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Impact of Exposure to Particulate Matter from an International Airport on Cerebral Palsy and Epilepsy

A thesis submitted in partial satisfaction of the  
requirements for the degree Master of Science in Epidemiology

by

Devin Teichrow

2024

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## ABSTRACT OF THE THESIS

Impact of Exposure to Particulate Matter from an International Airport on Cerebral Palsy and Epilepsy

by

Devin Teichrow

Master of Science in Epidemiology

University of California, Los Angeles 2024

Professor Beate Ritz, Chair

Ultrafine particulate matter (UFP) exposure from aircraft emissions is a growing concern for infant health. This study investigates the association between UFP exposure during pregnancy and the risk of cerebral palsy (CP) and epilepsy in infants born within a 15 km radius of Los Angeles International Airport (LAX) between 2008 and 2016. Using birth records from the California Department of Public Health and ground level air pollution data, we evaluated maternal residential UFP exposures, adjusting for neighborhood socioeconomic status, race of the mother, and sex of the infant. The study included 187,289 individuals with 284 CP cases and 120 epilepsy cases. Logistic regression analyses found a consistent increase in the odds of CP for UFP exposure in the third trimester for the second and third quartiles of exposure and close to null associations after adjustment for race, SES and infant sex in the third and fourth exposure quartile ( $\text{adjOR}_{2\text{nd Q}} = 1.45$  [95% CI = 1.00, 2.10];  $\text{adjOR}_{3\text{rd Q}} = 1.19$  [95% CI = 0.80, 1.74]  $\text{adjOR}_{4\text{th Q}} = 1.08$  [95% CI = 0.71, 1.66]). For epilepsy, we found no associations with airport UFPs ( $\text{adjOR}_{2\text{nd Q}} = 1.04$  [95% CI = 0.62, 1.73];  $\text{adjOR}_{3\text{rd Q}} = 0.82$  [95% CI = 0.48, 1.41]);  $\text{adjOR}_{4\text{th Q}} = 0.80$  [95% CI = 0.44, 1.45]). However, the sample size for epilepsy cases was small and our statistical power

to estimate effects was quite limited. This study is one of the first studies to assess air pollution's health impacts on these outcomes and the small sample size limited our ability to assess the risks associated with airport UFP exposure.

The thesis of Devin Teichrow is approved.

Kimberly Paul

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Beate Ritz, Committee Chair

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2024

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## **1. Introduction**

Cerebral palsy (CP), a neurodevelopmental disorder most commonly diagnosed in infancy or early childhood, impacts roughly three infants per 1,000 births in the United States, with infants experiencing preterm birth having a greater risk of CP. CP is usually attributed to lesions in the brain impacting movement and muscle coordination (Rosenbaum et al., 2006). The symptoms of CP vary from person to person, ranging from a single limb being affected (e.g. a limp) to severe disability (e.g. wheelchair-bound and/or intellectually disabled) (Jonsson et al., 2019). Other symptoms include mental disability, behavioral problems, and concurrent epilepsy (Rosenbaum et al., 2006). Preterm birth is associated with increased risks of CP (Tegegne 2023), and air pollution in the form of Ultra Fine Particulate matter (UFP) from aircraft has been found to increase the risk of preterm birth (Wing et al., 2020). Thus, here we will for the first time examine the impacts of UFP on CP and the other common neurodevelopmental disorder epilepsy.

Epilepsy has been found to impact roughly six in 1,000 births and to be comorbid with CP, with epilepsy co-occurring in an estimated 41% of CP cases (Christensen et al., 2014; Fiest et al., 2017). Previous studies have highlighted the impact of prenatal factors on neurodevelopment and the subsequent risk of developing epilepsy. There is not only an overlap between CP and epilepsy in terms of their developmental origin but possibly also in terms of shared risk factors. For instance, complications of preterm birth and low birth weight have been found to contribute to the development of CP and epilepsy (Otinashvili et al., 2024), as are brain lesions (El-Tallawy et al., 2014; Pavone et al., 2021).

Additional potential prenatal and postnatal risk factors for CP summarized in a systematic review include placental abnormalities, birth defects (major and minor), meconium aspiration,

cesarean delivery, birth asphyxia, neonatal seizures, hypoglycemia, and neonatal infection (McIntyre et al. 2012). Epilepsy has some evidence for common risk factors in preterm birth, neonatal seizures, and neonatal infection (Walsh et al., 2017). Some studies found disparate CP rates by socio-economic status (SES), with lower levels of parental SES being associated with higher rates of CP in offspring (Wu et al., 2010). Additionally, Hispanic and Black individuals in California have higher rates of CP than White and Asian individuals (Fecht et al., 2015). This may also suggest that disparate environmental exposures, such as air pollution may contribute to the development of such brain lesions with subsequent CP.

Recently, a cohort study in Canada found ambient levels of PM<sub>2.5</sub> to be associated with an increased risk of CP (Hu et al., 2022). However, prenatal exposure to particulates in the UFP range have not yet been investigated for CP and epilepsy, although there is some evidence that airport UFP exposure confers an increase in risk of preterm birth, a risk factor for CP and epilepsy (Wing et al. 2020). In the UFP range, no studies have examined the impact of exposure to UFPs originating from aircraft during pregnancy and any neurodevelopmental outcome, to our knowledge. In contrast, the impact of air pollution from road traffic on neurodevelopment has been more extensively studied. For example, PM<sub>2.5</sub>, Ozone, and Diesel exhaust have been found to increase the risk of, Autism Spectrum Disorder, Attention Deficit Hyperactivity Disorder, Schizophrenia, and behavioral disorders (Backes et al., 2016; Castagna et al., 2022; Chiu et al., 2016; Cory-Slechta et al., 2023; Costa et al., 2016; D'Anguilli, 2018; Rahman et al., 2022). There is a lack of evidence on the impacts of aircraft emissions on neurodevelopment and especially CP and epilepsy.

Following up on a recent study from our team finding that UFP from aircraft emissions at LAX increase preterm birth risk (Wing et al., 2020), this study aims to investigate the impact of

UFP, in the LAX area on the risk of CP and epilepsy using 2008-2016 California Department of Public Health (CDPH) birth records.

## **2. Methods**

Using birth records from the CDPH, we identified all mothers living within 15 km of LAX, using geocoded addresses, who gave birth from 2008 through 2016. We excluded birth records with gestational ages <20 or >50 weeks ( $n = 386$ ), those with birth weights <500g or >6,300 g ( $n = 211$ ), as well as those with missing covariate data ( $n = 12,962$ ), leaving 174,342 individuals in total for the analyses. All procedures described here were approved by the Institutional Review Boards of the Universities of California, Los Angeles (IRB# 22-000701) and CA state IRB (IRB# 12-10-0861).

According to CDPH, CP was defined in their data as a child having one of two types of motor dysfunction: (1) non-progressive lesion or disorder in the brain occurring during intrauterine life or the perinatal period and characterized by paralysis, spasticity, or abnormal control of movement or posture, which is manifest before two or three years of age, and (2) other significant motor dysfunction appearing before age eighteen. Epilepsy may be diagnosed after at least one unprovoked seizure, with high risk of recurrent seizures (Fisher et al., 2014). Therefore, epilepsy was defined as “recurrent, unprovoked seizures, where seizures can cause loss of muscle control, tremors, loss of consciousness, and other symptoms” (California Department of Developmental Services, 2016).

### ***Exposure Assessment – UFP***

Estimates of UFP measures were generated using an AERMOD dispersion model, which has been validated with spatially extensive ground-level measurements. More details have been

reported elsewhere (Hudda et al., 2014; Wing et al. 2020). Briefly, the U.S. Environmental Protection Agency's (U.S. EPA) AERMET model was first used to generate meteorological parameters at LAX, using hourly wind speed and direction averages. The AERMOD meteorological dispersion model was used to predict air quality in the area surrounding the airport. These sources were aligned with the runways, extending from ground level to 1,000m elevation, and the model factored in plume direction and the angle of approach. Due to historical uncertainty in UFP emissions, a nominal daily average total emission rate was assumed, with variations based on flight activity patterns. AERMOD predictions were then regressed against direct downwind measurements, with a model  $R^2$  of 0.71, and sensitivity tests were conducted for different configurations. The model was run from January 2008 through December 2016 and UFP estimates were generated for geocoded maternal addresses reported in the birth certificate.

### *Covariates*

Demographic factors listed on birth certificates, including maternal age, maternal race/ethnicity [Hispanic (any race), non-Hispanic Black, non-Hispanic White, non-Hispanic Asian, and non-Hispanic Other (including Native American and Hawaiian/Pacific Islander)], and maternal education (educational attainment was recorded in 3 ordinal categories: high school degree or less, some college to college degree, and more than a college degree) were included in the analyses. We used a neighborhood socioeconomic status (nSES) variable based on a principal component analysis of seven indicator variables generated from the United States census data. Mothers were assigned a quintile of nSES (1 = low, 5 = high) at the census block group level from a composite score of the following indicator variables median household income, median rent, median house value, percent living 200% below the level of poverty, percent of blue-collar workers, percent unemployed, and education index (Yost et al. 2001).

## *Statistical Analysis*

We used logistic regression to examine the association between residential-based aircraft UFP concentrations during pregnancy and the neurodevelopmental outcomes of CP and epilepsy (RStudio, R Core Team, 2022). Averaged monthly UFP concentration was treated as a 4-level categorical variable defined by quartiles in each of the trimesters of pregnancy, with cutoffs being the same for each trimester. Full pregnancy and trimester specific UFP exposure quartiles were calculated based on the exposure data from controls with cutpoints at 5,418 particles/cc, 8,661 particles/cc, and 14,622 particles/cc. We adjusted for infant sex, maternal race, nSES, maternal educational attainment, age maternal age. Trimester-specific effects were estimated using separate models for each trimester due to the high collinearity between the trimester exposure variables (See Table 6). In order to better understand UFP as a risk factor with regards to CP specifically, we ran a subgroup analysis on those with CP who did not have concurrent epilepsy.

We implemented stratified logistic regression models to address possible differences in UFP exposure by nSES and maternal education. Due to our small number of cases, convergence issues were encountered in some stratified models. Maternal smoking during pregnancy was reported for 4 cases of CP and 1 case of epilepsy, therefore, this variable was ignored due to model fit issues.

We performed additional analyses to evaluate whether preterm birth (PTB) is a possible mediator of the relationship between UFP and both CP and epilepsy, respectively. We compared effect sizes in models that included preterm birth with those that did not, allowing us to observe how the inclusion of preterm birth affected the relationships between UFP and each of the two neurodevelopmental disorders. These comparisons provided preliminary insights into the

potential mediating role of preterm birth.

**Table 1. Maternal and Infant Demographics (Mean and SD unless otherwise noted)**

<b>Demographic Variable</b>	<b>No CP or Epilepsy</b>	<b>CP</b>	<b>Epilepsy</b>
<b>Cases and Controls</b>	187,289	284	120
<b>Gestational age in weeks</b>	39.22 (2.18)	37.34 (4.32)	38.29 (3.87)
<b>Birth weight in grams</b>	3,283.28 (528.83)	2,703.55 (856.27)	3,000.10 (857.77)
<b>nSES Grouped [n (%)]</b>			
Quintile 1	102,529 (51.4)	202 (71.5)	79 (65.3)
Quintile 2- 3	43,292 (35.1)	47 (11.5)	25 (12.4)
Quintile 4-5	41,468 (13.5)	34 (5.8)	16 (8.3)
<b>Age Group [n (%)]</b>			
< 20	14,697 (7.5)	19 (6.9)	8 (7.2)
20 to 24	29,320 (15.1)	43 (15.7)	16 (14.4)
25 to 39	43,590 (23.1)	66 (23.0)	35 (27.9)
30 to 34	50,128 (27.2)	66 (23.4)	26 (22.5)
35 +	49,554 (27.1)	90 (31.0)	35 (27.9)
<b>Race (maternal) [n (%)]</b>			
White	32,488 (18.5)	27 (10.3)	16 (14.4)
Black	28,250 (14.8)	56 (20.7)	18 (16.2)
Hispanic	110,219 (57.5)	187 (63.6)	79 (63.1)
Asian	16,332 (9.2)	14 (5.4)	7 (6.3)
<b>Education (maternal) [n (%)]</b>			
High School Degree or Less	100,024 (51.3)	189 (63.6)	76 (61.3)
Some College to College Degree	63,566 (35.1)	74 (28.4)	37 (32.4)
More than a College Degree	23,699 (13.5)	21 (8.0)	7 (6.3)

<sup>a</sup>Educational attainment was recorded in 3 ordinal categories: High School Degree or Less, Some College to College Degree, and More than a College Degree.

### 3. Results

Demographic factors by CP and epilepsy status for infants born within a 15 km radius of LAX from 2008 to 2016 are summarized in Table 1. Most mothers were of Hispanic ethnicity and most had a high school diploma or less. Mean maternal age at delivery was 29 years (SD = 6.5 years). CP and epilepsy occurred in 0.16% and .07% of the births, respectively, and both were more common in children of Black and Hispanic mothers and mothers with less education compared with White and Asian mothers and those with a higher level of education. Higher

quartiles of exposure tended to contain mothers who were on average younger, more often Hispanic or Black, and had less education than mothers with lower exposure (See Table S1 for demographic variables stratified by UFP quartile). The mean UFP exposure concentration during the entire pregnancy was 11,971 particles/cc, with a minimum concentration of 2,535 particles/cc and a maximum concentration of 118,820 particles/cc (IQR of 9,200 particles/cc). We found nSES and UFP exposure to be negatively correlated ( $r = -0.27$ ,  $p < .0001$ ), with mothers living in areas of lower nSES having higher average exposure concentrations in pregnancy of aircraft-origin UFPs relative to those living in areas of higher nSES (See Table S3).

For the entire pregnancy period, the odds ratio for CP in the crude model was 1.30 [95% CI = 0.91, 1.85] when comparing exposure to the highest quartile of UFP level ( $\geq 14,622$  particles/cc) with the lowest quartile ( $< 5,418$  particles/cc). The ORs for quartiles 2 and 3 relative to the lowest quartile were slightly higher, at 1.51 [95% CI = 1.07, 2.13] and 1.40 [95% CI = 0.99, 1.99], respectively (See Table 2). Controlling for demographic factors the OR of CP for the highest quartile compared to the lowest quartile changed to 1.10 [95% CI = 0.76, 1.58]. The ORs for quartiles 2 and 3 relative to the lowest quartile were also higher but diminished with adjustment to an OR of 1.32 [95% CI = 0.93, 1.87] for quartile 2 and an OR of 1.12 [95% CI = 0.78, 1.60] for quartile 3 (See Table 2).

**Table 2. ORs (95% CI) from logistic regression models for CP by quartile of UFP exposure (Case N = 284, Control N = 187,289)**

Variable	N (cases)	Unadjusted Model	Adjusted Model <sup>a</sup>
<b>UFP</b>			
<b>Quartile 1</b> ( <b>&lt; 5,340 particles/cc</b> )	54	Ref.	Ref.
<b>Quartile 2</b> ( <b>5,340 – 8,600 particles/cc</b> )	82	1.51 (1.07, 2.13)	1.32 (0.93, 1.87)
<b>Quartile 3</b> ( <b>8,600 – 14,600 particles/cc</b> )	77	1.40 (0.99, 1.99)	1.12 (0.78, 1.60)



<b>Quartile 4</b> <b>(&gt;14,600 particles/cc)</b>	71	1.30 (0.91, 1.85)	1.10 (0.76, 1.58)
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<sup>a</sup> Adjusted for Infant sex, Maternal Age, Maternal Educational Attainment, nSES, and Maternal Race

### *Trimester-specific effects of UFP on CP*

In adjusted models, the highest quartile of first trimester UFP exposure was associated with an OR of 1.24 [95% CI = 0.88, 1.76], 1.15 [95% CI = 0.81, 1.64], and 1.02 [95% CI = 0.84, 1.71] for quartiles 2, 3 and 4, respectively. The highest quartile for second trimester UFP exposure was associated with adjusted ORs of 1.27 [95% CI = 0.89, 1.81], 1.27 [95% CI = 0.90, 1.80], and 1.03 [95% CI = 0.71, 1.48] for quartiles 2, 3 and 4, respectively. The highest quartile of third trimester UFP exposure was associated with an adjusted OR of 1.33 [95% CI = 0.94, 1.90], 1.32 [95% CI = 0.93, 1.87], and 1.02 [95% CI = 0.70, 1.48] for quartiles 2, 3 and 4, respectively (See Table 3).

**Table 3. Adjusted ORs<sup>a</sup> (95% CIs) of Ultrafine Particulate Matter on Cerebral Palsy by pregnancy trimester-specific exposures to UFP**

Variable	N (case)	Trimester 1	Trimester 2	Trimester 3
<b>UFP</b>				
<b>Quartile 1</b> <b>(&lt; 5,340 particles/cc)</b>	54	Ref.	Ref.	Ref.
<b>Quartile 2</b> <b>(5,340 – 8,600 particles/cc)</b>	82	1.24 (0.88, 1.76)	1.27 (0.89, 1.81)	1.33 (0.94, 1.90)
<b>Quartile 3</b> <b>(8,600 – 14,600 particles/cc)</b>	77	1.15 (0.81, 1.64)	1.27 (0.90, 1.80)	1.32 (0.90, 1.90)
<b>Quartile 4</b> <b>(&gt;14,600 particles/cc)</b>	71	1.02 (0.84, 1.71)	1.03 (0.71, 1.48)	1.02 (0.70, 1.48)

<sup>a</sup> Adjusted for Infant Sex, Maternal Age, Maternal Educational Attainment, nSES, and Maternal Race

### *Subgroup analysis of UFP on CP without concurrent epilepsy*

For the entire pregnancy period, the odds ratio of CP without concurrent epilepsy in the crude model was 1.42 [95% CI = 0.93, 2.16] when comparing the highest quartile of exposure to the lowest. Again, the ORs for quartiles 2 and 3 were slightly higher at 1.52 [95% CI = 1.01, 2.31] for quartile 2 and 1.57 [95% CI = 1.04, 2.35] for quartile 3. After adjusting for demographic factors, the highest quartile of UFP exposure was associated with adjusted ORs of 1.32 [95% CI = 0.87, 2.02], 1.24 [95% CI = 0.81, 1.90], and 1.19 [95% CI = 0.78, 1.84], for

quartiles 2, 3, and 4, respectively (See Table 4).

**Table 4. ORs (95% CI) from logistic regression models for CP without concurrent epilepsy by quartile of UFP exposure (Case N = 206, Control N = 187,289)**

Variable	N (cases)	Unadjusted Model	Adjusted Model <sup>a</sup>
<b>UFP</b>			
<b>Quartile 1</b> ( <b>&lt; 5,340 particles/cc</b> )	37	Ref.	Ref.
<b>Quartile 2</b> ( <b>5,340 – 8,600 particles/cc</b> )	57	1.53 (1.01, 2.31)	1.33 (0.87, 2.02)
<b>Quartile 3</b> ( <b>8,600 – 14,600 particles/cc</b> )	59	1.56 (1.04, 2.36)	1.24 (0.81, 1.90)
<b>Quartile 4</b> ( <b>&gt;14,600 particles/cc</b> )	53	1.42 (0.93, 2.15)	1.19 (0.78, 1.84)

<sup>a</sup> Adjusted for Infant sex, Maternal Age, Maternal Educational Attainment, nSES, and Maternal Race

In adjusted trimester specific models, first trimester UFP exposure on CP without concurrent epilepsy was associated with adjusted ORs of 1.19 [95% CI = 0.78, 1.81], 1.24 [95% CI = 0.82, 1.87], and 1.14 [95% CI = 0.75, 1.75], for quartiles 2, 3, and 4 respectively. Second trimester UFP exposure was associated with ORs of 1.28 [95% CI = 0.84, 1.95], 1.42 [0.94, 2.14], and 1.11 [95% CI = 0.72, 1.72], for quartiles 2, 3, and 4, respectively. The associated adjusted ORs for third trimester exposure of UFP were 1.32 [95% CI = 0.86, 2.03], 1.44 [95% CI = 0.95, 2.19], and 1.20 [95% CI = 0.77, 1.85], for quartiles 2, 3, and 4.

**Table 5. Adjusted ORs<sup>a</sup> (95% CIs) of Ultrafine Particulate Matter on CP without concurrent epilepsy by pregnancy trimester-specific exposures to UFP**

Variable	N (case)	Trimester 1	Trimester 2	Trimester 3
<b>UFP</b>				
<b>Quartile 1</b> ( <b>&lt; 5,340 particles/cc</b> )	37	Ref.	Ref.	Ref.
<b>Quartile 2</b> ( <b>5,340 – 8,600 particles/cc</b> )	57	1.19 (0.78, 1.81)	1.28 (0.84, 1.95)	1.32 (0.86, 2.03)
<b>Quartile 3</b> ( <b>8,600 – 14,600 particles/cc</b> )	59	1.24 (0.82, 1.87)	1.42 (0.94, 2.14)	1.44 (0.95, 2.19)
<b>Quartile 4</b> ( <b>&gt;14,600 particles/cc</b> )	53	1.14 (0.75, 1.75)	1.11 (0.72, 1.72)	1.20 (0.77, 1.85)

<sup>a</sup> Adjusted for Infant sex, Maternal Age, Maternal Educational Attainment, nSES, and Maternal Race

## *Epilepsy*

Demographic factors by epilepsy status for infants born within a 15-km radius of LAX from 2008 to 2016 are shown in Table 1. Epilepsy occurred in 0.06% of births and was more common in children of Hispanic mothers or mothers with less years of education. The dip in effect size in the fourth quartile seen in the CP analyses was more pronounced in epilepsy cases, likely due to a lack of power contributing to widened confidence intervals.

In crude models, only exposure at the second quartile of UFP during the entire pregnancy period was positively associated with epilepsy (OR = 1.19 [95% CI = 0.72, 1.96]) in comparison with the lowest quartile but not exposure to the 3<sup>rd</sup> (OR = 1.02 [95% CI = .61, 1.69]) or 4<sup>th</sup> quartile (OR = 0.88 [95% CI = 0.52 1.50]). In the adjusted model, the ORs for epilepsy comparing quartiles 2, 3 and 4 to the lowest quartile were 1.05 [95% CI = 0.63, 1.73], 0.83 [95% CI = 0.49, 1.40], and 0.74 [95% CI = 0.43, 1.27], respectively (See Table 4).

**Table 6. ORs (95% CI) from logistic regression models for Epilepsy by quartile of UFP exposure (Case N = 111, Control N = 174,342)**

Variable	N (case)	Unadjusted Model	Adjusted Model <sup>a</sup>
<b>UFP Quartile</b>			
<b>Quartile 1</b>			
(< 5,340 particles/cc)	29	Ref.	Ref.
<b>Quartile 2</b>			
(5,340 – 8,600 particles/cc)	35	1.19 (0.73, 1.95)	1.05 (0.64, 1.73)
<b>Quartile 3</b>			
(8,600 – 14,600 particles/cc)	30	1.02 (0.61, 1.69)	0.82 (0.49, 1.40)
<b>Quartile 4</b>			
(>14,600 particles/cc)	26	0.88 (0.52, 1.50)	0.73 (0.43, 1.27)

Adjusted for Infant Sex, Maternal Age, Maternal Educational Attainment, nSES, Maternal Race

### *Trimester-specific effects of UFP on Epilepsy*

First trimester UFP exposure was associated with an adjusted OR of 1.12 [95% CI = 0.68, 1.84], 0.89 [95% CI = 0.52, 1.], and 0.66 [95% CI = 0.36, 1.23] for quartiles 2, 3 and 4,

respectively (See Table 5). Second trimester UFP exposure was associated with an adjusted OR of 0.86 [95% CI = 0.52, 1.41], 0.74 [95% CI = 0.44, 1.25], and 0.59 [95% CI = 0.33, 1.07] for quartiles 2, 3 and 4, respectively (See Table 5). Third trimester UFP exposure was associated with an adjusted OR of 1.16 [95% CI = 0.71, 1.91], 0.85 [95% CI = 0.50, 1.45], and 0.61 [95% CI = 0.33, 1.14] for quartiles 2, 3 and 4, respectively (See Table 5). Lack of power restricted us from performing subgroup and sensitivity analyses on UFP and epilepsy.

**Table 7. Adjusted ORs<sup>a</sup> (95% CIs) of Ultrafine Particulate Matter on Epilepsy by pregnancy trimester-specific exposures to UFP**

Variable	N (case)	Trimester 1	Trimester 2	Trimester 3
<b>UFP</b>				
<b>Quartile 1</b> ( <b>&lt; 5,340 particles/cc</b> )	24	Ref.	Ref.	Ref.
<b>Quartile 2</b> ( <b>5,340 – 8,600 particles/cc</b> )	35	1.12 (0.68, 1.84)	0.86 (0.52, 1.41)	1.16 (0.71, 1.91)
<b>Quartile 3</b> ( <b>8,600 – 14,600 particles/cc</b> )	27	0.89 (0.52, 1.51)	0.74 (0.44, 1.25)	0.85 (0.50, 1.45)
<b>Quartile 4</b> ( <b>&gt;14,600 particles/cc</b> )	25	0.64 (0.36, 1.23)	0.59 (0.33, 1.07)	0.61 (0.33, 1.14)

<sup>a</sup> Adjusted for Infant Sex, Maternal Age, Maternal Educational Attainment, nSES, Maternal Race

Our limited sample of epilepsy cases did not allow for us to complete the same sensitivity analyses coming across convergence issues in our models. Adding PTB to the models did not attenuate change the effect estimates of UFP on CP or epilepsy, suggesting it does not mediate much of the effect of UFP on CP or epilepsy (See Table S5). We found PTB to be associated with higher odds of CP (OR = 4.16, 95%CI = 3.18, 5.44) and epilepsy (OR = 2.84, 95%CI = 1.81, 4.44) (See Table S6).

**Table 8. Pearson correlation coefficients (r) between UFP exposures by trimester**

	<b>UFP (Whole Pregnancy)</b>	<b>UFP (Trimester 1)</b>	<b>UFP (Trimester 2)</b>	<b>UFP (Trimester 3)</b>
<b>UFP (Whole Pregnancy)</b>	1.00			
<b>UFP (Trimester 1)</b>	0.97	1.00		
<b>UFP (Trimester 2)</b>	0.98	0.94	1.00	
<b>UFP (Trimester 3)</b>	0.97	0.89	0.94	1.00

#### **4. Discussion**

This study investigated the relationship between UFP exposure attributable to jet fuel exhaust and the incidence of CP and epilepsy in infants. In the area surrounding the Los Angeles International Airport (LAX), particulate matter (PM) counts tended to increase with proximity to the airport, with double the background particulate matter being found up to 16 km (10 miles) and a 4 to 5-fold increase 8-10 km (5-6 miles) downwind of the airport (Hudda et al. 2014). UFPs of jet aircraft origin may be an endocrine-disrupting chemical (EDC), exogenous chemicals that impact hormonal systems in the body, due to polycyclic aromatic hydrocarbons being a byproduct of jet fuel combustion (Howard et al., 2024). Exposure to UFP in occupational settings has been associated with placental hypoplasia, a known risk factor for CP (Pasquiou et al., 2021). Autopsies in children, young adults, and animals from cities with high levels of outdoor air pollution have found lesions in the frontal lobes, a common physiological symptom in CP (Herting et al., 2019).

The proposed mechanism by which particulate matter impacts neurodevelopment is thorough nanoparticles (smaller than 240 nm) bypassing the placenta, inducing changes in the maternal immune system, triggering higher levels of inflammatory cytokines and immune

response cells such as interleukin-6 (IL-6) and  $\text{tnf-}\alpha$ , impacting oxidative stress in the mother which influences fetal brain development, and potentially resulting in neurodevelopmental disorders such as CP and epilepsy (Habre et al., 2018; Herting et al., 2019, Leikauf et al., 2020). However, because air pollution has been implicated in preterm birth (Wing et al., 2020), increases in stress biomarkers (Nagiah et al., 2015), and placental abruption (Kioumourtzoglou et al., 2019), all of which have been implicated as causal factors in CP and epilepsy, the possible impacts of preterm exposure to air pollution on CP and epilepsy are valid concerns warranting investigation based on the triangulation of the evidence at hand.

Our findings suggest a positive association between UFP exposure and CP, especially for exposure in the second and third trimester. The association between UFP exposure and CP was most pronounced for CP cases without concurrent epilepsy, in the third trimester of pregnancy, for those in the third quartile of exposure (OR 1.44 , 95% CI: 0.95, 2.19) compared to the lowest quartile of UFP exposure after adjustment for demographic covariates. The unexpected trend of quartile 2 or 3 having higher ORs than quartile 4 may be due to lower cases of CP and epilepsy in our highest quartile of UFP exposure, a possible indicator of live birth bias (See Table S1 for demographics stratified by UFP quartile). Specifically, at the highest levels of UFP exposure there may be an increase in risk of fetal deaths and miscarriages of infants who also otherwise may develop CP. There is also a stronger effect observed for all but the highest quartiles of exposure with later gestational exposures to UFPs. Our results for moderate levels of UFP exposure are somewhat consistent with the literature suggesting in-utero exposure to air pollution increases the risk of neurodevelopmental disorders (Cory-Slechta et al., 2023).

We did not find a consistent pattern with increasing exposure levels between UFP and CP and no association with epilepsy possibly due to the limited sample size. However, the

suggestion of associations suggest that further research should be conducted to further explore the potential impact of UFP on CP and possibly even epilepsy risk.

While previous studies have found epilepsy to be associated with social deprivation, a measure commonly associated with increased air pollution exposure (Fecht et al., 2014), we failed to see an increase in epilepsy due to increased UFP exposure during pregnancy. However, these analyses were underpowered and researchers in the future should examine this question using larger datasets collected over a longer time period or using a multi-site.

Our study has several strengths. The UFP dispersion model we have available allows for the assessment of exposure profiles in a large population making it possible to study some rarer outcomes. Daytime wind directions in the area surrounding LAX is relatively consistent through the year (Hudda and Fruin, 2016). This consistency allowed for accurate exposure estimation due to improved AERMOD exposure model generalizability.

However, this study also has limitations. We were underpowered to detect small effects due to our limited sample size which also contributed to wide confidence intervals. We used a semi-ecological exposure assessment due to the usage of UFP exposures being estimated only at the home address provided on birth certificates. This does not allow for us to take into account possible movement patterns during pregnancy, with previous studies estimating moving rates of 9-32% among pregnant women (Bell and Belanger, 2012). Adjustment for PM<sub>2.5</sub> was not possible because of a lack of PM<sub>2.5</sub> monitors in the area. Only a single monitor was located in our 15km exposure area and did not provide the necessary spatial variation in measurements. Ground level traffic may also be a confounding factor here, however, with limited statistical power we opted to not control for NO<sub>2</sub>, as well as noise from the airport in order to avoid overfitting the models and potentially leading to unreliable effect estimates.

In conclusion, this study contributes to the growing body of literature on the health impacts of air pollution, suggesting that aircraft-related UFP exposure may affect CP. WE did not have enough sample size to sufficiently address epilepsy risk but generally we did not see consistent patterns with our modeled pollutants. Future studies are needed inquiries, particularly those that can leverage larger datasets with more cases to overcome the constraints of limited statistical power in our study. Future studies need to also consider the interplay of genetic predispositions, live-birth bias, and additional environmental toxins, which may allow for more insights into the etiology of these complex conditions.

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