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Residential Proximity to Major Roadways, Fine Particulate Matter, and Adiposity: The Framingham Heart Study

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Abstract

Objective—Higher traffic-related air pollution has been associated with higher body mass index (BMI) among children. However, few studies assessed the associations among adults.

Methods—2,372 participants from the Framingham Offspring and Third Generation cohorts who underwent multidetector computed tomography (MDCT) scans (2002-2005) were included. We estimated residential-based proximity to the nearest major roadway and one-year average levels of fine particulate matter (PM_{2.5}) air pollution. BMI was measured at Offspring examination 7 (1998-2001) and Third Generation examination 1 (2002-2005), subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) were measured using MDCT. We used linear regression models for continuous BMI, SAT, and VAT, and logistic models for the binary indicator of obesity (BMI ≥ 30 kg/m²), adjusting for demographic variables, individual- and area-level measures of socio-economic position, and clinical and lifestyle factors.

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Results—Participants who lived 60 m from a major roadway had 0.37 kg/m² higher BMI (95% CI: 0.10, 0.65 kg/m²), 78.4 cm³ higher SAT (95% CI: 4.5, 152.3 cm³), and 41.8 cm³ higher VAT (95% CI: -4.7, 88.2 cm³) than those who lived 440 m away.

Conclusions—Living closer to a major roadway was associated with higher overall and abdominal adiposity.

Keywords

Environmental Risk; Body-Mass index; BMI; Subcutaneous Adipose Tissue; Visceral Fat; Computed Tomography

Introduction

In 2011-2012, more than one-third of adults (34.9%) in the United States were obese (1). As obesity is an important and modifiable risk factor for cardiovascular disease, studying the origin and development of obesity is of great interest. Other than overall obesity, both abdominal subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) have been associated with adverse cardiometabolic risk profiles, with stronger associations seen for VAT than SAT (2-6).

In controlled animal studies, mice exposed to fine particulate matter (PM_{2.5}; particles with aerodynamic diameter $\leq 2.5\mu\text{m}$) had higher visceral fat or total abdominal fat compared with mice exposed to filtered air (7, 8). The hypothesized underlying biological mechanisms were the adverse effects of air pollution on inflammation, oxidative stress, and lipid metabolism (9-12). Although exposure to ambient air pollution has been linked to development of diabetes and cardiovascular disease in humans (13-16), few studies have examined the association between ambient air pollution and obesity (17-20), and little is known about the associations of ambient air pollution with abdominal adiposity among adults.

Therefore, we conducted the present investigation among participants from the multidetector computed tomography (MDCT) study, a sub-study of the Framingham Offspring and Third Generation cohorts. In the current study, we examined the associations of residential-based estimates of ambient PM_{2.5} exposure and proximity to the nearest major roadway with body mass index (BMI) and MDCT-based measures of abdominal adiposity. Our results may provide insight into the observed associations between air pollution and cardiovascular disease and diabetes.

Methods

Study population

We included participants from the Framingham Offspring cohort examination 7 (1998-2001) or Framingham Third Generation cohort examination 1 (2002-2005) who underwent the MDCT study. Selection criteria and study design of the two cohorts have been previously described (21, 22). For inclusion in the MDCT study, men were aged ≥ 35 years old, women were aged ≥ 40 years old and not pregnant, and because of physical constraints of the scanner, all participants weighed <350 lbs (160 kg) (3). Participants were scanned between

2002 and 2005. A total of 3,370 participants had either SAT or VAT measured, 520 were further excluded because of missing annual PM_{2.5} data. At each examination, physical examinations were performed following standardized protocols, and data on demographics, medication history, smoking history, and alcohol intake were collected by questionnaires. We further excluded participants with missing covariates data (N=478), leaving a total of 2,372 participants in the current analyses. All participants provided written informed consent, and Institutional Review Boards at Beth Israel Deaconess Medical Center, Boston University Medical Center, and Massachusetts General Hospital approved the study.

PM_{2.5} assessment

Participants' self-reported residential addresses were collected during the exam visit and geocoded using ArcGIS software. We used a spatial-temporal model to estimate PM_{2.5} concentrations at a 1×1 km² resolution based on residential addresses.

The satellite-based aerosol optical depth (AOD) is a measure of light attenuation in the atmospheric column, whereas the PM_{2.5} concentration is a measure of near surface dry mass (23). A number of statistical models have been developed in the past to estimate surface PM_{2.5} using satellite AOD retrieval, taking into account factors including vertical profile and meteorological parameters (24, 25). These models generally showed good correlations between AOD and surface PM_{2.5} in the eastern United States (25).

We used a novel hybrid spatial-temporal model that used AOD data from the Moderate Resolution Imaging Spectroradiometer (MODIS), spatial predictors (elevation, population density, traffic density, point and area emissions data for PM_{2.5}, PM₁₀, sulfur dioxide (SO₂), and nitrogen oxides (NO_x), and percentages of land use), and temporal predictors (meteorological parameters, MODIS Normalized Difference Vegetation Index, and the height of planetary boundary layer) (23). Furthermore, this hybrid model incorporated day-specific AOD calibration to ground level PM_{2.5}, which improved our ability to predict PM_{2.5} across the study region (26, 27). This approach allowed us to predict PM_{2.5} on days when AOD data were not available. Moreover, compared to the standard MODIS AOD product that had a resolution of 10 × 10 km², we used the advanced Multi-Angle Implementation of Atmospheric Correction (MAIAC) algorithms to achieve a higher resolution (1 × 1 km²) (23).

Briefly, we first fit a model regressing PM_{2.5} concentrations measured at local monitors against satellite-based AOD, adjusting for land use terms and meteorological predictors. Inverse probability weighting was used to address non-random missingness of daily AOD data. The predictions from this model (stage 1) have an excellent mean out-of-sample R² of 0.88 (year-to-year variation 0.82-0.90 for the years 2003-2011), with an excellent fit when comparing predictions with observations (slope=0.99, year-to-year variation 0.98-1.01 for the years 2003-2011) (23). Second, we predicted grid cells with AOD measurement but not ground monitors measurement using the above fitted model. Third, for grid cells/days that had missing AOD measurements, we imputed data by a generalized additive model with spatial smoothing and a random intercept for each grid cell. The overall mean out-of-sample R² for this stage of PM_{2.5} predictions was 0.88 with small year-to-year variation (0.84-0.91) (23). Last, we took the residuals (differences between monitor-based PM_{2.5} and predicted

PM_{2.5} for each cell) and regressed them against monitor-specific spatial and temporal variables such as traffic density and distance to A1 roadways to generate local predictions for each residential address, which allowed us to improve the daily predictions to a finer scale that could better capture pollution from local sources. The total PM_{2.5} daily estimates were the sum of grid and localized predictions. We used annual average PM_{2.5} of the same index year (2003) for all participants, similar to our previous work (28, 29).

Distance to the nearest major roadway

We defined major roadways as primary highways with limited-access (A1), primary roads without limited-access (A2), or secondary and connecting roads (A3). And we estimated residential distance to the nearest major roadway based on the geocoded addresses. We restricted our analyses to participants who lived within 1,000 meters from the nearest major roadway (N=2,118) when roadway proximity was the exposure of interest, because distance may not be an informative surrogate of traffic-related air pollution in semirural or rural areas. As in our previous work (28, 29), we classified participants into five groups based on the distance of their residential address to the nearest major roadway (0-50, 50-100, 100-200, 200-400, and 400-1,000 m). The cutpoints reflect the decreasing pattern of traffic-related pollutants, such as particulate matter mass and elemental carbon, from mobile sources (30).

Overall and abdominal adiposity

Both standing height and weight were measured without shoes according to a standardized protocol. Height was recorded to the nearest ¼ inch, and weight was recorded to the nearest pound (rounded up if ≥ 0.5 pound). BMI was calculated as weight (kg) / height (m)².

Participants underwent MDCT scan of the abdomen in the supine position by an eight-slice scanner (LightSpeed Ultra, General Electric, Milwaukee, WI) and 25 contiguous 5 mm thick slices (120 kVp, 400 mA, gantry rotation time 500 ms, table feed 3:1) were obtained above the S1 level. A semiautomatic segmentation technique that required manual definition of the abdominal muscular wall (Aquarius 3D Workstation, TeraRecon Inc., San Mateo, CA) was used to measure SAT and VAT. An image display window with width of −195 to −45 Hounsfield units was used to identify pixels containing fat. The MDCT-based volumetric measurements of abdominal adipose tissue have been shown to be reproducible with high intra-class correlation (ICC) for both intra-reader (ICC=0.99) and inter-reader (ICC=0.99) comparisons (31).

Statistical methods

We fit multivariable linear regression models for continuous BMI, SAT, and VAT, and multivariable logistic regression models for a binary indicator of obesity (BMI ≥ 30 kg/m²). We adjusted for age at examination, (age at examination)², sex, smoking status (current, former, or never), pack years of smoking, alcohol intake (drinks/week; calculated based on self-reported questionnaires and standardized to 0.5 oz alcohol/drink) (32), educational level, physical activity index (estimated based on self-reported questionnaires) (33), anti-hypertensive medication use, statin use, quartile of median household income in the

participant's census tract in 2000, cardiovascular disease, diabetes, and a cohort identifier. For MDCT analyses, we replaced age at examination with age at CT scan and additionally adjusted for height. Distance to the nearest major roadway was $\log_e$ transformed to account for hypothesized air pollution dispersion pattern and the log-linear relationship between residential distance to major roadway and cardiovascular outcomes as in our previous work (34, 35).

For sensitivity analyses, we excluded participants who were current smokers, or had previous cardiovascular disease or diabetes. We further examined the robustness of our findings by adjusting for additional measures of socioeconomic position, including individual-level self-reported usual occupation (laborer; sales/homemaker/clerical; professional/executive/supervisory/technical; and unspecified) (36), median value of owner occupied housing units in the census tract, and population density (population/km²) in the census tract. We additionally explored whether associations differed by median age (>/ 52 years old), sex, or a binary educational level indicator (high school or less vs. some college or higher) by adding interaction terms to the model. To estimate the influence of choosing the year 2003 as the index year, we assessed the associations between three-year average PM_{2.5} (2003-2005) and adiposity measures. We also evaluated the influence of adjusting for time by additionally including year of CT scan (categorical variable), date of CT scan (continuous variable), and days between CT scan and cohort examination visit for MDCT analyses. Additionally, we used quantile regression models to explore the associations at each quartile (25th, 50th, and 75th) of the distributions of these adiposity measures.

Results from the PM_{2.5} analyses were scaled to 1.5 $\mu\text{g}/\text{m}^3$, which is approximately the interquartile range of the 2003 annual average of PM_{2.5} concentration. Results from the residential proximity analyses were scaled by a factor of -2, which corresponds to contrasting participants who lived 60 m from a major roadway to those who lived 440 m from a major roadway, an approximation of the interquartile range of $\log_e$ -transformed distance. We examined the linear trend for road category analyses by assigning participants in each road category the median value of $\log_e$ -transformed distance within that category and then replaced the road category variables with this continuous variable in the models.

Scaled regression coefficients and odds ratios (ORs) were reported with 95% confidence intervals (CIs). A two-tailed p-value < 0.05 was considered statistically significant. Analyses were performed using PROC GLM, PROC GENMOD, and PROC QUANTREG in SAS 9.4 (SAS Institute, Inc., Cary, NC). Figures were plotted using Stata 13 (StataCorp LP, College Station, TX).

Results

Table 1 shows the characteristics of the study population. The mean age at the time of MDCT scan was 53.9 (standard deviation (SD): 11.8) years old and 52.1% were women. Of all the participants, 12.4% were current smokers, 8.1% had cardiovascular disease, and 7.3% had diabetes. The 2003 annual average PM_{2.5} concentration was 10.6 $\mu\text{g}/\text{m}^3$, which was lower than the current U.S. Environmental Protection Agency's National Ambient Air Quality Standard (annual average PM_{2.5}: 12.0 $\mu\text{g}/\text{m}^3$).

Table 2 shows the characteristics of the adiposity measures and Spearman partial correlation coefficients adjusting for sex. Of the 2,372 participants, 27.7% (N=657) were obese (BMI ≥ 30 kg/m²). BMI was highly correlated with both SAT and VAT, and SAT was moderately correlated with VAT.

Living closer to a major roadway was associated with higher BMI and higher SAT (Table 3 and Figure 1). Compared with participants who lived 440 m from the major roadway, those who lived 60 m from the major roadway had higher BMI ($\beta=0.37$ kg/m², 95% CI: 0.10, 0.65 kg/m²) and higher SAT ($\beta=78.4$ cm³, 95% CI: 4.5, 152.3 cm³). The positive association between living closer to a major roadway and higher VAT was weaker and the 95% CI overlapped the null ($\beta=41.8$ cm³, 95% CI: -4.7, 88.2 cm³). The 2003 annual average PM_{2.5} was not associated with adiposity measures.

Excluding participants who were current smokers or participants who had cardiovascular disease or diabetes did not alter our results substantially. Adjusting for individual-level usual occupation, census tract median value of owner occupied housing units, and census tract population density did not materially alter our results (Supplemental Figure S1). The associations were not altered when using the 2003-2005 average PM_{2.5} or additionally adjusting for time covariates. We found some evidence of stronger associations of living closer to a major roadway with BMI and SAT among younger (≤ 52 years old) or female participants (Supplemental Table S2). Quantile regression analyses between proximity to the nearest major roadway and adiposity measures confirmed our findings in the primary analyses: participants who lived closer to a major roadway had higher BMI, SAT, and VAT than those who lived further away, and the associations were consistent across quartiles of the distribution of each adiposity measure. Additionally, the associations of distance to a major roadway with higher percentiles of VAT appeared stronger than the associations with lower percentiles of VAT (Figure 2).

Discussion

In the present study, living closer to a major roadway was associated with higher BMI. We also observed similar associations between distance to the nearest major roadway and SAT but weaker for VAT. We found no association between annual average PM_{2.5} and BMI or measures of abdominal adiposity. We further found some evidence suggesting stronger associations among participants who had higher VAT.

Few studies have examined and reported the associations of residential proximity to the nearest roadway and ambient PM_{2.5} with BMI and abdominal adipose tissue measures among adults. Our results are consistent with findings from the Southern California Children's Health Study to some extent. In that study, higher levels of traffic-related pollution were associated with higher BMI growth and BMI after four (17) and eight years (18, 19) of follow-up. In a study conducted among adults, Ponticello *et al.* found higher mean BMI among traffic policemen compared with indoor police workers (20). However, the authors did not adjust for any characteristics that may have differed between the policemen and indoor workers.

Controlled animal studies have reported that mice exposed to PM_{2.5} had more visceral adipose tissue than mice exposed to filtered air. Among male C57BL/6 mice (6-week old) fed with high-fat chow, after a 24-week PM_{2.5} exposure (72.7 µg/m³; 6 hours/day, 5 days/week), Sun *et al.* found significantly higher visceral fat mass but not subcutaneous fat mass, compared to mice exposed to filtered air (7). Among a group of 3-week old male C57BL/6 mice fed with normal diet, exposure to PM_{2.5} (111.0 µg/m³; 6 hours/day, 5 days/week) was associated with an increase in both visceral and subcutaneous fat content compared to mice exposed to filtered air (8). In both experiments, exposure to PM_{2.5} induced adipose tissue inflammation and metabolic dysfunction (7, 8). However, the exposure concentrations in those animal studies were higher than the annual average PM_{2.5} concentration in our study, and the relevance of animal data to assessing the association between ambient air pollution and abdominal adiposity in humans is unknown. In the current study, we observed no association between residential-based estimates of annual average PM_{2.5} with adiposity measures among adults.

This discrepancy between results for the residential proximity to the nearest major roadway and the satellite model-based annual average PM_{2.5} might be explained by differences between these two exposures. The proximity to a major roadway could be viewed as an integrated measure of near-road exposures. It captures information about traffic-related components besides PM_{2.5}, such as traffic-related gaseous pollutants, road dust, traffic noise, traffic light, vibration, and possible psychological stress (17, 37). However, the satellite model-based PM_{2.5} estimation captures information about regional background pollution levels, local PM_{2.5} components that may be from emission sources far from major roadways, transported PM_{2.5} components from other regions, and local meteorology conditions (23). Residual confounding may also cause this discrepancy if there were some unmeasured variables that were consistently associated with living closer to a major roadway and higher adiposity measures but were not associated with satellite model-based PM_{2.5} predictions. However, this seems unlikely to be the explanation in our study because we have adjusted for a large set of potential confounders in our models, including neighborhood-level measures of socio-economic position that vary spatially, and the influence of residual confounding was expected to be small.

There are several limitations of our study that should be noted. First, participants enrolled in the MDCT study were a relatively healthy cohort and they were predominantly white individuals of European ancestry and middle-aged. Thus, our findings may not be generalizable to other ethnicities and age groups. Second, although we have adjusted for demographic factors, lifestyle factors, and socio-economic position, we cannot exclude the possibility of residual confounding. Third, the adipose tissue volumes were measured only once for each participant, we were not able to assess progression of adiposity. Last, we did not have statistical power to examine whether the observed associations differ by disease status, such as cardiovascular disease or diabetes. However, excluding participants with cardiovascular disease or diabetes did not materially change our results.

Our study also has several strengths. Our study population was from large well-characterized cohorts with standardized protocols for physical examinations and adipose deposition

assessments. The large sample size in our study allowed us to adjust for demographic characteristics, lifestyle factors, and individual- and area-level of socioeconomic position.

Although we were not able to directly measure walkability, we have adjusted for individual-level physical activity in the models. We used a novel spatial-temporal model to estimate PM_{2.5} at a high resolution, and we precisely quantified abdominal adipose tissue volumes using MDCT. The technique has high inter- and intra-reader reliability. Last, assessment of air pollution and adiposity were performed independently of each other, which decreased potential differential measurement errors in exposure and outcome assessments.

Conclusion

Among this relatively large cohort of adults living predominantly in the Northeastern U.S., we found evidence that living closer to a major roadway was associated with higher overall and abdominal adiposity. However, we observed no association of annual PM_{2.5} with adiposity measures. Future longitudinal studies with repeated adiposity measures are necessary to confirm or refute our findings and to extend our findings by exploring changes in adiposity measures associated with traffic-related air pollution.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Provide 1 to 3 bullet point answers. Remember to also include these in your Main Document before your abstract.

- What is already known about this subject? (or for Review Proposals/ Reviews, what major reviews have already been published on this subject?)

Experimental studies have demonstrated that exposure to concentrated fine particulate matter air pollution is associated with increased abdominal adiposity in animal models.

Living in areas with high traffic density is associated with higher body mass index (BMI) growth among children, but few studies examined this association among adults. One study found higher BMI among outdoor traffic policemen than indoor office workers.

- What does this study add?

This study among participants from the Framingham Heart Study demonstrated that living closer to a major roadway is associated with higher BMI and subcutaneous and visceral fat volumes.

The associations persisted after adjusting for a wide range of social, demographic, and behavioral characteristics.

Spatial-temporal model-based estimates of 2003 annual PM_{2.5} concentrations were not associated with any of the adiposity measures, suggesting that factors other than PM_{2.5} may be at least partially responsible for the observed associations.

a.

b.

Figure 1.

The associations between distance categories and (a) body mass index (BMI), (b) subcutaneous adipose tissue (SAT), (c) visceral adipose tissue (VAT), and (d) obesity (BMI ≥ 30 kg/m²). Models were adjusted for age at examination, and (age at examination)²; sex; smoking status (current, former, or never); pack years; alcohol intake; educational level; physical activity; anti-hypertensive medication use; statin use; quartile of median household

income in the participant's census tract in 2000; cardiovascular disease; diabetes, and a cohort identifier. For MDCT analyses, we replaced age at examination with age at CT scan and additionally adjusted for height. P-values from trend tests are shown in the plots. Error bars indicate the 95% confidence intervals.

a.

b.

Figure 2.

Associations between distance to the nearest major roadway and quartiles of the distributions of (a) body mass index (BMI), (b) subcutaneous adipose tissue (SAT), and (c) visceral adipose tissue (VAT). Models were adjusted for age at examination, and (age at examination)²; sex; smoking status (current, former, or never); pack years; alcohol intake; educational level; physical activity; anti-hypertensive medication use; statin use; quartile of median household income in the participant's census tract in 2000; cardiovascular disease; diabetes, and a cohort identifier. For MDCT analyses, we replaced age at examination with age at CT scan and additionally adjusted for height. Results were scaled to approximate comparing participants who lived 60 m from the nearest major roadway to those who lived 440 m from the nearest major roadway. Error bars indicate the 95% confidence intervals.

Table 1

Characteristics of the 2,372 participants.

	N (%) or Mean [SD]
Offspring cohort	1,090 (46.0%)
Age [*] , years	53.9 [11.8]
Women	1,236 (47.9%)
Alcohol, drinks/week	4.8 [7.2]
Current smoker	294 (12.4%)
Former Smoker	953 (40.2%)
Education	
< High school	41 (1.7%)
High School	521 (22.0%)
Some college	771 (32.5%)
College graduate	1,039 (43.8%)
Antihypertensive medication use	541 (22.8%)
Statins use	351 (14.8%)
Cardiovascular disease [*]	192 (8.1%)
Diabetes	173 (7.3%)
PM _{2.5} [‡] , µg/m ³	10.6 [1.4]
Distance [‡] , m	273 [254]
Distance categories [‡]	
0-50 m	487 (23.0%)
50-100 m	204 (9.6%)
100-200 m	373 (17.6%)
200-400 m	480 (22.7%)
400-1000 m	574 (27.1%)

Abbreviation: SD, standard deviation; PM_{2.5}, fine particulate matter.^{*} At the time of CT scan.[‡] 2003 annual average.[‡] 254 participants lived more than 1,000 meters from the nearest major roadway.

Table 2

Characteristics of adiposity measures and the correlation between these measures.

	N	Mean [SD]	Interquartile range	<u>Correlation coefficients</u> [*]	
				SAT	VAT
BMI, kg/m ²	2,372	27.8 [5.3]	6.4	0.83	0.73
SAT, cm ³	2,372	2,914 [1,391]	1,704		0.66
VAT, cm ³	2,372	1,828 [1,046]	1,535		

Abbreviation: SD, standard deviation; BMI, body mass index; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.

^{*} Spearman partial correlation coefficients, adjusted for sex.

Table 3

Associations of distance to a major roadway and PM_{2.5} with adiposity measures.

	<u>Closer to a major roadway</u>		<u>2003 annual average PM_{2.5}</u>	
	β *	95% CI	β *	95% CI
BMI, kg/m ²	0.37	0.10, 0.65	0.08	−0.14, 0.30
SAT, cm ³	78.4	4.5, 152.3	33.0	−25.3, 91.3
VAT, cm ³	41.8	−4.7, 88.2	−10.5	−46.9, 25.9
	Odds Ratio *	95% CI	Odds Ratio *	95% CI
Obesity †	1.10	0.97, 1.25	1.01	0.92, 1.12

Abbreviation: BMI, body mass index; SAT, subcutaneous adipose tissue; VAT, visceral adipose tissue.

* Models were adjusted for age at examination, and (age at examination)²; sex; smoking status (current, former, or never); pack years; alcohol intake; educational level; physical activity; anti-hypertensive medication use; statin use; quartile of median household income in the participant's census tract in 2000; cardiovascular disease; diabetes, and a cohort identifier. For MDCT analyses, we replaced age at examination with age at CT scan and additionally adjusted for height. Results from distance analyses were scaled to approximate comparing participants who lived 60 m from the nearest major roadway to those who lived 440 m from the nearest major roadway. Results from PM_{2.5} analyses were scaled to be as equivalent to per 1.5 µg/m³ increase in 2003 annual PM_{2.5} concentrations.

† Defined as BMI ≥ 30 kg/m².