indicating that the SOM classification aligns with the main variance captured by PCA and both methods capture similar underlying patterns in the data. The difference in classification by PCA and SOM might be explained by capturing non-linear relationships between data components by SOM (Peeters and Dassargues, 2006).

Ignoring co-exposure to nSEP as an important confounder, the estimated effects of air pollution on cognitive decline showed in Christensen et al. counterintuitive results with seemingly protective associations between air pollution and cognition (Christensen et al., 2022). The further SOM analysis, performed by the authors, demonstrated that this protective effect of air pollution might indeed be explained by higher nSEP in the areas with high air pollution burden. We saw similar findings in our PCA results. PC2, "High air pollution and High nSEP", demonstrated a positive, albeit non-significant, association with cognitive function in the PCA. In contrast, PC1, where all types of exposure were high, was aversively associated with cognitive function. The PC2 likely represents individuals residing in less deprived neighborhoods with greater exposure to air pollution and noise, often situated near city centers in the study region. It was hypothesized, that the individuals living in areas with higher nSEP experience less severe health effects from air pollution exposure compared to those in lower nSEP areas (Christensen et al., 2022; Wing et al., 2017). Also, previous studies have shown that interactions between air pollution and neighborhood deprivation can modify the associations of these risk factors with various health outcomes (Brunt et al., 2017).

Cluster 2 in the SOM analysis was distinguished by the high ozone concentrations. Geospatial mapping of this cluster, based on residential addresses, revealed that most individuals classified within this group resided in the southern areas of the study region. This region is predominantly rural, where higher ozone levels are anticipated (Yan et al., 2019), alongside relatively favorable nSEP. We didn't detect significant association of being classified to this cluster and poorer cognitive function. On the other hand, Cluster 4 ("High air pollution and noise") in the SOM analysis was significantly associated with poorer cognitive function. Most of the participants classified within this cluster resided in the northern part of the region, where the primary transportation artery of the entire area is located. The pattern of this cluster appears counterintuitive, exhibiting high levels of air pollution and traffic noise despite a low number of vehicles per resident. This observation can likely be attributed to a pattern of environmental injustice: high population density characterized by bigger family size in low-cost residential areas situated along heavily trafficked roads (Clark et al., 2014). This cluster might be also characterized by higher social inequality: it was shown that the least wealthy members of the societies do not have cars but are forced to endure elevated levels of crashes and pollution so that wealthier people can drive (Miner et al., 2024). The association with the poorer cognitive function for such mixture of disadvantageous conditions is approved in the literature (Dickerson et al., 2023).

Our results contribute to the existing body of evidence that underscores the complex effects of air pollution and nSEP as well as other environmental and neighborhood socioeconomic factors on cognitive function in adults. For instance, a cross-sectional study of an Australian cohort of adults found that the positive associations between built environment complexity (a composite index of four built environment measures such as population density, street intersection density, non-commercial and commercial land use) and memory were more pronounced in individuals living in areas with higher SEP and lower NO_2 concentrations (Cerin et al., 2023). Furthermore, a protective association between the natural environment (parkland and blue spaces) and memory emerged only among those living in areas with lower NO_2 concentrations and average or below-average SEP. The inverse association between $PM_{2.5}$ exposure and cognitive function was stronger among elderly who were also exposed to stressful neighborhood conditions (Ailshire et al., 2017). Moreover, it was shown that persons living in areas with low nSEP were most vulnerable to exposure to NO_x, $PM_{2.5}$ and CO (Li et al., 2022). In another study, the association between higher $PM_{2.5}$ exposure and poor cognitive function increased as area-level gross domestic product, an indicator of local overall economic condition, decreased (Wang et al., 2020).

In our analysis, Cluster 6 with high road traffic noise exposure and low to average exposure to other environmental and neighborhood socioeconomic factors tended to be negatively associated with GCS, but this association was not statistically significant. Moreover, in the PCA analysis, PC3 ("Low noise"), correlated with advantageous nSEP and average air pollution levels, showed no associations with GCS. Here, high road traffic noise occurred in a less detrimental combination with other exposures that might mitigate its harmful effects. Neighborhoods with higher SEP might have more access to restorative environments that may buffer noise effects on cognition (Hartig et al., 2014; von Lindern et al., 2016). This suggests a complex interaction between environmental and social exposures rather than simple independent effects. However, we are unaware of other studies examining the associations of environmental and socioeconomic exposure profiles with cognitive function that specifically included road traffic noise.

We also did not detect any associations between road traffic noise and cognitive function in single exposure models. The last finding contradicts our previous results (Tzivian et al., 2016a), where a significant association was identified between GCS scores and L_{den} in a single exposure model. It can be explained by the small methodological differences (the continuous noise variable in this study vs. using noise level thresholds in Tzivian et al. 2016) and the bigger sample size in Tzivian et al. (2016a).

4.2. Biological pathways

Adverse environmental factors can affect cognitive function through various biological pathways. Airborne ultrafine particles, when inhaled, can reach the brain directly through the nasal olfactory pathway. Bigger particle matter can penetrate deep into the lungs, reaching the alveoli and potentially entering the bloodstream (Thangavel et al., 2022). This process triggers inflammation in the nasal passages and lungs, releasing pro-inflammatory cytokines and increasing stress hormone levels like cortisol. These substances can cross the blood-brain barrier, leading to chronic inflammation and neurodegeneration (Genc et al., 2012). Additionally, particles affect vascular endothelium and possibly blood coagulability, potentially explaining cognitive changes in older adults as manifestations of vascular disease (Clifford et al., 2016).

Environmental noise impacts cognitive function, causing distraction, reduced sleep quality, impaired speech perception, heightened psychological stress, discomfort, and learned helplessness (Liang et al., 2024). Animal studies suggest that noise induces mild acute stress, leading to elevated levels of noradrenaline and dopamine in the hypothalamus, which impairs regulation of the prefrontal cortex responsible for cognitive abilities (Tzivian et al., 2015).

Regarding the neighborhood socioeconomic factors, studies suggest that social stressors may lower the brain's threshold for neurotoxicity, thus making those living in disadvantageous neighborhoods more vulnerable to the harmful effects of air pollution and noise (Lupien et al., 2009; McEwen and Tucker, 2011). In our analysis, PC1 ("High exposures") in the PCA and Cluster 1 ("Low nSEP") in the SOM analysis might support this hypothesis. Moreover, ecological research has indicated that the impact of neighborhood social dynamics and built infrastructure can substantially influence health behaviors and outcomes (Diez Roux, 2011; Pickett and Pearl, 2001). Traffic, as an integral component of this infrastructure, often is a common source of both air pollution and noise. Additionally, it is plausible that traffic has further implications on neurocognitive health beyond its direct influence on health through exposure to pollutants. For instance, it may hinder citizens' engagement in physical activity, active transportation, and social interactions. The same changes in behavior may be caused by disadvantageous social conditions. At the same time, advantageous social conditions might play a protective role against environmental stressors; in our analysis, PC2 ("High air pollution and High nSEP") might illustrate this hypothesis. Still, the available information on environmental and neighborhood socioeconomic factors remains limited, and there is insufficient evidence to firmly establish a conclusive causal and biological link between these factors and cognitive health.

4.3. Methodological aspects

In our analysis, the exposure profiles, found by employing unsupervised methods as PCA or SOM, were based on the amount of variance explained by given local exposure distribution and do not account for its relationship to the outcome or supported by any hypothesis, so these approaches limited the generalizability of the results (Hamra and Buckley, 2018) and did not focus on the patterns that were assumed being especially important to the outcomes. On the other hand, an unsupervised method can help identify patterns or groups (e.g. neighborhoods or population segments) that consistently show certain characteristics across several outcomes. This broader view could guide more holistic or integrated public health strategies.

While PCA is a linear, unsupervised dimensionality reduction method that identifies major axes of variation in the data, SOM is a nonlinear clustering technique that can capture more complex relationships and interactions among exposures. By applying both methods, we aimed to gain a broader understanding of the joint exposure patterns: PCA helped us interpret the dominant sources of variability, while SOM enabled us to identify meaningful exposure profiles that reflect real-world combinations individuals are likely to experience. The alignment between clusters and PCA axes further validated the robustness and interpretability of the patterns.

In the current study, we employed two distinct environmental mixture methods to investigate the relationships between exposure mixture profiles and cognitive function, revealing a synergy between environmental and social exposures. We acknowledge the growing use of advanced approaches in environmental epidemiology, such as quantile-based G-computation and Bayesian Kernel Machine Regression, both of which offer valuable frameworks for estimating joint effects and simulating hypothetical interventions. However, our focus was on exposure pattern discovery, rather than effect estimation per se. We chose SOM and PCA specifically to explore the structure of exposure mixtures. While PCA was not specifically designed for estimating mixture effects, utilizing this method, we showed, that a lower-dimensional disadvantageous exposure summary measure was associated with poorer cognitive function. Moreover, our results from SOM analysis were in line with PCA, showing that clusters exhibiting disadvantageous air pollution, road traffic noise, and nSEP exposure profiles similar to PC1 ("High exposures"), were significantly, robustly and adversely associated with cognitive function.

4.4. Implications

We estimated the impact of combined exposures on cognitive function, providing a realistic assessment of their effects under real-world conditions. Intercorrelated exposures may interact as antagonists or synergists. Although our analysis cannot confirm a hypothesis of synergy or antagonism, we observed cross-sectional patterns suggesting a potential interplay between environmental and social exposures.

Based on our findings, we can hypothesize that effective systematic public health interventions targeting the reduction of environmental exposures, namely air pollutants and road traffic noise, and the improvement of neighborhood socioeconomic factors could jointly contribute to cognitive health. The spatial distribution of exposure profiles across the region and their high concentration near major transport routes indicate a potential opportunity and a specific location for localized and practical interventions aimed at mitigating the negative health effects associated with road traffic pollution.

These results warrant confirmation through prospective longitudinal studies, and future research should focus on elucidating the potential biological or social mechanisms underlying the associations between nSEP, air pollutants, and road traffic noise with cognitive function.

4.5. Study strength and limitations

The primary limitation of this study is its cross-sectional design, which prevents a causal interpretation of our findings. Additionally, the environmental factors in our study were assessed at the individual level (based on residential addresses), whereas the socioeconomic measures were only available at the municipality level, which represents a relatively large spatial unit. Prior research has demonstrated that correlations between environmental factors and nSEP vary depending on the size of the defined "neighborhoods"—the larger the area, the stronger the correlations due to spatial smoothing (Fecht et al., 2015, 2016). Moreover, both air pollution models had different resolutions: ESCAPE-LUR predicts concentrations at each participant's address and EURAD-CTM had a grid of 1-km^2. Therefore, the mismatch in spatial scales may affect the results, adding a measurement error and making them sensitive in detecting smoothing effects, for example, related to nSEP characteristics. Additionally, the use of administrative data itself can introduce exposure misclassification: the administrative boundary may not precisely reflect the neighborhood and the nSEP exposures that residents experience. We used only a 2-year average to estimate long-term air pollution exposure and a 1-year average to estimate long-term traffic noise exposure, as these environmental pollutants in the study region have been relatively stable over time (Cyrys et al., 2012; Hennig et al., 2016; Hoffmann et al., 2015). This duration has also been used in previous studies investigating environmental impacts on cognitive function in older adults (Cyrys et al., 2012).

We also faced a temporal mismatch in our data sources. Environmental exposures and health outcomes were assessed during 2006–2008, while nSES data were only available for the years 2000–2004. However, we assumed that socioeconomic deprivation levels in German municipalities remain relatively stable and the earlier data likely provide a reasonable representation of chronic exposure to neighborhood social conditions, even six years later.

Our data is prone to measurement error and exposure misclassification. Individual exposure to air pollution from daily mobility patterns and behavior, that might result in higher exposure misclassification for specific subgroups, was not assessed. Due to the limitations of the dispersion chemical transport model with a resolution of 1 km^2, we were unable to consider the heterogeneous distribution of accumulation mode particles on a finer spatial scale, particularly near highways or other busy inner-city roads, that might be crucial for the dynamics of these particles and might lead to substantial errors in exposure assessment. Data on individual noise sensitivity or hearing impairment that might be an important modifier of personal perception of noise and a possible mediator in the linkage to dementia were not available. The geographical area of participants' residence, characterized by relatively high levels of air pollution, maintains homogeneity in pollution and living conditions with a narrow contrast in exposure in comparison to nationwide studies, which limits the ability to detect associations. Furthermore, our study sample participants tended to have better health and higher iSEP than the general German population. Also, the study itself is prone to the selection bias. The included individuals were more likely to have higher education and healthier behaviors, and may respond differently to the exposures. As a result, the associations observed in our study may be attenuated, and the true associations, particularly among more disadvantaged individuals, could have been stronger. This characteristic restricts the generalizability of our results and the potential to address environmental injustice.

Our study boasts several strengths. This is the first study on associations of joint environmental and socioeconomic exposure factors with cognitive function that included road traffic noise as a co-exposure and is based on data from Europe. Notably, it incorporates rich demographic and lifestyle data, enabling the adjustment for numerous potential confounders. The population-based nature of the study, along with standardized outcome assessment methods and a large sample size, further enhances its robustness. Furthermore, employing various methods to model the association of the exposure mixture and the outcome allowed to understand the interplay between exposures better as well as improve the robustness of the results. The mixture methods we used were designed to deal with correlated exposures, so we enriched the information in the analysis by including as many pollutants as possible.

5. Conclusion

We found associations between distinct combinations of air pollution, road traffic noise, and nSEP exposure with poorer cognitive function using two different dimensionality reduction methods. Understanding the effects of exposure patterns through future longitudinal studies could confirm causality, strengthen the case for policy and practice, and thus inform the development of targeted prevention programs addressing the environmental and neighborhood socioeconomic risk factors systematically.

CRediT authorship contribution statement

Katherine Ogurtsova: Writing – review & editing, Writing – original draft, Visualization, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Grace M. Christensen:** Writing – review & editing, Software, Methodology, Conceptualization. **Vanessa J. Soppa:** Writing – review & editing. **Martha Jokisch:** Writing – review & editing, Data curation. **Lilian Tzivian:** Writing – review & editing. **Christian Weimar:** Writing – review & editing, Data curation. **Nico Dragano:** Writing – review & editing, Funding acquisition, Data curation. **Börge Schmidt:** Writing – review & editing, Data curation. **Anke Hüls:** Writing – review & editing, Supervision, Resources, Methodology, Conceptualization. **Barbara Hoffmann:** Writing – review & editing, Supervision, Resources, Funding acquisition, Conceptualization.

Ethics

The HNR study was approved by the ethics committee of the University Hospital Essen. All participants gave their written informed consent. All study procedures complied with the Declaration of Helsinki.

Funding

The HNR study was supported by grants from the German Research Council (ER 155/6-1, ER 155/6-2, SI 236/8-1, SI 236/9-1) and the Kulturstiftung Essen, Germany. The exposure assessment was funded through the European Community's Seventh Framework Program (FP7/2007–2011; grant 211250) and by the German Research Council (HO 3314/4-3). Assessment of residential history and neighborhoods variables were additionally funded by the Volkswagen Foundation as part of the funding initiative "Individual and social perspectives on ageing". The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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.

Acknowledgements

We thank the North Rhine-Westphalia State Agency for Nature, Environment and Consumer Protection (LANUV) for providing emission and land use data for North Rhine-Westphalia. We are indebted to the investigative group and the study personnel of the HNR study. We also thank the Heinz Nixdorf Foundation for the generous support of this study. We are thankful for Anna Buschka for the data management.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2025.121830.

Data availability

The authors do not have permission to share data.

References

Abdi, H., Williams, L.J., 2010. Principal component analysis. Wiley Interdiscip Rev Comput Stat 2, 433–459. https://doi.org/10.1002/WICS.101.

Abo Hamza, E., Tindle, R., Pawlak, S., Bedewy, D., Moustafa, A.A., 2024. The impact of poverty and socioeconomic status on brain, behaviour, and development: a unified framework. Rev. Neurosci. 35, 597–617. https://doi.org/10.1515/REVNEURO-2023-0163/ASSET/GRAPHIC/J_REVNEURO-2023-0163_FIG_001.JPG.

Ailshire, J., Karraker, A., Clarke, P., 2017. Neighborhood social stressors, fine particulate matter air pollution, and cognitive function among older U.S. adults. Soc. Sci. Med. 172, 56–63. https://doi.org/10.1016/j.socscimed.2016.11.019.

The problem of multicollinearity. In: Allen, M.P. (Ed.), 1997. Understanding Regression Analysis. Springer US, Boston, MA, pp. 176–180. https://doi.org/10.1007/978-0-585-25657-3_37.

Amariglio, R.E., Donohue, M.C., Marshall, G.A., Rentz, D.M., Salmon, D.P., Ferris, S.H., Karantzoulis, S., Aisen, P.S., Sperling, R.A., 2015. Tracking early decline in cognitive function in older individuals at risk for Alzheimer's disease dementia: the Alzheimer's disease cooperative study cognitive function instrument. JAMA Neurol. 72, 446. https://doi.org/10.1001/JAMANEUROL.2014.3375.

Astel, A., Tsakovski, S., Barbieri, P., Simeonov, V., 2007. Comparison of self-organizing maps classification approach with cluster and principal components analysis for large environmental data sets. Water Res. 41, 4566–4578. https://doi.org/10.1016/J.WATRES.2007.06.030.

Beelen, R., Hoek, G., Vienneau, D., Eeftens, M., Dimakopoulou, K., Pedeli, X., Tsai, M.Y., Künzli, N., Schikowski, T., Marcon, A., Eriksen, K.T., Raaschou-Nielsen, O., Stephanou, E., Patelarou, E., Lanki, T., Yli-Tuomi, T., Declercq, C., Falq, G., Stempfelet, M., Birk, M., Cyrys, J., von Klot, S., Nádor, G., Varró, M.J., Dedele, A., Gražulevičiene, R., Mölter, A., Lindley, S., Madsen, C., Cesaroni, G., Ranzi, A., Badaloni, C., Hoffmann, B., Nonnemacher, M., Krämer, U., Kuhlbusch, T., Cirach, M., de Nazelle, A., Nieuwenhuijsen, M., Bellander, T., Korek, M., Olsson, D., Strömgren, M., Dons, E., Jerrett, M., Fischer, P., Wang, M., Brunekreef, B., de Hoogh, K., 2013. Development of NO2 and NOx land use regression models for estimating air pollution exposure in 36 study areas in Europe – the ESCAPE project. Atmos. Environ. 72, 10–23. https://doi.org/10.1016/J.ATMOSENV.2013.02.037.

Besser, L.M., McDonald, N.C., Song, Y., Kukull, W.A., Rodriguez, D.A., 2017. Neighborhood environment and cognition in older adults: a systematic review. Am. J. Prev. Med. 53, 241–251. https://doi.org/10.1016/J.AMEPRE.2017.02.013.

Birmili, W., Weinhold, K., Rasch, F., Sonntag, A., Sun, J., Merkel, M., Wiedensohler, A., Bastian, S., Schladitz, A., Löschau, G., Cyrys, J., Pitz, M., Gu, J., Kusch, T., Flentje, H., Quass, U., Kaminski, H., Kuhlbusch, T.A.J., Meinhardt, F., Schwerin, A., Bath, O., Ries, L., Wirtz, K., Fiebig, M., Gerwig, H., Wirtz, K., Fiebig, M., 2016. Long-term observations of tropospheric particle number size distributions and equivalent Black carbon mass concentrations in the German Ultrafine Aerosol Network (GUAN). Earth Syst. Sci. Data 8, 355–382. https://doi.org/10.5194/essd-8-355-2016.

Bloomberg, M., Muniz-Terrera, G., Brocklebank, L., Steptoe, A., 2024. Healthy lifestyle and cognitive decline in middle-aged and older adults residing in 14 European countries. Nat. Commun. 15, 5003. https://doi.org/10.1038/s41467-024-49262-5.

Bowe, B., Xie, Y., Yan, Y.Y., Al-Aly, Z., 2019. Burden of cause-specific mortality associated with PM2.5 air pollution in the United States. JAMA Netw. Open 2, e1915834. https://doi.org/10.1001/JAMANETWORKOPEN.2019.15834.

Brunt, H., Barnes, J., Jones, S.J., Longhurst, J.W.S., Scally, G., Hayes, E., 2017. Air pollution, deprivation and health: understanding relationships to add value to local air quality management policy and practice in Wales, UK. J. Public Health 39, 485–497. https://doi.org/10.1093/PUBMED/FDW084.

Castellani, B., Bartington, S., Wistow, J., Heckels, N., Ellison, A., Van Tongeren, M., Arnold, S.R., Barbrook-Johnson, P., Bicket, M., Pope, F.D., Russ, T.C., Clarke, C.L., Pirani, M., Schwannauer, M., Vieno, M., Turnbull, R., Gilbert, N., Reis, S., 2022. Mitigating the impact of air pollution on dementia and brain health: setting the policy agenda. Environ. Res. 215, 114362. https://doi.org/10.1016/J.ENVRES.2022.114362.

Cerin, E., Barnett, A., Wu, Y.T., Martino, E., Shaw, J.E., Knibbs, L.D., Poudel, G., Jalaludin, B., Anstey, K.J., 2023. Do neighbourhood traffic-related air pollution and socio-economic status moderate the associations of the neighbourhood physical environment with cognitive function? Findings from the AusDiab study. Sci. Total Environ. 858, 160028. https://doi.org/10.1016/J.SCITOTENV.2022.160028.

Chaix, B., Leal, C., Evans, D., 2010. Neighborhood-level confounding in epidemiologic studies: unavoidable challenges, uncertain solutions. Epidemiology 21, 124–127. https://doi.org/10.1097/EDE.0B013E3181C04E70.

Chen, J.H., Kuo, T.Y., Yu, H.L., Wu, C., Yeh, S.L., Chiou, J.M., Chen, T.F., Chen, Y.C., 2020. Long-term exposure to air pollutants and cognitive function in Taiwanese community-dwelling older adults: a four-year cohort study. J Alzheimers Dis 78, 1585–1600. https://doi.org/10.3233/JAD-200614.

Choy, C.T., Wong, C.H., Chan, S.L., 2019. Embedding of genes using cancer gene expression data: biological relevance and potential application on biomarker discovery. Front. Genet. 10, 1–10. https://doi.org/10.3389/fgene.2018.00682.

Christensen, G.M., Li, Z., Pearce, J., Marcus, M., Lah, J.J., Waller, L.A., Ebelt, S., Hüls, A., 2022. The complex relationship of air pollution and neighborhood socioeconomic status and their association with cognitive decline. Environ. Int. 167, 107416. https://doi.org/10.1016/j.envint.2022.107416.

Christensen, G.M., Marcus, M., Vanker, A., Eick, S.M., Malcolm-Smith, S., Suglia, S.F., Chang, H.H., Zar, H.J., Stein, D.J., Hüls, A., 2023. Joint effects of indoor air pollution and maternal psychosocial factors during pregnancy on trajectories of early childhood psychopathology. CIDRI Clin. Fellowsh. Wellcome Trust. https://doi.org/10.1101/2023.04.07.23288289v1.

Clark, L.P., Millet, D.B., Marshall, J.D., 2014. National patterns in environmental injustice and inequality: outdoor NO2 air pollution in the United States. PLoS One 9, e94431. https://doi.org/10.1371/JOURNAL.PONE.0094431.

Clifford, A., Lang, L., Chen, R., Anstey, K.J., Seaton, A., 2016. Exposure to air pollution and cognitive functioning across the life course – a systematic literature review. Environ. Res. 147, 383–398. https://doi.org/10.1016/J.ENVRES.2016.01.018.

Cyrys, J., Eeftens, M., Heinrich, J., Ampe, C., Armengaud, A., Beelen, R., Bellander, T., Beregszaszi, T., Birk, M., Cesaroni, G., Cirach, M., de Hoogh, K., De Nazelle, A., de Vocht, F., Declercq, C., Dėdelė, A., Dimakopoulou, K., Eriksen, K., Galassi, C., Grąulevičienė, R., Grivas, G., Gruzieva, O., Gustafsson, A.H., Hoffmann, B., Iakovides, M., Ineichen, A., Krämer, U., Lanki, T., Lozano, P., Madsen, C., Meliefste, K., Modig, L., Mölter, A., Mosler, G., Nieuwenhuijsen, M., Nonnemacher, M., Oldenwening, M., Peters, A., Pontet, S., Probst-Hensch, N., Quass, U., Raaschou-Nielsen, O., Ranzi, A., Sugiri, D., Stephanou, E.G., Taimisto, P., Tsai, M.-Y., Vaskövi, É., Villani, S., Wang, M., Brunekreef, B., Hoek, G., 2012. Variation of NO2 and NOx concentrations between and within 36 European study areas: results from the ESCAPE study. Atmos. Environ. 62, 374–390. https://doi.org/10.1016/j.atmosenv.2012.07.080.

Das, G., Chattopadhyay, M., Gupta, S., 2016. A comparison of self-organising maps and principal components analysis. Int. J. Mark. Res. 58, 815–834. https://doi.org/10.2501/IJMR-2016-039.

Delgado-Saborit, J.M., Guercio, V., Gowers, A.M., Shaddick, G., Fox, N.C., Love, S., 2021. A critical review of the epidemiological evidence of effects of air pollution on dementia, cognitive function and cognitive decline in adult population. Sci. Total Environ. 757, 143734. https://doi.org/10.1016/J.SCITOTENV.2020.143734.

Dickerson, A.S., Frndak, S., Gorski-Steiner, I., Deng, Z., Jenson, T.E., Mohan, A., Kim, J., Boerner, V.Q., Thorpe, R.J., 2023. Outdoor air pollution, environmental injustice, and cognitive decline: a review. Curr Epidemiol Rep 10, 158–167. https://doi.org/10.1007/s40471-023-00326-y.

Diez Roux, A.V., 2011. Investigating neighborhood and area effects on health, 1783–1789. https://doi.org/10.2105/AJPH.91.11.1783.

Dlugaj, M., Weimar, C., Wege, N., Verde, P.E., Gerwig, M., Dragano, N., Moebus, S., Jöckel, K.H., Erbel, R., Siegrist, J., 2010. Prevalence of mild cognitive impairment and its subtypes in the Heinz Nixdorf recall study cohort. Dement. Geriatr. Cogn. Disord 30, 362–373. https://doi.org/10.1159/000320988.

Dreger, S., Schüle, S.A., Hilz, L.K., Bolte, G., 2019. Social Inequalities in Environmental Noise Exposure: a Review of Evidence in the WHO European Region, 16, p. 1011. https://doi.org/10.3390/IJERPH16061011.

Eeftens, M., Beelen, R., De Hoogh, K., Bellander, T., Cesaroni, G., Cirach, M., Declercq, C., Dedele, A., Dons, E., De Nazelle, A., Dimakopoulou, K., Eriksen, K., Falq, G., Fischer, P., Galassi, C., Gražulevičiene, R., Heinrich, J., Hoffmann, B., Jerrett, M., Keidel, D., Korek, M., Lanki, T., Lindley, S., Madsen, C., Mölter, A., Nádor, G., Nieuwenhuijsen, M., Nonnemacher, M., Pedeli, X., Raaschou-Nielsen, O., Patelarou, E., Quass, U., Ranzi, A., Schindler, C., Stempfelet, M., Stephanou, E., Sugiri, D., Tsai, M.Y., Yli-Tuomi, T., Varró, M.J., Vienneau, D., Klot, S. Von, Wolf, K., Brunekreef, B., Hoek, G., 2012. Development of land use regression models for PM2.5, PM 2.5 absorbance, PM10 and PMcoarse in 20 European study areas; results of the ESCAPE project. Environ. Sci. Technol. 46, 11195–11205. https://doi.org/10.1021/ES301948K/SUPPL_FILE/ES301948K_SI_001.PDF.

European Parliament and the Council, 2002. Directive 2002/49/EC of european parliament and of the council of 25 June 2002 relating to the assessment and management of environmental noise. Offic. J. L 189.

European Parliament, Council of the European Union, 2008. Directive 2008/50/EC of the European Parliament and of the Council of 21 May 2008 on Ambient Air Quality and Cleaner Air for Europe. EU.

Fecht, D., Fischer, P., Fortunato, L., Hoek, G., De Hoogh, K., Marra, M., Kruize, H., Vienneau, D., Beelen, R., Hansell, A., 2015. Associations between air pollution and socioeconomic characteristics, ethnicity and age profile of neighbourhoods in England and the Netherlands. Environ. Pollut. 198, 201–210. https://doi.org/10.1016/J.ENVPOL.2014.12.014.

Fecht, D., Hansell, A.L., Morley, D., Dajnak, D., Vienneau, D., Beevers, S., Toledano, M. B., Kelly, F.J., Anderson, H.R., Gulliver, J., 2016. Spatial and temporal associations of road traffic noise and air pollution in London: implications for epidemiological studies. Environ. Int. 88, 235–242. https://doi.org/10.1016/J.ENVINT.2015.12.001.

Genc, S., Zadeoglulari, Z., Fuss, S.H., Genc, K., 2012. The adverse effects of air pollution on the nervous system. J. Toxicol. https://doi.org/10.1155/2012/782462.

Glaubitz, L., Stumme, J., Lucht, S., Moebus, S., Schramm, S., Jockwitz, C., Hoffmann, B., Caspers, S., 2022. Association between long-term air pollution, chronic traffic noise, and resting-state functional connectivity in the 1000BRAINS study. Environ. Health Perspect. 130. https://doi.org/10.1289/EHP9737.

Greenland, S., Pearl, J., Robins, J.M., 1999. Causal diagrams for epidemiologic research. Epidemiology 10.

Hajat, A., Hsia, C., O'neill, M.S., 2015. Socioeconomic disparities and air pollution exposure: a global review compliance with ethics guidelines human and animal rights and informed consent HHS public access. Curr. Environ. Health Rep. 2, 440–450. https://doi.org/10.1007/s40572-015-0069-5.

Hamra, G.B., Buckley, J.P., 2018. Environmental exposure mixtures: questions and methods to address them. Curr Epidemiol Rep 5, 160–165. https://doi.org/10.1007/S40471-018-0145-0/TABLES/1.

Hartig, T., Mitchell, R., De Vries, S., Frumkin, H., 2014. Nature and health. Annu. Rev. Publ. Health 35, 207–228. https://doi.org/10.1146/ANNUREV-PUBLHEALTH-032013-182443/1.

Health Effects Institute, 2022. Systematic Review and meta-analysis of Selected Health Effects of Long-Term Exposure to Traffic-Related Air Pollution. Health Effects Institute, Boston, MA, US.

Hennig, F., Sugiri, D., Tzivian, L., Fuks, K., Moebus, S., Jöckel, K.-H.H., Vienneau, D., Kuhlbusch, T.A.J., de Hoogh, K., Memmesheimer, M., Jakobs, H., Quass, U., Hoffmann, B., 2016. Comparison of land-use regression modeling with dispersion and chemistry transport modeling to assign air pollution concentrations within the Ruhr area. Atmosphere 7, 48. https://doi.org/10.3390/atmos7030048.

Hill, R.C., Fomby, T.B., Johnson, S.R., 2007. Communications in statistics-theory and methods component selection norms for principal components regression. https://doi.org/10.1080/03610927708827494.

Hoffmann, B., Weinmayr, G., Hennig, F., Fuks, K., Moebus, S., Weimar, C., Dragano, N., Hermann, D.M., Kälsch, H., Mahabadi, A.A., Erbel, R., Jöckel, K.H., 2015. Air quality, stroke, and coronary events: results of the Heinz Nixdorf recall study from the ruhr region. Dtsch Arztebl Int 112, 195–201. https://doi.org/10.3238/ARZTEBL.2015.0195.

Ilango, S.D., Leary, C.S., Ritchie, E., Semmens, E.O., Park, C., Fitzpatrick, A.L., Kaufman, J.D., Hajat, A., 2023. An examination of the joint effect of the social environment and air pollution on dementia among US older adults. Environ. Epidemiol. 7, E250. https://doi.org/10.1097/EE9.0000000000000250.

Iungman, T., Khomenko, S., Nieuwenhuijsen, M., Barboza, E.P., Ambròs, A., Padilla, C. M., Mueller, N., 2021. The impact of urban and transport planning on health: assessment of the attributable mortality burden in Madrid and Barcelona and its distribution by socioeconomic status. Environ. Res. 196, 110988. https://doi.org/10.1016/J.ENVRES.2021.110988.

Jolliffe, I.T., 2002. Principal component analysis. Encyclopedia of Statistics in Behavioral Science 30, second ed. https://doi.org/10.2307/1270093

Jönsson, L., 2022. The personal economic burden of dementia in Europe. Lancet Regional Health - Europe 20. https://doi.org/10.1016/j.lanepe.2022.100472.

Kohonen, T., 2013. Essentials of the self-organizing map. Neural Netw. 37. https://doi.org/10.1016/j.neunet.2012.09.018.

Kohonen, T., 2001. Self-organizing maps. Springer Inf. Sci. 30. https://doi.org/10.1007/978-3-642-56927-2.

Li, Z., Christensen, G.M., Lah, J.J., Marcus, M., Russell, A.G., Ebelt, S., Waller, L.A., Hüls, A., 2022. Neighborhood characteristics as confounders and effect modifiers for the association between air pollution exposure and subjective cognitive functioning. Environ. Res. 212, 113221. https://doi.org/10.1016/j.envres.2022.113221.

Liang, P., Li, Jiangjing, Li, Z., Wei, J., Li, Jing, Zhang, S., Xu, S., Liu, Z., Wang, J., 2024. Effect of low-frequency noise exposure on cognitive function: a systematic review and meta-analysis. BMC Public Health 24, 1–14. https://doi.org/10.1186/S12889-023-17593-5/FIGURES/6.

Lucht, S., Glaubitz, L., Moebus, S., Schramm, S., Jockwitz, C., Caspers, S., Hoffmann, B., 2022. Long-term air pollution, noise, and structural measures of the default mode network in the brain: results from the 1000BRAINS cohort. Int. J. Hyg Environ. Health 239, 113867. https://doi.org/10.1016/j.ijheh.2021.113867.

Lupien, S.J., McEwen, B.S., Gunnar, M.R., Heim, C., 2009. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat. Rev. Neurosci. 10 (6 10), 434–445. https://doi.org/10.1038/nrn2639.

Mauderly, J.L., Samet, J.M., 2009. Is there evidence for synergy among air pollutants in causing health effects? Environ. Health Perspect. 117, 1–6. https://doi.org/10.1289/EHP.11654/ASSET/A50646C7-E1EE-48B8-8A54-86EEE6CE2728/ASSETS/GRAPHIC/EHP-117-1E1.JPG.

McEwen, B.S., Tucker, P., 2011. Critical biological pathways for chronic psychosocial stress and research opportunities to advance the consideration of stress in chemical risk assessment. Am. J. Publ. Health 101, 131–139. https://doi.org/10.2105/AJPH.2011.300270.

Memmesheimer, M., Friese, E., Ebel, A., Jakobs, H.J., Feldmann, H., Kessler, C., Piekorz, G., 2004. Long-term simulations of particulate matter in Europe on different scales using sequential nesting of a regional model. Int. J. Environ. Pollut. 22, 108. https://doi.org/10.1504/IJEP.2004.005530.

Miner, P., Smith, B.M., Jani, A., McNeill, G., Gathorne-Hardy, A., 2024. Car harm: a global review of automobility's harm to people and the environment. J. Transport Geogr. 115, 103817. https://doi.org/10.1016/J.JTRANGEO.2024.103817.

Nandi, A., Counts, N., Bröker, J., Malik, S., Chen, S., Han, R., Klusty, J., Seligman, B., Tortorice, D., Vigo, D., Bloom, D.E., 2024. Cost of care for Alzheimer's disease and related dementias in the United States: 2016 to 2060. npj Aging 10 (1 10), 1–8. https://doi.org/10.1038/s41514-024-00136-6.

Nonnemacher, M., Jakobs, H., Viehmann, A., Vanberg, I., Kessler, C., Moebus, S., Möhlenkamp, S., Erbel, R., Hoffmann, B., Memmesheimer, M., 2014. Spatio-temporal modelling of residential exposure to particulate matter and gaseous pollutants for the Heinz Nixdorf recall cohort. Atmos. Environ. 91, 15–23. https://doi.org/10.1016/J.ATMOSENV.2014.03.052.

Ogurtsova, K., Soppa, V.J., Weimar, C., Jöckel, K.-H.K.-H., Jokisch, M., Hoffmann, B., 2023. Association of long-term air pollution and ambient noise with cognitive decline in the Heinz Nixdorf recall study. Environ. Pollut. 331, 121898. https://doi.org/10.1016/j.envpol.2023.121898.

Ohlwein, S., Hennig, F., Lucht, S., Matthiessen, C., Pundt, N., Moebus, S., Jöckel, K.-H., Hoffmann, B., 2019. Indoor and outdoor road traffic noise and incident diabetes mellitus: results from a longitudinal German cohort study. Environ. Epidemiol. 3, e037. https://doi.org/10.1097/EE9.0000000000000037.

Padilla, C.M., Kihal-Talantikite, W., Vieira, V.M., Rossello, P., Nir, G. Le, Zmirou-Navier, D., Deguen, S., 2014. Air quality and social deprivation in four French metropolitan areas—A localized spatio-temporal environmental inequality analysis. Environ. Res. 134, 315–324. https://doi.org/10.1016/J.ENVRES.2014.07.017.

Pearce, J.L., Waller, L.A., Chang, H.H., Klein, M., Mulholland, J.A., Sarnat, J.A., Sarnat, S.E., Strickland, M.J., Tolbert, P.E., 2014. Using self-organizing maps to develop ambient air quality classifications: a time series example. Environ. Health 13, 1–14. https://doi.org/10.1186/1476-069X-13-56/FIGURES/7.

Peeters, L., Dassargues, A., 2006. Comparison of Kohonen's self-organizing map algorithm and principal component analysis in the exploratory data analysis of a groundwater quality dataset. GeoENV2006.

Peters, R., Ee, N., Peters, J., Booth, A., Mudway, I., Anstey, K.J., 2019. Air pollution and dementia: a systematic review. J. Alzheim. Dis. 70, S145. https://doi.org/10.3233/JAD-180631.

Pickett, K.E., Pearl, M., 2001. Multilevel analyses of neighbourhood socioeconomic context and health outcomes: a critical review. J. Epidemiol. Commun. Health 55, 111–122. https://doi.org/10.1136/JECH.55.2.111, 1978.

Schmermund, A., Möhlenkamp, S., Stang, A., Grönemeyer, D., Seibel, R., Hirche, H., Mann, K., Siffert, W., Lauterbach, K., Siegrist, J., Jöckel, K.-H., Erbel, R., 2002. Assessment of clinically silent atherosclerotic disease and established and novel risk factors for predicting myocardial infarction and cardiac death in healthy middle-aged subjects: rationale and design of the Heinz Nixdorf RECALL study. Am. Heart J. 144, 212–218. https://doi.org/10.1067/mhj.2002.123579.

Song, Y., Liu, Y., Bai, X., Yu, H., 2024. Effects of neighborhood built environment on cognitive function in older adults: a systematic review. BMC Geriatr. 24, 1–28. https://doi.org/10.1186/S12877-024-04776-X/TABLES/4.

Stang, A., Moebus, S., Dragano, N., Beck, E.M., Möhlenkamp, S., Schmermund, A., Siegrist, J., Erbel, R., Jöckel, K.H., 2005. Baseline recruitment and analyses of nonresponse of the Heinz Nixdorf recall study: identifiability of phone numbers as the major determinant of response. Eur. J. Epidemiol. 20 (6 20), 489–496. https://doi.org/10.1007/S10654-005-5529-Z.

Thangavel, P., Park, D., Lee, Y.C., 2022. Recent insights into particulate matter (PM2.5)-mediated toxicity in humans: an overview. Int. J. Environ. Res. Publ. Health 19. https://doi.org/10.3390/IJERPH19127511. Page 7511 19, 7511.

Thompson, R., Smith, R.B., Bou Karim, Y., Shen, C., Drummond, K., Teng, C., Toledano, M.B., 2022. Noise pollution and human cognition: an updated systematic review and meta-analysis of recent evidence. Environ. Int. 158, 106905. https://doi.org/10.1016/J.ENVINT.2021.106905.

Thompson, R., Smith, R.B., Karim, Y.B., Shen, C., Drummond, K., Teng, C., Toledano, M. B., 2023. Air pollution and human cognition: a systematic review and meta-analysis. Sci. Total Environ. 859, 160234. https://doi.org/10.1016/J.SCITOTENV.2022.160234.

Tzivian, L., Dlugaj, M., Winkler, A., Hennig, F., Fuks, K., Sugiri, D., Schikowski, T., Jakobs, H., Erbel, R., Jöckel, K.H., Moebus, S., Hoffmann, B., Weimar, C., 2016a. Long-term air pollution and traffic noise exposures and cognitive function:a cross-sectional analysis of the Heinz Nixdorf recall study. J. Toxicol. Environ. Health A Curr. Issues 79, 1057–1069. https://doi.org/10.1080/15287394.2016.1219570.

Tzivian, L., Dlugaj, M., Winkler, A., Weinmayr, G., Hennig, F., Fuks, K.B., Vossoughi, M., Schikowski, T., Weimar, C., Erbel, R., Jöckel, K.H., Moebus, S., Hoffmann, B., 2016b. 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, 1361–1368. https://doi.org/10.1289/ehp.1509824.

Tzivian, L., Jokisch, M., Winkler, A., Weimar, C., Hennig, F., Sugiri, D., Soppa, V.J., Dragano, N., Erbel, R., Jöckel, K.-H., Moebus, S., Hoffmann, B., 2017. Associations of long-term exposure to air pollution and road traffic noise with cognitive function—An analysis of effect measure modification. Environ. Int. 103, 30–38. https://doi.org/10.1016/j.envint.2017.03.018.

Tzivian, L., Winkler, A., Dlugaj, M., Schikowski, T., Vossoughi, M., Fuks, K., Weinmayr, G., Hoffmann, B., 2015. Effect of long-term outdoor air pollution and noise on cognitive and psychological functions in adults. Int. J. Hyg Environ. Health 218, 1–11. https://doi.org/10.1016/j.ijheh.2014.08.002.

Vesanto, J., Alhoniemi, E., 2000. Clustering of the self-organizing map. IEEE Trans. Neural Network. 11, 586–600. https://doi.org/10.1109/72.846731.

von Lindern, E., Hartig, T., Lercher, P., 2016. Traffic-related exposures, constrained restoration, and health in the residential context. Health Place 39, 92–100. https://doi.org/10.1016/J.HEALTHPLACE.2015.12.003.

Wang, J., Li, T., Lv, Y., Kraus, V.B., Zhang, Y., Mao, C., Yin, Z., Shi, W., Zhou, J., Zheng, T., Kinney, P.L., Ji, J., Tang, S., Shi, X., 2020. Fine particulate matter and poor cognitive function among Chinese older adults: evidence from a community-based, 12-Year prospective cohort study. Environ. Health Perspect. 128, 1–9. https://doi.org/10.1289/EHP5304.

Wege, N., Dlugaj, M., Siegrist, J., Dragano, N., Erbel, R., Jöckel, K.H., Moebus, S., Weimar, C., 2011. Population-based distribution and psychometric properties of a short cognitive performance measure in the population-based Heinz Nixdorf recall study. Neuroepidemiology 37, 13–20. https://doi.org/10.1159/000328262.

Weuve, J., Bennett, E.E., Ranker, L., Gianattasio, K.Z., Pedde, M., Adar, S.D., Yanosky, J. D., Power, M.C., 2021a. Exposure to air pollution in relation to risk of dementia and related outcomes: an updated systematic review of the epidemiological literature. Environ. Health Perspect. 129. https://doi.org/10.1289/EHP8716.

Weuve, J., D'Souza, J., Beck, T., Evans, D.A., Kaufman, J.D., Rajan, K.B., de Leon, C.F.M. M., Adar, S.D., 2021b. Long-term community noise exposure in relation to dementia, cognition, and cognitive decline in older adults. Alzheimer's Dementia 17, 525–533. https://doi.org/10.1002/alz.12191.

Wilker, E.H., Osman, M., Weisskopf, M.G., 2023. Ambient air pollution and clinical dementia: systematic review and meta-analysis. BMJ 381, e071620. https://doi.org/10.1136/bmj-2022-071620.

Wimo, A., Seeher, K., Cataldi, R., Cyhlarova, E., Dielemann, J.L., Frisell, O., Guerchet, M., Jönsson, L., Malaha, A.K., Nichols, E., Pedroza, P., Prince, M., Knapp, M., Dua, T., 2023. The worldwide costs of dementia in 2019. Alzheimer's Dementia 19, 2865–2873. https://doi.org/10.1002/alz.12901.

Wing, J.J., Sánchez, B.N., Adar, S.D., Meurer, W.J., Morgenstern, L.B., Smith, M.A., Lisabeth, L.D., 2017. Synergism of short-term air pollution exposures and neighborhood disadvantage on initial stroke severity. Stroke 48, 3126–3129. https://doi.org/10.1161/STROKEAHA.117.018816.

Winkler, G., Döring, A., 1998. Validation of a short qualitative food frequency list used in several German large scale surveys. Z. Ernahrungswiss. 37, 234–241. https://doi.org/10.1007/PL00007377.

World Health Organization, Organization, W.H., 2021. WHO global air quality guidelines: particulate matter (PM2.5 and PM10), ozone, nitrogen dioxide. Sulfur Dioxide and Carbon Monoxide. World Health Organization, Geneva PP - Geneva.

Wu, Y.T., Prina, A.M., Brayne, C., 2015. The association between community environment and cognitive function: a systematic review. Soc. Psychiatr. Psychiatr. Epidemiol. 50, 351–362. https://doi.org/10.1007/S00127-014-0945-6.

Yan, Y., Lin, J., Pozzer, A., Kong, S., Lelieveld, J., 2019. Trend reversal from high-to-low and from rural-to-urban ozone concentrations over Europe. Atmos. Environ. 213, 25–36. https://doi.org/10.1016/J.ATMOSENV.2019.05.067.

Zare Sakhvidi, M.J., Yang, J., Lequy, E., Chen, J., de Hoogh, K., Letellier, N., Mortamais, M., Ozguler, A., Vienneau, D., Zins, M., Goldberg, M., Berr, C., Jacquemin, B., 2022. Outdoor air pollution exposure and cognitive performance: findings from the enrolment phase of the CONSTANCES cohort. Lancet Planet. Health 6, e219–e229. https://doi.org/10.1016/S2542-5196(22)00001-8.

Zhao, Y.-L., Qu, Y., Ou, Y.-N., Zhang, Y.-R., Tan, L., Yu, J.-T., 2021. Environmental factors and risks of cognitive impairment and dementia: a systematic review and meta-analysis. Ageing Res. Rev. 72, 101504. https://doi.org/10.1016/j.arr.2021.101504.