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Prenatal drug exposure and selective attention in preschoolers ☆

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Abstract

Deficits in sustained attention and impulsivity have previously been demonstrated in preschoolers prenatally exposed to cocaine. We assessed an additional component of attention, selective attention, in a large, poly-substance cocaine-exposed cohort of 4 year olds and their at-risk comparison group. Employing postpartum maternal report and biological assay, we assigned children to overlapping exposed and complementary control groups for maternal use of cocaine, alcohol, marijuana, and cigarettes. Maternal pregnancy use of cocaine and use of cigarettes were both associated with increased commission errors, indicative of inferior selective attention. Severity of maternal use of marijuana during pregnancy was positively correlated with omission errors, suggesting impaired sustained attention. Substance exposure effects were independent of maternal postpartum psychological distress, birth mother cognitive functioning, current caregiver functioning, other substance exposures and child concurrent verbal IQ.
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1. Introduction

Alterations in arousal modulation and attentional control have repeatedly been demonstrated in infants and toddlers in controlled studies of prenatal cocaine exposure [6,15, 31,46,49]. Similarly, infants with heavier prenatal cocaine exposure, compared with at-risk controls, have difficulty on tasks of inhibitory control [39]. The brain system that supports attention and inhibitory control, collectively called cognitive control, is the frontal–striatal system [8]. In experimental work with other species, this system is especially vulnerable to prenatal cocaine exposure because cocaine changes levels of neurotransmitters during gestation, which in turn have organizational effects on this brain system [34,51,52]. Recently, animal models of the behavioral effects of prenatal cocaine have suggested that the frontal–striatal systems necessary for establishing and maintaining selective response sets are at particular risk [24,25].

Functioning in frontal–striatal areas is different in ADHD, and these differences have been linked to the ability of children with ADHD to form selective attentional sets and to withhold impulsive responses [12]. Imaging studies confirm that at-least by 4 or 5 years of age, selective attention and inhibitory control depend on frontal–striatal functioning [5,13]. Deficits in selective attention, if found in cocaine-exposed preschoolers, would support the hypothesis that the frontal–striatal system is altered by prenatal cocaine exposure.

Bendersky and colleagues [7] recently reported an effect of prenatal cocaine exposure on impulsivity at 5 years of age. In a large cohort, prenatal cocaine exposure was associated with inferior ability to inhibited an non-rewarded motor response over time. In a modest sized group ($n = 30$, cocaine exposed) assessed at 6 and 10 years of age, Richardson and colleagues [42,43] reported deficits of sustained attention associated with cocaine exposure, with cocaine exposed children showing reduced sustained attention but not selective attention deficits. Bandstra and colleagues replicated the sustained attention findings with a larger, higher-risk cohort of cocaine-exposed preschoolers, but did not investigate selective attention [2].

Mayes and colleagues reported preliminary data suggesting that cocaine exposure is associated with selective attention effects in 5 year olds [38]. However, group differences in their study might be accounted for by variability in severity of maternal/caregiver risk factors and prenatal exposure to other substances [28]. In particular, the report must be considered preliminarily because potentially confounding prenatal exposure to cigarettes was not adequately controlled for.

Prenatal cigarette exposure has been associated with deficits in both selective and sustained attention during the preschool years [for a review, Ref. 20]. In two large, well-controlled prospective studies, prenatal cigarette exposure was associated with decreased selective attention in preschoolers assessed using the CPT task [32,53]. In Fried and colleagues' study, offspring of cigarette smokers had higher rates of commission errors on the CPT task at 4 [32] and 6 years [23]. This negative relationship between smoking and selective attention did not persist to later school ages [21]. Interestingly, this developmental pattern was replicated in another high-risk cohort, in which tobacco exposure was associated with sustained attention deficits at 6 years [33], but not 10 years of age [17]. There was a working memory deficit in the cigarette-exposed adolescents that suggests a developmentally persistent frontal–striatal effect of exposure [21].

Cocaine using mothers are also more likely to smoke marijuana than non-cocaine using women, and marijuana exposure also has effects that are suggestive of frontal–striatal deficits [23]. In separate, longitudinal studies, investigators [21,3] found marijuana effects on sustained attention at 6 years and older. Fried and colleagues failed to find a marijuana effect at 4 years of age [32] despite the presence of a cigarette effect on CPT errors at that age.

There are conflicting findings regarding prenatal alcohol exposure and performance on attention tasks. Several studies failed to find a relationship between prenatal alcohol exposure and performance on attention tasks at early school age [42,33,17,9], although one study did find such a relationship [53]. Coles and colleagues found performance on a sustained attention task affected by alcohol exposure in adolescents only for the subgroup with dysmorphology [14],

suggesting that sample differences might account for the conflict in the literature.

In the current study, two attention tasks, each with sustained and selective attention components, were presented to 330 4-year-old children as part of a longitudinal prospective study of the developmental effects of prenatal cocaine exposure. Both tasks were chosen for their demonstrated sensitivity to ADHD in preschoolers [11] and consequent neuropsychological specificity.

2. Methods

2.1. Subjects

A total of 330 children were presented with at least one of two attention tasks: a continuous performance task (CPT) and a picture deletion task (PDT). As participants in a prospective study by Singer and colleagues, they had been followed since birth [46,47]. The research was approved by hospital and university review boards and consent from custodial caregivers was obtained.

Of the 415 newborns recruited, 404 were living at 4 years. Of these, 28 children were unavailable at 4 years [49]. Of those children available at 4 years, 46 were not presented with either attention task. For 3 with a concurrent IQ of less than 45, testing was discontinued. Other children were not tested for the following reasons: a home visit could not accommodate the test, ($n = 4$); the attention tasks were still in piloting stage ($n = 10$); there was no examiner available trained in tasks ($n = 8$), the family had to leave before the attention battery could be administered, and they did not return to complete the visit ($n = 21$).

Of the 330 children offered at least one attention task, 149 were not offered the CPT task due to: inadequate time or personnel ($n = 78$); the CPT was still being piloted ($n = 18$) or the child ($n = 53$) had a concurrent IQ ≤ 70, an eligibility criterion for the CPT task. One child was not offered the PDT due to tester error. Neither the PDT nor the CPT was presented at different rates to exposure groups.

2.2. Assessments

2.2.1. Substance exposure assessment

The protocol for assessing exposure to cocaine, alcohol, marijuana and cigarettes employed by the Cleveland study has been described more extensively elsewhere [46,48]. Exposure was assessed with biological samples taken during the birth hospital stay and a post partum interview conducted at the first follow-up interview (approximately 2 weeks post partum).

Assignment into cocaine exposure groups (exposed, unexposed) and marijuana exposure groups (exposed, unexposed) was based on a positive response to either maternal self-report, meconium report, or infant/maternal urine reports. Meconium is the first bowel movement of the

newborn. Assignment into the alcohol-exposure group and cigarette-exposure group was based on maternal self-report and meconium assay. The biological assay for alcohol was based on a relatively new meconium procedure [3,4].

Self-report of drug-use was investigated with a standardized interview [46]. The frequency estimate (days/week) was multiplied by the daily amount (marijuana joints, cigarettes, drinks equivalent to .5 ounces absolute alcohol, or "rocks" of cocaine) to compute an estimate of use for each time period: the month prior to pregnancy, as well as during each trimester of pregnancy. These severity scores for the four time periods were also averaged into a single severity (avg. severity) score for each substance.

2.2.2. Attention assessment

The 4 year-old-visits were conducted in a single 3–4 h session at the research laboratory. Child testers were unaware of the substance exposure status of the children. The attention assessment was given after the Wechsler Preschool and Primary Scales of Intelligence-Revised [54] (WPPSI-R) [49], as well as a language [35] and an emotional functioning assessment. The presentation of the attention tasks was intermixed with an executive functioning assessment [40].

We employed preschool adaptations of two attention tasks: the CPT [44,16,26] and the picture deletion task ([16], PDT). The Byrne lab furnished original copies of the stimuli for both tasks.

For both tasks, commission and omission error rates were calculated as the proportion of opportunities for error (i.e. chances to miss a target or respond to a foil) in which the child made an error. Sustained attention is primarily necessary for low omission rates and selective attention contributes to lowering commission errors.

Picture Deletion Task for Preschoolers-Modified [26]. In this visual search task developed by Corkum, et al., children had to find 30 target pictures among 90 foils, with all 120 items presented simultaneously on two legal-size pieces of paper. Simple geometric shapes were employed, with triangles as the target and squares, diamonds, and circles as foils. Participation in this task requires passing a pretest involving one target exemplar and 5 foil exemplars [26]. If the child identified the target without making more than one error, they move on to the test phase. Children had up to 4 min to complete the task during the test phase.

Based on pilot testing, several modifications were made for the current cohort of children. Most notably, children did not make the responses themselves. Instead, the child pointed to an item to be marked and the tester marked it as soon as possible afterward. Also, there were scripted prompts that the experimenter made in response to strings of commission errors or periods of non-responding.

Continuous Performance Task (CPT) for Preschoolers-Modified [16]. In the CPT, the child must respond to the presentation of the target in a stream of serially presented targets and foils. We modified the computerized CPT task [42] to make it more structured. The tester was seated beside the child during training and test and gave scripted prompts for off-task behavior.

Line drawings were sequentially presented at a fixed rate for 750 ms each with an inter-trial interval of 1350 ms. in blocks of 6 items: the target (a pig face) and each of 5 foils (flower, lollipop, girl face, sun). The order of presentation was random within each block. The training session included up to 6 blocks of stimuli and also served as a pretest. Training continued until the child had correctly identified the target on two consecutive target trials without any intervening commission errors (criteria for passing pretest) or all six blocks of stimuli had been exhausted (failure of pretest). There were 25 blocks of stimuli during the test phase. If the child was off-task, and did not re-engage after 4 standardized prompts by the experimenter, testing was terminated.

2.2.3. Parental/environmental assessment

At the postpartum assessment several measures were administered to the current caregiver including: a questionnaire designed to yield a global index of psychiatric symptom severity (BSI: Brief Symptom Inventory: Derogatis, [18]); maternal verbal ability (PPVT-R: Peabody Picture Vocabulary Test-Revised: Dunn and Dunn, [19]); maternal performance IQ subtests (picture completion and block design from the WAIS-R).

At the 4-year-old visit, the preschool version of the HOME [10] was verbally administered to the current caregiver. Jacobson and Jacobson had previously adapted the interview version of the HOME to elicit responses that can take the place of the observed items and we further refined this adaptation [35,49]. The maternal substance abuse interview was updated, providing data on caregivers' current substance use. The Brief Symptom Inventory was also updated and, if there was a new caregiver, the PPVT-R, WAIS-R and BSI tests (subtests) were re-administered.

2.3. Methods of data analysis

Prior to analyses, several variables were normalized by a $\log_e(x+1)$ transformation, including drug self-report measures and the Global Severity Index (GSI). To stabilize the variance and correct for non-normality, the complimentary log–log (clog–log) transformation was used for the CPT and PDT attention variables. If we let p represent a proportion (e.g., CPT commission error rate) the clog–log transformation is $y = \log[-\log(1-p)]$. This transformation is undefined when $p=0$, therefore a constant of 0.01 was added to each value. Due to the high prevalence of 0% in the PDT omission outcome, which prohibited finding a suitable transformation, the variable was dichotomized at the 75th percentile.

Data were evaluated based on dichotomous substance exposure variables (exposed/non-exposed) using the two-

sample t-test and Pearson χ^2 tests for continuous and categorical variables, respectively. When unadjusted effects of exposures were found, they further explored.

Generalized additive models (GAM) [27] were used to identify the functional form (dose–response) of the relationship between the attention outcome variables and each drug exposure. The GAM models were fit with a non-parametric loess function of $\log_e$ (drug exposure) to describe the functional form. Based on the results from a plot of the predicted relationship, a threshold dose–response was identified, if suggested, and a piecewise linear model was then fit to allow for the threshold effect using multiple linear or logistic regression model. The process of fitting dose–response curves with these models allowed for: 1) an appropriate form of target exposure (e.g., group status, continuous, threshold effect) to be chosen, 2) for other prenatal exposures which may affect the target drug/outcome relation to be identified and 3) for the potential confounding effects of select primary variables (GSI,

HOME, caregiver current use of illicit drugs and alcohol) to be identified.

We employed a criterion method [29,30,45,49], of selecting secondary variables to consider as potential confounders. If they were both associated ($p < 0.10$) with target drug exposure and related ($p < 0.10$) to the outcome variables of interest the secondary variables were entered into the model. The following secondary variables were: gender, African-American ethnicity of birth mother, maternal age at birth, parity, prenatal care visit(s), maternal years of education, marital status, low socioeconomic status, biological and current caregiver mental functioning variables. The following variables were evaluated as potential mediators by the same criteria: length of gestation, birth length, birth weight, birth head circumference and child current verbal IQ.

Multiple linear and logistic regression models were used to evaluate the effects of prenatal substance exposure controlling for potential confounders and mediators.

Table 1a

Characteristics of mothers/caregivers of participants in PDT task, by cigarette exposure, group status

	Cigarette exposed $n=199$			Non-cigarette $n=100$			df	t/χ^2	p
	n (%)	Mean	SD	n (%)	Mean	SD			
Gestational drug use									
Cigarette, avg. severity[a]		11.5	11.2		–	–			
Alcohol, avg. severity[b]		6.7	14.3		1.7	9.6	258	−6.53	***
Marijuana, avg. severity[c]		.86	2.9		.72	3.7	284	−1.86	****
Cocaine, avg. severity[d]		16.2	40.5		1.84	7.9	287	−8.26	***
Use of less common drug	23 (15%)			0			1	12.7	***
Birth mother characteristics									
African-American ethnicity	153 (77%)			90 (90%)			1	7.5	**
Married	18 (9%)			19 (19%)			1	6.1	*
No prenatal care	28 (14%)			11 (11%)			1	.58	
Lower SES	193 (97%)			99 (99%)			1	1.2	
Age (years)		28.3	5.2		25.4	4.8	297	−4.6	***
Years education		11.6	1.6		12.1	1.2	244	2.4	*
Parity		3.2	1.9		2.8	1.9	297	−1.5	
PPVT-R score		76	14.3		75.5	15.4	287	−.3	
WAIS-R, block design		7.1	2.1		7.0	2.0	289	.6	
WAIS-R, picture completion		7.1	2.2		6.6	2.2	289	1.6	
Brief symptom Inventory		.68	.66		0.48	0.54	276	−2.7	**
Current caregiver									
Current alcohol, severity		2.4	68.3		1.6	4.6	272	−1.01	
Current marijuana, severity		0.2	1.0		0.6	4.3	141	0.1	
Current cocaine, severity		4.8	43.9		0	0	181	−2.0	*
HOME score		42	5.9		42	6.6	297	−.28	
PPVT_R score		80	15.7		75.9	15.9	277	2.0	*
WAIS-R block design		7.2	2.3		6.8	2.1	281	1.2	
WAIS-R picture completion		7.1	2.4		6.7	2.2	281	−1.6	
Brief symptom inventory		0.37	0.43		0.32	0.4	271	1.0	

[a] Mean number of cigarettes/day.
[b] Mean number of drinks/day × number days/week.
[c] Mean number of joints/day × number days/week.
[d] Mean number of rocks/day × number days/week.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.
**** $p < 0.10$.

Regardless of its relationship with the target exposure, if gender was related to performance ($p < 0.1$) then the role of gender as a possible modifiers of the outcome variables relationship with the exposure was evaluated.

Predictors of pretest success on the PDT and CPT measures were evaluated using logistic regression models. Predictors were identified by the $p < 0.10$ criterion as described above.

3. Results

3.1. Rate of passing pretests

Of the 329 children offered the PDT, most (301, 91%) passed the initial pretest and went on to participate in the test phase. Sixteen (5% of 329) failed the pretest and 12 (4% of the 329) refused to participate. The children in the cocaine-exposed group passed the pretest at a lower rate (88% passed) than the non-exposed children (95% passed, $\chi^2 = 4.4$, $p < 0.04$). Pretest success was not different by any other exposure grouping.

Of 181 children offered the CPT, most ($n = 154$, 85%) passed the pretest but there were some failures ($n = 18$, 10%) and some refusals ($n = 9$, 5%). Consistent with our findings from the PDT pretest, the children in the cocaine-exposed group passed the CPT pretest at a lower rate (78%) than the non-cocaine exposed group (91%, $\chi^2 = 6.1$, $p < 0.01$). The rate of passing was not significantly different by other exposure groupings.

3.2. Selective attention

3.2.1. Selective attention on the picture deletion task (PDT)

Selective attention on the PDT was evaluated through membership in the high commission error (>75th percentile of the sample distribution) or low commission error rate groups. Children in the cigarette-exposed group were twice as likely to be in the poor PDT selective attention group ($\chi^2 = 5.7$, $p < 0.02$, odds ratio (OR)$= 2.16[1.6 - 6.5]$).

To explore the association between cigarette exposure and PDT commission errors, we investigated potentially

Table 2
Effects of cigarette exposure group status on PDT commission errors

Predictor	Odds ratio (95% C.I.)	Wald χ^2	p
Cigarette exposure, group status	3.3 (1.6–6.5)	11.1	<0.001
Alcohol exposure, avg. severity	7 (.5–.9)	6.8	0.009
African-American ethnicity, maternal	2.8 (1.2–6.7)	5.5	0.019

$\chi^2 = 19.2$ ($df = 3$), $p < 0.001$.

confounding variables in the subset of 301 children who participated in the PDT. Although mothers in the cigarette-exposed group also reported more severe use of alcohol, marijuana and cocaine, as well as a higher rate of using other drugs during pregnancy (Table 1a), average severity of alcohol use was the only primary variable to qualify for the model.

As can be seen in Table 1a,b there were many of the secondary variables to be considered as potential confounders or mediators of the target relationship. However, of these potentially confounding secondary variables, only birth mother ethnicity met the criterion for entry into the model.

Adjusting for potential confounders, exposure to cigarettes was associated with a high rate of commission errors on the PDT task (Table 2).

3.1.2. Selective attention on the continuous performance task (CPT)

On the CPT, there was a significantly higher rate of commission errors in the cocaine-exposed group [exposed, $M = 27\%$, SD$= 22\%$ vs. non-exposed, $M = 19\%$, SD$= 17\%$, $t(152) = 2.39$, $p < 0.02$]. The children in the cigarette-exposed group also made commission errors at a higher rate [exposed, $M = 25\%$, SD$= 21\%$ vs. non-exposed, $M = 18\%$, SD$= 17\%$, $t(151) = 2.61$, $p < 0.01$] on the CPT task. Based on the estimated response curves from the GAM models, cocaine exposure was dichotomized (expose or non-exposed), and cigarette exposure was evaluated as average severity as it had been for the PDT task.

As can be seen in Table 3a,b, for the 154 CPT task participants, the cocaine exposed and non-cocaine exposure

Table 1b
Characteristics of PDT participants, by cigarette exposure, group status

	Cigarette exposed ($n = 199$)		Non-cigarette exposed ($n = 100$)				
	Mean	SD	Mean	SD	df	t	p
Birth characteristics							
Male (%)	92 (46%)		44 (44%)		1	.1	
Gestational age (weeks)	38.2	2.4	38.4	2.7	297	.7	
Birth weight (kg)	2.87	.59	3.09	.76	161	2.5	*
Birth length (cm)	48.3	3.5	48.9	4.0	174	1.22	
Head circumference (cm)	32.9	1.9	33.4	2.3	164	2.11	*
Concurrent functioning							
WPPSI-R Verbal IQ	82.3	11.2	82.9	12.3	297	.36	

Table 3a

Characteristics of mothers/caregivers of CPT task participants, by cocaine exposure grouping

	Cocaine exposed $n=69$			Non-cocaine-exposed $n=85$			df	t/χ^2	p
	n (%)	Mean	SD	n (%)	Mean	SD			
Gestational drug use									
Cigarette, avg. severity[a]		13.0	11.6		4.2	8.0	149	−5.2	**
Alcohol, avg. severity[b]		11.4	21.4		1.1	3.9	103	−6.1	**
Marijuana, avg. severity[c]		.92	2.5		1.0	4.9	147	−1.6	
Cocaine, avg. severity[d]		35.8	61.5		–	–	–		
Use of less common drug	12 (19%)			1 (1%)			1	14.6	**
Birth mother characteristics									
African-American ethnicity	55 (80%)			65 (76%)			1	0.23	
Married	7 (10%)			20 (23%)			1	5.1	*
No prenatal care	13 (24%)			7 (9%)			1	4.8	*
Lower SES	53 (96%)			71 (96%)			1	0.01	
Age (years)		29.8	5.2		26.3	5.0	152	−4.23	**
Years education		11.2	1.6		12.3	1.3	152	4.62	**
Parity		3.8	1.9		2.7	1.9	152	−3.46	**
PPVT-R score		71.8	13.5		79	16.0	150	2.96	**
WAIS-R, block design		7.0	2.0		7.3	2.2	150	.75	
WAIS-R, picture completion		6.9	2.2		7.0	2.4	150	.33	
Brief symptom inventory		0.54	0.35		0.32	0.27	113	−4.3	**
Current caregiver									
Current alcohol, severity		1.7	8.6		1.2	2.8	139	.02	
Current marijuana, severity		0.08	.6		0.7	4.6	110	1.25	
Current cocaine, severity		7.2	51.7		0	0	61	−1.78	
HOME score		42.5	6.2		43.4	5.5	131	.96	
PPVT_R score		80.5	16.5		79.4	17.1	146	−.27	
WAIS-R, block design		6.9	2.2		7.4	2.2	145	1.39	
WAIS-R, picture completion		7.2	2.4		7.0	2.4	145	−.48	
Brief symptom inventory		0.32	0.43		0.35	0.38	136	.68	

[a] Mean number of cigarettes/day.
[b] Mean number of drinks/day × number days/week.
[c] Mean number of joints/day × number days/week.
[d] Mean number of "rocks"/day × number days/week.
* $p<0.05$.
** $p<0.001$.

groups differed on many secondary variables. However, none of the secondary variables were related to CPT commission errors.

There were also several of the secondary variables related ($p<0.10$) to severity of cigarette exposure. How-ever, once again, none of these met the criteria for entry into the regression model.

Unadjusted, cocaine exposed grouping was associate with higher CPT commission errors (Table 4a), thus worse selective attention. In an unadjusted model,

Table 3b

Characteristics of CPT task participants, by cocaine exposure group

	Cocaine exposed ($n=69$)		Non-cocaine-exposed ($n=85$)		df	t/χ^2	p
	Mean	SD	Mean	SD			
Birth characteristics							
Male (%)	29 (39%)		43 (51%)		1	1.1	
Gestational age (weeks)	37.9	2.5	38.8	2.3	152	2.4	*
Birth weight (kg)	2.7	.58	3.1	.6	152	4.3	***
Birth length (cm)	47.6	3.6	49.3	3.3	152	3.0	**
Head circumference (cm)	32.5	1.7	33.6	1.9	152	3.7	***
Concurrent functioning							
WPPSI-R verbal IQ	85.5	8.8	88.7	11.1	152	3.3	***

* $p<0.05$.
** $p<0.01$.
*** $p<0.001$.

Table 4
Effects of exposure on CPT commission errors

Predictor	Beta (SE)	t	p
Model 1[a]			
Cocaine exposure, group status	.42 (.18)	2.4	.02
Model 2[b]			
Cigarette exposure, avg. severity	.15 (.07)	2.3	.03
Model 3[c]			
Cigarette exposure, avg. severity	10 (.08)	1.3	.18
Cocaine exposure, group status	.25 (.21)	1.2	.22
Model 4[d]			
Cigarette exposure, avg. severity	.23 (.10)	2.2	.03
Cocaine exposure, group status	.71 (.32)	2.2	.03
Interaction	−.28 (.15)	−1.8	.07

[a] $F(1, 152) = 5.7$, $p < 0.02$, $R^2 = 0.04$.
[b] $F(1, 148) = 5.1$, $p < 0.03$, $R^2 = 0.03$.
[c] $F(2, 147) = 3.3$, $p < 0.04$, $R^2 = 0.04$.
[d] $F(3, 146) = 3.4$, $p < 0.02$, $R^2 = 0.07$.

increasing exposure to cigarettes was also associated with higher CPT commission error rates (Table 4b). Due to the presence of confounding between these drug exposures, when both variables were entered into a single model, neither were significantly associated with commission errors (Table 4c). An interaction between cocaine and cigarettes was then estimated and found to have a probability of $p < 0.07$. When it was entered into the final model (Table 4d) there were positive relationships between both exposures and commission errors. Inspection of the interaction suggests that the negative effect of cocaine exposure on selective attention is only apparent at lower levels of cigarette exposure. It also suggests the linear negative relationship between cigarette exposure and selective attention is only apparent in the non-cocaine exposed children. However, results should be interpreted with caution since the interaction term is not statistically significant.

Table 6
Effects of first trimester marijuana exposure on PDT omission errors

Predictor	Beta (SE)	t	p
Model 1[a]			
Marijuana exposure, 1st trimester severity	.32 (.14)	2.3	.03
Cocaine exposure, 1st trimester severity	−.11 (.05)	−2.2	.03
Model 2[b]			
Marijuana exposure, 1st trimester severity	.29 (.15)	1.9	.06
Cocaine exposure, 1st trimester severity	−.14 (.05)	−2.6	.01
Caregiver current use of marijuana, severity	.26 (.22)	1.2	.25

[a] $F(2, 284) = 4.13$, $p < 0.02$, $R^2 = 0.03$.
[b] $F(3, 259) = 4.03$, $p < 0.01$, $R^2 = 0.04$.

3.3. Sustained attention and marijuana

There was a non-significant positive correlation between the avg. severity of marijuana exposure and the rate of omission errors on the PDT ($r = .11$, $p < 0.08$), suggesting that exposure was associated with worse sustained attention. Marijuana use during pregnancy co-occurred with use of the other drugs (Table 5). Using GAMs and linear regression severity of first trimester marijuana use was identified as the best marijuana exposure predictor of PDT omission error rate. Current caregiver marijuana use and severity of first trimester cocaine exposure were identified as potential confounders of this relationship.

The following secondary variables had positive correlations with severity of first trimester marijuana exposure: age, WAIS-R block design and picture completion subtests, and current caregiver block design. Birth mothers with lower SES status and who used more of the less common drugs used more marijuana during the first trimester. First trimester marijuana severity was negatively associated with birth weight and maternal education. Despite these relationships, no secondary variable met the criterion ($p < 0.10$) of being related to omission rate on the PDT.

Adjusted for prenatal cocaine exposure, severity of first trimester marijuana exposure was related to more omission

Table 5
Characteristics of polysubstance exposure of PDT task participants, by marijuana exposure grouping

Maternal use during pregnancy	Marijuana exposed $n = 85$			Non-marijuana-exposed $n = 216$			df	χ^2/t	p
	Users %	Mean	SD	Users %	Mean	SD			
Marijuana	100%	2.8[a]	5.4	0%	–	–			
							1	11	*
Tobacco	81%	11.2[b]	13.8	61%	6.1	8.6	290	−3.6	*
							1	18.8	*
Alcohol	84%	6.8[c]	13.7	57%	4.4	12.9	291	−3.7	*
							1	37.6	*
Cocaine	75%	11.9[d]	17.2	36%	11.4	39.0	293	−4.1	*

[a] Mean number of joints/day × number days/week.
[b] Mean number of cigarettes/day.
[c] Mean number of drinks/day × number days/week.
[d] Mean number of "rocks"/day × number days/week.
* $p < 0.001$.

errors (Table 6). However, caregiver current (while the child 2–4 years of age) use of marijuana was a partial confounder of this relationship. Adjusting for current caregiver marijuana use, which was associated with a large decrease (15%) in the regression coefficient of the 1st trimester marijuana variable, the latter was at the level of a non-significant trend (Table 6).

4. Discussion

Young children whose mothers had used cocaine during their pregnancies produced a higher rate of commission errors on the CPT than children without cocaine exposure. The finding suggests that cocaine-exposed children had difficulty in maintaining selective attention sets. None of the postnatal environmental risk factors, maternal risk factors, or other substances used could account for these differences apart from prenatal cigarette exposure. The negative effect of cocaine was only independent of cigarette exposure at lower levels of cigarette exposure. It is worth noting that participation in both tasks required passing a pretest, and cocaine exposed children had difficulty passing pretest. Because more cocaine-exposed children were screened out, the effects of cocaine exposure grouping on those who met the criterion for participation is all the more striking.

We found negative effects of prenatal cigarette exposure on commission errors on both the PDT and CPT assessments of selective attention. These effects appeared to be independent of all potentially confounding and potentially mediating variables.

Attention control decrements associated with severity of cigarette exposure have been found on CPT tasks with other cohorts of preschoolers [32,53], but this is the first for the PDT. Because the PDT requires self-directed search through simultaneously presented targets and distracters, it may have more ecological validity to the school classroom. Because secondary smoke was not accounted for in this study and has been found to have similar prenatal effects as primary cigarette use by the mother [41], environmental smoke may contribute to the relationship between maternal report of smoking and commission errors.

It should be emphasized that our finding effects for both cigarettes and cocaine on errors of commission, as compared with omission errors, does not justify interpreting the effect as an increase in impulsivity. The more conservative interpretation is that commission errors reflect failures to maintain a selective attention response set. This more conservative interpretation is especially appropriate given the modification made to the current tasks. The ongoing encouragement to produce a response may have caused some children to assume a compliant behavioral profile when they were no longer attempting to be selective in their responses [1]. Thus, it is especially problematic to conclude that the increased rate of commission errors associated with substance exposure in the current study reflects increased impulsivity.

Evidence for an effect of first trimester marijuana exposure on PDT omission errors was found, suggesting severity of marijuana use reported by the mother was positively related to failures to maintain vigilance. The finding that at 4 years of age marijuana-exposed children have some difficulty in sustained attention is relevant to current understanding of the age at which such effects emerge. Fried and colleagues found a relationship between marijuana exposure and attention at 6 years of age but not at 4 years of age [22,31]. Their assessment of attention at 4 years of age was sensitive to cigarette exposure, leading to the conclusion that the marijuana use impacted abilities emerging later in development [20]. The current results suggest that the relationship between prenatal marijuana and sustained attention is apparent as early as the preschool years.

The current findings confirm the previous reports that prenatal exposure to cocaine and cigarettes affects selective attention in preschoolers, with an additional novel finding that marijuana exposure has a negative effect on sustained attention at this age. It must be noted that prenatal substance exposure in these models is accounting for a very small percent of the variance in performance. However, the results must be extrapolated over the large number of substance exposure children in evaluating the public health risk. Given the very high risk status of these children, small shifts in the means of groups near the threshold for needing educational services can amount to large burdens on families and school systems.

Preschoolers are at the very beginning of a developmental progression in which attention becomes increasingly willful and effortful [44]. Despite the methodological challenges, assessing attention in preschool years is important in and of itself. First, it allows us to better characterize the difficulty children may be having adapting to structured situations, such as the preschool classroom. Second, it allows us to better understand early delays of attention, an understanding that may in turn inform our understanding of the neurological and functional development of attention. Recent longitudinal studies of ADHD have suggested that there are distinct subtypes of that disorder that can be distinguished by pattern symptom onset of symptoms during this period [50]. Therefore, a complete picture of the effects of prenatal substance exposure on attention requires an examination of the developmental progression of attentional skills from infancy through the school age years.

At preschool and school age, prenatal cocaine exposure has been associated with persistent behavioral problems in the same cohort [35,36]. It will be important to explore the relationship between impairments in selective attention and behavioral problems to ascertain whether attentional difficulties predispose preschoolers to later behavioral problems. There has been a consistently reported correlation between prenatal cigarette exposure and diagnosis of ADHD in retrospective reviews of clinically referred samples (see Ref. [37] for a review). The prospective design of the current study also presents a unique opportunity to consider

variables (both prenatal, child, and environmental) which may alter the degree to which preschool attentional problems predict the school age diagnosis of ADHD, as well as more minor attentional problems that may go undiagnosed.

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