Fetal exposure to propoxur and abnormal child neurodevelopment at 2 years of age

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Abstract

Objective—Our aim was to determine the effects of fetal exposure to propoxur and pyrethroids, on child neurodevelopment at 2 years of age.

Patients and Methods—Mothers were prospectively recruited during mid-pregnancy in Bulacan, Philippines where multiple pesticides including propoxur, cyfluthrin, chlorpyrifos, cypermethrin, pretilachlor, bioallethrin, malathion, diazinon and transfluthrin are used. To detect prenatal exposure to these pesticides, maternal hair and blood, infant's hair, cord blood, and meconium were analyzed for the pesticides by gas chromatography/mass spectrometry. Infants were examined at 2 years of age with 95.1% follow up rate and their neurodevelopment outcome was assessed by the Griffiths Mental Developmental Scale (N=754).

Results—Meconium analysis was the most sensitive method to detect fetal exposure to pesticides and exposure was highest for propoxur (21.3%) and the grouped pyrethroids (2.5% - bioallethrin, transfluthrin, cyfluthrin and cypermethrin). Path analysis modeling was performed to determine the effects of fetal exposure to propoxur and pyrethroids on the child's neurodevelopment at 24 months of age while controlling for confounders. Only singletons and those with complete data for the path analysis were included (N=696). Using a path analysis model, there was a significant negative (β= −0.14, p<0.001) relationship between prenatal pesticide exposure to propoxur and motor development at 2 years of age after controlling for confounders, e.g., infant gender, socioeconomic status, maternal intelligence, home stimulation (HOME), postnatal exposure to propoxur and blood lead level at 2 years of age.

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Conclusion—At 2 years of age, prenatal exposure to propoxur was associated with poorer motor development in children.

Introduction

There is such widespread use of pesticides that human exposure to these compounds is inevitable (USEPA, 2009; Waliszewski et al., 1998). Pesticide exposure in women while pregnant is a major concern, since most pesticides are neurotoxicants and the brain of the fetus and newborn infants are highly vulnerable to these toxicants due to the rapid growth and development of their brain (Bruckner, 2000; Eriksson, 1997; Barone et al., 2000), higher dose of pesticides per body weight (Weiss 2000) and lower activity and levels of enzymes that detoxify the pesticides (Holland et al. 2006). Although the recognizable effects of maternal exposure to low doses of environmental pesticides are minimal, serious concerns have been raised about their adverse effects on the fetus, particularly on subsequent neurodevelopmental, learning and behavioral difficulties in the children. A number of studies on prenatal exposure to organophosphate pesticides have been found to be associated with increased number of abnormal reflexes in newborn infants as assessed by the Brazelton Neonatal Behavioral Assessment Scale (Engel et al. 2007; Young et al. 2005). In young children, prenatal and/or postnatal exposure to organophosphates have been associated with decreased scores on the Stanford-Binet copying test, mean reaction time, poorer short term memory, executive function and lower MDI and PDI scores on the Bayley Scales of Infant Development term memory (Eskenazi et al. 2007; Handal et al. 2008; Rauh et al. 2006, Bouchard et al. 2010; Grandjean et al. 2006; Ruckart et al. 2004; Eskenazi 2007). The carbamates are another class of pesticides that have been increasingly used worldwide. Carbamates, e.g., propoxur, are similar to organophosphates in their action of inhibiting acetylcholinesterase, but unlike organophosphates, the carbamates are transient cholinesterase inhibitors and are hydrolyzed from the cholinesterase enzymatic site within 48 hours (Bjorling et al., 2008). Thus, carbamate toxicity tends to be of shorter duration compared to the organophosphates, although the mortality rates associated with exposure to these chemical classes are still similar (Rotenberg et al., 1995). Due to their lower toxicity and shorter half life, carbamates have been used widely in place of organophosphates, particularly for home pesticides. However, despite their widespread use, there has been no information on the reproductive or developmental effects of propoxur in humans, particularly on the fetus, newborn infant and young children (USEPA 1989; USEPA 1999) In a few animal studies on rats orally exposed to propoxur, fetotoxic effects e.g., decreased numbers of pups, and depressed fetal weight have been reported. Most studies on the adverse developmental effect of fetal or early childhood exposure to cholinesterase inhibitor pesticides have been on the organophosphates (Rosas & Eskenazi 2007). On the other hand, a review of the literature through PubMed has revealed no study dealing with the adverse effects of pre- and postnatal exposure to propoxur on the children's neurodevelopment. In the Philippines, the use of carbamate is widespread, particularly for home pesticides. The aim of this study is to report on the prevalence of prenatal and early childhood exposure to the carbamate pesticide, propoxur and its adverse effect on the neurodevelopment of children at 2 years of age.

Materials and Methods

Pesticide

Exposure Pregnant women were prospectively enrolled into the study at midgestation at the Bulacan Provincial Hospital (BPH) outpatient clinic. Bulacan is an agro-industrial province of the Philippines. A preliminary survey of the study area showed predominant use of the following pesticides at home or in the farm: cyfluthrin/propoxur (73%), chlorpyrifos (37%), cypermethrin (31%), pretilachlor (28%), bioallethrin (26%), malathion (15%), diazinon

(12%) and transfluthrin (11%). This study was approved by the Human Investigation Committee at Wayne State University, the University of the Philippines and the Bulacan Provincial Hospital. Informed consent was obtained from the mothers for themselves and their infants. Maternal blood and hair were obtained at midgestation and at birth cord blood, meconium, and infant hair were collected after birth to analyze for the above pesticides, including lindane and DDT. Pesticide analysis was by gas chromatography/mass spectrometry (GC/MS) using previously published procedures (Bielawski et al., 2005; Corrion et al., 2005; Ostrea et al., 2006, Posecion et al 2006).

Neurodevelopmental Outcome

The Griffiths test assesses five developmental scales: motor, social, hearing/language, eye/hand coordination and performance (Griffiths 1976; Huntley 1996). Based on the literature (Diamond A, 2007, Rendeli et al 2002, Burns et al 2004, Hart et al 2004, Bloom et al 2001) we choose three factors to represent neurodevelopment at 24 months. All three factors were from the Griffith Mental Development Scales (Griffiths 1976; Huntley 1996) 1) Locomotor subscale (gross motor development including balance and coordination of movements), 2) social development (Personal-Social [daily activities and child interaction] and Language subscales [receptive and expressive language]), and 3) Performance subscale (visuospatial skills and reaction time).

Neurobehavioral development of the children was assessed by the Griffiths Mental Developmental Scale (Griffiths 1976; Huntley 1996) by one of three Griffiths certified, developmental pediatricians at 24 months. Their inter-rater agreement by Cohen's kappa was 0.8525 (p<0.0001).

Covariates

Several potential confounders to the child's neurodevelopmental performance were also evaluated including infant's gender, maternal intelligence (assessed by a modified WAIS-III performance subscale; Wechsler 1981), status of the home stimulation of the child (Home Observation for Measurement of the Environment [HOME]; Caldwell & Bradley, 1984) and socioeconomic status ([SES] Roberto Scale; Roberto, 2002). The Roberto scale is widely used in the Philippines and is based on home structure and appearance. The scale ranges from A (highest) to E (lowest).

Prior to study inclusion, the validity of the WAIS-III for use this the study population was performed to determine subtests that were suitable for the study population. A group of 30 females that were not among the current subjects but from the same population were administered the performance subtest of the WAIS-III. Based on their performance scores, the following subtests were selected to comprise the short form for computing the performance IQ: Picture completion, matrix reasoning, picture arrangement and object assembly. For the Griffiths test, covariates included postnatal exposure to propoxur by hair analysis of the children, and serum lead at 24 months.

Statistical analysis

Mean (standard deviation) and frequency distribution were calculated to describe the demographic and socioenvironmental characteristics of the study population. Comparisons were made between pesticide exposed and non-exposed infants on multiple demographic/socioenvironmental characteristics as well as the infant's gestation, birth weight, length, and head circumference by the Student t-test or Mann-Whitney test for continuous variables and the Pearson's chi-square analysis or Fisher's Exact Test for categorical variables.

Structural Equation Modeling using LISERL 8.72 was performed to determine the effects of fetal exposure to pesticides (as determined by meconium analysis) on the child's neurodevelopment at 24 months as assessed by the Griffiths test while controlling for the following confounders: infant gender, socioeconomic status, maternal intelligence and HOME. Chlorpyrifos, pretilachlor, malathion, diazinon, lindane and DDT were excluded in the outcome analysis since only a few matrices were positive (<1.0 %) for these pesticides. Similarly, due to the very low prevalence of pyrethroids (2.5%), we preliminarily assessed the relationship of these pesticides with 24 month neurodevelopment before the structural equation model was tested. No significant bivariate relationships between pyrethroids and neurodevelopment at 24 months were found. As a result of the low prevalence and non-significant results, these pesticides were also excluded from the path analysis. Model fit was assessed using the comparative fit index (CFI), root mean square error of approximation (RMSEA) and 90% confidence interval for RMSEA. CFI> 0.95 and RMSEA <0.06 indicate a good fitting model (Hu & Bentler, 1999). Due to non-normality in the data the Satorra-Bentler scaled chi-square was used (Satorra & Bentler, 1994). Paths that were not significant at p 0.05 were removed from the model unless there were strong theoretical reasons for including them. Modifications to the model were based on both substantive clinical and statistical grounds. For the final model, results are reported as standardized regression coefficients. Prior to performing the path analysis, SPSS version 19 was used to assess the assumptions of linearity and multivariate normality. To identify multivariate outliers Mahalanobis distance, which is a measure of the multivariate distance of a case from the centroid of all other cases, was used (Tabachnick & Fidell, 2007). Mahalanobis distance can be evaluated using a χ^2 statistic. The probability of the χ^2 statistic is an indication of the probability that the values for that case come from the same multivariate distribution of the other cases. A criteria of $p < 0.001$ was used to indicate multivariate outliers. Cases with $p < 0.001$ have a very small probability of coming from the same multivariate distribution as the other cases. Using this criterion multivariate outliers were removed from the data set. An iterative process was used to clean the data. To reduce the influence of outlying cases, univariate outliers were winsorized and extremely skewed variables transformed.

Results

A total of 793 mother/infant dyads were initially enrolled at birth and 754 dyads (95.1%) were successfully followed up to 2 years of age. Among those not assessed at follow up (N=39), six children were deceased, 29 could not be located, and four mothers voluntarily withdrew from the study. The only significant difference between the 754 mother/infant pairs assessed at 2 years and those not assessed was marital status. Those not assessed were less likely to be married (43.6% vs 73.6%, p<0.03).

Of the 754 mother/infant pairs, only singletons were included in the analysis (N=741). Nine cases were identified as multivariate outliers among the set of predictors and outcomes using Mahalanobis distance, $p < 0.001$. The multivariate outliers were removed from the dataset leaving 732 cases. Overall only 1.3% of all data were missing. Complete data were available for 590 cases. Cases missing data on more than 25% of the variables of interest were dropped from further analyses (N = 9). Of the remaining data, 133 cases were missing data on at least one variable. Missing data were then imputed using PRELIS 2.52. Data could not be imputed for 27 cases leaving 697 cases with complete data after imputation. The data were then imported back into SPSS and a second evaluation for multivariate outliers was performed. One additional case was identified as a multivariate outlier and removed leaving a final data set of 696 cases with complete data for the path analysis.

From an initial survey of the study site, the predominant pesticides that were used in the homes included propoxur, cyfluthrin, bioallethrin, transfluthrin and chlorpyrifos. The

principal farm pesticides were chlopyrifos, cypermethrin, pretilachlor, malathion and diazinon. The prevalence of pesticide exposure based on the analysis of maternal hair, maternal blood, cord blood, infant hair or meconium obtained at birth, is shown in Table 1. Although most pesticides were detected in the various matrices, the prevalence of chlorpyrifos, pretilachlor, malathion, diazinon, lindane and DDT was <1.0% (Ostrea el al, 2009) and are excluded from the table and outcome analysis. Cyfluthrin, bioallethrin, transfluthrin and cypermethrin belong to the family of pyrethoids and are presented as a group because of similarity in their pharmacologic action. The number of samples was comparatively less for cord blood and meconium because cord blood was not obtained in those infants born at home or in an outside hospital. For meconium, some samples were insufficient in amount for analysis. The highest rate of pesticide exposure (Table 1) was to propoxur (21.3% in meconium and 21.1% in maternal hair) and to pyrethroids (2.5% in meconium and 13.9% in maternal hair), especially bioallethrin. In a previous publication, we compared pesticide exposure in subjects who had all five matrices available for analysis and the highest rate of pesticide exposure was detected in meconium followed by maternal hair (Ostrea et al., 2009). Thus, meconium and maternal hair are ideal matrices to analyze for prenatal exposure to pesticide.

Relation between exposure and neurodevelopment

To determine the relationship between fetal exposure to pesticide and the child's neurodevelopment at 2 years of age, fetal exposure to pesticide was based on meconium analysis, because meconium is a sensitive matrix to analyze for prenatal exposure to pesticide and, because, unlike maternal hair, meconium is produced by fetal tissue and therefore representative of fetal exposure to the pesticides. The demographic characteristics of the mother/infant dyads of this subgroup (N=680) are shown in Table 2. There were no significant differences in maternal and infant demographic characteristics or pregnancy complications in the pesticide-exposed versus non-exposed infants. Birth weight, head circumference, length and gestation were not significantly different between groups. The characteristics of the home and environment are shown in Table 3 and were not significantly different in the exposed versus non exposed groups except for a higher use of water seal toilet in the exposed group (87.4% versus 80.1%, p<0.04) and a higher use of well water in the unexposed group (44.9% versus 34.8%, p=0.02). Overall, there was an high (>90%) prevalence of flies, roaches and mosquitoes in the homes of both groups the subjects and the overall use of home pesticide was reported from 16.8% of the homes.

The final path model showing the effects of fetal exposure to environmental pesticides on child's neurodevelopment is shown in Figure 1. Only variables that were significantly related to neurodevelopmental outcome were included in the figure. Standardized coefficients are presented. Overall, model fit was excellent χ^2 (27, n=696) = 52.35, p=0.0006, RMSEA=0.037 (90%CI, 0.021–0.052), and CFI=0.98.

Direct effects on neurodevelopment

Exposure to propoxur was negatively related to motor development (β= −0.14, p<0.001), but was unrelated to social and performance development. Other variables were related to neurobehavioral development at 24 months. The HOME score (β=0.10, p=0.006), and infant gender with boys scoring higher than girls (β= −0.11, p=0.004) were related to motor development. Along with exposure to propoxur, the HOME score and gender accounted for 4% of the total motor development variance. Social development was predicted by 2-year lead exposure (β=−0.08, p=0.03), the HOME score (β=0.19, p<0.001), infant gender (girls scored higher than boys) (β=0.22, p<0.001), and maternal IQ (β=0.13, p<0.001). These variables accounted for 12% of social development variance. For performance development the related variables were HOME (β=0.20, p<0.001), infant gender, with girls scoring higher

than boys (β=0.09, *p*=0.046) and maternal IQ (β=0.11, *p*=0.01). These variables accounted for 7% of performance development variance.

Indirect and Total Effects

In addition to the direct effects listed above, the following variables had indirect effects on 24 month neurobehavioral development that were mediated by other study variables. SES had significant indirect effects on motor (β=0.02, *p*=0.02), social (β=0.06, *p*<0.001) and performance development (β=0.05, *p*<0.001). The effects of SES on development were mediated through lead exposure and HOME environment. In addition to its direct effects on development, maternal IQ also had significant indirect effects on motor (β=0.02, *p*=0.02), social (β=0.04, *p*<0.001) and performance development (β=0.04, *p*=0.002). The indirect effects of maternal IQ on development were mediated through the HOME environment.

Discussion

This prospective, cohort study of fetal exposure to environmental pesticides, specifically propoxur and pyrethroids, and their potential adverse effects on the neurodevelopment of the children at 2 years of age is the first study to examine five matrices (maternal hair, maternal blood, cord blood, infant hair and meconium) to determine antenatal pesticide exposure: As previously reported (Ostrea et al., 2009), meconium was found to have the highest positive rate to pesticides. This is consistent with the high detection rate of many xenobiotics in this matrix including licit and illicit drugs, nicotine metabolites and alcohol metabolites (Ostrea et al., 1999). The repository nature of meconium provides a wide window of xenobiotic exposure. Meconium is first formed at around the third or fourth week of gestation, thus, most xenobiotics that the fetus is exposed to during gestation are deposited in meconium through fetal swallowing and/or bile secretion (Ostrea et al., 1989). Since meconium, unlike fetal urine, is not normally excreted in utero, compounds that deposit in meconium accumulate and increase in concentration, thus enhancing their detection after birth.

The high exposure rate to <u>home pesticides</u>, even in an agricultural area such as Bulacan, is likely due to the high prevalence of flies, roaches and mosquitoes in the area. This observation parallels reports of high exposure rate to home pesticides among pregnant women and their infants residing in urban areas (Whyatt et al., 2003; Whyatt et al., 2004; Ostrea et al., 2002). Thus, whether in urban or rural areas, pesticide use is widespread and constitutes a serious health risk in pregnant women. In our study, spray pesticides were commonly used, principally Baygon™ (91.5%) which contains propoxur and cyfluthrin. Organophosphates were of low prevalence because they were not the common pesticides used at home. Improper use of these home pesticides was evident in a subgroup study showing that 39.9% of the spraying was done by the pregnant woman, themselves and reentry time to the sprayed area was   60 minutes in 73.2% of the cases. Poor education and inadequate labeling regarding the safe use of the pesticide were major reasons for their improper use.

The effects of prenatal exposure to pesticides on the neurodevelopmental outcome in the children was assessed at 24 months of age by the Griffiths Mental Development Scales since several investigators have suggested that the effects of prenatal exposures may not be obvious in early life (Waddington et al., 1957; Scarr-Salapetek, 1976; McCall 1981). Neuronal plasticity, which is the ability of the nervous system to continue to remodel and change throughout the developmental period in response to environmental insults (Rice & Barone, 2000; Barone et al., 2000; Bourgeois et al., 1993; Rakic et al., 1986; King et al., 1991) may act as a temporary compensating mechanism to interference in brain development and anatomical and functional effects of developmental insults may be subtle at early life but become apparent at later ages (Rice 1996; Qiao et al., 2002; Qiao et al.,

2003). We also chose to not examine the global overall Griffith's score (general quotient) but instead, to examine subfactors to see if there was a differential influence of pesticide exposure on specific neurodevelopmental outcomes. Since motor ability may influence performance in the cognitive, social, and performance domains, especially true in risk populations, (Rendeli et al., 2002; Burns et al., 2004) we chose to assess motor individually. As the literature has suggested there is a relation between sociability and language, (Diamond, 2007; Hart et al., 2004; Bloom et al., 2001; Carpenter, et al., 1998;), we chose to examine these scales as a single social/language factor and since both the Griffiths hand/eye coordination subscale and the performance subscales are performance measures we examined them as a single factor labeled performance.

Our results show that propoxur has a significant adverse effect on the Griffiths motor subscale at 24 months. This is important since motor development determines the sequence in which certain perceptual, language and cognitive abilities unfold. (Bushnell et al., 1993; Webster R et al., 2005; Diamond A, 2007). In a study of 378 children at age 5–6 years, quantitative and qualitative aspects of motor performance were related to several aspects of cognition, after controlling for the influence of attention (Wassenberg at al., 2005). Motor development is one of the earliest functions to develop in children. A study of Griffiths test among Filipino children at 24 months (Reyes et al., 2010), showed a relatively higher mean subquotient scores in motor tasks, self-help and social which coincide with developmental expectations during infancy, which is basically to develop ambulation and an awareness of their surroundings (First & Palfrey 1994). Mean subquotient in hearing and language have been found to be among the lowest, as emergence of speech is not generally expected until just before the toddler years (Capute & Accardo 1996). The early development of motor function in children may be a reason why adverse effect of prenatal exposure to propoxur was evident in motor compared to other functions (social and performance). However, because of delayed neurotoxicity, adverse effects on other neurobehavioral functions may occur later. Thus, it is important that follow up of the children is made which is what we are currently doing.

The influence of other factors on motor development were also observed in this study, such as HOME and infant gender. For social development the related variables were two year lead exposure, the HOME score, infant gender, and maternal IQ. For performance development the related variables were the HOME score, infant gender, and maternal IQ.

This is the first study to report on the adverse effect of propoxur, a carbamate, on the child's neurodevelopment. The strengths of this study are its large sample size (N=754 mother/infant dyads) that was prospectively studied with a high (95.1%) follow-up rate and the use of fetal tissue (meconium) as a sensitive biomarker of fetal exposure to pesticides. Propoxur, inhibits acetylcholinesterase and elicit cholinergic hyperstimulation similar to the action of organophosphates. However, unlike the organophosphates, the anticholinesterase action of propoxur is transient and may last only from minutes to a few hours (Bjorling et al., 2007). Yet, as shown in this study, prenatal exposure to propoxur is associated with neurodevelopmental delays in children similar to what have been observed with organophosphates (Eskenazi et al. 2007; Handal et al. 2008; Rauh et al. 2006, Bouchard et al. 2010; Grandjean et al. 2006; Ruckart et al. 2004; Eskenazi 2007), which indicates the high vulnerability of the fetal brain even to transient prolongation of acetylcholine action secondary to pesticide effect. On the other hand, other pharmacologic action of anticholinesterase pesticides may also play a role that is not mediated by a neurotransmitter (acetylcholine) effect. In undifferentiated PC12 cells which is a standard in vitro model for neuronal development, exposure of the cells to organophosphates and carbamate have shown inhibition of DNA synthesis, signs of oxidative stress as evidenced by measurements of lipid peroxidation, transcriptional effects on neurotrophic factors, their receptors and

modulators and a shift of the transmitter fate of the cells away from the cholinergic phenotype and toward the catecholaminergic phenotype. (Slotkin TA et al., 2007, Slotkin et al., 2008).

With regards to the pyrethroids, there was very little prenatal exposure as measured by meconium and there was no relationship between pyrethroid exposure and neurodevelopment at 24 months. However, the smaller sample size of infants positive for grouped pyrethroids (2.5%) compared to propoxur (21.3%) may have biased our results towards the null, resulting in our failure to observe an adverse effect. The absence of identifiable, significant adverse direct effects of pyrethroid at age 24 months should not be interpreted as a benign exposure. In animal studies following exposure to pyrethroids, delayed neurologic effects were observed. Early postnatal exposure to bioallethrin in rats showed that, as adults, the rats exhibited hyperactivity and a decrease in muscarinic ACh receptors, as well as decreased learning as measured by a Morris swim maze (Eriksson 1997; Talts, et al., 1998). Neonatal rats have been shown to be 4–17 times more vulnerable to the acute toxicity of pyrethroids (including permethrin (type I), deltamethrin (type II), cypermethrin (type II)) than adult rats (Sheets at al., 2000; Cantalamessa F, 1993). The higher toxicity in neonatal rats is affected by the lower capacity for metabolic detoxification doses (Sheets et al, 1994; Sheets LP 2000).

In the outcome analysis of pesticides as predictors of the Griffiths test, we did not include pesticides with very low prevalence (<1%) e.g., chlorpyrifos, pretilachlor, malathion, diazinon, and DDT (Ostrea el al, 2009) because of insufficient power to demonstrate any significant relationship. Interactions between pesticides with regards to the outcome measures were also not analyzed, except for propoxur and pyrethroids, since interactions between pesticides of very low prevalence would have given extremely low power. For propoxur and grouped pyrethroids, a post hoc simple regression analysis to determine interaction between the two groups of pesticide did not add anything to the prediction of Griffiths outcome.

In the follow up study of the children up to 2 years of age, we determined ongoing exposure to propoxur and pyrethroids in children's hair since these pesticides constituted the highest pesticide exposure antenatally. The ongoing exposure at 2 years of age to propoxur was 12.4% and 0.6% to bioallethrin. Unlike prenatal exposure, we did not find any significant association between postnatal exposure to propoxur and bioallethrin to the Griffiths test. This indicates that prenatal pesticide exposure has the highest risk to subsequent adverse neurodevelopment in children since it is during fetal life that brain growth and development are its maximum rate and vulnerability. (Bruckner, 2000; Eriksson, 1997; Barone et al., 2000).

In summary, a longitudinal study of a large group of children in the Philippines who were prenatally exposed to propoxur showed subsequent adverse effect of the pesticide on motor development at 24 months of age. This is an important observation since propoxur is widely used in the United States and globally, as well (USEPA 2009). The co-morbid association of motor performance and subsequent cognitive and language development is a compelling reason for the long term, longitudinal study of these prenatally, pesticide exposed children.

Acknowledgments

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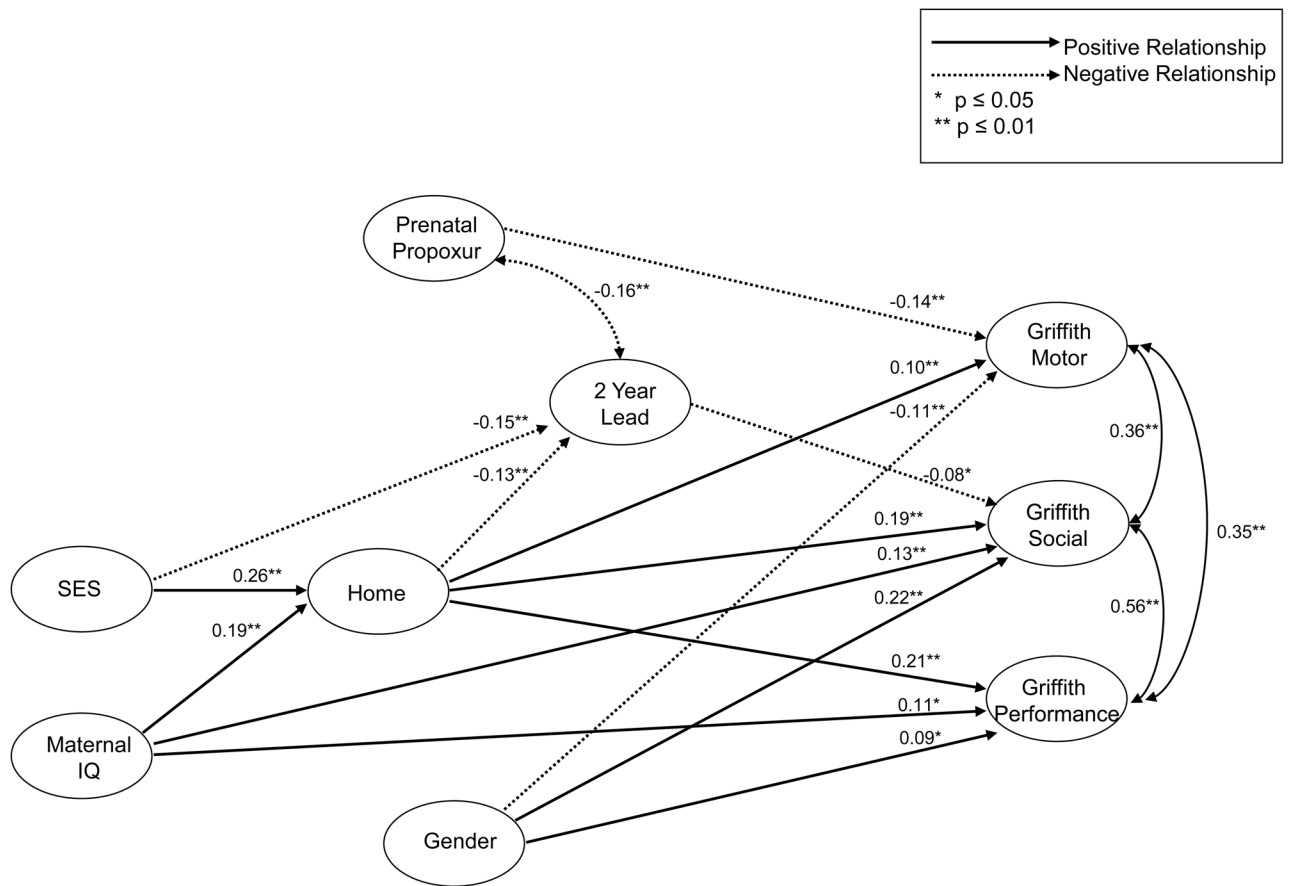
Figure 1.
Path analysis model showing the relationship between prenatal exposure to propoxur and confounders on child neurobehavioral development as assessed by the Griffiths test at 24 months of age

Table 1

Prevalence of prenatal exposure to propoxur and grouped pyrethroids (bioallethrin, cyfluthrin, transfluthrin and cypermethrin) by the analysis of meconium, cord blood, infant hair, maternal hair and maternal blood at birth.

	Meconium (N=717)	Cord blood (N=630)	Infant hair (N=730)	Maternal hair (N=740)	Maternal blood (N=740)
Propoxur	153 (21.3%)	12 (1.9%)	1 (0.1%)	156 (21.1%)	22 (3.0%)
Grouped pyrethroids	18 (2.5%)	0 (0.0%)	0 (0.0%)	103 (13.9%)	0 (0.0%)

Table 2

Demographics of the study population

	Total	Not exposed	Exposed	p^*
Maternal characteristics	(N=696)	(N=537)	(N=159)	
Maternal age (yr) **	25.8 (5.9)	25.7 (5.8)	26.2 (6.0)	0.38
Gravida **	2.4 (1.7)	2.4 (1.7)	2.3 (1.5)	0.52‡
Parity **	1.2 (1.5)	1.3 (1.6)	1.1 (1.4)	0.50‡
Married %	74.0	73.3	76.1	0.48
Oligohydramnios %	1.8	1.5	2.7	0.30†
Meconium stained %	11.6	11.4	12.2	0.78
C-section %	16.6	15.9	18.9	0.38
Vertex presentation %	97.2	97.4	96.9	0.78†
PROM > 24 %	0.9	1.0	0.6	1.00†
Hypertension/PIH %	5.2	6.0	2.5	0.08
Vaginal bleeding %	0.4	0.6	0	1.00†
Active smoking %	2.1	2.1	2.0	1.00†
Cocaine use %	0	0	0	
Opiate use %	0.3	0.4	0	1.00†
Marijuana use %	0.4	0.6	0	1.00†
Alcohol use %	0.7	0.7	0.6	1.00†
Methamphetamine use %	0.9	1.1	0	0.37†
Infant characteristics				
Male %	54.5	55.8	50.3	0.22
Gestation (wk) **	38.7 (1.2)	38.6 (1.2)	38.6 (1.4)	0.38
Weight (gm) **	2900.6 (424.4)	2911.9 (425.9)	2862.0 (418.3)	0.20
Length (cm) **	48.8 (2.4)	48.9 (2.4)	48.5 (2.6)	0.10
Head circumference (cm) **	33.1 (1.5)	33.1 (1.5)	33.0 (1.6)	0.27
Oxygen use after birth %	5.7	5.1	7.7	0.21
Resp distress %	1.0	0.7	1.9	0.20†
Transient tachypnea %	1.2	1.1	1.3	1.00†
Meconium aspiration syndrome %	0.4	0.4	0.6	0.54†
Asphyxia %	1.0	0.7	1.9	0.20†
Jaundice %	3.2	3.0	3.8	0.61
Sepsis %	11.1	10.1	14.6	0.12

*
Based on Student t-test or Mann-Whitney test ‡ for continuous variables and Pearson's chi-square analysis or Fisher's Exact Test† for categorical variables

**
Mean ± standard deviation

Table 3

Characteristics of the home and environment of the study population

	Total	Non-Exposed	Exposed	p^*
Home/Environment	**(N=696)**	**(N=537)**	**(N=159)**	
Roberto scale (A – C) %	38.9	37.6	43.4	0.19
Makeshift homes %	6.8	6.3	8.2	0.42
Water seal toilet %	81.8	80.1	87.4	0.04
Source of water (well) %	42.6	44.9	34.8	0.02
Waste water in canals/river %	62.4	61.7	64.8	0.48
Flies %	91.8	90.3	96.9	0.008
Cockroach %	90.7	90.5	91.2	0.79
Mosquitoes %	98.0	97.6	99.4	0.21[†]
Cellphone %	45.1	44.5	47.2	0.55
Use of home pesticides %	16.8	16.9	16.4	0.86
Lead recycling plant %	6.5	5.6	9.5	0.08

[*] Pearson's chi square analysis