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.

[Lederman et al. EHP 2004]

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

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). [Sjodin et al. Anal Chem 2004]
- 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 [Bernert et al. Clin Chem 1997]

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 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 1. Concentrations (ng/g lipid) of PBDEs and BB-153 in cord blood.

	Cord blood measurements ($n = 210$)				Cord measurements with > 1 neurodevelopmental test ($n = 152$)			
	n	% > LOD	Median	Maximum	*n*	% > LOD	Median	Maximum
BDE-47	210	81.4	11.2	613.1	152	83.6	11.2	613.1
BDE-85	189	18.5	0.7	16.6	141	17.7	0.7	16.6
BDE-99	210	59.5	3.2	202.8	152	57.9	3.2	202.8
BDE-100	209	63.6	1.4	71.9	152	69.1	1.4	71.9
BDE-153	201	49.8	0.7	28.9	143	55.9	0.7	28.9
BDE-154	200	6.0	0.6	11.1	146	6.2	0.6	11.1
BDE-183	204	3.9	0.6	2.8	147	4.1	0.6	2.8
BB-153	197	11.2	0.6	8.0	145	13.1	0.9	8.0

Characteristics of cohort members

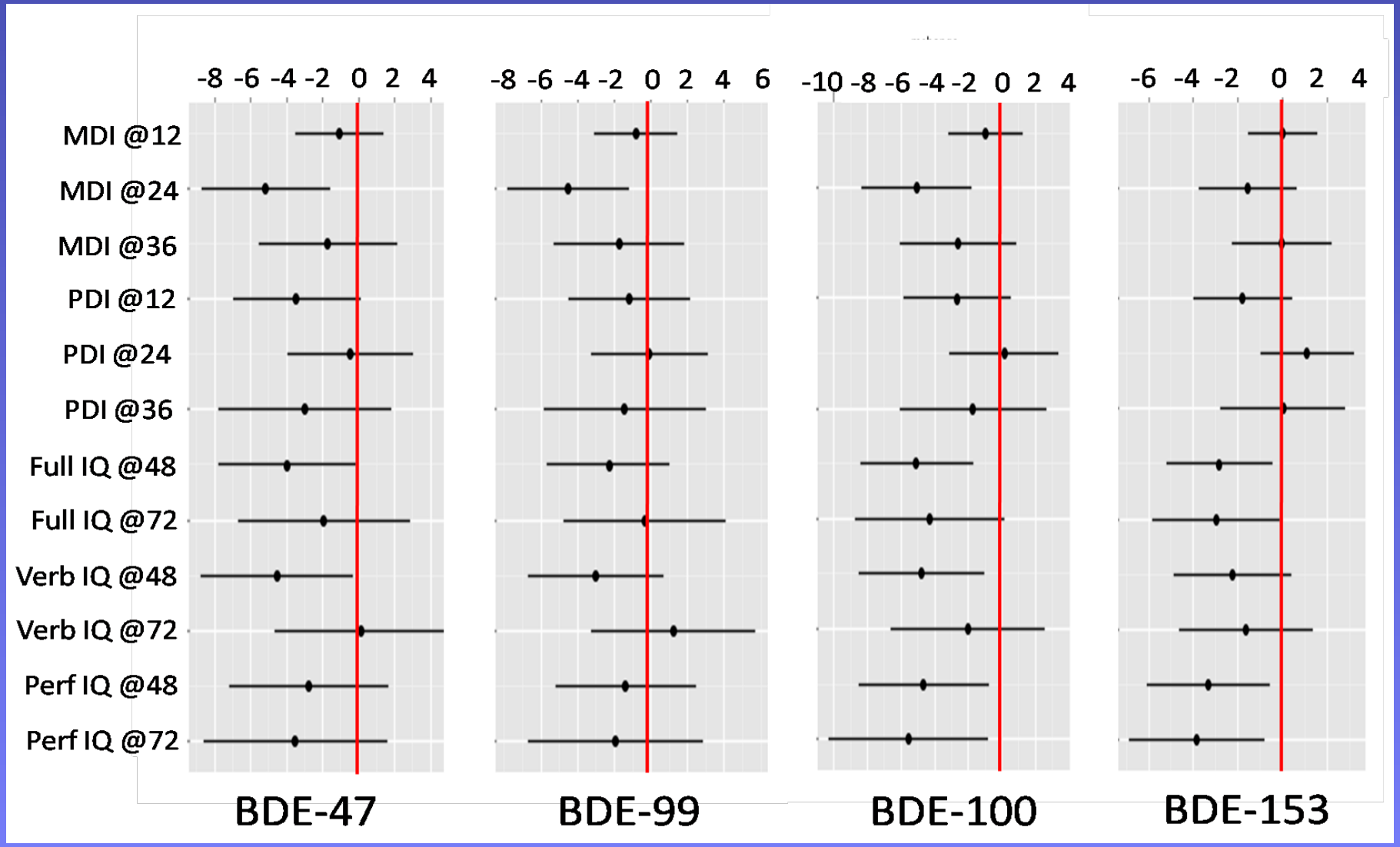
Table 2. Characteristics of all cohort members (n = 329), participants with cord blood measurement of PBDEs (n = 210), and those included in our study sample (n = 152).

	All participants (n = 329)	Cord PBDEs (n = 210)	Cord measurements > 1 neurodevelopmental test (n = 152)
Maternal characteristics			
Maternal age (years)	30.2 ± 5.2	30.4 ± 5.1	31.2 ± 4.9**
Maternal education			
< High school	61 (18.5)	45 (21.4)	21 (13.8)
High school	56 (17.0)	36 (17.1)	25 (16.4)
Some college	73 (22.2)	46 (21.9)	34 (22.4)
Four year college degree	72 (21.9)	41 (19.5)	34 (22.4)
Post college education	67 (20.4)	42 (20.0)	38 (25.0)
Race/ethnicity			
Chinese	92 (28.0)	72 (34.3)*	41 (27.0)
Asian (non-Chinese)	21 (6.4)	13 (6.2)	9 (5.9)
Black	50 (15.2)	27 (12.8)	23 (15.1)
White	133 (40.4)	77 (36.7)	62 (40.8)
Other	33 (10.0)	21 (10.0)	17 (11.2)
Married/ living with partner	265 (80.6)	172 (81.9)	126 (82.9)
TONI-2 score	95.8 ± 11.4	95.8 ± 11.3	95.8 ± 13.0
Missing TONI	118 (35.9)	82 (39.0)	26 (17.1)**
Maternal exposure to ETS, reported as smoker in the home (%)	59 (17.9)	36 (17.1)	26 (17.1)
Ate fish during the pregnancy	233 (70.8)	150 (71.4)	110 (72.4)
Material hardship	31 (9.4)	20 (9.5)	16 (10.5)
Infant characteristics			
Birth weight (g)	3419.5 ± 469.1	3399.2 ± 472.5	3412.0 ± 487.4
Birth length (cm)	50.8 ± 2.8	50.5 ± 2.7*	50.6 ± 2.7
Birth head circumference (cm)	34.2 ± 1.5	34.2 ± 1.4	34.3 ± 1.5
Gestational age (days)	276.8 ± 9.9	276.4 ± 10.4	276.6 ± 9.5
Male	161 (48.9)	105 (50.0)	77 (50.7)
Proportion of first year breast-fed (% of 1 year)	0.24 ± 0.28	0.22 ± 0.27	0.26 ± 0.28
Residential characteristics			
Worked and/or lived within 1 mile of the WTC during any of the 4 weeks after 9/11	62 (18.8)	43 (20.5)	32 (21.0)
Worked and/or lived within 2 mile of the WTC during any of the 4 weeks after 9/11	141 (42.8)	94 (44.8)	73 (48.0)

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

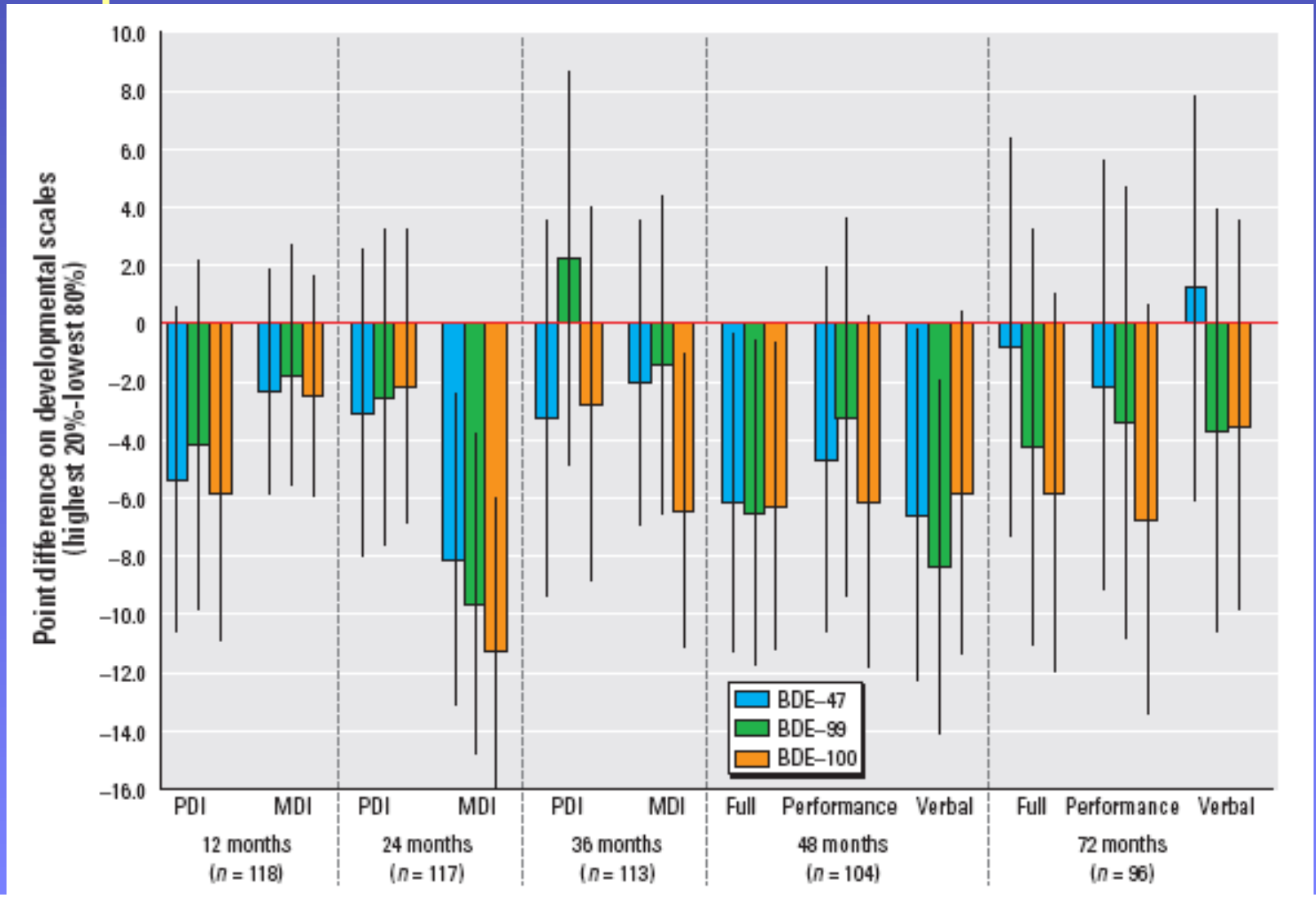
- slightly older
  - study: 31.2 yrs
  - cohort: 30.2 yrs)
- slightly more educated
  - study: 13.8% <HS
  - cohort: 18.5% < HS

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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