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Kristen Allen Date

The effects of intrauterine exposure to pesticides on cognition in early childhood in a cohort of mothers and daughters in Bristol, UK

By

Kristen Allen

MPH

Epidemiology

Terryl J. Hartman, PhD MPH RD

Committee Chair

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By

Kristen Allen

Bachelor of Arts

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Thesis Committee Chair: Terryl J. Hartman, PhD MPH RD

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Abstract

The effects of intrauterine exposure to pesticides on cognition in early childhood in a cohort of mothers and daughters in Bristol, UK

By Kristen Allen

Background: Prenatal exposure to pesticides may be associated with a negligible increase in development and communicative assessment scores in early childhood.

Objective: We explored associations of prenatal serum concentrations of hexachlorobenzene (HCH), beta-Hexachlorocyclohexane (HCCH), 2,2-Bis(4-chlorophenyl)-1,1-dichloroethene (DDE) and 2,2-Bis(4-chlorophenyl-1,1,1-trichloroethan (DDT) with maternal-reported measures of cognition and communication in 15 month-old girls, using the MacArthur Bates Communicative Inventory (MCDI).

Methods: We studied a sample of 309 singleton girls and their mothers participating in the Avon Longitudinal Study of Parents and Children (ALSPAC). Maternal serum samples were obtained at 15 weeks gestation and assessed for pesticide levels. Maternal demographic and health-related characteristics were recorded through questionnaires. Child characteristics and MCDI scores at 15 months were obtained through questionnaires mailed to the mothers at various time points after the child's birth. We explored associations between prenatal pesticide exposures and MCDI scores as well as total pesticide exposure and MCDI scores at 15 months of age in multivariate linear regression models after adjusting for maternal education, HOME score at 6 months of age, alcohol and tobacco use during the first trimester of pregnancy, maternal age at delivery and duration of breastfeeding (weeks).

Results: The geometric mean values of HCH and HCCH were similar, at 11.61 pg/g (95% CI 7.98, 16.89) and 11.27 pg/g (95% CI 6.94, 18.29), respectively. The geometric mean value of DDE, 25.77 pg/g (95 % CI 14.12, 46.99), was nearly four times that of DDT, 6.25 ph/g (95% CI 3.89, 10.06). Generally, crude associations between prenatal pesticides and MCDI components were null. In contrast, the adjusted multivariate linear regression models revealed several significant associations. For each twenty percent increase in HCB there was a 3.82 point (11.94%) increase in the social development score. A twenty percent increase in DDT was associated with a 24 point (8.96%) increase and a 29 point (8.79%) increase in the vocabulary and total communication components, respectively.

Conclusions: There is a slight positive association between serum pesticide levels and MCDI scores. These results, although unexpected, account for only small changes in MCDI scores.

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INTRODUCTION

Endocrine disrupting chemicals (EDC) are substances that may change the functioning of the body's endocrine system by binding to and activating various hormone receptors (2-5). Numerous substances identified as EDCS are also pesticides (1, 6-10). In addition, many pesticides are classified as persistent organic pollutants (POP). These substances persist long-term, accumulate in the fatty tissues of living organisms, and are widely diffused in the environment (11-14). Humans can be exposed to EDCs through inhalation of gases and particles in the air, ingestion of water, food and dust, and through the skin. A pregnant woman who is exposed to EDCs may also risk exposing the fetus or child via the placenta or breast milk (15). Because the endocrine system, which includes adrenal, gonadal, and thyroid hormones, is critical in the neurodevelopment of a fetus (16-19), exposure to EDCs in utero can be particularly harmful to a fetus (1, 20-22). Clinical and laboratory studies have documented that a developing brain is especially susceptible to exposures of neurodevelopmental toxicants such as EDCs, even at low levels that may not have a significant effect on a developed, adult brain (11, 23).

Abnormal communication and interpersonal behaviors before the age of 3 may be a characteristic of cognitive disorders, such as Autism Spectrum Disorders (ASDs) (17, 24, 25) . There is some debate as to whether cognitive function early in life will significantly affect the development of disorders like a learning disabilities (LDs), attention deficit disorder (ADD) and ASDs. More information is needed to determine how exposures to persistent organic pollutants can affect communication and cognition in infants, which could lead to a greater understanding of the relevancy of early cognitive screening and the development of issues later in life. Multiple prospective cohort studies have documented that environmental neurotoxicants in the blood or cord blood of mothers is negatively associated with cognition in early infancy of their children (11, 26). Moreover, a cross-sectional study by Lee, et al. (11) demonstrated positive relationships between certain POPs and LDs and ADD in older children. The population consisted of 278 children aged 12-15 identified from the 1999-2000 National Health and Nutrition Examination Survey (NHANES). Seven POPs, measured in blood serum samples of the children, were each analyzed separately for possible associations with LDs and ADD. Children were asked if they had ever had a history of diagnosis of an LD of ADD (11, 27).

In population-based studies, infant communication and development is often measured in the field through parent-reported assessments. The MacArthur Bates Communicative Inventory (28-30) has been widely used to measure communication and gestures in children with ASDs (31). Items that may be associated with abnormal communication and interpersonal behaviors include delayed onset of talking, late understanding of spoken language and intent to communicate or show gestures, relative to expectations for age (32).

Our overall objective was to evaluate the association between intrauterine exposure to selected pesticides and cognitive outcomes in infants. The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prenatal cohort of and mother-child pairs. The study contains information relating to pregnancy and birth characteristics, demographic factors, and childhood behavioral outcomes. Access is also available to previously analyzed prenatal blood samples to offer an ideal opportunity to explore this relationship.

METHODS

Population

The aim of this study is to investigate intrauterine exposure to EDCs, specifically persistent organic pollutants, and cognitive outcomes in offspring of women in a pregnancy cohort in Britain. The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective cohort study to investigate the development and health of children in the South West of England (33, 34). Pregnant women expected to deliver between April 1991 and December 1992 in three health districts in the county of Avon, Great Britain were enrolled in the ALSPAC. The cohort included 14,610 children who joined at birth. Methods of recruitment have been described elsewhere (34, 35). Questionnaires were mailed to mothers of children in the cohort four times during pregnancy, as well as at set time points postnatally to collect information on education, social circumstance, diet, and behavioral and cognitive outcomes of the child (36).

The participants in the current study were drawn from an ancillary study of puberty and development including 5,756 singleton, active, female participants at the age of 13 years in 2004-2005. Two valid assessments of pubertal status between the ages of 8 and 13 were returned from 3,682 of the girls. From this subset, a nested case-control study was designed to explore the effects of environmental exposures on selected health outcomes. The present study includes 309 girls selected from those who returned two valid assessments and had values for childhood cognitive assessments and maternal serum concentrations of POPs.

Cognitive Measures

At 15 months of age, mothers were mailed a form of the MacArthur Communicative Development Inventory (MCDI), which evaluates vocabulary comprehension and social activity in children (28-30). Parents complete the form based on current behaviors, therefore, the MCDI does not rely on the parent's memory. Shorter, adapted versions of the MCDI usually contain 100 words derived from the main form and are given at the same ages as the full MCDI (37). The ALSPAC adaptation of the MCDI includes an understanding score, vocabulary score, nonverbal communication score and social development score, as well as a total communication score. The understanding score was compiled from 12 questions (score ranges from 0 to 12), which ask if the child understands phrases such as "time for bed" and "come here." The vocabulary score was compiled from 133 questions (score ranges from 0 to 268) in which parents indicated whether the child understands but doesn't say or understands and says words such as "dog" and "milk." Nine questions asking if the child completes actions such as "blows kisses from a distance" or "shakes head 'no'" were compiled to derive the nonverbal communication score (score ranges from 0 to 20). To derive the social development score, 15 questions asking if the child completes actions such as "puts on a shoe or sock" or "brush teeth" were compiled (score ranges from 0 to 32). The total communication score (score ranges from 0 to 330) was compiled by combining the scores from each previous component (understanding, vocabulary, nonverbal communication, social development). We used the raw scores for the total and each MDCI component for our analysis.

Exposure Measures

Laboratory analysis was done at the National Center for Environmental Health of the Centers for Disease Control and Prevention (CDC) (Atlanta, GA) to measure serum concentrations of hexachlorobenzene (HCH), beta-Hexachlorocyclohexane (HCCH), 2,2-Bis(4-chlorophenyl)-1,1-dichloroethene (DDE) and 2,2-Bis(4-chlorophenyl-1,1,1-trichloroethan (DDT). HCH is created as a by-product from the manufacturing of other chemicals (38). The production of lindane, an insecticide, creates HCH as a byproduct (39). DDE is a result of the breakdown of DDT in the environment (40). Serum samples were taken at different times throughout the women's pregnancy, however, the average gestational age in weeks when samples were taken was 17.73 (Table 1). Analytical methods used have been described elsewhere [30, 33]. Limits of detection (LOD) were specific to each sample and each pesticide, and ranged from 20.21 pg/g serum to 231.48 pg/g serum for all 4 pesticides. Values for pesticide measurements below the limit of detection (1.52% of samples for HCCH and 11.25% of samples for DDT) were calculated by dividing the LOD by the square root of 2 [34-35].

Covariates

Potential confounders considered include, maternal age at delivery (<25 years, 25-29 years, >=30 years); parity (nulliparous, 1 to 2, >=3); maternal education (<O level,

O level, >O level), where O-level is the qualification obtained at age 16 when required schooling ends; maternal smoking during the first trimester of pregnancy (yes, no); alcohol use during the first trimester of pregnancy (yes, no); low birthweight as defined as less than 2500 grams (yes, no), according to the CDC criteria.; maternal depressive symptoms measured using the Crown-Crisp Experiential Index (CCEI; yes, no), which includes questions relating to depression, somaticism and free-floating anxiety; and an adapted version of the Home Observation for Measures of the Environment (HOME) score at both 6 months (0 to 12 points) and 18 months (1 to 12 points), which measures the quality of the parent and home environment.

Statistical Analysis

The sample of girls obtained for analysis was previously chosen to use in a nested case-control study examining associations of Polyfluoralkyl Compounds and age at menarche. The POPs and MCDI subset scores were examined for potential outliers. Due to a skewed distribution of the four POP variables, the values were log base 10-transformed in order to reduce the influence of extreme outliers. The relationships between potential covariates and the POPs were then explored. The MacArthur Bates Communicative Inventory obtained at 15 months was first analyzed continuously. The serum concentrations of four POPs that had less than 50% of values missing were analyzed continuously. Linear regression models were constructed to model the effect of intrauterine exposure to endocrine disrupting chemicals on cognitive and behavioral outcomes in 15-month old girls. A p-value of <0.05 was used to determine significance.

Multiple linear regression models were constructed separately for the five subsets of scores (total communication score, understanding score, vocabulary score, nonverbal communication score and social development score) for each pesticide exposure (HCB, HCCH, DDE, and DDT). A mixture analysis was also carried out to model the effect of the overall exposure of the four pesticides for each subject. The mean pesticide concentration was subtracted from each subjects' pesticide value, and then divided by the standard error to give a z-score. The z-scores from each of the 4 pesticides were combined to create a continuous variable to represent overall combined pesticide exposure. Using the all-possible subsets method, models were selected based on AIC and adjusted r-squared. Variables chosen a prior and deemed biologically plausible and relevant based on current literature were included in the model regardless of significance. After the initial model was selected, all exposure and covariate interaction terms were explored for statistical significance as well as biological plausibility. One overall set of variables was chosen as the final adjusted model for all exposures and outcomes.

RESULTS

Over half of the women included in the study were 25 to 24 years of age and had breastfed the child in the study for a duration of longer than 3 months, while nearly half had obtained an education level of O or greater and. Only about 3 percent of the children in the study were of low birth weight, defined as less than 2500 grams. Approximately 23% of mothers reported tobacco use during the first trimester of pregnancy and 16% reported consuming one or more servings of alcohol per week during this time (Table 2). The geometric mean values of HCH and HCCH were similar, at 11.61 pg/g (95% CI 7.98, 16.89) and 11.27 pg/g (95% CI 6.94, 18.29), respectively. The geometric mean value of DDE, 25.77 pg/g (95% CI 14.12, 46.99), was nearly four times that of DDT, 6.25 ph/g (95% CI 3.89, 10.06) (Table 1). With increasing maternal age, the geometric mean value of each pesticide subtly increased. Geometric mean values of HCB and HCCH for each covariate were similar. Geometric mean values of DDE were approximately two to four times greater than that of DDT for all of our assessed population characteristics (Table 2).

Table 3 includes results for both crude and multivariate adjusted linear regression models. For the most part, the crude associations between prenatal pesticides and MCDI components were null. In the adjusted models, we did not find any meaningful statistically significant interactions terms. The adjusted models revealed several significant associations. In the fully adjusted model, a twenty percent increase in HCB was associated with a 3.82 point (11.94%) increase in the social development score. For each twenty percent increase in DDT, there was a 24 point (8.96%) increase and a 29 point (8.79%) increase in the vocabulary and total communication components, respectively. In the overall measure of pesticide exposure regression analysis (Table 4), no significant associations were found.

DISCUSSION

Although many pesticides which were once widely used, including HCB, HCCH, DDE, and DDT are now prohibited to be used in most parts of the world (38, 40-

42), they still may persist in soils, sediments, and bioaccumulate in invertebrate and vertebrate tissues (1). In this population, the pesticide with the highest geometric mean concentration was DDE (25.52 pg/g). This pesticide is more persistent than DDT, and is formed as DDT breaks down in the environment. In addition, it may remain in human and animal tissues for a longer period of time than DDT. Humans are most commonly exposed to DDE through food (38).

Multiple studies have explored the effects of pesticide exposure on developmental scores of children using tools such as the Bayley Scales of Infant Development (BSID) (43), however, we are not aware of any studies evaluating the effects of pesticide exposure in utero on neurodevelopment and communication in children at 15 months using the MCDI. Current literature suggests that intrauterine exposure to DDT and DDE may impair psychomotor development in the first year of life (44-46). For example, a study in Mexico using the BSID found that DDE serum levels during the first trimester of pregnancy were associated with a decrease in the psychomotor development index (PDI) in the first year of a child's life. There was no association between prenatal DDE serum levels and the mental development index (MDI) (43, 46). Similarly, a study of 360 children tested at ages 6, 12 and 24 months in California showed that for each 10-fold increase in DDT levels at 6 and 12 months and DDE levels at 6 months, there was a 2-point decrease in PDI scores in infants (43, 44). In Spain, DDE cord serum levels were negatively associated with both MDI and PDI, while HCB had no effect of neurodevelopment in one year old infants (47, 50). On the other hand, a New York study of 263 women and their infants assessed cognition using the

Fagan test for Infant Intelligence (FTII) and found no significant associations between FTII scores and DDE cord blood levels (43, 47).

The National Health and Nutrition Examination Survey (NHANES) is a yearly cross-sectional survey of 5,000 United States citizens, designed to be a nationally representative sample. NHANES collects data on demographic characteristics, health behaviors, and laboratory data such as serum levels of various chemicals. During the 2003-2004 survey year, the geometric mean HCH serum level (whole weight) for women was 95 pg/g (95% CI 89, 100) and 97 pg/g (95% CI 92, 102) for those over 20 years of age (including men). Geometric mean HCCH serum levels for women were 51 pg/g (95% CI <limit of detection (LOD), 57) and for those over 20 (including men) geometric mean serum levels were 50 pg/g (95% CI <LOD, 58). For the same year, the geometric mean of DDE in women was 1,450 pg/g (95% CI 1,160, 1,820) and for those 20 years and older (including men) the geometric mean was 1,690 pg/g (95% CI 1,360, 2,100). For women and those over 20 years of age during the 2003-2004 survey year, geometric mean DDT serum levels were reported as below the limit of detection (LOD) (48). These levels are much higher than the geometric mean concentrations of HCH, HCCH, DDE, and DDT (11.70, 11.25, 25.53, 6.23 pg/g, respectively) in our population. This may be due to the fact that HCCH values for 1.52% of samples DDT values for 11.25% of samples had pesticide values below the limit of detection. To correct this, the LOD was divided by the square root of two to give a value to those below the LOD.

Our study found unexpected results, as the scores for several of the MCDI components in the adjusted model slightly increased with each one percent increase in pesticide exposure. Although these findings were significant, they presented only a small change change (<12%) in the scores. The significant findings were within the vocabulary, social development, and total communication components. It is possible that the MCDI components alone are not sensitive enough to detect a difference in communication and behavior between different levels of pesticide exposure. In addition, almost half (46.55%) of mothers in our student had achieved greater than an O level of education. This could possibly affect the way that mothers interact with their children, which in turn affects their development and communication. Controlling for the HOME score, which measures the child's environment, and the mother's education level, may not have been sufficient to account for confounding that could occur.

Possible mechanisms of exposure to these pesticides could have been through the consumption of animal products, particularly meats and dairy products that contain animal fat in which the pesticides may have bioaccumulated. Exposure from contaminated water or soil in which the pesticides have bioaccumulated is also possible, however, less likely (36). When pesticides are present in the body, they may act as endocrine disruptors. This is especially harmful to a developing fetus, and could be the mechanism by which pesticide exposure in utero affects the communication and development of a child (11).

There are several limitations to this study. Blood samples obtained at multiple time points during pregnancy may provide a more accurate estimate of intrauterine exposure, as opposed to our study which only measured serum levels in blood at one time point. Several of our covariates, as well as our outcomes measures, were self-report (tobacco and alcohol use) which could affect credibility. In addition, our models did not include maternal lead and mercury levels, which may also affect cognition. These covariates were not included as lead blood samples were missing for 207 mothers and mercury blood samples were missing for 211 mothers in the population. It is also possible that the MCDI scale we used may not be specific enough to explain the true effect of in utero pesticide exposure and communicative development. It is suggested that the MDCI be used in conjunction with other cognitive assessments (37), which our study did not include.

CONCLUSION

The literature presents differing evidence regarding the effects of pesticide exposure in utero on cognition and communication in early childhood. While our study revealed unexpected protective associations between pesticide exposure and these measures, the associations were for the most part negligible. More research is needed to determine more specifically how pesticides affect neurodevelopment in early life and which pesticides may have the most negative effects at certain time points during development. In addition, more information if needed to assess the accuracy of different infant development scales and the relevancy of infant development scales for predicting learning disabilities later in life.

TABLES

Table 1. Characteristics of Study Infants (girls) and Mothers.

Infant Characteristics (n=309)	Mean (SD)
HOME Score, 6 months[a]	8.07 (2.18)
HOME score, 18 months[a]	10.45 (1.51)
CCEI, 8 months[b]	10.19 (7.47)
Understanding Score	9.51 (2.33)
Vocabulary Score	95.24 (46.36)
Nonverbal Communication Score	14.87 (3.23)
Social Development Score	18.62 (5.31)
Total Communication Score (n=309)	138.39 (52.47)
Maternal Characteristics(n=309)	Mean (SD)
Gestational Age (weeks) when Sample was Taken	17.73 (9.94)
	Geometric Mean (95% CI)
HCH, pg/g	11.61 (7.98, 16.89)
HCCH, pg/g	11.27 (6.94, 18.29)
DDE, pg/g	25.77 (14.12, 46.99)
DDT, pg/g	6.25 (3.89, 10.06)

[a] n=298
[b] n=291

Table 2. Serum concentrations of pesticides (pg/g) within categories of maternal characteristics.

		HCB	HCCH	DDE	DDT
Maternal Characteristics	Frequency N (%)	Geometric Mean (95% CI)	Geometric Mean (95% CI)	Geometric Mean (95% CI)	Geometric Mean (95% CI)
Maternal age at delivery (years)					
<25	76 (24.44)	10.46 (10.15, 10.77)	9.65 (9.19, 10.13)	20.83 (19.80, 21.92)	5.72 (5.51, 5.93)
25-34	197 (63.34)	11.78 (11.50, 12.06)	11.59 (11.26, 11.92)	26.88 (25.89, 27.90)	6.31 (6.09, 6.53)
>= 35	38 (12.22)	12.94 (11.83, 14.16)	12.61 (11.18, 14.22)	31.62 (28.43, 35.17)	6.92 (6.30, 7.61)
Low birth weight (<2500 grams)					
No	311 (96.28)	11.60 (11.36, 11.85)	11.16 (10.86, 11.47)	25.34 (24.53, 26.18)	6.19 (6.04, 6.34)
Yes	12 (3.72)	11.50 (9.62, 13.76)	13.26 (11.29, 15.57)	34.48 (34.48, 45.27)	7.96 (5.65, 11.22)
Duration of breastfeeding					
Never	61 (19.87)	11.53 (10.97, 12.11)	11.08 (10.36, 11.85)	25.22 (23.35, 27.25)	6.20 (5.85, 6.57)
<3 months	79 (25.73)	11.69 (11.26, 12.15)	11.32 (10.76, 11.90)	26,32 (24.65, 28.10)	6.38 (5.98, 6.81)
3+ months	167 (54.40)	11.63 (11.27, 12.00)	11.33 (10.89, 11.79)	25.71 (24.51, 26.97)	6.20 (5.98, 6.41)
Tobacco use during the first trimester of pregnancy					
No	241 (76.27)	11.67 (11.38, 11.97)	11.20 (10.83, 11.57)	26.13 (25.14, 27.17)	6.28 (6.09, 6.48)
Yes	75 (23.73)	11.48 (11.04, 11.93)	11.53 (11.01, 12.09)	24.87 (23.19, 26.66)	6.19 (5.86, 6.53)
Maternal education					
<O level	53 (17.38)	11.93 (11.20, 12.72)	11.36 (10.53, 12.25)	25.71 (23.66, 27.95)	6.31 (5.89, 6.76)
O level	111 (36.39)	11.46 (11.10, 11.83)	11.05 (10.61, 11.50)	25.37 (23.97, 26.85)	6.14 (5.89, 6.40)
> O level	141 (46.23)	11.70 (11.34, 12.07)	11.49 (11.03, 11.97)	26.14 (24.82, 27.52)	6.30 (6.03, 6.59)
Parity					
Nulliparous	156 (49.84)	11.61 (11.31, 11.92)	11.25 (10.85, 11.67)	25.91 (24.69, 27.18)	6.29 (6.08, 6.53)
>1	157 (50.16)	11.65 (11.27, 12.05)	11.31 (10.84, 11.79)	25.79 (24.56, 27.08)	6.22 (5.97, 6.48)
Alcohol use during the first trimester of pregnancy					
<1 glass per week	262 (83.44)	11.60 (11.32, 11.87)	11.17 (10.84, 11.51)	25.40 (24.47, 26.37)	6.14 (5.97, 6.32)
1+ glasses per week	52 (16.56)	11.94 (11.44, 12.46)	11.79 (11.01, 12.63)	27.70 (25.64, 29.93)	6.65 (6.28, 7.05)

Table 3. Unadjusted and adjusted[1] associations between prenatal serum pesticide levels and MCDI components among 15-month old girls [β (95% CI)].

	MCDI Component				
Pesticide (pg/g)	Understanding	Vocabulary	Nonverbal Communication	Social Development	Total Communication
HCB					
Unadjusted	-0.2 (-1.54, 1.13)	-6.42 (-33.53, 20.69)	0.83 (-1.04, 2.71)	2.29 (-0.77, 5.35)	-0.42 (-31.48, 30.65)
Adjusted	0.08 (-1.52, 1.68)	6.85 (-23.08, 38.78)	0.97 (-1.16, 3.11)	3.82 (0.23, 7.41)*	11.72 (-22.15, 45.59)
HCCH					
Unadjusted	0.56 (-0.47, 1.59)	6.13 (-14.43, 26.70)	0.73 (-0.71, 2.17)	1.22 (-1.14, 3.57)	10.06 (-13.35, 33.46)
Adjusted	0.76 (-0.49, 2.01)	14.76 (-8.62, 38.15)	0.67 (-1.00, 2.34)	1.05 (-1.79, 3.88)	17.24 (-9.24, 43.71)
DDE					
Unadjusted	-0.14 (-0.99, 0.70)	-1.53 (-18.64, 15.57)	0.18 (-1.00, 1.35)	1.11 (-0.83, 3.05)	-0.08 (-19.47, 19.30)
Adjusted	0.17 (-0.87, 1.21)	12.81 (-6.53, 32.16)	0.44 (-0.94, 1.83)	1.1 (-1.24, 3.45)	14.53 (-7.38, 36.43)
DDT					
Unadjusted	0.24 (-0.18, 1.31)	4.14 (-18.38, 26.65)	1.1 (-0.36, 2.58)	2.25 (-0.16, 4.67)	8.69 (-16.88, 34.26)
Adjusted	0.82 (-0.45, 2.10)	24 (0.28, 47.72)*	1.48 (-0.22, 3.18)	2.56 (-0.31, 5.44)	28.87 (2.04, 55.70)*

[1] Adjusted for maternal education, HOME score at 6 months of age, alcohol consumption during the first trimester of pregnancy, tobacco use during the first trimester of pregnancy, maternal age at delivery, and duration of breastfeeding (weeks)

*$p<0.05$

Table 4. Adjusted[1] association between total serum pesticide exposure[a] during the first trimester of pregnancy and MCDI components among 15-month old girls [β (95% CI)].

	MCDI Component				
Pesticide (pg/g)	Understanding	Vocabulary	Nonverbal Communication	Social Development	Total Communication
Unadjusted	0.01 (-0.06, 0.08)	0.07 (-1.44, 1.57)	0.06 (-0.05, 0.16)	0.14 (-0.03, 0.31)	0.37 (-1.34, 2.09)
Adjusted	0.04 (-0.05, 0.13)	1.32 (-0.40, 3.03)	0.08 (-0.05, 0.20)	0.18 (-0.03, 0.38)	1.61 (-0.33, 3.55)

[1] Adjusted for maternal education, HOME score at 6 months of age, alcohol consumption during the first trimester of pregnancy, tobacco use during the first trimester of pregnancy, maternal age at delivery, and duration of breastfeeding (weeks)

[a] HCH, HCCH, DDE, DDT

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