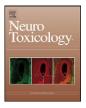
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Mother's environmental tobacco smoke exposure during pregnancy and externalizing behavior problems in children

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ABSTRACT

Background: While the impact of active maternal smoking during pregnancy on child health has been well investigated, the association between maternal passive smoking, or environmental tobacco smoke (ETS), or second-hand smoke, and behavioral development of offspring is less clear. This study examines the association between maternal ETS exposure during pregnancy and child behavior problems.

Methods: Cross-sectional data of 646 mother–child pairs from the Jintan China Cohort Study were used in the analyses. Mother's exposure to tobacco smoking at home, the workplace, and other places during pregnancy (for the determination of maternal ETS exposure) and children's behaviors (via Child Behavior Checklist) were assessed when the children were 5–6 years old. Logistic regression models were constructed to examine associations between maternal exposure to ETS during pregnancy and internalizing and externalizing behavior problems, adjusting for potential cofounders including child sex and parental characteristics.

Results: 37% of mothers reported ETS during pregnancy. Children of mothers exposed to ETS during pregnancy had higher scores for externalizing and total behavior problems, with 25% of children whose mothers were exposed to ETS compared to 16% of children of unexposed mothers. After adjusting for potential confounders, ETS exposure was associated with a higher risk of externalizing behavior problems in offspring of exposed mothers (OR = 2.08, 95% confidence interval [CI] 1.27–3.43). Analysis after multiple imputations and sensitivity analysis further verified the association, but no dose–response relationship was found. ETS exposure, however, was not associated with internalizing or total behavior problems.

Conclusion: This study suggests that maternal ETS exposure during pregnancy may impact child behavioral development, particularly externalizing behaviors.

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1. Introduction

According to the World Health Organization, the number of women who are smokers is growing rapidly, with a projected prevalence of 20% by 2025 (compared to only 12% in 2005) (The World Health Organization, 2007). Pregnancy is a critical period during which tobacco exposure may impact fetal development. Experimental studies have consistently shown histopathologic changes in the fetus from maternal smoking, particularly in the

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lungs and brain (Centers for Disease Control and Prevention, 2010). The changes in the brain are associated with adverse neurodevelopmental outcomes. Epidemiologic studies suggest maternal active smoking (i.e. direct intake of tobacco through cigarettes) during pregnancy is associated with child behavior problems, such as attention deficit and hyperactivity disorder (ADHD) (Button et al., 2005; Fergusson et al., 1993; Hutchinson et al., 2010; Kotimaa et al., 2003; Linnet et al., 2005; Milberger et al., 1996, 1998; Tiesler et al., 2011), conduct problems (Fergusson et al., 1993; Wakschlag et al., 1997, 2006), aggression, and other externalizing behaviors (Boutwell et al., 2011; Brook et al., 2006; Fergusson et al., 1998; Huijbregts et al., 2008; Orlebeke et al., 1997, 1999), as well as adult criminal behavior (Brennan et al., 1999). One possible mechanism for such an association involves the fetus potentially experiencing brain growth retardation, which may result in hypoxia or anoxia through pregnancy and

Abbreviations: ETS, environmental tobacco smoke; CBCL/1.5-5, Child Behavior Checklist; CJCCS, China Jintan Child Cohort Study.

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birth complications. It is known that hypoxia selectively damages the hippocampus, which brain-imaging research indicates is one component involved in aggression regulation (Raine et al., 2004; Liu, 2011). Furthermore, neurological deficits may represent a potential link between maternal smoking and adverse behavioral outcomes, such as criminal behavior in adolescence and adulthood (Brennan et al., 1999; Paradis et al., 2011).

While the impact of maternal active smoking on offspring behavior is well established, the impact of maternal environmental tobacco smoking (ETS) exposure during pregnancy has been less studied despite the large number of women exposed to ETS during pregnancy (Centers for Disease Control and Prevention, 2006). ETS, also known as second hand smoking, is a form of passive smoking, which is defined as inhalation of smoke by persons other than the intended 'active' smoker (Centers for Disease Control and Prevention, 2009). Few studies have examined maternal ETS exposure during pregnancy and the adverse behavior outcomes in offspring, and the U.S. Centers for Disease Control and Prevention has concluded that the evidence supporting a causal relationship between is inadequate (Centers for Disease Control and Prevention, 2006). Three studies included less than 200 mother-child pairs and found that child prenatal exposure through maternal ETS exposure was related to a higher risk of aggression and externalizing behavior problems (Gatzke-Kopp and Beauchaine, 2007; Hsieh et al., 2010; Makin et al., 1991). The only other study identified, which included more than 4000 mother-child pairs, did not support the previous findings (Roza et al., 2009).

Less than 2% of women in China are smokers (Li et al., 2011), but more than 60% of nonsmoking women are exposed to ETS (Yang et al., 1999). In fact, a recent survey found that 42% of women in China were exposed to ETS during pregnancy (Fu et al., 2008). The low active smoking prevalence but high ETS exposure rate makes women in China a unique population for studying health outcomes of maternal ETS exposure. This study aims to use the data from the China Jintan Child Cohort Study (CJCCS) (Liu et al., 2010) to address the gap in the literature regarding the effects of maternal ETS exposure during pregnancy and child behavioral outcomes. Outcomes may provide much-needed clarity on this relationship and are particularly important, as tobacco exposure and child psychopathology each represent significant public health issues.

2. Methods

2.1. Study population

The current study was part of a larger population-based community cohort study of 1656 Chinese children (55.5% boys, 44.5% girls) initially recruited in the Spring of 2005 from four preschools in the city of Jintan, located in the southeastern coastal region of Mainland China. Detailed sampling and research procedures of this larger cohort study have been described elsewhere (Liu et al., 2011b, 2010). Briefly, the China Jintan Child Cohort Study is an on-going prospective longitudinal study with the main aim of assessing the early health risk factors for the development of child neurobehavioral outcomes. Institutional Review Board approval was obtained from both the University of Pennsylvania and the ethical committee for research at Jintan Hospital in China.

Children were recruited in 2005 (included children in their junior (3 years old), middle (4 years old), and senior (5 years old) levels of preschool) and had their blood tested for lead levels (Liu et al., 2012). Children were followed periodically to evaluate physical and behavioral development. Two hundred and seventyone children dropped out of the study due to changing schools, leaving 1385 children in the later study waves. This analysis was based on cross-sectional data on mother's ETS exposure and children's neurobehavioral assessment during spring 2005 to spring 2007, when children were in their last year of preschool. Parents completed a questionnaire regarding child nutrition, behavior, prenatal characteristics, and family characteristics and Child Behavior Checklist for 1.5- to 5-year-olds (CBCL/1.5–5). CBCL assessments for 509 children were conducted after those children were older than 5 years, and these children were excluded from the primary analysis due to age cut-offs for CBCL/1.5–5 and for consistency with our recent publication (Liu et al., 2011a). Children of mothers who did not answer ETS exposure questions or provided incomplete ETS exposure information were not included (n = 230) in the primary analysis. Therefore, 646 mother-child pairs were included into the analysis.

2.2. Child behavior assessment

The CBCL is one of the most widely used scales for assessing behavioral and emotional problems in children and consists of 99 items which are scored on a 3-point scale ranging from "not true" (score = 0) to "often true" (score = 2) (Achenbach and Rescorla, 2000; Ivanova et al., 2010; Rescorla et al., 2011). The Chinese version of the CBCL has been validated (Leung et al., 2006; Liu et al., 2011a). The CBCL includes measures of seven syndromes: anxiety/ depression, emotional reaction, withdrawn, somatic complaints, sleep problems, attention problems, and aggression. Standardized T scores were calculated from raw scores. Standardized T scores for the syndromes equal to or greater than 65 (93rd percentile of Chinese norm group) indicate the presence of behavior problems in these areas in the borderline/clinical range (Achenbach and Rescorla, 2000). The CBCL also allows the examination of two behavioral problems: internalizing behavior problems (the sum of emotional reaction, anxiety/depression, withdrawn, and somatic complaints) and externalizing behavior problems (the sum of attention problems and aggression). The total problems score is the sum score of all 99 problem items. Those children with standardized T scores greater than 60 (83rd percentile) are considered having internalizing, externalizing, or total problems in borderline and clinical range (Achenbach and Rescorla, 2000).

2.3. Maternal exposure to ETS during pregnancy

In the questionnaire, mothers were asked how many persons smoked in the home, workplace, and other places where exposure could occur, and for how many minutes she was exposed to smoke in the environment each day during pregnancy. Exposure to ETS was considered present when at least one person smoked in the environment for at least 30 min each day. Maternal prenatal and postnatal active smoking status could not be assessed due to social stigma against women's smoking in China, especially in rural areas and small towns like Jintan. The dose of ETS exposure was categorized as no ETS exposure, <30 min, 30–60 min, and \geq 60 min under any one of those three circumstances.

2.4. Covariates

The first set of covariates included parental characteristics (father's education, father's occupation, whether the father smoked after the child was born, mother's age when the child was born, mother's occupation, parental psychopathologic problems, and marital status). Parental education at the time the children entered the study was categorized as less than high school, high school, and college or university. Parents reported the occupation that they had held for the longest period in their lives (unemployed, general labor, technician/ professional worker, and other). Fathers also reported current smoking status (no, yes but less than 10 cigarettes per day, 10–20

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