

WEB MATERIAL

Gestational Exposure to Organophosphate Pesticides and Longitudinally Assessed

Behaviors Related to Attention-Deficit/Hyperactivity Disorder and Executive Function

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<u>Contents</u>	<u>Page</u>
Web Appendix 1. Exclusions Based on Developmental Disorders.....	3
Web Appendix 2. Neurodevelopmental Assessments.....	3
Web Table 1. Demographic and Exposure Characteristics of All Children with Prenatal DAP Measurements and of Children Included by Timepoint, with Assessment for Differences Between Included and Excluded Children: CHAMACOS Study.....	7
Web Table 2. Mean attention and executive function scores by age point, based on teacher report, maternal report, and child assessment: CHAMACOS study.....	10
Web Table 3. Spearman Correlation of Select Measures within Timepoints: CHAMACOS Study.....	12
Web Table 4. Spearman Correlation of Repeated Measures across Timepoints: CHAMACOS Study.....	13
Web Table 5. Supplemental Table 5: Spearman Correlation Matrix of Measures, with Repeated Measures Represented as the Mean Score for that Child Across Age Points: CHAMACOS Study.....	14
Web Table 6. Change in maternal report and child-assessed attention and executive function scores per 10-fold increases in mean total prenatal urinary DM concentrations (nmol/L) using repeated measures (GEE) models, overall and stratified by sex, in the CHAMACOS study population, enrolled 1999-2000 in Salinas Valley, California.	15
Web Table 7. Change in maternal report and child-assessed attention and executive function scores per 10-fold increases in mean total prenatal urinary DE concentrations (nmol/L) using	

WEB MATERIAL

repeated measures (GEE) models, overall and stratified by sex, in the CHAMACOS study population, enrolled 1999-2000 in Salinas Valley, California..... 17

Web Table 8. Adjusted regression coefficients and 95% confidence intervals for multivariable linear regression models of association between mean total prenatal urinary DAP concentrations (nmol/L, log10 scale) and children's attention and executive function as reflected by teacher report, maternal report, and child assessment scores by time point per 10-fold increases in mean total prenatal urinary DAP concentrations (nmol/L), in the CHAMACOS study population, enrolled 1999-2000 in Salinas Valley, California..... 19

Web Figure 1. Directed acyclic graph (DAG) for associations of prenatal organophosphate exposure and executive function and attention-deficit/hyperactivity disorder-related behaviors..... 21

References..... 22

WEB MATERIAL

Web Appendix 1. Exclusions Based on Developmental Disorders

We excluded 6 children with diagnosed developmental conditions who could not complete all testing. These include 1 child with Down's Syndrome, 1 with CP/Hydrocephalus, 3 children with an ASD diagnosis, and 1 deaf child. Aside from incomplete testing for these 6 children, their cognitive and behavioral differences from other children in the cohort would be significant for reasons beyond early pesticide exposure.

Web Appendix 2. Neurodevelopmental Assessments

Although we assessed multiple aspects of children's cognitive and behavioral development during this time period, we selected several informant-report scales and child assessment measures with the explicit intention to characterize children's executive functioning and ADHD-related behaviors as discreet (and separate) domains. A priori, we selected the Behavior Rating Inventory of Executive Function¹ and the Wisconsin Card Sort Task⁵ as our key measures of executive functions and the Conners' ADHD/DSM-IV Scales² and the Conners' Continuous Performance Test⁶ as our key measures of attention. We also incorporated subscales from two other instruments we had administered as part of our overall assessment battery. The first were the Hyperactivity and Attention Problems scales of the Behavior Assessment Scales for Children³. In addition to the value of having another parent and teacher reported scale for ADHD-related behaviors in the BASC-2, we also administered the child BASC-2 self-report at age 10½, which offered a unique opportunity to consider how children's own perspective on their hyperactivity or attention problems compared to assessments from their teachers or parents as well as their own measured performance on tasks of attention. The second instrument from

WEB MATERIAL

which we mined additional data was the Wechsler Intelligence Scale for Children⁴ (see below for details).

The child behavior scales we administered are follows:

Behavior Rating Inventory of Executive Function (BRIEF)¹: At child ages 7, 9 and 12, parents completed the BRIEF, and at age 7, the child's teacher completed a BRIEF. We examined the Behavioral Regulation Index (concerning children's ability to inhibit inappropriate behavior; to shift easily between situations; or to control emotional reactions), the Metacognition Index (concerning their ability to initiate projects or play; to exhibit adequate working memory in their daily lives; to plan and organize their activities; to organize and keep track of their belongings; and to monitor both the quality of their work and the impact of their behavior on those around them), and the Global Executive Composite, which is the overarching summary score. Scores are age- and sex-standardized (T-scores; M=50, SD=10).

Conners' ADHD/DSM-IV Scales, Parent Version (CADS-P) and Teacher Version (CADS-T)²: At child ages 7, 9 and 12, parents completed the CADS-P, yielding four subscales: the Conners' ADHD index score, designed to identify children "at risk" for ADHD; and the DSM-IV-based Inattentive, Hyperactive/Impulsive, and Total subscales. Teachers completed the CADS-T when the child was age 7 years. All CADS data are age- and sex-standardized (T-scores; M=50, SD=10).

Behavior Assessment System for Children, 2nd edition Parent and Teacher Report (BASC-2) and Self Report of Personality (SRP)³: When the child was 7, parents and teachers completed the BASC-2. When the child was 10½, parents completed the BASC-2 and children completed specific scales of the parallel SRP. We examined the Hyperactivity and Attention Problems scales from these tests, both of which are age- and sex-standardized (T-scores; M=50, SD=10).

WEB MATERIAL

Due to the low literacy levels of mothers in CHAMACOS, maternal report scales were administered aloud by bilingual, bicultural study interviewers in the mother's language of choice. Teachers (at 7 years) completed paper versions of the child behavior scales in English, and children (at 10.5 years) completed a computerized version of the SRP in their primary language.

With regards to the direct neuropsychological assessments, we note that our psychometricians assessed children in their dominant language at ages 7 through 10½ years, as ascertained via direct assessment with the oral vocabulary subtest of the Woodcock–Johnson/Woodcock–Muñoz Tests of Cognitive Ability in both English and Spanish.¹⁸ Because nearly all children transitioned to English dominance during this period, all children were assessed in English at the age 12-year visit. The neuropsychological assessments we have used in this analysis are as follows:

Wechsler Intelligence Scale for Children - Fourth Edition (WISC-IV)⁴: At ages 7 and 10½, children were administered the WISC-IV. We examined the Processing Speed and Working Memory subscale scores (M=100; SD=15) as indicators of attention and executive function, respectively. Processing Speed scores were based on children's performance on two tasks – Coding and Symbol Search – both of which require rapid visual scanning of novel symbols and providing a quick and accurate response in accordance with task rules. While many skills, including visual perception and hand-eye coordination, are needed to complete these tasks well, the ability to attend to the visual materials and screen out distractions are critical components of good performance on these tasks. Working Memory scores were based on children's performance on two other tasks – Digit Span and Letter-Number Sequence – in which the children heard strings of numbers and/or letters read aloud by the tester, were required to reorder them mentally in accordance with task rules, and then verbally provided the reordered string of

WEB MATERIAL

numbers/letters to the tester. While several skills, including attention to verbal input, are needed to complete these tasks well, the ability to hold multiple numbers/letters in mind while also recalling and implementing the re-ordering rules require a high degree of executive functioning to perform well.

Wisconsin Card Sort Task-64: Computer Version 2- Research Edition (WCST)⁵: At ages 9 and 12, children completed this computerized task of set-shifting, which measures skills around strategic planning, ability to shift cognitive strategies, and impulse control. We examined T-scores for errors and perseverative errors.

Conners' Continuous Performance Test (CPT II)⁶: At ages 9 and 12, children completed this computerized vigilance task that assesses hit rate, accuracy, and impulse control (T-scores; M=50, SD=10). We examined continuous T-scores (standardized to a non-clinical population) for errors of commission (false positives), errors of omission (non-response), and hit rate standard error overall, and by block and interstimulus interval. Higher variability in hit rate indicates performance inconsistency, a symptom of ADHD.⁷ We also examined the continuous ADHD Confidence Index score, which indicates the probability that children are correctly classified as having clinical ADHD (note that this not equivalent to a clinical diagnosis of ADHD).

WEB MATERIAL

Web Table 1. Demographic and Exposure Characteristics of All Children with Prenatal DAP Measurements and of Children Included by Timepoint, with Assessment for Differences Between Included and Excluded Children: CHAMACOS Study.

	All Children with Prenatal DAPs	Any 7y Outcomes	<i>p</i> ^e	7y Teacher Report	<i>p</i> ^e	Any 9y Outcomes	<i>p</i> ^e	Any 10.5y Outcomes	<i>p</i> ^e	Any 12y Outcomes	<i>p</i> ^e
	(n=534)	(n=341)		(n=277)		(n=325)		(n=310)		(n=332)	
	n (%)^b	n (%)^b		n (%)^b		n (%)^b		n (%)^b		n (%)^b	
Child sex											
Male	264 (49)	159 (47)	0.08	127 (46)	0.09	155 (48)	0.32	144 (46)	0.10	156 (47)	0.15
Female	270 (51)	182 (53)		150 (54)		170 (52)		166 (54)		176 (53)	
Maternal country of birth											
U.S.	70 (13)	41 (12)	0.05	28 (10)	<0.01	41 (13)	0.03	39 (13)	0.05	41 (12)	0.08
Mexico	452 (85)	296 (89)		247 (89)		281 (86)		268 (86)		287 (86)	
Other	12 (2)	4 (1)		2 (1)		3 (1)		3 (1)		4 (1)	
Maternal years in US at child delivery											
≤1	129 (24)	76 (22)	0.07	66 (24)	0.02	68 (21)	0.03	66 (21)	0.10	73 (22)	0.27
2-5	144 (27)	90 (26)		74 (27)		85 (26)		82 (26)		90 (27)	
6-10	116 (22)	87 (25)		74 (27)		84 (26)		79 (25)		81 (24)	
11+	86 (16)	54 (16)		41 (15)		54 (17)		51 (16)		54 (16)	
Entire Life	59 (11)	34 (10)		22 (8)		34 (10)		32 (10)		34 (10)	
Maternal age at child delivery											
18-24	248 (46)	141 (41)	0.01	112 (40)	0.02	130 (40)	<0.01	120 (39)	<0.01	135 (41)	<0.01
25-29	163 (30)	113 (33)		97 (35)		108 (33)		109 (35)		112 (34)	
30-34	82 (15)	56 (16)		43 (16)		53 (16)		52 (17)		53 (16)	
35-45	40 (7)	31 (9)		25 (9)		34 (11)		29 (9)		32 (10)	
missing	1 (0)	0 (0)		0 (0)				0 (0)		0 (0)	
Maternal education at child delivery											
<6th grade	233 (44)	157 (46)	0.27	130 (47)	0.22	144 (44)	0.87	134 (43)	0.97	148 (45)	0.81
7th-12th grade	192 (36)	115 (34)		91 (33)		114 (35)		112 (36)		116 (35)	

WEB MATERIAL

Completed high school	109 (20)	69 (20)		56 (20)		67 (21)		64 (21)		68 (20)	
Maternal Verbal IQ (PPVT Score at child age 9)											
≤74	59 (11)	58 (17)	0.48	47 (17)	0.34	59 (19)	0.44	58 (19)	0.40	58 (17)	0.77
75-99	111 (21)	105 (31)		83(30)		108 (33)		104 (34)		107 (32)	
≥100	147 (28)	139 (41)		121 (44)		143 (44)		140 (45)		142 (43)	
missing	217 (41) ^g	39 (11)		26 (9)		15 (5)		8 (3)		25 (8)	
Smoked during pregnancy											
No	503 (91)	328 (96)	<0.01	267 (96)	0.02	313 (96)	<0.01	298 (96)	0.03	319 (96)	0.02
Yes	31 (6)	13 (4)		10 (4)		12 (4)		12 (4)		13 (4)	
Duration of breastfeeding											
Never breastfed	27 (5)	15 (4)	<0.01	12 (4)	<0.01	15 (5)	<0.01	15 (5)	<0.01	16 (5)	<0.01
≤1 month	107 (20)	43 (13)		35 (13)		41 (13)		39 (13)		43 (13)	
>1-6 months	181 (34)	115 (34)		92 (33)		110 (34)		105 (34)		110 (33)	
>6-12 months	102 (19)	75 (22)		64 (23)		68 (21)		65 (21)		71 (21)	
>12 months	107 (20)	93 (27)		74 (27)		91 (28)		86 (27)		92 (28)	
missing	10 (2)	0 (0)		0 (0)		0 (0)		0 (0)		0 (0)	
Mother depressed at 7 and/or 9 year visits											
No	227 (43)	213 (64)	0.58	176 (64)	0.77	205 (63)	0.18	192 (62)	0.02	208 (63)	0.49
Yes	126 (24)	120 (35)		96 (35)		119 (37)		117 (38)		118 (36)	
missing	181 (34) ^g	2 (2)		5 (2)		1 (0)		1 (0)		6 (2)	
	GM ± SD	GM ± SD	p^f	GM ± SD	p^f	GM ± SD	p^f	GM ± SD	p^f	GM ± SD	p^f
Dialkylphosphate urinary metabolites during pregnancy ^c											
∑DAPs (nmol/L)	136.5 ± 3.0	130.9 ± 2.7	0.24	128.5 ± 2.7	0.18	125.5 ± 2.7	0.03	124.6 ± 2.7	0.01	126.8 ± 2.8	0.04
∑DMs (nmol/L)	100.0 ± 3.4	96.1 ± 3.1	0.32	94.7 ± 3.1	0.29	92.4 ± 3.1	0.06	90.8 ± 3.0	0.03	93.3 ± 3.1	0.10
∑DEs (nmol/L)	21.3 ± 2.9	20.1 ± 3.0	0.11	19.4 ± 3.0	0.04	19.3 ± 3.0	<0.01	19.1 ± 3.0	<0.01	19.5 ± 3.0	0.02

WEB MATERIAL

Serum concentration during pregnancy^d

Σ PBDEs (47,99,100,153) (ng/g lipid)	26.2 ± 2.5 (n=468)	25.9 ± 2.5 (n=321)	0.67	25.2 ± 2.5 (n=262)	0.28	26.0 ± 2.5 (n=310)	0.81	25.7 ± 2.4 (n=297)	0.56	25.7 ± 2.4 (n=314)	0.51
DDT (ng/g lipid)	22.2 ± 5.3 (n=470)	22.6 ± 5.2 (n=323)	0.74	24.3 ± 5.4 (n=263)	0.18	23.2 ± 5.4 (n=313)	0.40	23.3 ± 5.5 (n=299)	0.40	23.7 ± 5.6 (n=317)	0.21

Abbreviations: CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; DDT, dichlorodiphenyltrichloroethane; DAP, dialkyl phosphate; GM, geometric mean; PPVT, Peabody Picture Vocabulary Test; PBDE, polybrominated diphenyl ether; SD, standard deviation.

^a Some analyses include fewer observations based on lower levels of participation in a specific outcome assessment.

^b Some percentages do not sum to 100 due to rounding.

^c Urinary metabolite concentrations based on the unadjusted average concentration in two pregnancy urine samples.

^d Measured in prenatal or delivery blood samples for ~83%; back-extrapolated from maternal serum concentrations at child age 9 years for ~17%. See Methods for details.

^e Statistical significance based on chi-square analysis comparing children with prenatal DAPs and non-missing values on the descriptive variable who were included in versus excluded from this analysis. Reasons for exclusion were twin status (n=6), birth defect affecting neurodevelopment or test validity (n=3), or autism diagnosis (n=3), and loss-to-follow-up, failure to complete visit, or teacher declining to participate for all others.

^f Statistical significance based on t-test of log-transformed values (not GM as shown) for children included versus excluded from this analysis.

^g Because these variables were assessed at 7y and/or 9y visits, they are missing for the sizable minority of families who were lost to follow-up before this point.

WEB MATERIAL

Web Table 2. Mean attention and executive function scores by age point, based on teacher report, maternal report, and child assessment: CHAMACOS study.

Outcome	orientation ^a	Age 7 Years		Age 9 Years	Age 10.5 Years	Age 12 Years	
		Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Behavioral Rating Scale							
		Teacher report	Maternal report	Maternal report	Maternal report	Maternal report	
Behavior Rating Inventory of Executive Function (<i>T</i> -scores) ^b							
Behavior Regulation Index	higher	50 ± 9	50 ± 10	51 ± 11		51 ± 11	
Metacognition Index	higher	52 ± 10	50 ± 11	49 ± 10		48 ± 9	
Global Executive Composite	higher	51 ± 10	50 ± 11	50 ± 10		49 ± 10	
Conners ADHD/DSM-IV Scales (<i>T</i> -scores) ^b							
ADHD Index	higher	53 ± 11	50 ± 8	52 ± 9		50 ± 8	
DSM-IV total scale	higher	52 ± 10	50 ± 8	52 ± 10		50 ± 8	
Inattentive subscale	higher	48 ± 9	49 ± 8	50 ± 9.0		48 ± 7	
Hyperactive/Impulsive subscale	higher	52 ± 10	52 ± 8	54 ± 11		52 ± 9	
Behavior Assessment System for Children-2 (<i>T</i> -scores) ^b							
Hyperactivity scale	higher	50 ± 10	46 ± 9		47 ± 8		
Attention Problems scale	higher	51 ± 8	50 ± 10		49 ± 10		
				Age 7 Years	Age 9 Years	Age 10.5 Years	Age 12 Years
				Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Child Assessment							
Wechsler Intelligence Scales for Children (standardized scores) ^b							
Processing Speed Index	lower		109 ± 13		98 ± 12		
Working Memory Index	lower		100 ± 14		91 ± 12		
Wisconsin Card Sort Test (<i>T</i> -scores) ^b							
Errors	lower			48 ± 11		54 ± 11	
Perseverative errors	lower			52 ± 14		57 ± 14	
Conners' Continuous Performance Test II (<i>T</i> -scores) ^b							
Errors of omission	higher			59 ± 17		49 ± 9	
Errors of commission	higher			50 ± 9		49 ± 11	
Hit rate standard error overall	higher			58 ± 11		48 ± 9	
Hit rate standard error by block	higher			51 ± 12		50 ± 10	

WEB MATERIAL

Hit rate standard error by inter-stimulus interval	higher	58 ± 10	50 ± 10
ADHD Confidence Index ^c	higher	55 ± 22	47 ± 17

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; SD, standard deviation.

^a higher scores indicate more symptomatic behavior/poorer performance; lower scores indicate poorer performance.

^b Behavior Rating Inventory of Executive Function, Conners' ADHD/ Diagnostic and Statistical Manual of Mental Disorders Scales, Behavior Assessment System for Children, Wisconsin Card Sort Task, and Conners' Continuous Performance Test T-scores are standardized to mean ± SD = 50 ± 10; Wechsler Intelligence Scale for Children T-standardized scores are standardized to mean ± SD = 100 ± 15.

^c The Conners' Continuous Performance Test ADHD Confidence Index is not a T-score, but is rather produced by discriminant function analysis and represents the percentage of children with this performance profile who would be correctly classified as having ADHD.

WEB MATERIAL

Web Table 3: Spearman Correlation of Select Measures within Timepoints: CHAMACOS Study

Age 7y Measures:	<i>M-GEC</i>	<i>M-CADS</i>	<i>M-BASC-H</i>	<i>M-BASC-AP</i>	<i>T-GEC</i>	<i>T-CADS</i>	<i>T-BASC-H</i>	<i>T-BASC-AP</i>	<i>WISC-PS</i>
Mat: BRIEF Global Executive Composite (M-GEC):	1.0000								
Mat: CADS ADHD Index (M-CADS):	0.7695*	1.0000							
Mat: BASC Hyperactivity (M-BASC-H):	0.7013*	0.6100*	1.0000						
Mat: BASC Attention Problems (M-BASC-AP):	0.5783*	0.6308*	0.4626*	1.0000					
Teach: BRIEF Global Executive Composite (T-GEC):	0.1952*	0.3030*	0.0876	0.2380*	1.0000				
Teach: CADS ADHD Index (T-CADS):	0.1642*	0.2640*	0.1197	0.2169*	0.8607*	1.0000			
Teach: BASC-2 Hyperactivity (T-BASC-H):	0.1012	0.1837*	0.1740*	0.2057*	0.7319*	0.7664*	1.0000		
Teach: BASC-2 Attention Problems (T-BASC-AP):	0.1772*	0.1955*	0.1254	0.2091*	0.7829*	0.8302*	0.7045*	1.0000	
Assess: WISC-IV Processing Speed (WISC-PS):	-0.1181	-0.0960	-0.0262	-0.0722	-0.2035*	-0.1688*	-0.1607	-0.1850*	1.0000
Assess: WISC-IV Working Memory (WISC-WM):	-0.1235	-0.1787*	-0.0470	-0.2344*	-0.2539*	-0.2173*	-0.1614	-0.3275*	0.3003*
Age 9y Measures:	<i>M-GEC</i>	<i>M-CADS</i>	<i>WCST-E</i>	<i>WCST-PE</i>	<i>CPT</i>				
Mat: BRIEF Global Executive Composite (M-GEC):	1.0000								
Mat: CADS ADHD Index (M-CADS):	0.8255*	1.0000							
Assess: WCST Errors (WCST-E)	-0.1742*	-0.2211*	1.0000						
Assess: WCST Perseverative errors (WCST-PE):	-0.1421	-0.1613*	0.7163*	1.0000					
Assess: CPT-II ADHD Confidence Index (CPT):	0.1686*	0.1352	-0.1276	-0.0665	1.0000				
Age 10.5y Measures:	<i>M-BASC-H</i>	<i>M-BASC-AP</i>	<i>C-BASC-H</i>	<i>C-BASC-AP</i>	<i>WISC-PS</i>	<i>WISC-WM</i>			
Mat: BASC-2 Hyperactivity (M-BASC-H):	1.0000								
Mat: BASC-2 Attention Problems (M-BASC-AP):	0.5250*	1.0000							
Child: BASC-2 Hyperactivity (C-BASC-H):	0.2075*	0.2757*	1.0000						
Child: BASC-2 Attention Problems (C-BASC-AP):	0.1764*	0.2926*	0.6955*	1.0000					
Assess: WISC-IV Processing Speed (WISC-PS):	-0.0340	-0.1751*	-0.2006*	-0.1563*	1.0000				
Assess: WISC-IV Working Memory (WISC-WM):	-0.1345	-0.2671*	-0.0921	-0.1904*	0.2135*	1.0000			
Age 12y Measures:	<i>M-GEC</i>	<i>M-CADS</i>	<i>WCST-E</i>	<i>WCST-PE</i>	<i>CPT</i>				
Mat: BRIEF Global Executive Composite (M-GEC):	1.0000								
Mat: CADS ADHD Index (M-CADS):	0.8150*	1.000							
Assess: WCST Errors (WCST-E)	-0.0413	-0.0945	1.000						
Assess: WCST Perseverative errors (WCST-PE):	-0.0805	-0.1115	0.7851*	1.0000					
Assess: CPT-II ADHD Confidence Index (CPT):	0.0535	0.0420	-0.0804	-0.1043	1.0000				

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; Assess, direct assessment of child; BASC-2, Behavior Assessment System for Children-2; BRIEF, Behavior Rating Inventory of Executive Function; CADS, Child, child self-report; Conners ADHD/DSM-IV Scales; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CPT-II, Conners' Continuous Performance Test II; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; Mat, maternal report; SD, standard deviation; WISC-IV, Teach, teacher report; Weschler Intelligence Scales for Children; WCST, Wisconsin Card Sort Test.

Shaded cells indicate that the scores being compared were from the same source (i.e., were all reported by the mother, teacher, child, or through direct assessment of the child).

*Indicates Spearman correlations that are statistically significant at $p < 0.01$.

WEB MATERIAL

Web Table 4: Spearman Correlation of Repeated Measures across Timepoints: CHAMACOS Study

Maternal Reports:				
BRIEF Global Executive Composite at:		zy	9y	12y
	7y	1.0000		
	9y	0.6856*	1.0000	
	12y	0.5856*	0.6617*	1.0000
CADS ADHD Index at:		7y	9y	12y
	7y	1.0000		
	9y	0.6782*	1.0000	
	12y	0.5457*	0.6398*	1.0000
BASC-2 Hyperactivity at:		7y	10.5y	
	7y	1.0000		
	10.5y	0.5383*	1.0000	
BASC-2 Attention Problems at:		7y	10.5y	
	7y	1.0000		
	10.5y	0.5816*	1.0000	
Child Assessments:				
WISC-IV Processing Speed at:		7y	10.5y	
	7y	1.0000		
	10.5y	0.4348*	1.0000	
WISC-IV Working Memory at:		7y	10.5y	
	7y	1.0000		
	10.5y	0.5122*	1.0000	
WCST Errors at:		9y	12y	
	9y	1.0000		
	12y	0.2122*	1.0000	
WCST Perseverative errors at:		9y	12y	
	9y	1.0000		
	12y	0.1702*	1.0000	
CPT-II ADHD Confidence Index at:		9y	12y	
	9y	1.0000		
	12y	0.3819*	1.0000	

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; Assess, direct assessment of child; BASC-2, Behavior Assessment System for Children-2; BRIEF, Behavior Rating Inventory of Executive Function; CADS, Child, child self-report; Conners ADHD/DSM-IV Scales; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CPT-II, Conners' Continuous Performance Test II; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; Mat, maternal report; SD, standard deviation; WISC-IV, Teach, teacher report; Weschler Intelligence Scales for Children; WCST, Wisconsin Card Sort Test, y, year.

*Indicates Spearman correlations that are statistically significant at $p < 0.01$.

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Supplemental Table 5: Spearman Correlation Matrix of Measures, with Repeated Measures Represented as the Mean Score for that Child Across Age Points: CHAMACOS Study

Measures: ^a	ρ^a	M-GEC _m	M-CADS _m	M-BASC- H _m	M-BASC- A _{pm}	T-GEC7	T-CADS7	T-BASC- H7	T-BASC- AP7	C-BASC- H10	C-BASC- AP10	WISC- PS _m	WISC- WM _m	WCST- Em	CPT _m
Mat: BRIEF Global Executive Composite, mean (M-GEC _m):	(+)	1.0000													
Mat: CADS ADHD Index, mean (M-CADS _m):	(+)	0.8636*	1.0000												
Mat: BASC Hyperactivity, mean (M-BASC-H _m):	(+)	0.7203*	0.6101*	1.0000											
Mat: BASC Attention Problems, mean (M-BASC-AP _m):	(+)	0.6830*	0.6946*	0.5721*	1.0000										
Teach: BRIEF Global Executive Composite, 7y (T-GEC7):	(+)	0.1983*	0.2961*	0.1095	0.2548*	1.0000									
Teach: CADS ADHD Index, 7y (T-CADS7):	(+)	0.1855*	0.2631*	0.1487	0.2436*	0.8607*	1.0000								
Teach: BASC-2 Hyperactivity, 7y (T-BASC-H7):	(+)	0.1549	0.2018*	0.2125*	0.2461*	0.7319*	0.7664*	1.0000							
Teach: BASC-2 Attention Problems, 7y (T-BASC-AP7):	(+)	0.2013*	0.1997*	0.1471	0.2723*	0.7829*	0.8302*	0.7045*	1.0000						
Child: BASC-2 Hyperactivity, 10.5y (C-BASC-H10):	(+)	0.2088*	0.2159*	0.1942*	0.2660*	0.2086*	0.2024*	0.1949*	0.2028*	1.0000					
Child: BASC-2 Attention Problems, 10.5y (C-BASC-AP10):	(+)	0.1849*	0.2053*	0.1621*	0.2756*	0.2571*	0.2263*	0.2578*	0.2664*	0.6955*	1.0000				
Assess: WISC-IV Processing Speed, mean (WISC-PS _m):	(-)	-0.1268	-0.1048	-0.0088	-0.1661*	-0.1812*	-0.1532	-0.1327	-0.2196*	-0.1947*	-0.1707*	1.0000			
Assess: WISC-IV Working Memory, mean (WISC-WM _m):	(-)	-0.2453*	-0.2560*	-0.1249	-0.2957*	-0.2660*	-0.2182*	-0.1273	-0.3205*	-0.0973	-0.2151*	0.2992*	1.0000		
Assess: WCST Errors, mean (WCST-Em)	(-)	-0.1614*	-0.2391*	-0.0184	-0.1785*	-0.1912*	-0.1802*	-0.1307	-0.1668*	-0.1091	-0.1418	0.1957*	0.2742*	1.0000	
Assess: CPT-II ADHD Confidence Index, mean (CPT _m):	(+)	0.1860*	0.1790*	0.2018*	0.2589*	0.1695*	0.1617*	0.1940*	0.1851*	0.1083	0.1179	-0.2204*	-0.2019*	-0.1844*	1.0000

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; Assess, direct assessment of child; BASC-2, Behavior Assessment System for Children-2; BRIEF, Behavior Rating Inventory of Executive Function; CADS, Child, child self-report; Conners ADHD/DSM-IV Scales; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CPT-II, Conners' Continuous Performance Test II; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; Mat, maternal report; SD, standard deviation; WISC-IV, Teach, teacher report; Weschler Intelligence Scales for Children; WCST, Wisconsin Card Sort Test. Shaded cells indicate that the scores being compared were from the same source (i.e., were all reported by the mother, by the teacher, by the child, or through direct assessment of the child).

^aIndicates Spearman correlations that are statistically significant at $p < 0.01$.

^a(+) higher scores indicate more symptomatic behavior; (-) lower scores indicate poorer performance.

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Web Table 6. Change in maternal report and child-assessed attention and executive function scores per 10-fold increases in mean total prenatal urinary DM concentrations (nmol/L) using repeated measures (GEE) models, overall and stratified by sex, in the CHAMACOS study population, enrolled 1999-2000 in Salinas Valley, California.

Outcome	orientation ^a	age (yrs) at assessment	Overall				Boys				Girls				<i>p</i> -value interaction
			No.	No. obs	β	(95% CI)	No.	No. obs	β	(95% CI)	No.	No. obs	β	(95% CI)	
Maternal Report^{b,c}															
Behavior Rating Inventory of Executive Function (<i>T</i> -scores) ^d		7, 9, 12													
Behavior Regulation Index	higher		347	978	3.1	(1.5,4.8)	163	460	5.0	(2.6,7.4)	184	518	1.9	(-0.1,4.0)	0.10
Metacognition Index	higher		347	978	3.4	(2.5,5.0)	163	460	4.6	(2.5,6.8)	184	518	2.6	(0.5,4.8)	0.23
Global Executive Composite	higher		347	978	3.5	(2.9,5.2)	163	460	5.2	(2.9,7.5)	184	518	2.5	(0.3,4.6)	0.13
Conners ADHD/DSM-IV Scales (<i>T</i> -scores) ^d		7, 9, 12													
ADHD Index	higher		349	988	1.7	(0.4,3.0)	163	464	1.5	(-0.3,3.3)	186	524	2.0	(0.2,3.8)	0.63
DSM-IV total scale	higher		349	988	1.7	(0.3,3.1)	163	464	2.1	(0.2,3.9)	186	524	1.6	(-0.4,3.7)	0.82
Inattentive	higher		349	988	1.6	(0.4,2.9)	163	464	2.0	(0.3,3.6)	186	524	1.5	(-0.2,3.3)	0.81
Hyperactive/Impulsive	higher		349	988	1.6	(0.1,3.1)	163	464	1.9	(-0.1,4.0)	186	524	1.4	(-0.7,3.5)	0.74
Behavior Assessment System for Children-2 (<i>T</i> -scores) ^d		7, 10.5													
Hyperactivity	higher		335	634	1.5	(0.2,2.8)	157	294	2.5	(0.4,4.6)	178	340	0.9	(-0.6,2.4)	0.40
Attention Problems	higher		335	634	2.5	(0.8,4.2)	157	294	1.8	(-0.6,4.2)	178	340	2.9	(0.5,5.2)	0.52
Child Assessment^{b,e}															
Weschler Intelligence Scales for Children (standardized scores) ^d		7, 10.5													
Processing Speed Index	lower		334	605	-0.8	(-3.0,1.3)	157	283	-1.5	(-5.2,1.1)	177	322	0.1	(-2.4,2.7)	0.32
Working Memory Index	lower		334	605	-3.5	(-6.2,-1.4)	157	283	-4.6	(-8.1,-1.0)	177	322	-2.2	(-5.0,0.5)	0.43
Wisconsin Card Sort Test (<i>T</i> -scores) ^d		9, 12													
Errors	lower		325	630	-2.7	(-4.5,-1.0)	153	295	-1.3	(-3.9,1.3)	172	335	-3.3	(-5.5,-1.1)	0.36
Perseverative errors	lower		325	630	-2.8	(-5.1,-0.5)	153	295	-1.7	(-5.3,1.9)	172	335	-3.2	(-6.2,-0.2)	0.68
Conners' Continuous Performance Test II (<i>T</i> -scores) ^d		9, 12													
Errors of omission	higher		325	634	1.6	(-0.3,3.6)	153	297	2.1	(-0.9,5.6)	172	338	0.8	(-1.8,3.4)	0.19
Errors of commission	higher		325	634	1.4	(-0.3,3.0)	153	297	-0.6	(-3.4,3.0)	172	338	3.2	(1.1,5.3)	0.01
Hit rate standard error overall	higher		325	634	1.2	(-0.2,2.9)	153	297	1.1	(-1.4,4.9)	172	338	1.3	(-1.0,3.6)	0.75

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Hit rate standard error by block	higher	325	634	0.6	(-1.3,2.5)	153	297	0.7	(-1.7,5.5)	172	338	0.7	(-2.2,3.6)	0.74
Hit rate standard error by inter-stimulus interval	higher	325	634	2.2	(0.6,3.8)	153	297	1.5	(-0.5,4.8)	172	338	3.1	(0.8,5.3)	0.21
ADHD Confidence Index ^f	higher	325	634	0.5	(-2.7,3.6)	153	297	1.0	(-3.7,5.8)	172	338	-0.4	(-4.7,3.9)	0.58

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CI, confidence interval; DM, dimethyl phosphate; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; GEE, generalized estimating equations.

^a higher scores indicate more symptomatic behavior; lower scores indicate poorer performance.

^b All models adjusted for maternal age, years in U.S., education, receptive language, and average depression score (7-9y); average HOME, Home Observation for the Measurement of the Environment score (7-12y); child age at assessment; and child sex.

^c Parent report models additionally adjusted for language of questionnaire administration.

^d Behavior Rating Inventory of Executive Function, Conners' ADHD/ Diagnostic and Statistical Manual of Mental Disorders Scales, Behavior Assessment System for Children, Wisconsin Card Sort Task, and Conners' Continuous Performance Test T-scores are standardized to mean \pm SD = 50 \pm 10; Wechsler Intelligence Scale for Children T-standardized scores are standardized to mean \pm SD = 100 \pm 15.

^e Child testing models additionally adjusted for psychometrician who administered test, language of testing, and, for Conners' Continuous Performance Test and Wisconsin Card Sort Task models only, video game usage.

^f The Conners' Continuous Performance Test ADHD Confidence Index is not a T-score but is rather produced by discriminant function analysis and represents the percentage of children with this performance profile who would be correctly classified as having ADHD.

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Web Table 7. Change in maternal report and child-assessed attention and executive function scores per 10-fold increases in mean total prenatal urinary DE concentrations (nmol/L) using repeated measures (GEE) models, overall and stratified by sex, in the CHAMACOS study population, enrolled 1999-2000 in Salinas Valley, California.

Outcome	orientation ^a	age (yrs) at assessment	Overall				Boys				Girls				<i>p</i> -value interaction
			No.	No. obs	β	(95% CI)	No.	No. obs	β	(95% CI)	No.	No. obs	β	(95% CI)	
Maternal Report^{b,c}															
Behavior Rating Inventory of Executive Function (<i>T</i> -scores) ^d		7, 9, 12													
Behavior Regulation Index	higher		347	978	1.1	(-0.6,2.7)	163	460	1.4	(-1.6,4.4)	184	518	0.7	(-1.1,2.6)	0.73
Metacognition Index	higher		347	978	1.4	(-0.4,3.1)	163	460	1.5	(-1.6,4.5)	184	518	1.4	(-0.5,3.4)	0.76
Global Executive Composite	higher		347	978	1.3	(-0.4,3.0)	163	460	1.6	(-1.5,4.6)	184	518	1.3	(-0.7,3.2)	0.97
Conners ADHD/DSM-IV Scales (<i>T</i> -scores) ^d		7, 9, 12													
ADHD Index	higher		349	988	1.3	(0.1,2.6)	163	464	1.1	(-1.0,3.2)	186	524	1.5	(-0.1,3.1)	0.58
DSM-IV total scale	higher		349	988	0.2	(-0.1,2.6)	163	464	1.2	(-1.0,3.4)	186	524	1.2	(-0.5,2.9)	0.94
Inattentive	higher		349	988	1.1	(-0.1,2.3)	163	464	1.2	(-0.8,3.2)	186	524	1.2	(-0.3,2.7)	0.84
Hyperactive/Impulsive	higher		349	988	1.1	(-0.3,2.6)	163	464	1.3	(-1.1,3.7)	186	524	0.9	(-0.9,2.6)	0.76
Behavior Assessment System for Children-2 (<i>T</i> -scores) ^d		7, 10.5													
Hyperactivity	higher		335	634	0.7	(-0.6,4.2)	157	294	1.8	(-0.6,4.2)	178	340	-0.1	(-1.5,1.3)	0.16
Attention Problems	higher		335	634	0.8	(-2.1,3.8)	157	294	0.9	(-2.1,3.8)	178	340	0.7	(-1.8,3.1)	0.84
Child Assessment^{b,e}															
Weschler Intelligence Scales for Children (standardized scores) ^d		7, 10.5													
Processing Speed Index	lower		334	605	-1.9	(-4.4,0.6)	157	283	-5.0	(-8.9,-1.2)	177	322	0.4	(-2.8,3.6)	0.03
Working Memory Index	lower		334	605	-0.7	(-3.3,1.8)	157	283	-3.1	(-6.5,0.3)	177	322	1.3	(-2.2,4.8)	0.18
Wisconsin Card Sort Test (<i>T</i> -scores) ^d		9, 12													
Errors	lower		325	630	-3.3	(-5.1,-1.5)	153	295	-3.1	(-5.8,0.4)	172	335	-2.6	(-4.9,-0.3)	0.98
Perseverative errors	lower		325	630	-3.4	(-5.8,-1.0)	153	295	-2.8	(-6.3,0.8)	172	335	-3.4	(-6.6,-0.2)	0.62
Conners' Continuous Performance Test II (<i>T</i> -scores) ^d		9, 12													
Errors of omission	higher		325	634	1.2	(-1.0,3.5)	153	297	1.4	(-2.0,4.9)	172	337	1.1	(-1.9,4.2)	0.77
Errors of commission	higher		325	634	1.1	(-0.7,2.9)	153	297	1.9	(-1.1,4.8)	172	337	0.5	(-1.7,2.8)	0.57
Hit rate standard error overall	higher		325	634	1.4	(-0.6,3.3)	153	297	3.5	(0.4,6.5)	172	337	0.1	(-2.5,2.6)	0.12

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Hit rate standard error by block	higher	325	634	1.4	(-0.2,3.0)	153	297	4.1	(1.5,6.6)	172	337	0.1	(-2.0,2.3)	0.02
Hit rate standard error by inter-stimulus interval	higher	325	634	0.9	(-0.7,2.5)	153	297	3.9	(1.2,6.5)	172	337	-1.1	(-3.1,1.1)	<0.01
ADHD Confidence Index ^f	higher	325	634	2.4	(-1.3,6.2)	153	297	4.1	(-1.6,9.8)	172	337	1.2	(-3.9,6.2)	0.40

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; BASC-2, Behavior Assessment System for Children-2; BRIEF, Behavior Rating Inventory of Executive Function; CADS, Conners ADHD/DSM-IV Scales; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CI, confidence interval; CPT-II, Conners' Continuous Performance Test II; DE, diethyl phosphate; DSM, Diagnostic and Statistical Manual of Mental Disorders; GEE, generalized estimating equations; HOME, Home Observation for the Measurement of the Environment; PPVT, Peabody Picture Vocabulary Test; WISC-IV, Wechsler Intelligence Scales for Children; WCST, Wisconsin Card Sort Test.

^a higher scores indicate more symptomatic behavior; lower scores indicate poorer performance.

^b All models adjusted for maternal age, years in U.S., education, receptive language, and average depression score (7-9y); average HOME score (7-12y); child age at assessment; and child sex.

^c Parent report models additionally adjusted for language of questionnaire administration.

^d Behavior Rating Inventory of Executive Function, Conners' ADHD/ Diagnostic and Statistical Manual of Mental Disorders Scales, Behavior Assessment System for Children, Wisconsin Card Sort Task, and Conners' Continuous Performance Test T-scores are standardized to mean \pm SD = 50 \pm 10; Wechsler Intelligence Scale for Children T-standardized scores are standardized to mean \pm SD = 100 \pm 15.

^e Child testing models additionally adjusted for psychometrician who administered test, language of testing, and, for Conners' Continuous Performance Test and Wisconsin Card Sort Task models only, video game usage.

^f The Conners' Continuous Performance Test ADHD Confidence Index is not a T-score but is rather produced by discriminant function analysis and represents the percentage of children with this performance profile who would be correctly classified as having ADHD.

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Web Table 8. Adjusted regression coefficients and 95% confidence intervals for multivariable linear regression models of association between mean total prenatal urinary DAP concentrations (nmol/L, log10 scale) and children's attention and executive function as reflected by teacher report, maternal report, and child assessment scores by time point per 10-fold increases in mean total prenatal urinary DAP concentrations (nmol/L), in the CHAMACOS study population, enrolled 1999-2000 in Salinas Valley, California.

Outcome	orientation ^a	Teacher Report						Maternal Report								
		Age 7 Years			Age 7 Years			Age 9 Years			Age 10.5 Years			Age 12 Years		
		No.	β	(95% CI)	No.	β	(95% CI)	No.	β	(95% CI)	No.	β	(95% CI)	No.	β	(95% CI)
Behavioral Rating Scale ^{b,c}																
Behavior Rating Inventory of Executive Function (<i>T</i> -scores) ^e																
Behavior Regulation Index	higher	276	0.2	(-2.2,2.6)	326	4.2	(2.0,6.4)	325	3.7	(1.4,6.0)				327	3.1	(0.8,5.4)
Metacognition Index	higher	276	2.2	(-0.4,4.7)	326	4.2	(1.8,6.5)	325	4.8	(2.9,6.8)				327	3.4	(1.3,5.5)
Global Executive Composite	higher	276	1.5	(-0.9,4.0)	326	4.4	(2.1,6.7)	325	4.6	(2.6,6.6)				327	3.7	(1.4,5.9)
Conners ADHD/DSM-IV Scales (<i>T</i> -scores) ^e																
ADHD Index	higher	275	2.9	(0.3,5.6)	339	1.9	(0.2,3.6)	324	3.4	(1.5,5.4)				325	1.9	(0.1,3.8)
DSM-IV total scale	higher	275	1.3	(-1.0,3.7)	339	2.1	(0.3,3.9)	324	3.4	(1.2,5.6)				325	1.4	(-0.4,3.3)
Inattentive	higher	275	1.6	(-0.6,3.7)	339	2.1	(0.5,3.8)	324	3.5	(1.5,5.3)				325	1.3	(-0.2,2.9)
Hyperactive/Impulsive	higher	275	0.5	(-1.9,3.0)	339	1.7	(-0.2,3.5)	324	2.9	(0.3,5.4)				325	1.4	(-0.5,3.3)
Behavior Assessment System for Children-2 (<i>T</i> -scores) ^e																
Hyperactivity scale	higher	276	0.0	(-2.4,2.4)	325	1.8	(0.1,3.5)				309	2.0	(0.3,3.8)			
Attention Problems scale	higher	276	2.0	(0.2,3.8)	325	2.0	(-0.3,4.4)				309	4.2	(1.9,6.5)			
Child Assessment ^{b,d}																
Wechsler Intelligence Scales for Children (standardized scores) ^e																
Processing Speed Index	lower				295	-2.1	(-5.2,1.0)				310	-1.7	(-4.6,1.2)			
Working Memory Index	lower				295	-2.8	(-6.0,0.4)				310	-4.9	(-7.6,-2.2)			
Wisconsin Card Sort Test (<i>T</i> -scores) ^e																
Errors	lower							315	-4.4	(-7.1,-1.8)				315	-2.7	(-5.3,0.0)
Perseverative errors	lower							315	-5.0	(-8.7,-1.4)				315	-2.5	(-5.9,0.1)
Conners' Continuous Performance Test II (<i>T</i> -scores) ^e																
Errors of omission	higher							316	4.0	(0.3,7.6)				319	-0.2	(-2.1,1.7)
Errors of commission	higher							316	3.0	(0.8,5.2)				319	0.2	(-2.4,2.7)
Hit rate standard error overall	higher							316	2.7	(0.2,5.3)				319	0.3	(-1.8,2.5)
Hit rate standard error by block	higher							316	2.1	(-0.7,5.0)				319	1.0	(-1.7,3.6)

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Hit rate standard error by inter-stimulus interval	higher	316	3.7	(1.3,6.0)	319	1.0	(-1.3,3.3)
ADHD Confidence Index ^f	higher	316	2.6	(-2.7,7.9)	319	-0.2	(-4.1,3.6)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; CHAMACOS, Center for the Health Assessment of Mothers and Children of Salinas; CI, confidence interval; DAP, dialkyl phosphate; DSM, Diagnostic and Statistical Manual of Mental Disorders; HOME, Home Observation for the Measurement of the Environment.

^a higher scores indicate more symptomatic behavior; lower scores indicate poorer performance.

^b All models adjusted for maternal age, years in U.S., education, receptive language, and average depression score (7-9y); average HOME score (7-12y); child age at assessment; and child sex.

^c Parent report models additionally adjusted for language of questionnaire administration.

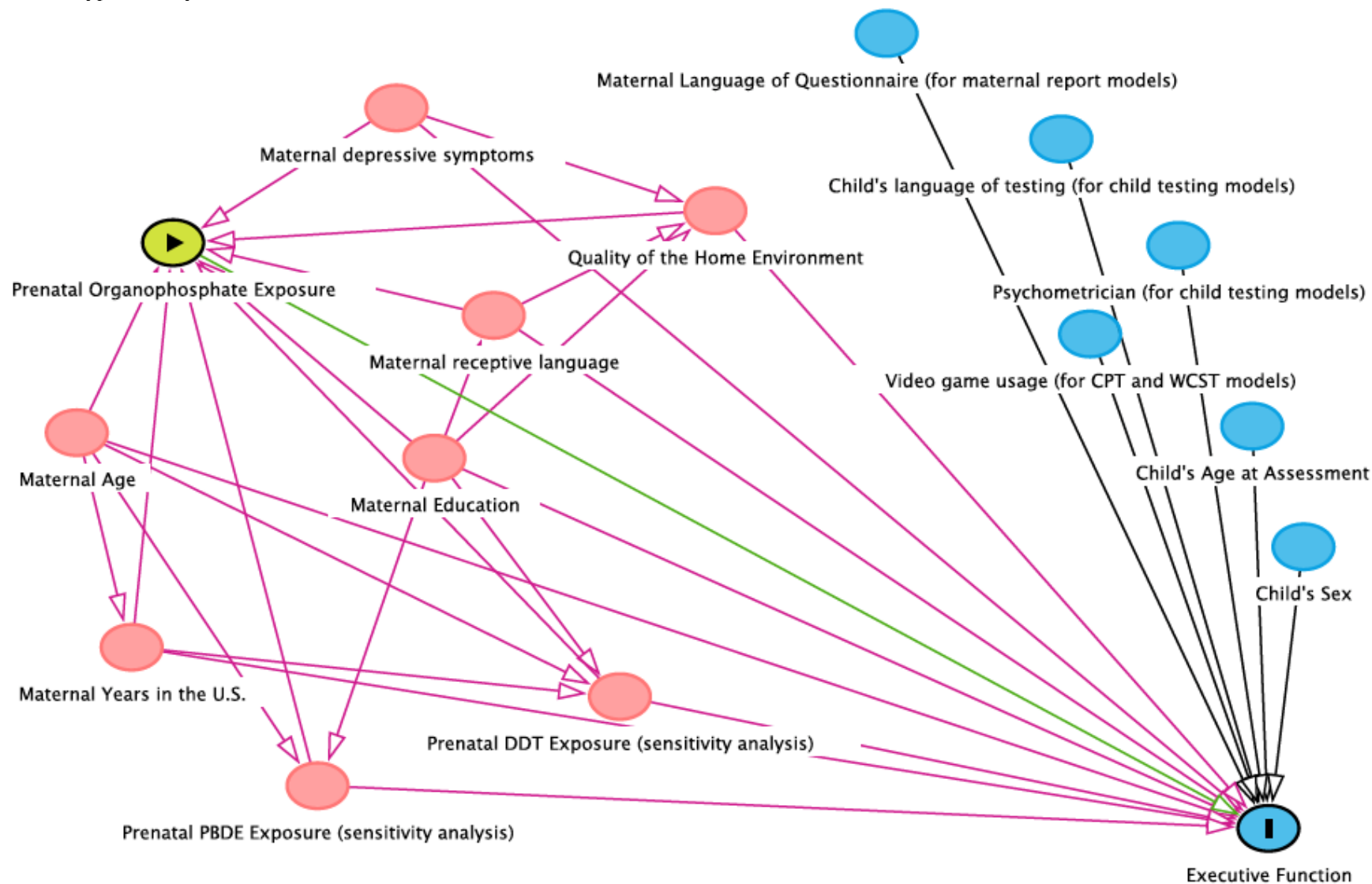
^d Behavior Rating Inventory of Executive Function, Conners' ADHD/ Diagnostic and Statistical Manual of Mental Disorders Scales, Behavior Assessment System for Children, Wisconsin Card Sort Task, and Conners' Continuous Performance Test T-scores are standardized to mean \pm SD = 50 \pm 10; Wechsler Intelligence Scale for Children T-standardized scores are standardized to mean \pm SD = 100 \pm 15.

^e Child testing models additionally adjusted for psychometrician who administered test, language of testing, and, for Conners' Continuous Performance Test and Wisconsin Card Sort Task models only, video game usage.

^f The Conners' Continuous Performance Test ADHD Confidence Index is not a T-score but is rather produced by discriminant function analysis and represents the percentage of children with this performance profile who would be correctly classified as having ADHD.

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Web Figure 1. Directed acyclic graph (DAG) for associations of prenatal organophosphate exposure and executive function and attention-deficit/hyperactivity disorder-related behaviors.



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