The Relationship Between Prenatal PAH Exposure and Child Neurocognitive and Behavioral Development

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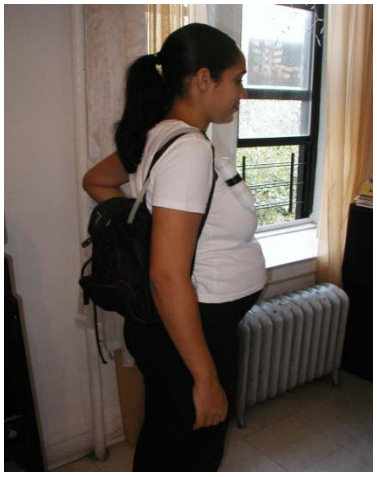
Research Overview



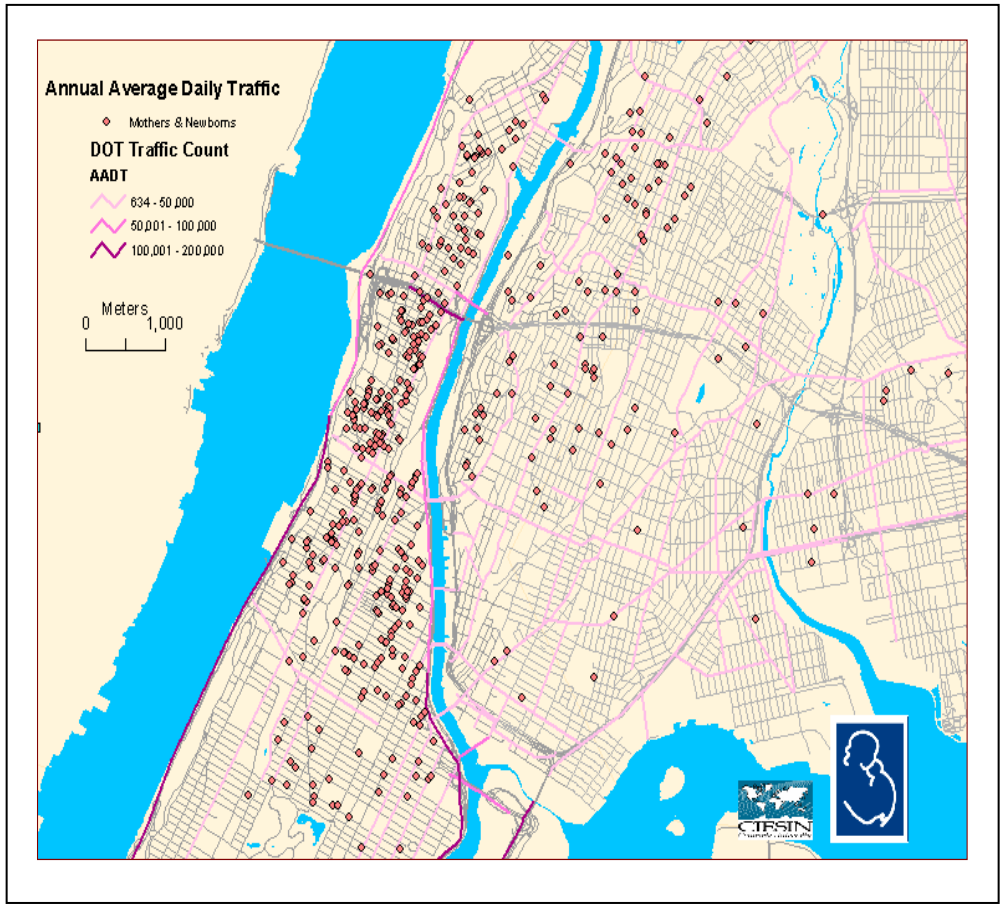
Mission: Prevention of childhood disease and neurodevelopmental impairment through early identification of environmental risk factors

Study Populations: NYC, Poland, and China

- Young, healthy pregnant women recruited during pregnancy (total ~ 2000 mothers and 2000 babies enrolled)
- Active smokers excluded; passive smokers included
- Subject to varying levels of environmental exposures

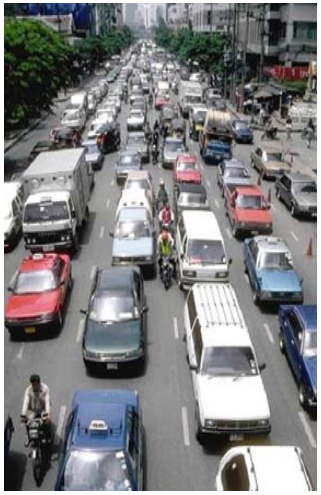
NYC Cohort

- >700 African-American and Latina mother-child pairs
- Exposures being studied: PAH, PM, ETS, pesticides, phthalates, BPA
- Prenatal personal air monitoring; maternal urine and blood, cord blood and placenta, child blood and urine



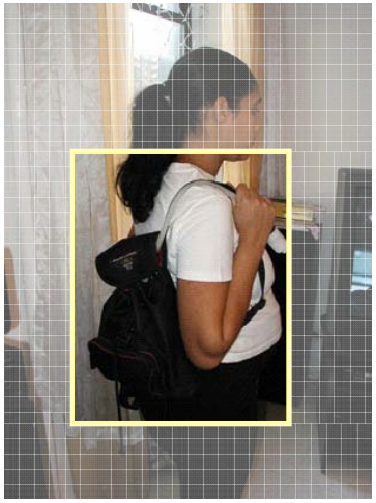
Why Polycyclic Aromatic Hydrocarbons?

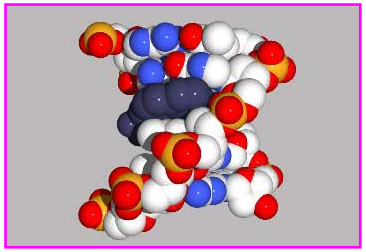
- Widespread urban air pollutants generated by fossil fuel burning and other combustion sources
- Carcinogenic, immunotoxic, neurotoxic, mutagenic, and endocrine disruptors
- Experimental animal data show:
    - exposure impairs memory and increases depression-like responses
    - pre- or perinatal exposure affects brain development, impairs learning, and affects emotional behavior
    - CCCEH data indicate that prenatal exposure in humans
    - y child develop



Measurement of Prenatal PAH Exposure in the NYC and Krakow Cohorts

Area Exposure	⇨	Personal Exposure	⇨	Internal Dose	⇨	Biologically effective dose
Area monitor (and GIS)		Backpack PAH		Urinary metabolite (e.g., 1-OH)		Adducts





CCCEH Cohort: Widespread Exposure to PAH in Air

- 100% of pregnant mothers exposed to PAH (mean 3.7 ng/m^3; range 0.36 -36.47 ng/m^3)
- PAH/aromatic-DNA adducts detected in 100% cord white blood cells
- PAH urinary metabolites detected in 100% pregnant mothers

Air Sampler

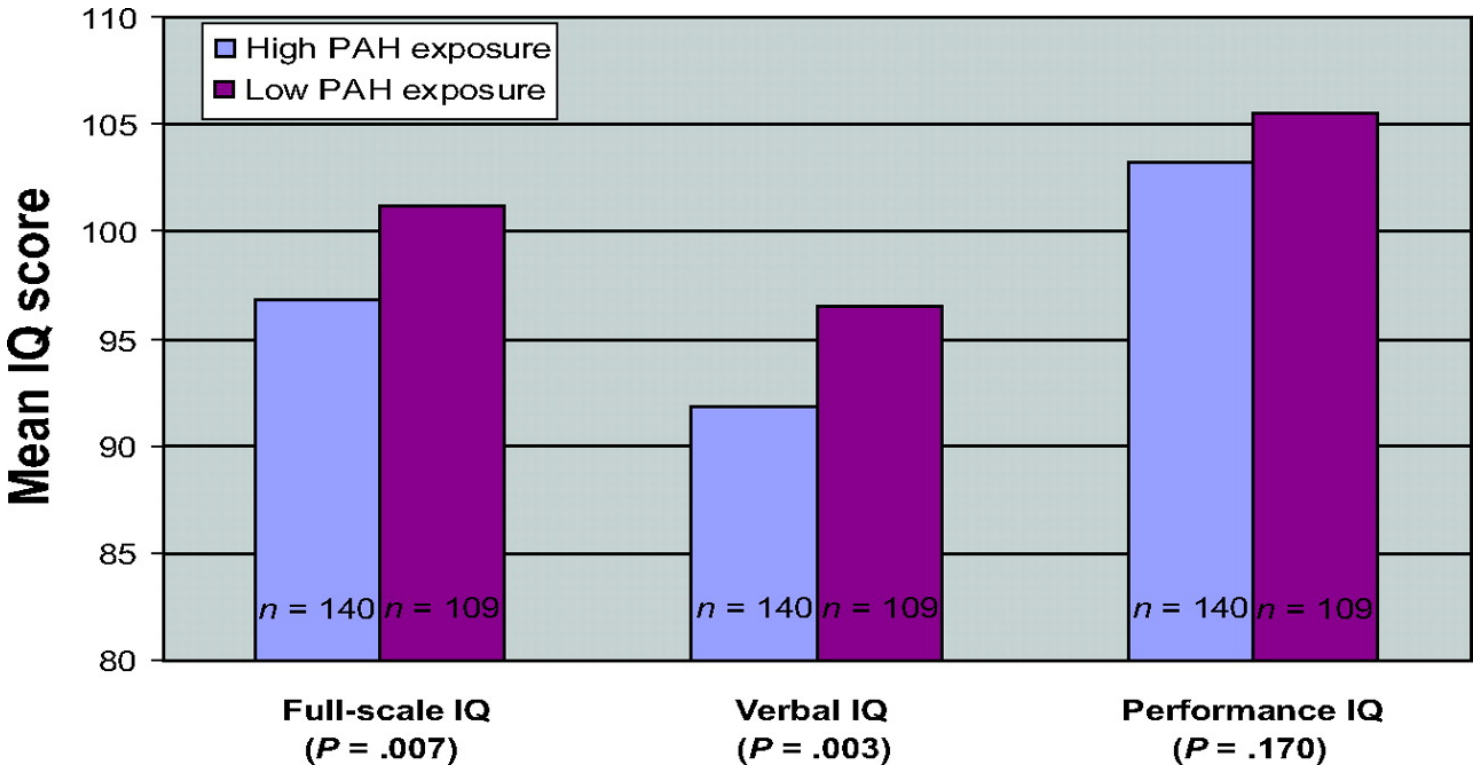
[Perera et al. 2003; 2004]

Previously Reported Associations between Prenatal PAH and Adverse Health Outcomes (NYC)

- Reduction in birth weight and head circumference
- Developmental delay* (MDI) at age 3 and reduced IQ at 5
- Childhood asthma
- Chromosomal aberrations
- Obesity
- Epigenetic Alterations

[Perera et al. 2009 ; Edwards et al. 2011]

PAH and Neurodevelopment: IQ at Age 5 in NYC



Differences in full-scale, verbal, and performance IQ scores associated with high levels of prenatal PAH exposure (N = 249)

[Perera, F. P. et al. Pediatrics 2009;124:e195-e202]

Results [age 5, 7]

Exposure assessment	Anxious /Depressed						Attention Problems					
	Poisson			Logistic Dichotomized T-scores			Poisson			Logistic Dichotomized T-scores		
	β	95% CI	p-value	OR	95% CI	p-value	β	95% CI	p-value	OR	95% CI	p-value
Cord ^{32}P adducts, age 5, (n=96)	0.34	(0.04, 0.64)	0.026*	8.14	(1.21, 54.94)	0.031*	0.38	(0.06, 0.69)	0.018*	5.66	(0.64, 50.05)	0.119
Cord ^{32}P adducts, age 7, (n=205)	-0.03	(-0.22, 0.16)	0.773	1.42	(0.45, 4.46)	0.544	0.22	(0.06, 0.38)	0.009*	3.30	(1.22, 12.54)	0.022*

	DSM-Oriented Anxiety Problems		
	Logistic Model		
	OR	95% CI	p-value
Cord ^{32}P adducts, age 5 (n=96)	8.30	(1.13, 60.71)	0.037*
Cord ^{32}P adducts, age 7, (n=205)	1.26	(0.42, 3.82)	0.683

- Adjusting for prenatal ETS, sex, gestational age, maternal IQ, home environment, maternal education, ethnicity, prenatal demoralization, and age at assessment

[Perera, F. P. et al. Pediatrics 2009;124:e195-e202]

Conclusion

- Adducts tell only part of the story. It is likely that PAH are also operating through mechanisms in addition to direct genotoxicity (epigenetic).
- This research provides evidence that prenatal exposure to environmental PAH at levels encountered in the air of New York City can adversely affect child cognition and behavior
- Results underscore the need for reduction of ambient PAH exposure

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I have no conflicts of interest to report