Published in final edited form as:
*Environ Res*. 2016 October ; 150: 128–137. doi:10.1016/j.envres.2016.05.048.

# Residential proximity to organophosphate and carbamate pesticide use during pregnancy, poverty during childhood, and cognitive functioning in 10-year-old children

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## Abstract

**Background—**Low-income communities and communities of color have been shown to experience disproportionate exposure to agricultural pesticides, which have been linked to poorer neurobehavioral outcomes in infants and children. Few studies have assessed health impacts of pesticide mixtures in the context of socioeconomic adversity.

**Objectives—**To examine associations between residential proximity to toxicity-weighted organophosphate (OP) and carbamate pesticide use during pregnancy, household- and neighborhood-level poverty during childhood, and IQ scores in 10-year-old children.

**Methods—**We evaluated associations between both nearby agricultural pesticide use and poverty measures and cognitive abilities in 10-year-old children (n = 501) using data from a longitudinal birth cohort study linked with data from the California Pesticide Use Reporting system and the American Community Survey. Associations were assessed using multivariable linear regression.

**Results—**Children of mothers in the highest quartile compared to the lowest quartile of proximal pesticide use had lower performance on Full Scale IQ [$\beta = -3.0$; 95% Confidence Interval (CI) = (−5.6, −0.3)], Perceptual Reasoning [$\beta = -4.0$; (−7.6, −0.4)], and Working Memory [$\beta = -2.8$; (−5.6, −0.1)]. Belonging to a household earning an income at or below the poverty threshold was associated with approximately two point lower scores on Full Scale IQ, Verbal Comprehension, and Working Memory. Living in the highest quartile of neighborhood poverty at age 10 was associated with approximately four point lower performance on Full Scale IQ, Verbal Comprehension, Perceptual Reasoning, and Working memory.

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**Conflict of Interest:** A.B. has participated as a volunteer member of the Board for The Organic Center, a nonprofit organization that provides information for scientific research about organic food and farming. The other authors declare they have no actual or potential competing financial interests.

**Conclusions—**Residential proximity to OP and carbamate pesticide use during pregnancy and both household- and neighborhood-level poverty during childhood were independently associated with poorer cognitive functioning in children at 10 years of age.

## Introduction

California is the largest agricultural state in the United States, producing nearly half of the country's nuts, vegetables, and fruits (California Department of Food and Agriculture 2014). In 2013, nearly 178 million pounds of pesticides were used in agriculture in California, including over four and a half million pounds of organophosphate (OP) and carbamate pesticides (California Department of Pesticide Regulation 2015). A growing body of research has linked prenatal exposure to OPs to abnormal reflexes in neonates, adverse mental and motor development in toddlers, and behavioral and cognitive deficits in children (Bouchard et al. 2011; Engel et al. 2007; Marks et al. 2010; Rauh et al. 2006; Young et al. 2005; Shelton et al. 2014). Little is known about the health effects of carbamates, although their mechanism of action is similar to OPs.

Research investigating neurodevelopmental effects of classes of currently-used pesticides is primarily limited to animal studies, with very few epidemiological studies assessing the effects of compounds other than OPs on humans (Burns et al. 2013). However, there has been an increasing interest in understanding how mixtures of pesticides may interact and affect human health (Hernandez et al. 2013; Mwila et al. 2013). Although OP pesticides have multiple documented neurotoxic mechanisms of action (Slotkin and Seidler 2007), both OP and carbamate pesticides produce neurotoxic effects through the inhibition of acetylcholinesterase (AChE), which results in an accumulation of the neurotransmitter acetylcholine and over-stimulation of acetylcholine receptors (Kwong 2002; Fuortes et al. 1993). Recent *in vitro* toxicological research using animal cells suggests that these two classes of pesticides combine to produce an additive inhibitory effect on AChE (Mwila et al. 2013; Tahara et al. 2005). Unfortunately, many pesticides, including carbamates, lack a biomarker of exposure. Although urinary dialkyl phosphate (DAP) metabolite levels are a widely used biomarker of OP exposure, they are limited in their ability to accurately reflect levels of exposure (Bradman et al. 2005; Bradman et al. 2013; Quiros-Alcala et al. 2012; Morgan et al. 2005; Lu et al. 2005; Zhang et al. 2008). The overall lack of biomarkers for many pesticides and limitations of those that do exist highlight the importance of exploring other methods to assess exposure.

Exposure to pesticides in California and elsewhere has been shown to disproportionately affect low-income communities and communities of color (Huang and London 2012; Griffith et al. 2007), consistent with a body of environmental justice research that has shown disproportionate environmental burdens by race, ethnicity, and socioeconomic status (Morello-Frosch and Shenassa 2006; O'Neill et al. 2003; Evans and Marcynyszyn 2004; Cureton 2011). Poverty during childhood has consistently been linked to negative outcomes among children, particularly in regards to cognitive ability and academic achievement (Duyme et al. 1999; Hair et al. 2015; Brooks-Gunn and Duncan 1997). Some have hypothesized additive and synergistic effects of cumulative environmental chemical and non-chemical social stressors on health (Gee and Payne-Sturges 2004; Morello-Frosch et al.

2011). However, the evidence for such cumulative effects has been isolated to research concerning air pollution and various health endpoints such as mortality and birth outcomes (Ponce et al. 2005; Morello-Frosch et al. 2010; Finkelstein et al. 2003; Gray et al. 2014). Thus far, no studies have examined the combined effects of pesticide exposure and social adversity on human health. Moreover, no studies have explored the combined effects of these exposures when occurring at disparate points during a child's life course, from the prenatal period to early adolescence.

The Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), a longitudinal birth cohort study of primarily low-income Latino farmworker families living in the agricultural Salinas Valley, California, aims to investigate the health effects of pesticides and other environmental exposures on pregnant women and children. In the present study, we investigate associations between residential proximity to OP and carbamate agricultural pesticide use during women's pregnancies, household- and neighborhood-level poverty experienced by their children at age 10 years, and the children's cognitive abilities at age 10.

## Methods

### Study sample and data collection

The CHAMACOS study has been described in detail elsewhere (Eskenazi et al. 2004; Sagiv et al. 2015). Families in this study were recruited in two waves. Recruitment of the initial "CHAMACOS 1" or CHAM1 cohort occurred between October 1999 and October 2000, when 601 pregnant women were enrolled at six prenatal clinics located throughout the Salinas Valley. To be eligible for the study, women had to be at least 18 years of age, 20 weeks or less of gestation, Spanish or English speaking, eligible for low-income health insurance (Medi-Cal), and planning to deliver at Navidad Medical Center, the local public hospital. A total of 532 pregnancies were followed to delivery and resulted in livebirths (between February 2000 and August 2001). Five pregnancies resulted in twins. For this analysis, we randomly selected and excluded one child from each pair of twins and excluded four children with diagnosed conditions that could impact cognitive assessment (autism, deafness, cerebral palsy, Down syndrome). CHAM1 mothers were interviewed by bilingual, bicultural staff twice during pregnancy, soon after delivery, and at child visits occurring at 6 months and 1, 2, 3.5, 5, 7, 9, and 10.5 years of age. A total of 316 CHAM1 children completed the 10.5-year neurodevelopmental assessment.

Recruitment of the "CHAMACOS 2" or CHAM2 portion of the cohort occurred between September 2009 and August 2011, when 305 additional 9-year old children and their mothers were recruited to participate. Eligibility criteria for CHAM2 were intended to mirror those of CHAM1 participants. Like CHAM1 children, CHAM2 children were born in the Salinas Valley to Spanish- or English-speaking women who were eligible for MediCal, sought prenatal care in the first trimester of pregnancy, and were at least 18 years old when their child was born. CHAM2 children were born between September 2000 and August 2002 (i.e., in a period that overlapped with CHAM1 children's birthdates). A total of 295 CHAM2 children completed the 10.5-year neurodevelopmental assessment, though for this analysis, we excluded one child with diagnosed autism.

From 610 CHAM1 and CHAM2 children with complete age 10.5-year neurodevelopmental assessments, we excluded from these analyses those with missing or invalid prenatal (n=106; all from CHAM2) address data. Eight children had missing or invalid age 10.5 address data; if available, we used age 7 or 9 address data instead (n=5; 3 from CHAM1, 2 from CHAM2), otherwise the children were excluded (n=3; 1 from CHAM1, 2 from CHAM2). The final analysis sample included 501 children (315 from CHAM1, 186 from CHAM2). A comparison of children included versus excluded from our analysis showed several differences; children included in analyses were significantly ($p < 0.05$) more likely to have older mothers, to have been breastfed for either more than 12 months or less than 1 month, to be more proficient in Spanish than English at age 10.5, and to live at or below the poverty threshold at 10.5 years of age. A comparison of CHAM1 and CHAM2 children included in our analysis also showed differences; CHAM1 children were significantly ($p < 0.05$) more likely to have not been breastfed and to live in a higher poverty neighborhood at 10.5 years of age.

Written informed consent was obtained from all mothers at enrollment and assent was obtained from all children starting at age 7 years for CHAM1 and enrollment for CHAM2. All study activities were approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley.

## Cognitive assessment

To assess cognitive abilities at the 10.5 year visit, we administered the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV), using methods similar to those used for the 7-year visit, which have been described in detail elsewhere (Bouchard et al. 2011; Wechsler 2003). Briefly, all assessments were conducted by one of three experienced bilingual psychometricians. Reported measures for each child included a Full Scale Intelligence Quotient (FSIQ) comprised of four subscales: Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed. All assessments were administered in the child's dominant language and scores were standardized against U.S. population-based norms for English- and Spanish-speaking children, with a mean of 100 and standard deviation of 15 for each scale. All analyses include the standardized cognitive scores as continuous variables.

## Geographic-based estimates of residential proximity to pesticide use

Using data from the California Pesticide Use Reporting (PUR) system, we estimated the total kilograms of OP and carbamate pesticides used in agriculture near the residence where each woman lived the longest during her pregnancy, applying methods that have been described in detail elsewhere (Gemmill et al. 2013; Gunier et al. 2011; Nuckols et al. 2007). The California PUR system reports the pounds of active pesticide applied, the date of application, and the location, which is reported by one-square mile sections (approximately 1.6 km × 1.6 km) as defined by the Public Land Survey System (PLSS) (U.S. Bureau of Land Management 2014). We calculated nearby use of 15 OP and 7 carbamate pesticides (see Table 1) by summing the kilograms applied in all the 1.6 km × 1.6km PLSS sections that fell within a 1 km radius of the maternal residence. In cases where the 1 km buffer intersected an adjacent PLSS section, the kilograms applied for that section were down-weighted to be proportional with the land area that fell within the buffer. We accounted for potential downwind pesticide drift from application sites to residences by incorporating historical wind direction data from the nearest meteorological station to each residence (California Irrigation Management Information System 2014). We calculated the extent of upwind pesticide use for each residence by using the proportion of each day that wind blew from each of eight directions (e.g. North, Northeast, East, Southeast, etc.). We identified the direction of centroids of all PLSS sections within the 1 km buffer from each residence and weighted the kilograms of pesticides applied within each section and each day by the proportion of time that the wind blew from that direction. The application dates included in the calculations for each woman were defined by the period between her reported last menstrual period date and her delivery date.

Relative Potency Factors (RPFs) were calculated for each OP and carbamate to weight their neurotoxicity relative to chlorpyrifos (U.S. Environmental Protection Agency 2001; Jensen et al. 2003; Caldas et al. 2006). Chlorpyrifos was selected as the index chemical because it is widely used in agriculture (California Department of Pesticide Regulation 2015). RPFs were calculated as the toxicologically relevant dose of chlorpyrifos divided by the toxicologically relevant dose of each remaining OP or carbamate pesticide under consideration. Because the primary shared neurotoxic effect of OP and carbamate pesticides is AChE inhibition, the toxicological relevant dose used in our calculations was the oral dose estimated to result in 10% male rat brain AChE inhibition (benchmark dose or $BMD_{10}$) as reported by the U.S. Environmental Protection Agency (EPA) and presented in Table 1 (U.S. Environmental Protection Agency 2006, 2007). The toxicity-weighted pesticide exposure variable used in these analyses was calculated by multiplying the wind-adjusted kilograms of each chemical used within the 1 km buffer during pregnancy by its RPF and summing the products for all 22 chemicals for each pregnancy; the resulting variable can be interpreted as kilogram-equivalents of chlorpyrifos applied within 1km of the maternal residence during pregnancy, adjusted for wind direction. The RPF values of each OP and carbamate pesticide included in this study, as well as the total number of kilograms and toxicity-weighted kilograms used in the Salinas Valley in 2000, are also presented in Table 1.

We assessed the linearity of the association between proximal pesticide use during pregnancy and cognitive measures using generalized additive models (GAMs) with three degrees of freedom on our continuous toxicity- and wind-adjusted pesticide use measure. The results of the GAMs indicated significant digression from linearity in the associations between proximal pesticide use and FSIQ and Working Memory and Perceptual Reasoning ($p < 0.2$). Because of this evidence of non-linearity, we analyzed pesticide exposure as a categorical variable defined by quartiles.

## Socioeconomic measures

The two socioeconomic measures of interest were household-level and neighborhood-level poverty status. At the 10.5-year visit, mothers were asked to select the range of values in which their monthly household income fell ($750 or less, $751–$1500, $1501–$2000, $2001–$2500, $2501–$3000, $3001 and above) and to report the number of individuals supported by that income. The midpoint of the reported monthly household income range and the number of individuals supported in each household were compared to the 2009 U.S.

Census Bureau weighted average poverty thresholds by size of family (U.S. Census Bureau 2009). Because of the low variability in household income in our sample—only one household earned above 200% of the poverty threshold—poverty status for each child was defined as a binary variable capturing whether a household was above or at/below the poverty threshold. To determine neighborhood poverty status, children's age 10.5 year residential addressed were mapped against 2010 census tracts, and the percentage of households within each census tract earning less than 200% of the Census Bureau poverty threshold, as reported in the 2008–2012 American Community Survey 5-year (ACS) estimates, were identified (United States Census Bureau 2013). For two children with uncertain street addresses but within a small town with only two-census tracts, we assigned the mean neighborhood poverty value of those two census tracts. We assessed the linearity of the association between neighborhood poverty status and cognitive measures using the same methods as those used for proximal pesticide use (i.e., GAMs), which indicated significant digression from linearity in the associations between neighborhood poverty status and FSIQ and all subscales except for Perceptual Reasoning ($p < 0.2$). Finding evidence of non-linearity, we analyzed neighborhood poverty status as a categorical variable defined by quartiles of the percent of households under 200% of the poverty threshold, with the first quartile representing the highest neighborhood socioeconomic status and the fourth quartile representing the lowest.

## Statistical analysis

We assessed the associations between residential proximity to OP and carbamate use during pregnancy, household poverty, neighborhood poverty, and cognitive scores at 10.5 years of age using multivariable linear regression. Our pesticide and poverty measures were included in the same models in order to assess their independent effects, resulting in a total of five main models, one for each cognitive scale. We conducted tests for trend across the quartiles of both residential proximity to OP and carbamate use and neighborhood poverty using orthogonal contrasts, with the assumption that the quartiles are evenly spaced. To control for potential confounding, all of our models included measures of maternal education, maternal intelligence, quality of home environment, maternal age at delivery, breastfeeding duration, language of WISC assessment, and the psychometrician who conducted the cognitive assessment. All covariates except for language of assessment and psychometrician were selected based on prior reports of significant associations between these measures and cognitive functioning in children (Tong et al. 2007; Fergusson and Woodward 1999; Jain et al. 2002). Covariates were categorized as in Table 2 unless otherwise noted. Maternal education was collected during enrollment of mothers for CHAM1 (1999–2000) and CHAM2 (2009–2011) and was categorized based on highest grade completed. Maternal receptive vocabulary as a proxy of intelligence was assessed at the 9-year visit using the Peabody Picture Vocabulary Test (PPVT) or the Test de Vocabulario en Imágenes Peabody (TVIP) in the mother's dominant language and included as a continuous variable (Dunn 1981). Quality of the child's home environment was assessed using the Home Observation Measurement of the Environment-Short Form (HOME-SF) at age 9 and included as a continuous variable. Maternal age at delivery was collected soon after delivery for CHAM1 and at enrollment for CHAM2 and included in analyses as a continuous variable. Information regarding breastfeeding duration was collected at each visit until age 3.5 for

CHAM1 and at enrollment for CHAM2 and is included as a categorical variable based on the number of months that the child was breastfed. Language of assessment was included as a binary variable indicating whether the assessment was taken in English or Spanish and psychometrician was included as a categorical variable. Missing values for maternal education (n=1), maternal PPVT scores (n=12), HOME score (n=4), and breastfeeding duration (n=4) were randomly imputed from other participant's values. We assessed bivariate associations between continuous toxicity-weighted OP/carbamate pesticide use within 1km of residences during pregnancy and continuous neighborhood poverty rate with each other as well as with household poverty and other covariates using Pearson's correlation, Wilcoxon rank-sum, and Kruskal-Wallis tests.

To explore potential interaction between residential proximity to OP and carbamate use during pregnancy and both household and neighborhood poverty, we stratified the full models separately by our categories of household and neighborhood poverty status. In additional models, we created an interaction term for the ordinal quartiles of pesticide use and ordinal quartiles of neighborhood poverty (i.e. the product of two variables, each with values of 1, 2, 3, or 4, corresponding to increasing quartiles of pesticide use and neighborhood poverty), while controlling for household poverty and other covariates. Similarly, we examined an interaction of ordinal quartiles of pesticide use and binary household poverty status (above the poverty threshold or at or below), while controlling for neighborhood poverty and other covariates. We also tested for potential interaction by cohort (CHAM1 and CHAM2) for cognitive outcomes that were associated with pesticide use in our main models.

We conducted a sensitivity analysis to assess the separate associations of OPs and carbamates with IQ scores. The models used were identical to those previously described but included only toxicity-weighted OPs or toxicity-weighted carbamates as opposed to the combination of both. We conducted an additional sensitivity analysis using a 3km buffer distance around the residences as opposed to the 1km buffer distance used in our primary analysis. All analyses were conducted using STATA (Version 13; StataCorp, College Station, TX).

We conducted an additional sensitivity analysis to explore the possibility of cognitive effects through mechanisms other than AChE inhibition as well as differential effects of diethyl (DEP) and dimethyl (DMP) OP pesticides, as has been suggested by other studies (Bouchard et al. 2011; Marks et al. 2010). Specifically, we fit the same models as previously described but included raw (i.e. not toxicity-weighted) wind-adjusted kilograms of DEPs plus carbamates and DMPs plus carbamates, separately. OPs included in each of the new pesticide measures are indicated in Table 1. As with the previous models, the new DEP/carbamate and DMP/carbamate measures were categorized as quartiles.

## Results

Almost all mothers identified as Latina (96.4%), 85.0% were born in Mexico, and nearly half (45.9%) had been in the United States less than five years at the time of the child's birth (Table 2). Most did not complete high school (75.4%), with 40.5% having no formal schooling beyond the sixth grade. More than one-quarter (28%) were engaged in agricultural work at some point during the child's pregnancy. Almost all children were breastfed (95.8%), with over half (50.9%) being breastfed for at least six months. At the time of the 10.5-year visit, 70.9% of the households earned an income that was at or below the poverty threshold.

Toxicity-weighted proximal OP and carbamate use during pregnancy had a mean value of 123.6kg (Median = 35.3kg; Range = 0kg – 1553.3kg), and was categorized as first quartile (≤5.5 kg), second quartile (>5.5 kg and ≤35.3 kg), third quartile (>35.3 kg and ≤135.4 kg), and fourth quartile (>135.4 kg). The mean IQ scores were 89.7 (SD = 10.7) for the Full Scale IQ, 96.3 (SD = 11.0) for Working Memory, 98.3 (SD = 12.1) for Processing Speed, 84.4 (SD = 11.4) for Verbal Comprehension, and 92.2 (SD = 14.1) for Perceptual Reasoning.

Toxicity-weighted OP/carbamate pesticide use within 1km of residences during pregnancy was negatively associated with both neighborhood and household poverty (Table 2). Among the covariates included in the main regression models, neighborhood poverty was negatively associated with maternal education, quality of home environment and positively associated with household poverty. Children who completed their cognitive assessment in Spanish lived in census tracts with higher neighborhood poverty rates compared to children who completed their assessments in English.

The adjusted associations between residential proximity to toxicity-weighted OP and carbamate agricultural pesticide use, household poverty, neighborhood poverty and IQ are shown in Table 3. Compared to children of mothers in the lowest quartile of proximal OP and carbamate use during pregnancy, children of mothers in the highest quartile of proximal use averaged three points lower on FSIQ (95% CI = −5.6, −0.3), four points lower on Perceptual Reasoning (95% CI = −7.6, −0.4), and 2.8 points lower on Working Memory (95% CI = −5.6, −0.1), after adjusting for potential confounders. Belonging to a household earning an income at or below the poverty threshold compared to a household earning an income above it was significantly associated with decreased performance of 2.4 points on FSIQ (95% CI = −4.5, −0.4), 2.3 points on Verbal Comprehension (95% CI = −4.5, −0.2), and 2.2 points Working Memory (95% CI = −4.4, −0.1). Independently of household poverty, living in a neighborhood in the lowest quartile of SES at 10.5 years of age compared to the highest was significantly associated with decreased performance of four points on FSIQ (95% CI = −6.9, −1.2), 4.3 points on Verbal Comprehension (95% CI = −7.2, −1.3), 4.4 points on Perceptual Reasoning (95% CI = −8.2, −0.5), and 3.6 points on Working Memory (95% CI = −6.6, −0.6). Tests for trend suggested declining trends across increasing quartiles of residential proximity to pesticide use for FSIQ and Perceptual Reasoning ($p < 0.05$). Similarly, results suggested declining trends across increasing quartiles of neighborhood poverty for FSIQ, Verbal Comprehension, and Perceptual Reasoning ($p < 0.05$).

The results of the multivariable regression models stratified by household poverty status as well as interaction terms between ordinal pesticide use and binary household poverty status are shown in Table 4. Although none of the interaction terms are statistically significant ($p > 0.2$), we observed statistically significant negative associations between living in the highest quartile of proximal pesticide use and FSIQ ($\beta = -3.8$; 95% CI = −7.0, −0.5), Perceptual Reasoning ($\beta = -4.4$; 95% CI = −8.7, −0.1), and Working Memory ($\beta = -3.8$; 95% CI = −7.2, −0.5) among children in households at or below the poverty threshold but not in those in households above the poverty threshold. Presented in Table 5, none of the interaction terms between ordinal pesticide use and ordinal quartiles of neighborhood poverty were statistically significant ($p > 0.2$), except in relation to Processing Speed ($\beta = -0.7$; $p = 0.15$), suggesting that the adverse association between proximal OP and carbamate use and Processing Speed may be enhanced across increasing quartiles of neighborhood poverty, and vice versa. In the regression models stratified by quartiles of neighborhood poverty, there were no clear trends for an interaction between residential proximity to pesticide use and neighborhood. We examined differences by cohort for outcomes that were related to OP and carbamate pesticide use and found no differences by cohort for FSIQ and Perceptual Reasoning ($p > 0.2$), but did observe an interaction for Working Memory (4th vs. 1st Quartile CHAM 1: $\beta = -3.3$; 95% CI = −6.9, 0.1; 4th vs. 1st Quartile CHAM 2: $\beta = -1.3$; 95% CI = −5.7, 3.2; overall $p = 0.09$).

The results of the sensitivity analysis examining the isolated effects of OP pesticides and carbamate pesticides separately show similar trends as the models assessing the combined effects of OP and carbamate pesticides, though smaller in magnitude and not statistically significant at $p < 0.05$ (see Supplemental Table 1). In the analysis using a three km buffer around the residence for OP and carbamate use instead of one km, the results were weaker than for one km with no significant associations between proximal pesticide use and children's WISC scores at age 10.5 (data not shown).

The results of the sensitivity analyses examining the isolated effects of non-toxicity-weighted DMPs plus carbamates and DEPs plus carbamates separately also show similar trends as the models assessing both the combined and isolated effects of OPs and carbamates (see Supplemental Table 2). Comparing the fourth quartile of pesticide use to the first quartile, the effects of DMPs plus carbamates are generally greater in magnitude compared to the effects of DEPs plus carbamates and only significant at $p < 0.05$ for the association between DMPs plus carbamates and Perceptual Reasoning.

## Discussion

Our findings suggest that residential proximity to agricultural use of OP and carbamate pesticides during pregnancy is associated with poorer cognitive functioning in children at 10.5 years of age. Children in the highest quartile of proximal pesticide use *in utero* had average deficits ranging from three to four points on multiple child intelligence scales, including Full Scale IQ, compared with those in the lowest quartile of proximal pesticide use. Moreover, our results also suggest that neighborhood poverty and household poverty are both independently associated with poorer cognitive abilities in 10.5-year-old children. Children in households earning incomes at or below the poverty threshold showed deficits of more than two points on multiple WISC subscales compared to children in households earning above the poverty threshold; likewise, children living in the lowest quartile of neighborhood SES had average deficits ranging from four to five points on multiple WISC subscales compared with those in the highest quartile of neighborhood SES.

Although we did not find that pregnant women with higher household or neighborhood poverty were exposed to greater pesticide use near their residences in our cohort of low-income families, prior studies have shown that agricultural pesticides are used disproportionately in or near low-income communities and communities of color (Huang and London 2012; Griffith et al. 2007). These disproportionate patterns of use highlight the importance of the independent, additive nature of our findings. Moreover, the results of our multivariable regression models stratified by household poverty suggest that children in poorer households may experience greater cognitive impacts in association with OP and carbamate exposures, although for the most part we did not observe statistically significant interaction. There was less evidence for interaction between proximity to pesticide use and neighborhood poverty, with the exception of a potentially stronger effect of proximal pesticide use on children's processing speed in poorer neighborhoods. It is important that future research explore these interactions in populations with greater variation in household and neighborhood socioeconomic status.

A previous study of the CHAMACOS cohort showed associations between prenatal exposure to OP pesticides, measured by urinary metabolite levels, and lower IQ at age 7 (Bouchard et al. 2011). Our toxicity weighted measure of residential proximity to organophosphate use, excluding carbamates, is not highly correlated with urinary OP metabolites in our cohort ($r = 0.04$), therefore we believe that these are complementary measures of exposure to OP pesticides. Regardless, our present findings are consistent with this previous study and suggest that the association between prenatal pesticide exposure and intellectual development is sustained as children age. Deficits in cognitive abilities during adolescence have been linked to lower academic and economic achievement, conduct disorder, delinquency, and increased risk of obesity and mortality during adulthood (Calvin et al. 2011; Fergusson et al. 2005; Murray and Farrington 2010; Yu et al. 2010).

This study has several limitations. We used residential proximity to agricultural use of OP and carbamate pesticides to classify exposure rank, not a true measure of exposure; however, there are no environmental or biological measurements available to characterize exposure to the full range of pesticides we examined and there are limitations to the most widely used biomarker for OP pesticides (DAPs). Indeed, DAP measurements capture only the 80% of OPs that actually devolve into these metabolites (Bradman et al. 2005), reflect only recent exposures due to short half-lives of the metabolites (Bradman et al. 2013), and may overestimate true OP exposure by reflecting exposure to both pre-formed DAPs in the environment and food as well as OPs (Quiros-Alcala et al. 2012; Morgan et al. 2005; Lu et al. 2005; Zhang et al. 2008). In addition, we used the single residence where each mother lived the longest during her pregnancy to estimate nearby pesticide use, which does not account for those who moved one or more times during pregnancy or those who spent a significant amount of time away from their residence for work or other reasons. We also did not assess proximal use of pesticides during early childhood; however, prior research suggests that postnatal exposure is less important to later neurodevelopment than exposure during the prenatal period (Bouchard et al. 2011; Marks et al. 2010). Furthermore, OP pesticides were commonly applied indoors until 2004, which could result in exposure misclassification and attenuation of the associations observed in our study. Another limitation is our use of census tracts to capture neighborhood socioeconomic status; census tract boundaries are defined independently of cultural or socioeconomic boundaries, which make them a relatively crude measure of an individual's immediate neighborhood. Finally, our study sample is comprised almost exclusively of low-income Latino families, which limits our ability to explore differences across racial/ethnic groups or across a wider spectrum of socioeconomic status.

This study also has considerable strengths. This is the first epidemiological study to assess the cognitive effects of multiple classes of pesticides known to affect the same neurochemical mechanism. Moreover, the present study advances methods to capture the relative toxicities of pesticides in an effort to enhance the assessment of potential cumulative health impacts. The results from our sensitivity analyses provide no evidence that proximal use of OPs is differentially associated with cognitive development compared to proximal use of carbamates, suggesting that our composite measure is valid. Since OPs and carbamates continue to be used together and alongside other classes of pesticides in the Salinas Valley and elsewhere, studies of the cumulative effects of these mixtures are important for understanding real world exposures and risks. Another contribution of this study is the assessment of the combined, additive effects of residential proximity to pesticide use, household poverty, and neighborhood poverty, which is essential for documenting and better understanding both the overlap and cumulative impact of environmental and social stressors to support the advancement of environmental and health equity.

Our methods and results have several implications for future research. The publicly available data of California's Pesticide Use Reporting System is a valuable resource for studying both the trends and potential health impacts of pesticide use, as demonstrated by our study. Continued use of these data should be pursued along with the development of methods to improve exposure classification, such as more advanced incorporation of meteorological data and more exact information on the location of pesticide applications. Furthermore, it is important that future research explore methods for studying the effects of pesticide mixtures as opposed to individual or classes of pesticides to further our understanding of potential hazards associated with real world exposures.

## Conclusion

The present study found independent negative associations between residential proximity to OP and carbamate agricultural pesticide use during pregnancy, household poverty, and neighborhood poverty and cognitive functioning in 10.5-year old children in a low-income agricultural community in California. The combined, additive effects of these environmental and social exposures deserve further investigation in populations that are more socioeconomically diverse.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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### Highlights

- Prenatal proximity to OP/carbamate pesticide use is linked to lower childhood IQ
- Neighborhood & household poverty during childhood are linked to lower childhood IQ
- Cognitive effects of proximal OP/carbamate pesticide use & poverty are independent

## Table 1

Toxicity characteristics and use of specific organophosphate and carbamate pesticides in the Salinas Valley in 2000

| | | | Actual | | Toxicity Weighted | |
|---|---|---|---|---|---|---|
| **Pesticide** | **BMD$_{10}$** | **RPF** | **Kg** | **Percent of Total** | **Kg** | **Percent of Total** |
| **Organophosphates** | | | | | | |
| Diazinon$^{DEP}$ | 9.62 | 0.16 | 55924 | 22.5% | 8720 | 0.7% |
| Malathion$^{DMP}$ | 212.02 | 0.01 | 45606 | 18.4% | 323 | 0.0% |
| Acephate | 0.77 | 1.95 | 33526 | 13.5% | 65310 | 5.6% |
| Chlorpyrifos$^{DEP}$ | 1.50 | 1.00 | 26630 | 10.7% | 26630 | 2.3% |
| Oxydemeton-methyl$^{DMP}$ | 0.07 | 21.43 | 27754 | 11.2% | 594727 | 50.7% |
| Dimethoate$^{DMP}$ | 0.35 | 4.29 | 16115 | 6.5% | 69064 | 5.9% |
| Bensulide | 40.88 | 0.04 | 17409 | 7.0% | 639 | 0.1% |
| Naled$^{DMP}$ | 1.00 | 1.50 | 9298 | 3.7% | 13947 | 1.2% |
| Disulfoton$^{DEP}$ | 0.10 | 15.00 | 5763 | 2.3% | 86440 | 7.4% |
| Methidathion$^{DMP}$ | 0.24 | 6.25 | 6926 | 2.8% | 43287 | 3.7% |
| Methamidophos | 0.07 | 21.43 | 619 | 0.2% | 13260 | 1.1% |
| Ethoprop | 1.35 | 1.11 | 472 | 0.2% | 524 | 0.0% |
| Azinphos-methyl$^{DMP}$ | 1.14 | 1.32 | 101 | 0.0% | 133 | 0.0% |
| Fenamiphos | 1.73 | 0.87 | 1114 | 0.4% | 966 | 0.1% |
| Phosmet$^{DMP}$ | 4.15 | 0.36 | 909 | 0.4% | 328 | 0.0% |
| **N-Methyl Carbamates** | | | | | | |
| Methomyl | 0.36 | 4.17 | 34815 | 61.1% | 145062 | 40.8% |
| Carbofuran | 0.10 | 15.00 | 7271 | 12.8% | 109072 | 30.7% |
| Carbaryl | 1.21 | 1.24 | 9169 | 16.1% | 11366 | 3.2% |
| Thiodicarb | 0.27 | 5.56 | 2227 | 3.9% | 12375 | 3.5% |
| Oxamyl | 0.24 | 6.25 | 3319 | 5.8% | 20741 | 5.8% |
| Methiocarb | 1.31 | 1.15 | 170 | 0.3% | 194 | 0.1% |
| Aldicarb | 0.06 | 25.00 | 2 | <0.1% | 38 | <0.1% |

BMD$_{10}$ = Benchmark dose estimated to result in 10% male rat brain AChE inhibition; RPF = Relative potency factor; Kg = kilogram

*DEP* Diethyl organophosphate pesticide

*DMP* Dimethyl organophosphate pesticide

## Table 2

Characteristics of study population at birth and during early childhood, CHAMACOS study, Salinas Valley, CA ($n = 501$)

| | | Proximal Pesticide Use During Pregnancy[a] | Neighborhood Poverty Rate at 10.5 years[b] |
|---|---|---|---|
| **Characteristics** | **n (%)** | **Median (IQR)** | **Median (IQR)** |
| **N** | 501 | 35 (6 – 135) | 57 (45 – 70) |
| **Child's sex** | | | |
| Male | 239 (47.7) | 37 (6 – 171) | 60 (45 – 70) |
| Female | 262 (52.3) | 33 (4 – 122) | 56 (45 – 70) |
| **Mother's Ethnicity**[†] | | | |
| Latina | 483 (96.4) | 36 (6 – 139) | 59 (45 – 70) |
| Other | 18 (3.6) | 13 (2 – 128) | 46 (32 – 62) |
| **Mother Engaged in Agricultural Work During Pregnancy** | | | |
| Yes | 142 (28.3) | 35 (6 – 152) | 60 (48 – 70) |
| No | 359 (71.7) | 35 (6 – 132) | 56 (45 – 70) |
| **Breastfeeding Duration** | | | |
| No breastfeeding | 21 (4.2) | 34 (5 – 183) | 66 (44 – 79) |
| Less than 1 month | 64 (12.8) | 44 (11 – 116) | 54 (44 – 67) |
| 1–6 months | 161 (32.1) | 47 (7 – 190) | 57 (45 – 70) |
| 6–12 months | 119 (23.8) | 20 (4 – 89) | 60 (45 – 70) |
| More than 12 months | 136 (27.1) | 38 (4 – 130) | 56 (45 – 69) |
| **Maternal education**[†] | | | |
| ≤ 6th grade | 203 (40.5) | 32 (4 – 122) | 60 (47 – 70) |
| Some middle/high school | 175 (34.9) | 35 (7 – 134) | 56 (45 – 70) |
| High school graduate | 123 (24.6) | 44 (9 – 190) | 54 (45 – 66) |
| **Maternal intelligence (PPVT Scores)**[‡] | | | |
| ≤ 74 | 106 (21.2) | 39 (9 – 124) | 60 (45 – 70) |
| 75–99 | 163 (32.5) | 38 (7 – 135) | 60 (46 – 70) |
| ≥ 100 | 232 (46.3) | 30 (3 – 153) | 56 (45 – 70) |
| **HOME-SF Score (Age 9)**[‡][†] | | | |
| ≤ 12 | 106 (21.2) | 40 (6 – 151) | 62 (47 – 71) |
| 13–16 | 163 (32.5) | 33 (4 – 126) | 56 (45 – 70) |
| ≥ 17 | 232 (46.3) | 40 (10 – 150) | 54 (45 – 66) |
| **Maternal age at birth**[‡] | | | |
| < 20 years | 36 (7.2) | 16 (2 – 81) | 56 (43 – 68) |
| 20–24 years | 165 (32.9) | 34 (6 – 156) | 61 (47 – 70) |
| 25–29 years | 158 (31.5) | 34 (7 – 134) | 56 (45 – 70) |
| 30–34 years | 89 (17.8) | 12 (5 – 128) | 54 (45 – 66) |
| ≥ 35 years | 53 (10.6) | 57 (7 – 171) | 54 (42 – 67) |
| **Maternal country of birth** | | | |

| | | Proximal Pesticide Use During Pregnancy[a] | Neighborhood Poverty Rate at 10.5 years[b] |
|---|---|---|---|
| **Characteristics** | **n (%)** | **Median (IQR)** | **Median (IQR)** |
| Mexico | 426 (85.0) | 40 (8 – 149) | 54 (43 – 66) |
| United States | 69 (13.8) | 34 (5 – 135) | 60 (45 – 70) |
| Other | 6 (1.2) | 65 (16 – 130) | 60 (45 – 66) |
| **Maternal years of residence in the U.S. at birth**[‡†] | | | |
| ≤ 5 years | 230 (45.9) | 29 (4 – 139) | 61 (48 – 71) |
| 6–10 years | 120 (24.0) | 30 (6 – 119) | 56 (45 – 70) |
| ≥ 11 years | 95 (19.0) | 59 (9 – 161) | 48 (42 – 62) |
| Entire life | 56 (11.2) | 56 (11 – 150) | 52 (42 – 68) |
| **Pesticide Use Within 1km of Residence During Pregnancy**[†] | | | |
| First quartile (≥0kg and ≤5.5kg%) | 126 (25.1) | N/A | 62 (45 – 79) |
| Second quartile (>5.5kg and ≤35.3kg) | 125 (25.0) | | 64 (45 – 71) |
| Third quartile (>35.3kg and ≤135.4kg) | 125 (25.0) | | 54 (45 – 64) |
| Fourth quartile (>135.4kg and ≤1553.3kg) | 125 (25.0) | | 52 (45 – 61) |
| **Family Income (Age 10.5)**[*†] | | | |
| At or below Census Bureau poverty threshold | 355 (70.9) | 48 (10 – 182) | 53 (42 – 66) |
| Above Census Bureau poverty threshold | 146 (29.1) | 31 (4 – 128) | 60 (47 – 70) |
| **Neighborhood Poverty (Age 10.5 years)**[*] | | | |
| First quartile (≥14.7% and ≤44.6%) | 129 (25.7) | 45 (6 – 155) | N/A |
| Second quartile (>44.6% and ≤57.0%) | 122 (24.4) | 81 (24 – 202) | |
| Third quartile (>57.0% and ≤69.7%) | 154 (30.7) | 33 (5 – 139) | |
| Fourth quartile (>69.7% and ≤92.8%) | 96 (19.2) | 14 (2 – 48) | |
| **Language of WISC-IV Assessment**[*†] | | | |
| English | 356 (71.1) | 46 (7 – 154) | 54 (45 – 70) |
| Spanish | 145 (28.9) | 18 (3 – 114) | 64 (52 – 70) |

[a] Continuous kilograms of toxicity-weighted OP/carbamate pesticide use within 1km of residence during pregnancy.

[b] Continuous percentage of households within child's census tract at age 10.5 that earn less than 200% of the Census Bureau poverty threshold

[*] $p < 0.05$ from Pearson's correlation, Wilcoxon rank-sum, or Kruskal-Wallis test assessing bivariate association between continuous toxicity-weighted OP/carbamate pesticide use within 1km of residence during pregnancy and maternal or child characteristic.

[†] $p < 0.05$ from Pearson's correlation, Wilcoxon rank-sum, or Kruskal-Wallis test assessing bivariate association between continuous neighborhood poverty rate at 10.5 years and maternal or child characteristic.

[‡] Bivariate associations assessed using continuous version of characteristic

## Table 3

Adjusted[a] regression coefficients and 95% confidence intervals for multivariable linear regression models assessing associations between categorical residential proximity to toxicity weighted[b] organophosphate and carbamate pesticide use during pregnancy and household and neighborhood poverty during childhood and WISC-IV scores (n = 501)

| | Full Scale IQ†‡ | Verbal Comprehension‡ | Perceptual Reasoning†‡ | Working Memory | Processing Speed |
|---|---|---|---|---|---|
| | β (95% CI) | β (95% CI) | β (95% CI) | β (95% CI) | β (95% CI) |
| **Pesticide Use Within 1km of Residence** | | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | Reference | Reference | Reference |
| Second Quartile | −0.3 (−2.9, 2.3) | −0.6 (−3.3, 2.1) | −0.5 (−4.0, 3.0) | −0.5 (−3.2, 2.2) | 1.0 (−2.0, 4.0) |
| Third Quartile | −0.7 (−3.4, 2.0) | −0.9 (−3.6, 1.9) | −1.9 (−5.5, 1.7) | 0.4 (−2.4, 3.2) | 1.1 (−2.0, 4.3) |
| Fourth Quartile (Highest Pesticide Use) | −3.0 (−5.6, −0.3) * | −1.3 (−4.1, 1.4) | −4.0 (−7.6, −0.4) * | −2.8 (−5.6, −0.1) * | −0.7 (−3.8, 2.4) |
| **Household Poverty** | | | | | |
| Above Federal Poverty Level | Reference | Reference | Reference | Reference | Reference |
| Below Federal Poverty Level | −2.4 (−4.5, −0.4) * | −2.3 (−4.5, −0.2) * | −1.0 (−3.8, 1.7) | −2.2 (−4.4, −0.1) * | −2.4 (−4.8, 0.0) |
| **Neighborhood Poverty** | | | | | |
| First Quartile (Lowest Poverty Rate) | Reference | Reference | Reference | Reference | Reference |
| Second Quartile | −0.6 (−3.2, 2.0) | −1.6 (−4.3, 1.1) | −1.1 (−4.7, 2.4) | −2.4 (−5.1, 0.4) | 3.8 (0.8, 6.9) * |
| Third Quartile | −0.7 (−3.2, 1.8) | 0.0 (−2.6, 2.6) | −1.9 (−5.3, 1.4) | −0.3 (−2.9, 2.3) | 0.9 (−2.0, 3.8) |
| Fourth Quartile (Highest Poverty Rate) | −4.0 (−6.9, −1.2) ** | −4.3 (−7.2, −1.3) ** | −4.4 (−8.2, −0.5) * | −3.6 (−6.6, −0.6) * | 1.0 (−2.3, 4.4) |

[a] All models adjust for maternal education, maternal intelligence, quality of home environment, maternal age at birth, breastfeeding duration, language of WISC assessment, and the psychometrician who conducted the cognitive assessment.

[b] Use was toxicity weighted using relative potency factors for AChE inhibition (U.S. Environmental Protection Agency, 2007, 2007).

[*] $p < 0.05$

[**] $p < 0.01$

[†] $p < 0.05$ from test for trend across quartiles of pesticide use within 1km of residence

[‡] $p < 0.05$ from test for trend across quartiles of neighborhood poverty

## Table 4

Adjusted[a] regression coefficients and 95% confidence intervals for multivariable linear regression models assessing categorical residential proximity to toxicity weighted[b] organophosphate and carbamate pesticide use during pregnancy within strata of household poverty status and interaction effects between ordinal quartiles of pesticide use and binary household poverty status.

| | At or Below Poverty Threshold (N = 355) | Above Poverty Threshold (N = 146) | | |
|---|---|---|---|---|
| | **β (95% CI)** | **β (95% CI)** | **β-int[c]** | **p-int[c]** |
| **Full-Scale IQ** | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | −0.9 | 0.34 |
| Second Quartile | 0.2 (−2.8, 3.3) | −1.3 (−6.7, 4.2) | | |
| Third Quartile | −0.3 (−3.6, 3.0) | −0.3 (−5.4, 4.8) | | |
| Fourth Quartile (Highest Pesticide Use) | −3.8 (−7.0, −0.5) * | −1.5 (−6.6, 3.7) | | |
| **Verbal Comprehension** | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | −0.8 | 0.44 |
| Second Quartile | −0.8 (−4.1, 2.4) | −1.6 (−6.9, 3.7) | | |
| Third Quartile | −0.5 (−4.0, 2.9) | −1.2 (−6.2, 3.8) | | |
| Fourth Quartile (Highest Pesticide Use) | −2.2 (−5.6, 1.3) | 0.9 (−4.1, 5.9) | | |
| **Perceptual Reasoning** | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | −0.6 | 0.64 |
| Second Quartile | 0.6 (−3.5, 4.7) | −1.5 (−8.9, 5.8) | | |
| Third Quartile | −1.6 (−6.0, 2.8) | 0.0 (−6.8, 6.8) | | |
| Fourth Quartile (Highest Pesticide Use) | −4.4 (−8.7, −0.1) * | −3.5 (−10.3, 3.4) | | |
| **Working Memory** | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | −1.2 | 0.23 |
| Second Quartile | −1.2 (−4.4, 2.0) | 2.2 (−3.8, 8.3) | | |
| Third Quartile | −0.1 (−3.5, 3.3) | 2.7 (−2.9, 8.3) | | |
| Fourth Quartile (Highest Pesticide Use) | −3.8 (−7.2, −0.5) * | −0.9 (−6.6, 4.7) | | |
| **Processing Speed** | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | −0.3 | 0.81 |
| Second Quartile | 2.6 (−1.0, 6.1) | −2.9 (−9.8, 4.0) | | |
| Third Quartile | 2.6 (−1.2, 6.4) | −2.0 (−8.4, 4.4) | | |
| Fourth Quartile (Highest Pesticide Use) | −0.9 (−4.6, 2.8) | −0.7 (−7.2, 5.7) | | |

[a] All models adjust for neighborhood poverty, maternal education, maternal intelligence, quality of home environment, maternal age at birth, breastfeeding duration, language of WISC assessment, and the psychometrician who conducted the cognitive assessment.

[b] Use was toxicity weighted using relative potency factors for AChE inhibition (U.S. Environmental Protection Agency, 2007, 2007).

[c] Coefficient and P-value for interaction effects between ordinal quartiles of pesticide use and binary household poverty status.

* $p < 0.05$

** $p < 0.01$

## Table 5

Adjusted[a] regression coefficients and 95% confidence intervals for multivariable linear regression models assessing categorical residential proximity to toxicity weighted[b] organophosphate and carbamate pesticide use during pregnancy within strata of neighborhood poverty status and interaction effects between the ordinal quartiles of pesticide use and ordinal quartiles of neighborhood poverty

| | Quartiles of Neighborhood Poverty Status | | | | | |
|---|---|---|---|---|---|---|
| | First Quartile (N = 129) | Second Quartile (N = 122) | Third Quartile (N = 154) | Fourth Quartile (N = 96) | | |
| | β (95% CI) | β (95% CI) | β (95% CI) | β (95% CI) | β-int[c] | p-int[c] |
| **Full-Scale IQ** | | | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | Reference | Reference | −0.1 | 0.89 |
| Second Quartile | 1.4 (−3.8, 6.5) | −0.1 (−7.3, 7.0) | −0.9 (−5.9, 4.1) | −0.6 (−6.2, 4.9) | | |
| Third Quartile | −2.1 (−7.0, 2.9) | 2.7 (−3.5, 9.0) | −1.8 (−7.3, 3.7) | −1.3 (−7.8, 5.1) | | |
| Fourth Quartile (Highest Pesticide Use) | 0.2 (−4.7, 5.2) | −2.3 (−8.6, 4.1) | −3.7 (−8.7, 1.2) | −2.4 (−9.8, 5.1) | | |
| **Verbal Comprehension** | | | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | Reference | Reference | −0.2 | 0.65 |
| Second Quartile | 2.8 (−2.7, 8.3) | 1.6 (−5.5, 8.8) | −3.1 (−8.2, 2.0) | −0.7 (−6.8, 5.3) | | |
| Third Quartile | 0.4 (−4.9, 5.7) | 2.0 (−4.3, 8.3) | −4.1 (−9.7, 1.5) | −1.1 (−8.1, 6.0) | | |
| Fourth Quartile (Highest Pesticide Use) | 3.3 (−2.0, 8.5) | −0.4 (−6.7, 5.9) | −2.6 (−7.7, 2.4) | −4.0 (−12.2, 4.1) | | |
| **Perceptual Reasoning** | | | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | Reference | Reference | 0.7 | 0.24 |
| Second Quartile | 0.0 (−7.8, 7.8) | 0.2 (−9.4, 9.9) | −0.8 (−7.1, 5.4) | −2.7 (−9.8, 4.4) | | |
| Third Quartile | −3.9 (−11.4, 3.7) | 2.0 (−6.5, 10.5) | −3.4 (−10.3, 3.5) | −1.1 (−9.4, 7.3) | | |
| Fourth Quartile (Highest Pesticide Use) | −4.5 (−12.0, 3.0) | −1.5 (−10.0, 7.1) | −5.7 (−11.9, 0.6) | | | |
| **Working Memory** | | | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | Reference | Reference | −0.2 | 0.71 |
| Second Quartile | −1.4 (−6.6, 3.8) | 0.5 (−5.8, 6.9) | 1.4 (−4.1, 6.9) | −0.7 (−7.1, 5.6) | | |
| Third Quartile | −2.9 (−7.9, 2.1) | 3.0 (−2.6, 8.6) | 4.2 (−1.9, 10.2) | −2.8 (−10.2, 4.6) | | |
| Fourth Quartile (Highest Pesticide Use) | −1.3 (−6.3, 3.7) | −1.8 (−7.4, 3.8) | −0.5 (−6.0, 5.0) | −2.8 (−11.3, 5.8) | | |
| **Processing Speed** | | | | | | |
| First Quartile (Lowest Pesticide Use) | Reference | Reference | Reference | Reference | −0.7 | 0.15 |
| Second Quartile | 2.0 (−4.4, 8.5) | −4.0 (−11.2, 3.1) | 0.9 (−5.3, 7.1) | 2.8 (−3.9, 9.5) | | |
| Third Quartile | 0.5 (−5.7, 6.7) | 1.9 (−4.4, 8.2) | −0.5 (−7.3, 6.2) | 1.5 (−6.3, 9.3) | | |

| | Quartiles of Neighborhood Poverty Status | | | | | |
|---|---|---|---|---|---|---|
| | **First Quartile (N = 129)** | **Second Quartile (N = 122)** | **Third Quartile (N = 154)** | **Fourth Quartile (N = 96)** | | |
| | **β (95% CI)** | **β (95% CI)** | **β (95% CI)** | **β (95% CI)** | **β-int**[c] | **p-int**[c] |
| Fourth Quartile (Highest Pesticide Use) | 4.6 (−1.5, 10.8) | −4.2 (−10.6, 2.1) | −1.8 (−7.9, 4.4) | −5.1 (−14.2, 3.9) | | |

[a] All models adjust for neighborhood poverty, maternal education, maternal intelligence, quality of home environment, maternal age at birth, breastfeeding duration, language of WISC assessment, and the psychometrician who conducted the cognitive assessment.

[b] Use was toxicity weighted using relative potency factors for AChE inhibition (U.S. Environmental Protection Agency, 2007, 2007).

[c] Coefficient and P-value for interaction effects between ordinal quartiles of pesticide use and ordinal quartiles of neighborhood poverty status.

* $p < 0.05$

** $p < 0.01$