Published in final edited form as:

Pediatr Obes. 2018 January ; 13(1): 54–62. doi:10.1111/ijpo.12188.

Effects of air pollution exposure on glucose metabolism in Los Angeles minority children

CM Toledo-Corral^{1,2,*}, TL Alderete^{2,3,*}, R Habre², K Berhane², FW Lurmann⁴, MJ Weigensberg⁵, MI Goran^{3,6}, and FD Gilliland²

¹California State University, Los Angeles, Department of Public Health ²University of Southern California, Department of Preventive Medicine, Division of Environmental Health ³University of Southern California, Department of Preventive Medicine, Diabetes and Obesity Research Institute ⁴Sonoma Technology, Inc ⁵University of Southern California, Department of Pediatrics ⁶University of Southern California, Department of Physiology and Biophysics

Abstract

Objective—Growing evidence indicates that ambient (AAP: NO₂, PM_{2.5}, and O₃) and traffic-related (TRAP) air pollutants contribute to metabolic disease risk in adults; however, few studies have examined these relationships in children.

Methods—Metabolic profiling was performed in 429 overweight and obese African-American and Latino youth living in urban Los Angeles, California. This cross-sectional study estimated individual residential air pollution exposure and used linear regression to examine relationships between air pollution and metabolic outcomes.

Results—AAP and TRAP exposure were associated with adverse effects on glucose metabolism independent of body fat percent. PM_{2.5} was associated with 25.0% higher fasting insulin ($p < 0.001$), 8.3% lower insulin sensitivity (SI) ($p < 0.001$), 14.7% higher acute insulin response to glucose (AIR_g) ($p = 0.001$), and 1.7% higher fasting glucose ($p < 0.001$). Similar associations were observed for increased NO₂ exposure. TRAP from non-freeway roads was associated with 12.1% higher insulin ($p < 0.001$), 6.9% lower SI ($p = 0.02$), 10.8% higher AIR_g ($p = 0.003$), and 0.7% higher fasting glucose ($p = 0.047$).

Conclusions—Elevated air pollution exposure was associated with a metabolic profile that is characteristic of increased risk for type 2 diabetes. These results indicate that increased prior year

Corresponding author: Frank D. Gilliland, MD, PhD, Southern California Environmental Health Sciences Center, Department of Preventive Medicine, University of Southern California, Keck School of Medicine of USC, 2001 N. Soto Street, Los Angeles, CA 90032, Phone: (323) 442-1309, gilliland@usc.edu.

* Authors contributed equally to this work.

Author contributions

C.M. Toledo-Corral and T.L. Alderete conceived the research question, study design, collected and reviewed data, ran analysis, and wrote the manuscript. M.I. Goran, M.J. Weigensberg, and F.D. Gilliland conceived the primary study design. R. Habre assembled residential data, guided geocoding efforts, designed and created the final analysis dataset combining exposures and clinical outcomes and contributed to analysis and writing of methods. K. Berhane provided statistical consultation and carefully reviewed results. F. Lurmann provided air pollution exposure data and contributed to manuscript writing. All authors reviewed the article. C. Toledo-Corral, T.L. Alderete, and F.D. Gilliland are the guarantors of this work, and as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors declare that they have no conflict of interest.

exposure to air pollution may adversely affect type 2 diabetes-related pathophysiology in overweight and obese minority children.

Keywords

childhood obesity; environmental factors; air pollution; insulin sensitivity; glucose metabolism; health disparities

Introduction

In the United States, the prevalence and incidence of type 2 diabetes more than doubled from 1990 to 2008 (1). While rates in Whites have plateaued or decreased since 2008, prevalence and incidence of type 2 diabetes in racial and ethnic minorities continue to increase (1). Although obesity is recognized as the strongest predictor of type 2 diabetes, environmental factors appear to confer additional risk. Historically, ambient air pollutants (AAP) and traffic-related air pollution (TRAP) have been associated with respiratory and cardiovascular disease (2), yet it is only recently that studies have begun to link elevated air pollution exposure with metabolic dysfunction in humans (3). At the same time, national and regional reports have detected significantly more air pollution in non-White neighborhoods (4,5), suggesting that increased rates and disparities in type 2 diabetes prevalence may be attributed to factors beyond increased adiposity. An improved understanding of the potential role of air pollution in type 2 diabetes is needed to develop effective interventions targeting the disparate burden of this disease.

Although air pollution has been associated with increased risk for type 2 diabetes (6–17), it is unclear the mechanism through which these pollutants increase risk. We hypothesized that elevated AAP increases type 2 diabetes occurrence by adversely affecting glucose metabolism and the underlying physiology starting early in life, including decreasing whole-body insulin sensitivity (SI) and pancreatic β -cell function. Further, few studies have investigated the detrimental effects of air pollution exposure on metabolic health in pediatric and minority populations (18–20). Therefore, the objective of this study was to determine whether prior exposure to AAP and TRAP were related to measures of glucose metabolism in overweight and obese African-American and Latino children living in Los Angeles, CA. We investigated the specific hypothesis that, independent of obesity, previous cumulative 12-month exposure to nitrogen dioxide (NO_2), ozone (O_3), particulate matter ($\text{PM}_{2.5}$) and nitric oxides (NO_x) increases type 2 diabetes risk as defined by higher fasting glucose in conjunction with lower whole-body insulin sensitivity (SI), insulin secretion, and pancreatic β -cell function.

Research Design and Methods

Participants

Analyses were conducted on participants from the Childhood Obesity Research Center (CORC)-Air Study, in which all participants had a common protocol for detailed phenotyping of body fat and risk factors for type 2 diabetes. The studies were conducted between 2001 and 2012 and participants included 429 overweight and obese African-

American and Latino (58 African-American and 371 Latino) aged 8 to 18 years who reported self, parents, and grandparents as African-American or Latino. A detailed description of these studies have been previously reported (21,22). Participants included in this study lived in urban Los Angeles, California (CA) and were recruited mostly from local metabolic clinics, but also through word-of-mouth, health fair recruitment, and advertisements in the local communities of East and South Los Angeles, which are areas well known of high obesity rates. Participants with Type 1 or Type 2 Diabetes were excluded from the study, as were those who were taking many medications that may interfere with insulin sensitivity. Before any testing, informed written consent/assent was obtained from the participant or parents. The University of Southern California Institutional Review Board approved these studies.

Residential Air Pollution Exposure Assessment

Street-level residential addresses of participants were geocoded at the parcel level and match codes were output using the Texas A&M Geocoder (<http://geoservices.tamu.edu/Services/Geocode/>). Addresses that did not initially match to a parcel centroid (e.g., address range interpolation or zip/city/state centroid) were manually corrected using Google Maps based on the best available knowledge of the participant's residence location. For AAP (NO₂, O₃, and PM_{2.5}), we assigned monthly air pollution exposure data for up to 12 months prior to each visit participant. Exposures were spatially interpolated from the air quality monitoring station's locations to the participant's residence at the finest geographic resolution possible (usually parcel-level) using inverse distance-squared weighting (more details in Supplement).

For TRAP, we conducted dispersion modeling to estimate annual-average exposure to local traffic pollution resulting from motor vehicle activity on roads within 5 km, for each residence with both an accurate street-level geocode (address range interpolation, building centroid or exact parcel centroid) and sufficient local traffic volume data. Specifically, TRAP was modeled as NO_x emissions from local, on-road traffic exhaust using local meteorological data, emission factors from EMFAC2011, and the CALINE4 line dispersion model (23). The model was applied to estimate the traffic impact from each of the four Feature Class Code (FCC) road classes: Freeway or highway (FCC1), major collector (FCC2), minor collector (FCC3), and arterial road (FCC4) (using Streetmap Premium database, ArcGIS 10.1, Environmental Systems Research Institute Inc., Redlands, CA). Non-freeway NO_x was defined as the sum of FCC2, FCC3 and FCC4 NO_x.

Metabolic and Adiposity Assessment

All participants attended two clinical visits at either the Los Angeles County Hospital or the USC University Hospital. The first visit was outpatient and participants received a comprehensive medical history and physical examination by a licensed health care provider. Pubertal stage (Tanner Staging) was determined by physical examination using breast stage for girls and pubic hair stage for boys (24,25). Clinical staff performed an 8–10 hour fasting blood draw followed by a 2-hour oral glucose tolerance test (OGTT) with an oral glucose challenge (1.75 g oral glucose solution/kg body weight to a maximum 75 g). Following the outpatient visit, participants were admitted for an overnight inpatient visit at the same

facility where a supervised fasting period of 8 hours took place. At 06:30 hr the following morning, a 13-sample insulin-modified frequently sampled intravenous glucose tolerance test (FSIVGTT) was performed as follows: Intravenous catheters were placed in the antecubital fossae of both arms, one for infusions and one for sampling. After two fasting blood samples were taken at -15 and -5 min, glucose (0.3 g/kg body weight) was administered at time 0 over a 1-min period. Subsequent blood samples were collected at 2, 4, 8, and 19 min. Insulin (0.02 U/kg body weight, Humulin R; Eli Lilly, Indianapolis, IN) was administered intravenously at 20 min, followed by blood sample collection at 22, 30, 40, 50, 70, 100, and 180 min. Glucose was assayed using a Yellow Springs Instruments analyzer (YSI INC., Yellow Springs, OH) and insulin was assayed using an automated enzyme immunoassay (Tosoh AIA 600 II analyzer, Tosoh Bioscience, Inc., South San Francisco, CA). Glucose and insulin data from the FSIVGTT were entered into MINMOD software (version 6.02; RN Bergman, Los Angeles, CA) for calculation of whole body insulin sensitivity (SI), the acute insulin response to glucose (AIR_g; an early phase secretion in response to intravenous glucose bolus) and the disposition index (DI = the product of SI and AIR_g). DI is a measure of the ability of the islet cells to secrete insulin normalized to the degree of insulin resistance and is routinely used as an assessment of β -cell function. HOMA-IR was calculated using the fasting glucose and insulin from the 2-hour OGTT using the standard formula for using glucose in units of mg/dl: $\text{HOMA-IR} = \text{glucose (mg/dL)} \times \text{insulin (}\mu\text{L)} / 405$ (26).

Total body composition was determined at either visit, based on availability of the participant and staff, by dual-energy x-ray absorptiometry using a Hologic QDR 4500 W (Hologic, Bedford, MA). Single-slice abdominal MRI scans were performed on a subset of the participants (N=179). Abdominal fat distribution was measured directly by magnetic resonance imaging (MRI) using a General Electric 1.5 Signa LX-Echospeed device with a General Electric 1.5-Telsa magnet (Waukesha, WI). A single-slice axial TR 400/16 view of the abdomen at the level of the umbilicus was analyzed for cross-sectional area of visceral adipose tissue and subcutaneous abdominal adipose tissue (27).

Social Position

To assess socioeconomic status, we utilized a modified version of the Hollingshead Four Factor Index of Social Status in those participants where relevant information was available (N=379; Supplement Table 1) (28). This index factors in occupation and education of each parent/guardian residing in the child's home in order to generate a single measure of a family's social status. An education score of 1 to 7 was assigned to parents/guardians living in the household where 1 corresponded to less than a seventh-grade education and 7 to graduate training. Individuals who reported being either homemakers, unemployed, or students did not have categories based on the Hollingshead method and would not be included in the household social position score (n=171). We utilized a modified scoring system where these individuals were assigned a score of 0 in order to retain them in the final score. Using this method, 1 corresponded to an unskilled employee and 7 was assigned to those with employment roughly corresponding to higher executives and major professionals. Education and occupation scores were weighted to obtain a single score for each parent/guardian and when there were multiple caretakers scores were averaged to obtain a single

household social position score or index. Social position was categorized into four categories: less than or equal to the 25th (n=116), greater than the 25th percentile and less than the 75th (n=158), greater than or equal to the 75th percentile (n=105), and missing education and occupational data (n=50).

Statistical Analysis

Our total sample size was 429 participants. All 429 participants had measures of ambient air pollution exposure, height, weight, and data from a 2-hour OGTT. Of the 429 participants, all but one had TRAP exposure data, 426 had measures of adiposity, and 387 had data from a FSIVGTT. Only 179 participants had data available for central adiposity including subcutaneous abdominal (SAAT) and intra-abdominal adipose tissue (IAAT).

Participants in this study were recruited between 2001 and 2012, a period of time in which ambient air pollution concentrations declined in Los Angeles, CA (29). To account for this, we explored a modeling strategy where we used mixed modeling to allow for a random intercept of year while *a priori* covariates included age, sex, and total percent fat mass where appropriate as well as pubertal stage (Tanner Stage), ethnicity, and seasonality (cool and warm). Results from this analysis revealed that the variance of year was very close to zero and non-significant. Moreover, results were similar to a linear model that did not include any random effects (data not shown). For this reason, we used multiple linear regression modeling for all subsequent analysis and controlled for *a priori* covariates. For each pollutant, we created a yearly average as well as a deviation variable that estimated the individual's estimated exposure over various monthly lags. Results were driven by yearly exposure and our final analysis contained pollutants at the individual level in which we examined cumulative 12-month exposure. Final models assessing effects of O₃ exposure adjusted for prior year NO₂ exposure due to observed confounding. Associations between outcomes and O₃ exposure are shown before and after adjusting for prior year NO₂ are shown in Supplemental Table 2. African Americans were excluded in a sensitivity analysis where final results were not significantly altered (data not shown).

Social position was categorized into four categories: less than or equal to the 25th (n=116), greater than the 25th percentile and less than the 75th (n=158), greater than or equal to the 75th percentile (n=105), and missing education and occupational data (n=50). This social position indicator variable was added as an additional covariate to each model where changes in effects sizes and significance of our exposure were examined. Parameter estimates for 1-unit or 1-SD increase in AAP and TRAP were back transformed to percent change. Results were considered significant at a two-sided p<0.05. All analyses were performed in SAS, version 9.4 (SAS, Institute, Cary, NC).

Results

Participants were between 8–18 years of age (12.5 ± 2.7 years), 56% were male, and 86% were Latino (Table 1). Participants had an average BMI percentile of 96.8 ± 3.2 . Fifty participants did not have social position data available but were similar in regards to age, sex, adiposity, and metabolic indices as those who reported this information (Supplemental Table 1). Among those with parental/guardian information (N=379), 67% had less than a

high school diploma/GED, and 93% classified at or below the level of skilled manual workers. Average levels of residential annual air pollution exposures are shown in Table 2. Significant correlations were observed among AAP and TRAP (Supplemental Table 3).

Ambient Air Pollution (AAP)

Cumulative 12-month AAP exposures were significantly associated with adverse metabolic outcomes. For example, both NO₂ and PM_{2.5} were associated with higher fasting glycemia and insulin, lower SI, and higher insulin secretion (Table 3). Specifically, each SD increase in NO₂ and PM_{2.5} exposure was associated with 22.8% ($p<0.001$) and 24.7% ($p<0.001$) higher fasting insulin, respectively. At the same time, each SD increase in NO₂ and PM_{2.5} exposure was associated with a 1.6% ($p<0.001$) and 1.6% ($p<0.001$) higher fasting glucose. HOMA-IR was 25.1% ($p<0.001$) and 26.9% ($p<0.001$) higher for each SD increase in NO₂ and PM_{2.5} exposure. NO₂ and PM_{2.5} was related to a 8.5% ($p=0.03$) and 11.2% ($p=0.003$) lower SI as well as a 12.7% ($p=0.006$) and 14.2% ($p=0.002$) higher AIR_g, per a SD increase in exposure. In regards to measures of adiposity, only elevated annual exposure to PM_{2.5} was associated with a higher BMI z-score ($\beta=0.05$; $p=0.04$). AAP was not related to 2-hour clinical glucose, DI, total body fat percent, SAAT, or IAAT (Supplemental Table 4). Results were unchanged after adjusting for social position (Table 3; **Model 2**). Cumulative monthly lag exposures were not associated with these outcomes (data not shown).

Traffic-Related Air Pollution (TRAP)

Annual measures of TRAP were associated with metabolic indices (Table 3). Non-freeway and total NO_x were associated with higher insulin and fasting glucose, lower SI, and higher insulin secretion. Each SD increase in non-freeway NO_x exposure was related to a 12.1% higher fasting insulin ($p<0.001$), 0.7% higher fasting glucose ($p=0.047$), 12.9% higher HOMA-IR ($p<0.001$), 6.9% lower SI ($p=0.02$), and 10.8% higher AIR_g ($p=0.002$). For total NO_x, each SD increase in exposure was related to a 6.7% higher fasting insulin ($p=0.02$), 7.5% higher HOMA-IR ($p=0.02$), and 7.6% higher AIR_g ($p=0.04$). TRAP was not associated with 2-hour clinical glucose, DI, BMI z-score, total body fat percent, SAAT, or IAAT (Supplemental Table 4). These results were unchanged after adjusting for social position (Table 3; **Model 2**).

Discussion

Our results demonstrate that air pollution exposure is related to an adverse metabolic profile that has been linked with increased risk for type 2 diabetes (6–17). Among overweight and obese minority youth, higher levels of cumulative 12-month exposure to NO₂, PM_{2.5}, and TRAP were related to small elevations in fasting glucose and decreased SI that were independent of adiposity and social position. Exposure to non-freeway NO_x was associated with higher insulin resistance and insulin secretion. Since metabolic indices were unrelated to freeway NO_x, exposure to NO_x from smaller and perhaps more proximal roadways appeared to be a more metabolically relevant metric of air pollution exposure in our cohort. Independent of adiposity, NO₂, PM_{2.5} and TRAP exposure were associated with adverse metabolic health, providing strong evidence that air pollution exposure contributes to the underlying pathophysiology of type 2 diabetes. These novel findings suggest that, in

response to environmental air pollutants, metabolic regulation is maintained via robust increases in fasting insulin and AIR_g that highlight pancreatic resiliency during adolescence (30).

In the current study, AAP and TRAP were associated with disruption of insulin and glucose function, however the exact underlying mechanisms are largely unknown. Since healthy mice exposed to $PM_{2.5}$ have been shown to have increased inflammation, endothelial dysfunction, and suppression of insulin signaling, leading to insulin resistance (31–33) we hypothesize that air pollution has direct effects on metabolic health independent of increases in adiposity. Supporting this, we found that air pollution exposure was unrelated to measures of total body fat or abdominal adiposity, indicating that increased air pollution exposure may have independent adverse effects on SI, insulin secretion, and glycemia. However, 12-month exposure to $PM_{2.5}$ was related to a slightly higher BMI z-score, yet without lifetime residential history we were unable to determine whether an extended history of air pollution exposure was related to obesity. In a separate study from our group, we showed that one-month AAP exposure was associated with type 2 diabetes risk factors in predominately female Mexican-American adults (9). This contrasts to our current study findings that showed no acute effects of ambient air pollution, but rather long-term cumulative effects on type 2 diabetes risk in a mixed population of Latino and African-American children. We hypothesize that due to the metabolic resilience observed in adolescence (30), children are less sensitive to the acute effects of AAP. However, future longitudinal studies are needed to fully characterize the short-term and lifelong effects of AAP exposure in children and adults.

To put the magnitude of the effects of AAP and TRAP into context, we compared the relative importance of air pollution exposure with effects of measures of adiposity on the metabolic outcomes of interest. We found that adiposity had adverse effects on glucose metabolism with a lower SI and higher AIR_g . The magnitude of the adverse effect of adiposity was on the same order of magnitude as the effect of elevated AAP and TRAP exposures (Supplemental Table 5). These findings suggest that independent of adiposity, increased air pollution exposure has clinical and public health importance in addressing type 2 diabetes prevention.

Despite the strengths of this study, we did not have diet and physical activity measures or lifetime residential history information. Therefore, results have the potential for residual confounding by poor diet and/or lack of physical activity since each of these factors are associated with increased adiposity, metabolic dysregulation, and residential proximity to sources of AAP and TRAP (33,34). However, our results are unlikely to be explained by residual confounding by these factors because adjustment for social position, a strong determinant of these factors, did not substantially change our results. The use of residential based estimates of air pollution exposure may have resulted in exposure misclassification; however, this misclassification likely attenuates our observed effects (35). Since this study excluded lean children and other racial/ethnic groups our study results had limited generalizability to overweight and obese minority youth mostly of a lower social position. We have previously shown that secondhand smoke exposure along with traffic-related air pollution can have synergistic effects on BMI (20), however this study population, we did not assess secondhand smoke exposure. Despite these limitations, our findings provide new

knowledge about the detrimental relationships between air pollution exposure and risk factors for type 2 diabetes in overweight and obese minority youth.

In summary, increased exposure to air pollution was associated with higher insulin resistance and secretion, which was observed in conjunction with higher glycaemia. Based on these findings, AAP and TRAP appear to act as environmental factors that contribute to risk factors for type 2 diabetes independent of adiposity. We speculate that prolonged exposure to increased air pollution may elicit a constant and strong compensatory response that would eventually lead to β -cell exhaustion and overt metabolic disease. These findings highlight the importance of the physical environment in metabolic health, particularly for vulnerable racial/ethnic groups as well as children who are highly susceptible to toxic elements during development. Results from this study strongly implicate the role of the physical environment in contributing to risk factors for type 2 diabetes, where independent of adiposity and social position, there appears to be direct effects of AAP and TRAP on glucose metabolism.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Grants

This work was funded by several NIH agencies: NCMHD P60MD002254 (MJW, MIG); NIDDK grant R01DK29511 (MIG); NIEHS: P30ES007048 (FDG).

References

1. Geiss LS, Wang J, Cheng YJ, Thompson TJ, Barker L, Li Y, et al. Prevalence and incidence trends for diagnosed diabetes among adults aged 20 to 79 years, United States, 1980–2012. *JAMA*. 2014 Sep 24; 312(12):1218–26. [PubMed: 25247518]
2. Brunekreef B, Holgate ST. Air pollution and health. *Lancet*. 2002 Oct 19; 360(9341):1233–42. [PubMed: 12401268]
3. Rajagopalan S, Brook RD. Air pollution and type 2 diabetes: mechanistic insights. *Diabetes American Diabetes Association*. 2012 Dec; 61(12):3037–45.
4. Clark, LP., Millet, DB., Marshall, JD. National Patterns in Environmental Injustice and Inequality: Outdoor NO₂ Air Pollution in the United States. In: Zhang, Y., editor. *PLoS ONE*. Vol. 9. 2014 Apr 15. p. e94431-8.
5. OEHHA. Analysis of Race/Ethnicity-California Communities Environmental Health Screening Tool (CalEnviroScreen 2.0). 2014 Aug 14. p. 1-7.
6. Krämer U, Herder C, Sugiri D, Strassburger K, Schikowski T, Ranft U, et al. Traffic-related air pollution and incident type 2 diabetes: results from the SALIA cohort study. *Environ Health Perspect*. 2010 Sep; 118(9):1273–9. [PubMed: 20504758]
7. Coogan PF, White LF, Jerrett M, Brook RD, Su JG, Seto E, et al. Air pollution and incidence of hypertension and diabetes mellitus in black women living in Los Angeles. *Circulation Lippincott Williams & Wilkins*. 2012 Feb 14; 125(6):767–72.
8. Chen H, Burnett RT, Kwong JC, Villeneuve PJ, Goldberg MS, Brook RD, et al. Risk of incident diabetes in relation to long-term exposure to fine particulate matter in Ontario, Canada. *Environ Health Perspect*. 2013 Jul; 121(7):804–10. [PubMed: 23632126]

9. Chen Z, Salam MT, Toledo-Corral C, Watanabe RM, Xiang AH, Buchanan TA, et al. Ambient Air Pollutants Have Adverse Effects on Insulin and Glucose Homeostasis in Mexican Americans. *Diabetes Care*. 2016 Apr; 39(4):547–54. [PubMed: 26868440]
10. Eze IC, Schaffner E, Zemp E, Eckardstein von A, Turk A, Bettschart R, et al. Environmental tobacco smoke exposure and diabetes in adult never-smokers. *Environmental Health*. 2014; 13(1): 74. [PubMed: 25253088]
11. Pearson JF, Bachireddy C, Shyamprasad S, Goldfine AB, Brownstein JS. Association between fine particulate matter and diabetes prevalence in the U.S. *Diabetes Care*. American Diabetes Association. 2010 Oct; 33(10):2196–201.
12. Park SK, Adar SD, O'Neill MS, Auchincloss AH, Szpiro A, Bertoni AG, et al. Long-Term Exposure to Air Pollution and Type 2 Diabetes Mellitus in a Multiethnic Cohort. *American Journal of Epidemiology*. 2015 Feb 24; 181(5):327–36. [PubMed: 25693777]
13. Tamayo, T., Rathmann, W., Krämer, U., Sugiri, D., Grabert, M., Holl, RW. Is particle pollution in outdoor air associated with metabolic control in type 2 diabetes?. In: Kronenberg, F., editor. *PLoS ONE*. Vol. 9. Public Library of Science; 2014. p. e91639
14. Chuang, K-J., Yan, Y-H., Chiu, S-Y., Cheng, T-J. *Occup Environ Med*. Vol. 68. BMJ Publishing Group Ltd; 2011 Jan. Long-term air pollution exposure and risk factors for cardiovascular diseases among the elderly in Taiwan; p. 64-8.
15. Kim JH, Hong YC. GSTM 1, GSTT 1, and GSTP 1 Polymorphisms and Associations between Air Pollutants and Markers of Insulin Resistance in Elderly Koreans. *Environmental Health*. 2012
16. Brook, RD., Sun, Z., Brook, JR., Zhao, X., Ruan, Y., Yan, J., et al. Hypertension. Vol. 67. Lippincott Williams & Wilkins; 2016 Jan. Extreme Air Pollution Conditions Adversely Affect Blood Pressure and Insulin Resistance: The Air Pollution and Cardiometabolic Disease Study; p. 77-85.
17. Brook RD, Xu X, Bard RL, Dvonch JT, Morishita M, Kaciroti N, et al. Reduced metabolic insulin sensitivity following sub-acute exposures to low levels of ambient fine particulate matter air pollution. *Sci Total Environ*. 2013 Mar 15; 448:66–71. [PubMed: 22901427]
18. Kelishadi R, Mirghaffari N, Poursafa P, Gidding SS. Lifestyle and environmental factors associated with inflammation, oxidative stress and insulin resistance in children. *Atherosclerosis*. 2009 Mar; 203(1):311–9. [PubMed: 18692848]
19. Jerrett, M., McConnell, R., Chang, CCR., Wolch, J., Reynolds, K., Lurmann, F., et al. Preventive Medicine. Vol. 50. Elsevier Inc; 2010 Jan 1. Automobile traffic around the home and attained body mass index: A longitudinal cohort study of children aged 10–18 years; p. S50-8.
20. McConnell R, Shen E, Gilliland FD, Jerrett M, Wolch J, Chang C-C, et al. A longitudinal cohort study of body mass index and childhood exposure to secondhand tobacco smoke and air pollution: the Southern California Children's Health Study. *Environ Health Perspect*. 2015 Apr; 123(4):360–6. [PubMed: 25389275]
21. Goran, MI., Bergman, RN., Avila, Q., Watkins, M., Ball, GDC., Shaibi, GQ., et al. *J Clin Endocrinol Metab*. Vol. 89. Endocrine Society; 2004 Jan. Impaired glucose tolerance and reduced beta-cell function in overweight Latino children with a positive family history for type 2 diabetes; p. 207-12.
22. Toledo-Corral, CM., Alderete, TL., Hu, HH., Nayak, K., Esplana, S., Liu, T., et al. *J Clin Endocrinol Metab*. Vol. 98. Endocrine Society Chevy Chase; MD: 2013 Mar. Ectopic fat deposition in prediabetic overweight and obese minority adolescents; p. 1115-21.
23. Benson PE. A review of the development and application of the CALINE3 and 4 models. *Atmospheric Environment Part B Urban Atmosphere*. 1992; 26B:379–90.
24. Marshall, WA., Tanner, JM. *Archives of Disease in Childhood*. Vol. 45. BMJ Publishing Group Ltd and Royal College of Paediatrics and Child Health; 1970 Feb 1. Variations in the Pattern of Pubertal Changes in Boys; p. 13-23.
25. Marshall, WA., Tanner, JM. *Archives of Disease in Childhood*. Vol. 44. BMJ Group; 1969 Jun. Variations in pattern of pubertal changes in girls; p. 291-303.
26. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia*. 1985 Jul; 28(7):412–9. [PubMed: 3899825]

27. Ross R, Léger L, Morris D, de Guise J, Guardo R. Quantification of adipose tissue by MRI: relationship with anthropometric variables. *J Appl Physiol*. 1992 Feb; 72(2):787–95. [PubMed: 1559959]
28. Hollingshead, AB. Four Factor Index of Social Status. In: Smith, P., editor. *Yale Journal of Sociology*. Vol. 8. 2011 Dec 3. p. 21-52.
29. Pollack IB, Ryerson TB, Trainer M, Neuman JA, Roberts JM, Parrish DD. Trends in ozone, its precursors, and related secondary oxidation products in Los Angeles, California: A synthesis of measurements from 1960 to 2010. *J Geophys Res Atmos*. 2013 Jun 13; 118(11):5893–911.
30. Kelly LA, Lane CJ, Weigensberg MJ, Toledo-Corral CM, Goran MI. Pubertal changes of insulin sensitivity, acute insulin response, and β -cell function in overweight Latino youth. *J Pediatr*. 2011 Mar; 158(3):442–6. [PubMed: 20888012]
31. Mendez, R., Zheng, Z., Fan, Z., Rajagopalan, S., Sun, Q., Zhang, K. *Am J Transl Res*. Vol. 5. e-Century Publishing Corporation; 2013. Exposure to fine airborne particulate matter induces macrophage infiltration, unfolded protein response, and lipid deposition in white adipose tissue; p. 224-34.
32. Zheng Z, Xu X, Zhang X, Wang A, Zhang C, Hüttemann M, et al. Exposure to ambient particulate matter induces a NASH-like phenotype and impairs hepatic glucose metabolism in an animal model. *J Hepatol*. 2013 Jan; 58(1):148–54. [PubMed: 22902548]
33. Xu, X., Yavar, Z., Verdin, M., Ying, Z., Mihai, G., Kampfrath, T., et al. *Arterioscler Thromb Vasc Biol*. Vol. 30. Lippincott Williams & Wilkins; 2010 Dec. Effect of early particulate air pollution exposure on obesity in mice: role of p47phox; p. 2518-27.
34. Hsieh S, Klassen AC, Curriero FC, Caulfield LE, Cheskin LJ, Davis JN, et al. Built environment associations with adiposity parameters among overweight and obese Hispanic youth. *Preventive Medicine Reports*. 2015; 2:406–12. [PubMed: 26339570]
35. Nerrière É, Zmirou-Navier D, Blanchard O, Momas I, Ladner J, Le Moullec Y, et al. Can we use fixed ambient air monitors to estimate population long-term exposure to air pollutants? The case of spatial variability in the Genotox ER study. *Environ Res*. 2005 Jan; 97(1):32–42. [PubMed: 15476731]

Table 1

General Characteristics of Overweight and Obese African-American and Latino Participants Living in Urban Los Angeles, CA

n=429	
Physical Characteristics	
Age (years)	12.5 ± 2.7
Sex (F/M)	189/240
Ethnicity (African Americans/Latinos)	58/371
Pubertal Status	
Tanner 1	108
Tanner 2	122
Tanner 3	41
Tanner 4	57
Tanner 5	101
Height (cm)	153.6 ± 12.8
Weight (kg)	70.9 ± 22.3
Adiposity	
BMI (kg/m ²)	29.4 ± 6.1
BMI Percentile	96.8 ± 3.2
BMI z-score	2.03 ± 0.44
Total Fat Mass (kg) ^a	32.5 ± 14.9
Total Lean Tissue Mass (kg) ^a	35.4 ± 11.1
Total Percent Fat (%) ^a	38.3 ± 6.4
Subcutaneous Abdominal Adipose Tissue (cm ²) ^b	338.5 ± 142.2
Intra-abdominal Adipose Tissue (cm ²) ^b	48.2 ± 20.9
Metabolic Outcomes	
2-Hour Oral Glucose Tolerance Test	
Fasting Glucose (mg/dL)	89.0 ± 6.8
2-hour Glucose (mg/dL) ^c	124.1 ± 20.3
Fasting Insulin (μU/mL) ^d	15.0 ± 10.4
2-hour Insulin (μU/mL) ^e	144.5 ± 137.0
HOMA-IR ^d	3.3 ± 2.4
Frequently Sampled Intravenous Glucose Tolerance Test	
Fasting Glucose (mg/dL) ^f	91.3 ± 6.2
Fasting Insulin (μU/mL) ^g	18.3 ± 11.1
Insulin Sensitivity (x10 ⁻⁴ min ⁻¹)/μU/mL ^h	2.1 ± 1.5
Acute Insulin Response (μU/mL × 10min) ^h	1,650.4 ± 1,219.6
Disposition Index ^h	2,513.7 ± 1,334.6

General characteristics of participants included in this study. The table shows the unadjusted means with the standard deviation.

N= ^a427, ^b179, ^c428, ^d419, ^e418, ^f384, ^g385, and ^h387.

Table 2

Average Levels of Residential Annual Air Pollution Exposures in Overweight and Obese African-American and Latino Youth Participants Living in Urban Los Angeles, CA

n=429	
12-Month Cumulative AAP	
NO ₂ (ppb)	27.3 ± 6.8
PM _{2.5} (µg/m ³)	17.8 ± 5.2
O ₃ (ppb)	20.9 ± 3.0
Annual TRAP	
Freeway NO _x	25.3 ± 24.3
Non-Freeway NO _x	7.6 ± 4.8
Total NO _x	32.9 ± 25.2

Average 12-month cumulative ambient air pollution (AAP) and traffic-related air pollution (TRAP) exposure with standard deviation at time of outpatient visit.

Table 3

Estimated Percent Change in Metabolic Indices for One-Standard Deviation Increase in Previous Cumulative 12-month Exposure to Ambient Air Pollutant (AAP) and Previous Year Exposure to Traffic-Related Air Pollution (TRAP) Among Overweight and Obese African-American and Latino Participants Living in Urban Los Angeles, CA ^a

	n	Model 1 Adjusted Estimates		Model 2 Adjusted Estimates Including Social Position	
		%	p-value	%	p-value
Fasting Glucose					
NO ₂	429	1.7	<0.001	1.6	<0.001
PM _{2.5}	429	1.7	<0.001	1.6	<0.001
O ₃ †	429	0.2	0.70	0.2	0.69
Freeway NO _x	427	0.5	0.12	0.5	0.17
Non-Freeway NO _x	427	0.7	0.047	0.7	0.045
Total NO _x	427	0.7	0.06	0.6	0.08
Fasting Insulin					
NO ₂	419	23.2	<0.001	22.8	<0.001
PM _{2.5}	419	25.0	<0.001	24.7	<0.001
O ₃ †	419	−0.2	0.95	−0.2	0.96
Freeway NO _x	417	4.4	0.13	3.6	0.22
Non-Freeway NO _x	417	12.1	<0.001	12.3	<0.001
Total NO _x	417	6.7	0.02	6.0	0.045
HOMA-IR					
NO ₂	419	25.6	<0.001	25.1	<0.001
PM _{2.5}	419	27.4	<0.001	26.9	<0.001
O ₃ †	419	−0.05	0.99	−0.04	0.99
Freeway NO _x	417	5.0	0.10	4.2	0.17
Non-Freeway NO _x	417	12.9	<0.001	13.1	<0.001
Total NO _x	417	7.5	0.02	6.7	0.03
SI					
NO ₂	387	−9.4	0.01	−8.5	0.03
PM _{2.5}	387	−12.0	<0.001	−11.2	0.003
O ₃ †	387	−1.2	0.78	−1.5	0.74
Freeway NO _x	386	−3.2	0.33	−2.5	0.44
Non-Freeway NO _x	386	−6.9	0.02	−7.0	0.02
Total NO _x	386	−4.5	0.16	−3.9	0.23
AIR _g					
NO ₂	387	13.2	0.004	12.7	0.006
PM _{2.5}	387	14.7	0.001	14.2	0.002

	n	Model 1 Adjusted Estimates		Model 2 Adjusted Estimates Including Social Position	
		%	p-value	%	p-value
O ₃ [†]	387	-3.2	0.50	-3.1	0.51
Freeway NO _x	386	5.4	0.13	5.1	0.16
Non-Freeway NO _x	386	10.8	0.002	10.9	0.002
Total NO _x	386	7.6	0.04	7.3	0.047

^a Estimated percent change in metabolic indicators as a function of each 1-standard deviation increase in 12-month cumulative ambient air pollution (AAP) exposure and annual traffic-related air pollution (TRAP).

[†] Two-pollutant model that also adjusts for cumulative 12-month NO₂ exposure. Model 1 adjusts for age, sex, ethnicity, pubertal stage, total percent fat mass, and seasonality. Model 2 also adjusts for social position.