Original Investigation

Prenatal Cigarette Smoke Exposure and Early Initiation of Multiple Substance Use

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Abstract

Introduction: Earlier studies have shown a relation between prenatal cigarette smoke exposure (PCSE) and offspring initiation of tobacco use. No prior study has examined the association between PCSE and early initiation of multiple substances (EIMS) including marijuana and alcohol in addition to tobacco. We investigated the association between PCSE and multiple substance use during adolescence.

Methods: Pregnant women attending an urban prenatal clinic were selected to participate in the prospective longitudinal study based on their substance use. This study is based on the 16-year follow-up phase and consists of 579 mother–offspring dyads. The women were of lower socioeconomic status, 54% were Black, and 53% reported smoking cigarettes. 52% of the offspring were female. EIMS is a measure of the number of substances initiated prior to age 16 by the adolescents; it ranged from 0 (no initiation, $N = 166$) to 3 (all, $N = 162$).

Results: Adolescents exposed to tobacco during first trimester of gestation were 1.4 times more likely to initiate multiple substances by age 16 than the nonexposed group. PCSE was a significant predictor of EIMS after controlling for other prenatal exposures, home environment, and demographic characteristics, using ordinal polytomous logistic regression. Other risk factors of EIMS were maternal and adolescent depression, less strict and less involved parenting, offspring attention problems, and lack of participation in a youth club.

Conclusions: There is a significant relation between PCSE and adolescent's EIMS.

Introduction

To date, most research on the association between prenatal exposure and subsequent offspring substance use has addressed the unitary association between prenatal cigarette smoke exposure (PCSE) and offspring tobacco use. Little research has evaluated the long-term effects of PCSE on the use of a broader spectrum of substances in the exposed offspring. Moreover, no

research has addressed the issue of early age of onset of multiple substance use. This is particularly important since early age of initiation is associated with multiple negative outcomes.

The association between PCSE and offspring tobacco use has been demonstrated in numerous studies. Kandel, Wu, and Davies (1994) reported a fourfold increase in tobacco use among girls aged 9–17 years with PCSE. Griesler, Kandel, and Davies (1998) showed that this association was a mediated relationship: PCSE was significantly associated with higher levels of child behavior problems that, in turn, increased the likelihood of lifetime smoking among daughters. In the Maternal Health Practices and Child Development (MHPCD) Project, 10-year-old PCSE offspring had a 5.5-fold increased risk for early tobacco experimentation (Cornelius, Leech, Goldschmidt, & Day, 2000). In the Ottawa Prenatal Prospective Study (OPPS; Porath & Fried, 2005), PCSE significantly predicted offspring cigarette smoking initiation. Thus, PCSE is associated with early initiation of tobacco use among offspring.

PCSE also predicts greater quantity and frequency of offspring cigarette use. At 14 years, offspring with PCSE in the MHPCD study smoked significantly more cigarettes than those without PCSE (Cornelius, Leech, Goldschmidt, & Day, 2005). Findings from a birth cohort of over 7,000 offspring demonstrated that maternal smoking during pregnancy had an independent effect on the quantity of cigarettes smoked among 14-year-olds (O'Callaghan et al., 2006). In a retrospective study of children in treatment for smoking cessation, PCSE predicted accelerated progression from experimentation to daily use among girls and earlier experimentation among the boys (Oncken, McKee, Krishnan-Sarin, O'Malley, & Mazure, 2004). PCSE has been also shown to be significantly related to lifetime tobacco dependence (Buka, Shenassa, & Niaura, 2003; Lieb, Schreier, Hildegard, & Wittchen, 2003).

While the association between PCSE and offspring tobacco use is well documented, there are few reports about the effects of PCSE on initiation and use of marijuana, alcohol, and other illicit drugs. In the MHPCD study, a significant bivariate relation between PCSE and offspring marijuana use at age 14 was not significant after controlling for home environment (Day, Goldschmidt, & Thomas, 2006). The OPPS also did not find a

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significant relation between PCSE and marijuana use at ages 16–21 (Porath & Fried, 2005). There are no reports of an association between PCSE and offspring alcohol use.

There is a biological basis for a relation between PCSE and offspring substance use. Prenatal nicotine exposure has been shown to increase plasma testosterone in mice offspring, and this alteration increases nicotine seeking in the offspring (Smith, Cloak, Poland, Torday, & Ross, 2003). In a study by Slotkin (2008), there was an upregulation of nicotinic acetylcholine receptors (nAChR) among adult rats exposed to nicotine in the immediate neonatal period, a time comparable to the third trimester in humans. Subsequently, the modification of the neurotransmitters affects the reward system and increases susceptibility to drug use. Lotfpour et al. (2010) showed that the $\alpha 6$ subunit of nAChR interacts with PCSE in humans to influence adolescence drug experimentation.

Risk factors associated with adolescent substance use must be considered when evaluating the relation between PCSE and substance use. Demographic characteristics, home environment, life events, and ethnicity are associated with adolescent drug initiation and are potential covariates of PCSE (Johnston, O'Malley, Bachman, & Schulenberg, 2010; Wills, Vaccaro, & McNamara, 1992). Prenatal exposures to other substances such as alcohol and marijuana have been associated with adolescent use of alcohol, marijuana, and cigarettes (Baer, Barr, Bookstein, Sampson, & Streissguth, 1998; Day et al., 2006; Porath & Fried, 2005) as well as a family history of alcoholism (Chassin, Curran, Hussong, & Colder, 1996). Other correlates of adolescent substance use include maternal and child depression (Cortes, Fleming, Mason, & Catalano, 2009; Weissman, Warner, Wickramaratne, Moreau, & Olsson, 1997), parental monitoring and involvement (Bogenschneider, Wu, Raffaelli, & Tsay, 1998; Ryan, Jorm, & Lubman, 2010; Steinberg, Fletcher, & Darling, 1994), attention deficit and hyperactivity (Galéra et al., 2010; Molina & Pelham, 2003), and participation in extracurricular activities (Eccles, Barber, Stone, & Hunt, 2003).

In this study, we examine the effects of PCSE on early initiation of multiple substances (EIMS) including tobacco, marijuana, and alcohol. Our hypothesis is that by age 16, PCSE is related not only to adolescent tobacco initiation but also to EIMS. The aim of the study is to compare those who have early onset to those who did not have an early onset of use. To our knowledge, this is the first prospective longitudinal study to investigate the effects of PCSE on the multiple substance use during adolescence. Our aim is also to identify other correlates of EIMS and to examine whether the association between PCSE and EIMS remains significant after inclusion of these correlates in the model.

Methods

Participants

The data come from MHPCD Project. The subjects were recruited between 1982 and 1984. Pregnant women who were 18 years or older and in their fourth prenatal month were sequentially selected from an urban hospital-based prenatal clinic to study the effects of prenatal marijuana and alcohol exposure. Informed consent was obtained from the mothers. The study was approved by the Institutional Review Board of the University

of Pittsburgh and Human Experimentation Committee of the Magee-Womens Hospital. The selection of the participants is described in detail elsewhere (Day, Wagener, & Taylor, 1985). Although the participants were recruited to study the effects of alcohol and marijuana use during pregnancy, women were also interviewed in detail about the frequency, quantity, and type of their cigarette smoking. Fifty-three percent of the women smoked tobacco during their first trimester of pregnancy, 41% smoked marijuana, and 64% used alcohol.

Women were reinterviewed in the seventh prenatal month and at delivery when data were collected on second and third trimester substance use, respectively. Postpartum study phases were conducted at 8 and 18 months, 3, 6, 10, 14, 16, and 22 years. This report presents data from the prenatal period and at the 16-year follow-up.

The birth cohort included 763 mothers and their live-born singletons. At 16 years, 592 subjects were interviewed. Subject loss between birth and this phase included refusals for the current phase ($n = 52$), moved out of Pittsburgh ($n = 35$), lost to follow-up ($n = 69$), child death ($n = 6$), or placed for adoption/foster care (9). Adolescents with diagnosed mental retardation ($n = 8$), fibrous dysplasia ($n = 1$), and cerebral palsy ($n = 2$) were excluded from the analyses. Two cases with missing drug use information were dropped from the analyses, resulting in a sample of 579 adolescents for this report. There was no difference in PCSE between those who participated in the study at age 16 ($n = 579$) and those who did not ($n = 184$).

The study participants represent a lower socioeconomic population. At the 16-year phase, the median family income was \$1700 per month (range 0–18,000), the average level of maternal education was 12.2 years (range 7–18), 39% of the mothers were married, 73% worked outside of the home, 46% were Caucasian, and 54% were Black. The average age of the adolescents was 16.9 years (range 16–19), 52% were female, and 16% did not live with their biological mothers. In these cases, the current caregiver completed the parent interview. For convenience, we refer to all caregivers as mothers.

Measures

Maternal tobacco, alcohol, and marijuana use was assessed at the fourth and seventh prenatal months and at delivery for the first, second, and third trimesters of pregnancy, respectively. During the interview at each trimester of pregnancy, women were asked whether they smoked cigarettes and how much they smoked per day. In the early phase, PCSE was measured as the number of packs smoked per day (none, less than half a pack, half a pack, etc.). This was translated into the average number of cigarettes per day using the median of each category, assuming each pack contains 20 cigarettes. Categories ranged from none to 3 packs/day. Women were interviewed about the quantity and frequency of alcohol (beer, liquor, and wine), and marijuana (cigarettes, hashish, and sinsemilla) use. Alcohol was expressed as the average number of drinks per day, and marijuana use was expressed as the average number of joints smoked per day. The validity of the substance use questionnaire used during pregnancy is described in detail by Day and Robles (1989). At 16 years, the mothers were asked the same questions about their substance use during the last year. The mothers and the caregivers were also asked whether the biological parents or any blood-related

relatives of the adolescent had drinking problems. Drinking problems were defined as problems with relatives, friends, at work, or with the authorities ([National Institute on Alcohol Abuse and Alcoholism, 1998](#)). Known first- and second-degree family histories of alcohol problems were described by dichotomous variables (yes = 1, no = 0).

Socioeconomic status (SES) was measured by family monthly income, mother's level of education, marital status (yes/no), work status, and race/ethnicity. Home environment was measured by questions adopted from the HOME Inventory ([Caldwell & Bradley, 1984](#)) that were pertinent to adolescence. The questions included subjects' interest in reading, music, sports, household chores and help cleaning, whether they ate regularly with their family, spent time with the biological father (or father figure), and any physical punishment. These questions were combined into a latent variable as a measure of the home environment ($M = 6$, $SD = 1.6$).

The Center for Epidemiological Studies Depression Scale ([Radloff, 1977](#)) was used to assess maternal depressive symptoms ($M = 39.9$, $SD = 10.5$). Number of life events was measured using the Psychiatric Epidemiology Research Interview life events scale ($M = 2.9$, $SD = 2.2$; [Dohrenwend, Krasnoff, Askenasy, & Dohrenwend, 1978](#)).

The My Parents instrument ([Steinberg, Lamborn, Dornbusch, & Darlin, 1992](#)), completed by the adolescents, assessed parenting practices. This instrument has three scales: acceptance/involvement (M at age 14 = 30.3, $SD = 4.3$), strictness/supervision ($M = 20$, $SD = 3.8$), and psychological autonomy granting scale ($M = 23.5$, $SD = 4.6$). The Cronbach alpha reliability measures for these scales were 0.72, 0.76, and 0.82, respectively.

The Health Behavior Questionnaire ([Jessor, Donovan, & Costa, 1989](#)) was used to assess the age of onset of tobacco, marijuana, and alcohol. The adolescents were interviewed in a private setting apart from their mothers. For cross-validation and to avoid recall bias, the offspring's report of the age of onset of substance use at phase 16 was compared with their 14-year report; if the answers differed, the earlier report was used for these analyses.

Data on ages of initiation were combined: For each substance, initiation prior to age 16 was scored as 1 point and initiation at or after age 16 was scored as 0, and the scores were summed. EIMS ranged from 0 (no initiation of any substance prior to age 16) to 3 (initiation of all 3 substances prior to age 16). Age 16 was used as the cutpoint because it was the youngest age within the assessment phase. To ensure accurate substance use reports, the adolescents were asked to provide a urine sample at age 14 and a saliva sample at age 16. While this does not validate age of initiation reports, the offspring were aware that we were assessing their use, and it is less likely that they would misreport initiation of use. All the adolescents with positive tetrahydrocannabinol (THC) urine toxicology screening did report that they had initiated marijuana use. We used the cutoff of 14 ng/ml saliva cotinine levels to validate self-report of cigarette smoking ([Cummings & Richard, 1988](#); [Hegaard, Kjærgaard, Møller, Wachmann, & Ottesen, 2007](#)). Only 10 adolescents (2%) with cotinine levels of at least 14 ng/ml reported no initiation of any type of cigarette use, but 7 of them

reported marijuana use, which could have been contaminated with nicotine. In contrast, 100 adolescents with negative THC toxicology reported marijuana initiation, and 119 adolescents with cotinine levels less than 14 ng/ml reported tobacco initiation. We concluded that the adolescent's self-report of initiation was reliable.

The comparison no-use group (EIMS = 0) in the analyses included all subjects who had not begun any substance use by age 16. This included both those who began after 16 ($N = 32$) and those who had not begun by the 16-year interview ($N = 134$). These two groups were combined because the focus of this analysis was on early initiation. In fact, these two groups did not differ on PCSE: The rates of first trimester PCSE were 38% and 36%, respectively, compared with a significantly higher rate of 61% PCSE among those who initiated two or more substances by age 16. The rates were similar for third trimester exposure.

The Children's Depression Inventory (CDI; [Kovacs, 1992](#)) was used to measure the adolescent's depressive symptoms. This inventory includes 27 self-rated items, including negative mood, interpersonal problems, and hedonic capacity ($M = 45.2$, $SD = 9.4$). The scale has a test-retest reliability of 0.82. Age- and gender-standardized CDI scores were used in the analyses. The attention problems syndrome scale from the Child Behavior Checklist (CBCL; [Achenbach, 1991](#)) was used to assess attention problems. This scale consists of 11 items and is completed by the caregiver ($M = 55.1$, $SD = 7.1$). The test-retest reliability of the measure is 0.90, and the scale is adjusted for age and gender. CBCL questions regarding sports and youth club activities were also used in the analyses.

Statistical Analysis

Two measures of PCSE were used in separate analyses to assess percent used (dichotomized to use/no use) and quantity of use (continuous). The correlation between first trimester smoking and second and third trimester smoking were .82 and .80, respectively. Although these correlations are high, analyses for the first and third trimesters are presented to capture any differences in effects due to timing of exposure.

The bivariate associations between EIMS and PCSE, covariates, and other risk/protective factors were tested using analysis of variance for the continuous variables and chi-square tests for the dichotomous variables. In addition, monotonic trend tests were used to determine whether the association between EIMS and PCSE were in increasing order ([Cochran, 1954](#)).

Multivariate analyses were done hierarchically. In the first step, ordinal polytomous logistic regression was applied to examine the association between PCSE and EIMS adjusting for differences between the groups on the core covariates including the adolescent's gender, race, home environment, family income, maternal education, work status, marital status, life events, and prenatal exposures to alcohol and marijuana. The analysis was done in a stepwise manner to avoid multicollinearity and to obtain a parsimonious model. The regression coefficients were estimated using maximum likelihood and represent the effect of the predictor on EIMS per increment of one unit in the predictor. In ordinal polytomous logistic regression, the odds ratios (ORs) represent the probability of being in a higher category of EIMS relative to lower levels. The analyses were repeated

Table 1. Prevalence of Maternal Cigarette Smoking (%)

Time of assessment	Average number of cigarettes per day				N
	0	>0-9	10-19	≥20	
First trimester	47.2	20.4	17.8	14.7	579
Second trimester	47.9	19.2	16.3	16.5	526
Third trimester	48.7	15.9	16.9	18.5	579
16 years postpartum	46.3	15.3	18.5	19.8	561

adding a second set of risk factors to the model to examine whether PCSE remained significant after controlling for these additional variables. These covariates included participation in sports and youth club activities, parenting practices, maternal and adolescent depression, and adolescent attention problems. Since the association between adolescent substance use and the latter variables can be recursive, data from the preceding 14-year phase were used.

The literature shows that current parental smoking is related to EIMS. In this cohort, PCSE was strongly correlated with the mother's current cigarette smoking. The correlations between first and third trimester exposure and current maternal smoking were .50 and .53, respectively. To separate the effects of prenatal from current exposure, four mutually exclusive groups were defined: (a) exposed both prenatally and currently ($n = 238$); (b) exposed prenatally only ($n = 89$); (c) exposed currently only ($n = 63$); and (d) no PCSE and no current maternal smoking ($n = 189$). Three dummy variables representing the first three groups were created and included together in the model in addition to the identified significant covariates. In this model, the last group is the reference group. The coefficients and significance of the groups, particularly for the second group, will allow us to determine whether prenatal exposure has an independent effect on EIMS.

Results

During first, second, and third trimesters of pregnancy, 52.8%, 52.1%, and 51.3% of the women, respectively, smoked and 14.7%, 16.5%, and 18.5% of the women, respectively, smoked one or more packs of cigarettes per day (Table 1). Women who smoked tobacco during pregnancy were more likely to be Caucasian and to have less education than the nonsmokers but did not differ in income, marital, or work status (Table 2). Women who smoked tobacco were more likely to use marijuana and alcohol than were the nonsmokers. Also, while most women decreased their use of marijuana and alcohol as their pregnancies progressed, they did not change the pattern of their tobacco use. During the first, second, and third trimesters of pregnancy, 14.3%, 5.3%, and 5.4% of the women, respectively, smoked one or more joints of marijuana per day and 18.0%, 2.5%, and 3.6%, respectively, drank one or more alcoholic drinks per day.

PCSE was significantly related to early initiation (prior to age 16) of alcohol, marijuana, and tobacco individually. Sixty-three percent of the adolescents with PCSE in the first trimester had initiated alcohol use by age of 16 compared with 45% among nonexposed offspring ($\chi^2 = 17.5, p = .000$). The percentages

Table 2. Maternal Characteristics Associated With First Trimester PCSE

	No cigarette smoking	Cigarette smoking	<i>p</i> Value ^a
	<i>N</i> = 273	<i>N</i> = 306	
<i>M</i> age (years)	22.7	23.1	.16
<i>M</i> education (years)	12.0	11.6	.00
% Caucasian	36.3	53.9	.00
% Married	32.6	31.4	.75
% Work/attend school	27.8	25.2	.47
Family income (\$/month)	439	455	.52
% Used marijuana	32.6	48.4	.00
Average joints/day	0.26	0.56	.00
% Drank alcohol	52.4	74.2	.00
Average drinks/day	0.23	0.85	.00

Note. PCSE = prenatal cigarette smoke exposure.

^a*t* test for continuous variables, Mann-Whitney for skewed variables, and χ^2 test for the dichotomous variables. *p* values are two-tailed.

of early marijuana use among PCSE and nonexposed adolescents were 53% and 39%, respectively ($\chi^2 = 11.6, p = .001$). Similarly, 56% of the PCSE offspring initiated cigarette smoking by age of 16 compared with 43% among nonexposed adolescents ($\chi^2 = 9.7, p = .002$). The pattern was similar for the third trimester exposure.

Next, we examined the relation between PCSE and EIMS. The prevalence of EIMS was as follows: 166 scored 0, 114 scored 1 (23 initiated marijuana only, 39 tobacco, and 52 alcohol), 137 scored 2 (35 cases initiated marijuana & tobacco, 48 initiated marijuana & alcohol, and 54 initiated alcohol & tobacco), and 162 scored 3. Adolescents with first trimester PCSE were 1.4 times more likely to initiate 2 or more substances by age 16 than the nonexposed group. A more detailed relation between PCSE and EIMS is presented in Table 3. There was a significant and monotonically increasing bivariate relation between PCSE and EIMS. For example, the average first trimester PCSE was 5.7 cigarettes/day for those with no EIMS, 6.6 cigarettes/day for those with one EIMS, 9.2 for those with two EIMS, and 10.4 for those with three EIMS. This pattern was not observed with prenatal marijuana and alcohol exposures.

In the first step of the multivariate analysis, PCSE was significantly associated with EIMS after controlling for the core covariates (Table 4). PCSE was a significant predictor of EIMS whether expressed as a continuous variable or dichotomized as use/no use, although the dichotomized variable was a stronger predictor ($\chi^2 = 11.2, p = .001$) of EIMS than the continuous measure ($\chi^2 = 4.6, p = .03$). The adjusted odds of an adolescent with first trimester PCSE progressing to multiple substance use prior to age of 16 were 1.7 times larger than the odds of the nonexposed offspring. The cumulative OR for third trimester tobacco exposure compared with the nonexposed offspring was 1.6 ($\chi^2 = 10.2, p = .001$).

Among the covariates, poorer home environment, more life events, and Caucasian race were significantly associated with EIMS (Table 4). There were no differences in the rates of EIMS by gender, prenatal alcohol, or marijuana exposure.

Table 3. Bivariate Association Between EIMS, Prenatal Substance Use, and Other Variables

EIMS	None	One	Two	Three	<i>p</i> Value ^a
<i>N</i>	166	114	137	162	
Prenatal maternal substance use					
First trimester					
% Smoked cigarettes	36.1	57.0	59.9	61.1	.000
Average cigarettes/day	5.7	6.6	9.2	10.4	.000
Average drinks/day	0.49	0.41	0.58	0.67	NS
Average joints/day	0.37	0.51	0.47	0.36	NS
Third trimester					
% Smoked cigarettes	38.6	50.0	58.4	59.3	.000
Average cigarettes/day	6.6	7.4	10.4	11.8	.001
Average drinks/day	0.10	0.09	0.19	0.09	NS
Average joints/day	0.14	0.22	0.15	0.16	NS
Basic covariates					
Race (% Caucasian)	31.3	43.9	45.3	61.7	.000
Gender (% male)	49.4	53.5	42.3	46.9	NS
Current caregivers education	12.6	11.9	12.6	11.7	.000
Work status (% work)	75.5	73.2	73.7	70.1	NS
Marital status (% married)	37.3	32.1	43.2	41.9	NS
Monthly family income (\$)	2,177	2,141	2,257	2,043	NS
Life events (<i>n</i>)	2.4	2.7	3.0	3.5	0.000
Home environment	6.3	6.2	6.0	5.6	0.001
Other risk/protective factors					
% Participate in clubs	50.0	58.9	46.7	25.5	.000
% Participate in sports	92.1	88.5	85.4	85.1	NS
Parental involvement at 16 years	31.0	30.8	30.0	28.9	.000
Psychological autonomy	24.7	23.7	23.6	24.3	NS
Strictness/supervision	20.1	19.3	18.5	17.3	.000
Parental involvement at 14 years	30.9	30.8	29.8	29.7	.03
Psychological autonomy	23.7	24.0	23.1	23.2	NS
Strictness/supervision	21.3	20.0	19.6	18.9	.000
CBCL attention problems at 16	52.7	53.4	55.1	57.1	.000
CBCL attention problems at 14	53.7	53.0	55.8	57.4	.000
Adolescent depression (CDI) at 16	41.1	43.2	45.7	46.4	.000
Adolescent depression (CDI) at 14	41.3	43.2	47.0	49.2	.000
Caregivers' depression at 16	37.9	39.8	40.4	41.7	.01
Caregivers' depression at 14	36.8	37.2	38.5	39.4	NS
Family history of alcohol problems					
First degree (%)	42.8	50.9	57.1	57.3	.03
Second degree (%)	50.9	47.3	53.4	58.0	NS
Not in maternal custody (%)	18.2	16.1	12.8	17.2	NS

Note. CDI = Children's Depression Inventory; EIMS = early initiation of multiple substances; NS = not significant.

^aBased on analysis of variance *F* test for continuous variables and χ^2 test for the dichotomous variables.

The polytomous logistic regression was repeated including the significant covariates identified in the first step and the additional risk factors listed in Table 3. To avoid multicollinearity, the predictors were included in the model in a stepwise manner. With inclusion of these variables, PCSE remained a significant predictor of EIMS (Table 4). Other significant factors included parental strictness/supervision, adolescent's depressive symptoms, attention problems, and participation in a youth club.

To test whether prenatal cigarette smoking affected EIMS independent of current maternal smoking, three variables representing (a) exposed only to prenatal smoking, (b) exposed

only currently, and (c) exposed both prenatally and currently were simultaneously entered in the multivariate analyses. Descriptively, 38.6% of the nonexposed adolescents initiated two or more substances prior to age 16 compared with 57.3% among exposed prenatally only, 57.1% among exposed currently only, and 58.4% among exposed both prenatally and currently (χ^2 with three degrees of freedom = 19.1, p = .003). All three groups were significantly related to EIMS controlling for other significant covariates. The cumulative ORs of the three groups were 1.8 (χ^2 = 5.2, p = .02), 2.0 (χ^2 = 6.4, p = .01), and 1.9 (χ^2 = 12.4, p = .00), respectively. Hence, PCSE and current exposure have independent effects on EIMS.

Table 4. Significant Predictors of EIMS Using Ordinal Polytomous Logistic Model

Variables	Coefficient	Significance (<i>p</i> value)	Cumulative OR (95% CI)
Results with basic covariates and prenatal exposure			
Race	0.82	.000	2.3 (1.6–3.1)
Home environment	–0.22	.000	0.8 (0.7–0.9)
Life events	0.13	.000	1.14 (1.1–1.2)
PCSE			
First trimester continuous ^a	0.16 ^b	.03	1.2 (1.01–1.4)
First trimester none/any ^a	0.53	.001	1.7 (1.2–2.3)
Third trimester continuous ^a	0.14 ^b	.03	1.1 (1.01–1.3)
Third trimester none/any ^a	0.50	.001	1.6 (1.2–2.2)
Results with basic covariates, other risk factors, and prenatal exposure			
Race	0.67	.000	2.0 (1.4–2.7)
Life events	0.10	.01	1.1 (1.01–1.2)
Parenting strictness/supervision	–0.10	.000	0.9 (0.86–0.94)
CBCL attention problems	0.03	.03	1.03 (1.003–1.1)
Adolescent depression (CDI)	0.05	.000	1.06 (1.03–1.1)
Club participation	–0.57	.000	0.6 (0.4–0.8)
PCSE			
First trimester none/any ^a	0.48	.003	1.6 (1.2–2.2)
Third trimester none/any ^a	0.42	.009	1.5 (1.1–2.1)

Note. CBCL = Child Behavior Checklist; CDI = Children's Depression Inventory; EIMS = early initiation of multiple substances; OR = odds ratio; PCSE = prenatal cigarette smoke exposure.

^aAnalyses were run separately but are shown together for ease of presentation.

^bOne unit represents 10 cigarettes/day.

Discussion

We have found a significant association between PCSE and the early initiation of tobacco, marijuana, and alcohol use individually. Further, PCSE predicted the early initiation of multiple substance use among the exposed offspring. This relation remained significant after controlling for demographic, environmental, child and maternal psychological factors, and prenatal exposure to alcohol and marijuana. This is the first report of an association between PCSE and EIMS including substances other than tobacco. This has important implications as early marijuana use, for example, has been shown to be related to academic achievement, neurocognitive performance, health (Brook, Stimmel, Chenshu, & Brook, 2008), and later drug abuse (Anthony & Petronis, 1995).

Multiple factors are likely to contribute to the observed association between PCSE and multiple substance use. As we noted in the introduction, there is a plausible biological explanation for finding early use of multiple substances. In addition, environmental factors play a role in the development of substance use. Although we have identified, examined, and controlled for environmental variables used in the literature, it is possible that we may have not included some variables.

Genetic and gene-environment interactions may also contribute to this association and require further study. Kendler, Jacobson, Prescott, & Neale (2003) found that genetic influences played an important role in predicting dependence on marijuana and other illicit substances but were not as significant in predicting the use of these substances. Environmental factors, however, played a bigger role in substance use than dependence. These analyses did not include prenatal substance exposures.

PCSE predicted an increased probability of EIMS in adolescence independent of current maternal tobacco smoking. This latter result parallels reports by Lieb et al. (2003). These results indicate that there is a unique contribution of PCSE to the development of EIMS. We found no gender differences in the rate of EIMS. The literature about gender differences is not equivocal due to the type of the substance and the timing. Males are at higher risk than females for early initiation of alcohol and marijuana use (Thomas, 1996), while females are more likely to smoke cigarettes (Young et al., 2002). The gender differences may surface, as the offspring grow older. Further, recent national surveys show that the gender gap in substance use has narrowed (Johnston et al., 2010). We also did not find a significant association between prenatal exposure to marijuana and alcohol and EIMS, although each of these substances has been reported to predict increased use (Baer et al., 1998; Day et al., 2006). It is possible that the effects of prenatal marijuana and alcohol on offspring use are specific to the individual substances and do not extend to multiple use. More research is needed to examine potential interactions among PCSE, environmental and genetic risk factors, and potential gender differences. It will be interesting to follow these adolescents to young adulthood to examine whether the relation between PCSE and EIMS predicts more serious drug use.

Use of illicit drugs other than marijuana was not included in the calculation of EIMS since use of these drugs by the adolescents was sporadic. However, within the four groups of EIMS (from 0 to 3), 0.6%, 3.5%, 9.5%, and 27% of the adolescents, respectively, reported using other illicit substances, suggesting a relationship between EIMS and other illicit substance use. Further research extending EIMS to include these illicit drugs is needed.

There are limitations to these findings. The women and offspring in this sample were generally of lower SES, and these results should be replicated in a sample with different characteristics. However, we have controlled for a number of variables that are associated with lower SES and found that the effect of PCSE on EIMS remained significant. It is also possible that some women misreported their tobacco use when asked during their pregnancy. The prenatal data, however, were collected in the early 1980s when tobacco use during pregnancy was not as stigmatized as it is now. To increase the accuracy of reporting, we constructed and tested detailed questions and trained our staff extensively in interviewing techniques. The fact that the correlations between trimesters and across each follow-up phase were high indicates consistency in reporting.

We have demonstrated that PCSE predicts early onset of multiple substances. These findings have significant public health implications. Approximately 12% of pregnant women in the United States smoke (Dietz et al., 2010), and the rate is higher among lower SES populations (Willford, Day, & Cornelius, 2006). Intervening prior to pregnancy would have a twofold effect on decreasing tobacco use. If offspring are not exposed during gestation, they would be protected from the known effects of PCSE, and they would not be at increased risk of EIMS. Further research to define the mechanism of the association between PCSE and early onset of use is important for designing effective intervention programs.

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Declaration of Interests

Lidush Goldschmidt—None. Marie Cornelius—None. Nancy Day—None.

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