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Problematic substance use in urban adolescents: Role of intrauterine exposures to cocaine and marijuana and post-natal environment

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ABSTRACT

Background: Linkages between intrauterine exposures to cocaine and marijuana and adolescents' problematic substance use have not been fully delineated.
Methods: Prospective longitudinal study with assessors unaware of intrauterine exposure history followed 157 urban participants from birth until late adolescence. Level of intrauterine exposures was identified by mother's report and infant's meconium. Problematic substance use, identified by the Voice Diagnostic Interview Schedule for Children (V-DISC) or the Audio Computer Assisted Self-Interview (ACASI) and urine assay, was a composite encompassing DSM-IV indication of tolerance, abuse, and dependence on alcohol, marijuana, and tobacco and any use of cocaine, glue, or opiates.
Results: Twenty percent (32/157) of the sample experienced problematic substance use by age 18 years, of whom the majority (22/157) acknowledged abuse, tolerance or dependence on marijuana with or without other substances. Structural equation models examining direct and indirect pathways linking a Cox survival model for early substance initiation to a logistic regression models found effects of post-natal factors including childhood exposure to violence and household substance use, early youth substance initiation, and ongoing youth violence exposure contributing to adolescent problematic substance use.
Conclusion: We did not identify direct relationships between intrauterine cocaine or marijuana exposure and problematic substance use, but did find potentially modifiable post-natal risk factors also noted to be associated with problematic substance use in the general population including earlier substance initiation, exposure to violence and to household substance use.

1. Introduction

Substance misuse is widespread among America's youths and young adults (Shih et al., 2010; Wu et al., 2011). Among 12 to 17 year olds in the United States, 7.3% reported dependence or abuse of illicit drugs or alcohol during the past year. The national prevalence of past year dependence or abuse of illicit drugs or alcohol was 16.6% among 18 year olds and 20.0% among 19 and 20 year olds (Substance Abuse and Mental Health Services Administration, 2011).

Studies have delineated racial/ethnic, male/female, and regional variability in substance use, dependence, and abuse (Shih et al., 2010). Among high school students in Boston, 2.3% of males and 1.2% of females reported using any form of cocaine, while 21.2% of females and 32.7% of males in reported using marijuana in the past 30 days. These data, derived from high school students, may underestimate actual prevalence of use in the age cohort, since they cannot account for use by adolescents who have dropped out of

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school, a population with higher rates of use (Substance Abuse and Mental Health Services Administration, 2011).

The predictors of adolescent substance use and abuse are complex, encompassing exogenous social factors, the adolescent's cognitive and behavioral characteristics, and endogenous factors including intrauterine exposures, genetic predisposition, sex, race/ethnicity (Galea et al., 2004). Exogenous factors are diverse and numerous. For example, in a retrospective study of Adverse Childhood Experiences (ACEs) exposure to household substance use, household dysfunction such as criminal behavior or observing a mother treated violently, and physical, sexual, and psychological abuse as a child were found to be risk factors for later alcoholism and illicit drug use (Felitti, 2002). Studies have shown that the relationship between ACEs and the risk of alcohol misuse and abuse in adulthood are independent of a history of parental alcoholism (Dube et al., 2006). Substance dependent parents, externalizing behaviors in adolescents, low commitment to school (Stone et al., 2012), poly-substance use in adolescence (Schmid et al., 2007) family conflicts, poor impulse control, living in a neighborhood with high crime rates or drug use (Ali et al., 2011), and victimization by violence (Doherty et al., 2012) may promote and perpetuate later drug dependence and problematic substance use in young adulthood.

Research conducted among children of alcoholics (King and Chassin, 2007) and more representative samples of the U.S. population (Chen et al., 2009; Grant and Dawson, 1998) found early initiation of cocaine and marijuana use in adolescence to be associated with an increased risk of later drug dependence (Chen et al., 2009; Grant and Dawson, 1998; King and Chassin, 2007) and alcohol dependence (Grant and Dawson, 1998). However, one study found early initiation of drug use may not predict later alcohol and drug dependence among 20th century Black populations (Grant and Dawson, 1998). Conversely several potential protective factors have been identified including close parental supervision and religiosity (Schulenberg et al., 2005; Stone et al., 2012).

Intrauterine exposures to alcohol and other psychoactive substances have been associated in prospective investigations with early initiation of licit and illicit substances. In a longitudinal study, intrauterine marijuana exposure (IUME) was found to be associated with marijuana initiation at age 14 (Day et al., 2006). Among 16 to 21 year olds, intrauterine tobacco exposure (IUTE) was associated with marijuana initiation (Day et al., 2006; Porath and Fried, 2005), while IUTE but not IUME was associated with tobacco initiation (Porath and Fried, 2005). In a prospective cohort of white and black adolescents, intrauterine cocaine exposure (IUCE), as well as a family history of alcohol problems and adolescent's history of exposure to violence, were been found to be associated with early adolescent marijuana and alcohol use (Richardson et al., 2013). In contrast, Lester et al. (2012) found that there was no direct association between IUCE and age of substance use initiation once neurobehavioral disinhibition (based on a composite indicator of externalizing behaviors at ages 8, 9 years) was considered as a mediator (Lester et al., 2012).

Recent studies examining the relationship between IUCE and the offspring's cocaine use in adolescence yield mixed results. A prospective IUCE cohort study conducted in Detroit found a more than two-fold increased risk of cocaine use, measured using hair, sweat, or urine samples, at the age of 14 years among young adolescents with IUCE (Delaney-Black et al., 2011). In contrast, a prospective IUCE cohort study from rural Florida found no significant differences in pre-teen cocaine use, identified by positive hair specimens, between those with and without IUCE (Warner et al., 2011).

In both studies, the interpretation of adolescent cocaine use is somewhat uncertain because of reliance primarily on hair samples, which may not unequivocally differentiate the adolescent's own cocaine use from environmental contamination (Romano et al., 2001).

Standard criteria of substance use disorder as laid out in the Diagnostic and Statistical Manual-IV (DSM-IV) do not appear to have the same validity among adolescents as among adults (Winters et al., 2011). There are a number of complex factors to take into account with subsyndromic substance use that may cause physical or other harm in adolescent populations. These diverse potential negative consequences of use (Mason et al., 2007) have been evaluated by other researchers in varying composites with the more classic definitions of substance use disorders such as tolerance, addiction, or dependence under the rubric which we will also use of "problematic substance use" (Roeloffs et al., 2001).

In addition to the obvious concern that mothers' use of psychoactive substances in pregnancy may be a marker for genetic vulnerability to substance use disorders, the earlier initiation of psychoactive substance found in some, but not all, studies of adolescents with intrauterine substance exposures, raises concern that this may be a group at increased risk for problematic substance use by later adolescence.

Data regarding prenatal exposures and later problematic substance use (as opposed to early initiation of substance use) are sparse. Intrauterine alcohol exposure (IUAE) has been associated with an increased risk of alcohol problems at age 21 years in the United States (Baer et al., 2003), but not in an Australian cohort (Alati et al., 2005). Little is known about intrauterine exposures to illicit substances and later problematic substance use.

Taken as a whole, prior research findings suggest that linkages between intrauterine substance exposure and later problematic substance use have not yet been fully delineated, particularly with regard to the relative roles played by endogenous factors such as sex and intrauterine exposures and exogenous forces in the social environment.

In the current cohort, the association between intrauterine substance exposures (IUSE), environmental factors and the early initiation of substance use have been previously reported (Frank et al., 2011), with findings largely consistent with the subsequent reports of other investigators (Minnes et al., 2013; Richardson et al., 2013). We reported heavier IUCE and lighter IUME were both significantly associated with initiation of any substance use by the age of 16 (Frank et al., 2011). Adolescents in our cohort who reported higher levels of violence exposure were at increased risk of early initiation of any substance by 16 compared to adolescents who reported lower levels of violence exposure. In addition, marijuana use by a member of the adolescent's household was associated with an increased risk of the adolescent's own marijuana use (Frank et al., 2011).

The goal of the current analysis is to extend our previous work on age of substance initiation to evaluate whether there are direct or indirect associations between levels of IUCE and IUME and problematic substance use by late adolescence (16–18) after controlling for relevant covariates.

2. Methods

2.1. Sample recruitment

As has been previously reported in greater detail (Frank et al., 1999; Tronick et al., 1996), sample recruitment occurred 8–72 h after delivery during post-partum hospitalization at Boston City Hospital (now Boston Medical Center) between October 1990 and March 1993, with screening for eligibility conducted 7 days a week with the exception of major holidays or interviewer illness. Mother and infant medical records, interviews conducted by trained research staff, biological measures and infant physical examinations were assessed to identify the following inclusion criteria: infant gestational age ≥36 weeks; no neonatal intensive care; no obvious major congenital malformations; no diagnosis of fetal alcohol syndrome in the neonatal record; no positive HIV history noted in the mother's or infant's medical record; no indication by neonatal or maternal urine toxicology screen or history in medical record of mother's use during pregnancy of illegal opiates, methadone,