Neurotoxicology and Teratology 34 (2012) 534–541

Contents lists available at SciVerse ScienceDirect

Neurotoxicology and Teratology

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

Does the home environment and the sex of the child modify the adverse effects of prenatal exposure to chlorpyrifos on child working memory?

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ARTICLE INFO

Article history:
Received 1 March 2012
Received in revised form 10 July 2012
Accepted 16 July 2012
Available online 21 July 2012

Keywords:
Chlorpyrifos
Neurodevelopment
Working memory
HOME inventory
Sex-specific

ABSTRACT

Prenatal exposure to chlorpyrifos (CPF), an organophosphorus insecticide, has long been associated with delayed neurocognitive development and most recently with decrements in working memory at age 7. In the current paper, we expanded the previous work on CPF to investigate how additional biological and social environmental factors might create or explain differential neurodevelopmental susceptibility, focusing on main and moderating effects of the quality of the home environment (HOME) and child sex. We evaluate how the quality of the home environment (specifically, parental nurturance and environmental stimulation) and child sex interact with the adverse effects of prenatal CPF exposure on working memory at child age 7 years. We did not observe a remediating effect of a high quality home environment (either parental nurturance or environmental stimulation) on the adverse effects of prenatal CPF exposure on working memory. However, we detected a borderline significant interaction between prenatal exposure to CPF and child sex (B (95% CI) for interaction term = −1.714 (−3.753 to 0.326)) suggesting males experience a greater decrement in working memory than females following prenatal CPF exposure. In addition, we detected a borderline interaction between parental nurturance and child sex (B (95% CI) for interaction term = 1.490 (−0.518 to 3.499)) suggesting that, in terms of working memory, males benefit more from a nurturing environment than females. To our knowledge, this is the first investigation into factors that may inform an intervention strategy to reduce or reverse the cognitive deficits resulting from prenatal CPF exposure.

1. Introduction

1.1. Background

Chlorpyrifos (CPF) is an organophosphorus (OP) insecticide widely recognized for its neurotoxic properties and effectiveness at eliminating household pests including cockroaches. Once the leading insecticide used throughout the Unites States in residential and agricultural settings, widespread use resulted in ubiquitous exposure (Landrigan et al., 1999; Whitemore et al., 1994) until the US EPA curtailed its residential use in 2001 (U.S. EPA, 2000). Previous studies have reported that prenatal and early childhood exposure to OP insecticides, including CPF, is associated with indicators of delayed neurodevelopment (Berkowitz et al., 2004; Engel et al., 2007; Eskenazi et al., 2007; Guillette et al., 1998; Lizardi et al., 2008; Young et al., 2005). Most recently, results from three separate longitudinal birth cohort studies demonstrate that prenatal exposure to OP insecticides is negatively associated with cognitive development at 7-years of age (Bouchard et al., 2011; Engel et al., 2011; Rauh et al., 2011). Rauh et al. (2011) reported evidence of deficits in 7-year working memory and full scale IQ scores as a function of prenatal CPF exposure (Rauh et al., 2011). Working memory is one of the core processes of executive function. It encompasses the ability to memorize new information, hold it in short-term memory, concentrate, and manipulate information to produce results (Baddeley and Logie, 1999; Smith and Jonides, 1997). Insufficient development of executive functioning during early childhood has been associated with an array of adverse outcomes including psychopathology (Pennington and Ozonoff, 1996), increased physical aggression (Tremblay et al., 2005), cortisol reactivity (Blair et al., 2005), and lack of school readiness (Blair, 2002).

It is recognized that biologic and social factors interact to affect neurologic development in children (Escanola, 1982), including the development of executive functions such as working memory (Diamond, 2009). The quality of the home environment is a particularly important social factor that predicts child neurodevelopment. Numerous prior studies demonstrate associations between the home environment and child cognition, including assessment among groups that differed by ethnicity, socioeconomic status, child weight, child disabilities, maltreatment and/or exposures to neurotoxicants (Bradley, 1993). Intervention studies suggest that improving the quality of the home environment can improve child cognitive performance (Wasik et al., 1990). The Home Observation for the Measurement of the Environment (HOME) (Caldwell and Bradley,

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doi:10.1016/j.ntt.2012.07.004

1984) is a well-validated instrument for assessing the quality of the home environment. It was designed to assess a child's physical, intellectual, and emotional milieu through both direct observation and unstructured interview with the child's primary caregiver. Notably, the HOME scale includes subscales measuring specific aspects of the child's home life such as parental nurturance and environmental stimulation. Farah et al. (2008) used the HOME scale to demonstrate that these different aspects of the home environment affect different components of cognitive development in humans (Farah et al., 2008). Parental nurturing was associated with improved working memory while environmental stimulation facilitated improved language development. In the current study, we evaluate whether specific aspects of the home environment can remediate the adverse effects of environmental toxicants on children's cognitive development.

There is growing evidence that child sex is also an important determinant of behavior and cognition. Research has shown that developing males and females respond differently to the effects of chemical stressors (e.g. polychlorinated biphenyls) and nonchemical stressors (e.g. poverty) on child behaviors (Weiss, 2002; Werner and Ruth, 1992). In the guinea pig, prenatal social stress resulted in elevated cortisol levels in male offspring with no effect in female offspring (Kaiser and Sachser, 1998, 2001). While clinical evidence suggests males are generally more susceptible to infectious disease, hypertension (cardiovascular disease), and aggressive behaviors (Wang et al., 2007), it is less clear how sex may influence the impact of toxicant exposure on developmental outcomes. In a recent epidemiologic study examining the impact of prenatal exposure to phthalates, common plasticizers, on reproductive development, adverse effects were only observed in male children (Swan et al., 2005). Conversely, in a study examining the impact of bisphenol A (BPA) exposure on behavior in children, effects were observed especially among female children (Braun et al., 2011). Notably, many studies of the adverse effects of endocrine disrupting compounds on cognition and behavior do not investigate differential effects in males vs. females (Engel et al., 2009; Whyatt et al., 2012). In general, the evaluation of child sex as a potential effect modifier of the effects of environmental toxicants on child development has received little attention in epidemiologic studies to date (Schwartz, 2003; Vahter et al., 2007a,b).

In the current study, we built on our prior investigation of prenatal CPF exposure (Rauh et al., 2011) to evaluate how the quality of the home environment (specifically, parental nurturance and environmental stimulation) and child sex interact with the adverse effects of prenatal CPF exposure on working memory at child age 7 years. We hypothesize that a nurturing home environment may moderate the adverse effects of prenatal CPF exposure on children's working memory at age 7. Further, we hypothesize that the moderation effect may be stronger in males than in females.

2. Methods

2.1. Participants

The sample consisted of 335 mother–child pairs selected from an ongoing prospective cohort study (Columbia Center for Children's Environmental Health) of inner-city mothers and their children (Perera et al., 2002). The larger parent cohort (N = 725), enrolled between 1998–2006, comprised pregnant women age 18–35 years who self-identified as either African-American or Dominican, did not smoke, were low-risk pregnancies (classified as free of diabetes, hypertension, and known HIV infection), lived in the designated neighborhoods for at least one year, and had registered at the Obstetrics and Gynecology prenatal clinics at New York Presbyterian Medical Center or Harlem Hospital by the 20th week of pregnancy. All participants gave informed consent and the Institutional Review Board of Columbia University approved the study.

For the current study, we selected all offspring from this cohort who had reached age 7 at the time of this analysis and had complete data in the following areas: maternal prenatal and 7-year interview; biomarkers of prenatal CPF exposure, HOME assessment completed at 3 years of age; and WISC-IV administered at 7 years of age. The characteristics of this subsample are presented in Table 1. In general, the 335 subjects selected for the current study did not differ from the full parent cohort with respect to demographic characteristics.

2.2. Maternal interview and HOME assessment

Mothers were interviewed in the 3rd trimester of pregnancy and annually thereafter by a trained bilingual interviewer. Interviews included questions about demographics; residential history; living conditions; maternal education; maternal income and employment; illness, alcohol and drug use during pregnancy; and chemical exposures, including pesticides, polycyclic aromatic hydrocarbons (PAHs), lead and environmental tobacco smoke (ETS).

Children's home environments were evaluated at 3 years of age (mean = 3.6 years; range = 1.1–6.3 years) using the HOME Inventory (Bradley, 1993; Caldwell and Bradley, 1984). The HOME Inventory is an unstructured 1-hour observational interview administered by a trained researcher and widely used as a predictor of child intelligence and achievement (Bradely et al., 1989). The 55-item checklist is divided into eight subscales. Based on previous literature employing the HOME inventory to examine the association between childhood experience and cognitive development (Farah et al., 2008), we divided the 8 subscales into two composite scales, Environmental Stimulation and Parental Nurturance. The Environmental Stimulation variable was created by summing the z-scores of the Learning Materials, Language Stimulation, Academic Stimulation, and Variety subscales, which measure the availability of intellectually stimulating materials in the home and the mother's encouragement of learning. The Parental Nurturance variable was created by summing the z-scores of the Responsivity, Modeling, and Acceptance subscales, which measure such maternal behaviors as attentiveness, displays of physical affection, encouragement of delayed gratification, limit setting, and the ability of the mother to control her negative reactions.

In addition to the primary predictors included in the final models described below, we examined other maternal toxicant exposures with the potential to impact children's cognitive development including prenatal exposure to PAHs (Perera et al., 2006), ETS (Eskenazi and Castorina, 1999), and lead (Lanphear et al., 2005). PAHs were measured in personal

Table 1
Demographic characteristics of the study population, New York City, 2009–2010 (N = 335).

Characteristics	N	%
Family income		
<$20,000	172	51.3
≥$20,000	163	48.7
Maternal education (years)		
<12 years	230	68.7
≥12 years	105	31.3
Race/ethnicity		
Dominican	132	39.4
African American	203	60.6
	Median	Range
Prenatal CPF (ng/g)	0.36	0.25–32.1
	Mean	SE
HOME score (total score)	39.8	0.34
WISC_IV*		
Full Scale IQ	99.3	0.70
Working memory	98.3	0.77
Perceptual reasoning	100.5	0.75
Verbal comprehension	96.97	0.65
Processing speed	102.0	0.87

* Wechsler Intelligence Scale for Children, 4th edition, composite scores of We.