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Long-term exposure to traffic-related air pollution is associated with impaired odor identification: Results from the population-based KORA FIT study in Augsburg, Germany

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ABSTRACT

Ambient air pollution has been linked to neurodegenerative diseases. Nevertheless, the literature on the effects of air pollution on the olfactory system and early cognitive impairment is scarce. In this study, we investigated the association between long-term air pollution exposure and odor identification, which can serve as an early indicator of various neurodegenerative conditions. We used data collected in Augsburg, Germany in 2018–2019 for the population-based KORA FIT study of 3,059 participants born between 1945–1964. The Sniffin' Sticks 12-Item Test was used to assess each participant's odor identification. Air pollution concentrations at residential addresses were estimated using land use regression modeling. We dichotomized the odor identification score to normosmia (score $\geq$ 10) versus hyposmia (score $<$ 7) or anosmia (score $<$ 10) and applied logistic regression. The models were adjusted for age, sex, socioeconomic characteristics (education, income, socioeconomic status), lifestyle factors (physical activity, smoking, body mass index, alcohol consumption) and disease history (e.g., allergies). We observed increased odds of hyposmia or anosmia compared to normosmia per interquartile range increase in the concentrations of PNC, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2 and NO_x [OR (95 % CI): 1.12 (1.02, 1.24), 1.10 (0.98, 1.25), 1.14 (1.00, 1.30), 1.20 (1.06, 1.35), 1.20 (1.06, 1.36), 1.20 (1.06, 1.37) and 1.13 (1.01, 1.27); respectively]. For O_3, no clear effects were detected. Females and physically active people appeared to be more susceptible. No further significant indications of effect modification were found. The results were consistent across sensitivity analyses. This study provides robust evidence for an association between long-term exposure to traffic-related air pollution and poor odor identification, even in a region with relatively low air pollution levels. These findings suggest a potential link between prolonged air pollution exposure and early changes in the olfactory system and could be indicative of early signs of detrimental effects on the brain.

1. Introduction

Air pollution is one of the greatest environmental risks to human health and poses a major challenge both globally and locally for communities. It is the second highest risk factor for mortality (Health Effects Institute, 2024) and a major contributor to the attributable disability-adjusted life years (Murray, 2024). Air pollution has been extensively associated with various health problems, including cardio-metabolic (Wolf et al., 2021; Guo et al., 2022), respiratory (Park et al., 2021), and neurological (Kim et al., 2020) diseases, disproportionately affecting vulnerable sub-populations such as the elderly, children, and people with pre-existing cardiovascular disease or lower socioeconomic status (SES) (Tibuakuu et al., 2018).

Odor identification refers to our ability to identify and recall known, previously experienced smells (Murphy, 2019), and it relies on our executive (Westervelt et al., 2005) and semantic (Larsson et al., 2000) memory, going beyond mere sensory detection. Impaired olfaction entails severe risks and negatively impacts health (Devanand et al., 2015)

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and well-being (Croy et al., 2014). Low scores can be associated with cognitive impairment (Dintica et al., 2019) and serve as an early indicator of several neurodegenerative conditions (Marin et al., 2018), such as Parkinson's and Alzheimer's disease (Doty and Kamath, 2014).

Air pollution can harm our olfactory and brain health through various pathways, as described in previous studies (Ajmani et al., 2016; Shehab et al., 2024). Briefly, the olfactory mucosa is directly and constantly exposed to the external environment and houses olfactory neurons that interact with harmful air pollutants. These pollutants can penetrate the protective blood–brain barrier by either compromising the olfactory barrier or traveling via axonal transport to the olfactory bulb (Merz, 2021). For example, there is evidence that fine particles ($PM_{2.5}$, particulate matter with an aerodynamic diameter of 2.5 μm or less) accumulate in the olfactory bulb causing local inflammation (Ajmani et al., 2016). Additionally, ultrafine particles (UFP, particulate matter with an aerodynamic diameter of 100 nm or less) and other $PM_{2.5}$ constituents can move along the olfactory nerve and travel from various organs to the brain's vasculature, triggering inflammatory responses and contributing to neuronal damage (Peters, 2023).

Despite increasing interest in the effects of air pollution on the olfactory system and early cognitive impairment, significant uncertainties and gaps remain in the literature. Existing studies focus on a limited and specific range of air pollutants, primarily $PM_{2.5}$ and nitrogen dioxide (NO_2) (Adams et al., 2016; Ekström et al., 2022; Cao et al., 2023; Ajmani et al., 2016; Zhang et al., 2021; Andersson et al., 2022), with only one study addressing particulate matter with an aerodynamic diameter of 10 μm or less (PM_{10}) (Scussiatto et al., 2023). There is a complete lack of research on UFP or particle number concentration (PNC) which is often used as a proxy for UFP, particulate matter with aerodynamic diameter between 2.5 μm and 10 μm (PM_{coarse}), $PM_{2.5}$ absorbance ($PM_{2.5abs}$), and ozone (O_3). Previous studies have also had limitations in their exposure measurement and design, such as relying on weather station data (Adams et al., 2016) or indirect methods for assessing exposure to air pollution (Ranft et al., 2009), small sample sizes, and using ecological study designs (Guarneros et al., 2009; Hudson et al., 2006). Additionally, previous studies have had strong potential for significant confounding (such as by age, sex, smoking, alcohol and residential characteristics) and challenges in establishing statistically significant associations due to constraints inherent in their data sources (Shehab et al., 2024).

We examined long-term associations between various air pollutants and odor identification using cross-sectional data from a population-based cohort in Augsburg, Germany. We hypothesized that prolonged residential air pollution exposure would be negatively associated with odor identification, an indicator of worse olfactory function and an early sign of impacts on the brain. To examine vulnerable sub-populations, we further evaluated several participant characteristics as effect modifiers.

2. Methods

2.1. Study population

Health and individual data were retrieved from the Cooperative Health Research in the Region of Augsburg (KORA) study in Southern Germany, a population-based cohort in the region of Augsburg which consists of the city of Augsburg and two adjacent districts (Fig. S1). KORA is a regional research platform for population-based studies, consisting of four cross-sectional baseline surveys (in 1984/1985, 1989/1990, 1994/1995, and 1999/2001). Details of the design of the KORA cohort study can be found elsewhere (Holle et al., 2005). We specifically used data from KORA FIT (2018/2019), which is a follow-up examination of all participants who participated in the four initial KORA baseline surveys. The KORA FIT follow-up study was conducted from 22.01.2018 to 29.06.2019, covering the period from the first participant's examination to the last participant's examination. All living participants born between 1945 and 1964 that had provided informed consent to be contacted again were invited for a re-examination (n = 3,059 or 64.4 % of all eligible persons). KORA FIT participants underwent thorough, standardized physical examinations and completed in-person interviews (Rooney et al., 2022).

The study methods were approved by the Ethics Committees of the Bavarian Chamber of Physicians (KORA-Fit EC No 17040).

2.2. Outcome measurement

Odor identification was evaluated using the Sniffin' Sticks 12-Item Test (SST-12 Item Test, Burghart Messtechnik, Germany), a well-established and validated olfactory assessment tool (Hummel et al., 2001). Each participant was sequentially presented with 12 pens containing everyday odors one at a time and tasked with identifying the correct odor from the four options provided (Table S1). The SST-12 Item Test toolkit included the following odors: peppermint, fish, coffee, banana, orange, rose, lemon, pineapple, cinnamon, cloves, leather, and licorice. The odor identification score was calculated as the total number of correct responses out of the 12 pens. This score was then dichotomized into 1) normal olfactory ability (normosmia), defined as a score of 10 or higher, and 2) limited olfactory ability (hyposmia) or lack of olfactory ability (anosmia), defined as a score below 10 (Cao et al., 2023; Hummel et al., 2001; Stogbauer et al., 2020).

2.3. Exposure assessment

Annual mean concentrations of air pollutants were estimated through land use regression (LUR) models using data from a 2014–2015 measurement campaign of 20 air pollution monitoring stations in the Augsburg region. These estimates were mapped in a 50 × 50 m grid and then assigned to the geocoded residential addresses of the KORA participants. These air pollutants included PNC ($10^3/cm^3$), $PM_{2.5}$ ($\mu g/m^3$), $PM_{2.5abs}$ ($10^{-5}/m$) (a surrogate for black carbon linked to vehicle emissions), PM_{coarse} ($\mu g/m^3$), PM_{10} ($\mu g/m^3$), nitrogen oxides (NO_2, NO_x) ($\mu g/m^3$), and O_3 ($\mu g/m^3$). Key methodological details on measurement standards, monitoring tools, and missing data handling can be found in the Supplementary material (Supplementary materials M1). The LUR models performed well, with adjusted leave-one-out cross-validation R^2 of 0.55 (PM_{coarse}), 0.69 ($PM_{2.5}$), 0.76 (PM_{10}), 0.81 (O_3), 0.82 (NO_x), 0.82 (PNC), 0.83 ($PM_{2.5abs}$), and 0.89 (NO_2). Further information about the modeling approach and the models' performance can be found elsewhere (Wolf et al., 2017).

2.4. Confounders and effect modifiers

We used data on participants' demographics including age (years) and sex (female/male); socioeconomic features including education (years), monthly income (€), and socioeconomic status (SES, measured by the Helmert Index (Helmert and Shea, 1994), with a range from 1 to 27, where lower scores indicate lower SES); lifestyle factors including physical activity (active or inactive), smoking status (current, ex-, and never smokers – Table S2), body mass index (BMI, kg/m^2), and alcohol consumption (grams per day – Table S2); and chronic diseases including diabetes (yes or no), asthma (yes or no), chronic obstructive pulmonary disease (COPD, yes or no), hay fever (yes or no), allergies (yes or no), and hypertension (yes or no). In addition, we used residential information, including an indicator for urbanization, so whether the participant resides in Augsburg city or in a surrounding district (©GeoBasis-DE/BKG [2019]), a satellite-based index for greenness (normalized difference vegetation index [NDVI], 0 to 1) (Dandolo et al., 2022), and yearly mean air temperature values (°C) provided by a high-resolution multi-stage regression-based modeling approach (Nikolaou et al., 2023). A concise summary with key details on NDVI and mean air temperature estimations is provided in the Supplementary material (Supplementary materials M2). Additionally, we used data on each participant's subjective self-reported odor identification ability. Each

participant selected the most accurate response for themselves from the following options: I have a very good sense of smell, I cannot smell everything, sometimes I cannot smell something that other people can smell, or I have a very bad sense of smell. We then dichotomized these responses into 1) having a very good sense of smell versus 2) not. All these variables served as either confounders or effect modifiers in our analysis.

2.5. Statistical analysis

We calculated means and standard deviations (SD) for continuous health and individual characteristics and residential exposure features, and absolute numbers and percentages for categorical variables. To assess differences between normosmic and hyposmic or anosmic participants, a two-sample *t*-test was used for continuous variables, a Wilcoxon rank-sum test if the distribution was deviating from normal, and a Chi-square test of independence for categorical variables. We present various statistics for air pollution levels: means and SDs, minimum–maximum ranges, and interquartile ranges (IQR). Spearman's correlation coefficient was used to evaluate the correlations between air pollutants.

We used logistic regression to examine the associations between long-term air pollution exposure and odor identification. Selected covariates were added stepwise to the model. The minimum model included basic demographics (sex and age). The main model additionally included socioeconomic features (education, income, and SES) and lifestyle factors (physical activity, smoking status, BMI, and alcohol consumption). Finally, the extended model also included chronic diseases (diabetes, asthma, COPD, hay fever, allergies, and hypertension).

Two-pollutant models were used to evaluate the independent effects of each exposure. Using the main model structure, we ran two-pollutant models for all combinations of air pollutants with a Spearman correlation coefficient less than or equal to 0.7.

We examined several potential effect modifiers: sex (female vs. male), age ($<$ vs. $\geq$ 65 years old), physical activity (inactive vs. active), smoking status (never or ex- vs. current smokers), BMI (non-obese vs. obese, i.e., BMI $\geq$ 30 kg/m^2), subjective odor identification ability (very good sense of smell vs. not), indicator for city vs. district, greenness ($<$ vs. $\geq$ 0.5), and mean air temperature ($<$ first quartile Q1 vs. Q1 $-$ Q3 vs. $>$ third quartile Q3).

To evaluate the robustness of our results, we conducted several sensitivity analyses: 1) Categorizing the odor identification score differently: $\leq$ 9 for hyposmia or anosmia and $>$ 10 for normosmia, effectively excluding a score of 10, which was previously classified under normosmia. This approach accounted for an ongoing debate about whether a score of 10 should be included in the dichotomization and specifically in normosmic subjects (Vandersteen et al., 2022). 2) Excluding subjects who reported having a stuffy nose, in two levels. Stuffy nose information derived from the question "How freely are you breathing through your nose at the moment?" with a response scale of 1–10 (10 to be completely free) dichotomized into yes or no. We considered participants to have a stuffy nose (yes) in two scenarios, with a stuffy nose being defined as a score less than 8 and also as a score less than 5. 3) Conducting a Bayesian information criterion (BIC) selection for the covariates, evaluating all possible combinations.

Results are presented as Odds Ratios (OR) of hyposmia or anosmia vs. normosmia together with their corresponding 95 % Confidence Intervals (95 % CI) per IQR increase of each air pollutant. Analysis was conducted in R 4.3.0 (R Core Team, 2023) and package mgcv (Wood, 2017). Statistical significance was determined by two-sided p-values $<$ 0.05.

3. Results

3.1. Study population and air pollutants

The flowchart of the study population is shown in Fig. S2. The minimum model includes 2,943 participants. For the main model, participants with missing values in at least one of the selected covariates (age, sex, education, income, SES, physical activity, smoking status, BMI, alcohol consumption, diabetes, asthma, COPD, hay fever, allergies, and hypertension; n = 237 and n = 390 for the main and extended models, respectively) were excluded, leaving the main model with 2,706 participants and the extended model with 2,553 participants.

The continuous odor identification score as initially retrieved by the SST-12 test had a mean of 10.08 with an SD of 1.6 (Table 1) and was left-skewed (Fig. S3). After dichotomizing, the binary odor identification score categorized 2,143 subjects as normosmic and 800 as hyposmic or anosmic (Table 1 and Fig. S3).

The study population and air pollutants are described based on the sample size of the minimum model in Table 1 (N = 2,943). The sex distribution was balanced, with 54.1 % female participants. Participants had a mean examination age of 63.1 years. Over one third (37.1 %) of the study population was located in the city of Augsburg. Sex, income, allergies, hypertension, stuffy nose, subjective odor identification ability and indicator for city vs. district were statistically significantly different between normosmic and hyposmic or anosmic people (Table 1). The yearly mean concentrations of $PM_{2.5}$ (11.6 μg/m^3), PM_{10} (16.3 μg/m^3), and NO_2 (13.6 μg/m^3), were below the current limits set by the European Union air quality standards (UNION P., 2008) but exceeded the latest guidelines established by the World Health Organization (WHO) (World Health Organization., 2021) (Table 2). The hyposmic or anosmic group had statistically significantly higher yearly mean levels of air pollution in comparison with the normosmic group for all air pollutants except O_3 (Table S3). Moderate to strong correlations were observed among the air pollutants, excluding O_3 (Table 2).

3.2. Air pollution and odor identification

Higher levels of air pollution were found to be associated with worse odor identification for all air pollutants (PNC, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2, NO_x) except O_3 across all models (minimum, main, and extended). Most of these associations (PNC, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2, NO_x) remained statistically significant throughout all three models, while the association for $PM_{2.5}$ persisted only for the minimum model. More specifically, as demonstrated in Fig. 1 and Table S4, we observed increased odds of hyposmia or anosmia compared to normosmia per IQR increase in the yearly mean concentrations of PNC, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2, and NO_x [main model: OR (95 % CI): 1.12 (1.02, 1.24), 1.10 (0.98, 1.25), 1.14 (1.00, 1.3), 1.20 (1.06, 1.35), 1.20 (1.06, 1.36), 1.20 (1.06, 1.37) and 1.13 (1.01, 1.27); respectively]. For O_3, no clear effects were detected.

3.2.1. Two-pollutant models

The results of the two-pollutant models are presented in Fig. 2 and Table S5. After adjusting for NO_2, the effect of PM_{10} was no longer statistically significant, and vice versa. No other differences were observed.

3.2.2. Effect modification

We did not observe statistically significant changes in the associations between air pollution and odor identification when testing for effect modification in most cases (Fig. 3 and Tables S6-S14). Females appeared more vulnerable than males, particularly for PNC, $PM_{2.5abs}$, PM_{10}, and NO_x, where the OR (95 % CI) were 1.24 (1.07, 1.44), 1.28 (1.05, 1.56), 1.34 (1.12, 1.61), and 1.26 (1.07, 1.49), respectively in females, compared to 1.02 (0.89, 1.16), 1.01 (0.84, 1.21), 1.07 (0.91, 1.26), and 1.01 (0.87, 1.18), respectively in males, with p-interaction =

Table 1
Descriptive statistics of participant characteristics in the KORA FIT cohort study (N = 2,943).

Variable category	Variable	Mean ± SD / N (%)			Missings	P-value
		Hyposmia or anosmia (N = 800)	Normosmia (N = 2,143)	Total (N = 2,943)		
Demographic	Sex (female)	379 (47.4)	1,214 (56.6)	1,593 (54.1)	–	< 0.001
	Age (years)	64.6 ± 5.4	62.6 ± 5.4	63.1 ± 5.5	–	0.064
Lifestyle	Education (years)	11.9 ± 2.6	12.0 ± 2.6	12 ± 2.6	–	0.120
	Alcohol (g/day)	15.7 ± 20.8	14.4 ± 18.8	14.7 ± 19.4	2	0.226
	BMI (kg/m^2)	28.2 ± 5.4	28.1 ± 5.3	28.2 ± 5.3	2	0.070
	Smoking status				2	0.584
	Current smoker	121 (15.1)	302 (14.1)	423 (14.4)		
	Former smoker	318 (39.8)	894 (41.7)	1,212 (41.2)		
	Never smoker	360 (45.0)	946 (44.1)	1,306 (44.4)		
	Physical activity (active)	568 (71.0)	1,557 (72.7)	2,125 (72.2)	–	0.729
Socioeconomic	Social class (1 to 27)	14.4 ± 5.0	15.0 ± 5.0	14.9 ± 5.0	15	0.240
	Income (€)	1,631 ± 838.9	1,769 ± 863.5	1,731 ± 858.9	236	< 0.001
Medical	Allergies (yes)	229 (28.6)	699 (32.6)	928 (31.5)	79	0.048
	COPD (yes)	25 (3.1)	49 (2.3)	74 (2.5)	62	0.236
	Asthma (yes)	66 (8.3)	161 (7.5)	227 (7.7)	70	0.506
	Hay fever (yes)	118 (14.8)	382 (17.8)	500 (17.0)	55	0.057
	Diabetes (yes)	75 (9.4)	159 (7.4)	234 (8.0)	4	0.098
	Hypertension (yes)	435 (54.4)	1,027 (47.9)	1,462 (49.7)	8	0.002
	Stuffy nose (yes)					
	Cut-off 8	300 (37.5)	672 (31.6)	972 (33.0)	–	< 0.001
	Cut-off 5	40 (5.0)	102 (4.8)	142 (4.8)	–	0.862
	Subjective odor identification ability (very good)	359 (44.9)	1,323 (61.7)	1,681 (57.1)	1	< 0.001
Residential	Indicator for city versus district (city)	331 (41.3)	763 (35.6)	1,094 (37.1)	–	0.005
	Mean air temperature (°C)	9.9 ± 0.4	9.8 ± 0.3	9.8 ± 0.4	168	0.058
	NDVI (0 to 1)	0.45 (0.09)	0.46 (0.09)	0.46 (0.09)	–	0.006
Outcome	Odor identification (0 to 12)	–	–	10.08 (1.6)	–	–

Hyposmia or anosmia: odor identification score < 10; normosmia: odor identification score ≥ 10; Differences between normosmic versus hyposmic or anosmic were quantified by two-sample *t*-test or Wilcoxon test, if not normally distributed, and Chi^2 test, respectively; SD = standard deviation; The numbers in brackets represent percentages, while the ± values indicate SD; BMI = body mass index; NDVI = normalized difference vegetation index.

Table 2
Descriptive statistics for the annual average air pollution concentrations at the residential locations of the KORA FIT participants (N = 2,943).

Air pollutant	Mean ± SD	Range	IQR	Spearman correlation coefficients							
				PNC	$PM_{2.5}$	$PM_{2.5abs}$	PM_{coarse}	PM_{10}	NO_2	NO_x	O_3
PNC (10^3/cm^3)	7.0 ± 1.7	3.0–13.7	1.9	1							
$PM_{2.5}$ (μg/m^3)	11.6 ± 1.0	7.8–14.2	1.4	0.72	1						
$PM_{2.5abs}$ (10^{-5}/m)	1.2 ± 0.2	0.7–1.7	0.3	0.77	0.69	1					
PM_{coarse} (μg/m^3)	4.8 ± 1.1	2.5–8.2	1.4	0.74	0.59	0.81	1				
PM_{10} (μg/m^3)	16.3 ± 1.4	12.9–22.0	2.0	0.82	0.60	0.77	0.79	1			
NO_2 (μg/m^3)	13.6 ± 4.2	6.9–28.3	6.3	0.77	0.77	0.85	0.81	0.70	1		
NO_x (μg/m^3)	21.3 ± 6.7	3.9–44.0	8.7	0.91	0.80	0.74	0.72	0.74	0.85	1	
O_3 (μg/m^3)	39.1 ± 2.3	31.7–45.7	3.5	−0.07	−0.23	−0.08	0.16	0.06	−0.18	−0.14	1

SD = standard deviation; The ± values indicate SD; IQR = interquartile range; PNC = particle number concentration; $PM_{2.5}$ = particulate matter (PM) with an aerodynamic diameter less than 2.5 μm; $PM_{2.5abs}$ = $PM_{2.5}$ absorbance; PM_{coarse} = PM between 2.5 and 10 μm; PM_{10} = PM with an aerodynamic diameter less than 10 μm; NO_2 = nitrogen dioxide; NO_x = nitrogen oxides; O_3 = ozone.

0.05, 0.07, 0.09, and 0.04, respectively (Table S6). Similarly, physically active individuals showed stronger associations than the inactive ones, for example for PNC, $PM_{2.5abs}$, and NO_x [OR (95 % CI): 1.18 (1.04, 1.33) vs. 0.99 (0.83, 1.19), 1.19 (1.01, 1.39) vs. 1.01 (0.79, 1.30), and 1.19 (1.04, 1.36) vs 1.00 (0.81, 1.23)] (Table S8). Additionally, smokers tended to have consistently higher ORs compared to non-smokers, with the strongest difference observed for $PM_{2.5abs}$, where smokers had OR (95 % CI) of 1.31 (0.92, 1.87) vs. 1.10 (0.95, 1.27) in non-smokers (Table S9). High levels of air pollution did impact individuals who perceived their odor identification ability as very good more than those who did not. The strongest differences were observed for $PM_{2.5abs}$ and NO_2 [OR (95 % CI): 1.29 (1.06, 1.56) vs. 0.99 (0.82, 1.20), p-interaction = 0.05, and 1.36 (1.12, 1.64) vs. 1.06 (0.89, 1.27), p-interaction = 0.08, respectively] (Table S11).

3.2.3. Sensitivity analysis

By excluding scores of 10 from the normosmic category, 795 individuals were dropped for each model. The results were consistent with those from the main analysis (Fig. S4 and Table S15). Additionally, excluding participants with a stuffy nose resulted in the removal of 972 and 142 subjects for the cut-offs of 8 and 5, respectively. The results from this sensitivity test were largely consistent with the main analysis, except for the OR for $PM_{2.5}$, which became statistically significant for participants with almost completely clear noses (Fig. S5 and Table S16). The BIC-based selection resulted in a model only adjusting for age, sex, and SES, yet the results remained consistent with the main analysis (Fig. S6).

4. Discussion

The present study investigated associations between long-term exposure to a wide spectrum of dominant air pollutants and odor identification, an indicator of olfactory and early cognitive impairment. We used cross-sectional data from 2,943 middle-aged to older

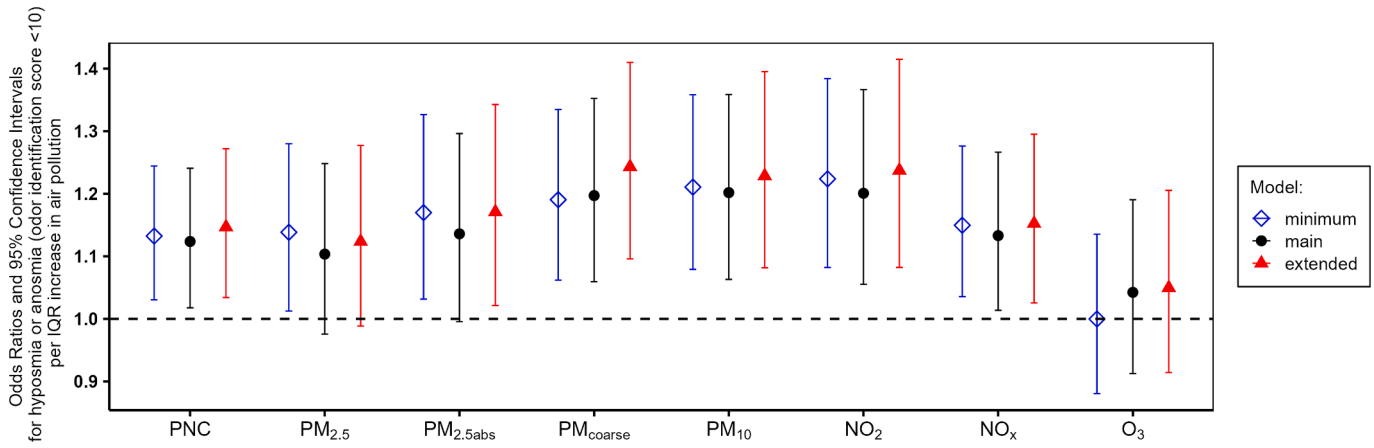

Fig. 1. Associations between various air pollutants and odor identification; Odds Ratios are presented for hyposmia or anosmia (odor identification score < 10) vs. normosmia (odor identification score ≥ 10) per interquartile range (IQR) increase in each air pollutant (PNC, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2, NO_x and O_3); Error bars present 95 % Confidence Intervals; Minimum model: each pollutant, sex and age; Main model: minimum model, education, income, socioeconomic status, physical activity, smoking status, body mass index and alcohol consumption; Extended model: main model, diabetes, asthma, chronic obstructive pulmonary disease, hay fever, allergies and hypertension; PNC = particle number concentration; $PM_{2.5}$ = particulate matter (PM) with an aerodynamic diameter less than 2.5 μm; $PM_{2.5abs}$ = $PM_{2.5}$ absorbance; PM_{coarse} = PM between 2.5 and 10 μm; PM_{10} = PM with an aerodynamic diameter less than 10 μm; NO_2 = nitrogen dioxide; NO_x = nitrogen oxides; O_3 = ozone.

individuals who participated in a population-based cohort in Augsburg, Germany. We observed that long-term exposure to higher air pollution levels was associated with impaired odor identification, and the findings were robust in sensitivity analyses. We observed strong associations for traffic-related pollutants such as NO_2, PNC, and $PM_{2.5abs}$. Females and physically active people were found to be more susceptible to this negative air pollution impact on odor identification.

To our knowledge, our study is the first to explore the association between long-term exposure to such a broad range of air pollutants and odor identification, including air pollutants such as PNC, $PM_{2.5abs}$ and PM_{coarse}, utilizing a comprehensive, population-based cohort dataset. Moreover, this study is the first to report statistically significant associations between impaired odor identification and PNC, $PM_{2.5abs}$, and PM_{coarse}.

Air pollution, even at relatively low levels like those in the Augsburg region of southern Germany, was shown to be adversely linked with odor identification. While Germany's air quality is generally considered good, it still falls short of the more stringent 2021 air quality guidelines set by the WHO, which recommends annual average levels of no more than 5 $\mu g/m^3$ for $PM_{2.5}$, 15 $\mu g/m^3$ for PM_{10}, and 10 $\mu g/m^3$ for NO_2 (World Health Organization., 2021). Currently, there are no established thresholds for UFP. Our research demonstrated that prolonged exposure to these air pollutants, even at concentrations below the European Union guideline thresholds, is associated with poor odor identification, so problematic olfaction and indicative of early impairments in brain function. This underscores the need for more rigorous air quality standards to protect public health.

Traffic-related air pollution has a key role. Shi et al. found a strong statistical link between annual $PM_{2.5}$ levels from traffic and fossil fuel combustion and the incidence of dementia (Shi et al., 2023). $PM_{2.5}$ particles, ranging down to nanometers in size, are influenced by fuel type, the chemical reactions that occur during formation, and absorbed substances. For example, black carbon, which is a primary UFP from combustion, can grow into larger fine particles over time (Peters, 2023). Additionally, there are secondary components such as sulfates, nitrates, and ammonium which are formed from gaseous precursors and which indicate aged and combustion-related $PM_{2.5}$. While these secondary components are less toxic, they are still associated with various health risks (Peters, 2023).

Odor identification is a well-established early marker of cognitive decline and various neurodegenerative disorders, making it a critical tool of extensive scientific investigation (Adams et al., 2016; Ekström et al., 2022; Cao et al., 2023; Ajmani et al., 2016; Andersson et al., 2022; Scussiatto et al., 2023). Despite its importance, other key components of olfactory testing such as odor threshold (the lowest concentration of a particular odor that one can detect) and odor discrimination (the ability to identify the unique odor among three options) (Hummel et al., 1997) are often overlooked in research (Shehab et al., 2024), mostly due to practical considerations such as examination time constraints. When combined with odor identification, these tests form a comprehensive score known as the threshold-discrimination-identification score (Trentin et al., 2022). Inclusion of all three tests in new cohort studies and follow-ups of existing studies would enhance the comprehensiveness of olfactory assessment and provide a more holistic measure of early cognitive decline for future research.

Impaired olfactory function, particularly the sense of smell which is closely connected to brain areas such as the hippocampus (Dhilla Albers et al., 2016), assessed through standardized tests, has been widely acknowledged as a potential early marker of cognitive impairment (Dintica et al., 2019; Tian et al., 2023; Tahmasebi et al., 2020), and a significant predictor of conditions such as Alzheimer's disease (Devanand, 2016; Wilson et al., 2009). Moreover, there is evidence of a harmful impact of air pollution on cognitive health (Schikowski and Altuğ, 2020) with studies linking long-term exposure to $PM_{2.5}$ and NO_2 with an increased risk for neuroinflammation, oxidative stress, and subsequent cognitive dysfunction (Power et al., 2016). Thus, existing evidence suggests that both reduced olfactory function and air pollution exposure serve as critical predictors of cognitive impairment.

Our olfactory system is directly and consistently exposed to air pollution. Particles, such as $PM_{2.5}$, accumulate in the olfactory bulb, causing local inflammation (Ajmani et al., 2016). UFP and $PM_{2.5}$ constituents are also able to travel to the brain's vasculature, triggering inflammatory responses and contributing to neuronal damage (Peters, 2023). UFP is particularly important. Given their size (equal to or less than 100 nm), they can translocate along the olfactory nerve to reach the olfactory region of the brain (Peters, 2023), and it is more plausible that they can directly penetrate the blood–brain barrier instead of working through systemic inflammation to neuronal inflammation (Oberdörster et al., 2004). Additionally, smaller particle sizes are linked with higher levels of oxidative stress (Underwood, 2017).

However, there is a lack of evidence clarifying or suggesting mechanisms underlying our findings in females and physically active

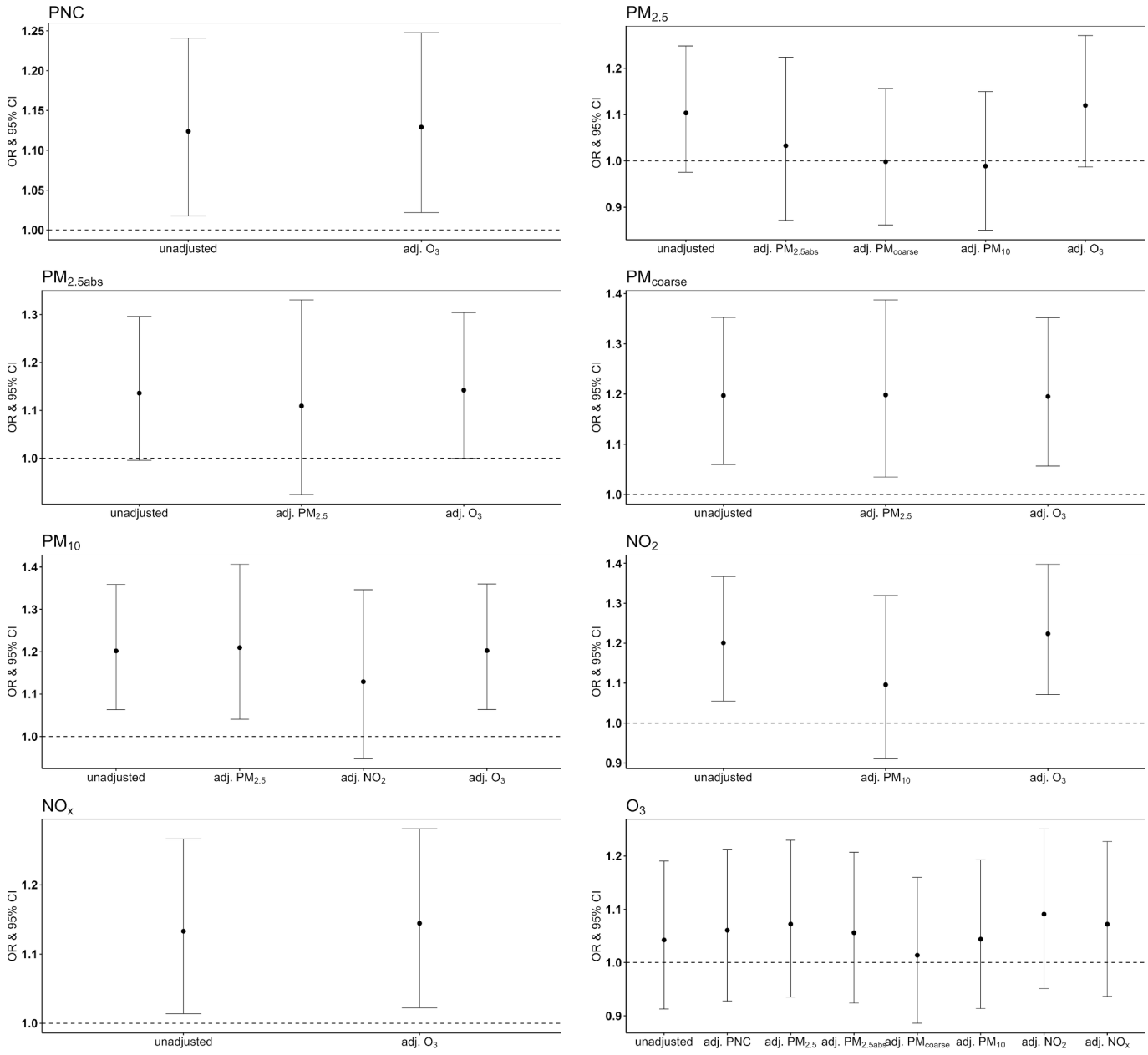

Fig. 2. Associations between selected air pollutants and odor identification for single-exposure main model and two-exposure main model; Odds Ratios (OR) are presented for hyposmia or anosmia (odor identification score < 10) vs. normosmia (odor identification score ≥ 10) per interquartile range (IQR) increase in each air pollutant (PNC, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2, NO_x and O_3); Error bars present 95 % Confidence Intervals (CI); Main model: each pollutant, sex, age, education, income, socioeconomic status, physical activity, smoking status, body mass index and alcohol consumption; PNC = particle number concentration; $PM_{2.5}$ = particulate matter (PM) with an aerodynamic diameter less than 2.5 μm; $PM_{2.5abs}$ = $PM_{2.5}$ absorbance; PM_{coarse} = PM between 2.5 and 10 μm; PM_{10} = PM with an aerodynamic diameter less than 10 μm; NO_2 = nitrogen dioxide; NO_x = nitrogen oxides; O_3 = ozone; unadjusted: single-exposure main model; adj.: adjusted with a second exposure variable additional to the main model.

individuals. The greater susceptibility observed in females may be related to hormonal changes, such as the significant decline in estrogen levels during and after menopause, which aligns with the age range of our study. This hormonal shift is associated with cognitive issues (Sherwin, 2003), and air pollution has been suggested to disrupt sex hormones during the menopausal transition (Wang et al., 2024). Biological factors, such as differences in blood–brain barrier permeability, may also play a role, as the integrity of this barrier seems to have a more direct impact on cognitive impairment in females due to the influence of hormones on its structure (Moon et al., 2021). Additionally, females' higher number of neurons and glial cells than males in olfactory regions (Oliveira-Pinto et al., 2014) could make them more vulnerable to olfactory damage (Doty, 2015). Physically active individuals may be more susceptible to the effects of air pollution on impaired sense of smell and cognitive decline due to increased respiratory rates and higher exposure levels during exercise, which can lead to greater inhalation of harmful pollutants. Exercise-induced oxidative stress (Powers et al., 2020) may exacerbate the neurotoxic effects of air pollution and undermine the health benefits of physical activity in the context of higher air pollution levels (Pasqua et al., 2018). We additionally observed consistently higher OR for the smokers, even if not statistically significant, which can be attributed to the high concentration of UFP in smoke. This increased exposure may make smokers more susceptible to related olfaction and cognitive impairment (Underwood, 2017).

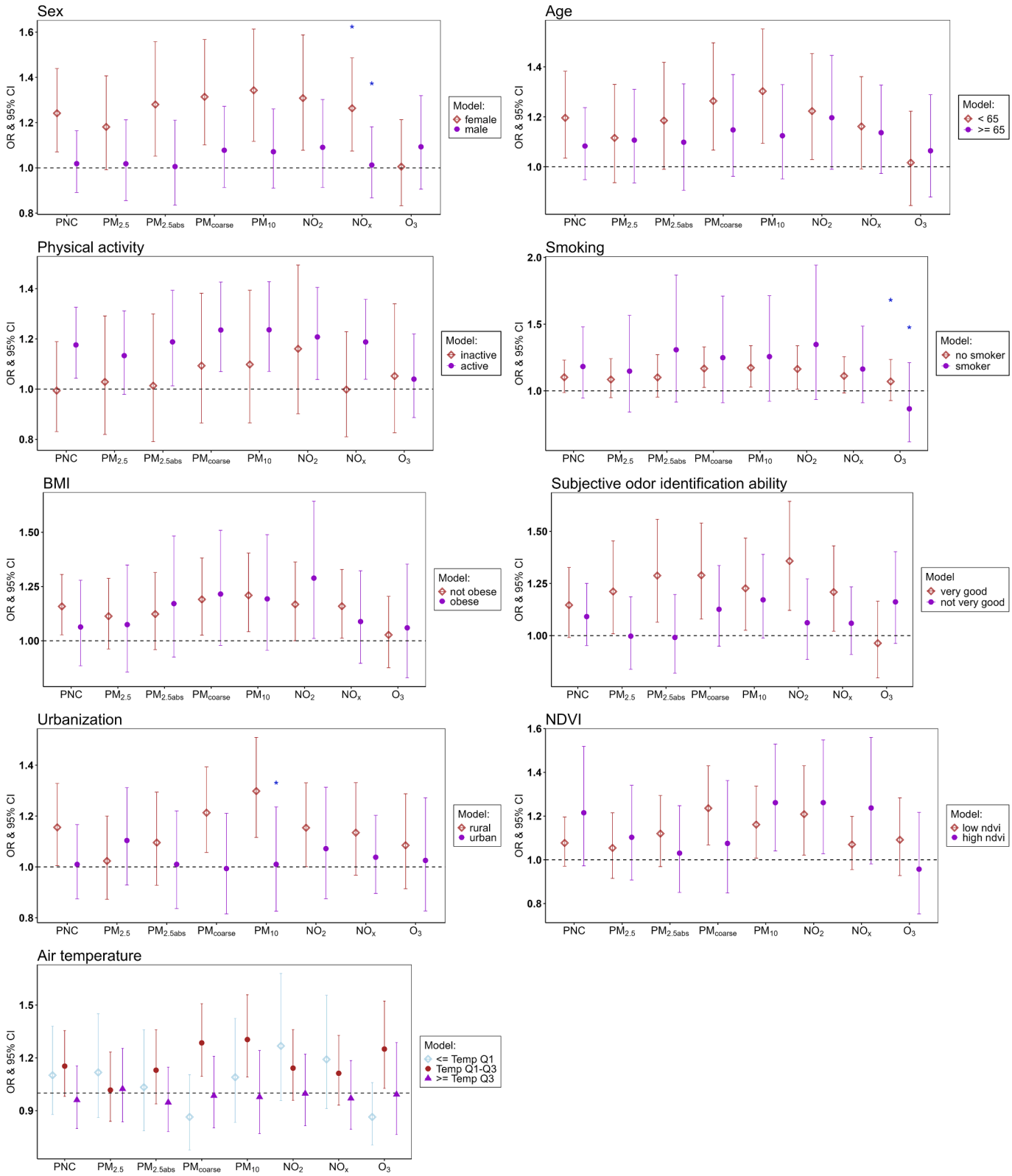

Fig. 3. Associations between various air pollutants and odor identification modified by sex, age, physical activity, smoking, body mass index (BMI), subjective odor identification ability, urbanization, normalized difference vegetation index (NDVI) and air temperature; Main model was used: minimum model (each pollutant, sex and age), education, income, socio-economic status, physical activity, smoking status, body mass index and alcohol consumption; Odds Ratios (OR) are presented for hyposmia or anosmia (odor identification score < 10) vs. normosmia (odor identification score ≥ 10) per interquartile range (IQR) increase in each air pollutant (PNC, $PM_{2.5}$, $PM_{2.5abs}$, PM_{coarse}, PM_{10}, NO_2, NO_x and O_3); Error bars present 95 % Confidence Intervals (CI); PNC = particle number concentration; $PM_{2.5}$ = particulate matter (PM) with an aerodynamic diameter less than 2.5 μm; $PM_{2.5abs}$ = $PM_{2.5}$ absorbance; PM_{coarse} = PM between 2.5 and 10 μm; PM_{10} = PM with an aerodynamic diameter less than 10 μm; NO_2 = nitrogen dioxide; NO_x = nitrogen oxides; O_3 = ozone; Stars indicate statistically significant interaction (p-value < 0.05).

In Germany, we were only able to identify one comparable study which was published 15 years ago. Ranft et al. found an adverse association between traffic-related air pollution, estimated by the proximity of the home address to a busy road, and mild cognitive impairment in older women (Ranft et al., 2009). In Europe, two additional studies have been published to date, both conducted in Sweden. Andersson et al. observed that long-term exposure to $PM_{2.5}$ improved odor identification ability (Andersson et al., 2022), which contradicts most of the literature and our own findings. Ekstroem et al. showed that exposure to residential $PM_{2.5}$ and NO_x over a 5-year period had a negative impact on olfaction (Ekström et al., 2022), consistent with our results. All other studies have been carried out in the Americas, mostly in the United States (US) and Mexico. Ajmani et al. observed that prolonged $PM_{2.5}$ exposure was associated with poor olfactory functioning in older US urban residents (Ajmani et al., 2016). Similarly, Adams et al. found that NO_2 was linked with worse olfaction in older US subjects (Adams et al., 2016), which aligns with our results. Zhang et al. also reported an association between $PM_{2.5}$ and anosmia in middle-aged to older individuals in the US (Zhang et al., 2021). Cao et al., using data from the Sister Study which focused exclusively on women, did not find strong evidence connecting $PM_{2.5}$ and NO_2 with reduced odor identification (Cao et al., 2023). In contrast, our study showed stronger associations in females. In Mexico, studies comparing young and middle-aged subjects living in highly polluted cities versus those in less polluted cities reported that residents of the highly polluted cities had worse olfactory ability (Guarneros et al., 2009; Hudson et al., 2006). A study in Brazil exhibited a strong relationship between high PM_{10} levels and poor olfactory function, with the effects being more pronounced in men (Scussiatto et al., 2023). Conversely, our findings indicated that the association was stronger in females.

Two reviews (Ajmani et al., 2016; Shehab et al., 2024) have highlighted common limitations in previous studies. They noted that previous studies have used proxies for air pollution exposure, had small sample sizes, had potential for significant confounding, and had challenges in establishing statistically significant associations. Both reviews reached similar conclusions and emphasized the need for more comprehensive research to address the existing gaps in the evidence. In our approach, we employed highly resolved and reliable LUR models for assessing air pollution exposure, focusing on traffic-related air pollutants at the residential addresses of our participants. Our study utilized a substantial sample size of almost 3,000 subjects and included a comprehensive, well-established cohort with an extensive dataset covering demographic, lifestyle, socioeconomic, and medical information. Additionally, we applied three distinct covariate models to thoroughly account for potential confounding factors. As a result of these rigorous methodologies, the statistically significant associations we found for many air pollutants can be considered robust and reliable.

This study is also subject to some limitations. We lacked data on odor threshold and discrimination scores, which prevented a more comprehensive olfactory assessment. However, odor identification alone serves as a well-established indicator of olfactory dysfunction and an early sign of neurodegeneration and is used in most existing research, providing reliable insights and meeting our study's objectives. The use of one- and two-pollutant models limited our ability to adopt a holistic exposure approach due to the challenge of multi-collinearity, a common issue in air pollution and health analyses. Not all environmental variables were available for KORA FIT's examination years (2018 and 2019), and exposure periods longer than one-year averages were not considered, which may have increased the risk of exposure misclassification. However, studies conducted in Europe have shown that while overall air pollution levels may change over time, the spatial variability of air pollutants remains relatively stable over long periods (Eeftens et al., 2011; Wang et al., 2013; Cesaroni et al., 2012; De Hoogh et al., 2018; Brunekreef et al., 2021). The study population comes from a small region, making it challenging to generalize the findings to populations with different demographic or exposure conditions. The population does, however, encompass both rural and urban areas. Our study also focuses on a specific age range, which may explain the absence of effects of aging. While we adjusted for known confounders, the possibility of residual confounding due to unmeasured factors or the cross-sectional nature of our study, which does not account for time-varying variables for example, cannot be entirely ruled out. However, we adjusted for multiple confounders in different models and the results remained robust. The seasonal variability of O_3 may affect its association with olfactory function, but our annual exposure averages with comparably low concentration levels and small exposure contrasts cannot capture this. Future research should incorporate season-specific analyses to better understand the impact of O_3 on olfactory function.

Recognizing the lack of such analyses at a national level in Germany and beyond, as well as the literature gap concerning the use of large and comprehensive cohort data, our next step is to build on the presented results by conducting a countrywide analysis using data from the German National Cohort (NAKO) (Peters et al., 2022). Furthermore, to bridge another evidence gap on this topic, we plan to integrate data from the KORA (Holle et al., 2005) FFF4 study and combine insights from two cohorts (KORA and SALIA (Schikowski et al., 2005) to further enhance the current evidence in the field through a longitudinal study.

Researchers in this field should take note of the lack of research conducted in Asia, Africa, and Oceania, as well as in multi-country studies. Addressing these gaps could yield valuable and insightful contributions to the field. Additionally, it would be beneficial for future research to consider the role of neurodegenerative disease status in data collection, as olfactory function is closely linked to these conditions. Integrating information on neurodegeneration could provide deeper insights into the observed associations.

5. Conclusion

This study provides robust evidence for significant associations between long-term exposure to traffic-related air pollution and impaired odor identification, even in regions with comparatively low air pollution levels. Additionally, this study found heightened vulnerability among females and physically active people. The study results highlight a potential connection between sustained air pollution exposure and cognitive decline and supports the evidence for particle translocation from the nose to the brain.

CRediT authorship contribution statement

Nikolaos Nikolaou: Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis. **Kathrin Wolf:** Writing – review & editing, Methodology, Data curation. **Susanne Breitner:** Writing – review & editing, Methodology. **Regina Pickford:** Writing – review & editing, Methodology. **Tamara Schikowski:** Writing – review & editing, Conceptualization. **Annette Peters:** Writing – review & editing, Supervision, Conceptualization. **Alexandra Schneider:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Ethics approval and consent to participate

The study methods were approved by the Ethics Committees of the Bavarian Chamber of Physicians (KORA-Fit EC No 17040). The study was performed in accordance with the Declaration of Helsinki. All study participants gave written informed consent.

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.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2025.109528.

Data availability

The datasets analyzed during the current study are not publicly available due to national data protection laws, since the informed consent given by KORA study participants does not cover data posting in public databases. Data are available upon request by means of a project agreement from KORA. Requests should be sent to kora.passt@helmholtz-munich.de and are subject to approval by the KORA Board. The analysis R scripts are available from the authors upon reasonable request.

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