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School achievement in 14-year-old youths prenatally exposed to marijuana

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ABSTRACT

The relation between prenatal marijuana exposure (PME) and school achievement was evaluated in a sample of 524 14-year-olds. Women were recruited during pregnancy and assessed, along with their offspring, at multiple phases from infancy to early adulthood. The sample represents a low-income population. Half of the adolescents are male and 55% are African American. School achievement was assessed with the Wechsler Individual Achievement Test (WIAT) Screener (Psychological Corporation, 1992). A significant negative relation was found between PME and 14-year WIAT composite and reading scores. The deficit in school achievement was mediated by the effects of PME on intelligence test performance at age 6, attention problems and depression symptoms at age 10, and early initiation of marijuana use. These findings suggest that the effects of PME on adolescent achievement are mediated by the earlier negative effects of PME on child characteristics. The negative impact of these characteristics on adolescent achievement may presage later problems in early adulthood.

1. Introduction

Academic achievement during adolescence is critical to the acquisition of skills for future employment. Thus, it is important to identify the causes and pathways that lead to achievement deficits. Earlier analyses from the Maternal Health Practices and Child Development Project (MHPCD), a large low-income cohort enrolled to study the effects of prenatal substance exposure, found a significant relation between PME and deficits in academic achievement at age 10 (Goldschmidt et al., 2004): PME predicted poorer performance on the reading and spelling scores of the Wide Range Achievement Test—Revised (WRAT-R) (Jastak and Wilkinson, 1984) and the Peabody Individual Achievement Test—Revised (PIAT-R) (Markwardt, 1998) reading comprehension score. Children with PME also did less well on the teacher's evaluation of their school performance and had a higher rate of underachievement, defined as a significant disparity between school achievement and intellectual ability. These findings were specific to heavy marijuana exposure (≥1 joints/day) and remained significant after controlling for the child's home environment and sociodemographic status (Goldschmidt et al., 2004).

In the only other longitudinal study of PME, the Ottawa Prenatal Prospective Study (OPPS), PME was not associated with academic achievement during childhood in a predominantly white middle class sample (Fried and Smith, 2001; Fried et al., 1997). However, at ages 13 to 16 in the OPPS, heavy PME (≥6 joints/week) was associated with poorer performance on the spelling recognition subtest of the PIAT (Fried et al., 2003). The different findings between the OPPS and the MHPCD may be due to socioeconomic differences between the cohorts.

PME also has significant effects on cognitive and behavioral development, which affect how well adolescents perform in school. In the MHPCD, PME predicted poorer performance on the short-term memory and verbal reasoning subscales of the Stanford–Binet Intelligence Scale at age 3 (SBIS; Thorndike et al., 1986) (Day et al., 1994). At age 6, heavy PME (≥1 joints/day) was associated with lower composite, verbal reasoning, short-term memory, and quantitative scores on the SBIS (Goldschmidt et al., 2008). At age 10, PME predicted poorer performance on the design memory and screening indices of the Wide Range Assessment of Memory and Learning (WRAML; Sheslow and Adams, 1990) (Richardson et al., 2002). In the OPPS, there was a significant association between PME and lower scores on the verbal and memory domains of the McCarthy Scales of Children's Abilities at age 4 and deficits in impulse control and visual analysis and hypothesis testing at ages 9 to 12 (Fried and Smith, 2001). Thus, PME has been found to affect cognitive development in both of these long-term studies.

Further, PME was significantly associated with self-reported depression symptoms (Gray et al., 2005) and inattention (Goldschmidt et al., 2000) in the MHPCD cohort at age 10. In the OPPS, PME predicted increased errors of omission, a measure of inattention, and higher rates of hyperactivity at age 6 (Fried et al., 1992b). Depression and attention deficits have also been shown to affect school performance (Fergusson and Horwood, 1995; Kovacs and Goldston, 1991; Rapport

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et al., 1999) and therefore, it is important to consider these factors in evaluating the association between PME and achievement.

In the MHPCD, PME significantly predicted an earlier age of onset and more frequent marijuana use in the offspring, controlling for significant covariates from the prenatal period as well as the postnatal environment at age 14 (Day et al., 2006). In the OPPS, PME predicted marijuana use in subjects ranging in age from 16 to 21, although this analysis did not control for factors in the postnatal environment (Porath and Fried, 2005). Early initiation of marijuana use among adolescents also has a negative effect on school achievement (Brook et al., 1999; Fergusson et al., 2003). Thus, the effect of PME on offspring substance use should be taken into account while examining the overall effects of PME on academic achievement.

Environmental and demographic factors that are associated with PME and with academic achievement also need to be considered (Day et al., 1993). For example, lower socioeconomic status, ethnicity (Yeung and Conley, 2008), mother's education, and characteristics of the home environment (Hill et al., 2004) are associated with academic success and are potential covariates in studies examining the effects of prenatal drug exposures and offspring outcomes (Day et al., 1993; Huizink and Mulder, 2006). In addition, prenatal exposure to other drugs such as tobacco and alcohol often co-occurs with PME (Day et al., 1993) and research has shown that prenatal exposures to these drugs have independent, adverse effects on children's psychological and cognitive functioning (Day et al., 2000; Fried et al., 1992a, 2003; Olson et al., 1997; Willford et al., 2004).

The goals of this study are: 1) to examine whether the effects of PME on school achievement that we found at 10 years of age persist into adolescence; and 2) to evaluate whether the relation between PME and academic achievement is mediated by earlier effects of PME on child intelligence at age 6, child's depressive symptoms and attention problems at age 10, and adolescent early initiation of marijuana use (before age 14). Understanding the significance and strength of each pathway between PME and academic achievement in adolescence is an important tool in directing resources for intervention.

2. Methods

2.1. Study design

The study sample consists of women and their offspring who were participating in the MHPCD project, a longitudinal study investigating the effects of prenatal exposure to marijuana and alcohol on the growth, cognitive development, and behavior of the offspring. The women were first interviewed about their first trimester substance use at their fourth or fifth prenatal month visit to the Magee-Womens Hospital prenatal clinic. All women who used two or more joints of marijuana per month during the first trimester, along with a random sample of women who used less than this amount, were enrolled in the marijuana study cohort. In a second study, all women who drank three or more drinks per week during the first trimester and a random sample of women who used less than this amount were selected. Women could be in either or both cohorts. These two cohorts are combined for this analysis. Further details about the studies are in Day et al. (1985).

The women selected for the studies were interviewed again at their seventh month prenatal visit and after delivery, when they were asked about their second and third trimester substance use, respectively. Women and their offspring were assessed at birth, 8 and 18 months, 3, 6, 10, 14, 16, and 22 years of age. At each phase, maternal interviews included questions about substance use, sociodemographic and environmental characteristics, and psychological status. Age-appropriate instruments were used at each phase to assess offspring growth, cognitive and neuropsychological development, and behavior. The current report focuses on the 14-year follow-up that was conducted from 1996 through 2000.

2.2. Description of the study cohort

The MHPCD cohort consisted of 763 live singleton infants at birth. The current study is based on a sample of 524 mother-child dyads who were seen at 14 years, representing 69% of the birth cohort. The attrition from birth to 14 years was due to death of the child (n = 6), placement for adoption/foster care (n = 7), refusal (n = 52), moving out of the area (n = 49), and lost to follow-up (n = 69). Thirty-four children were interviewed by phone at age 14 and could not be tested, combined mother/child assessments were not available for 11 cases, and 11 children with mental or physical disabilities were excluded from these analyses. There were no differences in gender, birth weight, maternal income, or education between subjects who participated in the study (n = 524) and those who did not (n = 239). Participants were more likely to be African American (55% versus 44%, $\chi^2 = 7.1$, $p < 0.01$) and to have been exposed to marijuana during the third trimester of gestation (21% versus 12%, $\chi^2 = 8.9$, $p < 0.01$) than were those who did not participate at 14 years.

The demographic characteristics of the sample are shown in Table 1. At recruitment, between 1982 and 1985, most of the women (74%) had a high school education and 32% were married. They were generally of lower socioeconomic status with a median monthly family income of $350. Forty-five percent of the women were Caucasian and 55% were African American. At the 14-year phase, 42% of the mothers were married, and 75% worked or went to school. Their median monthly family income was $1500. Half of the offspring were males. Their average age was 14.75 (SD = 0.44). At 14 years, 11.6% of the offspring were not in maternal custody. For these children, we interviewed the child's caregiver and have included the data from these subjects.

2.3. Measures

2.3.1. Prenatal substance exposure

Prenatal marijuana use was measured as the quantity and frequency of marijuana, sinsemilla, and hashish used during each month of the first trimester and across the second and third trimesters of pregnancy. Because the concentration of Δ-9-tetrahydrocannabinol (THC) in each of these substances differs, the quantities of sinsemilla and hashish were transformed into two and three joints of marijuana, respectively (Gold, 1989; Julien, 1992). Marijuana exposure was calculated as average daily joints (ADJ) and was considered separately for each trimester of pregnancy. In this analysis, marijuana exposure was used both as a

Table 1
Demographic characteristics.

		Range
First trimester maternal characteristics		
Age (mean years)	23.2	18–42
Education (mean years)	11.8	7–18
Race (% Caucasian)	45.2	
Monthly family income (median $)[a]	350	0–1000+
Married (%)	31.5	
Work and/or attend school (%)	26	
14 year maternal characteristics		
Education (mean years)	12.4	6–18
Monthly family income (median $)	1500	0–9990
Married (%)	42.2	
Work and/or attend school (%)	74.6	
14 year child characteristics		
Gender (% male)	49.6	
Age (mean years)	14.75	14–16
Presence of an adult male in the household (% present)	51.9	
Not in maternal custody (%)	11.6	
Number of siblings	1.5	0–7
HOME-SF (mean)	11.3	2.5–18

[a] Measured from 1982 to 1985.

continuous variable and as a dichotomous variable, heavy (≥1 joints/day) versus non-heavy (<1 joint/day) use. This dichotomy was based on our previous findings at age 10, which showed that deficits in school achievement were related to heavy use (Goldschmidt et al., 2004). Further details about the MHPCD substance use questions, including the assessment of pattern, duration, and quantity of use, and methods to minimize recall error and maximize honest reporting, can be found in Day et al. (1985).

Prenatal alcohol exposure was measured in the same manner as marijuana exposure and included questions about specific categories of alcoholic beverages (e.g., beer, wine, liquor). The average daily volume (ADV) was calculated for each trimester of pregnancy. Prenatal tobacco exposure was measured by the number of cigarettes smoked per day for each trimester of pregnancy. Information regarding the quantity and frequency of cocaine use and illicit drugs other than marijuana was also collected, but due to their low prevalence in this cohort, illicit drug use was dichotomized to use (=1) versus no use (=0) across pregnancy.

2.3.2. Dependent variable

Academic achievement at age 14 was assessed with the Wechsler Individual Achievement Test (WIAT) Screener (Psychological Corporation, 1992). The WIAT Screener is composed of three subtests: basic reading (decoding letters and words), mathematics reasoning (problem-solving strategies), and spelling (encoding dictated sounds and words). The age-adjusted composite screener and subtest scores were used in this analysis. The internal consistency reliability coefficient for this age range is 0.95 (Psychological Corporation, 1992).

2.3.3. Mediators

The Stanford–Binet Intelligence Scale (SBIS) Fourth Edition (Thorndike et al., 1986) was used to measure the child's cognitive development at 6 years. The SBIS composite score at age 6 has an internal consistency reliability score of 0.96 (Thorndike et al., 1986). Children were assessed by trained examiners who were blind to maternal prenatal and current substance use. The mean SBIS score at age 6 was 91.6 (S.D. = 14). This value is below the standardized mean of the general population (100), which is characteristic of a sample with lower educational and socioeconomic status.

Childhood depressive symptoms at age 10 were assessed by the Children's Depression Inventory (CDI; Kovacs, 1992), a measure of general psychopathology and distress. The test–retest reliability and internal consistency coefficients of the CDI are 0.82 and 0.86, respectively. The average CDI raw and t-scores were 7.4 (S.D. = 6.5) and 46.3 (S.D. = 8.7), respectively. We used the raw scores in the analyses because they were more highly correlated with the WIAT.

The Swanson, Noland, and Pelham (SNAP; Pelham and Bender, 1982) attention subscale was used to measure the child's attention problems at age 10. This scale consists of 5 questions based on the DSM-III definition of attention deficit disorder, such as easily distracted or failing to finish things. The questions range from never (=1) to all the time (=4). The average inattention score for this cohort was 9.0 (S.D. = 3.0).

Questions regarding adolescent age of onset, quantity, and frequency of marijuana use over the past year were adapted from the Health Behavior Questionnaire (Jessor et al., 1989). The adolescents were interviewed separately from their mothers for all questionnaires. A biological validation of substance use also was included to check on the adolescent's self-report. The adolescents were asked to provide a urine sample during their appointment and were informed that the sample would be analyzed for substance use. All of the adolescents whose urine was positive for THC had also reported that they had initiated marijuana use. For this study, early age of onset was defined as initiation of marijuana use prior to age of 14. This cut-point was selected because it represented initiation prior to the 14-year assessment of academic achievement. One hundred and two adolescents (19.5%) used marijuana before the age of 14.

2.3.4. Covariates

The covariates included in the analyses were selected based on their association with school achievement according to the literature. These included adolescent gender and ethnicity, home environment, maternal socioeconomic status, prenatal exposure to alcohol and tobacco, and current maternal substance use. Home environment was measured by the Home Observation for Measurement of the Environment—Short Form (HOME-SF; Baker and Mott, 1989), presence of an adult male in the household (yes/no), whether the adolescent was in maternal custody (yes/no), and number of siblings. Maternal variables included depression as measured by the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977), hostility measured by the State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970), number of life events (Dohrenwend et al., 1978), support from friends and relatives and overall coping ability (Berkman and Syme, 1979). Socioeconomic status was measured by average monthly family income, maternal education, and work status (yes/no). At 14 years postpartum, maternal substance use was assessed for the preceding year, using the same questions as in the prenatal questionnaires. To reduce the number of covariates, a measure of overall current maternal substance use was created: current maternal alcohol use (2 or more drinks/day), marijuana use (1 or more joints/month), and other illicit drugs (any/none) were combined into one variable ranging from zero (none) to three (all).

2.4. Statistical analysis

The analyses followed a mediational model. First, the direct relation between PME and the WIAT Screener composite score at age 14 was examined controlling for other prenatal substance exposures, socioeconomic status, and the home environment using stepwise regression analysis. One-tailed probabilities were used because it was hypothesized that PME would predict lower WIAT scores. The covariates considered for inclusion in the regression analysis are listed in the Measures section. Variables significant at an alpha level of ≤0.05 were included in the model. When the relation between PME and the WIAT composite score was found to be significant, the WIAT reading, spelling, and mathematics subscales were analyzed separately to identify the specific achievement domains that were significantly related to PME.

Regression errors were screened to identify outliers and influential cases and to examine the regression assumptions. No influential cases were identified and the residual diagnostics did not indicate violation of the regression assumptions. Because the sample at 14 years differed from the birth cohort by race and third trimester marijuana exposure, the regression analyses were repeated and weighted to adjust for these differences. The weights were calculated as the inverse of the predicted propensities, the probability of response by each racial and exposure group. The results of the weighted regressions did not differ from the unweighted regressions with regard to the effects of PME. The estimated regression coefficients presented here are based on the unweighted data for ease of interpretation.

The mediators were selected based on their significant associations with PME and academic achievement and their temporal position preceding the assessment of academic achievement at age 14. The mediating effects of IQ as measured by the SBIS composite score, depressive symptoms (CDI), inattention (SNAP), and early initiation of marijuana use (before age 14) were tested using structural equation models (SEM). All covariates that were significantly related to academic achievement in the regression analysis were included in the mediating model. The significance of each mediator was assessed by MacKinnon's z' distribution (MacKinnon et al., 2002), and the combined indirect effect was estimated by the sum of the product of path coefficients (Mueller, 1996). The statistical package LISREL (Jöreskog and Sörbom, 1994) was used to estimate the parameters of the model.

3. Results

The distribution of marijuana use at each trimester of pregnancy and at 6, 10, and 14 years, the phases included in these analyses, is shown in Table 2. For descriptive purposes, women were categorized as abstainers (ADJ = 0), light/moderate users (ADJ > 0 and ADJ < 1), and heavy users (ADJ ≥ 1). In general, women decreased their use early in pregnancy. Forty-two percent of the women used marijuana during the first trimester of pregnancy compared to 24.6% and 20.6% at the second and third trimesters of pregnancy, respectively. During the first trimester, 15.1% of the women were heavy users, and by second and third trimesters the rates of heavy use were 5.6% and 6.5%, respectively. Only a few women initiated marijuana use after their first trimester. Of the women who used marijuana during pregnancy, 93% (218/234) used marijuana in the first trimester. On average, first, second, and third trimester heavy users smoked 2.4, 2.1, and 2.4 joints of marijuana per day, respectively. A postpartum decrease in marijuana use with age was also observed (Table 2). At the 14-year phase, only 15.5% of the caregivers reported any marijuana use and heavy users reported smoking on average 2.3 joints of marijuana per day.

The bivariate associations between the WIAT Screener, the hypothesized mediators, and first trimester PME are presented in Table 3. There was a clear demarcation in WIAT scores between those with heavy use (ADJ ≥ 1) compared to those with no exposure and those with low to moderate exposure. The mean WIAT composite, reading, and mathematics scores of adolescents who were exposed to an average of one or more joints of marijuana/day during first trimester of gestation were significantly lower than those of their peers. There was no significant relation between first trimester PME and the spelling subscale. There were no significant associations between any of the WIAT scores and either second or third trimester PME.

In the second step, stepwise regression analyses were used to evaluate the significance of these associations after controlling for significant covariates (Table 4). One-tailed probabilities are reported to reflect the hypothesis that PME is related to poorer school achievement. Exposure to one or more joints of marijuana/day during the first trimester significantly predicted the WIAT Screener composite score after adjusting for other covariates. The magnitude of the deficit was 2.9 points ($t = 1.8$, $p < 0.05$) after taking into account race, maternal education, gender, number of siblings, family income, and home environment.

Basic reading was the only subscale of the WIAT that was significantly associated with first trimester marijuana exposure after controlling for other significant predictors of school achievement (coefficient = −3.3, $t = 2.2$, $p < 0.05$). Other predictors of lower reading subscale scores were African American race, lower maternal education, male gender, and lower family income.

Second and third trimester PMEs were not related to academic achievement at age 14. Exposure to one or more alcoholic drinks/day in the second trimester of pregnancy significantly predicted a reduction in the Basic Reading subscale of WIAT (coefficient = −7.7, $t = 2.2$, $p < 0.05$). There were no other significant associations between prenatal substance exposure and the measures of academic achievement.

Table 2
Prevalence of maternal marijuana use (%).

Time of assessment	Abstainer[a]	Light/moderate[b]	Heavy users[c]	Total n[d]
First trimester	58.4	26.5	15.1	524
Second trimester	75.4	19.0	5.6	479
Third trimester	79.4	14.1	6.5	524
Six years	76.8	18.8	4.4	504
Ten years	76.8	20.2	3.0	505
Fourteen years	84.5	13.8	1.7	523

[a] Abstainer: no use.
[b] Light/moderate: greater than zero and less than one joint/day.
[c] Heavy: one or more joints/day.
[d] Sample sizes differ due to missing data.

Table 3
Unadjusted mean scores of WIAT Screener and mediators by levels of first trimester marijuana exposure.

	Non-exposed n = 306	Light/moderate[a] n = 139	Heavy exposure[b] n = 79	p[c]
WIAT screener at 14				
Composite	89.9	89.8	83.9	0.003
Basic reading	93.8	93.1	87.8	0.001
Mathematics	90.7	90.7	86.0	0.02
Spelling	93.8	94.4	90.1	N.S.
SBIS composite score at 6	91.6	94.1	87.1	0.002
CDI total raw score at 10	6.9	6.9	10.3	0.0002
SNAP inattention at 10	8.7	9.2	9.7	0.02
Marijuana initiation prior to age 14 (%)	15.7	24.5	25.3	0.03

N.S. = not significant.
[a] Light/moderate: less than one joint/day.
[b] Heavy: one or more joints/day.
[c] Overall significance using F test for the continuous variables and χ^2 test for dichotomous variables.

Figs. 1 and 2 show the effects of PME on the WIAT composite score before and after inclusion of the intervening variables in the model. The mediators were intelligence at 6 years, depression symptoms and inattention at 10 years, and initiation of marijuana before age 14. The pathways between the variables are labeled with the standardized coefficients for comparison of the magnitude of relations between variables. For example, Fig. 2 shows that, controlling for all other factors in the model, IQ at 6 was the most significant predictor of the WIAT composite score with a standardized coefficient of 0.53, followed by inattention (Std. Coef. = −0.11), and then by depression symptoms (Std. Coef. = −0.09). The relation between marijuana use prior to age 14 and the WIAT composite score was not significant at alpha level of 0.05 (Std. Coef. = −0.05), after adjusting for the effects of other mediators on achievement. The adequacy of the fitted model was assessed using adjusted goodness-of-fit (AGFI) and comparative fit indices (CFI). The values for both these indices were above 0.90, indicating overall adequate fit (Mueller, 1996). The Root Mean Square Error of Approximation (RMSEA) was less than 0.05, which is also an indicator of good fit. The SEM also included covariation among the exogenous variables (i.e., PME, race, maternal education, and income), but this is not shown in the figures.

Table 4
Regressions on the WIAT scales in which first trimester marijuana exposure was a significant predictor.

WIAT scales	Significant predictors	Coefficient[a]	R^2
Composite score	Race[b]	8.09***	0.10
	Maternal education	1.27***	0.03
	Gender[c]	−3.4**	0.01
	Number of siblings	−1.14**	0.01
	Family income (increments of $100)	0.11*	0.01
	HOME-SF	0.5*	0.005
	Heavy 1st trimester marijuana exposure[d]	−2.9*	0.005
Reading subscale	Race	6.4***	0.08
	Maternal education	1.25***	0.03
	Gender	−3.6***	0.02
	Family income (increments of $100)	0.09**	0.01
	Heavy 1st trimester marijuana exposure	−3.3*	0.01

[a] Regression coefficient represents the magnitude of effect per unit change.
[b] Caucasian = 1, African American = 0.
[c] Male = 1, female = 0.
[d] Heavy exposure = 1, all others = 0.
*** $p < 0.001$.
** $p < 0.01$.
* $p < 0.05$.

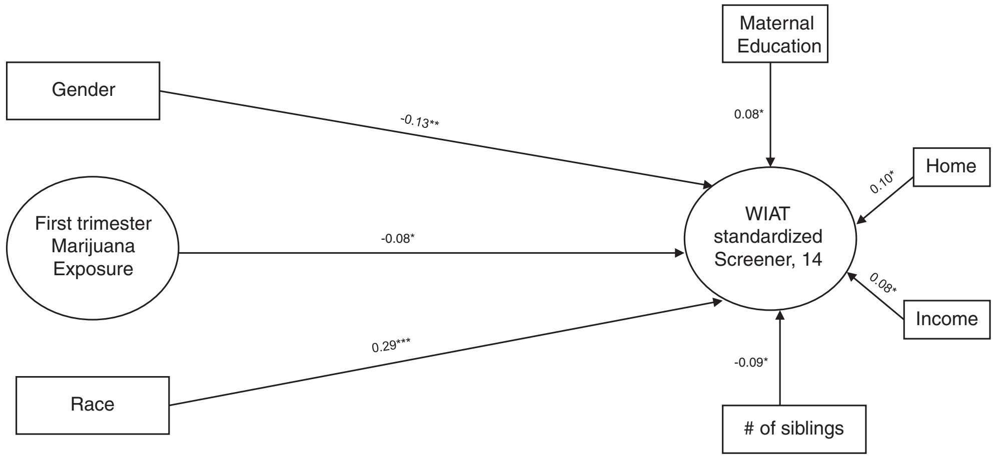

Fig. 1. Direct effects of first trimester marijuana exposure on WIAT composite score at 14.

The direct effect of PME on the WIAT composite score before inclusion of the mediators was significant (Fig. 1). The indirect effects of PME on school achievement through the SBIS composite score at age 6, CDI depression symptoms at age 10, SNAP inattention at 10 years, and early initiation of marijuana use were each individually significant, using MacKinnon's z' distribution. The most significant mediated pathway was through depression symptoms (z' = −2.0), followed by IQ (z' = −1.8), and inattention (z' = −1.7). The weakest path was through early initiation of marijuana use (z' = −1.1). The direct effect of PME on achievement was no longer significant once the mediating effects were taken into account (Fig. 2).

The total effect of PME on school achievement was decomposed into direct and indirect effects. The combined indirect effect was calculated as the sum of the products of the coefficients. The standardized total effect of PME on school achievement of the model in Fig. 2 was equal to −0.083 (−3.5 raw score, t = −1.9, $p<0.05$) and the indirect effect was equal to −0.071 (−3.0 raw score, t = −2.6, $p<0.005$). Thus, 85% (0.071/0.083) of the effect of PME on the WIAT composite score was due to the mediators.

The same pattern was observed with the WIAT reading score, with only slight differences. Controlling for all other factors in the model, the standardized coefficients between IQ, attention problems, depression, early marijuana use and WIAT reading scores were 0.45 ($p<0.0005$), −0.11 ($p<0.005$), −0.06 ($p<0.1$), and −0.06 ($p<0.1$), respectively. Similar to what we reported above with the WIAT composite score, the indirect effects of PME on the reading score through these mediators were all significant using MacKinnon's z' distribution. The strongest path between PME and the WIAT reading subscale was through the SBIS composite score at 6 years (z' = −1.8), followed by SNAP inattention scale (z' = −1.64), CDI depression symptoms (z' = −1.4), and early initiation of marijuana use (z' = −1.2). The direct effect of PME on the reading score was not significant after inclusion of the mediators in the model. The standardized total effect of PME on the WIAT reading subscale was −0.103 (−3.9 raw score, t = −2.3, $p<0.05$), and 60% of the total effect of PME on the WIAT reading score was explained by the mediators.

4. Discussion

This study evaluated the association between PME and the performance of the offspring on a test of academic achievement. First trimester PME significantly predicted poorer scores on the composite score and the reading score of the WIAT at 14 years of age. This association was

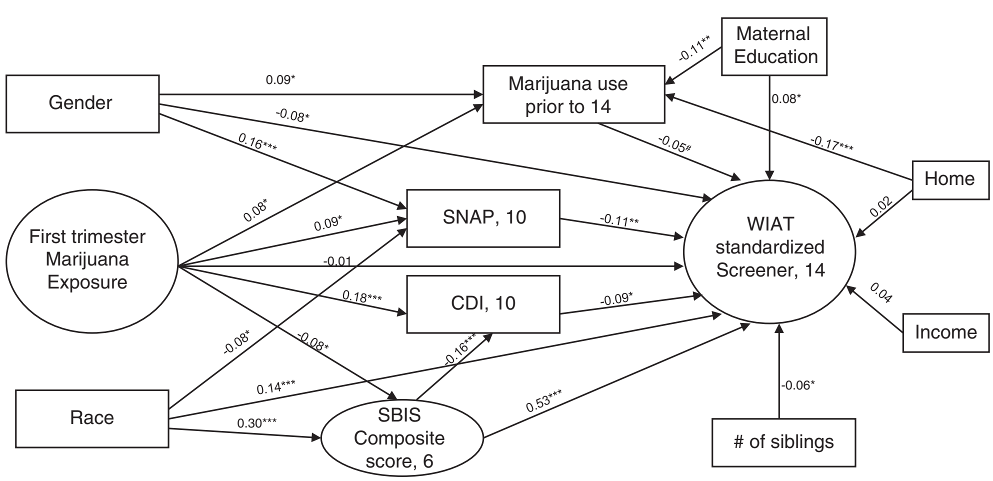

Fig. 2. Total effects of first trimester marijuana exposure on WIAT composite score through intervening variables.

found at an exposure level of one or more joints/day during the first trimester. There were no significant effects of first trimester PME on the other subscales of the WIAT. PME in the second and third trimesters did not predict academic performance. The direct effects of PME on the WIAT composite score and the reading subscale remained significant after controlling for covariates of PME and achievement such as home environment, race, and maternal education.

We further hypothesized that if there was a significant association between PME and academic performance, this significant relation would be explained by the earlier effects of PME on the cognitive, emotional, and behavioral development of the children. We demonstrated in earlier analyses that PME predicted IQ deficits at age 6 (Goldschmidt et al., 2008), attention problems at 10 years (Goldschmidt et al., 2000), a higher rate of depressive symptoms in offspring at age 10 (Gray et al., 2005), and an earlier onset of marijuana use (Day et al., 2006). When these variables were considered as mediators, the direct associations between PME and the composite scale and the reading subscale of the WIAT were no longer significant. The effects of PME on academic achievement were mediated by the earlier effects of PME on IQ, attention problems, depressive symptoms, and an early age of marijuana initiation. These findings are unique, as the only other study of PME did not evaluate the potential for mediating effects on academic achievement.

Pre-clinical studies with animals have shown that PME affects CNS development by disrupting the development and functioning of the fetal endocannabinoid system (Fride, 2008; Harkany et al., 2008). Prenatal exposure to THC disrupts the position, postsynaptic target selectivity, and differentiation of the developing axons in fetal brain (Berghuis et al., 2005). Exposure affects dopamine activity (Navarro et al., 1994) and processes in the prefrontal cortical dopamine system (Fride and Mechoulam, 1996). The resultant changes in the endocannabinoid system, in turn, lead to behavioral sequelae in animals such as responses to stress and novelty, emotional reactivity, and drug sensitivity (Harkany et al., 2007; Willford et al., in press). Thus, these pre-clinical studies support our findings that PME affects the domains of mood, attention, and drug use.

A limitation of this study is that the cohort was selected from a prenatal clinic and largely consisted of women of lower socioeconomic status. As a result, these findings may not be generalizable to other socioeconomic levels. This limitation is balanced by the methodological strengths of the study. Information about maternal sociodemographic, environmental and psychological characteristics, and current substance use was collected, which allowed an examination of the effects of PME while controlling for these factors. Current offspring substance use was also carefully assessed. In addition, the large sample size and excellent follow-up rates allowed for statistically powerful tests of the hypotheses.

The effects of PME were associated with exposure in the first trimester. Therefore, prevention and education programs should be directed at women who are planning their pregnancies and toward advising women to stop using marijuana as soon as they realize that they are pregnant. In addition, the relationship between PME and achievement was only significant for those with exposure levels of one or more joints/day. Although this does not allow us to say that there would not be effects at lower levels, it does identify a group of women who use marijuana and whose offspring have the highest risk of consequences.

Our findings demonstrate that there are PME-related cognitive, mood, attention, and substance use problems in childhood, which then have a negative influence on academic achievement. These early effects of PME may be compounded as the offspring experience the greater curricular demands of high school. Thus, among children with PME, early intervention on these characteristics could preclude later difficulties in academic performance, as well as other tasks of adolescence. On the obverse side, it is important to consider that children who have difficulties in school may be experiencing the sequelae of PME. This would direct counselors and teachers to the potential for interventions that are better tailored to the exposed adolescent's needs.

Conflict of interest statement

None.

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