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Non-nutritive suck and airborne metal exposures among Puerto Rican infants

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Abstract

Air pollution has been shown to impact multiple measures of neurodevelopment in young children. Its effects on particularly vulnerable populations, such as ethnic minorities, however, is less studied. To address this gap in the literature, we assess the associations between infant non-nutritive suck (NNS), an early indicator of central nervous system integrity, and air pollution exposures in Puerto Rico.

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CRediT authorship contribution statement

Sarah Morton: Formal analysis, Writing – original draft, Writing – review & editing, Visualization. **Trenton Honda:** Writing – review & editing. **Emily Zimmerman:** Data curation, Supervision, Writing – review & editing. **Kipruto Kirwa:** Formal analysis, Writing – review & editing. **Gredia Huerta-Montanez:** Supervision. **Alaina Martens:** Data curation. **Morgan Hines:** Data curation. **Martha Ondras:** Visualization, Data curation. **Ki-Do Eum:** Formal analysis. **Jose F. Cordero:** Supervision, Project administration, Funding acquisition. **Akram Alshawabekeh:** Supervision, Project administration, Funding acquisition. **Helen H. Suh:** Supervision, Conceptualization, Project administration, Funding acquisition, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

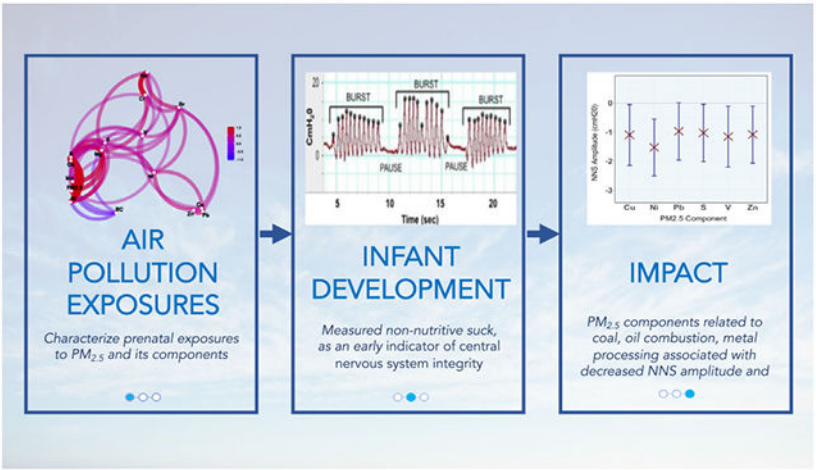
Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2021.148008.

Among infants aged 0–3 months enrolled in the Center for Research on Early Childhood Exposure and Development (CRECE) cohort from 2017 to 2019, we examined associations between exposure to fine particulate matter ($PM_{2.5}$) and its components on infant NNS in Puerto Rico. NNS was assessed using a pacifier attached to a pressure transducer, allowing for real-time visualization of NNS amplitude, frequency, duration, cycles/burst, cycles/min and bursts/min. These data were linked to 9-month average prenatal concentrations of $PM_{2.5}$ and components, measured at three community monitoring sites. We used linear regression to examine the $PM_{2.5}$-NNS association in single pollutant models, controlling for infant sex, maternal age, gestational age, and season of birth in base and additionally for household smoke exposure, age at testing, and NNS duration in full models.

Among 198 infants, the average NNS amplitude and burst duration was 17.1 cmH_2O and 6.1 s, respectively. Decreased NNS amplitude was consistently and significantly associated with 9-month average exposure to sulfur (−1.026 ± 0.507), zinc (−1.091 ± 0.503), copper (−1.096 ± 0.535) vanadium (−1.157 ± 0.537), and nickel (−1.530 ± 0.501). Decrements in NNS frequency were associated with sulfur exposure (0.036 ± 0.018), but not other examined PM components. Our findings provide new evidence that prenatal maternal exposure to specific PM components are associated with impaired neurodevelopment in Puerto Rican infants soon after birth.

GRAPHICAL ABSTRACT



Keywords

Air pollution; Neurodevelopment; Non-nutritive suck; Prenatal exposures

1. Introduction

Prenatal air pollution exposures have been linked to a variety of adverse neurodevelopmental outcomes in children (Basu et al., 2014; Bell et al., 2012; Chiu et al., 2016; Church et al., 2018; Coker et al., 2015; Hyder et al., 2014; Li et al.,2019). Previous studies have shown prenatal exposures to fine particulate air pollution ($PM_{2.5}$) to be significantly associated with adverse birth outcomes (Li et al., 2019) and to a lesser extent, fetal and infant

neurodevelopment (Xu et al., 2016), including autism spectrum disorder (Volk et al., 2011), impaired cognition (Porta et al., 2016; Perera et al., 2006a), and neurodevelopmental delays (Chiu et al., 2016). Further, polycyclic aromatic hydrocarbon (PAHs) exposures have been associated with increased risk of cognitive delay (Perera et al., 2006b), while pre-natal exposures to particulate matter and NO_2 have been associated with developmental, verbal, and fine motor delays at 2.5 years (Kim et al., 2014; Yorifuji et al., 2016). Additionally, several components of $PM_{2.5}$, such as black carbon (BC) and nickel, have been associated with low birth weight (Ebisu and Bell, 2012), a risk factor for subsequent cognitive delays and poorer health outcomes (Ylijoki et al., 2019).While providing important evidence linking $PM_{2.5}$ to neurodevelopmental delays, findings from these and other studies, however, are limited by (1) the heterogeneity in their findings and (2) the non-specificity of birth outcome measures, and (3) the long latency period between prenatal exposures and the manifestation of clinical neurodevelopment indicators in children. As a result, they provide little evidence to assess whether and through what pathways $PM_{2.5}$ affects neurodevelopment in utero.

It is possible, however, that non-nutritive suck (NNS), defined as sucking on an object (i.e. a finger or pacifier) without receiving nutrients (Zimmerman and Foran, 2017; Zimmerman et al., 2017), may provide a means through which the impacts of prenatal air pollution exposures on neurodevelopment can be assessed in neonates. NNS is a developmental reflex antecedent to the development of complex neuromuscular feeding behavior (Pineda et al., 2019) that can be measured in infants easily using non-invasive methods. NNS is controlled by the suck central pattern generator in the brainstem, and infants begin NNS in utero at around 15 weeks' gestation (Humphrey, 1970). Importantly, NNS is known to be altered in conditions associated with abnormal neurological development, including: Prematurity, respiratory distress syndrome, and small for gestational age (Estep et al., 2008; Da Costa et al., 2010; Lau et al., 2000). NNS has also been linked to neonatal brain injuries, with 35–48% of infants with neonatal brain injuries having delayed NNS (Pineda et al., 2019; Zimmerman et al., 2020), and to subsequent neurodevelopmental outcomes. For example, in one recent study, neonatal measures of NNS were associated with multiple markers of neuromuscular development, intelligence, and language at age five (Wolthuis-Stigter et al., 2017).

In this study, we examined whether NNS is associated with prenatal exposures to $PM_{2.5}$ and its constituents in a cohort of Puerto Rico infants participating in the Center for Research on Early Childhood Exposure and Development in Puerto Rico (CRECE).

2. Methods

2.1. Study population

Details on the study cohort are published elsewhere (Manjourides et al., 2020). Briefly, the study population included 198 mother-infant dyads living in the North Shore of Puerto Rico (Fig. 1) and participating in CRECE and the Puerto Rico Testsite for Exploring Contamination Threats (PROTECT) studies, respectively. Pregnant women who visited one of two hospitals or five clinics were recruited for study participation, with most recruited at approximately the 14th week of pregnancy. Women were eligible if they were between 18

and 40 years of age, resided in a municipality in the Northern karst region of the island, did not use oral contraceptives for at least three months before becoming pregnant, did not use in vitro fertilization to become pregnant, and had no known medical or obstetrical complications, including diabetes. After the initial screening at the time of enrollment, pregnant women attended three additional study visits [26].

Women were contacted one week after giving birth to inquire about participation in CRECE. Mothers who agreed to participate with their infant gave their informed consent, after which we accessed the child's birth and medical records and began follow-up of their children.

2.2. NNS measurements

NNS was measured for 5 minutes for each of 198 singleton infants born between April 7, 2017 and July 26, 2019. Infants were measured between 0 and 3 months of age using a pressure transducer attached to a Soothie pacifier. The transducer sent information to ADInstrument's Power Lab, a data acquisition system, which was connected to a laptop with ADInstrument's LabChart software (Manjourides et al., 2020). Two minute periods of sucking were analyzed to quantify several measures of NNS, including cycle count, amplitude (cmH_20), burst duration (s), frequency (Hz), bursts/min, cycles/min, and cycles/burst. A burst was defined as the group of cycles between two pauses taken by the infant for respiration (Zimmerman et al., 2020).

2.3. Individual-specific covariates

Covariates were selected based upon their prior associations with NNS or air pollution. Infant-related covariates included sex, gestational age, and season of birth. Gestational age was estimated from a combination of ultrasounds, the mother's last menstrual period, and postpartum medical abstraction, and was recorded in a binary fashion (0 = full term, 1 = preterm), with preterm birth defined as gestational age of less than 37 weeks (Organization, 2012). Season of birth was accounted for by grouping birth month into the following seasons: January–March (Winter), April–June (Spring), July–September (Summer), and October–December (Fall) and included in the model as a 4-level categorical variable.

Maternal covariates included maternal age and household smoke exposure. Age was included as a continuous variable. Household smoke exposure was assessed by maternal report if they or anyone in their household smoked and was recorded in a binary fashion (0 = no household exposure, 1 = household exposure).

2.4. $PM_{2.5}$ and $PM_{2.5}$ component exposures

$PM_{2.5}$ and its components were measured from June 2016–June 2019 at stationary ambient monitoring sites located in Manati, Arecibo, and Morovis, communities centrally located to our CRECE participants (Fig. 1). Of the participants, 42% lived closest to the Arecibo monitor, 34% to the Manati monitor and 24% to the Morovis monitor. Fifty percent of the participants lived within 9.5 km (km) (5.8 miles) of an air pollution monitoring site. The minimum and maximum distance a participant lived to the closest monitor was 1.1 and 37.6 km, respectively, 95% of the participants living with 9.7 km from the nearest monitor. At each monitoring site, the samplers were sited away from large roadways and major air

pollution sources. Sampler inlets were placed 1.5 m above the ground in an open area in the backyard of the CRECE clinic at Manati and on the rooftop of 3 to 4 story office buildings in Morovis and Arecibo. $PM_{2.5}$ samples were collected at each site over week-long periods on 37 mm Teflon Harvard Impactor filters (Marple et al., 1987). Pre- and post- sampling, filters were weighed on an electronic microbalance (MT-5 Mettler Toledo, Columbus, OH). Static charge was removed by passing over alpha ray before measuring the weight. Filters were subsequently analyzed for black carbon using a reflectometer and for individual elements using X-ray fluorescence (XRF, Model Epsilon 5, PANalytical, The Netherlands) (Kellogg and Winberry, 1999). Information on the Quality Assurance and Control of XRF analysis has been reported in detail elsewhere (Kang et al., 2014).

We estimated infant-specific exposures to $PM_{2.5}$ and its components during pregnancy, as the mean pollutant exposure during the 9-months prior to each infant's date of birth at the maternal ZIP code of residence during this timeframe. Exposures were calculated using inverse distance weighted interpolation (Shepard, 1968). To do so, we identified the population-weighted ZIP code centroid based on 2019 data, accounting for participant changes in ZIP code of residence by year. We calculated the Euclidean distance between the ZIP code centroid for each participant and the sampling sites. For each ZIP code, we calculated inverse distance-weighted monthly average concentrations, from which nine-month moving average $PM_{2.5}$ and $PM_{2.5}$ component concentrations were calculated for each participant.

2.5. Statistical analysis

We used least-squares multiple linear regression to examine associations between prenatal $PM_{2.5}$ and single $PM_{2.5}$ component concentrations and each NNS measure, controlling for maternal age and infant sex, gestational age, and season of birth. Full models additionally controlled for household smoke exposure, the age of the infant at the time of the NNS test, and NNS burst duration for other NNS measures; NNS burst duration may confound the relationship between PM components and other measures of NNS. In sensitivity analyses, we ran full models excluding burst duration as a covariate. All statistical analysis was performed with R version 3.6.1 (R Core Team, 2017). The study was approved by the institutional review boards at Tufts University and Northeastern University.

3. Results

Table 1 presents demographic information on all 198 participants. Sex was approximately evenly distributed between male (48%) and female (52%) infants. Most (94%) infants were full-term, and births were distributed across seasons, with the largest proportion (29%) born in the winter, and the least in summer (18%). NNS was most variable for cycles/min (60.5 ± 20.1) and amplitude (17.1 cmH_20 ± 6.85) measures (Table 1). NNS amplitudes were higher in female versus male infants (17.4 cmH_20 ± 6.8 vs 16.7 cmH_20 ± 7.0), preterm versus full-term infants (19.2 cmH_20 ± 8.3 vs 16.9 cmH_20 ± 6.8), and those born to younger (18–20 years) versus older (>36 years) mothers (21.5cmH_20 ± 7.9 vs 15.8 cmH_20 ± 6.5) (Supplementary Table 1). $PM_{2.5}$ concentrations were relatively low, wth mean levels of 5.37

(2.31) ug/m^3. Of the components, sulfur, sodium, and chlorine comprised the largest fraction of $PM_{2.5}$.

Pair-wise correlations between pollutant components were generally highest for pollutants sharing common sources. For example, correlations were high between markers of metal processing (e.g. zinc, copper), oil processing (e.g. vanadium, nickel), and crustal materials (e.g. calcium, potassium), with statistically significant correlation coefficients of 0.37, 0.41, and 0.94, respectively (all *p*-values <0.05) (Thurston et al., 2011). $PM_{2.5}$ was most strongly correlated with calcium (r = 0.91, p-value<0.001), followed by manganese ((r = 0.89, p-value<0.001) and silicon (r = 0.89, p-value<0.001).

Table 2 presents associations between $PM_{2.5}$ and component concentrations and NNS measures. In base models, we observed statistically significant decrements in NNS amplitude (cmH_20) associated with 9-month average exposure to zinc (−1.016 ± 0.500), vanadium (−1.141 ± 0.528), and nickel (−1.478 ± 0.497), with suggestive, although non-significant, inverse associations for lead, copper, and sulfur. In fully adjusted models, associations for zinc (−1.091 ± 0.503), vanadium (−1.157 ± 0.537), and nickel (−1.530 ± 0.501) were largely unchanged, while that for copper (−1.096 ± 0.535) and sulfur (−1.026 ± 0.507) became statistically significant. No other examined pollutant, including $PM_{2.5}$, was associated with NNS amplitude. Associations between pollutants and NNS frequency (Hz) were null for all pollutants, except sulfur (0.036 ± 0.018). Associations with other investigated NNS metrics (i.e. burst duration, bursts/min, cycles/min, and cycles/burst) were also null for all examined pollutants (Supplementary Table 2). In sensitivity analyses in which burst duration was removed as a covariate, results were comparable (data not shown).

4. Discussion

Our study is the first to examine associations between $PM_{2.5}$ and its component exposures and NNS, an early indicator of central nervous system integrity. We found decreased NNS amplitude to be strongly and consistently linked with several $PM_{2.5}$-associated metals, including vanadium and nickel, markers of oil combustion, zinc and copper, tracers of metal processing, and sulfur, a marker of coal combustion. Sulfur was also significantly associated with increased NNS frequency, with null associations for other examined pollutants possibly due to low variability in NNS frequency. Null associations were also observed for other examined pollutants, including $PM_{2.5}$, and other investigated NNS metrics.

While relatively little data are available on NNS, especially for infants residing in Puerto Rico, NNS metrics in our study participants are largely consistent with prior literature reported on infants 0–3 months (Zimmerman and Foran, 2017; Zimmerman et al., 2020). For example, in a study of 26 full-term infants, Martens et al. (2020) reported comparable ranges of NNS, with mean NNS frequency of 2.09 Hz (versus 1.9 ± 0.2 Hz in our study), mean cycles per burst of 9.6 (versus 11.5 ± 6.5 in our study), and average amplitude of 14.05 cmH_2O (versus 17.1 ± 6.9 cmH_2O in our study). (Martens et al., 2020) The concordance of our NNS measures with prior research, together with our finding showing NNS to be similar across gender, maternal age, and pre-term birth status, suggest that our NNS measures may

be generalizable to other populations; however, further characterization of NNS in other populations is needed.

Our findings linking prenatal exposures to specific $PM_{2.5}$ components are consistent with the few prior studies of $PM_{2.5}$ components and adverse birth outcomes, although the specific components associated with adverse birth outcomes differed by study. As in our study, Ebisu and Bell (2012) found null associations for $PM_{2.5}$ and positive associations for several $PM_{2.5}$ components, including elemental carbon, aluminum, nickel, and titanium, and risk of low birth weight (LBW), with 4.7% (95% CI: 3.2, 6.2%), 4.9% (95% CI: 3.4, 6.5%), 5.7% (95% CI: 2.7 8.8%), and 5.0% (95% CI: 3.1, 7.0%) increased LBW risks per IQR increase, respectively, in a study of infants born in northeastern and mid-Atlantic US (Ebisu and Bell, 2012). While not robust to adjustment for other pollutants, an IQR increase in zinc exposures was also associated in single pollutant models with higher LBW risk (4.4%; 95% CI: 1.7, 7.2%), as in our study. Contrary to our findings, this study did not find significant associations of sulfate, vanadium, or copper on low birth weight risk, possibly reflecting differences in their cohort, which was comprised of mostly White infants, and their outcome based on birth certificate records.

In a California study with a larger percentage of Hispanic infants, Basu et al. (2014) found significant associations between prenatal $PM_{2.5}$ and numerous component exposures and decreased birth weight, with markers of traffic, industrial sources, oil combustion, and metal production (sulfur, sulfate, vanadium, iron, manganese, bromine, ammonium, zinc, copper) most strongly associated with lower birth weight. Although $PM_{2.5}$ exposures were not associated with decreased NNS in our study, our findings for component-related associations were largely similar. Notably, the magnitude of the associations with $PM_{2.5}$ were greater for Hispanic and Black infants as compared to White and Asian infants, but were lower for most $PM_{2.5}$ components for Hispanic, Asian, and Black as compared to White infants, which is contrary to previous reports (Bell et al., 2010; Darrow et al., 2011; Salihu et al., 2011).

In studies of air pollutant exposures and neurodevelopment, Perera et al. found that prenatal exposure to polycystic aromatic hydrocarbons during the 3rd trimester of pregnancy was associated with decrements in measures of mental development (Bayley Scale of Infant Development) in a small (n = 183) US cohort, with the highest quartile of exposure having 2.89 times the risk of cognitive delay (95% CI: 1.33, 6.25), relative to the least exposed (Perera et al., 2006b). This is consistent with a Korean study, which found that PM_{10} and NO_2 exposure over the entire gestational period were associated with decrements in both the mental development index and psychomotor development index, as measured using the Korean Bayley Scale of Infant Development II (Kim et al., 2014). In a Massachusetts cohort of mother-child dyads, Harris et al. found that maternal proximity to major roadways, but not black carbon or $PM_{2.5}$ exposures, during the prenatal period was associated with lower non-verbal IQ (Harris et al., 2015). In a large Japanese cohort (n = 33,911) Yorifuji et al. found that prenatal exposure to PM and NO_2 were associated with delay in developmental milestones, verbal, and fine motor development at age 2.5, and with behavioral problems (poor inhibition, impulsive behavior) at 5.5 years (Yorifuji et al., 2016). While we found no significant associations with $PM_{2.5}$, our study is the only such examination in a Puerto Rican cohort, and our findings of significant associations with various PM components, but not

with $PM_{2.5}$, may indicate that the composition of PM across the studies may be driving the differences in results.

Prenatal $PM_{2.5}$, but not component, exposures have also been linked to the development of neurodevelopmental disorders, such as autism. For example, in a large case-control study (979 cases, 14,666 controls) Kalkbrenner et al. found that prenatal exposure to PM_{10} during the 3rd trimester was associated with 1.36 (95% CI 1.13, 1.63) times the risk of autism spectrum disorder (Kalkbrenner et al., 2015). Similarly, in a small study of infants in California, Volk et al. found that high levels of $PM_{2.5}$, PM_{10}, and NO_2 exposure during 1st, 2nd, and 3rd trimesters of pregnancy were also associated with elevated autism risk (Volk et al., 2011), while Raz et al. found that each 4.42 $\mu g/m^3$ increase in prenatal $PM_{2.5}$ exposure was associated with a 57% increased risk (95% CI 22%–103%) of ASD (Raz et al., 2015). As dysregulated breastfeeding behavior has recently been associated with future development of autism, it is possible that the associations we observe between PM components and NNS may be early indicators of future neurodevelopmental risk (Lucas and Cutler, n.d.).

A number of potential mechanisms through which prenatal air pollution exposure may impair NNS and neurodevelopment have been described. Maternal $PM_{2.5}$ exposure can result in 1) activation of alveolar macrophages, resulting in systemic inflammation, and 2) translocation of metals and PM components directly into the maternal blood stream and into the fetal side of the placenta (Bové et al., 2019), all of which may contribute to oxidative stress and neuroinflammation in both the maternal and fetal brains (Xu et al., 2016; U.S. Environmental Protection Agency, Washington, DC, U.S. EPA, 2019). Animal studies support that prenatal air pollution exposures can result in detrimental neurodevelopmental changes. For example, in a 2017 study, Klocke et al., showed that controlled, prenatal exposure in mice was associated with the development of fetal neuroinflammation and ventriculomegaly, which in humans has been associated with the development of neurocognitive and neurodevelopmental disorders (Klocke et al., 2017). A 2018 study also found that concentrated maternal exposure during the gestational period in mice was associated with autism-like alterations in behavior after birth (Church et al., 2018).

Our study has a number of important limitations. First, the generalizability of our results is limited by the homogenous study population on a single island. Second, our exposure models assume that participants' mothers spent most time at home during the 9 months of pregnancy, and does not differentiate between indoor and outdoor exposure, which raises the possibility of exposure misclassification. Further, participants' mothers lived at varying distances from the monitoring sites, potentially resulting in greater exposure error for mothers living further from the closest monitoring site. These concerns are balanced, however, by the fact that the majority of mothers lived less than 10 km of a monitoring site, with the furthest distance between a mother's residence and a monitoring site being 37 km. These distances are well within the exposure limits used in numerous epidemiological studies, with essentially no impact on resulting risk estimates when exposure buffer zones are increased from 10 km to the closest monitor to 40 km to the closest monitor (Pun et al., 2017). While exposure error is still a concern, our use of inverse distance weighting, accounting for residential moves, to estimate individual ambient exposure levels decreases

the likelihood of differential misclassification. Third, our study has a relatively small sample size, which raises the possibility that our results may have been impacted by insufficient power. Fourth, we lack information on potentially important confounders which have been previously associated with NNS measures, such as whether the infants are breast or bottle fed. Last, while we are able to document that $PM_{2.5}$ component exposures are associated with changes in NNS, whether these changes are indicative of increased risk of developing specific neurodevelopmental disorders is unclear.

These limitations are counterbalanced by a number of important strengths. Our study participants are drawn from an established, Puerto Rican prospective cohort, allowing us to explore associations in a particularly vulnerable population and to link infant outcomes to important maternal variables. Second, our air pollution measurements were taken using state-of-the-art equipment and standard protocols, helping to ensure that our exposure assignments are both precise and accurate. Third, our use of NNS, a non-invasive index of early neurodevelopment, ensured that we had an accurate and reliable outcome measure, and last our findings were robust to various model specifications in which we controlled for multiple potential confounders.

5. Conclusion

Among infants residing in Puerto Rico, our study is the first to find that prenatal maternal exposures to zinc, copper, sulfur, vanadium, and nickel were associated with lower NNS amplitudes, while decrements in NNS frequency were associated with sulfur exposure, but not other examined PM components. As NNS is an early indicator of CNS integrity, our findings add to mounting evidence of the detrimental effect of $PM_{2.5}$ and its components on infant neurodevelopment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations:

NNS	non-nutritive suck

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HIGHLIGHTS

- PM2.5 component exposures are associated with altered infant non-nutritive suck (NNS)
- Strongest associations for NNS amplitude and S, Zn, Cu, V, and Ni
- NNS frequency was associated with sulfur exposure
- Findings suggestive that prenatal PM2.5 component exposure may impact CNS integrity

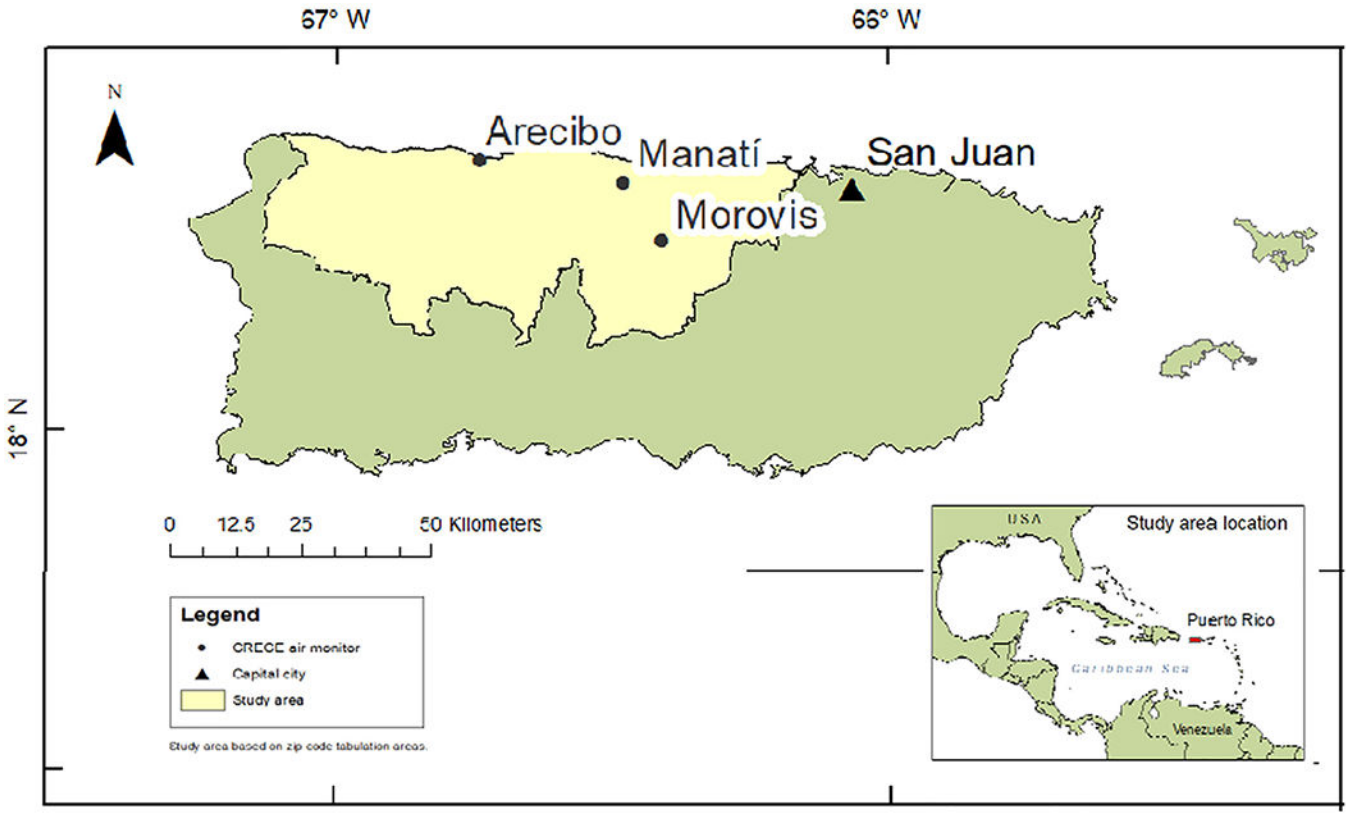

Fig. 1.
Map of study area.

Table 1

Study population characteristics: 2017–2019.[a]

Variable	Number (%) or mean (SD)
Sex	
Male	96 (48)
Female	102 (52)
Birth term	
Preterm (<37 weeks)	11 (6)
Full term (>37 weeks)	187 (94)
Season of birth	
Winter	58 (29)
Spring	51 (26)
Summer	36 (18)
Fall	53 (27)
Mother's age, mean (SD), years	28.7 ± 5.2
Marital status	
Legally married	106 (54)
Not married, living together	64 (32)
Divorcee, widow, maiden	24 (12)
Unknown	4 (2)
Home smoking	
No	171 (86)
Yes	27 (14)
NNS (mean, SD)	
Height (cmH_2O)	17.1 (6.9)
Frequency (cycles/s)	1.9 (0.2)
Duration (s)	6.1 (3.6)
Cycles per burst	11.5 (6.5)
Cycles per minute	60.5 (20.1)
Bursts per minute	6.3 (2.5)
Pollutant concentrations (mean, SD)	
$PM_{2.5}$ ($\mu g/m^3$)	5.37 (2.31)
Black carbon ($\mu g/m^3$)	0.19 (0.04)
Bromine (ng/m^3)	0.97 (0.41)
Calcium (ng/m^3)	54.1 (35.7)
Chlorine ($\mu g/m^3$)	0.24 (0.11)
Copper (ng/m^3)	1.92 (1.22)
Lead (ng/m^3)	1.99 (1.18)
Magnesium (ng/m^3)	37.4 (29.4)
Manganese (ng/m^3)	1.68 (1.61)
Nickel (ng/m^3)	0.67 (0.35)

Variable	Number (%) or mean (SD)
Potassium (ng/m^3)	54.9 (28.1)
Silicon (μg/m^3)	0.29 (0.31)
Sodium (μ/m^3)	0.23 (0.07)
Sulfur (μg/m^3)	0.23 (0.06)
Vanadium (ng/m^3)	0.82 (0.22)
Zinc (ng/m^3)	3.50 (2.94)

[a]Total number of births equaled 198.

Table 2

Effect estimates (standard error) for NNS outcome per standard deviation increment in air pollutant levels (N = 198).

Pollutant	NNS amplitude (cmH_20)		NNS frequency (Hz)	
	Base model[1]	Full model[2]	Base model[1]	Full model[2]
$PM_{2.5}$	−0.41 (0.50)	−0.46 (0.50)	0.01 (0.02)	0.01 (0.02)
Mg	0.26 (0.49)	0.20 (0.50)	0.01 (0.02)	0.01 (0.02)
Mn	−0.55 (0.50)	−0.62 (0.51)	0.02 (0.02)	0.02 (0.02)
Si	−0.53 (0.50)	−0.61 (0.51)	0.02 (0.02)	0.02 (0.02)
Ca	−0.64 (0.50)	−0.70 (0.50)	0.02 (0.02)	0.02 (0.02)
K	−0.40 (0.49)	−0.52 (0.50)	0.02 (0.02)	0.02 (0.02)
BC	0.18 (0.53)	0.06 (0.54)	0.02 (0.02)	−0.02 (0.02)
Br	−0.77 (0.51)	−0.77 (0.51)	0.02 (0.02)	0.02 (0.02)
Pb	−0.88 (0.50)*	−0.98 (0.51)*	0.01 (0.02)	0.01 (0.02)
Zn	−1.02 (0.50)**	−1.09 (0.50)**	0.02 (0.02)	0.02 (0.02)
Cu	−1.02 (0.53)*	−1.10 (0.54)**	0.02 (0.02)	0.02 (0.02)
S	−1.00 (0.50)*	−1.03 (0.51)**	0.03 (0.02)*	0.04 (0.02)**
Cl	0.48 (0.49)	0.44 (0.50)	0.01 (0.02)	0.00 (0.02)
Na	0.26 (0.50)	0.23 (0.50)	0.01 (0.02)	0.01 (0.02)
V	−1.14 (0.53)**	−1.16 (0.54)**	0.03 (0.02)	0.03 (0.02)
Ni	−1.48 (0.50)**	−1.53 (0.50)**	0.03 (0.02)	0.03 0.02)

[1] Base model adjusted for infant gender, maternal age, gestational age, and season of birth.

[2] Fully adjusted model additionally adjusted for household smoke exposure, NNS burst duration, and infant age at NNS testing.

** $p < 0.05$.

* $p < 0.10$.