Environmental Research 150 (2016) 128–137

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

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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ARTICLE INFO

Article history:
Received 3 March 2016
Received in revised form
5 May 2016
Accepted 27 May 2016
Available online 6 June 2016

Keywords:
agricultural
children
neurodevelopment
pesticides
poverty

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.
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.

1. 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).

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http://dx.doi.org/10.1016/j.envres.2016.05.048
0013-9351/

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.

2. Methods

2.1. 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.

2.2. 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