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Prenatal air pollution exposure and ultrasound measures of fetal growth in Los Angeles, California ☆

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ABSTRACT

Background: Few previous studies examined the impact of prenatal air pollution exposures on fetal development based on ultrasound measures during pregnancy.
Methods: In a prospective birth cohort of more than 500 women followed during 1993–1996 in Los Angeles, California, we examined how air pollution impacts fetal growth during pregnancy. Exposure to traffic related air pollution was estimated using CALINE4 air dispersion modeling for nitrogen oxides (NO_x) and a land use regression (LUR) model for nitrogen monoxide (NO), nitrogen dioxide (NO_2) and NO_x. Exposures to carbon monoxide (CO), NO_2, ozone (O_3) and particles < 10 μm in aerodynamic diameter (PM_{10}) were estimated using government monitoring data. We employed a linear mixed effects model to estimate changes in fetal size at approximately 19, 29 and 37 weeks gestation based on ultrasound.
Results: Exposure to traffic-derived air pollution during 29 to 37 weeks was negatively associated with biparietal diameter at 37 weeks gestation. For each interquartile range (IQR) increase in LUR-based estimates of NO, NO_2 and NO_x, or freeway CALINE4 NO_x we estimated a reduction in biparietal diameter of 0.2–0.3 mm. For women residing within 5 km of a monitoring station, we estimated biparietal diameter reductions of 0.9–1.0 mm per IQR increase in CO and NO_2. Effect estimates were robust to adjustment for a number of potential confounders. We did not observe consistent patterns for other growth endpoints we examined.
Conclusions: Prenatal exposure to traffic-derived pollution was negatively associated with fetal head size measured as biparietal diameter in late pregnancy.

1. Introduction

Epidemiologic studies have associated prenatal air pollution exposure with various measures of intrauterine growth restriction, including small for gestational age, term low birth weight, and reductions in birth weight, length and head circumference (Shah and Balkhair, 2011; Woodruff et al., 2009). Most studies used ambient concentrations from government monitoring stations to assess exposure. European and Canadian studies focusing specifically on air pollution from motor vehicles, reported more consistent positive associations for these outcomes and exposures based on land use regression (LUR) or dispersion models than simpler proximity to roadway measures (Aguilera et al., 2010; Ballester et al., 2010; Estarlich et al, 2011; Brauer et al., 2008; Gehring et al., 2011a, 2011b; Genereux et al., 2008; Malmqvist et al., 2011; Slama et al., 2007; van den Hooven et al., 2012b; Wilhelm and Ritz, 2005). Ambient and personal measures of polycyclic aromatic hydrocarbons (PAHs) – fuel combustion by-products – have also been associated with reduced fetal growth (Choi et al., 2008; Dejmek et al., 2000). PAHs can be carried into the body by ultrafine particles (< 0.1 μm in aerodynamic diameter), and may disturb fetal development through adverse changes in placental transport or through oxidative stress pathways (Jedrychowski et al., 2010; Sram et al., 1999).

The relatively short 9 month period of fetal development provides unique opportunities to study exposures acting during

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narrow susceptibility windows. However, there is a lack of toxicological information to help guide selection of relevant exposure periods for most environmental toxins and fetal growth end-points. Currently there is no consensus on pregnancy periods most susceptible to air pollution impacts, although associations have been reported somewhat more consistently for first and third trimester averages (Woodruff et al., 2009). Exposures during early pregnancy may result in disruption of placental formation and function leading to growth retardation throughout gestation (Dejmek et al., 2000) while exposures during later pregnancy may interfere with the fastest period of fetal body mass accumulation (Kline et al., 1989). Furthermore, inflammation and oxidative stress in the early of pregnancy or toward the end of pregnancy are also related to the onset of parturition. We have previously reported air pollution exposure to be associated with increased C-reactive protein concentrations (> 8 μg/ml) in early pregnancy (Lee et al., 2011) and a Dutch cohort study recently confirmed these observations (van den Hooven et al., 2012a).

Five previous European and Australian studies measured fetal growth via ultrasound to examine air pollution impacts (Aguilera et al., 2010; Hansen et al., 2008; Slama et al., 2009; van den Hooven et al., 2012b; Iñiguez et al, 2012). Here, we present the first U.S. results in a prospective birth cohort study conducted 1993–1996 in the heavily polluted region of Los Angeles, California. We used government monitoring data to assess prenatal exposures to several criteria air pollutants (carbon monoxide, CO; NO_2; ozone, O_3; PM_{10}), and also estimated prenatal exposures to nitrogen oxides as markers of traffic-related air pollutants using the CALINE4 air dispersion model (Benson, 1989) and a LUR model we developed for the LA basin (Su et al., 2009).

2. Methods

2.1. Study population

The Behavior in Pregnancy Study conducted at Cedars-Sinai Medical Center followed 688 ethnically and socioeconomically diverse women prospectively to assess the impact of chronic stress on preterm birth and low birth weight from 1993 to 1996 (Hobel et al., 1999). Detailed demographic data and information on maternal behaviors and medical conditions were collected three times at gestational ages: 18 to 20 weeks (mean = 19.1), 28 to 30 weeks (mean = 28.8), and 35 to 37 weeks (mean = 36.7). Gestational age was estimated from self-reported date of last menstrual period. For about one quarter of participants, a first-trimester dating ultrasound was available and those for whom the two gestational age measures differed by more than 10 days, the date determined from the first-trimester ultrasound estimate was used as the actual gestational age. For all participants, the estimated gestational age was corroborated by ultrasound estimates at each follow-up visit. At each visit, real-time ultrasound was conducted using an ATL, HDI 3000 ultrasound machine (Philips Medical Systems, Best, the Netherlands). Measurements of the following parameters were obtained by 5 sonographers trained and supervised by an author (CH): femur length, abdominal circumference, head circumference and biparietal diameter. From among 688 pregnant women who completed a baseline screening interview, 639 gave birth to a live infant, and 578 completed one or more study visits. Eligible pregnant women were those aged 18 years or older, English- or Spanish-speaking, and less than 20 weeks pregnant with a single gestation. We also excluded women whose pregnancy ended in stillbirths (n = 2), or infants with birth weights < 500 g (n = 5) or gestational age > 308 days (n = 1), leaving 566 women and 17 women reporting illegal drug use during pregnancy (marijuana, cocaine, heroin or speed). Of those remaining, 478 (84%) completed three ultrasound visits, 66 (12%) two and 22 (4%) one visit.

2.2. Air pollution exposure assessment

Air pollution exposures were based on participants' residential addresses reported at baseline and mapped using three methods: 406 (72%) were geocoded to the parcel level using the TeleAtlas Address Point database, 117 (21%) were geocoded using address interpolation via the TeleAtlas EZ Locate geocoding service, and 38 (7%) were mapped using Google Earth (equivalent to highest quality match using EZ Locate). Three addresses could only be located to a ZIP code centroid and were assigned regional air quality but not traffic exposures. Addresses for two subjects could not be mapped resulting in missing air pollution assignments.

2.2.1. Regional air quality exposure assignments

Prenatal exposures for the criteria pollutants CO, NO_2, PM_{10}, and O_3 were estimated using measurement data from the U.S. EPA's Air Quality System (http://www.epa.gov/ttn/airs/airsaqs/) and the University of Southern California's Children's Health Study conducted in 1992–1996 (Peters et al., 2004). NO_2 and O_3 data from the Children's Health Study versus the Air Quality System were used when both were available for a station because the Children's Health Study data were subjected to greater quality assurance (Alcorn and Lurmann, 2004). However, Air Quality System Federal Reference Method (FRM) PM_{10} data were used instead of Children's Health Study non-FRM data when both existed for a station because the U.S. National Ambient Air Quality Standard for PM_{10} is defined in terms of FRM measured data. Data on particles < 2.5 μm in aerodynamic diameter ($PM_{2.5}$) levels were unavailable for this time period from either source.

The following averages were first generated for each day if at least 75% of required hourly readings were available (see also Supplemental Table 1): 8-h daily maximum averages for CO (ppm), 12-h daytime (6 am to 6 pm) averages for NO_2 (ppb), 8-h daytime (10 am to 6 pm) averages for O_3 (ppb) and 24-h averages for PM_{10} (μg/m^3). The daily averages were then averaged for each woman over the following three pregnancy periods: estimated date of conception to first ultrasound date, approximately 0–19 weeks gestation (period 1); first to second ultrasound date, 19–29 weeks gestation (period 2); and second to third ultrasound date, 29–37 weeks gestation (period 3). Gaseous pollutant exposures were generated if there were valid daily averages for ≥ 75% of each pregnancy period. For PM_{10}, this criterion was lowered to ≥ 12.5% since most 24-h measures were only available every 6 days.

Average pregnancy period exposures were estimated at each residence location based on inverse distance-squared weighting of values from up to the four closest monitoring stations within 50 km (31.1 mi) for NO_2, O_3 and PM_{10} and 25 km (15.5 mi) for CO. However, whenever one or more stations were located within 5 km (3.1 mi) of a residence, only these stations were used for interpolation. For consistency, interpolations for all three periods of pregnancy were based on data from the same stations. Because large offshore – onshore pollutant gradients have been shown to exist along the southern California coast (Main et al., 1991), the interpolations were carried out with pseudo-stations located ~30 km offshore and assigned the following concentrations based on long-term measurements at a clean coastal location (Lompoc, CA): 0.3 ppm CO, 4 ppb NO_2, 29 ppb O_3, and 15 μg/m^3 PM_{10}. For CO and NO_2, 17% and 18% of exposure estimates were based on stations within 5 km of residences, respectively. For O_3 and PM_{10}, 19% and 10% of exposure estimates were based on stations within 5 km of residences, and 81% and 89% within 5–25 km of residences, respectively.

2.2.2. CALINE4 nitrogen oxides (NO_x) exposure estimates

We used the CALINE4 line source dispersion model (Chen et al., 2009; Benson, 1989) which accounts for traffic emissions, roadway characteristics and meteorological conditions, to estimate pregnancy period exposures to local, traffic-derived NO_x, including roadways within 5 km of subjects' residences. This approach has proven useful in studies of traffic and health effects in southern California (e.g. Gauderman et al., 2007). Traffic count data from Tele Atlas/Geographic Data Technology (GDT) (http://www.teleatlas.com) were assigned to streets as explained in Supplemental material.

Hourly surface wind speeds and directions were acquired from 20 routine, ambient air quality stations in the study region for the 1992–1996 study time period (http://www.epa.gov/ttn/airs/airsaqs/). Due to lack of adequate information for 1992–1993, estimates were based on average hourly wind direction and speed values for the period 1994–1996. Thus, the modeling reflects average, within-year seasonal fluctuations in wind direction and speed, but not year-to-year variation in these factors across 1992–1996. We assigned subgroups of residences to 14 meteorological stations with sufficiently complete hourly data (> 75%) during 1994–1996 using Thiessen polygons and terrain data.

Vehicle fleet average emission factors were based on the California Air Resource Board's EMFAC2007 (version 2.3) model. Summer and winter average emission factors for vehicles in Los Angeles County in 1993, 1994, 1995, and 1996 were calculated using California Air Resource Board recommended default parameters. The emission factors for 65, 50, 35, and 30 mph were used for travel on freeways, state highways, arterials, and collectors, respectively. Diurnal and weekday/weekend volume variation profiles were based on average conditions observed at weigh-in-motion sensor locations in Southern California (Coe et al., 2004).

2.2.3. Land use regression (LUR) exposures

We extracted nitrogen monoxide (NO), NO_2, and NO_x concentration estimates at residential locations from land use regression (LUR) model surfaces we developed for the LA Basin (see Su et al., 2009). The LUR surfaces were based on 2-week average Ogawa NO_2 and NO_x measures we collected in September 2006 and February 2007 at 181 locations (196 samplers in total) simultaneously throughout LA County. Final regression models explained 81%, 86% and 85%, respectively, of the variance in measured NO, NO_2 and NO_x concentrations. Cross-validation analyses suggested high prediction accuracy in the range of 87–91%. The LUR models most closely approximate annual average concentrations, and thus provide spatial but not temporal contrasts.