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Residential proximity to agricultural fumigant use and IQ, attention and hyperactivity in 7-year old children

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ABSTRACT

Objectives: Our objective was to examine the relationship between residential proximity to agricultural fumigant use and neurodevelopment in 7-year old children.

Methods: Participants were living in the agricultural Salinas Valley, California and enrolled in the Center for the Health Assessment of Mothers and Children Of Salinas (CHAMACOS) study. We administered the Wechsler Intelligence Scale for Children (4th Edition) to assess cognition and the Behavioral Assessment System for Children (2nd Edition) to assess behavior. We estimated agricultural fumigant use within 3, 5 and 8 km of residences during pregnancy and from birth to age 7 using California's Pesticide Use Report data. We evaluated the association between prenatal (n = 285) and postnatal (n = 255) residential proximity to agricultural use of methyl bromide, chloropicrin, metam sodium and 1,3-dichloropropene with neurodevelopment.

Results: We observed decreases of 2.6 points (95% Confidence Interval (CI): −5.2, 0.0) and 2.4 points (95% CI: −4.7, −0.2) in Full-Scale intelligence quotient for each ten-fold increase in methyl bromide and chloropicrin use within 8 km of the child's residences from birth to 7-years of age, respectively. There were no associations between residential proximity to use of other fumigants and cognition or proximity to use of any fumigant and hyperactivity or attention problems. These findings should be explored in larger studies.

1. Introduction

Methyl bromide, chloropicrin, metam sodium and 1, 3-dichloropropene (1,3-DCP) are common agricultural fumigants used primarily to reduce pathogens and pests in soil prior to planting crops. Approximately 44 – 51 million kilograms (kg) of these four fumigants are applied annually in the United States (Grube et al., 2011), and 13 million kg are applied annually in California (CDPR, 2016c), constituting one sixth of all pesticide use in California. Fumigants are more likely than other pesticides to drift from application sites due to their high vapor pressure (California Department of Pesticide Regulation, 2015, 2016a, 2016b). In 2012, California implemented a pesticide air monitoring network in several agricultural communities. Fumigants were frequently detected at each of the air monitoring sites, indicating repeated, low-level community exposures (CDPR, 2014). Acute human exposure to methyl bromide has produced symptoms including headaches, seizures, muscle weakness, memory problems (Bishop, 1992; Reidy et al., 1994), and neuropathy (Ben Slamia et al., 2006; Cavalleri et al., 1995). More attention and concentration problems have been reported in workers exposed to methyl bromide (Magnavita, 2009). Residents exposed to metam sodium after a train spill experienced increased psychological problems (e.g., depression and anxiety) (Bowler et al., 1994b). Symptoms of chloropicrin intoxication are also primarily neurologic, including tremors and seizures (TeSlaa et al., 1986). Although there is no evidence of neurotoxicity from limited human and animal research of 1,3-DCP (ATSDR, 2008), increased use of 1,3-DCP as a replacement for methyl bromide warrants further studies on the human health effects of this fumigant. A survey of pesticide related illnesses reported in 11 states from 1998 to 2006 found that soil applications of fumigants were responsible for the largest percentage of acute illnesses (45%) and non-occupational cases (61%) (Lee et al., 2011). In a risk assessment using California air monitoring data, these

Abbreviations: 1, 3-DCP, 1,3-dichloropropene; BASC-2, Behavioral Assessment System for Children 2; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CI, confidence interval; DAP, dialkyl phosphate; DDT, *p, p′*-dichlorodiphenyltrichloroethylene; DDE, *p, p′*-dichlorodiphenyldichloroethylene; HOME, Home Observation for Measurement of the Environment; IQ, intelligence quotient; OP, organophosphate; OR, odds ratio; PBDE, polybrominated diphenyl ether; PPVT, Peabody Picture Vocabulary Test; TVIP, Test de Vocabulario en Imagenes Peabody; WISC-IV, Wechsler Intelligence Scale for Children, 4th edition

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four high-use fumigants (methyl bromide, chloropicrin, metam sodium and 1,3-DCP) were the top four pesticides ranked in terms of chronic health risks and an estimated 5 million U.S. residents live in areas of high agricultural fumigant use (Lee et al., 2002).

Currently, there are no reliable biomarkers to assess human exposure to fumigants in epidemiologic studies (Hustinx et al., 1993; Magnavita, 2009; Verberk et al., 1979). Thus, residential proximity to fumigant use is currently the best method to characterize potential exposure. Since 1990, California has maintained a Pesticide Use Reporting (PUR) system which requires commercial growers to report all agricultural pesticide use to a one square mile (~259 ha) area (CDPR, 2016c). A study using PUR data showed that methyl bromide use within a 7 × 7 square mile area (~8 km radius) around monitoring sites explained 95% of the variance in methyl bromide air concentrations, indicating a direct relationship between nearby agricultural use and potential community exposure (Li et al., 2005). Several epidemiologic studies have used PUR data and observed associations between higher nearby agricultural pesticide use during pregnancy and adverse neurodevelopmental outcomes including birth defects (Carmichael et al., 2014; Rull et al., 2006; Yang et al., 2014), autism (Roberts et al., 2007; Shelton et al., 2014) and cognitive function (Gunier et al., 2016; Rowe et al., 2016).

We previously found that living within 5 km of methyl bromide use in the second trimester of pregnancy was associated with decreased birth weight, length, and head circumference (Gemmill et al., 2013). Methyl bromide was banned by the Montreal Protocol due to harmful effects on the ozone layer and is currently being phased out of use, resulting in increased usage of chloropicrin, metam sodium and1,3-DCP in recent years (CDPR, 2016c). In the present study, we investigate associations between residential proximity to agricultural use of four fumigants during the prenatal and postnatal periods and child neurodevelopment and behavior at age 7 in children participating in the Center for the Health Assessment of Mothers and Children of Salinas (CHAMACOS), a longitudinal birth cohort study of primarily low-income Latino families living in the agricultural community of the Salinas Valley, California.

2. Methods

2.1. Study population

We enrolled 601 pregnant women between October 1999 and October 2000 as part of the CHAMACOS study. Women were eligible if they were ≥ 18 years of age, < 20 weeks gestation, eligible for California's subsidized low-income prenatal health care, spoke English or Spanish, and were planning to deliver at the county hospital. We followed the women through the delivery of 537 live born children. We excluded children with medical conditions that could affect neurodevelopmental assessment (n = 4, one child each with Downs syndrome, autism, deafness, and hydrocephalus). We included children who had a neurodevelopmental assessment at age 7 (n = 336) and excluded two participants who did not have prenatal measurements of dialkyl phosphate (DAP) metabolites of organophosphate pesticides (OPs) because a previous analysis in this cohort found that DAPs were associated with neurodevelopment (Bouchard et al., 2011). For analyses of proximity to fumigant use, we included participants whose residential location was known for at least 80% of the time during pregnancy (n = 285) for the prenatal period and from birth to the 7-year neurodevelopmental assessment (n = 255) for the postnatal period. Written informed consent was obtained from all women and oral assent from all children at age 7; all research was approved by the University of California, Berkeley, Committee for the Protection of Human Subjects prior to commencement of the study.

2.2. Maternal interviews and assessments

Bilingual interviewers conducted maternal interviews in Spanish or English twice during pregnancy (~13 and 26 weeks gestation), after delivery and when the children were 6 months and 1, 2, 3.5, 5 and 7-years of age. Interviews obtained demographic information including maternal age, education, country of birth, number of years lived in the United States, marital status, paternal education, and family income. We collected residential history information by asking participants if they had moved since the last interview and, if so, the dates of all moves. We conducted home visits shortly after enrollment (~16 weeks gestation) and when the child was 6 months and 1, 2, 3.5 and 5-years of age. For each visit, latitude and longitude coordinates of the participant's home were determined using a handheld global positioning system unit.

Mothers were administered the Peabody Picture Vocabulary Test (PPVT) for English speakers or the Test de Vocabulario en Imagenes Peabody (TVIP) for Spanish speakers at the six-month visit to assess verbal intelligence (Dunn and Dunn, 1981). If maternal PPVT or TVIP scores were unavailable from the 6-month visit, we used scores from the re-administration of the test conducted at a 9-year visit (n = 5) or assigned the mean score of the sample (n = 2). A short version of the HOME (Home Observation for Measurement of the Environment) inventory was completed during the 7-year visit (Caldwell and Bradley, 1984).

2.3. Cognitive and behavior assessments

We assessed cognitive abilities when the children were 7-years of age using the Wechsler Intelligence Scale for Children, 4th edition (WISC-IV) (Wechsler, 2003). All assessments were completed by a single bilingual psychometrician, who was trained and supervised by a pediatric neuropsychologist. Index scores for four domains were calculated based on the following subtests: Verbal Comprehension (composed of Vocabulary and Similarities subtests), Perceptual Reasoning (Block Design and Matrix Reasoning subtests), Working Memory (Digit Span and Letter-Number Sequencing subtests), and Processing Speed (Coding and Symbol Search subtests). We administered all subtests in the dominant language of the child using either the WISC-IV English or Spanish edition, which was determined through administration of the oral vocabulary subtest of the Woodcock–Johnson/Woodcock–Munoz Tests of Cognitive Ability (Woodcock and Munoz-Sandoval, 1990) in both English and Spanish at the beginning of the assessment as recommended in the WISC-IV Spanish Manual. The psychometrician was blinded to exposure status. We standardized WISC-IV scores against U.S. population–based norms for the English and Spanish versions of WISC-IV. We did not administer Letter-Number Sequencing or Symbol Search subtests for the first 3 months of assessments, therefore 27 participants lack scores for Processing Speed and Working Memory domains. A Full-Scale IQ was available for 255 children.

Children's behavior was assessed by maternal and teacher report at age 7 using the Behavior Assessment System for Children 2 (BASC-2) (Reynolds, 2004). The behavior assessments were interviewer-administered to the mother (due to low literacy rates) and self-administered by the child's teacher. The BASC-2 has been validated in English and Spanish. The BASC-2 Parent Rating Scale asks how often the child exhibits certain behaviors in the home setting (160 questions), while the Teacher Rating Scale asks about similar behaviors at school (139 questions). Scales of interest from the BASC-2 were hyperactivity and attention problems. Standardized T-scores were computed using age-standardized national norms, with higher values indicating more frequent problem behaviors.

2.4. Geographic-based estimates of agricultural fumigant use

To characterize potential exposure, we estimated agricultural