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The association of prenatal cocaine exposure, externalizing behavior and adolescent substance use

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ABSTRACT

Prenatal cocaine exposure (PCE) may increase adolescent substance use through alterations of neurotransmitter systems affecting fetal brain development. The relationship between PCE and substance use at 15 and 17 years was examined. Subjects (365: 186 PCE; 179 non-cocaine exposed (NCE)) supplied biologic and self-report data using the Youth Risk Behavior Surveillance System (YRBSS) and Computerized Diagnostic Interview Schedule for Children (C-DISC 4) at ages 15 and 17. The relationship between PCE and substance use was assessed using General Estimating Equation (GEE) analyses controlling for confounding factors including violence exposure and preschool lead level. Teens with PCE vs. NCE teens were 2 times more likely to use tobacco (OR = 2.1; 95% CI 1.21–3.63; $p < .001$) and marijuana (OR = 1.85; CI 1.18–2.91; $p < .001$) and have a substance use disorder at age 17 (OR = 2.51; CI 1.00–6.28; $p < .05$). Evaluation of PCE status by gender revealed an association between PCE and marijuana use that was more pronounced for boys than girls at 17 years. Violence exposure was also a significant predictor of alcohol ($p < .001$), tobacco ($p < .05$), and marijuana ($p < .0006$) use and substance abuse/dependence ($p < .01$). Externalizing behavior at age 12 fully mediated the effects of PCE on substance use disorder at age 17 and partially mediated effects of PCE on tobacco use, but did not mediate effects on marijuana use. The percentage of substance use reported increased between 15 and 17 years, with no differences between the PCE and NCE groups. Data suggest specialized drug use prevention measures for children with PCE may benefit this high risk group.

1 Introduction

Adolescent substance use is a significant concern in the United States, with 6.5% of 12th graders reporting daily marijuana use (Johnston et al., 2014), 1.0% of 12–17 year-olds reporting five or more drinks at one time at least five days during the past 30 days (Center for Behavioral Health Statistics and Quality, 2015) and 20.8% of high school students reporting binge drinking five or more drinks in a row on at least one day in the past 30 days (Kann et al., 2014). In 2014, the national rate of past year substance use disorder for adolescents aged 12–17 was estimated to be 5%, with 2.7% of youth aged 12–17 having an alcohol use disorder and 3.5% having an illicit drug use disorder (Center for Behavioral Health Statistics and Quality, 2015). Earlier initiation of substance use for children and adolescents is associated with a number of problems including academic failure (Yule and Prince, 2012), not attending or completing college (King et al., 2006), and risk for development of a substance use disorder later in life (Substance Abuse Mental Health Services Administration (SAMHSA), 2013).

Problematic substance use is regarded as multi-causal and children born with prenatal cocaine-exposure (PCE) often have more risk factors than those with no PCE. Risks specific to children with PCE include direct teratological effects of cocaine on the developing brain and self-regulatory systems (King et al., 2006; Nigg et al., 2006; Thompson et al., 2009; Zucker et al., 2011; Yule and Prince, 2012; Substance Abuse Mental Health Services Administration (SAMHSA), 2013; Kann et al., 2014; Johnston et al., 2014), genetic transmission of substance use traits (Agrawal and Lynskey, 2008), and/or accumulation of negative environmental experiences such as exposure to violence (Lynskey et al., 2010).

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1.1. Prenatal cocaine exposure and adolescent substance use

Prenatal cocaine exposure is hypothesized to have direct teratologic effects on fetal brain development via cocaine induced hypoxia resulting from vasoconstriction in uterine and placental blood vessels (Malanga and Kosofsky, 1999) and negative effects on monoamine neurotransmitter functions of the developing fetal brain (Kosofsky et al., 1994; McCarthy et al., 2014). Evidence suggests that PCE alters prenatal responses to stress in reaction to environmental insults (Lester and Padbury, 2009). The combination of these early alterations in brain development can result in pervasive, subtle developmental problems of self-regulation, including executive functioning deficits, behavioral problems and poor impulse control (Singer et al., 2008; Thompson et al., 2009; Minnes et al., 2010; Minnes et al., 2014a, 2014b).

Existing research on adolescents who have experienced PCE has found that they are about 2–3 times more likely to use substances or develop substance use problems than their non-cocaine exposed peers. At age 14, adolescents with PCE were twice as likely to use cocaine as non-exposed teens (Delaney-Black et al., 2011). Fifteen-year olds with PCE were found to be 1.8 times more likely to have early initiation of alcohol or marijuana use (Richardson et al., 2013), about twice as likely to have used alcohol, marijuana, or tobacco at age 15 (Minnes et al., 2014a,b), and 2.8 times more likely to have problems related to substance use than their non-exposed peers (Min et al., 2014b). The risk of developing problematic substance use appears to increase with the amount of prenatal exposure the adolescent experienced (Frank et al., 2011). To our knowledge no studies have looked beyond adolescent substance use among youth with PCE to examine the percentage of those who meet diagnostic criteria for substance use disorders.

1.2. Externalizing behavior as a mediator of cocaine's association with adolescent substance use

There is converging evidence that an indirect pathway to adolescent substance use among children with PCE may occur through increased externalizing behavior. Externalizing typically refers to overt behavior problems that involve impulsivity and insufficient self-regulation of behavior or emotion, but can also be considered broadly as a neurodevelopmental style of self-regulation and learning that is more responsive to environmental than internal influences (Tucker et al., 2015). PCE has been associated with increased behavioral dysregulation throughout infancy and early childhood, and increased externalizing, disruptive, and risk-taking behaviors through middle childhood and into adolescence (Richardson et al., 2011; Lambert and Bauer, 2012). Problems with poor inhibitory control can manifest in behaviors that show impulsivity and poor judgment for adolescents with PCE. Examples of such behavior include earlier initiation of sexual activity (De Genna et al., 2014; Min et al., 2015), more engagement in risky sexual behavior (Min et al., 2016), and more damage, theft, and status offenses by age 15 (Richardson et al., 2015) than non-exposed adolescents.

Relatively few studies have examined the mediating effect of externalizing behavior in the relationship between prenatal cocaine exposure and teen substance use. Only the Maternal Life Style (MLS) study reported that childhood externalizing problems mediated the effects of PCE on the risk of initiating use of any substance by age 16 (Lester et al., 2012). Other studies have found direct relationships between PCE and increased risk of problematic substance use. However, they have either not directly examined the mediating effects of externalizing behaviors (Frank et al., 2011; Warner et al., 2011; Richardson et al., 2013) or have not found a significant mediating effect (Frank et al., 2011; Warner et al., 2011; Richardson et al., 2013). Additional investigation is warranted to clarify a potential pathway to substance use among prenatally drug exposed teens.

Differential relationships based on gender may exist between PCE and externalizing behaviors, as some studies have found boys with PCE to have higher levels of externalizing behaviors than girls (Greenwald et al., 2011; Bennett et al., 2013), while others have found only girls with PCE report more externalizing (Minnes et al., 2010; McLaughlin et al., 2011) and risk taking behaviors (Min et al., 2015). Increased levels of PCE are also linked to lower caregiver ratings of executive functioning at age 12 in girls but not boys, indicating dysfunction in the areas of the brain related to judgment and behavioral regulation (Minnes et al., 2014a,b). To date, it is not clear how gender may interact with PCE to predict adolescent substance use.

1.3. Other prenatal drug exposure and environmental covariates

Children with PCE also have higher levels of prenatal exposure to other drugs of abuse, including alcohol, opiates, and tobacco (Singer et al., 2000). These additional prenatal drug exposures have been associated with both neurobehavioral regulatory problems and increased risk of substance use in adolescence (Glantz and Chambers, 2006).

Environmental influences can constitute up to 70% of the variation in initiation and problematic substance use (Lynskey et al., 2010) and are important to consider when evaluating the association of PCE and substance use. A potent negative environmental influence, violence exposure, has been associated with early initiation of alcohol use (Taylor and Kliewer, 2006; Bossarte and Swahn, 2008), marijuana use (Mason, 2010; Richardson et al., 2013), cocaine use (Delaney-Black et al., 2011), and general substance use (Pinchevsky et al., 2014) for adolescents. Repeated exposure to violence is reported to set the stage for greater rates of substance abuse and other mental and physical health problems later in development (Moffitt, 2013). There is also existing evidence that violence exposure is a contributing factor to substance abuse after accounting for PCE (Frank et al., 2014; Minnes et al., 2014a,b).

Additionally, *post*-natal exposure to ongoing substance use by household members for children with PCE has been associated with a nearly six-fold increase in risk of problematic adolescent substance use (Frank et al., 2014). Furthermore, PCE and caregiver current substance use were both found to independently predict adolescent cocaine use by 14 years (Delaney-Black et al., 2011). Elevated blood lead levels, which often co-occur within low socioeconomic status households and, therefore, at high rates in our sample (Min et al., 2009), are also associated with increased risk of behavioral problems in childhood through early adulthood in the general population (Wasserman et al., 1998; Burns et al., 1999; Lane et al., 2008; Wright et al., 2008), and were found to be related to alcohol use in adolescents with PCE (Minnes et al., 2014a,b). Other caregiver characteristics known to independently influence behavioral outcomes include caregiver psychological distress, receptive vocabulary skills, non-verbal reasoning ability and quality of the home environment (Bennett et al., 2008; Singer et al., 2008; Singer et al., 2015). Generally, poor environmental and socioeconomic conditions are often prevalent among parents with substance use disorders and are important factors to consider in evaluating the relationship between PCE and teen substance use. These multiple factors have rarely been evaluated simultaneously in a large well-defined prospective sample.

1.4. Purpose and hypotheses

The purpose of the current study advances previous research by aiming to better understand the relationship between PCE and substance use patterns in the teen years, controlling for important