Prenatal Exposure to EDCs and Developmental and Health Outcomes in a New York City Cohort

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Research Overview

Mission: Prevention of childhood neurodevelopmental impairment, asthma, obesity and cancer through early identification of environmental risk factors and translation to intervention.
MULTIPLE EXPOSURES TO EDCs AND OUTCOMES IN THE CCCEH COHORT

SES/Exposure Biomarkers Outcomes

PAH BPA Phthalates CPF PBDEs ETS

Neurodevelopment
Birth Outcomes
Obesity/metabolic disorders
Asthma/Wheeze/Air way inflamm.
Cancer risk
MULTIPLE EXPOSURES TO EDCs AND OUTCOMES IN THE CCCEH COHORT

SES/Exposure  Biomarkers  Outcomes

Neurodevelopment
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Mechanisms:
• Epigenetics
• MRI

PAH  BPA
Phthalates  CPF
PBDEs  ETS
CCCEH NYC Cohort Study:
720 Mother-Child Pairs Enrolled

- Mothers non-smoking and healthy, ages 18-35
- African American and Dominican Residents of northern Manhattan and the S. Bronx
- 63.5% of mothers had completed high school education or more
- Mostly low income, on Medicaid
- 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
- GIS
RESEARCH FINDINGS: PAH

- Prenatal exposure associated with:
  - Developmental delay age 3 (OR= 2.89, 0.01)
  - IQ reduction at age 5 (β=4.31; p=.007)

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

[Perera et al., 2006; 2009; 2012]
RESEARCH FINDINGS: PAH

- Behavioral problems (e.g., anxiety/depression symptoms) ages 6-7
- Prenatal PAH exposure associated with MRI brain changes (age 7-9)

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Syndrome Scales</th>
<th>Anxious /Depressed</th>
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<tbody>
<tr>
<td></td>
<td>Exp beta</td>
<td>95% CI</td>
</tr>
<tr>
<td>PAH (high/low) (n=253)</td>
<td>1.45</td>
<td>(1.22, 1.72)</td>
</tr>
<tr>
<td>Maternal adducts (n=223)</td>
<td>1.23</td>
<td>(1.04, 1.46)</td>
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<tr>
<td>Cord adducts (n=148)</td>
<td>1.46</td>
<td>(1.19, 1.78)</td>
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Adjusting for potential confounders

[Peterson et al., submitted, Perera et al., 2012]
**Research Findings: PAH**

- Prenatal PAH exposure associated with **obesity** over childhood years

  \[
  \text{RR}=1.79 \text{ at age 5;} \\
  2.26 \text{ at age 7}
  \]

- High prenatal and high postnatal exposure to PAH (pyrene) associated with **asthma** in children (OR=1.90; 95% CI:1.13-3.20)

- **Cockroach allergen and prenatal PAH exposures predict cockroach allergic sensitization** at ages 5-7

*All analyses adjusting for relevant covariates: environmental co-exposures and social factors*

[Rundle et al., 2012; Jung et al., 2012; Perzanowski et al., 2013]
**Research Findings: CPF**

- Prenatal CPF exposure associated with reduction in Working Memory at age 7 (p=0.003)

- Brain changes at ages 7-9 (MRI scan) appear to mediate the adverse neurodevelopmental effects of CPF

* All analyses adjusting for relevant covariates

High CPF exposure associated with enlargement of superior temporal, posterior middle temporal, and inferior postcentral gyri bilaterally, and enlarged superior frontal gyrus, gyrus rectus, cuneus, and precuneus along the mesial wall of the right hemisphere

[Rauh et al., 2011, 2012]
RESEARCH FINDINGS: PHTHALATES

• Phthalates associated with **airway inflammation**
  - DEP and BBzP associated with increase in fractional exhaled nitric oxide (FeNO)

• Phthalates associated with **eczema**
  - MBzP with early onset eczema (RR=1.52, p=0.0003)

• Phthalates associated with **adverse child mental, motor, and behavioral development**
  - Psychomotor Development Index (PDI) with MnBP and MiBP
  - Mental Development Index (MDI) with MnBP in girls
  - Clinically withdrawn behavior with MnBP

Metabolites:
• BBzP - butylbenzyl phthalate
• DEP - diethyl phthalate
• MBzP - mono-benzyl phthalate
• MiBP - mono-isobutyl phthalate
• MnBP - mono-n-butyl phthalate

*All analyses adjusting for relevant covariates: environmental co-exposures and social factors

[Just et al., 2012; Whyatt et al., 2011]
After adjustment for potential confounders, children with higher concentrations of BDEs 47, 99, or 100 scored lower on tests of mental and physical development at 12-48 and 72 months (1-6 yrs.).
PBDE: health effects

Cord PBDE concentrations and Neurodevelopment

[Herbstman et al. EHP 2010]
**Research Findings: BPA**

- **Prenatal BPA associated with adverse neurobehavioral outcomes at ages 3-5**
  - Among boys—high exposure associated with significantly higher CBCL scores on Emotionally Reactive (1.62 times greater) and Aggressive Behavior syndromes (1.29 times greater)
  - Among girls—higher exposure associated with lower scores on all syndromes

- **Postnatal BPA (urinary concentrations) associated with asthma**
  - BPA at age 3 associated with wheeze at age 5 (OR, 1.4; p=.02) and age 6 (OR=1.4; p=.03)
  - BPA at age 7 associated with wheeze at age 7 (OR, 1.4; p=.04) and FeNO (β = 0.1; p=.02)
  - BPA at ages 3, 5, and 7 associated with asthma (OR, 1.5; p=.005; OR, 1.4; p=.03; and OR, 1.5; p=.04, respectively)

*All analyses adjusting for relevant covariates: environmental co-exposures and social factors*

[Perera et al., 2012; Donohue et al., 2013]
Experimental Studies: Effects of Prenatal BPA Exposure on the Developing Brain

Brain development
Sexual differentiation (BPA)
Behavior
Learning

Epigenetic mechanisms?
**Experimental Studies: Epigenetic and Behavioral Effects of BPA**

- Sex-specific curvilinear effects of gestational BPA exposure on ERα mRNA in the offspring hypothalamus
- Changes in ERα gene expression are associated with changes in DNA methylation also in the offspring hypothalamus
- Changes in ERα gene expression are associated with alteration in social and anxiety-like behavior

[Kundakovic, Champagne et al., 2013]
TRANSLATION OF RESEARCH TO PREVENTION

• The Center’s *Healthy Homes Healthy Child Campaign*

• Communication by Center investigators and WEACT to cohort families, the community and policy-makers

• Impact on policy:
  - Supported reduction of emissions from diesel buses and trucks, cars, and other combustion sources in the City*
  - Supported clean heating fuel policy in NYC
  - Supports clean energy and climate policy
  - Demonstrated benefit of EPA phase-out of residential CPF
  - Prompted passage of Local Law 37, placing New York at the forefront of safer pest control methods in the United States*
  - Demonstrated efficacy of Integrated Pest Management (IPM) interventions in public housing (Kass et al., 2009)

• Brought attention to need for coordinated social and environmental interventions

*Commendation from Mayor Michael Bloomberg, 2009*
CPF in cord blood (N=395)* (pg/g)

*EPA Ban on residential use of chlorpyrifos took effect in 2001
[Whyatt et al., 2003]

Personal Prenatal Exposure to PAH in the NYC Cohort Declined from 1998 to 2006
[Narvaez, et al. 2008]
Overall Conclusion

- Prenatal and continuing environmental exposures can affect children’s health and development with implications for children’s ability to learn and their future well-being.
- Preventive policies are needed to protect this vulnerable life stage.
- Benefits will be seen in childhood and are likely to accrue over the entire life course.
- This calls for more preventive research and translation.
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