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Effects of prenatal cocaine exposure on adolescent development ☆

Gale A. Richardson [a,*], Lidush Goldschmidt [b], Cynthia Larkby [a], Nancy L. Day [a]

[a] University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, United States
[b] University of Pittsburgh Medical Center, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, United States

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ABSTRACT

The associations between prenatal cocaine exposure (PCE) and adolescent behavior, cognitive development, and physical growth were examined in 219 15-year-olds who have participated in a longitudinal study since their fourth gestational month. During the first trimester, 42% of the women used cocaine, with use declining across pregnancy. At the 15-year follow-up, the caregivers were, on average, 43 years old, had 13 years of education, and 50% were African American. First trimester PCE was not associated with global cognitive development or with measures of learning and memory. First trimester PCE was significantly related to adolescent-reported delinquent behavior, poorer problem solving and abstract reasoning, and reduced weight, height, and head circumference at 15 years. These results were significant after other factors that affect these domains were controlled in regression analyses. In addition, exposure to violence partially mediated the effect of PCE on delinquent behavior. These adolescent domains are important because they are predictors of poorer adult functioning.

1. Introduction

This report addresses three domains of adolescent development: behavior, cognition, and physical growth, each of which has been reported to be associated with prenatal cocaine exposure (PCE). These domains are important areas of adolescent development as they may portend early adult functioning.

We have found persistent associations between PCE and child temperament and behavior problems at 1, 3, 7, and 10 years of age (Richardson et al., 2008, 2009, 2011, 2013a), which is consistent with reviews suggesting that the behavior domain is most likely to be affected (Ackerman et al., 2010; Behnke and Smith, 2013; Buckingham-Howes et al., 2013). Others have also reported that PCE is associated with child or adolescent behavior problems, particularly externalizing behaviors such as aggression and delinquency (Bada et al., 2011, 2012; Bennett et al., 2007, 2013; Delaney-Black et al., 2000; Fisher et al., 2011; McLaughlin et al., 2011; Min et al., 2014a, 2014b; Minnes et al., 2010; Nordstrom Bailey et al., 2005; Sood et al., 2005; Whitaker et al., 2011). However, not all reports have confirmed these findings (Accornero et al., 2002, 2006; Allen et al., 2014; Bada et al., 2008; Bennett et al., 2002; Bridgett and Mayes, 2011; Gerteis et al., 2011; Greenwald et al., 2011; Linares et al., 2006; Savage et al., 2005; Warner et al., 2006b). This is an important domain to investigate because adolescent behavior problems predict poorer outcomes in adulthood, including substance abuse, risky sex, psychiatric disorders, and less successful adjustment (Doherty et al., 2008; Fergusson et al., 2007; Ramrakha et al., 2007).

A second domain that has implications for adult functioning is child and adolescent cognitive development. We found a significant association between PCE and short-term memory (Richardson et al., 2009), and other researchers have reported deficits in specific areas such as verbal reasoning/memory (Bennett et al., 2002), executive function (Minnes et al., 2014; Warner et al., 2006a), cognitive processing/learning (Bridgett and Mayes, 2011; Mayes et al., 2005, 2007), visual spatial/math skills (Singer et al., 2004, 2008), visual motor integration (Arendt et al., 2004; Schroder et al., 2004), and attention, inhibitory control, and impulsivity (Accornero et al., 2007; Bandstra et al., 2001; Bendersky et al., 2003; Carmody et al., 2013; Noland et al., 2005; Rose-Jacobs et al., 2009). However, there are also reports that show no negative effects of PCE on specific areas of cognition (Betancourt et al., 2011; Eyler et al., 2009; Hurt et al., 2009; Li et al., 2009; Rose-Jacobs et al., 2011), and most groups, including ours, do not find a relation between PCE and global cognitive development (Accornero et al., 2007; Bandstra et al., 2002; Frank et al., 2005; Hurt et al., 1997, 2001; Messinger et al., 2004; Morrow et al., 2004, 2006; Singer et al., 2004).

In terms of the third domain of growth, it is unclear whether the association between PCE and early childhood growth deficits persists into adolescence. We found significant associations between PCE and growth deficits at follow-ups through 10 years of age (Richardson et al., 1999, 2008, 2009, 2011, 2013a). Some other studies have also reported that PCE has a detrimental effect on childhood growth (Covington et al., 2002; Minnes et al., 2006; Rivkin et al., 2008; Shankaran et al., 2011). However, others have reported that it has no

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* Corresponding author. Tel.: +1 412 681 3482; fax: +1 412 246 6875.
E-mail address: gar@pitt.edu (G.A. Richardson).

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effect at younger ages (Arendt et al., 2004; Bada et al., 2012; Frank et al., 2002; Lumeng et al., 2007; Warner et al., 2006a), and two studies reported that PCE was associated with increased body mass index and obesity in some subgroups of children (LaGasse et al., 2011; Shankaran et al., 2010). To our knowledge, there have been no reports on the effects of PCE on adolescent growth.

It is also important to consider the effects of the postnatal environment on development. Offspring with PCE are at greater risk of being raised in an adverse environment as a consequence of their PCE-associated deficits and of having a mother with a problematic lifestyle. Women who use drugs are less capable of providing a good home environment, more likely to use other drugs, more transient, have less social support, and have more psychiatric problems (Stratton et al., 1996), factors that predict poorer offspring outcomes (Greenberg and Crnic, 1988; Sameroff et al., 1987; Sroufe and Rutter, 1984; Werner and Smith, 1992). Some of the inconsistent findings described above could be due to differential consideration of environmental variables. Further, childhood exposure to violence and abuse are associated with both PCE and behavior problems (Bada et al., 2011; Delaney-Black et al., 2011; Frank et al., 2011; Richardson et al., 2013a; Schwab-Stone et al., 2013) and, therefore, could function as mediators of the effects of PCE.

The purpose of these analyses was to investigate the effects of PCE on adolescent behavior, cognition, and growth. We carefully measured postnatal environmental exposures, and considered their effects in the analyses. Based on the literature and our previous findings, we hypothesized that there would be detrimental effects of PCE on behavior and growth. However, because of the inconsistency in the literature, we did not hypothesize an expected effect of PCE on cognition.

2. Methods

2.1. Study design

Women 18 years or older who attended the prenatal clinic at Magee-Womens Hospital (MWH) in Pittsburgh, PA from March 1988 to December 1992 were eligible to participate. Written consent was obtained according to the guidelines of the University of Pittsburgh's Institutional Review Board and the Research Review and Human Experimentation Committee of MWH. A Certificate of Confidentiality was obtained from the Department of Health and Human Services to assure participants that their responses could not be subpoenaed.

Women were initially approached for interview during their fourth or fifth prenatal month by trained research staff. Women were not enrolled if they came in for their first prenatal visit after the fifth month or if they did not speak English. No information was obtained from the medical charts about a woman's drug use before she was asked to participate in the study. Ninety percent of the women approached agreed to be interviewed. Medical chart reviews were conducted to assess whether refusal to participate was associated with drug use. A random sample of those women who were approached but refused to participate was selected: Only 5% had a history of drug use during the current pregnancy.

At the initial assessment, women were interviewed about their use of cocaine, crack, alcohol, marijuana, tobacco and other drugs for the year prior to pregnancy and for the first trimester. The core data set consisted of information about sociodemographic characteristics, life events (Dohrenwend et al., 1978), social support (Berkman and Syme, 1979), and psychiatric symptomatology (Center for Epidemiologic Studies-Depression Scale [CES-D], Radloff, 1977; Spielberger State–Trait Anxiety Inventory [STAI], Spielberger et al., 1970).

All women who reported using any cocaine or crack during the first trimester were enrolled, along with the next woman interviewed who reported no cocaine or crack use during pregnancy or in the year before pregnancy. Of the women initially interviewed, 320 (18%) met the inclusion criteria and were enrolled in the study. Women selected for the study were interviewed at seven months about their substance use during the second trimester and the core data set was repeated. The women were interviewed again at 24 to 48 h postpartum, when they were asked about third trimester substance use and the core data set. All newborns received comprehensive physical examinations, generally within 24 to 48 h of delivery, by study nurse clinicians who were unaware of prenatal exposure status. The mothers and offspring were assessed at 1, 3, 7, 10, and 15 years postpartum. At all assessment phases, the mothers were interviewed with the core data set, including questions about substance use over the past year.

2.2. Sample characteristics

Of the 320 women selected for the study, 17 became ineligible for participation because of abortion/miscarriage/infant death (N = 5), home delivery (N = 1), or moving out of the area (N = 11). Of the remaining 303 eligible women, 1 was lost to follow-up and 2 refused further participation. Thus, delivery assessments were completed on 300 mothers. Four pairs of twins and 1 child with Trisomy 21 were excluded from further follow-up, yielding a birth cohort of 295 mothers and infants.

At the 15-year follow-up, 219 subjects out of the 295 in the birth cohort were seen (74% of the birth cohort). Seven women refused the 15-year phase only, 12 refused any further contact, 31 were lost to follow-up, 17 moved, 3 offspring were in foster care and could not be located, and 6 offspring had died. Subjects who participated in the 15-year phase (N = 219) did not differ from those who did not participate (N = 76) on the following: prenatal alcohol, tobacco, or other illicit drug exposure; maternal race, age, income, marital status, work status; parity, pregnancy, labor, or delivery complications; or infant birth weight, length, head circumference, or gestational age. The subjects who did not participate had fewer years of education at delivery (11.6 vs. 12.0 years, $p < 0.05$), were more likely to be marijuana users during the first trimester (46% vs. 30%, $p < 0.01$), and were less likely to be cocaine users during the second trimester (1% vs. 10%, $p < 0.05$) than those who did participate.

At the 15-year follow-up, 19% of the offspring were not in maternal custody, in which case the current caregiver was interviewed. The mean age of the women was 43 years (range = 33–75), their mean level of education was 13.1 years (range = 9–20), 50% were African American, 58% were single, 53% had a man living in the household, the median family income was $2000/month (range = $0–$12,083), and 70% worked and/or attended school.

The mean age of the offspring at the 15-year assessment was 15.6 years (median = 15.3; SD = 0.8; range = 15–18). Ninety-two percent were seen before 17 years of age. Fifty-two percent were males. The average weight was 154.4 lb (SD = 43; range = 90–340), the average height was 66.2 in (SD = 3.5; range = 57–76), and the average head circumference was 561 mm (SD = 18; range = 521–620). The mean Wechsler Intelligence Scale for Children—III (WISC-III) (Wechsler, 1991) composite score was 87.9 (SD = 17.4; range = 47–129). The mean grade in school was 9.4 (median = 9.0, SD = 0.9, range = 7–12).

2.3. Variables

2.3.1. Maternal cocaine and other substance use

Maternal cocaine and crack, tobacco, alcohol, marijuana, and other illicit drug use were assessed during confidential interviews by research staff at each assessment phase. Cocaine and crack use were reported in lines, rocks, or grams, or in cost at 15 years if the woman could not report quantity. For these analyses, cocaine use was dichotomized into any use vs. no use for each of the three trimesters and for the 15-year phase. The alcohol and marijuana variables were average number of drinks or joints per day, respectively, and were log transformed to reduce skewness. Tobacco use was analyzed as number of cigarettes