Are air pollution and traffic noise independently associated with atherosclerosis: the Heinz Nixdorf Recall Study

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Aims	Living close to high traffic has been linked to subclinical atherosclerosis, however it is not clear, whether fine particulate matter (PM) air pollution or noise, two important traffic-related exposures, are responsible for the association. We investigate the independent associations of long-term exposure to fine PM and road traffic noise with thoracic aortic calcification (TAC), a reliable measure of subclinical atherosclerosis.
Methods and results	We used baseline data (2000–2003) from the German Heinz Nixdorf Recall Study, a population-based cohort of 4814 randomly selected participants. We assessed residential long-term exposure to PM with a chemistry transport model, and to road traffic noise using façade levels from noise models as weighted 24 h mean noise (L_{den}) and night-time noise (L_{night}). Thoracic aortic calcification was quantified from non-contrast enhanced electron beam computed tomography. We used multiple linear regression to estimate associations of environmental exposures with $\ln(TAC+1)$, adjusting for each other, individual, and neighbourhood characteristics. In 4238 participants (mean age 60 years, 49.9% male), $PM_{2.5}$ (aerodynamic diameter $\leq 2.5\ \mu m$) and L_{night} are both associated with an increasing TAC-burden of 18.1% (95% CI: 6.6; 30.9%) per 2.4 $\mu g/m^3$ $PM_{2.5}$ and 3.9% (95% CI 0.0; 8.0%) per 5dB(A) L_{night}, respectively, in the full model and after mutual adjustment. We did not observe effect measure modification of the $PM_{2.5}$ association by L_{night} or vice versa.
Conclusion	Long-term exposure to fine PM and night-time traffic noise are both independently associated with subclinical atherosclerosis and may both contribute to the association of traffic proximity with atherosclerosis.
Keywords	Atherosclerosis • Epidemiology • Air pollution • Traffic noise

Introduction

Long-term fine particulate matter (PM) air pollution and long-term exposure to high ambient noise levels are environmental exposures, which share similar sources, often occur conjointly and affect large portions of the population. Both exposures, occurring over years, are linked to the incidence of acute cardiovascular events.[1–3] Due to their overlapping sources such as road traffic, it has been difficult to tease apart the independent effects of long-term PM and noise exposure.[4] Furthermore, PM and noise exposure share many hypothesized biological pathways, including the elicitation of autonomic imbalance with sympathetic preponderance, an increase of arterial blood pressure, and increased blood coagulability.[4–6]

Recently, two studies have shown an association of high residential traffic exposure—the most important source of inner-urban variability of PM and noise—with different measures of atherosclerosis of

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the coronary and large conduit vessels.[7,8] Other studies have suggested that long-term fine PM exposure is associated with atherosclerosis of the larger vessels[9–14] and with narrowing of the microvasculature.[15] While these studies built on elaborate assessments of long-term residential PM exposure, none has been able to adequately control for the simultaneous occurrence of traffic noise and therefore has not been able to tease apart the detrimental effects of particle and noise exposure.

In this analysis, we use long-term exposure estimates for traffic noise and for fine PM exposure concurrently to investigate their independent associations with thoracic aortic calcification (TAC), a measure of subclinical atherosclerosis, in a large cardiovascular cohort study.[16,17] While sharing cardiovascular risk factors with coronary calcification,[16] which has been studied by our group before,[17] TAC is independently related to the incidence of cardiovascular events.[18,19] Furthermore, TAC has a higher prevalence among middle-aged adults than coronary calcification, making it specifically suitable for epidemiological analyses.[17,19,20]

We investigate whether long-term residential exposure to PM and traffic noise are independently associated with the degree of TAC, and whether concurrent traffic noise exposure modifies the association of PM with subclinical atherosclerosis or vice versa. The study extends prior analyses of coronary calcification in the Heinz Nixdorf Recall Study, a well-characterized, ongoing population-based prospective cohort in Germany, which has been subjected to intense state-of-the-art fine PM and noise exposure assessment campaigns.

Methods

Study design

Participants for this analysis were drawn from the Heinz Nixdorf Recall Study, an ongoing population-based cohort study located in three large adjacent cities of the densely populated Ruhr Area. Details of the study have been described elsewhere.[21,22] Participants were randomly selected from mandatory lists of residence. Between 2000 and 2003, 4814 participants aged 45–75 years of age were enrolled. All participants provided written informed consent and the study was approved by the institutional ethics committees. Traditional cardiovascular risk factors were measured at baseline using self-administered questionnaires, face-to-face interviews, clinical examinations, and comprehensive laboratory tests according to standard protocols.[21,23]

Exposure assessment

Air pollution

The study area covers a region of $\sim$600 km^2. We used a residence-based approach to characterize long-term exposure to urban air pollution.[13] In short, a validated chemistry transport model (EURAD-CTM) was applied to model the average daily mass concentrations of urban background PM with an aerodynamic diameter less than 10 µm (PM$_{10}$) and less than 2.5 µm (PM$_{2.5}$) on a grid of 1 km^2.[24] The EURAD-CTM uses input data from official emission inventories on a scale of 1 km^2, including industrial sources, household heating, traffic and agriculture, data on hourly meteorology and regional topography. Surface concentrations are calculated by dispersing emissions in horizontal strata, taking chemical reactivity, mass transport between horizontal strata and deposition into account. Daily average surface concentrations of each pollutant were modelled for each grid cell of 1 km^2 size for the time period from

November 2000 until July 2003 and assigned to the addresses of the participants, using a geographic information system (ArcView 9.2, ESRI, Redlands, CA, USA). For the assessment of long-term residential exposure, the average of the 365 daily values of the participant's grid cell prior to the participant's individual examination date was calculated.

Road traffic noise

Long-term road noise was modelled according to the European Union directive (2002/49/EC) for the year 2005 as weighted 24-h mean (L$_{den}$) and weighted night-time (226– h) mean (L$_{night}$) and given in dB(A), 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 façade values from local city administrations. We used the maximum noise value in a 10 m buffer around the participants' geographic address coordinates in all cities. For 60 participants, noise values were imputed from isophone bands. Noise values were investigated as categories of 5 dB(A) with the exception of the lowest category (0– 45dB(A)).

Measurement of thoracic aortic calcification

At baseline, subjects underwent cardiac CT. The methodology for acquisition and interpretation of the scans has been reported previously.[21–23] Electron beam-CT (EBCT) scans were performed utilizing a C-100 or C-150 scanner (GE Imatron, South San Francisco, CA, USA) without the use of contrast media. Imaging was prospectively triggered at 80% of the RR interval and contiguous 3 mm thick slices from the right pulmonary artery to the apex of the heart were obtained at an image acquisition time of 100 ms. A CT threshold of 4 pixels and 130 Hounsfield units (Hu) was used for the identification of a calcified lesion using the Agatston method.[25] Thoracic aortic calcification was assessed by summation of all calcified lesions.

As the EBCT scans were primarily performed for quantification of coronary calcification, assessment of TAC burden was possible in segments of the ascending and descending thoracic aorta that were included in the coronary calcium scan. The aortic arch and the infrarenal abdominal aorta were not included in the scan.

Cardiovascular risk factor assessment

We classified education as a marker of socioeconomic status (SES) according to the International Standard Classification of Education as total years of formal education. Equivalent monthly household income was calculated by dividing total net household income by weighted number of household members. To account for small-area differences in SES apart from individual-level SES, we assessed the unemployment rate of the neighbourhood, supplied by the city administrations for the 106 administrative districts of the study area for the year 2001. Smoking status was categorized as current smoker, ex-smoker, and never smoker. Current smoking was defined as a history of cigarette smoking during the past year. Lifetime cumulative exposure was assessed in pack-years. Environmental tobacco smoke (ETS) at home, at the workplace, or in other places was combined in one variable. Physical activity was assessed as hours of weekly exercise, and alcohol intake as drinks per week (0, 1–3, 4–6, >6 drinks per week). Anthropometry and blood pressure were measured according to the standardized protocols. Diabetes mellitus was defined as prior physician diagnosis of diabetes or taking an anti-diabetic drug or having a blood glucose ≥200 mg/dL or having a fasting blood glucose ≥126 mg/dL. Current medications were

coded according to the Anatomical Therapeutic Chemical Classification Index.

Analytical strategy

This cross-sectional analysis was performed on 4238 participants for whom data on TAC and all covariates were available. In a first step, we used linear regression models to analyse the association of proximity to high traffic, long-term particulate matter exposure (PM_{10}, $PM_{2.5}$), and long-term road traffic noise exposure (L_{den}, L_{night}) with the natural logarithm (ln) of (TAC+1) in separate, single exposure models. We adjusted for covariates, which were *a priori* believed to potentially influence the exposure-outcome association. These included age, sex, education, neighbourhood unemployment rate, smoking status, cumulative cigarette exposure, ETS, physical activity, weekly alcohol consumption, and body mass index (BMI). City of residence was added in an extended model to examine the association of within-city variability of exposures with TAC. Second, we constructed two-exposure models including both exposures simultaneously by adding $PM_{2.5}$ to the noise models and L_{night} to the $PM_{2.5}$ and PM_{10} models. To investigate whether high traffic noise modified the association of PM with TAC and vice versa, we included product terms of PM and dichotomized traffic noise exposure and vice versa. Similarly, potential effect measure modification was analysed for specific participant characteristics, which have been suggested to act as effect modifiers in prior studies.[7,12,13] A nonlinear estimation of the exposure response relationship was conducted using regression splines. In extension of our previous study, which was based on an earlier version of the EURAD model,[7] we repeated the analyses outlined above with coronary artery calcification score (CAC) as outcome.

To take possible clustering of the outcome into account, we conducted a random effects model with neighbourhood district as random effect. We included equivalent income in the subgroup of participants for whom this information was available (n = 3998). Hypertension, systolic blood pressure, antihypertensive medication, markers of inflammation, and diabetes mellitus were added in extended models since they might act as intermediates. To proof robustness of effect estimation in our main model, we estimated the association of $PM_{2.5}$ and TAC-Score in a subset excluding most influential participants (Cook's D > 4/N). All estimates are presented as percent change in (TAC+1) per interquartile range (IQR) for PM, per 5 dB(A) (continuously or as a category) for noise, and per 50% reduction of the distance to highly trafficked roads.

Results

Study population and environmental exposures

The mean age of the 4238 included participants (49.9% male) was 59.6 ± 7.8 years (*Table 1*). Exposure to 24 h mean noise had a skewed distribution with more than 60% included in the reference category (≤45 dB(A)), while exposure to night-time noise was distributed more equally among categories (*Figure 1*). Modelled urban background PM_{10} and $PM_{2.5}$ exposures were highly correlated, while fine PM and noise exposures showed only a low correlation (*Table 2*).

Association of traffic proximity, particulate matter and traffic noise with thoracic aortic calcification

Distance to highly trafficked roads, long-term exposure to fine PM, and long-term exposure to night-time road traffic noise were all associated with increasing TAC burden in the crude and in the fully

Table 1 Summary statistics of 4238 analysed participants of the Heinz Nixdorf Recall Study

	Total sample (n = 4238)
TAC (median, IQR)	20.0 (143.3)
CAC (median, IQR)	17.0 (157.6)[a]
Age [years] (mean ± SD)	59.6 ± 7.8
Male sex (N, %)	2114 (49.9)
Educational attainment (N, %)	
<10 years	454 (10.7)
11−13 years	2369 (55.9)
14−18 years	958 (22.6)
>18 years	457 (10.8)
Smoking status (N, %)	
Current smoker	965 (22.8)
Former smoker	1491 (35.2)
Never smoker	1782 (42.0)
Packyears in ever smokers (mean ± SD)	27 ± 27.1
Environmental tobacco smoke (N, %)	1522 (35.9)
Alcohol consumption	
0 times/week (N, %)	2102 (49.6)
1−3 times/week (N, %)	748 (17.6)
>3−6 times/week (N, %)	413 (9.7)
>6 times/week (N, %)	975 (23.0)
Physical activity (mean ± SD)	2.1 ± 1.3
Body mass index [kg/m^2] (mean ± SD)	27.9 ± 4.5
Systolic blood pressure [mmHg] (mean ± SD)	133.1 ± 20.9[a]
LDL/HDL ratio (mean ± SD)	2.7 ± 1.1
Fibrinogen [mg/dL] (mean ± SD)	333.9 ± 77.2[a]
Coronary heart disease (N, %)	275 (6.5)
Lipid-lowering medication (statins) (N, %)	416 (9.8)
Diabetes mellitus (N, %)	573 (13.5)
Hypertension (N, %)[b]	2267 (53.5)[a]
Antihypertensive medication (N, %)	1483 (35.0)[a]
City of residence (N, %)	
Mülheim	1526 (36.0)
Essen	1432 (33.8)
Bochum	1280 (30.2)

[a]Excluding missings.
[b]Systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg.

adjusted single exposure models (*Table 3*). Weighted 24 h noise exposure L_{den} was not associated in the adjusted model. Adjusting for city attenuated most estimates slightly. In the mutually adjusted two exposure models of $PM_{2.5}$ and L_{night}, estimates did not change relevantly with a 18.1% (95% CI 6.6; 30.9%) increase in TAC per IQR of 2.4 μg/m^3 for $PM_{2.5}$ and a 3.9% (95% CI 0.0; 8.0%) increase per 5 dB(A) L_{night}. Exposure-response analyses yielded no evidence of a threshold for the effects of $PM_{2.5}$, PM_{10}, and L_{night} below which exposures seemed to have no effect. Predicted TAC increased in a linear fashion until an exposure of ~16 μg/m^3 $PM_{2.5}$ (20 μg/m^3

Figure 1 Distribution of L_{den} and L_{night} in 5 dB(A) categories.
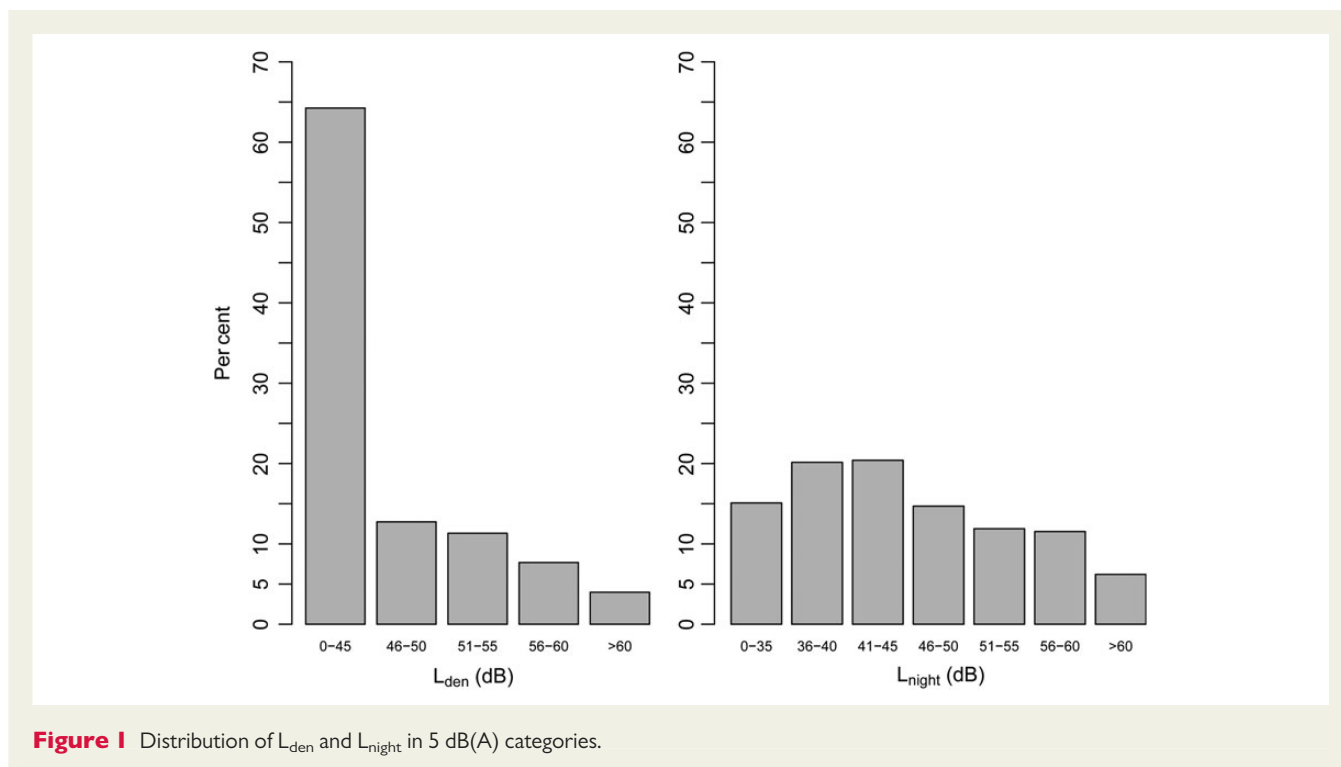
Table 2 Summary statistics for long-term exposure variables for 4238 participants of the Heinz Nixdorf Recall Study

Exposure	Mean (SD)	Median	Q1	Q3	Min	Max	Correlation (ρ)			
							PM_{10}	Distance	L_{den}	L_{night}
$PM_{2.5}$ [μg/m^3]	16.62 (1.60)	16.42	15.43	17.82	13.28	22.38	0.81	-0.02	0.07	0.10
PM_{10} [μg/m^3]	20.64 (2.59)	20.64	18.46	22.46	15.83	29.35		0.01	0.17	0.19
Distance to highly trafficked road [m]	910.40 (785.75)	709.50	326.90	1264.0	1.35	4877.0			0.21	0.21
L_{den} [dB(A)]	54.38 (8.76)	52.41	46.84	61.13	44.00	84.56				0.77
L_{night} [dB(A)]	45.37 (8.66)	43.80	38.20	52.14	34.00	76.29				

Particulate matter (PM) concentrations are given as the individual 365-day moving average before the day of examination. Mean noise exposures are modelled according to the EU directive 2002/49/EC.
L_{den}, weighted 24 h mean of road traffic noise; L_{night}, mean of night-time noise (22–6 h); PM, particulate matter.

PM_{10}) and levelled off at higher exposures (*Figure 2*). There was no evidence for a nonlinear relationship for L_{night}.

Similar to our already published finding based on an earlier version of the EURAD-CTM, fine PM was not clearly associated with CAC. Per IQR increase in $PM_{2.5}$, CAC increased by 7.0% (95% CI -6.1; 22.0%) in the fully adjusted model (main model+city). Neither L_{den} nor L_{night} were associated with CAC [-1.3% (95%CI -6.4; 4.1%) and 1.0% (95%CI -2.5; 4.6%), respectively]. Estimates for CAC did not change upon mutual adjustment and no interaction between PM and noise was observed.

Random effects models displayed unchanged results for the association of environmental exposures with TAC. Inclusion of possible intermediates such as hypertension, systolic blood pressure, fibrinogen concentration, and diabetes mellitus slightly reduced the positive estimates for PM and night-time noise.

Additional adjustment for income did not change the estimate for PM. Exclusion of most influential covariates led to an increase in effect estimates for TAC and to a decrease in effect estimates for CAC.

Effect modification

The effect of PM on TAC was not clearly modified by traffic-noise exposure (*Figure 3*). Only at high L_{night} exposure, a higher estimate for PM_{10} was suggestive of a positive effect modification. However, confidence intervals were wide due to a low sample size in this group of participants with high L_{night} exposure. Similarly, PM did not modify the association of night-time traffic noise with TAC (*Figure 3*). We observed an interaction of $PM_{2.5}$ and PM_{10} with age, displaying clearly stronger associations for younger participants (45–65 years), participants with prevalent CHD, and participants

Table 3 Estimated % change in thoracic aortic calcification per change in particulate matter air pollutant by interquartile range, for exposure to high traffic per 100 m decrease in distance and for traffic-noise in 5dB(A) categories compared with the reference category
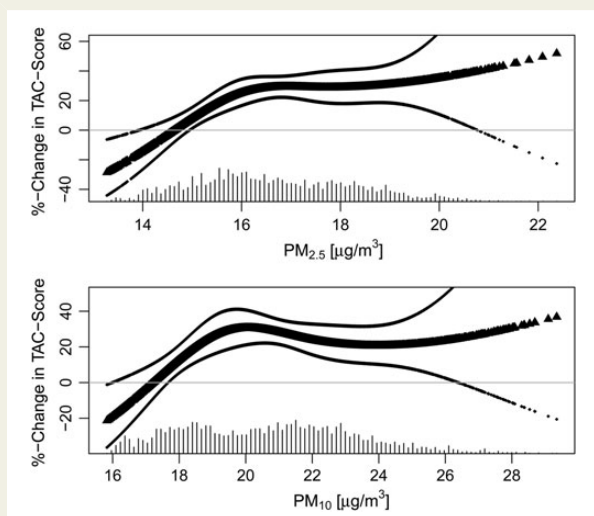
Exposure	% change estimate (95%-CI) in TAC Score			
	Crude	Main[a]	Main + city	Main + L_{night}^{b} or main + $PM_{2.5}^{c}$
$PM_{2.5}$ (per 2.4 $\mu g/m^3$)	26.5 (12.8; 41.8)	19.5 (7.9; 32.4)	15.7 (0.3; 33.5)	18.1 (6.6; 30.9)[b]
PM_{10} (per 4.0 $\mu g/m^3$)	19.6 (6.2; 34.7)	11.6 (0.4; 24.1)	0.4 (−13.6; 16.7)	9.4 (−1.8; 21.9)[b]
Distance to highly trafficked road (per reduction by 50%)	12.9 (−0.4; 24.5)	12.1 (0.1; 22.7)	12.3 (0.3; 22.8)	8.8 (−4.2; 20.3)[b]
L_{den} (per 5dB with a cut point at 45 dB)	2.5 (−3.9; 9.4)	2.5 (−3.3; 8.6)	2.1 (−3.6; 8.2)	1.9 (−3.8; 8.0)[c]
L_{night} (per 5 dB with a cut point of 35 dB)	5.5 (1.0; 10.1)	4.6 (0.7; 8.7)	4.1 (0.1; 8.2)	3.9 (0.0; 8.0)[c]

L_{den}, weighted 24 h mean of road traffic noise; L_{night}, weighted mean of night-time noise(22−6 h); PM, particulate matter; TAC, thoracic aortic calcification.
[a]main: sex, age, unemployment rate in neighbourhood, smoking status, packyears of smoking, ETS, physical activity, BMI, alcohol intake.
[b]Plus L_{night}.
[c]Plus $PM_{2.5}$.

Figure 2 Level of long-term particulate matter (PM) exposure at participants' residence and the estimated percent change in thoracic aortic calcification (TAC) Score, modelled by cubic regression spline with 3 degrees of freedom. Percentage change in TAC Score is shown relative to the 10th percentile of $PM_{2.5}$ (14.6 $\mu g/m^3$) and PM_{10} (17.3 $\mu g/m^3$).

taking statins. The PM_{10} estimate differed across cities, with a positive association restricted to the city of Bochum. Other individual characteristics or related exposures did not clearly lead to an effect modification of the PM estimates.

Discussion

The most important finding of our study is that both, long-term exposure to fine PM and to night-time road traffic noise, are independently associated with TAC. While confirming earlier studies linking residential proximity to high traffic with subclinical atherosclerosis, we can now show that both of the two major types of exposure

which occur in densely populated urban areas, namely fine particles and traffic noise, contribute to the explanation for the observed associations between living close to high traffic and subclinical atherosclerosis.[7,8] In addition, the associations of $PM_{2.5}$ and road traffic noise were not modified by each other. The associations for $PM_{2.5}$ and road traffic noise with TAC were robust to the inclusion of risk factors for atherosclerosis, including those that lie on the hypothesized biologic pathway. Compared with cross-sectional age-related differences in TAC, an increase of 20% in TAC for an interquartile increase in long-term $PM_{2.5}$ of 2.4 $\mu g/m^3$ corresponds to ∼1 year of older vascular age in our cohort.[17]

This is the first study to examine simultaneously the associations of fine PM and road traffic noise with the degree of subclinical atherosclerosis. Fine PM and traffic noise exposure do not only share high traffic as a common source, but they are also believed to act through similar biologic pathways and increase the risk for the same group of diseases.[5] Both, noise and PM exposure, lead to an imbalance of the autonomic nervous system with a relative increase in sympathetic tone; noise through the activation of the pituitary−adrenal−cortical axis and the sympathetic−adrenal−medullary axis,[26] while PM is hypothesized to interact with pulmonary receptors or nerves.[1] Furthermore, stress hormones, released after noise exposure, feed into complex mechanisms regulating blood pressure, blood lipids, glucose level, clotting, and viscosity.[5] All of these processes have also been shown to be influenced by PM exposure, most likely through the combination of parasympathetic withdrawal, elicitation of local pulmonary and systemic inflammation, and direct action of particles or their components that reach the systemic compartment.[1] It seems likely that these physiological processes after noise, respectively PM exposure, might interact and possibly aggravate each other. However, in this study, we did not see clear effect modification of the PM effect by noise or vice versa, which does not support our prior hypothesis of interaction.

Interestingly, we observed slightly different patterns of effect modification by personal characteristics between exposures. While young age clearly increased the association of PM with TAC, no differences between age groups were seen for the associations of noise with TAC. Similarly, we found suggestive evidence that
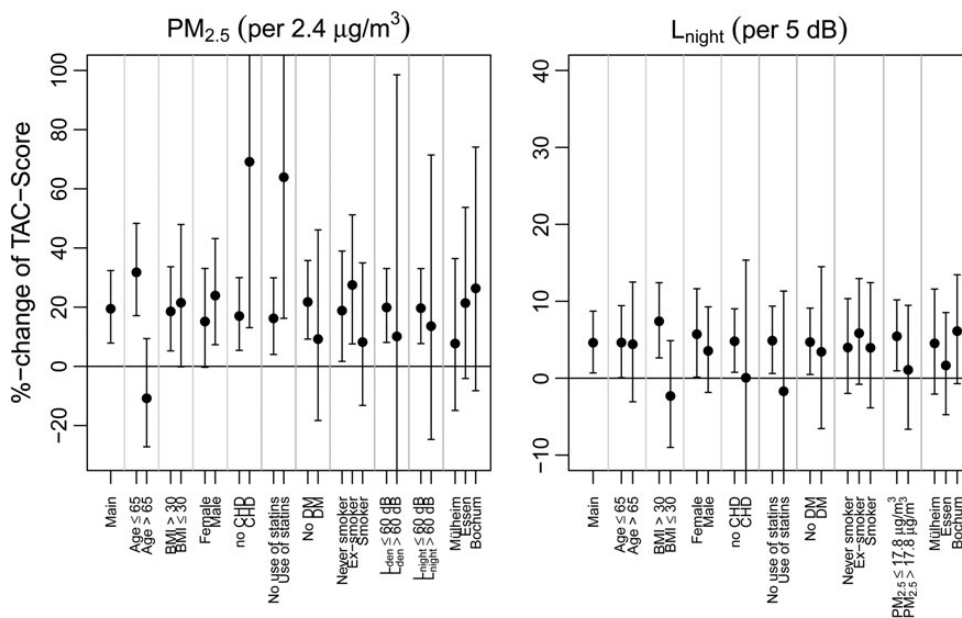
Figure 3 Effect modification: % change in TAC Score per IQR increase in PM$_{2.5}$ and PM$_{10}$, proximity to highly trafficked road per 100 m and per 5dB(A) increase in night-time noise. Estimates calculated from product terms in the fully adjusted models.

participants with CHD and participants on statins were especially susceptible to the effects of PM, while they displayed no association of noise with TAC. These findings suggest that, even though noise and PM share many biological pathways, the individual mechanisms feeding into these pathways may differ and may lead to differences in the manifestations of health outcomes.[1,5]

To effectively protect the population from adverse environmental effects, it is important to investigate the respective effects of both exposures independently of each other, because interventions regarding PM and road traffic noise can differ. In our study, we found a clinically relevant particle-independent association of night-time road traffic noise in the general population, and a noise-independent association of PM$_{2.5}$ with TAC. Other studies have additionally shown effects of other transportation noise sources such as aircraft noise or railway noise.[27,28] In our study, however, aircraft noise levels were low because our study area does not include an airport. Railway noise levels were not available and could therefore add to the adverse effects of noise observed in our study.

This study showed a robust and relevant association of PM with TAC, while we could not show an association with CAC. This result is similar to our previous study, which was based on an earlier version of the EURAD-CTM.[7] Coronary artery calcification and TAC differ with regard to pathogenic pathways: while CAC is mostly entirely atherosclerotic, TAC involves two pathophysiological processes: intimal, which is atherosclerotic and associated with lipid, macrophages, and vascular smooth muscle cells, and medial, which exists independently of atherosclerosis and is associated with elastin and therefore contributes to increased aortic stiffness.[17] Furthermore, risk factors regarding the two different arterial sites may differ considerably, with systemic hypertension frequently noted as most important in the development of aortic lesions.[29,30]

This is in line with our observation of increased arterial blood pressure in participants subjected to higher residential PM air pollution.[6] Moreover, the higher prevalence of TAC makes this outcome more suitable for analytical strategies building upon continuous outcomes, thereby increasing the power of the analysis in comparison with the analysis of CAC.

For PM exposure, we applied the EURAD-CTM, which has been shown to predict several cardiovascular or inflammatory outcomes before.[10,11,13,31] This model estimates the average level of PM in 1 km^2 grid cells across the study region. The EURAD modelling technique therefore estimates the urban background concentration and captures an average exposure within the neighbourhood of the participant's residence. This is different from commonly used land use regression models, which estimate pollutant levels for exact locations with a spatial resolution in the range of meters (i.e. at the participant's front entrance door, depending on the available reference point for each building). land use regression (LUR) models are strongly based on distance measures to traffic and land use variables. While these models reflect peaks in especially traffic-related exposures due to nearby heavily trafficked roads well, they are very sensitive to a change of location by participants, for example when leaving the immediate vicinity of the house. LUR model estimates are also more strongly correlated with modelled noise values, which partly results from using the same predictor variables. This makes it difficult to separate noise and PM effects in an epidemiological study using LUR models for exposure estimation. With the EURAD model, however, we were able to differentiate PM from noise exposure, since EURAD models the urban background concentration and is less dependent on traffic proximity.

Major strengths of our study include the availability of both, fine PM and noise exposure data in a large, population-based cohort.

Traditional cardiovascular risk factors were measured using highly standardized protocols and TAC was quantified using a reproducible method. All measurements were conducted in a well-controlled study environment with strict adherence to standards and quality control measures. The detailed information on known and candidate cardiovascular risk factors allowed an extensive control of confounding.

Individual characteristics such as room ventilation patterns, hearing abilities, etc. contribute to misclassification of noise exposure. However, we expect this misclassification to be non-differential, thereby most likely biasing our results towards the null. Pathogenic noise characteristics are not well understood and the estimation of ambient road traffic noise with the EU noise models may not be optimal to assess pathogenic noise characteristic(s). Furthermore, one important pathway through which road traffic noise acts is annoyance, which was not investigated in this analysis.

Since the Heinz Nixdorf Recall Study was initially designed to evaluate the predictive role of subclinical atherosclerosis by assessment of CAC additionally to traditional risk factors for modern cardiac risk stratification, the EBCT scans were primarily performed for quantification of CAC. The aorta was examined in the available range, excluding the aortic arch and the infrarenal abdominal aorta to keep the radiation exposure to a minimum. The positive correlation between calcification in the aortic arch with calcification in the ascending and descending thoracic aorta[32] and the relative ease in identifying TAC during a standard CAC scan, without requiring additional radiation exposure, are advantages as TAC can be a good estimate of the presence and extent of overall calcific atheroma burden.[18]

A limitation of this study is the lack of progression data on TAC and CAC. Participants were re-examined at years 5 and 10 of follow-up and progression data will be available in the future. We will then be able to investigate the role of environmental exposures in a longitudinal design, which will have a stronger claim on causality. Furthermore, we have not taken relocations prior to the TAC and CAC measurement into account. This might have introduced some degree of non-differential exposure estimation misclassification, which most likely biases the estimate towards the null. In addition, as our study was conducted in a predominantly Caucasian population, generalization to other ethnic groups remains uncertain.

Conclusion

In summary, we found that long-term exposure to fine PM air pollution and to road traffic noise are both independently associated with TAC as a measure of subclinical atherosclerosis and may both contribute to the association of traffic proximity with atherosclerosis. The considerable size of the associations underscores the importance of long-term exposure to air pollution and road traffic noise as risk factors for atherosclerosis.

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