Pre- and postnatal urinary BPA concentrations and childhood neurodevelopment over the first 3 years of life

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  - Participants

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Bisphenol A

- Estrogenic monomer used in the production of polycarbonate plastics and resins
- Concern that prenatal exposure may result in adverse growth and development via endocrine pathways
- Recent expert panels have expressed concern over BPA toxicity
Sources of BPA Exposure

- Canned foods
- Bottles and formula
- Thermal receipts
- Cigarette Filters (Braun 2010)

Ubiquity of BPA has led to nearly universal exposure
Bisphenol A and Neurodevelopment

- Prenatal exposure may result in adverse neurodevelopment
  - Sex steroid mediated processes (Palanza 2008)

- Animal studies show prenatal exposure associated with:
  - Aggression, altered spatial learning
  - Changes in sexually dimorphic behaviors

- Only one human study (Braun et al. 2009)
BPA and Childhood Behavior

- Prenatal BPA exposure was associated with externalizing behaviors in girls at 2 years
  - Early exposures were most important

- Suggests that BPA may disrupt development of sexually dimorphic behaviors

- Limitations
Specific Aims

1. Determine if associations between prenatal BPA exposure and neurodevelopment persist to 3 years of age
   • Examine behavior, mental/psychomotor development, and executive function

2. Examine association between prenatal BPA exposure and cognitive, language, and psychomotor development in Mexico City children
Aim 1: Neurodevelopment at 3 Years

The HOME Study
Data Source: Aim 1

- HOME Study
- Prospective cohort of mothers and their singleton children (n=237)
- Enrolled between 13 and 19 weeks gestation
- Cincinnati metro area
- Recruited 2003-2005
HOME Study Exposures and Outcomes

Prenatal BPA Measures

16W  26W Birth

Covariates

Postnatal Neurobehavior and BPA Measures

1Y: BPA

2Y: BPA

3Y: BPA

3Y: BASC, BRIEF-P, and BSID-II
BPA Exposure

- Spot urine samples collected
  - Prenatal:
    - 16 and 26 weeks
    - Birth
  - Postnatal:
    - 12, 24, and 36 months
  - HPLC-MS/MS

- Creatinine standardized/adjusted
Neurodevelopmental Outcomes

- **BASC-2**
  - Problem and adaptive behaviors:
    - Externalizing, internalizing, and behavioral symptom index

- **BRIEF-P**
  - Parent report of executive function
  - Flexibility, self-control, ability to shift, etc.

- **BSID-II**
  - Structured examination of mental and psychomotor development
BPA Exposure

- Prenatal median: 2.0 µg/L
- Postnatal median: 4.4 µg/L

- Very low correlation between measures
  - $R^2=0$ to 0.3
Aim 2: Pilot Study of BPA and Neurodevelopment in Mexico

The ELEMENT Study
Data Source: Aim 2

- ELEMENT Study
- Ongoing prospective cohort of ~1200 women
- Enrolled ~20 weeks gestation
- Mexico City
- Women were recruited through Mexican Social Security System

- Pilot study of 100 women and their children
ELEMENT Study Exposures and Outcomes

Prenatal BPA Measures

$\text{20W}$

Covariates

Postnatal Neurobehavior

6, 12, and 18 Months: BSID-III
BPA Exposure

- Spot urine samples collected at 20 and 30 weeks gestation
  - Analyzed 20 week samples

- Analyzed with ESI-LC-MS

- Creatinine standardized/adjusted
Neurodevelopmental Outcomes

- BSID-III
  - Structured examination of mental and psychomotor development
  - Global cognition
  - Receptive/express language
  - Gross/fine motor
BPA Exposure in Mexico City at 20 Weeks Gestation

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<td>&lt;LOD</td>
<td>4.4</td>
<td>20</td>
<td>150</td>
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52% (n=52) of women had detectable urinary BPA concentrations ~20 weeks gestation.
Conclusions: Behavior and Executive Function

- Behavior
  - Externalizing and internalizing behaviors
  - Females
  - Early 2nd trimester
  - Persists at 3 years

- Executive function
  - Corroborates behavior result
  - Neuropsychological tests of EF
Conclusions: Mental/psychomotor Development

- BSID Results
  - Conflicting evidence between cohorts

- Differences:
  - Exposure
  - BSID-II vs. BSID-III
  - Small sample in Mexico
Discussion

- Animal literature supports results
  - ↑ Morphine induced locomotion among animals with early exposure (Narita 2007)
  - Increased anxiety (Tian 2010)
    - Changes NMDA and domaninergic systems
  - Sex specific effects of BPA on spatial memory (Bryce 2006, Carr 2003)
Discussion

- BPA may impact sexual differentiation of the brain
  - Importance of sex steroids
Strengths and Limitations

- Neurodevelopmental and exposure data
- Longitudinal follow-up
- Rich set of confounders
- Temporal variability of BPA
- Multiple exposures
- Still early in childhood
- Residual confounding
Future Research

- Continued follow-up of both cohorts

- Enrich Mexico City cohort with:
  - Additional mother-child pairs
  - 3rd trimester sample

- Sexually dimorphic computerized tests
  - VMWM
Conclusions

- BPA exposure may adversely affect childhood behavior
- Role of BPA in cognitive development uncertain
- Research Needs:
  - Comparable animal tests
  - Exposure assessment