Environmental Research 163 (2018) 201–207

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Chronic exposure to inhaled, traffic-related nitrogen dioxide and a blunted cortisol response in adolescents

Sam E. Wing[a,*], Gretchen Bandoli[b], Donatello Telesca[c], Jason G. Su[d], Beate Ritz[a]

[a] Department of Epidemiology, Fielding School of Public Health, University of California, Los Angeles, 650 Charles E Young Dr S, Los Angeles, CA 90095, USA
[b] Department of Pediatrics, University of California, San Diego, 9500 Gilman Drive #0828 La Jolla, CA 92093, USA
[c] Environmental Health Sciences Division, School of Public Health, University of California, Berkeley 50 University Hall #7360, Berkeley, CA 94720, USA
[d] Department of Biostatistics, Fielding School of Public Health, University of California, Los Angeles, 650 Charles E Young Dr S, Los Angeles, CA 90095, USA

ARTICLE INFO

Keywords:
Air pollution
Adolescents
Epidemiology
Cortisol
HPA Axis
Neighborhood

ABSTRACT

Background: Chronic health effects of traffic-related air pollution, like nitrogen dioxide (NO_2), are well-documented. Animal models suggested that NO_2 exposures dysregulate cortisol function.
Objectives: We evaluated the association between traffic-related NO_2 exposure and adolescent human cortisol concentrations, utilizing measures of the cortisol diurnal slope.
Methods: 140 adolescents provided repeated salivary cortisol samples throughout one day. We built a land use regression model to estimate chronic NO_2 exposures based on home and school addresses. We then generated model-based estimates of the association between cortisol and NO_2 exposure one year prior to cortisol sampling, examining changes in cortisol diurnal slope. The final model was adjusted other criteria pollutants, measures of psychosocial stress, anthropometry, and other demographic and covariates.
Results: We observed a decrease in diurnal slope in cortisol for adolescents exposed to the estimated 75th percentile of ambient NO_2 (high exposure) relative to those exposed at the 25th percentile (low exposure). For a highly exposed adolescent, the log cortisol was lower by 0.06 μg/dl at waking (95% CI: −0.15, 0.02), 0.07 μg/dl at 30 min post waking (95% CI: −0.15, 0.02), and higher by 0.05 μg/dl at bedtime (95% CI: 0.05, 0.15), compared to a low exposed adolescent. For an additional interquartile range of exposure, the model-based predicted diurnal slope significantly decreased by 0.12 (95% CI: −0.23, −0.01).
Conclusions: In adolescents, we found that increased, chronic exposure to NO_2 and the mixture of pollutants from traffic sources was associated with a flattened diurnal slope of cortisol, a marker of an abnormal cortisol response which we hypothesize may be a mechanism through which air pollution may affect respiratory function and asthma in adolescents.

1. Introduction

Exposure to air pollution in human studies has been consistently associated with a wide range of negative health outcomes (Park et al., 2010; Brook et al., 2013). Animal studies have suggested that air pollution may impact a major endocrine subsystem, the hypothalamic-pituitary-adrenal (HPA) axis, and alter the typical release of cortisol from the adrenal gland (Sirivelu et al., 2006; Thomson, 2013). Dysregulation of this neuroendocrine subsystem has been associated with metabolic disorders (Martins et al., 2016), cardiovascular dysfunction (Feldt-Rasmussen and Klose, 2016), and neuropsychiatric disorders (Vedder, 2007). Cortisol is also responsible for assisting in the regulation of immune and inflammatory responses in the airways (Chen and Miller, 2007), but repeated, long-term exposure to high levels of cortisol may cause a counterregulatory response by the white blood cells that limits the inhibitory effects of cortisol and results in the promotion of inflammatory diseases like asthma (Miller et al., 2002). Even though mechanistic evidence for air pollution's action on the HPA axis and cortisol has largely come from animal models (Martrette et al., 2011), there is an overlap between HPA axis-related diseases and diseases that have been associated with air pollution exposure, like depression (Lim et al., 2012; Szyszkowicz et al., 2010). To date, few studies of air pollution and cortisol response in humans exist, especially in children and adolescents (Ising et al., 2004).

Cortisol is a steroid hormone produced in the adrenal gland and readily sampled from saliva (Saxbe, 2008). Cortisol concentrations follow a diurnal rhythm where daily values peak approximately 30–45 min after waking, followed by a steady decline throughout the

* Correspondence to: 650 Charles Young Drive, South, Box 951772, Los Angeles, CA 90095, USA.
E-mail addresses: samwing@ucla.edu (S.E. Wing), gbandoli@ucsd.edu (G. Bandoli), dtelesca@ucla.edu (D. Telesca), jasonsu@berkeley.edu (J.G. Su), britz@ucla.edu (B. Ritz).

https://doi.org/10.1016/j.envres.2018.01.011
Received 29 September 2017; Received in revised form 16 December 2017; Accepted 15 January 2018

day. Lowest daily cortisol values typically occur overnight, with values cyclically increasing again in the hours prior to waking (Saxbe, 2008).

Due to the time-dependent nature of the measure, cortisol analyses necessarily include multiple measurements during the day. Diurnal slope, or the change in cortisol values from post-waking peak to their nighttime low point, is a frequently used measure of HPA axis function. Flattened diurnal slopes are a marker of an abnormal cortisol response and have previously been associated with chronic exposures to psychosocial stress (Smith and Vale, 2006). These flattened slopes are more generally described as having a lower post-waking cortisol peak and higher end-of-day values. Additionally, flattened diurnal slopes have been identified as a superior predictor of both psychosocial stress and potential HPA axis dysregulation relative to other measures of cortisol, like total daily cortisol output ("area under the curve") or cortisol awakening response (Saxbe, 2008; Adam and Kumari, 2009).

Here, we investigate the degree to which land use regression (LUR) modeled nitrogen dioxide (NO_2) exposure from traffic-related air pollution is associated with a flattened diurnal cortisol slope in adolescents ages 12–17 years who participated in the Los Angeles Family and Neighborhood Survey (LAFANS), wave 2, that contained information on self-reported psychosocial stressors, demographic information, and collected repeated saliva cortisol samples from participants.

2. Materials and methods

2.1. Sample Population

Participants were enrolled in the Los Angeles Family and Neighborhood Survey (LAFANS), Wave 2, a population-based study in Los Angeles County, California to study the complex, multilevel influence that neighborhoods and families have on child development (Sastry et al., 2006). Data were collected in two waves, the first conducted in 2000 and 2001 and the second from 2006 through 2008. Wave 1 sampled 3090 households from 65 census tracts. Within each household sampled, adults and children were enrolled and consented/assented for their participation in the interviews. The second wave comprised of participants who responded in the first wave and remained in their neighborhood or had moved away but could still be traced, and new entrants into the original neighborhoods. Wave 2 re-interviewed 1091 of the original 3140 children who participated in Wave 1 and added 296 new neighborhood entrants under the age of 18, for a total of 1387 children.

In addition to interviewing, Wave 2 introduced health assessments for a random subset of 492 participants between 3 and 17 years of age, which included anthropometry, spirometry, and salivary cortisol measurements. Older children, between the ages of 12 and 17, were asked a more detailed battery of questions that included information on psychosocial stressors. Because both acute (Kinlein et al., 2015) and chronic stress (Wingenfeld et al., 2009; McEwen, 2000) modulate the HPA axis and subsequent cortisol release, only adolescents were included in this analysis (n = 140) to allow for adequate covariate control. Data collection occurred with approval from the RAND Institutional Review Board. Subsequent data analyses were carried out with approvals from the RAND and the University of California, Los Angeles Institutional Review Boards.

2.2. Saliva Cortisol

Parents of the participating children were trained by interviewers to gather saliva samples using absorbent, cellulose-cotton tipped sorbette swabs on the end of short plastic sticks, previously identified as practically advantageous relative to other saliva collection techniques (Strazdins et al., 2005; de Weerth et al., 2007). This method harvested more than adequate amounts of saliva for laboratory assays of cortisol, remained stable at refrigerator temperatures for a week, was comfortable for the study subject, and could be accurately carried out with minimal training.

Parents were instructed to collect samples at three time points during a single day: immediately when the adolescent woke up, 30 min after waking, and at bedtime. Also known as "sponge-pops", parents placed these into the adolescent's mouth, under their tongue for 60 s in order to collect an adequate amount of saliva. Subsequently, the swabs were sealed in test tubes, stored in home refrigerators, and sent out the following day for laboratory analysis.

Participants were not allowed to provide samples if they ate or drank prior to the sample collection time point and were required to abstain from alcohol and dental work in the preceding 24 h before the day of collection. Samples were also rejected if they were contaminated with blood or if cortisol values exceeded maximum assay sensitivity or had abnormally large intra-assay differences. Detailed information on saliva collection protocols is available from the RAND Corporation and collection device manufacturer (Sastry et al., 2006; Salmetrics, 2017). The second sample must have been collected between 15 and 60 min after waking to be included and the third sample taken at bedtime was only included if the subject was awake for at least 10 but no longer than 20 h.

2.3. Exposure assessment

An LUR model to estimate annual NO_2 exposures was created for Los Angeles County using data collected over two weeks from 201 passive air samplers (part number PS-100, Ogawa & Company USA, Inc, Pompano Beach, FL) placed in the LAFANS neighborhoods during both October 2006 and February 2007. The final prediction surfaces explained 85% in the variation of NO_2 concentrations over the two weeks. Detailed information about these air pollution estimates has been published previously (Singer et al., 2004; Ritz et al., 2009). The estimated NO_2 exposure was for the one year prior to the LAFANS, wave 2 data collection date and was not adjusted for seasonality. Fig. 1 displays the final prediction surface for NO_2, a marker for the mixture of pollutants from traffic sources.

In addition to the unadjusted effect of NO_2, in adjusted models we also controlled for $PM_{2.5}$ (fine particulate with aero-dynamic diameter $\leq$ 2.5 μm) and ozone exposure measures to isolate the role of near-source, traffic-related mixture of exposure, as represented by NO_2 in our LUR model from spatially more homogeneous, area-wide exposures. These two pollutants and our LUR traffic marker were not highly correlated in the Los Angeles region ($\rho < .70$). $PM_{2.5}$ and ozone exposure measures were generated via interpolation using a kriging algorithm with routinely collected, government ambient monitoring station data from 2002 and 2000, respectively (Ritz et al., 2009). Thus, $PM_{2.5}$ and ozone concentrations represent background levels for both pollutants and both are more homogeneously distributed across the LA basin. Air pollution exposure estimates were time-weighted for 3 locations: current home, any previous homes (within the preceding 12 months), and 1080 h spent at school per year.

2.4. Demographic, socioeconomic, and health characteristics

An adult household participant reported on previous year's household income. Race/ethnicity of the child was reported by the adult in the home as being White, Black, Latino, Asian, Pacific Islander, or Native American. The latter two categories were collapsed into "Other" in this analysis due to small subgroup sizes. The household's adult also reported on smokers living in the home and the use of air conditioning. A previous analysis of LAFANS wave 2 data found that less than 2% of adolescents reported smoking (Bandoli et al., 2016), which was deemed too low of a prevalence for inclusion in further analysis. Interviewers measured the height and weight of participants during study visits and recorded the child's use of medications for controlling asthma.