Prenatal exposure to chemical mixtures and working memory among adolescents

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**Supplemental Tables**

**Supplemental Table 1.** Sex-stratified results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)1 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the main analysis group2.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Verbal Working Memory | | | Symbolic Working Memory | | | Working Memory Index | | |
|  |  | |  |  | |  |  | |  |
|  | Males  Difference (95% CI) | Females  Difference (95% CI) | p3 | Males  Difference (95% CI) | Females  Difference (95% CI) | p3 | Males  Difference (95% CI) | Females  Difference (95% CI) | p3 |
| Log2 DDE | -0.30 (-0.73, 0.12) | -0.32 (-0.74, 0.10) | 1 | -0.11 (-0.55, 0.32) | -0.15 (-0.58, 0.27) | 0.8 | -1.15 (-3.25, 0.94) | -1.29 (-3.26, 0.68) | 0.9 |
| Log2 HCB | 0.06 (-0.41, 0.52) | 0.15 (-0.28, 0.58) | 0.6 | 0.09 (-0.38, 0.57) | 0.48 (0.04, 0.91)\* | 0.1 | 0.46 (-1.82, 2.75) | 1.72 (-0.29, 3.73) | 0.3 |
| Log2 ΣPCB4 | 0.40 (-0.07, 0.88) | 0.31 (-0.15, 0.76) | 0.9 | 0.17 (-0.31, 0.65) | 0.05 (-0.41, 0.51) | 0.9 | 1.56 (-0.76, 3.87) | 1.00 (-1.13, 3.14) | 1 |
| Log2 Pb | 0.14 (-0.40, 0.68) | -0.27 (-0.61, 0.08) | 0.2 | -0.06 (-0.61, 0.49) | -0.14 (-0.49, 0.21) | 0.9 | 0.24 (-2.41, 2.89) | -1.15 (-2.76, 0.46) | 0.5 |
| Log2 Mn | -0.88 (-1.70, -0.07)\* | -0.38 (-1.14, 0.39) | 0.6 | 0.03 (-0.80, 0.86) | -0.57 (-1.34, 0.19) | 0.3 | -2.45 (-6.44, 1.54) | -2.47 (-6.02, 1.09) | 0.9 |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Main analysis group: complete working memory outcome, covariate and exposure data for PCBs, DDE, HCB, Pb and Mn. Total n=373; Males n= 179; Females n=194. 3P-value for chemical-sex interaction term included in multivariable linear regression model.\*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese

**Supplemental Table 2.** Prenatal social disadvantage index (PNSDI)1-stratified results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)2 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the main analysis group3.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Verbal Working Memory | | | Symbolic Working Memory | | | Working Memory Index | |  |
|  | PNSDI < 3  Difference (95% CI) | PNSDI ≥ 3  Difference (95% CI) | p4 | PNSDI < 3  Difference (95% CI) | PNSDI ≥ 3  Difference (95% CI) | p4 | PNSDI < 3  Difference (95% CI) | PNSDI ≥ 3  Difference (95% CI) | p4 |
| Log2 DDE | -0.04 (-0.37, 0.30) | -0.60 (-1.16, -0.03)\* | 0.1 | 0.02 (-0.32, 0.37) | -0.21 (-0.78, 0.36) | 0.5 | -0.04 (-1.66, 1.57) | -2.22 (-4.88, 0.44) | 0.2 |
| Log2 HCB | 0.32 (-0.05, 0.70) | -0.30 (-0.85, 0.26) | 0.1 | 0.41 (0.02, 0.80)\* | -0.12 (-0.68, 0.44) | 0.2 | 2.03 (0.22, 3.84)\* | -1.13 (-3.74, 1.49) | 0.1 |
| Log2 ΣPCB4 | 0.10 (-0.27, 0.47) | 0.73 (0.11, 1.35)\* | 0.2 | -0.09 (-0.47, 0.30) | 0.40 (-0.24, 1.03) | 0.3 | 0.06 (-1.73, 1.85) | 3.10 (0.15, 6.05)\* | 0.2 |
| Log2 Pb | -0.31 (-0.67, 0.06) | 0.11 (-0.43, 0.64) | 0.3 | -0.06 (-0.44, 0.32) | -0.21 (-0.75, 0.33) | 0.6 | -1.01 (-2.78, 0.77) | -0.32 (-2.85, 2.20) | 0.8 |
| Log2 Mn | -1.00 (-1.66, -0.35)\* | -0.41 (-1.41, 0.58) | 0.3 | -0.80 (-1.48, -0.11)\* | 0.19 (-0.82, 1.19) | 0.1 | -4.91 (-8.11, -1.70)\* | -0.51 (-5.22, 4.19) | 0.1 |

1Prenatal social disadvantage index (PNSDI) was constructed as the sum of five adverse social or economic exposures at the time of the child’s birth where presence of each risk factor was assigned a value of 1, absence a value of 0: mother unmarried, mother’s education as high school graduate or less, father’s education as high school graduate or less, annual household income less than $20,000, and mother’s age at birth less than 20 years.2Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 3Main analysis group: complete working memory outcome, covariate and exposure data for PCBs, DDE, HCB, Pb and Mn. Total n=373; PNSDI < 3 n= 241; PNSDI ≥ 3 n=132.4P-value for chemical-PNSDI interaction term included in multivariable linear regression model.\*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese.

**Supplemental Table 3.** Inverse probability weighted results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)1 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the main analysis group2.

|  |  |  |  |
| --- | --- | --- | --- |
| Exposure | Verbal Working Memory  Difference (95% CI) | Symbolic Working Memory  Difference (95% CI) | Working Memory Index  Difference (95% CI) |
| Log2 DDE | -0.28 (-0.56, 0.00) | -0.10 (-0.39, 0.19) | -1.04 (-2.39, 0.32) |
| Log2 HCB | 0.09 (-0.22, 0.39) | 0.18 (-0.13, 0.50) | 0.77 (-0.70, 2.24) |
| Log2 ΣPCB4 | 0.37 (0.06, 0.68)\* | 0.14 (-0.18, 0.46) | 1.40 (-0.09, 2.88) |
| Log2 Pb | -0.08 (-0.37, 0.21) | -0.08 (-0.38, 0.22) | -0.44 (-1.85, 0.97) |
| Log2 Mn | -0.74 (-1.29, -0.20)\* | -0.40 (-0.96, 0.16) | -3.09 (-5.72, -0.46)\* |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Main analysis group: complete working memory outcome, covariate and exposure data for PCBs, DDE, HCB, Pb and Mn, n=373.\*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese.

**Supplemental Table 4.** Inverse probability weighted sex-stratified results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)1 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the main analysis group2.

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Verbal Working Memory | | | Symbolic Working Memory | | | Working Memory Index | | |
|  |  | |  |  | |  |  | |  |
|  | Males  Difference (95% CI) | Females  Difference (95% CI) | p3 | Males  Difference (95% CI) | Females  Difference (95% CI) | p3 | Males  Difference (95% CI) | Females  Difference (95% CI) | p3 |
| Log2 DDE | -0.34 (-0.77, 0.08) | -0.36 (-0.78, 0.06) | 1 | -0.13 (-0.55, 0.30) | -0.15 (-0.58, 0.27) | 0.7 | -1.31 (-3.36, 0.75) | -1.40 (-3.35, 0.55) | 0.8 |
| Log2 HCB | 0.00 (-0.46, 0.47) | 0.14 (-0.29, 0.57) | 0.5 | 0.04 (-0.43, 0.50) | 0.42 (-0.02, 0.86) | 0.1 | 0.17 (-2.08, 2.42) | 1.54 (-0.47, 3.54) | 0.2 |
| Log2 ΣPCB4 | 0.45 (-0.02, 0.92) | 0.33 (-0.12, 0.78) | 0.7 | 0.27 (-0.20, 0.74) | 0.03 (-0.42, 0.49) | 0.7 | 1.96 (-0.31, 4.24) | 1.03 (-1.06, 3.12) | 0.7 |
| Log2 Pb | 0.16 (-0.38, 0.71) | -0.24 (-0.59, 0.10) | 0.3 | -0.06 (-0.60, 0.48) | -0.14 (-0.49, 0.21) | 0.8 | 0.31 (-2.32, 2.93) | -1.08 (-2.68, 0.52) | 0.6 |
| Log2 Mn | -0.85 (-1.67, -0.03)\* | -0.38 (-1.14, 0.37) | 0.7 | 0.16 (-0.66, 0.98) | -0.62 (-1.39, 0.14) | 0.1 | -2.00 (-5.97, 1.97) | -2.60 (-6.12, 0.92) | 0.6 |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Main analysis group: complete working memory outcome, covariate and exposure data for PCBs, DDE, HCB, Pb and Mn. Total n=373; Males n=179; Females n=194.3P-value of chemical-sex interaction term included in multivariable linear regression model.\*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese.

**Supplemental Table 5.** Inverse probability weighted prenatal social disadvantage index (PNSDI)1-stratified results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)2 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the main analysis group3.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Verbal Working Memory | | | Symbolic Working Memory | | | Working Memory Index | | | |
|  |  | |  |  | |  |  | |  | |
|  | PNSDI < 3  Difference (95% CI) | PNSDI ≥ 3  Difference (95% CI) | p4 | PNSDI < 3  Difference (95% CI) | PNSDI ≥ 3  Difference (95% CI) | p4 | PNSDI < 3  Difference (95% CI) | PNSDI ≥ 3  Difference (95% CI) | | p4 |
| Log2 DDE | -0.06 (-0.38, 0.26) | -0.61 (-1.17, -0.04)\* | 0.1 | 0.01 (-0.32, 0.34) | -0.18 (-0.75, 0.40) | 0.6 | -0.14 (-1.69, 1.42) | -2.17 (-4.85, 0.51) | | 0.2 |
| Log2 HCB | 0.33 (-0.05, 0.70) | -0.26 (-0.80, 0.28) | 0.1 | 0.38 (-0.01, 0.77) | -0.13 (-0.68, 0.43) | 0.2 | 1.98 (0.16, 3.80)\* | -1.02 (-3.59, 1.55) | | 0.1 |
| Log2 ΣPCB4 | 0.13 (-0.22, 0.49) | 0.72 (0.11, 1.33)\* | 0.2 | -0.03 (-0.41, 0.34) | 0.33 (-0.30, 0.95) | 0.5 | 0.29 (-1.46, 2.03) | 2.89 (-0.01, 5.79) | | 0.3 |
| Log2 Pb | -0.30 (-0.67, 0.06) | 0.11 (-0.43, 0.66) | 0.3 | -0.05 (-0.43, 0.33) | -0.19 (-0.75, 0.36) | 0.6 | -0.97 (-2.75, 0.81) | -0.25 (-2.83, 2.32) | | 0.8 |
| Log2 Mn | -1.02 (-1.68, -0.36)\* | -0.43 (-1.41, 0.55) | 0.3 | -0.81 (-1.50, -0.12)\* | 0.18 (-0.82, 1.19) | 0.1 | -4.98 (-8.19, -1.77)\* | -0.56 (-5.23, 4.11) | | 0.1 |

1Prenatal social disadvantage index (PNSDI) was constructed as the sum of five adverse social or economic exposures at the time of the child’s birth where presence of each risk factor was assigned a value of 1, absence a value of 0: mother unmarried, mother’s education as high school graduate or less, father’s education as high school graduate or less, annual household income less than $20,000, and mother’s age at birth less than 20 years. 2Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 3Main analysis group: complete working memory outcome, covariate and exposure data for PCBs, DDE, HCB, Pb and Mn. Total n = 373; PNSDI < 3 n = 241; PNSDI ≥ 3 n = 132. 4P-value of chemical-sex interaction term included in multivariable linear regression model. \*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese.

**Supplemental Table 6.** Characteristics of all New Bedford Cohort participants who were included in the secondary analysis group1 and all of those who were excluded.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Descriptive Characteristic | Secondary analysis group, n=235 | | | Excluded group, n=553 | | |  |
| Working Memory Measures3 | n(%) | Mean (SD) | Range | n(%) | Mean ± SD | Range | p-value2 |
| Verbal Working Memory | 235 | 9.3 ± 2.5 | 1-16 | 293 | 8.5 ± 2.9 | 1-17 | < 0.01\* |
| Symbolic Working Memory | 235 | 10.1 ± 2.6 | 1-17 | 292 | 9.3 ± 2.8 | 1-19 | < 0.01\* |
| Working Memory Index | 235 | 97.9 ± 12.1 | 55-133 | 292 | 93.6 ± 13.8 | 57-142 | < 0.01\* |
|  |  |  |  |  |  |  |  |
| Exposure Measures4 |  |  |  |  |  |  |  |
| Cord serum DDE (ng/g) | 235 | 0.6 (1.4) | 0.02-14.9 | 516 | 0.4 (0.7) | 0-10.2 | 0.04\* |
| Cord serum HCB (ng/g) | 235 | 0.03 (0.02) | 0-0.1 | 516 | 0.03 (0.04) | 0-0.7 | 0.2 |
| Cord serum ΣPCB4 (ng/g) | 235 | 0.3 (0.3) | 0.01-2.3 | 516 | 0.2 (0.3) | 0.01-4.4 | 0.2 |
| Cord blood Pb (μg/dL) | 235 | 1.4 (0.9) | 0-9.4 | 513 | 1.6 (1.5) | 0-17.4 | 0.01\* |
| Cord blood Mn (µg/dL) | 235 | 4.3 (1.6) | 1.7-11.2 | 473 | 4.2 (1.9) | 0.2-22.1 | 0.8 |
| Maternal hair total Hg (μg/g) | 235 | 0.6 (0.6) | 0.03-3.1 | 276 | 0.6 (0.7) | 0.03-9.2 | 0.3 |
| Maternal toenail As (μg/g) | 235 | 0.1 (0.1) | 0.02-0.8 | 181 | 0.1 (0.1) | 0.02-1.0 | 0.5 |
|  |  |  |  |  |  |  |  |
| Covariate Measures5 |  |  |  |  |  |  |  |
| Child Characteristics |  |  |  |  |  |  |  |
| Race/Ethnicity |  |  |  |  |  |  | < 0.01\* |
| Non-Hispanic White | 186 (79.1) |  |  | 345 (62.4) |  |  |  |
| Hispanic | 16 (6.8) |  |  | 73 (13.2) |  |  |  |
| Other | 33 (14.0) |  |  | 133 (24.1) |  |  |  |
| Missing | 0 |  |  | 2 (0.4) |  |  |  |
| Sex |  |  |  |  |  |  | 0.3 |
| Male | 114 (48.5) |  |  | 294 (53.2) |  |  |  |
| Female | 121 (51.5) |  |  | 259 (46.8) |  |  |  |
| Age at Exam | 235 | 15.5 (0.6) | 14.4-17.7 | 293 | 15.6 (0.6) | 13.9-17.9 | 0.5 |
| Home Score | 235 | 44.4 (6.0) | 27-56 | 256 | 42.8 (6.5) | 21-56 | < 0.01\* |
| Year of Birth |  |  |  |  |  |  | 0.03\* |
| 1993-1994 | 76 (32.3) |  |  | 183 (33.1) |  |  |  |
| 1995-1996 | 104 (44.3) |  |  | 196 (35.4) |  |  |  |
| 1997-1998 | 55 (23.4) |  |  | 174 (31.5) |  |  |  |
| Maternal Characteristics |  |  |  |  |  |  |  |
| Marital status at birth |  |  |  |  |  |  | < 0.01\* |
| Not married | 74 (31.5) |  |  | 257 (46.5) |  |  |  |
| Married | 161 (68.5) |  |  | 241 (43.6) |  |  |  |
| Missing | 0 |  |  | 55 (9.9) |  |  |  |
| **Supplemental Table 6 (Continued)** | | | | | | | |
| Maternal IQ | 235 | 100.6 (9.7) | 67-124 | 400 | 96.3 (10.5) | 57-126 | < 0.01\* |
| Seafood during pregnancy (serv/day) | 235 | 0.5 (0.6) | 0-5.3 | 398 | 0.6 (0.7) | 0-6 | 0.5 |
| Smoking during pregnancy |  |  |  |  |  |  | 0.3 |
| No | 171 (72.8) |  |  | 311 (56.2) |  |  |  |
| Yes | 64 (27.2) |  |  | 140 (25.3) |  |  |  |
| Missing | 0 |  |  | 102 (18.4) |  |  |  |
| Maternal education |  |  |  |  |  |  | < 0.01\* |
| ≤ High School | 108 (46.0) |  |  | 313 (56.6) |  |  |  |
| > High School | 127 (54.0) |  |  | 183 (33.1) |  |  |  |
| Missing  Household Characteristics at Birth | 0 |  |  | 57 (10.3) |  |  |  |
| Paternal Education |  |  |  |  |  |  | 0.01\* |
| ≤ High School | 152 (64.7) |  |  | 360 (65.1) |  |  |  |
| > High School | 83 (35.3) |  |  | 125 (22.6) |  |  |  |
| Missing | 0 |  |  | 68 (12.3) |  |  |  |
| Annual Household Income |  |  |  |  |  |  | < 0.01\* |
| < $20,000 | 62 (26.4) |  |  | 203 (36.7) |  |  |  |
| ≥ $20,000 | 173 (73.6) |  |  | 286 (51.7) |  |  |  |
| Missing | 0 |  |  | 64 (11.6) |  |  |  |
| Examination Characteristics |  |  |  |  |  |  |  |
| Examiner |  |  |  |  |  |  | 0.3 |
| 1 | 171 (72.8) |  |  | 227 (41.0) |  |  |  |
| 2 | 64 (27.2) |  |  | 66 (11.9) |  |  |  |
| Missing | 0 |  |  | 260 (47.0) |  |  |  |

1Secondary analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, PCBs, Pb Mn, MeHg, and As, n=235. 2P-values represent results comparing characteristics between participants included in the secondary analysis group and those excluded from the secondary analysis group using t-tests and chi-square tests. Categorical covariate comparisons based on the distribution of non-missing values. 3NBC participants with missing working memory measures: Verbal Working Memory n=260; Symbolic Working Memory n=261; Working Memory Index n=261. 4NBC participants with missing exposure measures: DDE n=37; HCB n=37; ΣPCB4 n=37; Pb n= 40; Mn n=80; Hg n=277; As n=372. 5NBC participants with missing covariate measures: age at exam n=260; HOME score n= 297; maternal IQ n=153; seafood during pregnancy n= 155. \*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese; Hg: mercury; As: arsenic.

**Supplemental Table 7.** Complete-case results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)1 assessing the relation of prenatal exposure to a seven-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the secondary analysis group2.

|  |  |  |  |
| --- | --- | --- | --- |
| Exposure | Verbal Working Memory  Difference (95% CI) | Symbolic Working Memory  Difference (95% CI) | Working Memory Index  Difference (95% CI) |
| Log2 DDE | -0.08 (-0.46, 0.30) | -0.02 (-0.42, 0.37) | -0.33 (-2.17, 1.52) |
| Log2 HCB | 0.11 (-0.25, 0.48) | 0.17 (-0.21, 0.55) | 0.83 (-0.94, 2.60) |
| Log2 ΣPCB4 | 0.11 (-0.33, 0.54) | 0.00 (-0.44, 0.45) | 0.31 (-1.77, 2.39) |
| Log2 Pb | -0.21 (-0.57, 0.15) | -0.03 (-0.41, 0.34) | -0.66 (-2.41, 1.09) |
| Log2 Mn | -0.49 (-1.16, 0.18) | 0.01 (-0.68, 0.70) | -1.40 (-4.62, 1.83) |
| Log2 MeHg | 0.07 (-0.27, 0.40) | 0.02 (-0.33, 0.37) | 0.29 (-1.33, 1.91) |
| Log2 As | 0.10 (-0.22, 0.43) | -0.02 (-0.36, 0.32) | 0.28 (-1.29, 1.85) |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Secondary analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, PCBs, Pb, Mn, MeHg, and As, n=235. \*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese; MeHg: methylmercury; As: arsenic.

**Supplemental Table 8.** Inverse probability weighted results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)1 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition working memory scaled scores among adolescents in the secondary analysis group2.

|  |  |  |  |
| --- | --- | --- | --- |
| Exposure | Verbal Working Memory  Difference (95% CI) | Symbolic Working Memory  Difference (95% CI) | Working Memory Index  Difference (95% CI) |
| Log2 DDE | -0.12 (-0.50, 0.26) | -0.05 (-0.43, 0.33) | -0.50 (-2.31, 1.31) |
| Log2 HCB | 0.04 (-0.32, 0.41) | 0.12 (-0.25, 0.48) | 0.47 (-1.26, 2.20) |
| Log2 ΣPCB4 | 0.19 (-0.25, 0.63) | 0.09 (-0.35, 0.53) | 0.77 (-1.32, 2.86) |
| Log2 Pb | -0.22 (-0.59, 0.15) | -0.04 (-0.42, 0.33) | -0.70 (-2.48, 1.08) |
| Log2 Mn | -0.30 (-0.99, 0.39) | 0.30 (-0.39, 0.99) | -0.09 (-3.36, 3.17) |
| Log2 MeHg | 0.16 (-0.20, 0.51) | 0.06 (-0.29, 0.41) | 0.63 (-1.04, 2.31) |
| Log2 As | 0.09 (-0.26, 0.44) | -0.05 (-0.40, 0.29) | 0.15 (-1.49, 1.79) |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Secondary analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, PCBs, Pb, Mn, MeHg, and As, n=235. \*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese; MeHg: methylmercury; As: arsenic.

**Supplemental Table 9.** Results of multivariable linear regression analyses (difference in scaled scores associated with a twofold increase in exposure and 95% CI)1 assessing the relation of prenatal exposure to a five-chemical mixture with Wide Range Assessment of Memory and Learning, 2nd Edition Verbal Working Memory scaled scores among adolescents in the main analysis group2 stratified by maternal seafood consumption during pregnancy.

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| --- | --- | --- | --- |
| Exposure | Verbal Working Memory  Maternal seafood consumption during pregnancy  ≤ 2 servings/week  Difference (95% CI) | Verbal Working Memory  Maternal seafood consumption during pregnancy  > 2 servings/week  Difference (95% CI) | P-value for log2 ΣPCB4 \* Maternal seafood consumption during pregnancy interaction term in overall model |
| Log2 ΣPCB4 | -0.36 (-0.89, 0.17) | 0.50 (0.07, 0.92)\* | 0.31 |

1ΣPCB4 has been log2-transformed and models have been adjusted for all DDE, HCB, Pb, Mn, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Main analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, ΣPCB4, Pb and Mn, n=373.\*p < 0.05.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese.

**Supplemental Figures**

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| **Supplemental Figure 1.** Estimated exposure-response functions and 95% credible intervals1 associating DDE, HCB, PCBs, Pb, Mn, MeHg, and As with the Wide Range Assessment of Memory and Learning 2nd Edition working memory scaled scores, where all of the remaining exposures are assigned to their median value, among adolescents in the secondary analysis group2. | |
| Verbal Working Memory | Symbolic Working Memory |
| A close up of a map  Description automatically generated | Chart  Description automatically generated |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Secondary analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, PCBs, Pb, Mn, MeHg, and As, n=235.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; PCBs: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese; MeHg: methylmercury; As: arsenic.

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| **Supplemental Figure 2.** Bivariate exposure-response functions1 associating each of 7 exposures (DDE, HCB, PCBs, Pb, Mn, MeHg, As) and a second exposure fixed at various quantiles with the Wide Range Assessment of Memory and Learning 2nd Edition working memory scaled scores, while the remaining exposures are assigned to their median value, among adolescents in the secondary analysis group2. | |
| Verbal Working Memory | Symbolic Working Memory |
| A close up of text on a white background  Description automatically generated | Diagram  Description automatically generated |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Secondary analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, PCBs, Pb, Mn, MeHg, and As, n=235.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese; MeHg: methylmercury; As: arsenic.

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| **Supplemental Figure 3.** Joint association of the chemical mixture composed of DDE, HCB, PCBs, Pb, Mn, MeHg, and As (estimates and 95% credible intervals1) with the Wide Range Assessment of Memory and Learning 2nd Edition working memory scaled scores, comparing chemical mixture levels at various percentiles compared to their median levels, among adolescents in the secondary analysis group2. | |
| Verbal Working Memory | Symbolic Working Memory |
| A close up of a logo  Description automatically generated | A picture containing water, group  Description automatically generated |

1Exposures have been log2-transformed and models have been adjusted for all listed exposures, child race, sex, age at exam, year of birth, and HOME score; maternal marital status at child’s birth, IQ, seafood consumption during pregnancy, and smoking during pregnancy; maternal and paternal education and annual household income at child’s birth; study examiner. 2Secondary analysis group: complete working memory outcome, covariate and exposure data for DDE, HCB, PCBs, Pb, Mn, MeHg, and As, n=235.

Abbreviations: DDE: dichlorodiphenyldichloroethylene; HCB: hexachlorobenzene; ΣPCB4: Sum of 4 PCB congeners (118, 138, 153, 180); Pb: lead; Mn: manganese; MeHg: methylmercury; As: arsenic.