Prenatal Exposure to PBDEs and Neurodevelopment

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Study Objective

• While the association between prenatal exposure to PBDEs and adverse neurodevelopment has been observed in animal models, this association has not been adequately explored in human populations.

• We explored the relationship between prenatal PBDE exposure measured in umbilical cord blood and indicators of neurodevelopment at ages 1, 2, 3, 4, and 6 years.
World Trade Center Pregnancy Study

Women pregnant with a single child were enrolled between December 2001 and June 2002 during labor at 3 participating hospitals located within 2 miles of the WTC site.

Eligibility:
- Healthy
- 18-39 years old
- Not a smoker, drug user
- No known HIV infection

Complete enrollment:
- Cord or maternal blood
- Postpartum interview (in English, Spanish, or Mandarin)
- Allowed access to their medical record information

[Lederman et al. EHP 2004]
Methods: Data Collection

- Information about the pregnancy and delivery was collected from the medical records of the mother and newborn.

- Neurodevelopmental testing:
  - Ages 12, 24, and 36 months using Bayley Scales of Infant Development II
    - Mental and Psychomotor Developmental Index
  - Age 48 and 72 months using Wechsler Preschool and Primary Scale of Intelligence-Revised
    - Verbal, Performance, and Full Scale IQs
Methods: Biological Sample Analysis

Cord blood samples were processed at Columbia University

Shipped to the laboratories of the Centers for Disease Control and Prevention for plasma measurements of:

- **PBDEs**
  - semiautomated high-throughput extraction and cleanup method
  - quantified using gas chromatography isotope dilution high resolution mass spectrometry (GC-IDHRMS).


- **Lipids (total triglycerides and cholesterol)**
  - commercially available test kits from Roche Diagnostics Corp. (Indianapolis, IN)

- **Cotinine**
  - liquid chromatography in conjunction with atmospheric pressure ionization tandem mass spectrometry

Methods: Statistical Analyses (1)

• Lipid- and natural log-adjusted

• For BDEs that are components of the penta-formulation:
  – values below LOD were imputed using the $\text{LOD} / \sqrt{2}$
    BDE-47, 99, 100, and 153.
  – compared participants in the highest quintile of exposure to those in the lowest 80% of the population distribution.
  – BDE-85 and 183 were treated as dichotomous measures: detected versus non-detected.
Methods: Statistical Analyses (2)

- Multivariate linear regression analyses
- Inclusion of covariates based on their *a priori* association with neurodevelopment
  - child's exact age at test administration, ethnicity, maternal IQ, sex of child, ETS (yes/no)
- Inclusion of additional covariates based on >10% change in BDE beta coefficient
  - Gestational age at birth, maternal age, maternal education, material hardship during pregnancy, breast feeding index
- Additional model including language and location of assessment
Results: PBDE Exposure

<table>
<thead>
<tr>
<th></th>
<th>Cord blood measurements (n = 210)</th>
<th>Cord measurements with &gt; 1 neurodevelopmental test (n = 152)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>% &gt; LOD</td>
</tr>
<tr>
<td>BDE-47</td>
<td>210</td>
<td>81.4</td>
</tr>
<tr>
<td>BDE-85</td>
<td>189</td>
<td>18.5</td>
</tr>
<tr>
<td>BDE-99</td>
<td>210</td>
<td>59.5</td>
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<tr>
<td>BDE-100</td>
<td>209</td>
<td>63.6</td>
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<tr>
<td>BDE-153</td>
<td>201</td>
<td>49.8</td>
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<tr>
<td>BDE-183</td>
<td>200</td>
<td>6.0</td>
</tr>
<tr>
<td>BB-153</td>
<td>197</td>
<td>11.2</td>
</tr>
</tbody>
</table>

*Table 1. Concentrations (ng/g lipid) of PBDEs and BB-153 in cord blood.*
Characteristics of cohort members

Those included in the study sample were similar to the underlying cohort except:

- slightly older
  - study: 31.2 yrs
  - cohort: 30.2 yrs

- slightly more educated
  - study: 13.8% < HS
  - cohort: 18.5% < HS
Change* in score per increase in BDE IQR

* Adjusted for multiple confounders
Difference in (adj.) mean developmental scores comparing individuals in the highest quintile to those in the lower 80%
Discussion (1)

- Children who had higher cord blood concentrations of BDE 47, 99, and 100 scored, on average, lower on tests of mental and physical development at ages 12-48 and 72 months.

- Concentrations of cord blood PBDEs in this cohort are similar to other U.S. populations.

- Neurodevelopmental effects of prenatal PBDE exposure is consistent with what has been observed in animal models.

- Results are not consistent with the only other human study (Roze et al. 2009); however, differences in exposure concentrations, analytic approaches, and sample size limit comparability.
Discussion (2)

• Mechanisms by which prenatal PBDE exposure affect neurodevelopment are not completely understood:
  – direct neurotoxic effects on neuronal and glial cells [Costa et al. 2008]
  – changes in the quantity of cholinergic nicotinic receptors in the hippocampus [Viberg et al. 2003]
  – induction of apoptotic cerebellar granule cell death [Reistad et al. 2006]
  – thyroid hormone disruption

• Future work:
  – Replication in other study populations
  – Evaluation of effects on child behavior
  – Measurement of thyroid hormones as possible mediators

• While additional studies are underway, identification of opportunities to reduce PBDE exposure
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