Neurotoxicology and Teratology xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Neurotoxicology and Teratology

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

Brief communication

Prenatal tobacco exposure, maternal postnatal nicotine dependence and adolescent risk for nicotine dependence: Birth cohort study

Natacha M. De Genna [a,*], Lidush Goldschmidt [b], Nancy L. Day [a], Marie D. Cornelius [a]

[a] Department of Psychiatry, University of Pittsburgh School of Medicine and Department of Epidemiology, Graduate School of Public Health, 3811 O'Hara Street, Pittsburgh, PA 15213, USA
[b] University of Pittsburgh Medical Center, Program in Epidemiology, 817 Bellefield Tower, 100 North Bellefield Avenue, Pittsburgh, PA 15213, USA

ARTICLE INFO

Article history:
Received 15 June 2016
Received in revised form 21 February 2017
Accepted 23 February 2017
Available online xxxx

Keywords:
Prenatal tobacco exposure
Nicotine dependence
Adolescence
Smoking
Pregnancy

ABSTRACT

Aims: The goals of this study are to determine if there is (a) a threshold effect for prenatal tobacco exposure (PTE) on adolescent risk for nicotine dependence, and (b) an additive effect of PTE and maternal postnatal nicotine dependence on adolescent risk for nicotine dependence.
Methods: Pregnant women were recruited in their 4th or 5th gestational month and asked about cigarette use during the first trimester. Mothers reported on third trimester cigarette use at delivery. Sixteen years postpartum, mothers and offspring reported on current levels of cigarette use (N = 784). Nicotine dependence was assessed in both using a modified Fagerström questionnaire.
Results: Based on the results of a threshold analysis for PTE, four groups were created: threshold PTE only (10+ cigarettes per day), maternal nicotine postnatal dependence with no-low PTE (0– <10 cigarettes per day), threshold PTE + maternal postnatal nicotine dependence, and a referent group with no-low PTE and no maternal postnatal nicotine dependence. Adolescents in the PTE-only group and the PTE + maternal postnatal nicotine dependence group were significantly more likely to be at risk for nicotine dependence than the offspring from the referent group. However, there was no evidence for an additive effect of maternal postnatal nicotine dependence, and maternal nicotine dependence was not a significant predictor of adolescent risk for nicotine dependence in regression models including prenatal tobacco exposure.
Conclusions: Bivariate analysis revealed a threshold effect for PTE of 10 cigarettes per day. In multivariate analysis, PTE remained significantly related to risk for offspring nicotine dependence, after controlling for maternal postnatal nicotine dependence and other covariates associated with adolescent cigarette use.

1. Introduction

Over a third of all adolescents in the U.S. try smoking, and at least one-fifth of those who experiment with cigarettes will develop nicotine dependence (ND) (Colby et al., 2000; Dierker et al., 2012). Parental smoking is a well-known predictor of adolescent smoking and ND (Gilman et al., 2009; Hu et al., 2012; Kandel et al., 2007, 2015; Mays et al., 2014; Selya et al., 2012; Weden & Miles, 2012). However, many adolescents whose parents currently smoke also have prenatal tobacco exposure (PTE). Offspring with PTE are more likely to smoke than unexposed offspring (Agrawal et al., 2010; Cornelius et al., 2000, 2005; Goldschmidt et al., 2012; Weden & Miles, 2012) and to progress from smoking to ND (Buka et al., 2003; Rydell et al., 2012; Shenassa et al., 2015). Preclinical studies provide a plausible biological mechanism for the effects of PTE on ND: PTE rodents respond differently to nicotine administration and withdrawal during adolescence than unexposed rodents (Slotkin et al., 2006).

Of note, prior studies of the effects of PTE on ND in humans did not focus on the effects of maternal postnatal ND. PTE and maternal postnatal ND may represent separate pathways to ND in adolescents. PTE may have a teratological effect, priming exposed offspring to become smokers and then dependent smokers by sensitizing them to the effects of nicotine at smoking initiation (Bidwell et al., 2016; Pomerleau, 1995). There may also be indirect teratogenic effects of PTE on ND in adolescents via attention and behavior problems (Clark et al., 2016; Cornelius et al., 2007, 2011; Day et al., 2000) that promote disengagement at school, antisocial peer relations and daily smoking. On the other hand, PTE may simply be a marker for maternal postnatal ND (Agrawal et al., 2008) or genetic and environmental influences (Rydell et al., 2016). In addition, dependent mothers are more likely to continue smoking during pregnancy, exposing the offspring to higher levels of tobacco.

To date, most research on ND has focused on the effects of PTE or maternal postnatal ND separately. Only one study previously took into account both exposures, by including a retrospective report of PTE as a

* Corresponding author at: University of Pittsburgh School of Medicine, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213, USA.
E-mail addresses: degennan@pitt.edu (N.M. De Genna), lidush@pitt.edu (L. Goldschmidt), nday@pitt.edu (N.L. Day), mdc1@pitt.edu (M.D. Cornelius).

http://dx.doi.org/10.1016/j.ntt.2017.02.004
0892-0362/

covariate. In this study, Kandel et al. (2007) found that maternal postnatal ND, but not PTE, predicted ND in smoking adolescents. This study merits replication because it was a small community sample (353 students in Chicago public schools) and the measure of PTE was a retrospective caregiver's report of any smoking by the adolescent's biological mother at any point during the pregnancy. The goals of this study are to use prospective birth cohort data to determine if there is (a) a threshold effect for PTE on adolescent risk for ND, using a prospective measure of PTE for each trimester of pregnancy, and (b) an additive effect of PTE and maternal postnatal ND on adolescent risk for ND.

2. Method

2.1. Design

Pregnant girls and women were recruited in their 4th or 5th prenatal month from a teaching hospital in Pittsburgh, PA. They were seen again with their offspring at delivery and 6, 10, 14, and 16 years post-partum. At the 16-year follow-up visit, nicotine dependence (ND) was assessed in mothers and adolescent offspring.

2.2. Participants

The mothers in this study were recruited for three birth cohorts from a consortium of studies on the effects of prenatal substance use on physical and neurobehavioral development. Participants were from two studies of pregnant adults (AA06390; DA03874: PI Day) recruited from 1982 to 1985 and one study of pregnant adolescents recruited from 1990 to 1995 (DA09275: PI Cornelius). A new dataset combining the birth cohorts was created for the purposes of this study. The participants were drawn from the same prenatal clinic, seen at same follow-up time periods, and the same measures and personnel were used, so we avoid most sources of between-subject heterogeneity in the merged dataset (Curran and Hussong, 2009).

At birth, the combined sample size was 1176 mothers. By the 16-year follow-up, 103 offspring were lost to follow up, 67 refused participation, 13 children had died, 15 were adopted or in foster care, and 52 had moved out of the area. Ten adolescents did not complete the drug assessment at age 16, and 27 caregivers were not assessed. We also excluded 105 dyads because the biological mother was not interviewed at the last follow-up. Complete data on ND in both biological mother and child were available for 784 dyads. This sample differed from the birth sample by race and PTE. The analyses were repeated with sampling weights, to adjust for attrition and to examine whether the results remained stable. The weights were calculated as the inverse probability of response for each racial group and tobacco exposure group. The results of the analyses were the same with and without the sampling weights, so unweighted values are presented for ease of interpretation.

2.3. Measurements

2.3.1. Prenatal tobacco exposure

Pregnant mothers were first interviewed in their 4th or 5th prenatal month in a private setting in the prenatal clinic by female interviewers who were comfortable discussing tobacco, alcohol and drug use. Quantity and frequency of cigarette use during the first trimester were assessed in this interview. Mothers were interviewed again within 48 h of delivery, reporting on 3rd trimester cigarette use. About half of the mothers smoked during pregnancy (48% during the first trimester, 52% by the third trimester). The increase in smoking during pregnancy in the combined sample was influenced by the inclusion of a large number of adolescent mothers in the study, because smoking increased across pregnancy in this younger group (Cornelius et al., 1994, 2001). In comparison, among the adult-aged mothers, smoking prevalence was more stable across pregnancy (Cornelius et al., 2007).

2.3.2. Maternal postnatal nicotine dependence

Mothers were interviewed about their cigarette use 16 years post-partum, and also completed the 6-item Fagerström Test for Nicotine Dependence (FTND) (Heatherton et al., 1991). Similar to other epidemiological studies (e.g., Azagba & Asbridge, 2013; Breslau & Johnson, 2000) ND was coded for mothers endorsing at least 4 items on the FTND.

2.3.3. Adolescent offspring risk for nicotine dependence

Offspring were also interviewed about their substance use 16 years post-partum. Adolescent ND was assessed in offspring who had ever tried cigarettes via the FTND questionnaire. A score of 4 on this scale indicates moderate dependence (Prokhorov et al., 2001). Adolescent offspring who scored 3 or higher were considered at risk of ND (outcome variable).

2.3.4. Covariates

Characteristics associated with smoking in previous research (including child age, race, maternal education, and prenatal exposure to alcohol and marijuana) were included in all of the multivariate analyses as covariates. Child sex was also included in preliminary analyses.

2.4. Statistical analyses

Bivariate analyses were first used to examine whether there was a linear relationship between PTE and adolescent ND. Next, a logistic regression was used to test whether PTE was a significant predictor of adolescent ND controlling for race, prenatal exposure to alcohol and marijuana, maternal education and child age at the 16-year assessment. In the second step of the regression, maternal postnatal ND was added to the model and the change in the relation between PTE and adolescent risk for ND was observed. In the last step, we introduced an interaction term to test whether the influence of PTE on adolescent risk for ND was sex-specific.

To determine if there was an additive effect of PTE and maternal postnatal ND, a separate analysis was conducted using the following four exposure groups: PTE only (at the threshold of 10+ cigarettes per day), maternal postnatal ND + no-low PTE (0 ≤ 10 cigarettes/day), PTE + maternal postnatal ND (adolescents with both exposures), and a referent group with no maternal postnatal ND and no-low PTE (0 ≤ 10 cigarettes per day). Adolescent risk for ND in the reference group was first compared to adolescent risk for ND in the three exposure groups using a χ^2 test. Logistic regression was then applied to simultaneously compare adolescent risk for ND in the PTE and maternal ND/low-no PTE groups relative to the reference group, controlling for demographic covariates. Finally, to test whether the effects of PTE and maternal postnatal ND were additive, adolescent risk for ND in the PTE + ND group relative to the PTE only and the ND/low-no PTE groups was compared.

3. Results

3.1. Sample characteristics

On average, the pregnant mothers were young (M = 20.6 years, SD = 4.6, range = 13–42) single mothers (65%). The sample was 61% Black and 39% White. At the 16-year follow up, 92% of the mothers had completed high school/GED (M = 12.5 years of education, SD = 1.9). Monthly family income ranged from 0 to 18,000 US$ (M = 2198, SD = 1741). More than half of the mothers were current smokers 16 years post-partum (55%), and 25% of mothers in the study were ND. Maternal postnatal ND was significantly correlated with maternal number of cigarettes smoked daily (r = 0.48). Paternal ND was not assessed in this study.

Adolescent offspring (half female) were 16.7 years on average (SD = 0.66, range = 16–19) and 39% had tried smoking. One in five of all the adolescent offspring was a current smoker (M = 6.3

Please cite this article as: De Genna, N.M., et al., Prenatal tobacco exposure, maternal postnatal nicotine dependence and adolescent risk for nicotine dependence: Birth cohort study, Neurotoxicol Teratol (2017), http://dx.doi.org/10.1016/j.ntt.2017.02.004