Drug and Alcohol Dependence 176 (2017) 169–175

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Full length article

Intrauterine exposure to tobacco and executive functioning in high school

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ARTICLE INFO

Keywords:
Intrauterine tobacco exposure
Executive functioning
High school students
Teacher behavior rating of executive functioning

ABSTRACT

Background: Executive functioning (EF), an umbrella construct encompassing gradual maturation of cognitive organization/management processes, is important to success in multiple settings including high school. Intrauterine tobacco exposure (IUTE) correlates with negative cognitive/behavioral outcomes, but little is known about its association with adolescent EF and information from real-life contexts is sparse. We evaluated the impact of IUTE on teacher-reported observations of EF in urban high school students controlling for covariates including other intrauterine and adolescent substance exposures.

Methods: A prospective low-income birth cohort (51% male; 89% African American/Caribbean) was followed through late adolescence (16–18 years old). At birth, intrauterine exposures to cocaine and other substances (52% cocaine, 52% tobacco, 26% marijuana, 26% alcohol) were identified by meconium and/or urine assays, and/or maternal self-report. High school teachers knowledgeable about the student and unaware of study aims were asked to complete the Behavior Rating Inventory of Executive Functioning-Teacher Form (BRIEF-TF) annually.

Results: Teachers completed at least one BRIEF-TF for 131 adolescents. Multivariable analyses included controls for: demographics; intrauterine cocaine, marijuana, and alcohol exposures; early childhood exposures to lead; and violence exposure from school-age to adolescence. IUTE was associated with less optimal BRIEF-TF Behavioral Regulation scores ($p < 0.05$). Other intrauterine substance exposures did not predict less optimal BRIEF-TF scores, nor did exposures to violence, lead, nor adolescents' own substance use.

Conclusions: IUTE is associated with offspring's less optimal EF. Prenatal counseling should emphasize abstinence from tobacco, as well as alcohol and illegal substances.

1. Introduction

Approximately 12% of pregnant U.S. women in 2008 reported smoking tobacco during the third trimester, despite increased long-term health risks for themselves and offspring (Tong et al., 2013). Executive functioning (EF) encompasses a set of higher-level neurocognitive functions (e.g., working memory, inhibitory control, organization, and planning) necessary for independent, purposeful, goal-directed day-to-day activity. Intrauterine tobacco exposure (IUTE) has been associated with less optimal performance on measures of children's neurocognitive abilities (Fried et al., 2003) including working memory (Fried and Watkinson, 2001), attention, emotion and behavioral regulation (Cornelius et al., 2012; Wiebe et al., 2014) and aggression/other anti-social behaviors in older children and adolescents (Huizink and Mulder, 2006; Wakschlag et al., 2011). Few studies specifically examine IUTE effects on executive functioning (EF) during adolescence (Clifford et al., 2012). EF encompasses a set of higher-level neurocognitive functions (e.g., working memory, inhibitory control, organization, and planning) necessary for independent, purposeful, goal-directed day-to-day activity including helping to manage competing performance demands (Alvarez and Emory, 2006; Lezak et al., 2012).

Prior studies evaluating IUTE effects on neurobehavioral outcomes usually focus on individualized, laboratory-based assessments rather than measures of functioning in real-life contexts where environmental stimuli may influence individuals' behavior (Chaytor et al., 2006;

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http://dx.doi.org/10.1016/j.drugalcdep.2017.02.022
Received 28 September 2016; Received in revised form 14 February 2017; Accepted 22 February 2017
Available online 10 May 2017
0376-8716/

Clifford et al., 2012). Context is known to be an important factor influencing EF (Williams et al., 2009). For example, success in high school requires constant adaptation to variable, unpredictable conditions, but it is not known whether adolescents with versus without IUTE show observable EF differences in this "real world", rather than a controlled laboratory environment (Diamantopoulou et al., 2007).

Regardless of setting, studies of specific effects of any single intrauterine substance exposure also must evaluate potential environmental, demographic and biologic covariates, particularly other intrauterine substance exposures and adolescents' own substance use (Fried et al., 2003; Richardson et al., 2013; Rose-Jacobs et al., 2011). As evident in substance-exposure literature, outcomes may be influenced by specific samples, ages tested, assessments used, and covariates included (Clifford et al., 2012; Piper and Corbett, 2012). Potential covariates based on published literature should be evaluated to avoid misinterpretation of results. For example, in low-income, urban populations, environmental exposure to second-hand tobacco smoke (Cornelius and Day, 2009), lead (Min et al., 2009), and violence (Frank et al., 2011; Perkins and Graham-Bermann, 2012) may influence EF.

The present study goal is to evaluate possible associations between IUTE and EF reported by participants' high school teachers. We hypothesize that after controlling for contextual variables including demographics, childhood blood lead levels, childhood and adolescent exposure to violence, other intrauterine substance exposures, and the adolescent's own substance use, IUTE will be negatively associated with high school teachers' ratings of students' classroom EF.

2. Methods

2.1. Sample

Participants were high school students from low-income, urban backgrounds enrolled in a prospective, longitudinal birth cohort study evaluating potential developmental sequelae of intrauterine exposure to cocaine and other substances. As previously reported (Frank et al., 1999), participants were recruited (1990–1993) postpartum at an urban hospital serving a large Medicaid population. Inclusion criteria were: gestational age ≥36 weeks, no level III NICU care, no diagnosed Fetal Alcohol Syndrome or HIV infection; mother's English fluency, age ≥18 year, and no documented use during index pregnancy of opiates, benzodiazepines, amphetamines, phencyclidine, barbiturates or hallucinogens (Mirochnick et al., 1991). Exclusion criteria included known major risk factors (e.g., preterm birth, adolescent mother, genetic syndromes) that might confound the effects of intrauterine substance exposures. The Institutional Review Board of Boston City Hospital/Boston University Medical Center approved the study. A Certificate of Confidentiality was obtained.

2.2. Intrauterine substance exposure classification

Research staff interviewed postpartum mothers about cocaine, alcohol, marijuana, cigarette, and other illicit drug use during pregnancy via an adaptation of the Addiction Severity Index (ASI) (McLellan et al., 1992). At that time, cotinine assays (to measure gestational tobacco exposure) were prohibitively expensive and there were no biological markers for gestational alcohol exposure. For analytic purposes, we created a 3-level intrauterine tobacco exposure variable (none = no cigarettes during pregnancy, lighter (< 10 cigarettes/day on average, and heavier ≥ 10 cigarettes/day.). We categorized prenatal alcohol use as none, lighter (< 0.5 average drinks/day), and heavier (≥0.5 drinks/day).

Urine samples were analyzed for benzoylecgonine, opiates, amphetamines, benzodiazepines and cannabinoids by radioimmunoassay using commercial kits (Abuscreen RIA, Roche Diagnostics Systems, Inc., Montclair, N.J.). Meconium specimens were analyzed by radioimmunoassay for the cocaine metabolite benzoylecgonine, metabolites of opiates, amphetamines, benzodiazepines, and cannabinoids (Mirochnick et al., 1991; Ostrea et al., 1989). We classified IUCE exposure as "unexposed", "lighter", or "heavier" based on composite information derived from maternal self-report, mother or infant urine, and/or the meconium assays (Tronick et al., 1996). Identification of intrauterine marijuana exposure was based on a composite index of the urine assays, meconium assay, and maternal self-report and categorized as "unexposed", "lighter" or "heavier." (Frank et al., 2011).

2.3. Procedures

Primary caregivers and their child/adolescent completed multiple follow-up evaluations at a developmental laboratory between the target child's birth and late adolescence. At follow-up visits, research assistants masked to the target child's intrauterine exposure status interviewed caregivers regarding family demographics, psychosocial variables, and cigarette smoking among household contacts. Another research assistant masked to the intrauterine exposures and previous assessments administered the developmental and behavioral protocol assessments to target children/adolescents.

2.3.1. Age groups and problematic substance use determination

During three adolescent visits, early (ages 12–14.4 years), middle (14.5–16.4 years), and late (16.5–18 years), adolescents reported their own substance use history using an auditory computer-assisted self-interview (ACASI). Questions about cocaine, marijuana, alcohol, tobacco, and other substance use were taken from the U.S. Center for Disease Control (2005) Youth Risk Behavior Surveillance System and the Wisconsin Youth Risk Behavior Surveillance middle and high school questionnaires (Eaton et al., 2006). Adolescents voluntarily provided urine samples at each visit to screen for legal and illegal substances (Frank et al., 2011). Urine samples were tested by the United States Drug Testing Laboratories, Inc., using the No-Excuse Urine Panel that has a limit of detection panel using enzyme multiplied immunoassay technique at the lowest validated concentrations achieved. Gas chromatography–mass spectrometry confirmations were used for some drug classes: cannabinoids, opiates, amphetamines and cocaine metabolites. Enzyme-linked immunosorbent assay technique was used for cotinine. The No-Excuse Urine test level gives a detection window of up to a week for most drugs, and even longer for marijuana. We classified adolescents as currently substance-positive if they self-reported use of alcohol, marijuana, and other substances excluding tobacco experimentation during the past 30 days or if their urine assay was positive. We classified adolescents reporting substance use prior to the past 30 days and with negative urine assay as "ever" having used a particular substance. To maintain adequate cell sizes for statistical analyses, adolescents' own cigarette or cocaine use each were categorized as two-level variables, "never" and "ever". Problematic substance use was identified by a composite of ACASI substance use answers, and/or urine assays encompassing the DSM-IV indication of tolerance, abuse, and dependence on alcohol, marijuana, and tobacco and any use of cocaine, glue or opiates during adolescence (Frank et al., 2014).

2.3.2. Measures

The primary outcome for these analyses, the BRIEF-TF (Behavior Rating Inventory of Executive Functioning-Teacher Form), is a standardized 86 item three-point scale (Never, Sometimes, Often) teacher-reported questionnaire developed to rate observations of student classroom EF-related behavioral tendencies (Gioia et al., 2000; Toplak et al., 2008). The BRIEF-TF consists of eight subscales summarized as two indexes measuring day-to-day functioning. Behavioral Regulation (subscales: Inhibit, Shift, Emotional Control) represents abilities to shift attention between different tasks, efficiently adapt to changing situations, and use inhibitory control to modulate strong or automatic behavioral/emotional responses. Meta-cognition (subscales: Initiate,