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# Differential effects on cognitive functioning in 13- to 16-year-olds prenatally exposed to cigarettes and marihuana

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**Abstract**

Cognitive performance was examined in 145 thirteen- to sixteen-year-old adolescents for whom prenatal exposure to marihuana and cigarettes had been ascertained. The subjects were from a low-risk, predominantly middle-class sample participating in an ongoing, longitudinal study. The assessment battery included tests of general intelligence, achievement, memory, and aspects of executive functioning (EF). Consistent with results obtained at earlier ages, the strongest relationship between prenatal maternal cigarette smoking and cognitive variables was seen with overall intelligence and aspects of auditory functioning whereas prenatal exposure to marihuana was negatively associated with tasks that required visual memory, analysis, and integration. The interpretation of the results is discussed in terms of the differential observations related to in utero exposure to cigarettes and marihuana and the nature of the cognitive variables associated with the two drugs.



*Keywords:* Marihuana; Cigarettes; Pregnancy; Cognition; Adolescent

## 1. Introduction

The Ottawa Prenatal Prospective Study (OPPS) is an ongoing longitudinal project that was initiated in 1978. It has examined the neurobehavioral and developmental effects of prenatal exposure to cigarettes and marihuana in a low-risk cohort assessed from birth through adolescence. By examining these two substances within the same sample, the ability to contrast the putative impact of maternal use of the two drugs is facilitated. Recently, we have published articles describing outcomes in 13- to 16-year-olds in the domains of growth [9] and attention [16]. The present report is an examination of cognitive performance in this age group.

Lower scores on tests of general cognitive performance have been reported in preschool and school-aged children born to women who smoked cigarettes during pregnancy both within the OPPS sample [11,4,19,28] and in other cohorts [31,40]. These dose-related findings persist after statistical adjustment for demographic factors and other drug use. A recurring theme in the investigation of this relationship is that the primary variables differentiating the children of smokers from those born to nonsmokers [11,14,19] or to women who quit smoking during pregnancy [40] were aspects of cognition that required auditory processing and verbal comprehension. These effects were apparent in the verbal subscales of standardized global intelligence tests [14,19,31], as well as in altered auditory habituation in neonates [10,17,34,39], auditory-based behaviors in infants [13], deficits in auditory processing [30], and phonological aspects of reading [20] in school-aged children.

Another association with prenatal exposure to cigarettes found in the OPPS sample has been in the area of memory. At both 5 and 6 years of age [11], a negative dose–response relationship was observed between maternal smoking and the child's performance on the Memory subscale of the McCarthy Scales of Children's Abilities [29] with three of the four subtests requiring verbal responses. Between 9 and 12 years of age [19], after controlling for prenatal confounding variables, a negative linear trend was noted with a digit span memory assessment and an auditory working memory task.

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Although there have been relatively few studies that have considered cognitive performance in offspring born to marihuana users, quite consistent observations have been noted. Furthermore, the findings differ from those reported among the children exposed prenatally to cigarettes.

In children participating in the OPPS, maternal marihuana use was not associated with cognitive outcome variables after controlling for potentially confounding variables at ages 2 [13] and 3 years old [14]. At 4 years of age [14], several cognitive domains distinguished the children of heavy ($\geq$6 joints/week) marihuana users from the remainder of the sample. In particular, memory, verbal, and perceptual outcome measures were negatively associated with maternal marihuana use. These observations are similar to those reported by Day et al. [3] with 3-year-olds from a predominantly African American, high-risk, low-socioeconomic sample recruited in the Pittsburgh area. In that work, the children of marihuana users were negatively affected in short-term memory, verbal, and abstract/visual reasoning tasks. Further concordance was noted in a study [23] investigating the interaction between prenatal cocaine use and a number of drugs including marihuana in 3-year-old offspring. In this work, maternal marihuana use was also related to poorer performance on abstract/visual reasoning tasks. In the three cohort studies with preschoolers, in contrast to the impact of prenatal cigarette exposure described earlier, there was no prenatal marihuana effect on the composite intelligence scores. The lack of an association between global IQ and prenatal marihuana exposure continued in the OPPS subjects at 5–6 [11] and 9–12 years of age [19].

A large, well-controlled study using a high-risk cohort from Pittsburgh is the only non-OPPS study that has examined cognitive functioning in school-aged children prenatally exposed to marihuana and their findings are similar to those noted in the OPPS cohort. In a preliminary report from this group [36], prenatal marihuana use was negatively associated with abstract/visual reasoning at 10 years of age, an observation that was consistent with findings noted in the same cohort at 3 years of age [3]. A recent, more detailed description of the findings with the 10-year-old cohort [37] indicated that prenatal marihuana was associated with poorer performance on the design memory subscale and the composite index score of the Wide Range Assessment and Learning test [42] as well as measures of impulsivity. Finally, preliminary analysis from 14-year-olds in this cohort [47] indicated an association between prenatal marihuana exposure and the Wechsler Intelligence Scale for Children (WISC) Mazes and Coding subtests [46] suggesting vulnerability in the visual–cognitive domain.

Thus, in addition to the contrasting findings in terms of an impact on IQ, the consequences of maternal use of marihuana differed from maternal use of cigarettes within specific cognitive dimensions. Whereas prenatal cigarette exposure impacted the auditory domain, in utero marihuana was associated with deficits in tasks requiring visuo-planning, visuo-construction, and visuo-analysis, and with impulse control in tasks requiring sustained attention [19,15] but did not impact on tasks that involved basic visuo-perceptual abilities [15]. Prenatal marihuana exposure was also significantly associated with decreased consistency in response latencies in a timed visual attention task [16].

The combination of an absence of lowering of global IQ scores, the negative association with abstract visual reasoning, and the failure to find a negative impact until the children were 3 or 4 years of age has served as support for the hypothesis that prenatal marihuana exposure may impact upon particular facets of the behavioral–cognitive construct of executive function (EF). As elaborated in detail elsewhere [7,8,12], it has been proposed that visual analysis, hypothesis testing, and sustained attention are negatively associated with maternal use of marihuana. This type of integrative 'top-down' behavior [4,5] involves the interplay of subordinate cognitive operations and is considered an important facet of EF.

The tests in the present work examine aspects of cognition that have been shown to be impacted at earlier ages by maternal use of either cigarettes or marihuana. The assessment instruments were part of a large battery administered to 13- to 16-year-old OPPS subjects with the overall objective of examining the potential effects of prenatal exposure to the two drugs. The domains described in this report include cognitive achievement, memory, facets of EF, and general intelligence. As in previous reports, careful consideration is given to nondrug variables including demographic factors that may differ among women in the various drug groups.

## 2. Methods

### 2.1. OPPS cohort and pregnancy information

Six hundred and ninety-eight women volunteered to enter the OPPS in the late seventies and early eighties after learning of the study through the media or through notices in obstetricians' offices. The women were interviewed during each of the remaining trimesters in their pregnancies. The repetition of interviews and the use of the same female interviewer throughout the pregnancy enhanced the rapport between the subject and the interviewer and provided an opportunity to assess the consistency of the self-report [17]. Maternal data collected included amounts and patterns of drug use before and during pregnancy, caffeine use, nutrition, age, height, prepregnancy weight, weight gained during pregnancy, regular exposure to the cigarette smoke of others, general health (both present and prior to pregnancy), and history of previous pregnancies. The father's medical history, parents' level of education, and the family's socioeconomic status (SES) were also recorded. A nicotine score was derived by multiplying the number of cigarettes smoked on a daily average by the nicotine content of the brand

specified. Marihuana use was recorded in terms of number of joints per week. Measurement of alcohol consumption included beer, wine, and liquor use: both quantity and pattern of consumption were recorded and subsequently converted to ounces of absolute alcohol (AA) per day.

A cohort of children was selected for follow-up beyond birth: 140 children of women who reported any use of marihuana or drank alcohol beyond a daily average of 0.85 oz AA or smoked an average of at least 16 mg nicotine/day during pregnancy and a random selection of 50 children of women who were nonusers of marihuana, who abstained or drank little alcohol and who were nonsmokers. Of these 190 subjects, 157 children ranging in age from 13 to 16 years inclusive were available for testing. The 33 children not tested involved participants who had moved out of the Ottawa area, two families who had withdrawn from the study, and a few children unavailable for the testing. No differential loss of subjects with respect to drug variables occurred. The data for three children whose primary language was French and for four children who attended French school were not included in the analyses because the language emphasis at school and/or at home was thought to influence the outcome variables in the present report. Five children on Ritalin medication (none born to heavy marihuana users; three born to heavy smokers and two born to nonsmokers) were excluded because of concern regarding the effect of Ritalin on the children's performance in a number of tasks. The final sample comprised 145 subjects, 78 boys and 67 girls, with 45 thirteen-year-olds, 36 fourteen-year-olds, 51 fifteen-year-olds, and 13 sixteen-year-olds.

### 2.2. Instruments and procedure

The following tests were used to assess multiple aspects of cognition: Wide Range Achievement Test (WRAT) and the Peabody Spelling for general reading and language skills; Missing Numbers, Abstract Designs, Sentence Memory, and Knox Cube tasks for different aspects of auditory and visual memory; the Wisconsin Card Sorting Test (WCST) and the Stroop Test for inhibition of prepotent responding; and a short form of the WISC-III for overall general intelligence. Further detail and references regarding these tests are presented in Table 1. The age of the subject was taken into consideration either by age-normed standard scores provided with the test or by adjustment of raw scores and transformation to *t* scores.

Table 1
Measures and tests

*General reading and language skills*

WRAT [25]: The three components were the following: Reading—written words of increasing difficulty to be pronounced; Spelling—orally presented words of increasing difficulty to be written; Arithmetic—written arithmetic problems of increasing difficulty.

Peabody Individual Achievement Test—Spelling Recognition subtest [6]: The subject must visually select the correct spelling of a orally presented word from four minimally different written alternatives.

*Aspects of auditory and visual memory*

Missing Numbers [32]: Numbers from 1 to 10 were read in random sequence omitting one number. The subject was required to state which number was missing at the end of each of 10 trials.

Abstract Designs [33]: The subject was instructed to touch 1 of 12 abstract designs on the first of 12 pages and a different design on each successive page without touching any particular design twice. Latency and errors were recorded.

Sentence Memory Test [26]: The subject was asked to repeat 25 tape-recorded sentences of increasing length and complexity.

Knox Cube Test [44]: The subject was required to imitate prearranged sequences of increasing length and complexity as touched (at a rate of 1/s) on a row of four cubes affixed on a strip of wood.

*Inhibition of prepotent responding*

WCST [24]: The subject must determine a matching principle based on either color, form, or number. The response category is changed without warning after 10 correct responses. The number of perseverative errors was analysed.

Stroop Test [22]: From three separate pages, the subject is required to (1) read aloud the words 'red', 'green,' and 'blue' printed repeatedly in black ink; (2) name the colors of stimuli 'XXXX' printed repeatedly in red, green, or blue; and (3) name colors of the words 'red', 'green,' and 'blue' printed repeatedly in a manner in which the words did not match their printed color. An interference score calculated from the three tasks was used.

*Overall general intelligence*

WISC-III [46] Short Form [38]: The tetrad of block design, arithmetic, picture arrangement and vocabulary was transformed into a short-form deviation quotient to provide an estimate of full-scale IQ.

### 2.3. Statistical procedures

#### 2.3.1. Group categorization

Maternal cigarette smoking, after averaging use over pregnancy trimesters, was categorized into three groups: nonsmoking, light, heavy ($\geq$16 mg nicotine/day, which is approximately a minimum of one package of average strength). These three categories have been used in previous OPPS publications and were retained for the current analysis due to negative effects reported in both the light and heavy smoking groups with the same subjects at younger ages. Maternal average marihuana use across pregnancy was categorized into two groups: no use plus infrequent/moderate use ($<$6 joints/week) and heavy use ($\geq$6 joints/week). In a number of OPPS publications reporting effects of maternal marihuana use with the same subjects at younger ages, analyses involved three marihuana categories, comprising nonusers, heavy users, and a separate infrequent/moderate user group. Since no negative impact has been found with this intermediate use category it has been combined, as in a few previous articles [11,15,18], with the no-use group for the current report.

#### 2.3.2. Analysis

Both univariate and multivariate approaches were used in the analysis of the data. The former was considered an important complement to the multivariate analysis by pre-

senting all the unadjusted and adjusted cognitive/drug use relationships. The multivariate approach was used to control Type 1 error, to examine the total variance explained by a combination of cognitive outcomes, and to study the relationships among the cognitive variables in their association with the maternal drug groups.

For the univariate analyses, the relationship between each cognitive variable and drug use categories was examined separately for marihuana and cigarette smoking groups by means of analysis of variance (ANOVA) and, where warranted, analysis of covariance (ANCOVA) to control for potential confounds.

Stepwise discriminant function analysis (DFA), used as the multivariate approach, allows variables that discriminate across drug levels to enter in order of predictive power and yields the optimal combination of outcome variables to classify drug group membership. If two highly correlated predictors are eligible for entry at the criterion of $P \leq =.05$, the more powerful would enter first, bringing both its unique explanation of variance and the variance it shares with the less powerful predictor. This latter variable rarely has sufficient remaining explanatory power to enter the equation. However, with DFA, structure coefficients (SC) are available for further interpretation. These coefficients represent the correlation between each cognitive variable and the discriminant function(s). Therefore, if a variable fails to enter because of its high correlation with other variables that have stepped into the equation, its relative predictive power for the discriminant function is quantified by the SC. Another possible source of interpreting the importance of the individual predictors is by the size and direction of the standardized discriminant function coefficients that modify the cognitive variables in the equation. However, when these variables are correlated, which is the case with the cognitive measures in the present work, these coefficients or weights are limited in their interpretive value. For example, with two highly correlated variables similarly associated with the factor, often only one of the variables will have a large coefficient due to the predictor redundancy [1].

As in previous OPPS publications [11,19], cross-validation procedures were undertaken to examine the stability of the discriminant functions. Each case was classified by the functions derived from all cases other than that case and the shrinkage of correctly classified cases from the originally grouped cases to the cross-validated cases was examined.

#### *2.3.3. Confounding and moderating variables*

Other variables that might affect the relationship between the cognitive outcomes and the drug of interest were evaluated if related to the drug of interest at an alpha level of .10 or less and to the cognitive outcomes at an alpha level of .05 or less. Potentially confounding prenatal variables considered were SES (family income and average parental education), maternal age, maternal drug use, and mother's secondhand cigarette smoke exposure during pregnancy. Maternal pregnancy alcohol use and drug use that was not of primary interest (marihuana or cigarettes) were always included as covariates. Postnatal moderating or intervening variables examined were current SES (family income, maternal education), current marital status, current maternal cigarette and marihuana use, the home environment, the secondhand cigarette smoke exposure of the subject, sex of subject, and subject's current smoking habits. The home environment was assessed by maternal self-report with the Home Environment Questionnaire (HEQ) [43], which comprised subscales evaluating Achievement, Aggression-External, Aggression-Home, Aggression-Total, Supervision, Change, Affiliation, Separation, and Sociability. Active smoking by subjects was based on self-report that was confirmed by urinalysis and was coded as yes/no. The subject's postnatal secondhand smoke exposure was calculated as a proportion of life in which the subject was regularly exposed at least 2 hours/day to sources both within and outside the home. ANCOVAs were conducted by first selecting relevant prenatal potential confounds followed by subsequent entry of any postnatal variables satisfying the above criteria.

## 3. Results

Drug usage and characteristics across levels of maternal cigarette and marihuana use during pregnancy are described in Table 2. The average age and grade for the subjects did not vary across levels of the drug groups. The OPPS sample was representative of the Ottawa population with the average age, parity, and family income for the mothers being similar to those of women giving birth at the participating hospitals in the same years [17].

Assumptions regarding singularity, lack of Factor × Covariate interactions, and homogeneity of variance–covariance matrices were satisfied for the DFA and ANCOVA analyses. The prenatal maternal values for one nicotine, two alcohol, and four marihuana cases, as well as one current maternal marihuana value were extreme univariate outliers with respect to their distributions ($z$ score>4). Each score was adjusted to one unit greater than the next heaviest user in the distribution to maintain their rank [45], retain the cases for analysis, and reduce the influence of extreme values. When used as covariates, these continuous drug variables were log transformed to reduce positive skewness.

### *3.1. Prenatal cigarette smoking*

Table 3a presents, for each cognitive variable, the unadjusted mean and standard deviation (S.D.) as well as the mean and standard error (S.E.) adjusted for prenatal and postnatal covariates across the three cigarette smoking groups. The strongest relationships between maternal cigarette use and cognitive variables were seen with overall general intelligence represented by the short-form WISC

Table 2
Drug usage and characteristics of the groups

| | Cigarettes (mg nicotine/day) | | | Marihuana (joints/week) | |
|---|---|---|---|---|---|
| | None (0) | Light (>0 to <16) | Heavy (≥16) | None/light (<6) | Heavy (≥6) |
| Sample size | 64 | 45 | 36 | 120 | 25 |
| Prenatal characteristics | | | | | |
| Maternal marihuana use (joints/week) | 2.6 | 5.1 | 2.2 | 0.35 | 17.5*** |
| Maternal nicotine use (mg/day) | 0.0 | 5.7 | 25.5[a,***] | 8.1 | 8.4 |
| Maternal alcohol use (oz AA/day) | 0.18 | 0.16 | 0.18 | 0.18 | 0.14 |
| Mother's passive smoke exposure (% responding yes) | 26.6 | 61.4 | 90.6[a,***] | 45.7 | 83.3** |
| Mother's age at birth (years) | 29.5 | 27.0 | 26.7[b,**] | 28.9 | 23.9*** |
| Family income at birth (×CAN$1000) | 35.5 | 29.3 | 25.2[c,*] | 32.7 | 22.8* |
| Average parental education at birth[†] | 3.0 | 2.5 | 2.0[a,***] | 2.8 | 1.9*** |
| Postnatal characteristics | | | | | |
| Mother's current marihuana (joints/week) | 0.05 | 0.67 | 0.85* | 0.2 | 1.5*** |
| Mother's current smoking (cigarettes/day) | 0.42 | 8.1 | 16.5[a,***] | 6.1 | 9.9 |
| Current family income (×CAN$1000) | 57.2 | 58.0 | 45.8[d,**] | 56.7 | 44.8** |
| Mother's current education[†] | 2.9 | 2.4 | 2.2[b,***] | 2.7 | 2.0*** |
| Current marital status (% together) | 75.0 | 53.3 | 69.4 | 73.0 | 40.0** |
| Adolescent's age at testing (years) | 14.6 | 14.5 | 14.7 | 14.6 | 14.6 |
| Adolescent 's grade at testing | 8.6 | 8.4 | 8.5 | 8.5 | 8.4 |
| Sex of adolescent (% female) | 40.6 | 46.7 | 55.6 | 46.7 | 44.0 |
| Adolescent's postnatal passive smoke exposure (proportion of life) | 0.16 | 0.52 | 0.83[a,***] | 0.38 | 0.75*** |
| Adolescent 's current smoking (% responding yes) | 9.4 | 17.8 | 30.6[c,*] | 14.2 | 32.0* |
| HEQ Achievement | 57.0 | 56.3 | 48.5[d,***] | 55.5 | 51.1 |
| HEQ Aggression External | 47.9 | 47.5 | 54.6[d,**] | 49.7 | 48.0 |
| HEQ Aggression Home | 44.6 | 48.8 | 52.0[c,***] | 47.4 | 49.0 |
| HEQ Aggression Total | 44.8 | 48.3 | 53.9[d,***] | 48.0 | 48.7 |
| HEQ Supervision | 46.9 | 46.5 | 40.9[c,*] | 46.1 | 42.0 |
| HEQ Change | 49.6 | 49.9 | 51.3 | 49.5 | 53.1 |
| HEQ Affiliation | 52.3 | 52.2 | 49.9 | 52.6 | 47.2* |
| HEQ Separation | 49.4 | 52.6 | 52.3 | 50.1 | 56.0* |
| HEQ Sociability | 50.6 | 51.3 | 51.7 | 51.3 | 49.8 |

Statistical tests were one-way between-subjects ANOVAs with the Scheffé [41] test used for post hoc comparisons.

[a] All groups differ pairwise.

[b] *None* differs from *light* and *heavy.*

[c] *None* differs from *heavy.*

[d] *None* and *light* differ from *heavy.*

* $P \leq .05$.

** $P \leq .01$.

*** $P \leq .001$.

[†] Education was coded as 1: did not finish high school, 2: graduated from high school, 3: graduated from college or university, and 4: obtained a postgraduate degree.

(after controlling for parental education at birth and other drug use during pregnancy) and auditory memory in the form of Sentence Memory (after controlling for mother's other drug use and secondhand smoke exposure during pregnancy). Maternal cigarette smoking was associated with the WRAT achievement measures of reading and arithmetic but not after controlling for parental education at birth and other drug use during pregnancy. Visual memory, as assessed by the Knox Cube, was negatively associated with maternal cigarette smoking but no longer significantly related after adjusting for family income at birth, other prenatal drug use, and two HEQ subscales (Aggression-External and Supervision). No aspects of EF (WCST perseverative errors, inhibition of prepotent responses, working memory) were associated with maternal smoking. The covariates described above (and those included in subsequent analyses) differed from one analysis to another depending on which potential confounds met the criteria as specified in the Methods section.

Parental education as recorded at the time of the subject's birth was the covariate that mediated the relationship between prenatal maternal smoking and the two measures of WRAT-Reading and WRAT-Arithmetic but it only partially reduced the association of prenatal smoking with the short-form WISC. Parental education at birth was significantly correlated ($r$=.64, $P$<.001) with current maternal education as recorded at the time of the 13- to 16-year-old testing and thus current maternal education lacked sufficient

Table 3a
Unadjusted and adjusted outcome variables across smoking groups

| | Smoking (mg/day) | | | | | |
|---|---|---|---|---|---|---|
| | Unadjusted, mean (S.D.) | | | Adjusted, mean (S.E.) | | |
| | None (0) | Light (>0 to <16) | Heavy (≥16) | None (0) | Light (>0 to <16) | Heavy (≥16) |
| Sample size | 64 | 45 | 36 | 64 | 45 | 36 |
| General reading and language skills | | | | | | |
| WRAT-Reading | 114.3 (10.9) | 110.2 (11.0) | 107.1[a,**] (13.4) | 113.6 (1.6) | 110.6 (1.8) | 108.0 (2.2) |
| WRAT-Spelling | 106.8 (11.8) | 104.3 (12.2) | 102.4 (12.2) | | | |
| WRAT-Arithmetic | 102.1 (13.6) | 98.3 (15.4) | 93.8[a,*] (14.2) | 100.0 (1.9) | 99.0 (2.1) | 96.5 (2.6) |
| Peabody Spelling | 103.1 (10.4) | 100.4 (11.8) | 99.6 (12.2) | | | |
| Aspects of auditory and visual memory | | | | | | |
| Missing Numbers (errors) | 48.0 (9.1) | 51.1 (10.5) | 52.1 (10.5) | | | |
| Abstract Designs (errors) | 49.1 (6.2) | 50.5 (7.9) | 50.9 (5.9) | | | |
| Abstract Designs (latency) | 49.0 (8.8) | 50.9 (9.9) | 50.6 (8.4) | | | |
| Sentence Memory | 53.2 (10.1) | 49.4 (7.7) | 44.9[a,***] (10.2) | 53.1 (1.3) | 49.5 (1.4) | 45.0** (1.7) |
| Knox Cube | 50.6 (10.3) | 52.3 (8.7) | 46.0[b,*] (10.0) | 49.4 (1.2) | 52.0 (1.4) | 48.6 (1.6) |
| Inhibition of prepotent responding | | | | | | |
| WCST perseverative errors | 56.9 (9.4) | 58.3 (8.9) | 55.2 (7.7) | | | |
| Stroop interference | 51.5 (9.5) | 50.7 (6.9) | 50.1 (6.2) | | | |
| Overall general intelligence | | | | | | |
| Short-form WISC | 115.0 (14.3) | 109.1 (12.4) | 103.2[a,***] (11.8) | 113.4 (1.7) | 109.8 (2.0) | 105.2* (2.4) |
| Discriminant scores | 54.4 (10.8) | 49.1 (8.6) | 43.4[c,***] (10.0) | 53.4 (1.4) | 49.5 (1.5) | 44.6** (1.9) |

Statistical tests were one-way between-subjects ANOVAs with the Scheffé [41] test used for post hoc comparisons.
[a] *None* differs from *heavy*.
[b] *Light* differs from *heavy*.
[c] All groups differ pairwise.
[d] *None* and *light* differ from *heavy*.
[e] *None* differs from *light* and *heavy*.
* $P \leq .05$.
** $P \leq .01$.
*** $P \leq .001$.
[†] Education was coded as per Table 2.

power to be entered as a covariate in the ANCOVAs with these three measures. When the mediating role of the latter variable was examined, a pattern and degree of influence similar to that of parental education at birth was found.

The DFA revealed significant association between the smoking groups and the cognitive variables [$\chi^2(4, n = 145) = 25.8$, $P < .001$; Wilks' lambda=.83]. The first discriminant function accounted for 99% of the total discriminatory variance and discriminated in a linear manner maximally distinguishing the nonsmoking from the heavy smoking group. The mean discriminant *t* scores for each smoking group (group centroids) were 54.4, 49.1, and 43.4 for the nonsmoking, light, and heavy smoking groups, respectively. The primary predictors, as indicated by the SC, were the measure of general intelligence (short-form WISC; SC=.82) and Sentence Memory (SC=.80). Other moderately predictive variables were the WRAT-Reading (SC=.53), Knox Cube (SC=.42), Peabody Spelling (SC=.41), WRAT-Spelling (SC=.41), and WRAT-Arithmetic (SC=.40). The two variables that stepped into the DFA were the short-form WISC and subsequently Sentence Memory. These variables were moderately correlated ($r$=.38, $P < .001$) and therefore their associated discriminant function coefficients were not reliable for interpretative purposes. After controlling for parental education at birth, mother's secondhand cigarette exposure, alcohol and marihuana use during pregnancy, the association between maternal smoking and the discriminant scores remained [$F(2,138) = 5.7$, $P < .01$].

Classification results indicated that 49.7% of the original grouped cases were correctly classified. With the cross-validation procedure, 48.3% of grouped cases were correctly classified. These figures are considerably above the 33.3% correct classification expected based on chance.

### 3.2. Prenatal marihuana smoking

The unadjusted and adjusted means of the cognitive variables across the two levels of maternal marihuana use are presented in Table 3b. A significant association was found between Abstract Designs latency and the marihuana groups with the subjects born to heavier users displaying slower response times. This relationship remained significant after controlling for other maternal pregnancy drug use and the HEQ Supervision subscale, the only potential confounds that required adjustment. Performance on the Peabody Spelling was also negatively associated with maternal marihuana use after controlling for prenatal drug

Table 3b
Unadjusted and adjusted outcome variables across marihuana groups

| | Marihuana (joints/week) | | | |
|---|---|---|---|---|
| | Unadjusted, mean (S.D.) | | Adjusted, mean (S.E.) | |
| | None/ light < 6 | Heavy ≥ 6 | None/ light < 6 | Heavy ≥ 6 |
| Sample size | 120 | 25 | 120 | 25 |
| General reading and language skills | | | | |
| WRAT-Reading | 111.8 (11.9) | 108.6 (11.7) | | |
| WRAT-Spelling | 105.4 (12.4) | 102.8 (10.4) | | |
| WRAT-Arithmetic | 99.8 (14.5) | 94.1 (14.4) | | |
| Peabody Spelling | 102.3 (11.1) | 97.1* (11.7) | 102.3 (1.0) | 97.3* (2.2) |
| Aspects of auditory and visual memory | | | | |
| Missing Numbers (errors) | 49.9 (10.2) | 50.3 (8.7) | | |
| Abstract Designs (errors) | 50.0 (6.6) | 50.1 (7.2) | | |
| Abstract Designs (latency) | 49.1 (8.3) | 54.2* (11.3) | 49.2 (0.8) | 53.7* (1.8) |
| Sentence Memory | 50.1 (10.2) | 49.4 (9.1) | | |
| Knox Cube | 50.2 (10.0) | 48.9 (9.7) | | |
| Inhibition of prepotent responding | | | | |
| WCST perseverative errors | 56.7 (8.6) | 57.8 (10.3) | | |
| Stroop interference | 50.9 (8.3) | 51.1 (6.3) | | |
| Overall general intelligence | | | | |
| Short-form WISC | 111.1 (14.3) | 106.1 (11.1) | | |

[†]Education was coded as per Table 2.
Statistical tests were one-way between-subjects ANOVAs.
** $P \leq .01$; *** $P \leq .001$.
* $P \leq .05$.

use. No other prenatal or postnatal potential confounds were found to influence this latter association.

The DFA for the marihuana groups resulted in a univariate structure with only one variable, Abstract Designs latency, stepping into the function.

### 3.3. Influence of the subjects' cigarette smoking

Of the 145 subjects in this age group, 25 were active smokers as determined by self-report and confirmed by urinalysis (Table 1). In addition to the subject's smoking habits being considered as potentially confounding variables in the above analyses, an examination of any combined effects with either maternal cigarette or marihuana use during pregnancy was undertaken. Using factorial ANOVA with both subject's smoking and either maternal cigarette or marihuana use as independent variables, no potentiating or ameliorative effects were noted among the cognitive variables examined.

## 4. Discussion

The cognitive results obtained in the present report from the 13- to 16-year-old OPPS subjects continue some of the major observations found at younger ages, both in this sample and in other cohorts. The continuity is reflected in two ways. On the one hand, the areas that appear vulnerable to prenatal exposure to either cigarettes or marihuana are within those spheres that were identified at earlier ages and, on the other, in utero exposure to these two drugs continues to impact differentially on varying aspects of cognition.

In the OPPS sample, from the ages of 3–12 years [11,14,19], measures of overall intelligence were related to maternal use of cigarettes in a negative dose–response manner after controlling for potentially confounding variables. Extending this in the present work, among the 13- to 16-year-olds utilizing a short form of the WISC-III, the derived IQ was linearly and negatively associated with in utero exposure to cigarettes.

It is apparent from the DFA that, of all of the cognitive variables considered in the present battery, the short form of the WISC had the strongest association with maternal smoking. After the entry of the WISC into the function, many of the other cognitive variables did not have sufficient power to enter because of their shared variance with the WISC outcome. An important exception was found in the tests used to assess memory. Sentence Memory, a task requiring verbal processing, retained enough explanatory variance to enter the function arising from the DFA. On the other hand, the nonverbal, visual memory task, Knox Cube, did not. These differential findings in the 13- to 16-year-olds within the sphere of memory that appear related to either auditory or visual demands are consistent with the observations at younger ages of maternal smoking impacting upon auditory-based functioning. The results of the ANCOVA support these observations. After controlling for potentially confounding variables, Sentence Memory but not the Knox Cube task remained associated with prenatal cigarette exposure. At the earlier ages in the OPPS sample and other cohorts, the auditory–verbal domain was the dimension that maximally discriminated among the different levels of prenatal cigarette exposure when the full IQ battery was administered. The present results in the 13- to 16-year-old offspring continue to suggest that prenatal cigarette smoking is associated with deficits in auditory functioning.

A further consistency with earlier results obtained from the subjects exposed prenatally to cigarettes can be seen when comparing those cognitive outcomes derived from tests that were given both in the present battery and when the subjects were between 9 and 12 years of age [19,20]. In the current work, both overall intelligence and most measures of achievement (WRAT-Arithmetic; WRAT-Reading; composite WRAT score) were negatively associated with prenatal cigarette smoking before controlling for potentially confounding variables. The most influential covariate with smoking during pregnancy and both of the two categories of

outcomes was parental education. This covariate proved to mediate their relationships but to different degrees. In the case of the achievement measures, parental education strongly mediated the relationship with maternal smoking resulting in a reduction to nonsignificance. With the overall general intelligence measure, parental education reduced the magnitude of the relationship but, in contrast to the WRAT results, a statistically significant association remained. A similar pattern of mediation by parental education occurred with the same sample when tested at 9–12 years of age. At this age, the significant associations between WRAT-Reading and the WISC-III Full-Scale IQ with maternal smoking were differentially affected when the strong influence of parental education was statistically controlled. As found with the 13- to 16-year-olds in the current report, after controlling for this confounding factor in the 9- to 12-year-olds, maternal cigarette smoking was no longer associated with the WRAT-Reading whereas its relationship with the Full-Scale IQ, although diminished, remained statistically significant [20].

Why the general intelligence measures demonstrate a unique association with prenatal cigarette exposure whereas the achievement tests do not can only be speculated upon at this time. In terms of assessment, the WRAT achievement tests evaluate the mechanical abilities within arithmetic, reading, and spelling [25], whereas the WISC subtests examine the application of basic abilities in new and different ways. While intelligence tests, by assessing capabilities that are learned in a wide variety of life experiences, are more a measure of learning potential [38], achievement tests are more highly dependent upon formal learning experiences that are acquired in school or at home. Thus, the latter may be mediated, to a great degree, by parental education.

In the present study, as in earlier reports [11,15,19], the consequences of prenatal exposure to marihuana appear to differ from those following maternal cigarette use. In contrast to cigarette smoking during pregnancy and its negative association with both the overall IQ and verbal memory, these outcomes were not related to prenatal marihuana use even prior to any consideration of potential confounding factors. This lack of association with IQ parallels the results reported previously when these subjects were younger [11,14,19], where it was consistently noted that maternal marihuana use did not impact composite measures representing general or overall intelligence. In addition, as reported elsewhere [16], heavy maternal marihuana use was not associated with the ability to inhibit prepotent responding as assessed by the WCST and the Stroop Test.

However, particular aspects of cognition at different ages have been negatively associated with in utero exposure to marihuana. Effects have been found in the OPPS with memory at 4 years of age [14], with attention at the age of 6 years [18], with visual integration [15] and attention- and visual-related aspects of EF in 9- to 12-year-olds [19], and with stability of attention in 13- to 16-year-old teens [16].

Among the tests given in the present battery, only two tasks were associated with maternal marihuana use and both were unrelated to maternal smoking. Compared to the other tests used in the battery, these two tasks, Abstract Designs and Peabody Spelling, depend, to a lesser degree, on cognitive manipulation or comprehension and, to a greater degree, on visual memory, analysis and integration.

Peabody Spelling required the subject to visually analyze and recognize the correct spelling of commonly misspelled words. The words were pronounced and used in sentences by the examiner. The adolescent pointed to the correct spelling from among four similar alternatives presented on a page. The format of this test differed considerably from the WRAT-Spelling test in which subjects were also read sentences containing the word to be spelled but subsequently had to write the word using recall memory. The WRAT-Spelling test was not associated with prenatal marihuana exposure.

That deficits in the Peabody Spelling task were associated with prenatal marihuana exposure is consistent with earlier reports arising from both the OPPS and other cohorts. In these studies, subjects ranging in age from 3 [3,23] to 9–12 [15,19,36,37] to 14 years [46] exposed prenatally to marihuana performed significantly worse than appropriate controls on tasks requiring visual analysis and reasoning.

The finding that errors on Abstract Designs, a visual memory task, were not associated with heavy maternal marihuana exposure is consistent with earlier findings [15]. In that work, the performance of 9- to 12-year-old OPPS subjects exposed prenatally to marihuana was not negatively affected with respect to visual memory or visual–spatial relations in tasks that placed little demand on integrative analytical skills [21]. However, in those tasks, no measure of latency was available. The apparent slowing of processing speed in the Abstract Designs task may have served to enhance accuracy resulting in the subjects born to heavy marihuana users performing no worse than the other adolescents in terms of errors. The longer latency may reflect a subtle vulnerability to prenatal marihuana exposure in a task that requires visual analysis of complex figures combined with substantial demands on memory and attention, all three elements representing the general pattern of prenatal marihuana's impact noted in the extant literature described earlier.

This observation and interpretation is consistent with earlier reports from both non-OPPS and OPPS cohorts. Leech et al. [27], based on slower response times in a visual search paradigm [35] and performance on timed attention tasks, speculated that prenatally, marihuana-exposed 6-year-old children may enhance their accuracy at the cost of slowing their processing speed. Within the OPPS cohort, in a motor tracing task [2] in which both carefulness and speed were emphasized, the 13- to 16-year-old offspring of heavy marihuana users did not differ from the control group

in terms of precision but did manifest significantly slower latencies (unpublished data).

In summary, the present findings are consistent with and extend the observations in the cognitive domain made in this sample when they were 9–12 years of age. As noted at the younger age, maternal cigarette usage is negatively associated with particular outcomes that differ from those impacted by maternal marihuana use. The current results extend to adolescence the negative dose–response relationship between overall intelligence and prenatal exposure to cigarettes. In addition, the observation that memory subtests based on verbal functioning were more vulnerable to such exposure than were memory tasks based on other modalities parallels and extends the negative impact of cigarette use during pregnancy on the auditory–verbal domain noted in this cohort and others at earlier ages. The absence of a relationship of maternal use of marihuana and global intelligence in the offspring in the present sample, which contrasts with the findings associated with prenatal cigarette exposure, is also consistent with this sample at earlier ages. The vulnerability of the offspring of marihuana users in a task requiring visual analysis is in further contrast to the impact of prenatal cigarette exposure and is also consistent with similar observations of prenatally marihuana exposed offspring noted in this and other cohorts. Such deficits have been interpreted as suggesting that in utero exposure to marihuana impacts in a negative fashion upon particular aspects of cognitive performance that comprise the broad area of EF.

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