PRENATAL EXPOSURE TO AIR POLLUTION AND NEURODEVELOPMENT IN A NEW YORK CITY COHORT

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CHE Partnership Call
March 19, 2014

THE GROWING BURDEN OF NEURODEVELOPMENTAL DISORDERS IN CHILDREN

- 15% of children in the U.S. ages 3 to 17 years are affected by neurodevelopmental disorders such as ADHD, learning disorders, or intellectual disability

- 20% global prevalence of child and adolescent mental disorders

- Rates of these conditions have increased in recent decades—the US, Europe, and China

DISPROPORTIONATE EXPOSURE/RISK

- Toxic sources such as for PAH are disproportionately sited in lower income communities of color

- Higher exposure to pesticides and certain EDC chemicals in buildings, food and consumer products

- These communities also experience more material hardship and psychosocial stress

- Pollutants and psychosocial stress may act through common mechanistic and physiological pathways

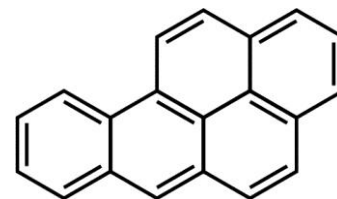- Need to document interactions in order to intervene effectively

Multiple Environmental Exposures Occur During Pregnancy and Early Childhood

- **PAH/air pollution**
- Pesticides
- Chemicals (BPA, Phthalates PBDEs etc.)
- Metals
- Often co-occur with social stressors and adverse genetic and nutritional factors

PAH

- Linked to neurodevelopmental toxicity, asthma, immunotoxicity, carcinogenicity, obesity

- PAH are both genotoxic <u>and</u> endocrine disruptors

  – PAH form DNA adducts and cause mutations

  – PAH such as B[a]P resemble steroid hormones

  – Induce estrogen-dependent cell proliferation

  – Affect gene expression in hormonal regulatory pathways (e.g., bind to the AH receptor) and activate transcription of CYP1A1 and CYP1B1)
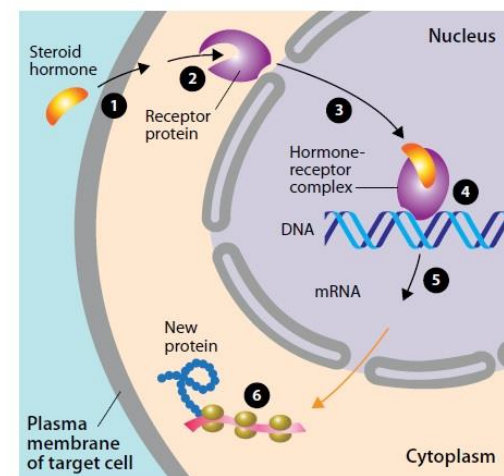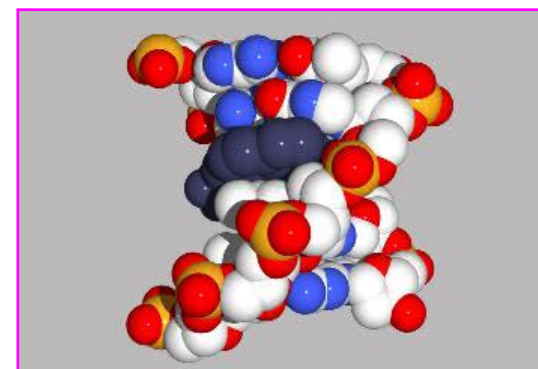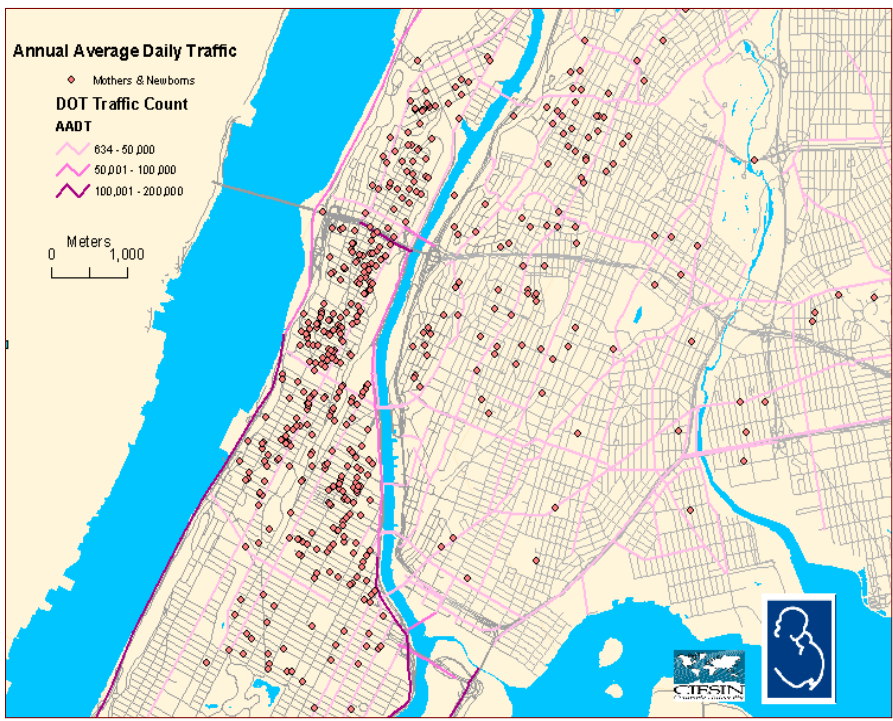

[State of the Science of Endocrine Disrupting Chemicals, 2012]

CCCEH NYC Cohort Study: 720 Mother-Child Pairs Enrolled

Annual Average Daily Traffic
- Mothers & Newborns

DOT Traffic Count AADT
- 634 - 50,000
- 50,001 - 100,000
- 100,001 - 200,000

Meters 0 | 1,000

- Mothers non-smoking and healthy, ages 18-35

- African American and Dominican Residents of northern Manhattan and the S. Bronx

- 64% of mothers had completed high school education

- Mostly low income

- Recruited during pregnancy: maternal urine and blood collected
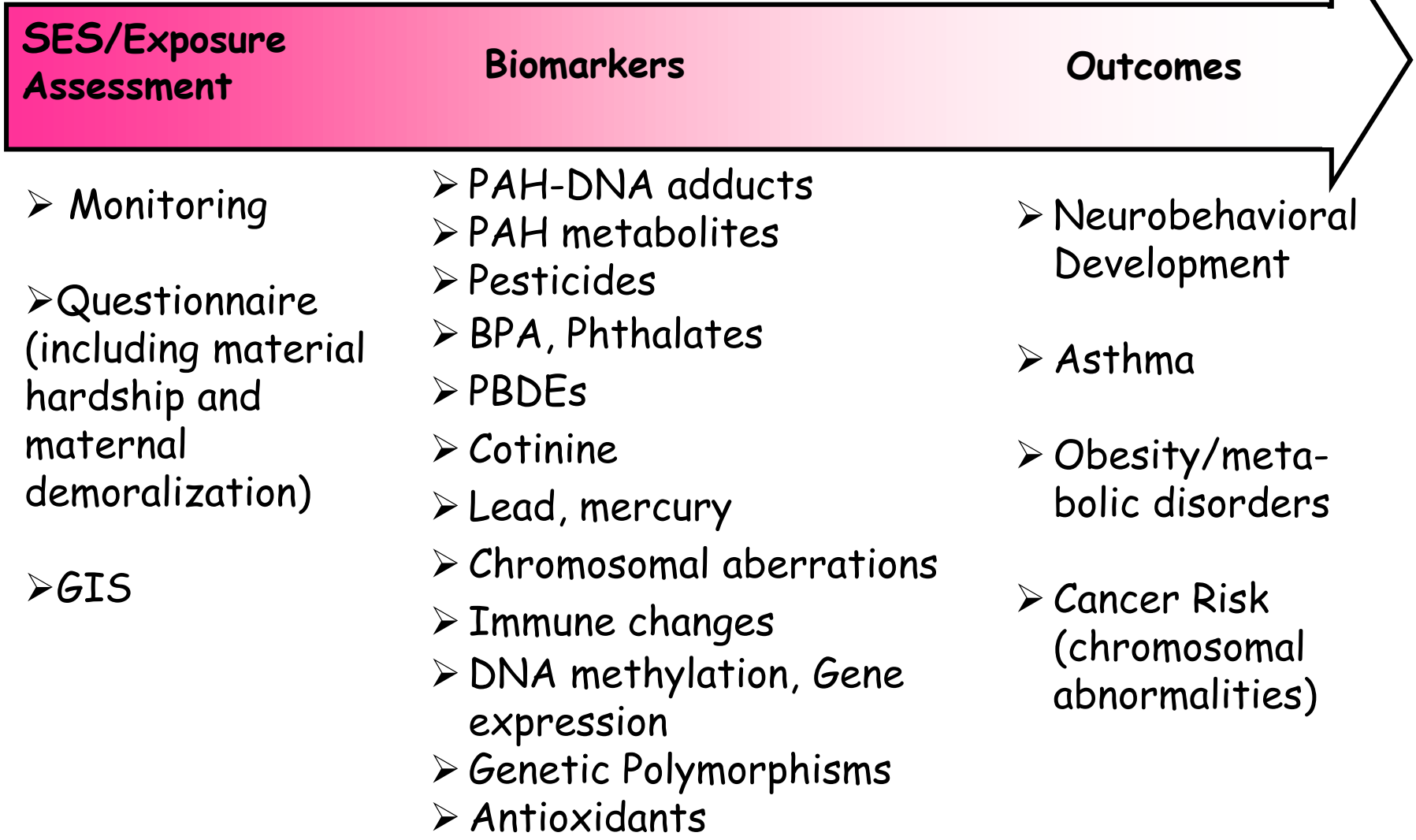
- Prenatal personal air monitoring

Cord blood and placenta collected at birth, blood and urine from children (2 yr-adolescence)

Follow-up of children through adolescence

COHORT STUDIES: REPEAT MEASURES ON WOMEN AND CHILDREN (PREGNANCY ⟶ ADOLESCENCE)

SES/Exposure Assessment

Biomarkers

Outcomes

➢ Monitoring

➢ Questionnaire (including material hardship and maternal demoralization)

➢ GIS

➢ PAH-DNA adducts
➢ PAH metabolites
➢ Pesticides
➢ BPA, Phthalates
➢ PBDEs
➢ Cotinine
➢ Lead, mercury
➢ Chromosomal aberrations
➢ Immune changes
➢ DNA methylation, Gene expression
➢ Genetic Polymorphisms
➢ Antioxidants

➢ Neurobehavioral Development

➢ Asthma

➢ Obesity/meta-bolic disorders

➢ Cancer Risk (chromosomal abnormalities)

WIDESPREAD EXPOSURE TO PAH

- 100% of pregnant mothers exposed to airborne PAH

  - mean 3.7 ng/m^3, range 0.36 ng/m^3 to 36.47 ng/m^3

- 40% of cord and maternal white blood cells had detectable PAH-DNA adducts

- 100% pregnant mothers had detectable levels of PAH metabolites

- >98% of 3 year olds have at least 6 detectable metabolites in their urine
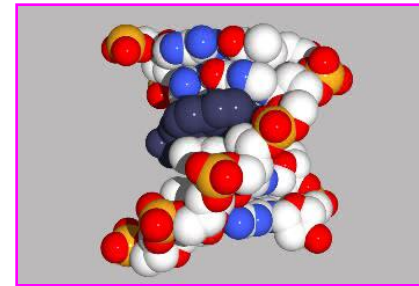
Air Sampler

[Perera et al., 2003; 2004]
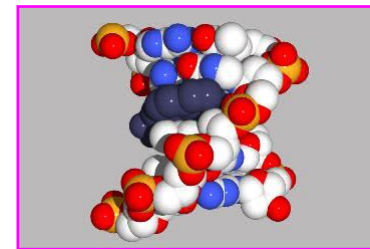
PRENATAL PAH AND COGNITIVE/ BEHAVIORAL PROBLEMS IN THE CCCEH COHORT: METHODS

- PAH: personal monitoring

- PAH-DNA Adducts
  - specifically B[a]P-DNA adducts
  - measured by HPLC-Fluorescence

- Bayley Scales, WPPSI,WISC etc.

- CBCL, Child Behavior Checklist (screen for behavioral problems), Connors (ADHD) etc.

PAH and Developmental Delay At Age 3 in the CCCEH Cohort

- High prenatal exposure to PAH (upper quartile) was associated with lower mental development index at age 3 [β= –5.69; 95% CI, –9.05 to –2.33; p < 0.01).

[Perera et al., 2006]

- Among the highly exposed children the odds of having developmental delay were 2.89 times greater than the odds among unexposed children

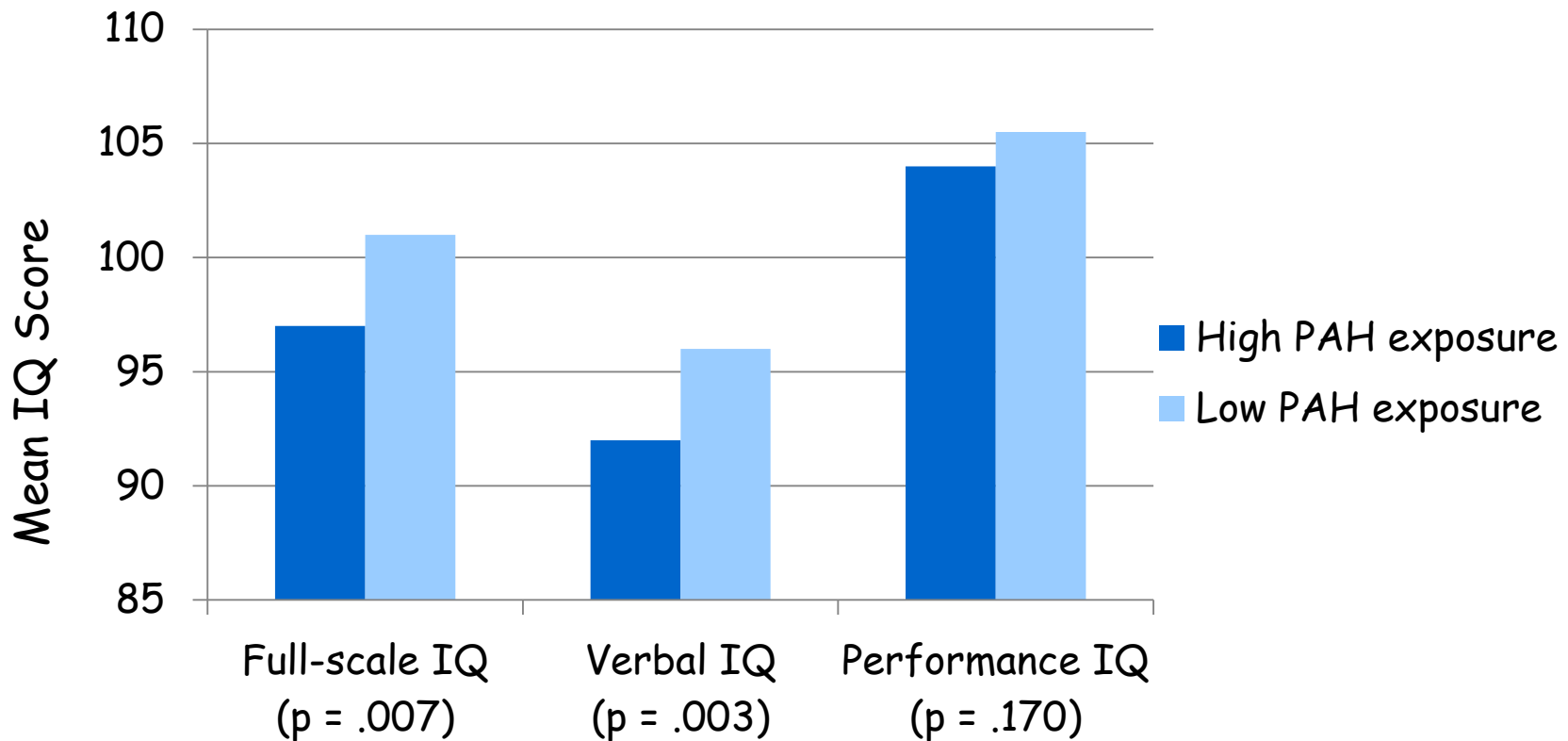Adjusting for sex, ethnicity, gestational age, quality of home (caretaking) environment, prenatal exposure to ETS and CPF, age at assessment.

Prenatal PAH and IQ
At Age 5 in the CCCEH Cohort

High prenatal PAH levels associated with reduced full-scale and verbal IQ scores

Adjusting for prenatal ETS, sex, gestational age, maternal IQ, home environment, maternal education, ethnicity, diet and other covariates (N=249)

[Perera et al., 2009]

PRENATAL PAH/PAH-DNA ADDUCTS AND CHILD BEHAVIORAL PROBLEMS (AGE 6–8)

Exposure	Syndrome Scales Anxious /Depressed			DSM-Oriented Scales Anxiety Problems		
	Poisson Raw			Logistic Model		
	Exp beta	95% CI	p-value	OR	95% CI	p-value
PAH (high/low) (n=253)	1.45	(1.22, 1.72)	**<0.0001**	4.59	(1.46, 14.27)	**0.009**
Maternal HPLC adducts (n=223)	1.23	(1.04, 1.46)	**0.019**	2.19	(0.79, 6.07)	0.133
Cord HPLC adducts (n=148)	1.46	(1.19, 1.78)	**<0.001**	2.53	(0.84, 7.65)	0.100

Adjusting for prenatal ETS, sex, gestational age, maternal IQ, home environment, maternal education, ethnicity, prenatal demoralization, and age at assessment00

[Perera et al., 2012]

CUMULATIVE PAH EXPOSURE (HIGH/LOW) AND ADHD AT AGE 9

	Air PAH			Maternal adduct			Cord adduct		
	n	Est.	p-value	n	Est.	p-value	n	Est.	p-value
CBCL DSM: ADHD									
Connors Subscales:									
ADHD Index									
DSM-IV ADHD Total									
DSM-IV Hyper active-Impulsive									
DSM-IV Inattentive									

Adjusting for ETS, gender, maternal education, ethnicity, gestational age, maternal demoralization, home caretaking environment, maternal ADHD

INTERACTIONS BETWEEN POLLUTANTS AND PSYCHOSOCIAL FACTORS

Does the combination of physical and psychosocial stressors during fetal development magnify the effect of each exposure?

Documentation of interactions will allow more effective interventions to protect the most vulnerable.

Everyone benefits.

Interaction of Prenatal PAH Exposure with Material Hardship on Child IQ at Age 7 (NYC)

- **Hypothesis: Material hardship exacerbates the effect of PAH on child IQ at age 7**

- Material hardship: a measure of the inability of families to meet their basic needs for housing, clothing, food

- PAH-DNA adducts measured in cord blood as an individual biomarker of prenatal PAH exposure

- Child IQ assessed via the Wechsler Intelligence Scale for Children (WISC-IV) at 7 years

[Vishnevetsky et al., in revision]

IQ Scores in the Low and High Cord Adduct Groups Stratified by Cumulative Hardship

[Perera et al., in revision]

INVESTIGATION OF MECHANISMS ONGOING

- MRI

- PARALLEL LABORATORY STUDIES

- EPIGENETIC ANALYSES

Spearman Rank-Order Correlations of White Matter Surface with Prenatal PAH Levels

Figure 2
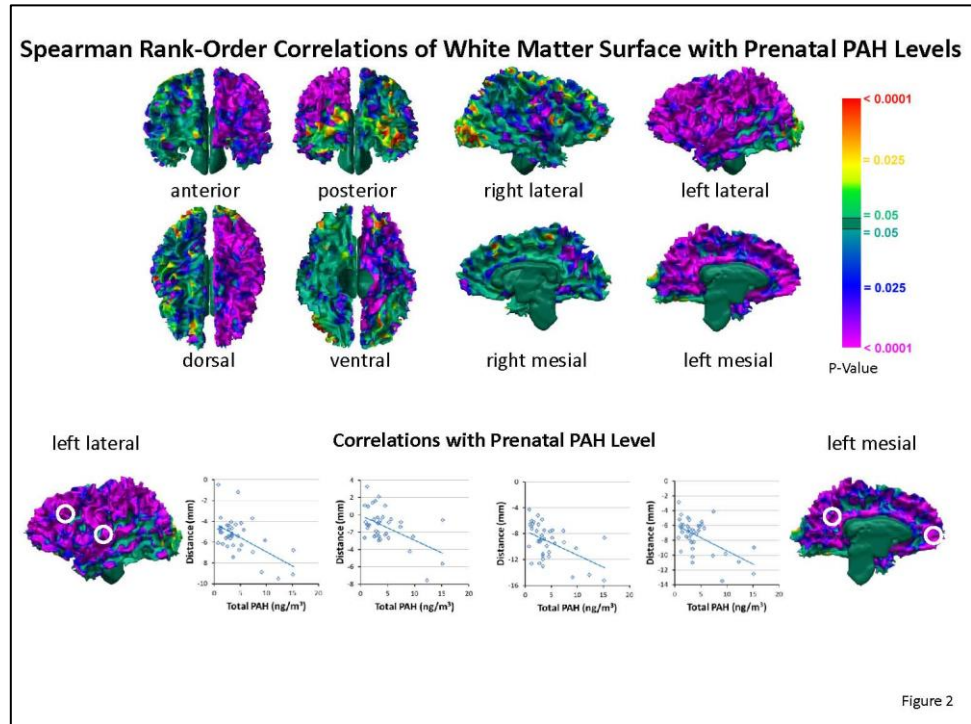
Environmental exposures — Epigenetics (with access to target tissue) — F2
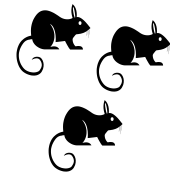
Neurobiology, behavior, metabolism, and immune function

CONCLUSION

- Evidence of continuing effects of prenatal or cumulative exposure to PAH on child cognitive and neurobehavioral development through age 9

- Evidence of interactions with psychosocial stressors

- Implications for children's academic performance and lifetime earnings

- Need for multi-faceted interventions to reduce neurotoxic exposures and alleviate stress due to poverty

COLLEAGUES

THIS RESEARCH HAS BEEN MADE POSSIBLE BY JOINT FUNDING FROM:

Special thanks to the families and children

I have no conflicts of interest to report.