

Online supplement for Lees et al., Association of Prenatal Alcohol Exposure With Psychological, Behavioral, and Neurodevelopmental Outcomes in Children From the Adolescent Brain Cognitive Development Study. *Am J Psychiatry* (doi: 10.1176/appi.ajp.2020.20010086).

Methods: Additional Details

The validated Developmental History Questionnaire, originally developed by the Adolescent Component of the National Comorbidity Survey (Merikangas et al., 2009, Kessler et al., 2009), was modified by the ABCD team to include additional questions on maternal use of substances during pregnancy.

ABCD Baseline Alcohol Use Questions During Pregnancy

- Before you/biological mom found out you/biological mom were pregnant, but while you might have been pregnant with this child, did you use any of the following? Alcohol?
- Before knowing of pregnancy, what was the maximum number of drinks consumed in one sitting?
- Before knowing of pregnancy, what was the average number of drinks consumed per week?
- Once you/biological mom knew you/she were pregnant, were you/biological mom use any of the following? Alcohol?
- After knowing of pregnancy, what was the maximum number of drinks consumed in one sitting?
- After knowing of pregnancy, what was the average number of drinks consumed per week?

Examining prenatal alcohol exposure.

The categorical PAE variable included all youth with any parent-reported prenatal alcohol exposure before or after knowledge of pregnancy. To examine the dose-dependent relationship of PAE on outcomes of interest, an estimate of the total number of drinks consumed during pregnancy was calculated. This was based on: a) average number of drinks consumed per week before pregnancy knowledge, b) the week the mother learned of pregnancy, c) average number of drinks consumed per week following pregnancy knowledge, and d) gestational week of birth. Two weeks were subtracted from reported week of pregnancy knowledge to adjust for conception date.

$$\text{Estimate of total drinks} = ab + c(d - b - 2)$$

To explore the effect of common PAE patterns, maternal drinking was categorized into abstinent (< 1 standard drink/occasion throughout pregnancy), light (1-2 drinks/occasion, <7 drinks/week), moderate (3-4/occasion, <7/week), heavy (<5/occasion, 7+/week), or binge drinking (5+/occasion) before and after knowing of pregnancy, based on established prenatal alcohol use classification (O'Leary et al., 2010). Common patterns were identified:

- 1) Abstinent throughout pregnancy;
- 2) Light reducers (light before knowing, abstinent after knowing of pregnancy);
- 3) Heavier reducers (moderate, heavy, and binge drinkers before knowing, abstinent or light drinking after knowing);
- 4) Stable light drinkers throughout pregnancy;
- 5) Stable heavier drinkers throughout pregnancy;
- 6) Increasesers (drank more after knowledge of pregnancy).

Additional Results

Table S1. Psychological, behavioral and cognitive characteristics.

	Total	No prenatal alcohol exposure		Prenatal alcohol exposure		<i>p</i>
	N	N	%	N	%	
Past/present mental disorders						
Depression	264	195	2.7	69	2.7	1.0
Generalized Anxiety Disorder	409	288	4.0	121	4.8	.10
Panic Disorder	27	18	0.2	9	0.4	.51
Separation Anxiety	834	554	7.7	280	11.1	<.001
Social Anxiety/Selective Mutism Disorder	453	326	4.5	127	5.0	.32
Hallucinations	46	28	0.4	18	0.7	.06
Delusions	163	116	1.6	47	1.9	.45
Attention Deficit Hyperactivity	1,870	1,314	18.2	556	22.1	<.001
Oppositional Defiant Disorder	1,283	868	12.1	415	16.5	<.001
Conduct Disorder	271	190	2.6	81	3.2	.15
Obsessive-Compulsive Disorder	844	597	8.3	247	9.8	.02
Unspecific Bipolar and Related Disorder	324	251	3.5	73	2.9	.18
Post Traumatic Stress Disorder	170	116	1.6	54	2.1	.10
Specific Phobia	2,511	1,826	25.4	685	27.2	.08
Cash Choice Task – delayed gratification	5,535	4,067	56.5	1,468	58.3	.29
	Mean	Mean	SD	Mean	SD	<i>p</i>
Psychological problems (CBCL)						
Total problems	45.6	45.0	11.3	47.2	10.8	<.001
Externalizing	45.4	45.0	10.1	46.6	10.3	<.001
Rule breaking behavior	52.6	52.5	4.6	52.9	4.9	<.001
Aggressive behavior	52.7	52.5	5.2	53.1	5.7	<.001
Internalizing	48.4	48.0	10.6	49.5	10.4	<.001
Anxious/Depressed	53.4	53.3	5.9	53.8	6.0	<.001
Withdrawn/Depressed	53.4	53.3	5.6	53.7	5.9	.005
Somatic complaints	54.9	54.7	6.0	55.4	6.2	<.001
Social problems	52.7	52.6	4.6	52.8	4.6	.129
Thought problems	53.7	53.5	5.7	54.3	6.1	<.001
Attention problems	53.8	53.6	5.9	54.2	6.3	<.001
Impulsivity (UPPS-P)						
Lack of planning	7.8	7.7	2.4	7.9	2.3	<.001
Sensation seeking	9.8	9.7	2.7	10.0	2.6	<.001
Negative urgency	8.5	8.4	2.6	8.6	2.6	.02
Positive urgency	8.0	8.0	3.0	7.9	2.9	.62
Lack of perseverance	7.0	7.0	2.2	7.1	2.2	.07
Motivation (BIS/BAS)						
Behavioral inhibition	5.5	5.5	2.9	5.5	2.8	.47
Reward responsiveness	8.8	8.8	2.4	8.7	2.4	.09
Drive	4.1	4.1	3.1	4.0	2.9	.04
Fun seeking	5.7	5.7	2.7	5.7	2.5	.04
NIH Toolbox fluid intelligence						
Processing Speed (Pattern Comparison)	93.8	93.7	22.0	94.2	22.2	.43
Working memory (List Sorting)	100.9	100.2	14.7	102.9	14.4	<.001
Episodic memory (Picture Sequence)	101.4	101.0	16.0	102.50	16.4	<.001
Executive function / attention / inhibition (Flanker)	95.6	95.2	13.7	96.8	13.3	<.001
Executive function / cognitive flexibility (Dimensional Change Card Sort)	96.9	96.4	15.1	98.3	15.3	<.001
RAVLT						
Learning (Trials I-V avg)	8.9	8.8	2.0	9.1	1.9	<.001
Immediate delay (Trial VI)	9.7	9.6	3.0	10.0	2.9	<.001
Long (30 min) delay (Trial VII)	9.2	9.1	3.2	9.6	3.1	<.001

PAE Dichotomous Analysis: Additional Results

Table S2: Psychological, behavioral, and cognitive outcomes associated with any prenatal alcohol exposure, when adjusting for random effects only (family, site).

	<i>B</i> (95% CI)	<i>p</i>	<i>R</i> ²
CBCL			
Total problems	2.61 (2.08, 3.13)	<.001	.007
Externalizing	1.95 (1.47, 2.43)	<.001	.005
Rule breaking behavior	0.56 (0.34, 0.78)	<.001	.002
Aggressive behavior	0.70 (0.45, 0.95)	<.001	.002
Internalizing	1.91 (1.42, 2.41)	<.001	.004
Anxious/depressed	0.69 (0.41, 0.97)	<.001	.001
Withdrawn/depressed	0.50 (0.23, 0.77)	<.001	.001
Somatic complaints	0.78 (0.49, 1.07)	<.001	.002
Social problems	0.28 (0.06, 0.49)	.01	<.001
Thought problems	0.93 (0.66, 1.21)	<.001	.003
Attention problems	0.79 (0.50, 1.07)	<.001	.002
KSADS			
Depression	0.01 (-0.13, 0.15)	.93	<.001
Generalized Anxiety Disorder	0.19 (0.08, 0.30)	.08	<.001
Panic Disorder	0.35 (-0.06, 0.76)	.39	<.001
Separation Anxiety	0.41 (0.33, 0.49)	<.001	.003
Social Anxiety/Selective Mutism Disorder	0.10 (0.00, 0.21)	.33	<.001
Hallucinations	0.60 (0.30, 0.91)	.05	<.001
Delusions	0.15 (-0.03, 0.32)	.40	<.001
Attention Deficit Hyperactivity	0.25 (0.19, 0.30)	<.001	.002
Oppositional Defiant Disorder	0.38 (0.31, 0.44)	<.001	.004
Conduct Disorder	0.20 (0.06, 0.33)	.14	<.001
Obsessive-Compulsive Disorder	0.20 (0.12, 0.28)	.01	<.001
Unspecific Bipolar and Related Disorder	-0.19 (-0.33, -0.06)	.15	<.001
Post Traumatic Stress Disorder	0.29 (0.12, 0.45)	.08	<.001
Specific Phobia	0.09 (0.04, 0.14)	.09	<.001
UPPS-P			
Lack of planning	0.29 (0.18, 0.40)	<.001	.003
Sensation seeking	0.26 (0.13, 0.38)	<.001	.002
Negative urgency	0.09 (-0.04, 0.21)	.17	<.001
Positive urgency	-0.02 (-0.16, 0.12)	.80	<.001
Lack of perseverance	0.11 (0.00, 0.21)	.05	<.001
BIS/BAS			
Behavioral inhibition	0.09 (-0.04, 0.22)	.19	<.001
Reward responsiveness	-0.07 (-0.18, 0.04)	.23	<.001
Drive	-0.10 (-0.25, 0.04)	.15	<.001
Fun seeking	0.05 (-0.08, 0.17)	.43	<.001
NIH Toolbox			
Processing Speed (Pattern Comparison)	0.07 (-0.96, 1.09)	.90	<.001
Working memory (List Sorting)	2.63 (1.95, 3.32)	<.001	.007
Episodic memory (Picture Sequence)	1.46 (0.71, 2.22)	<.001	.002
Executive function / attention / inhibition (Flanker)	1.55 (0.92, 2.19)	<.001	.003
Executive function / cognitive flexibility (Dimensional Change Card Sort)	1.81 (1.10, 2.52)	<.001	.003
RAVLT			
Learning	-0.23 (-0.24, -0.22)	<.001	.003
Immediate delay	0.37 (0.23, 0.51)	<.001	.003
Long (30 min) delay	0.46 (0.32, 0.61)	<.001	.004
Cash Choice Task			
	0.08 (0.03, 0.12)	.12	<.001

Unstandardized regression coefficients and associated 95% confidence interval, p-value and R² value are presented for the effects of prenatal alcohol exposure compared to no exposure. GAMMs controlled for random effects (family, scanner/site).

Table S3: Structural brain measures associated with any prenatal alcohol exposure, when adjusting for random effects only (family, site).

Region		B (95% CI)	p	R ²
Cortical volume				
Frontal				
Caudal middle frontal	L	162.2 (90.0-234.4)	<.001	.003
Lateral orbitofrontal	L	160.2 (111.2-209.2)	<.001	.005
	R	128.2 (78.7-177.7)	<.001	.005
Pars opercularis	L	100.8 (51.3-150.2)	.004	.002
Pars orbitalis	L	60.0 (42.1-77.9)	<.001	.005
	R	46.2 (24.7-67.6)	.002	.002
Precentral	L	191.5 (101.4-281.7)	.002	.002
	R	174.1 (84.4-263.8)	.01	.002
Rostral middle frontal	L	265.7 (141.2-390.2)	.002	.002
	R	289.9 (164.2-415.5)	<.001	.002
Superior frontal	L	343.2 (191.0-495.4)	<.001	.003
	R	392.4 (240.2-544.5)	<.001	.004
Frontal pole	L	16.3 (7.7-25.0)	.01	.001
	R	23.2 (12.0-34.5)	.004	.002
Caudal middle frontal	L	152.2 (79.4-224.9)	<.001	.002
Medial orbitofrontal	R	81.5 (45.7-117.3)	<.001	.003
Parietal				
Postcentral	L	210.2 (126.0-294.4)	<.001	.003
Precuneus	L	219.4 (143.1-295.7)	<.001	.003
	R	257.3 (176.2-338.5)	<.001	.004
Superior parietal	L	263.3 (158.1-368.4)	<.001	.003
	R	251.9 (146.5-357.3)	<.001	.002
Supramarginal	L	209.6 (109.2-310.1)	.003	.002
	R	259.3 (166.1-352.5)	<.001	.003
Inferior parietal	L	266.8 (158.1-375.5)	<.001	.002
Inferior parietal	R	292.7 (166.4-418.9)	<.001	.002
Temporal				
Fusiform	L	230.0 (150.7-309.4)	<.001	.005
	R	201.6 (124.1-279.1)	<.001	.004
Parahippocampal	L	37.0 (16.2-57.7)	.03	.002
	R	49.4 (29.1-69.6)	<.001	.003
Superior temporal	L	188.5 (102.7-274.2)	<.001	.002
	R	214.8 (137.1-292.5)	<.001	.004
Transverse temporal	L	24.6 (11.8-37.4)	.01	.002
	R	22.9 (12.8-33.0)	<.001	.003
Banks of superior temporal sulcus	L	53.9 (29.9-78.0)	<.001	.002
Inferior temporal	L	343.0 (246.2-439.8)	<.001	.006
	R	236.3 (144.2-328.3)	<.001	.003
Middle temporal	L	303.9 (217.9-390.0)	<.001	.006
	R	339.3 (248.9-429.8)	<.001	.006
Temporal pole	R	38.2 (21.6-54.8)	<.001	.002
Occipital				
Cuneus	L	56.6 (28.5-84.6)	.005	.002
	R	76.0 (44.1-107.9)	<.001	.002
Lingual	L	124.1 (66.7-181.5)	.002	.003
	R	125.6 (70.0-181.2)	<.001	.003
Lateral occipital	L	319.0 (228.3-409.7)	<.001	.005
	R	300.9 (203.9-397.9)	<.001	.004
Cingulate				
Caudal anterior	L	53.6 (25.3-81.9)	.01	.001
Isthmus	L	58.8 (29.5-88.2)	.006	.002

Region		B (95% CI)	p	R²
Posterior	L	66.5 (34.7-98.3)	.003	.002
Rostral anterior	L	57.2 (29.3-85.1)	.004	.002
Insula	L	72.8 (32.2-113.3)	.03	.002
Subcortical volume				
Cerebellum	L	563.3 (311.0-815.6)	<.001	.003
	R	618.3 (359.7-876.9)	<.001	.004
Thalamus	L	73.7 (40.-107.4)	<.001	.001
	R	59.8 (27.4-92.3)	.01	.001
Hippocampus	L	39.4 (19.3-59.4)	.004	.001
	R	48.2 (28.4-68.0)	<.001	.002
Amygdala	L	18.5 (8.5-28.4)	.01	.001
	R	18.7 (8.7-28.8)	.01	.001
Ventral diencephalon	L	30.5 (11.8-49.2)	.05	.001
	R	47.2 (28.4-65.9)	<.001	.003
Intracranial		17582.0 (11190.3-23972.7)	<.001	.002
Cerebrum		15586.0 (10642.9-20529.7)	<.001	.005
Total grey		532.5 (300.2-764.8)	<.001	.002
Surface area				
Frontal				
Caudal middle frontal	L	50.2 (29.0-71.3)	.002	.003
	R	49.1 (27.5-70.8)	<.001	.003
Lateral orbitofrontal	L	37.3 (23.0-51.5)	<.001	.004
	R	32.9 (18.0-47.8)	<.001	.004
Medial orbitofrontal	L	25.4 (13.5-37.2)	.002	.003
	R	26.2 (16.0-36.4)	<.001	.004
Pars opercularis	L	25.9 (11.7-40.1)	.02	.002
Pars orbitalis	L	12.0 (7.8-16.1)	<.001	.004
	R	10.5 (5.4-15.7)	.004	.002
Precentral	L	54.3 (25.3-83.3)	.02	.002
Rostral middle frontal	L	73.1 (33.8-112.4)	.02	.002
	R	91.4 (50.7-132.1)	<.001	.003
Superior frontal	L	103.5 (59.1-147.9)	<.001	.004
	R	110.0 (65.4-154.5)	<.001	.004
Frontal pole	R	5.1 (2.7-7.4)	.002	.002
Parietal				
Inferior parietal	L	69.6 (35.6-103.6)	.004	.003
	R	74.9 (35.8-114.0)	.01	.002
Postcentral	L	53.1 (26.7-79.6)	.006	.003
Precuneus	L	64.0 (39.1-88.8)	<.001	.003
	R	78.0 (50.5-105.5)	<.001	.003
Superior parietal	L	81.1 (46.2-116.0)	<.001	.003
	R	78.8 (44.5-113.2)	<.001	.003
Supramarginal	L	54.7 (23.6-85.8)	.04	.002
	R	70.0 (41.2-98.7)	<.001	.004
Temporal				
Fusiform	L	56.0 (35.2-76.9)	<.001	.004
	R	52.0 (31.2-72.8)	<.001	.004
Middle temporal	L	58.5 (37.4-79.6)	<.001	.005
	R	65.2 (42.7-87.7)	<.001	.005
Banks of superior temporal sulcus	R	14.7 (7.1-22.3)	.01	.002
Inferior temporal	L	77.9 (53.4-102.4)	<.001	.006
	R	55.4 (32.7-78.0)	<.001	.004
Superior temporal	R	46.1 (25.5-66.7)	<.001	.004
Traverse temporal	R	5.7 (3.0-8.3)	.002	.002
Occipital				

Region		B (95% CI)	p	R²
Lingual	L	35.0 (14.9-55.1)	.04	.002
	R	39.3 (19.8-58.7)	.005	.002
Lateral occipital	L	90.8 (60.4-121.2)	<.001	.006
	R	76.9 (45.7-108.2)	<.001	.004
<i>Cingulate</i>				
Caudal anterior	L	14.7 (7.2-22.2)	.009	.002
Isthmus	L	18.4 (8.7-28.1)	.01	.002
Posterior	L	19.3 (9.4-29.3)	.01	.002
Cortical thickness				
<i>Parietal</i>				
Postcentral	L	.01 (.01-.02)	.03	<.001
<i>Temporal</i>				
Middle temporal	R	.01 (.01-.020)	.04	<.001
<i>Occipital</i>				
Cuneus	L	.01 (.01-.02)	.01	.001
	R	.02 (.01-.03)	<.001	.002
Lateral occipital	L	.01 (.00-.02)	.04	-.001
	R	.01 (.01-.02)	.004	-.001
Lingual	L	.01 (.01-.02)	.03	.001

Unstandardized regression coefficients and associated 95% confidence interval, false discovery rate adjusted p-value and R² value are presented for the effects of prenatal alcohol exposure compared to no exposure. Only regions where the model passed the FDR correction for volume, surface area or cortical thickness are presented. These generalized additive mixed models controlled for random effects only (family, scanner/site).

Table S4: Functional connectivity indices associated with any prenatal alcohol exposure. Only the associations which passed FDR correction in unadjusted models are presented.

	B (95% CI)	p	R²
Unadjusted Models			
Between networks			
Sensorimotor hand – salience	0.007 (0.002, 0.011)	.03	.002
Network – subcortical region			
Auditory – right ventral diencephalon	-0.001 (-0.018, -0.006)	<.001	.002
Default – left amygdala	0.013 (0.005, 0.020)	.02	.001
Salience – left ventral diencephalon	-0.010 (-0.016, -0.004)	.01	.001
Adjusted Models			
Between networks			
Sensorimotor hand – salience	0.010 (0.002, 0.012)	.002	.027
Network – subcortical region			
Auditory – right ventral diencephalon	-0.010 (-0.018, -0.006)	.001	.012
Default – left amygdala	0.015 (0.004, 0.019)	.09	.003
Salience – left ventral diencephalon	-0.008 (-0.015, -0.001)	.48	.006

Unstandardized regression coefficients and associated 95% confidence interval, false discovery rate adjusted p-value and R² value are presented for the effects of prenatal alcohol exposure compared to no exposure. Only the network connectivity associations where the model passed the FDR correction in unadjusted models are presented. Unadjusted generalized additive mixed models controlled for random effects only (family, scanner/site). Adjusted models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use) and random (family, scanner/site) effects.

Note, hyperconnectivity between the default network and left amygdala, and hypoconnectivity between the salience network and left ventral diencephalon, among PAE compared to unexposed youth was no longer significant in the covariate-adjusted models.

Table S5: Functional connectivity within and between major networks which have previously been associated with fetal alcohol spectrum disorder. No associations were significant in unadjusted or adjusted models.

	B (95% CI)	p	R²
Unadjusted models			
<i>Within networks</i>			
Default	0.002 (-0.002, 0.006)	.30	-.0002
Saliience	-0.005 (-0.014, 0.005)	.33	.0002
Dorsal attention	0.002 (-0.002, 0.006)	.42	-.0003
Fronto-parietal	-0.001 (-0.005, 0.003)	.56	<.0001
<i>Between networks</i>			
Default – saliience	0.001 (-0.003, 0.005)	.64	.0000
Default – dorsal attention	-0.001 (-0.004, 0.003)	.67	-.0003
Default – fronto-parietal	0.000 (-0.003, 0.003)	.87	-.0001
Saliience – dorsal attention	0.000 (-0.004, 0.004)	.91	.0004
Saliience – fronto-parietal	0.000 (-0.005, 0.004)	.82	<.0001
Dorsal attention – fronto-parietal	0.000 (-0.002, 0.003)	.81	<.0001
Covariate-adjusted models			
<i>Within networks</i>			
Default	0.001 (-0.003, 0.004)	.79	.027
Saliience	-0.008 (-0.018, 0.002)	.13	.004
Dorsal attention	0.000 (-0.004, 0.004)	.96	.012
Fronto-parietal	-0.002 (-0.006, 0.002)	.33	.012
<i>Between networks</i>			
Default – saliience	0.000 (-0.006, 0.004)	.69	.008
Default – dorsal attention	0.000 (-0.003, 0.004)	.82	.027
Default – fronto-parietal	0.000 (-0.003, 0.003)	.77	.006
Saliience – dorsal attention	0.001 (-0.003, 0.006)	.52	.006
Saliience – fronto-parietal	-0.001 (-0.006, 0.003)	.61	.002
Dorsal attention – fronto-parietal	0.000 (-0.002, 0.003)	.71	.002

Unstandardized regression coefficients and associated 95% confidence interval, p-value and R² value are presented for the effects of prenatal alcohol exposure compared to no exposure. Unadjusted generalized additive mixed models controlled for random effects only (family, scanner/site). Adjusted models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use) and random (family, scanner/site) effects.

Table S6: Dichotomous PAE variable follow-up analysis for regional brain ROIs when including intracranial volume as an additional covariate.

		B (95% CI)	p	R²
<i>Volume</i>				
Inferior parietal	L	118.1 (25.1, 211.0)	.08	.356
Supramarginal	R	89.1 (9.0, 169.1)	.18	.358
Inferior temporal	L	126.4 (46.9, 205.8)	.01	.323
Middle temporal	L	82.1 (12.9, 151.2)	.12	.439
	R	79.5 (11.6, 147.4)	.13	.498
Lateral occipital	L	89.3 (15.1, 163.5)	.11	.412

Unstandardized regression coefficients and associated 95% confidence interval, false discovery rate adjusted p-value and R² value are presented for generalized additive model results for the effects of prenatal alcohol exposure compared to no exposure. Only regional brain ROIs identified from first series of analyses are presented. These generalized additive mixed models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use) and random (family, scanner/site) effects.

Table S7: Significant associations between covariates included in GAMMs and outcomes

	Structural MRI	Resting-state functional MRI	Behavioral outcomes	Cognitive outcomes
			<i>Higher scores = Greater problems</i>	<i>Higher scores = Better performance</i>
Youth measures				
↑ Age	-	+/-	+	+
Being female	+	-	+	-
Race (compared to white)	-	+/-	+/-	+/-
Born premature	+		+	
↑ Birthweight	+	-		+
↑ School grades	+		-	+
Tobacco exposure		-	+	
Cannabis exposure			+	
Heroin exposure				
Cocaine exposure			+	
↑ School grade		+		
Parent measures				
↑ Parent education	+		-	+
Maternal depression			+	+/-
↑ Maternal age	+		-	+

"+" = positive association, "-" = negative association, "+/-" = both positive and negative associations were observed. If there is no + or -, no significant association was observed in the GAMMs.

Dose-Dependent Relationship Analysis Results

Table S8: Generalized additive model results for alcohol use as a continuous measure, using an estimate of total drinks throughout pregnancy, when adjusting for fixed and random effects.

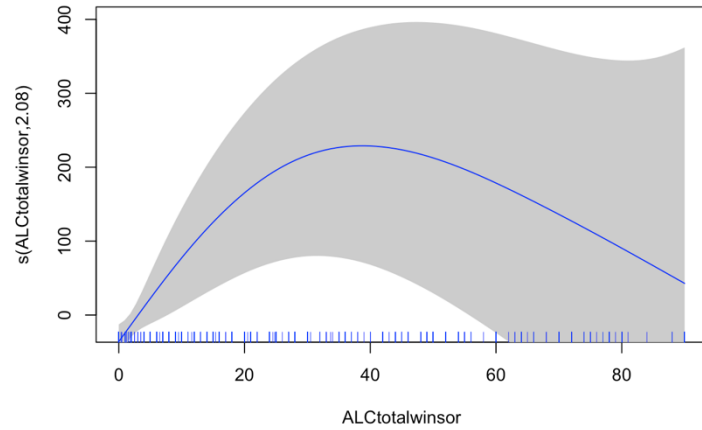
	<i>B</i> (95% CI)	<i>p</i>	<i>R</i> ²
CBCL			
Total problems	0.02 (0.00, 0.03)	.009	.137
Externalizing	0.01 (0.00, 0.03)	.07	.107
Rule breaking behavior	0.00 (0.00, 0.01)	.47	.111
Aggressive behavior	0.00 (0.00, 0.01)	.35	.089
Internalizing	0.02 (0.00, 0.32)	.02	.076
Anxious/depressed	0.01 (0.00, 0.01)	.14	.051
Withdrawn/depressed	0.01 (0.00, 0.01)	.14	.071
Somatic complaints	0.01 (0.01, 0.02)	.001	.042
Social problems	0.00 (0.00, 0.01)	.63	.102
Thought problems	0.00 (0.00, 0.01)	.22	.078
Attention problems	0.01 (0.00, 0.02)	.04	.169
KSADS			
Depression	0.00 (-0.01, 0.00)	.83	.027
Generalized Anxiety Disorder	0.00 (-0.01, 0.00)	.53	.026
Panic Disorder	0.00 (-0.01, 0.00)	.54	.003
Separation Anxiety	0.00 (-0.01, 0.00)	.31	.026
Social Anxiety/Selective Mutism Disorder	0.00 (-0.01, 0.00)	.50	.015
Hallucinations	0.00 (-0.01, 0.00)	.42	.004
Delusions	0.00 (-0.01, 0.00)	.95	.010
Attention Deficit Hyperactivity	0.00 (0.00, 0.00)	.11	.130
Oppositional Defiant Disorder	0.00 (0.00, 0.00)	.46	.049
Conduct Disorder	-0.01 (-0.01, 0.00)	.19	.040
Obsessive-Compulsive Disorder	0.00 (0.00, 0.01)	.12	.019
Unspecific Bipolar and Related Disorder	0.00 (-0.01, 0.00)	.33	.017
Post Traumatic Stress Disorder	0.00 (-0.01, 0.00)	.42	.030
Specific Phobia	0.00 (0.00, 0.00)	.25	.019
UPPS-P			
Lack of planning	0.002 (-0.002, 0.005)	.35	.030
Sensation seeking	0.006 (0.002, 0.009)	.003	.026
Negative urgency	0.002 (-0.002, 0.005)	.42	.017
Positive urgency	0.001 (-0.003, 0.006)	.47	.049
Lack of perseverance	0.001 (-0.002, 0.004)	.46	.049
BIS/BAS			
Behavioral inhibition	0.003 (-0.001, 0.007)	.12	.010
Reward responsiveness	0.001 (-0.002, 0.005)	.48	.023
Drive	0.001 (-0.004, 0.005)	.77	.060
Fun seeking	0.003 (-0.001, 0.007)	.99	.023
NIH Toolbox			
Processing Speed (Pattern Comparison)	-0.006 (-0.037, 0.024)	.67	.056
Working memory (List Sorting)	0.013 (-0.006, 0.032)	.18	.151
Episodic memory (Picture Sequence)	0.000 (-0.022, 0.021)	.97	.091
Executive function / attention / inhibition (Flanker)	0.023 (0.005, 0.042)	.01	.051
Executive function / cognitive flexibility (Dimensional Change Card Sort)	0.014 (-0.007, 0.035)	.18	.080
RAVLT			
Learning	-0.66 (-0.97, -0.35)	<.001	.130

Immediate delay		0.00 (0.00, 0.01)	.45	.130
Long (30 min) delay		0.00 (0.00, 0.01)	.10	.137
Cash Choice Task		-0.001 (-0.002, 0.000)	.55	.005
Brain structure				
<i>Volume</i>				
Cerebrum		8005.30 (3654.66, 12355.96)	<.001	.342
Inferior parietal	L	206.53 (98.71, 314.34)	.01	.150
Supramarginal	R	167.17 (74.34, 260.01)	.03	.135
Inferior temporal	L	214.54 (120.51, 308.57)	<.001	.194
Middle temporal	L	154.07 (71.46, 236.67)	.02	.205
	R	162.64 (78.3, 246.9)	.01	.258
Lateral occipital	L	155.15 (69.8, 240.5)	.02	.248
<i>Surface area</i>				
Precuneus	R	48.62 (22.3, 74.9)	.02	.215
Inferior temporal	L	51.46 (27.75, 75.17)	.001	.196
Lateral occipital	L	53.64 (24.8, 82.5)	.02	.213
Functional connectivity				
Sensorimotor hand – salience		0.00 (0.00, 0.00)	.45	.005
Auditory – right ventral diencephalon		-0.0002 (-0.0003, -0.00002)	.03	.011

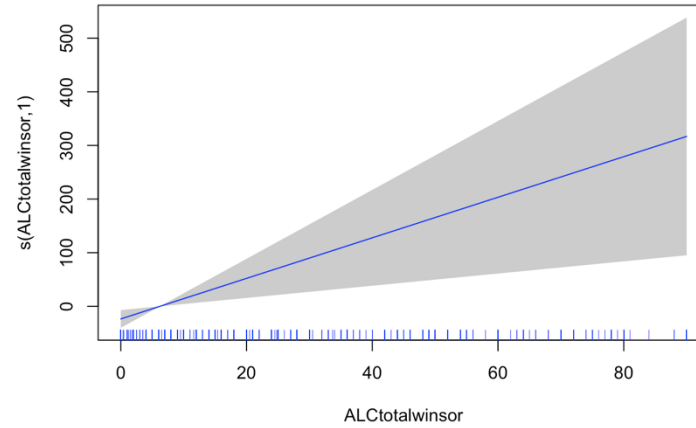
Unstandardized regression coefficients and associated 95% confidence interval, p-value/false discovery rate adjusted p-value (for brain ROIs) and R^2 value are presented for generalised additive model results for alcohol use as a continuous measure, using an estimate of total drinks throughout pregnancy. Only brain ROIs identified from first series of analyses are presented. These generalized additive mixed models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects. N=8811. Data winsorized at .015.

Figure S1: Spline models for estimated total number of alcoholic drinks consumed during pregnancy with offspring brain volume and surface area, when adjusting for fixed and random effects.

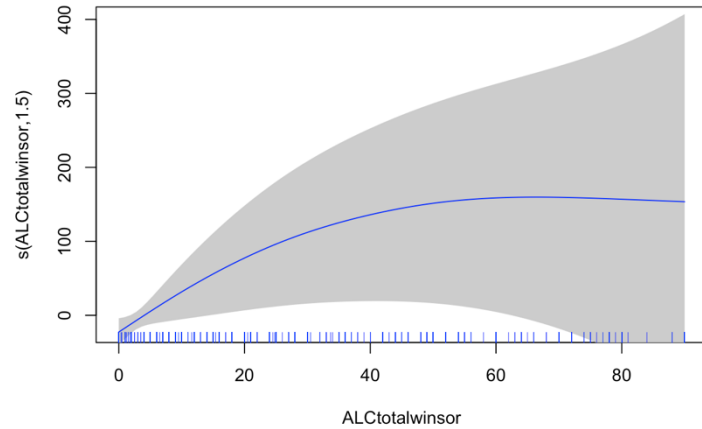
A. Left inferior parietal volume



B. Right supramarginal volume



C. Left inferior temporal volume



D. Left middle temporal volume

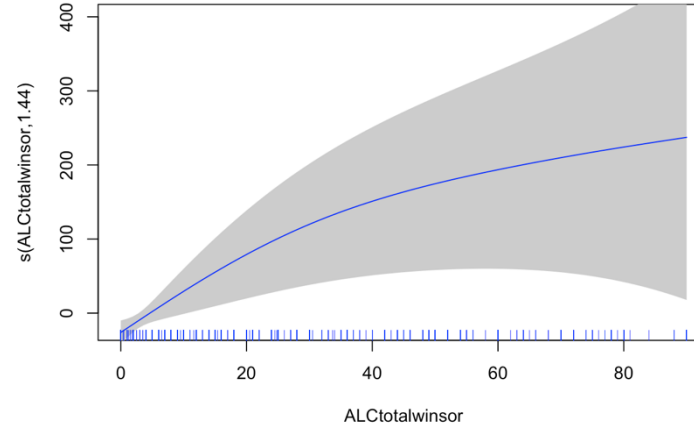
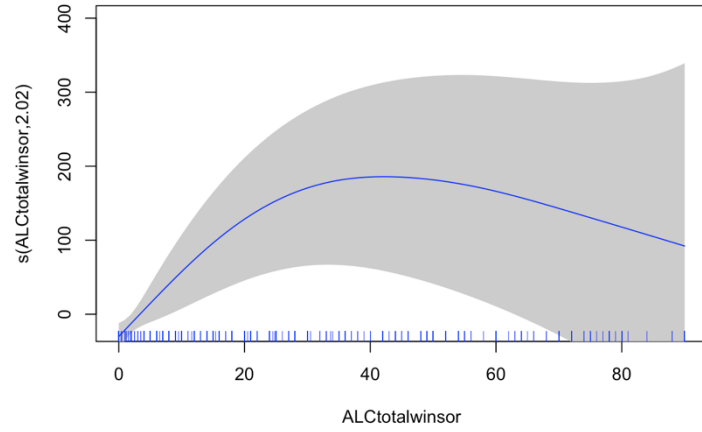
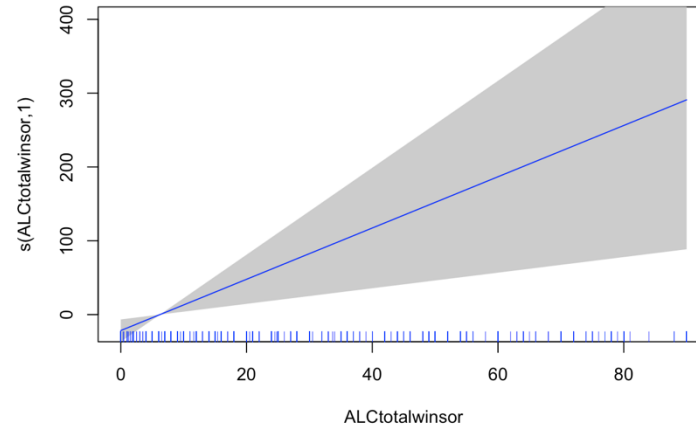


Figure S1 continued:

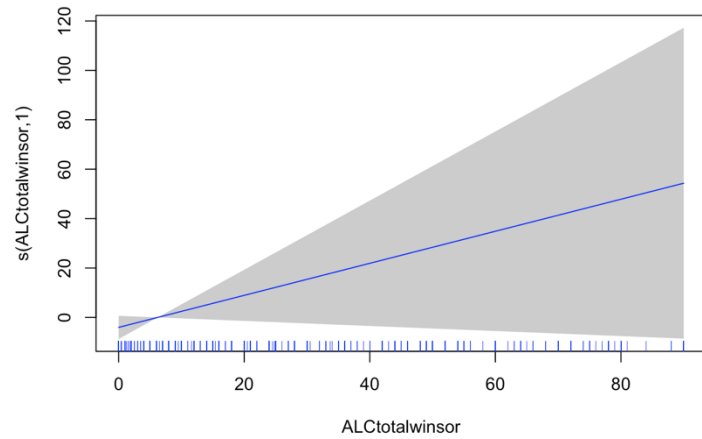
E. Right middle temporal volume



F. Left lateral occipital volume



G. Right precuneus surface area



H. Left Inferior temporal surface area

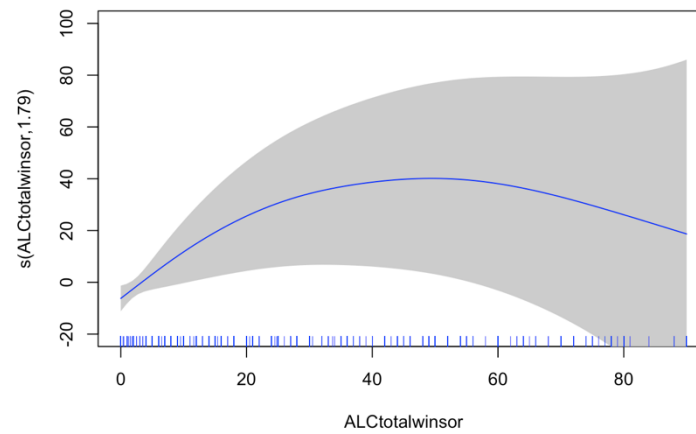


Figure S1 continued:

I. Left lateral occipital surface area

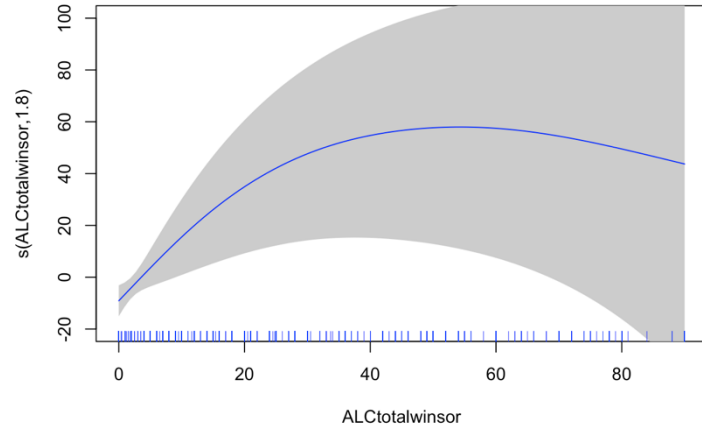
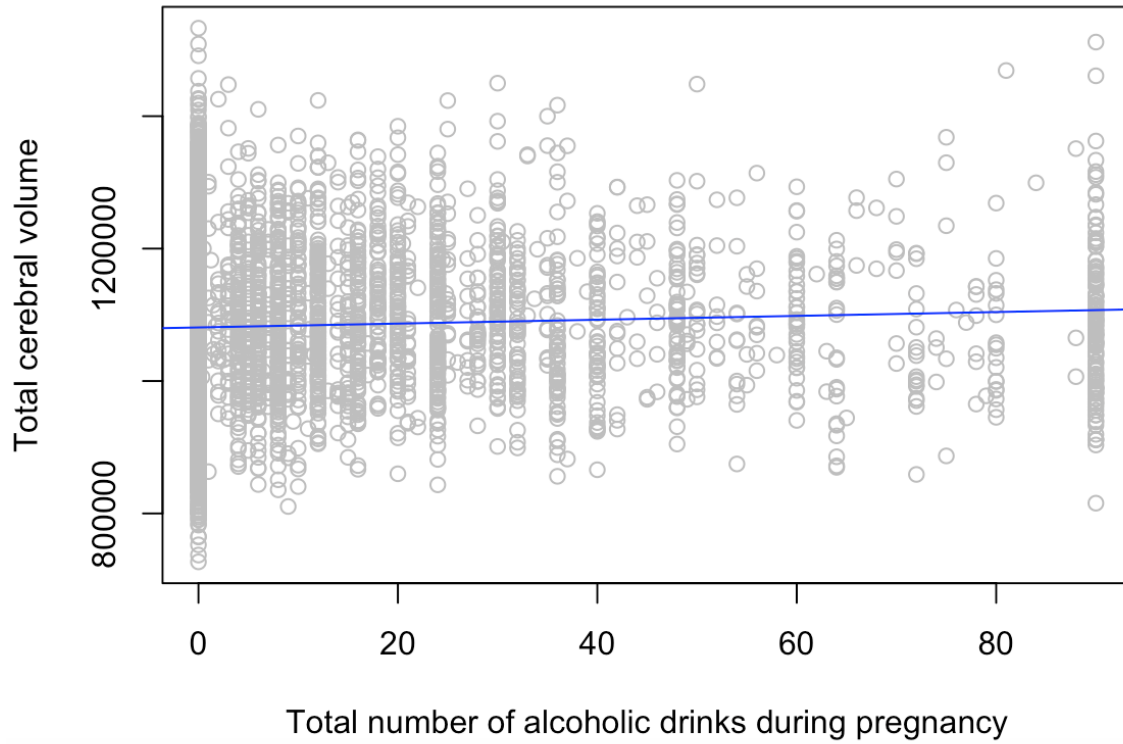


Figure S2: Data points on plot of total drinks consumed during pregnancy and total cerebral volume

Total alcohol use during pregnancy on total cerebral volume



Association of Prenatal Alcohol Exposure and Associated Outcomes

Exposure Pattern Analysis Results

Table S9: Demographic, psychological, behavioral, and cognitive characteristics for unexposed, light reducers, stable light drinkers and heavier reducers.

	No prenatal alcohol exposure n=6669	Light reducer n=1203	Stable light n=93	Heavier reducer n=755	<i>p</i>
Age (mean [SD])	9.9 (0.6)	9.9 (0.6)	9.9 (0.6)	9.9 (0.6)	.82
Sex (%)					.24
Female	47.7	527.7	48.0	51.3	
Male	52.3	47.3	52.0	48.7	
Race (%)					<.001
White	51.4	81.7	64.9	68.9	
Hispanic	21.6	10.8	15.5	17.1	
Black	15.1	2.2	8.4	6.0	
Asian	1.8	0.0	1.5	0.4	
Other	10.1	5.4	9.6	7.7	
Highest Parent Education (%)					<.001
<HS Diploma	7.2	0.0	1.7	1.5	
HS Dip/GED	11.2	3.2	4.2	6.1	
Some College	30.4	12.9	21.9	33.2	
Bachelor	28.0	34.4	35.3	30.6	
Post Grad	23.1	49.5	36.7	28.6	
Birth weight (lbs [SD])	6.5 (1.5)	6.7 (1.4)	6.9 (1.6)	6.6 (1.5)	<.001
Maternal age (mean [SD])	29.3 (6.2)	30.9 (5.5)	33.5 (4.6)	29.4 (5.9)	<.001
Found out pregnant (weeks [SD])	6.9 (7.0)	6.8 (5.6)	5.7 (4.4)	6.8 (5.1)	.10
Total drinks	0.0 (0.0)	15.8 (14.7)	44.0 (25.8)	36.2 (25.5)	
Maternal Depression (%)					<.001
Yes	21.2	22.6	22.4	29.1	
No	76.5	74.2	74.9	67.3	
Unknown	2.3	3.2	2.7	3.6	
Born premature (%)					.14
Yes	79.5	81.7	82.6	80.1	
No	20.2	17.2	17.2	19.7	
Unknown	0.3	1.1	0.2	0.1	
Tobacco exposure (%)					<.001
Yes	8.8	8.6	15.0	35.1	
No	91.0	91.4	84.8	63.8	
Unknown	0.2	0.0	0.2	1.1	
Cannabis exposure (%)					<.001
Yes	2.8	9.7	6.2	18.4	
No	97.1	89.2	92.7	80.1	
Unknown	0.1	1.1	1.1	1.5	
Heroin exposure (%)					.40
Yes	0.1	0.0	0.0	0.1	
No	99.9	100.0	99.9	99.6	
Unknown	0.0	0.0	0.1	0.3	
Cocaine exposure (%)					<.001
Yes	0.1	0.0	0.5	1.3	
No	99.8	100.0	99.3	97.9	
Unknown	0.0	0.0	0.2	0.8	
Impulsivity (m [SD])					
Negative urgency	8.4 (2.6)	8.6 (2.6)	8.1 (2.5)	8.6 (2.6)	.04
Positive urgency	8.0 (3.0)	7.9 (2.9)	7.4 (2.8)	8.1 (2.9)	.26
Lack of planning	7.7 (2.4)	8.0 (2.3)	8.0 (2.2)	7.8 (2.3)	<.001
Lack of perseverance	7.0 (2.3)	7.1 (2.1)	7.3 (2.3)	7.1 (2.2)	.28

Association of Prenatal Alcohol Exposure and Associated Outcomes

	No prenatal alcohol exposure n=6669	Light reducer n=1203	Stable light n=93	Heavier reducer n=755	<i>p</i>
Sensation seeking	9.7 (2.7)	10.0 (2.5)	10.2 (2.7)	10.2 (2.7)	<.001
Emotional/behavioural problems (m [SD])					
Total problems	45.0 (11.3)	46.2 (9.9)	47.5 (9.7)	48.1 (11.4)	<.001
Externalizing	44.9 (10.1)	45.7 (9.4)	46.3 (9.1)	47.3 (11.1)	<.001
Rule breaking behavior	52.5 (4.6)	52.3 (4.0)	51.9 (4.1)	53.5 (5.6)	<.001
Aggressive behavior	52.5 (5.2)	52.5 (4.6)	52.7 (3.9)	53.7 (6.6)	<.001
Internalizing	48.0 (10.6)	48.6 (9.9)	49.1 (10.2)	50.4 (10.9)	<.001
Anxious/Depressed	53.3 (5.9)	53.4 (5.4)	53.8 (6.4)	54.4 (6.6)	.001
Withdrawn/Depressed	53.3 (5.9)	53.0 (5.2)	52.9 (5.1)	54.1 (6.2)	.001
Somatic complaints	54.7 (6.0)	55.0 (5.8)	55.6 (6.5)	55.8 (6.5)	<.001
Social problems	52.6 (4.6)	53.7 (5.3)	52.4 (4.1)	53.2 (5.1)	.009
Thought problems	53.5 (5.7)	53.6 (5.3)	54.4 (5.9)	54.6 (6.4)	<.001
Attention problems	53.6 (5.9)	52.4 (4.1)	54.7 (6.1)	54.8 (7.1)	<.001
Past/presented mental disorders (%)					
Depression	2.8	2.3	1.9	3.6	.15
Generalized Anxiety	4.3	4.7	4.4	6.6	.03
Panic	0.2	1.2	0.3	0.3	.44
Separation Anxiety	8.2	14.0	11.8	11.1	<.001
Social Anxiety/Selective Mutism	4.9	5.8	5.1	5.4	.92
Hallucinations	0.4	1.2	0.6	0.7	.55
Delusions	1.7	1.2	1.7	1.9	.95
Attention Deficit Hyperactivity	19.0	24.4	19.8	26.5	<.001
Oppositional Defiant Conduct	12.7	14.0	15.0	20.4	<.001
Obsessive-Compulsive	2.7	2.3	2.7	2.6	.99
Unspecific Bipolar and Related Disorder	8.5	7.0	9.3	9.8	.52
Post Traumatic Stress	3.6	2.3	3.1	2.6	.47
Specific Phobia	1.7	1.2	1.5	2.8	.17
Specific Phobia	26.6	38.4	28.1	28.7	.05
Motivation (m [SD])					
Behavioral inhibition	5.5 (2.9)	5.5 (2.7)	5.9 (2.9)	5.6 (2.8)	.56
Reward responsiveness	8.8 (2.4)	8.8 (2.4)	8.5 (2.3)	8.7 (2.3)	.38
Drive	4.1 (3.1)	4.0 (3.0)	3.8 (3.1)	4.0 (3.0)	.18
Fun seeking	5.7 (2.7)	5.7 (2.5)	6.1 (2.8)	5.8 (2.5)	.33
NIH Toolbox fluid intelligence (m [SD])					
Processing Speed (Pattern Comparison)	93.8 (22.0)	94.6 (22.3)	97.5 (18.0)	94.2 (22.5)	.33
Working memory (List Sorting)	100.4 (14.5)	102.8 (14.3)	105.9 (12.7)	103.4 (14.5)	<.001
Episodic memory (Picture Sequence)	101.2 (16.0)	102.9 (16.3)	102.1 (16.1)	102.1 (16.4)	.005
Executive function / attention / inhibition (Flanker)	95.2 (13.7)	97.0 (13.0)	99.2 (13.0)	96.6 (13.1)	<.001
Executive function / cognitive flexibility (Dimensional Change Card Sort)	96.5 (15.2)	98.6 (15.1)	99.2 (14.4)	98.9 (15.7)	<.001
RAVLT (m [SD])					
Learning (Trials I-V avg)	8.8 (2.0)	9.2 (1.9)	8.9 (2.1)	9.1 (1.9)	<.001
Immediate delay (Trial VI)	9.7 (3.0)	10.1 (2.9)	9.7 (3.1)	10.0 (2.9)	<.001
Long (30 min) delay (Trial VII)	9.1 (3.2)	9.7 (3.0)	9.4 (3.4)	9.6 (3.1)	<.001
Cash Choice Task delayed gratification (%)	58.4	61.0	58.1	58.6	.70

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S10: GAMM results for common patterns of alcohol exposure during pregnancy, when compared to unexposed youth.

	<i>Light reducer</i> n=1203		<i>Stable light</i> n=93		<i>Heavier reducer</i> n=755		<i>R</i> ²
	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>	
CBCL							
Total problems	1.39 (0.72, 2.07)	<.001	3.13 (0.94, 5.33)	.005	1.82 (0.96, 2.68)	<.001	.136
Externalizing	1.06 (0.44, 1.69)	<.001	2.18 (0.13, 4.22)	.04	1.38 (0.59, 2.18)	<.001	.106
Internalizing	0.77 (0.11, 1.43)	.02	1.51 (-0.66, 3.68)	.17	1.56 (0.72, 2.41)	<.001	.076
Anxious Depressed	0.13 (-0.24, 0.51)	.49	0.60 (-0.63, 1.83)	.34	0.59 (0.11, 1.07)	.02	.050
Withdrawn	-0.07 (-0.42, 0.29)	.71	0.09 (-1.08, 1.25)	.89	0.50 (0.05, 0.95)	.03	.070
Somatic	0.35 (-0.04, 0.74)	.08	1.06 (-0.21, 2.33)	.10	0.72 (0.23, 1.22)	.004	.041
Thought	0.20 (-0.16, 0.56)	.28	0.97 (-0.21, 2.15)	.11	0.44 (-0.02, 0.89)	.06	.076
Attention	0.17 (-0.18, 0.53)	.34	1.40 (0.23, 2.57)	.02	0.55 (0.10, 1.01)	.02	.167
Rule breaking	0.01 (-0.27, 0.29)	.96	0.03 (-0.90, 0.95)	.96	0.59 (0.23, 0.95)	.001	.111
Aggressive	0.05 (-0.28, 0.38)	.75	0.47 (-0.61, 1.55)	.40	0.57 (0.15, 0.99)	.008	.087
KSADS							
Separation Anxiety	0.28 (0.17, 0.39)	.008	0.41 (-0.09, 0.74)	.20	0.05 (-0.19, 0.09)	.71	.025
Attention Deficit Hyperactivity	0.03 (-0.06, 0.12)	.71	0.39 (0.01, 0.66)	.15	0.22 (0.11, 0.32)	.04	.130
Oppositional Defiant Disorder	0.11 (0.01, 0.20)	.26	-0.01 (-0.33, 0.32)	.99	0.26 (0.15, 0.37)	.02	.046
Specific Phobia	0.07 (0.00, 0.14)	.34	0.56 (0.33, 0.79)	.01	-0.05 (-0.15, 0.04)	.57	.020
UPPS-P							
Lack of planning	0.22 (0.07, 0.37)	.004	0.25 (-0.25, 0.75)	.32	0.06 (-0.13, 0.25)	.53	.029
Sensation seeking	0.13 (-0.05, 0.30)	.15	0.40 (-0.17, 0.96)	.17	0.30 (0.08, 0.52)	.007	.026
BIS/BAS							
Fun seeking	0.11 (-0.06, 0.28)	.20	0.64 (0.08, 1.20)	.02	0.05 (-0.17, 0.26)	.66	.024
NIH Toolbox							
Working memory (List Sorting)	0.50 (-0.37, 1.38)	.26	1.96 (-0.92, 4.85)	.18	2.12 (1.00, 3.23)	<.001	.152
Executive function / attention / inhibition (Flanker)	0.84 (-0.02, 1.69)	.06	2.95 (0.11, 5.78)	.04	1.17 (0.07, 2.26)	.04	.051
Executive function / cognitive flexibility (Dimensional Change Card Sort)	0.85 (-0.10, 1.79)	.08	0.57 (-2.57, 3.70)	.72	2.01 (0.80, 3.22)	.001	.082

Association of Prenatal Alcohol Exposure and Associated Outcomes

	<i>Light reducer</i> n=1203		<i>Stable light</i> n=93		<i>Heavier reducer</i> n=755		<i>R</i> ²	
	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>		
RAVLT								
Learning	-0.55 (-1.24, 1.39)	.12	-0.14 (-2.38, 2.11)	.90	-0.12 (-0.21, 0.00)	.006	.131	
Immediate delay	0.11 (-0.07, 0.29)	.23	-0.52 (-1.12, 0.09)	.09	0.21 (-0.02, 0.44)	.08	.131	
Long (30 min) delay	0.20 (0.01, 0.39)	.04	-0.38 (-1.01, 0.26)	.24	0.30 (0.06, 0.55)	.02	.138	
Brain Structure								
<i>Volume</i>								
Cerebrum	7122.20 (1494.00, 12750.48)	.01	20544.50 (2551.57, 38537.43)	.03	10844.80 (3754.16, 17935.39)	.003	.338	
Inferior parietal L	263.04 (123.50, 402.57)	.001	710.07 (259.74, 1160.41)	.01	126.15 (-50.34, 302.63)	.97	.149	
Supramarginal R	156.29 (36.90, 276.68)	.07	140.00 (-249.18, 529.18)	.48	162.21 (9.85, 314.56)	.22	.134	
Inferior temporal L	209.35 (87.89, 330.81)	.004	219.71 (-172.90, 612.32)	.27	212.27 (58.62, 365.92)	.02	.190	
Middle temporal L	162.54 (55.47, 269.19)	.02	134.14 (-210.88, 479.16)	.45	161.54 (26.35, 296.73)	.12	.201	
	R	160.87 (52.02, 269.73)	.02	151.36 (-199.35, 502.06)	.40	167.58 (29.96, 305.20)	.10	.251
Lateral occipital L	159.90 (49.77, 270.03)	.03	359.49 (3.96, 715.01)	.29	128.41 (-10.88, 267.71)	.42	.245	
<i>Surface area</i>								
Precuneus R	37.99 (2.85, 72.13)	.09	114.06 (3.82, 224.29)	.13	57.92 (14.77, 101.08)	.03	.210	
Inferior temporal L	44.13 (13.48, 74.79)	.01	38.04 (-60.85, 136.93)	.45	63.9 (25.08, 102.64)	.004	.192	
Lateral occipital L	47.53 (10.33, 84.73)	.04	104.57 (-15.36, 224.50)	.26	69.67 (21.62, 115.72)	.01	.212	
Functional connectivity								
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.008	0.00 (-0.02, 0.02)	.86	0.01 (0.00, 0.02)	.02	.006	
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.002	-0.01 (-0.04, 0.01)	.42	-0.01 (-0.02, 0.00)	.20	.011	

Unstandardized regression coefficients and associated 95% confidence interval, p-value/false discovery rate adjusted p-value (for brain ROIs) and *R*² value are presented for generalized additive model results for common patterns of alcohol exposure during pregnancy, when compared to unexposed youth. Only brain ROIs identified from first series of analyses are presented. These generalized additive mixed models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

N= 8720.

PAE Sensitivity Analysis: Participant between group one-to-one matching on demographic characteristics.

The dichotomous PAE groups were demographically matched after excluding all cases of rare phenotypes on which groups were mismatched, including other in utero substance use exposure and positive reports of maternal depression. All PAE association analyses were then repeated with this more homogenous subsample.

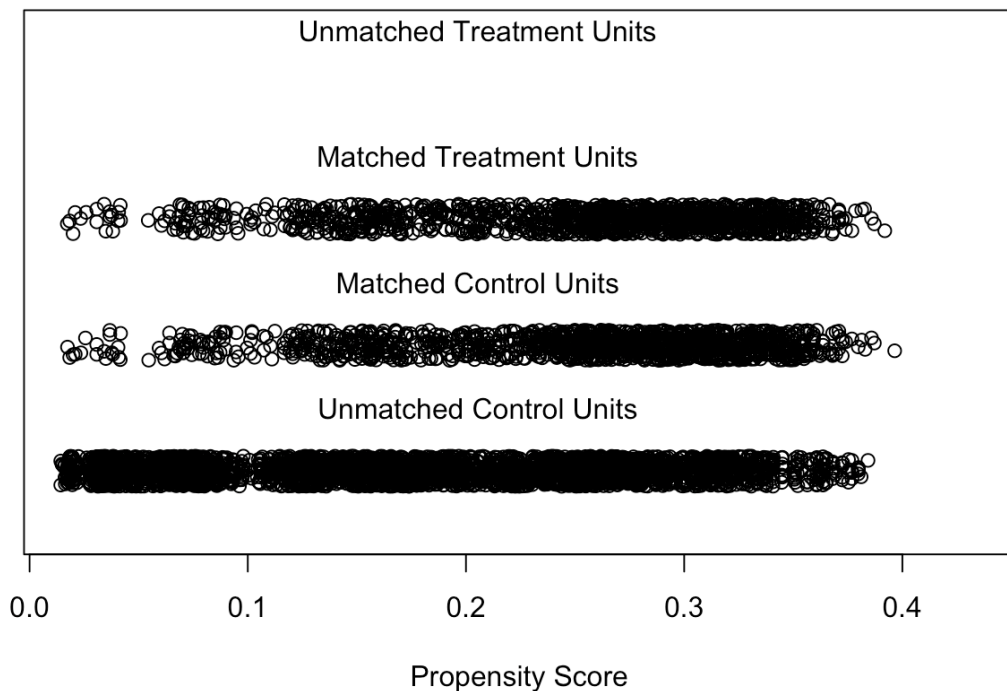
Table S11: Sample Sizes

	Unexposed	Exposed
All	4,928	1,271
Matched	1,271	1,271
Unmatched	3,657	0

Table S12: Summary of balance for matched data

	Means Exposed	Means Unexposed	Mean Diff
Distance	0.25	0.25	0.00
Race (white)	0.70	0.70	0.00
Race (black)	0.05	0.06	-0.01
Race (Hispanic)	0.15	0.15	0.00
Race (Asian)	0.02	0.01	0.00
Race (Other)	0.08	0.08	0.00
Birth weight	6.72	6.78	-0.05
Maternal age	31.59	31.49	0.10
<HS Diploma	0.03	0.02	0.00
Some College	0.17	0.18	0.00
Bachelor	0.37	0.38	-0.01
Post Grad	0.42	0.41	0.01

Distribution of Propensity Scores



Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S13: Demographic characteristics that participants were matched one-to-one on for sensitivity analyses.

	Unexposed n=1,271	Exposed n=1,271	<i>p</i>
Age (M [SD])	9.9 (0.6)	9.9 (0.6)	.38
Sex (F; n [%])	605 (47.6)	631 (49.6)	.32
Race (n [%])			.95
White	894 (70.3)	889 (69.9)	
Black	71 (5.6)	64 (5.0)	
Hispanic	186 (14.6)	190 (14.9)	
Asian	19 (1.5)	21 (1.7)	
Other	101 (7.9)	107 (8.4)	
Born premature (n [%])	202 (15.9)	211 (16.6)	.53
Birth weight (M [SD])	6.8 (1.3)	6.7 (1.4)	.32
Maternal age (M [SD])	31.5 (5.3)	31.6 (5.2)	.63
Highest Parent Education (n [%])			.92
<HS Diploma	13 (1.0)	13 (1.0)	
HS Dip/GED	27 (2.1)	32 (2.5)	
Some College	227 (17.9)	222 (17.5)	
Bachelor	483 (38.0)	468 (36.8)	
Post Grad	521 (41.0)	536 (42.2)	

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S14: Sensitivity matched-participant analysis – GAMMs for any alcohol use (dichotomous variable) in pregnancy on all outcomes of interest.

	<i>B</i> (95% CI)	<i>p</i>	<i>R</i> ²
CBCL			
Total problems	2.28 (1.48, 3.09)	<.001	.021
Externalizing	1.64 (0.90, 2.37)	<.001	.018
Rule breaking behavior	0.22 (-0.07, 0.50)	.14	.018
Aggressive behavior	0.23 (-0.11, 0.56)	.19	.007
Internalizing	1.45 (0.67, 2.33)	<.001	.007
Anxious/depressed	0.47 (0.04, 0.90)	.03	.002
Withdrawn/depressed	0.27 (-0.11, 0.64)	.16	.019
Somatic complaints	0.40 (-0.03, 0.83)	.07	.005
Social problems	0.16 (-0.13, 0.45)	.28	.012
Thought problems	0.54 (0.14, 0.93)	.01	.009
Attention problems	0.52 (0.12, 0.91)	.01	.017
KSADS			
Depression	0.08 (-0.57, 0.74)	.80	.008
Generalized Anxiety Disorder	0.10 (-0.30, 0.51)	.62	.001
Panic Disorder	0.41 (-2.54, 3.35)	.79	-.012
Separation Anxiety	0.31 (0.02, 0.60)	.03	<.001
Social Anxiety/Selective Mutism Disorder	-0.05 (-0.44, 0.34)	.81	-.001
Hallucinations	0.16 (-0.86, 1.18)	.76	.004
Delusions	-0.34 (-1.09, 0.41)	.36	-.004
Attention Deficit Hyperactivity	0.16 (-0.06, 0.38)	.14	.021
Oppositional Defiant Disorder	0.25 (0.01, 0.49)	.04	.007
Conduct Disorder	-0.02 (-0.61, 0.56)	.93	.004
Obsessive-Compulsive Disorder	0.16 (-0.14, 0.45)	.30	.006
Unspecific Bipolar and Related Disorder	-0.07 (-0.58, 0.44)	.78	.008
Post Traumatic Stress Disorder	-0.71 (-1.63, 0.21)	.13	<.001
Specific Phobia	0.23 (0.03, 0.43)	.02	.001
UPPS-P			
Lack of planning	0.19 (0.02, 0.36)	.03	.021
Sensation seeking	0.29 (0.09, 0.49)	.005	.029
Negative urgency	0.15 (-0.05, 0.35)	.13	.008
Positive urgency	0.15 (-0.06, 0.37)	.17	.024
Lack of perseverance	0.07 (-0.10, 0.24)	.40	.014
BIS/BAS			
Behavioral inhibition	0.13 (-0.08, 0.35)	.22	.003
Reward responsiveness	0.04 (-0.14, 0.22)	.63	.025
Drive	0.08 (-0.14, 0.31)	.46	.034
Fun seeking	0.17 (-0.02, 0.37)	.09	.011
NIH Toolbox			
Processing Speed (Pattern Comparison)	-0.15 (-1.86, 1.55)	.86	.030
Working memory (List Sorting)	0.61 (-0.48, 1.70)	.27	.052
Episodic memory (Picture Sequence)	0.61 (-0.67, 1.89)	.25	.035
Executive function / attention / inhibition (Flanker)	1.05 (-0.00, 2.10)	.05	.004
Executive function / cognitive flexibility	1.19 (-0.28, 2.41)	.06	.015

Association of Prenatal Alcohol Exposure and Associated Outcomes

		<i>B</i> (95% CI)	<i>p</i>	<i>R</i> ²
(Dimensional Change				
Card Sort)				
RAVLT				
Learning		0.04 (-0.11, 0.18)	.60	.111
Immediate delay		0.02 (-0.20, 0.24)	.85	.080
Long (30 min) delay		0.01 (-0.22, 0.24)	.95	.080
Cash Choice Task		0.09 (-0.07, 0.25)	.27	.010
Brain Structure				
<i>Volume</i>				
Cerebrum		9907.80 (3023.09, 16792.56)	.005	.294
Inferior parietal	L	245.92 (75.87, 415.97)	.03	.119
Supramarginal	R	184.68 (36.07, 333.29)	.08	.104
Inferior temporal	L	239.59 (90.34, 388.84)	.01	.142
Middle temporal	L	140.83 (10.75, 270.90)	.20	.163
	R	58.52 (-74.76, 191.80)	.39	.205
Lateral occipital	L	161.47 (23.59, 299.36)	.13	.177
<i>Surface area</i>				
Precuneus	R	82.12 (41.25, 122.98)	<.001	.167
Inferior temporal	L	71.86 (33.58, 110.15)	<.001	.151
Lateral occipital	L	52.70 (6.43, 98.97)	.08	.162
Functional connectivity				
Sensorimotor hand – salience		0.01 (0.00, 0.01)	.24	.008
Auditory – right ventral diencephalon		-0.13 (-0.02, 0.00)	.01	.006

Unstandardized regression coefficients and associated 95% confidence interval, p-value/false discovery rate adjusted p-value (for brain analyses) and *R*² value are presented for generalised additive model results for alcohol use as a categorical measure. Only brain ROIs identified from first series of analyses are presented. These generalized additive mixed models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S15: Sensitivity matched-participant analysis – GAMM results for alcohol use as a continuous measure, using an estimate of total drinks throughout pregnancy, when adjusting for fixed and random effects.

	<i>B</i> (95% CI)	<i>p</i>	<i>R</i> ²
CBCL			
Total problems	0.03 (0.00, 0.05)	.02	.054
Externalizing	0.02 (0.00, 0.05)	.02	.033
Rule breaking behavior	0.00 (-0.01, 0.01)	.48	.043
Aggressive behavior	0.01 (0.00, 0.02)	.20	.023
Internalizing	0.01 (-0.01, 0.04)	.29	.012
Anxious/depressed	0.00 (-0.01, 0.02)	.71	.019
Withdrawn/depressed	0.00 (-0.01, 0.01)	.96	.023
Somatic complaints	0.00 (-0.01, 0.02)	.66	.005
Social problems	0.00 (-0.01, 0.01)	.98	.054
Thought problems	0.01 (0.00, 0.02)	.13	.022
Attention problems	0.01 (0.00, 0.02)	.04	.119
KSADS			
Depression	0.00 (-0.02, 0.02)	.91	.006
Generalized Anxiety Disorder	0.00 (-0.01, 0.01)	.67	.009
Panic Disorder	0.13 (-0.05, 0.31)	.14	.429
Separation Anxiety	0.01 (0.00, 0.01)	.13	.005
Social Anxiety/Selective Mutism Disorder	0.01 (-0.01, 0.02)	.34	-.003
Hallucinations	0.00 (-0.04, 0.04)	.97	.015
Delusions	0.00 (-0.02, 0.02)	.81	.018
Attention Deficit Hyperactivity	0.00 (0.00, 0.01)	.16	.114
Oppositional Defiant Disorder	0.00 (0.00, 0.01)	.34	.013
Conduct Disorder	-0.01 (-0.03, 0.01)	.44	.034
Obsessive-Compulsive Disorder	0.01 (0.00, 0.01)	.10	.007
Unspecific Bipolar and Related Disorder	0.00 (-0.02, 0.01)	.60	.004
Post Traumatic Stress Disorder	0.00 (-0.04, 0.03)	.63	.028
Specific Phobia	0.00 (-0.01, 0.00)	.47	.003
UPPS-P			
Lack of planning	0.00 (0.00, 0.01)	.56	.018
Sensation seeking	0.01 (0.00, 0.02)	.002	.028
Negative urgency	0.00 (0.00, 0.01)	.13	.012
Positive urgency	0.00 (0.00, 0.01)	.27	.035
Lack of perseverance	0.00 (0.00, 0.00)	.99	.039
BIS/BAS			
Behavioral inhibition	0.01 (0.00, 0.01)	.02	.006
Reward responsiveness	0.00 (0.00, 0.01)	.49	.033
Drive	0.00 (-0.01, 0.01)	.78	.045
Fun seeking	0.01 (0.00, 0.01)	.09	.014
NIH Toolbox			
Processing Speed (Pattern Comparison)	0.03 (-0.02, 0.08)	.30	.045
Working memory (List Sorting)	0.00 (-0.03, 0.04)	.80	.090
Episodic memory (Picture Sequence)	0.00 (-0.04, 0.04)	.94	.062
Executive function / attention / inhibition (Flanker)	0.05 (0.02, 0.08)	.002	.020
Executive function / cognitive flexibility	0.03 (0.00, 0.07)	.06	.042

Association of Prenatal Alcohol Exposure and Associated Outcomes

		<i>B</i> (95% CI)	<i>p</i>	<i>R</i> ²
(Dimensional Change				
Card Sort)				
RAVLT				
Learning		0.00 (-0.01, 0.00)	.37	.140
Immediate delay		0.00 (-0.01, 0.00)	.26	.100
Long (30 min) delay		0.00 (-0.01, 0.00)	.18	.099
Cash Choice Task		0.00 (0.00, 0.01)	.16	.005
Brain Structure				
<i>Volume</i>				
Cerebrum		119.10 (-87.73, 325.88)	.26	.30
Inferior parietal	L	2.71 (-2.47, 7.89)	.17	.117
Supramarginal	R	1.76 (-2.74, 6.27)	.56	.102
Inferior temporal	L	0.95 (-3.64, 5.55)	.29	.144
Middle temporal	L	2.28 (-1.63, 6.19)	.63	.156
	R	-0.99 (-5.01, 3.04)	.55	.189
Lateral occipital	L	6.56 (2.45, 10.66)	.01	.186
<i>Surface area</i>				
Precuneus	R	0.20 (-1.05, 1.45)	.75	.157
Inferior temporal	L	0.24 (-0.92, 1.41)	.26	.150
Lateral occipital	L	1.55 (0.19, 2.92)	.08	.176
Functional connectivity				
Sensorimotor hand – salience		0.00 (0.00, 0.00)	.15	.006
Auditory – right ventral diencephalon		0.00 (0.00, 0.00)	.23	.006

Unstandardized regression coefficients and associated 95% confidence interval, p-value/false discovery rate adjusted p-value (for brain analyses) and *R*² value are presented for generalised additive model results for alcohol use as a continuous measure. Only brain ROIs identified from first series of analyses are presented. These generalized additive mixed models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S16: Sensitivity matched-participant analysis – GAMM results for common patterns of alcohol exposure during pregnancy compared to no exposure, when adjusting for fixed and random effects.

	<i>Light reducer</i> n=729		<i>Stable light</i> n=53		<i>Heavier reducer</i> n=284		<i>R</i> ²
	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>	
CBCL							
Total problems	1.69 (0.73, 2.64)	<.001	5.06 (2.33, 7.78)	<.001	3.18 (1.85, 4.51)	<.001	.066
Externalizing	1.40 (0.52, 2.27)	.002	3.79 (1.28, 6.30)	.003	2.19 (0.98, 3.41)	<.001	.047
Internalizing	0.64 (-0.32, 1.59)	.19	3.17 (0.44, 5.91)	.02	1.84 (0.51, 3.16)	.007	.013
Anxious Depressed	0.06 (-0.48, 0.59)	.84	1.48 (-0.05, 3.02)	.06	0.51 (-0.23, 1.26)	.18	.017
Withdrawn	0.04 (-0.39, 0.47)	.86	0.60 (-0.66, 1.86)	.35	0.24 (-0.36, 0.84)	.44	.025
Somatic	0.14 (-0.39, 0.66)	.62	1.42 (-0.09, 2.94)	.07	0.59 (-0.14, 1.32)	.12	.006
Thought	0.23 (-0.24, 0.70)	.34	1.45 (0.08, 2.82)	.04	0.36 (-0.30, 1.01)	.29	.026
Attention	0.06 (-0.40, 0.52)	.79	2.27 (0.94, 3.61)	<.001	0.79 (0.14, 1.42)	.02	.137
Rule breaking	0.16 (-0.17, 0.49)	.35	0.10 (-0.86, 1.06)	.84	0.53 (0.07, 0.99)	.03	.043
Aggressive	0.10 (-0.29, 0.50)	.61	0.79 (-0.35, 1.94)	.18	0.64 (0.09, 1.19)	.02	.032
KSADS							
Depression	0.27 (-0.67, 1.21)	.58	1.69 (0.05, 3.35)	.04	0.70 (-0.44, 1.84)	.22	.015
Separation Anxiety	0.34 (0.01, 0.67)	.05	0.98 (0.22, 1.74)	.01	0.17 (-0.32, 0.66)	.48	.011
Attention Deficit	0.07 (-0.20, 0.34)	.64	0.79 (0.21, 1.48)	.02	0.41 (0.06, 0.76)	.03	.119
Hyperactivity							
Oppositional Defiant Disorder	0.37 (0.08, 0.66)	.01	0.45 (-0.35, 1.25)	.26	0.38 (-0.01, 0.77)	.06	.021
Specific Phobia	0.25 (0.01, 0.49)	.03	0.82 (0.23, 1.41)	.007	0.22 (-0.02, 0.46)	.18	.007
UPPS-P							
Lack of planning	0.27 (0.06, 0.48)	.01	0.32 (-0.30, 0.94)	.31	0.21 (-0.09, 0.50)	.17	.029
Sensation seeking	0.29 (0.04, 0.54)	.02	0.62 (-0.08, 1.33)	.08	0.40 (0.56, 0.74)	.02	.033
BIS/BAS							
Behavioral inhibition	0.00 (-0.26, 0.25)	.98	1.10 (0.35, 1.85)	.004	0.09 (-0.27, 0.45)	.64	.011
Fun seeking	0.03 (-0.20, 0.27)	.77	0.56 (-0.12, 1.25)	.11	-0.01 (-0.33, 0.32)	.97	.013
NIH Toolbox							
Working memory (List Sorting)	0.23 (-1.08, 1.54)	.73	1.76 (-2.01, 5.53)	.36	2.45 (0.63, 4.28)	.008	.076
Executive function / attention / inhibition (Flanker)	1.38 (0.13, 2.63)	.03	3.24 (-0.37, 6.85)	.08	1.30 (-0.46, 3.04)	.14	.025

Association of Prenatal Alcohol Exposure and Associated Outcomes

	<i>Light reducer</i> n=729		<i>Stable light</i> n=53		<i>Heavier reducer</i> n=284		<i>R</i> ²	
	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>	<i>B</i> (95% CI)	<i>p</i>		
Executive function / cognitive flexibility (Dimensional Change Card Sort)	0.53 (-0.92, 1.98)	.47	0.04 (-4.13, 4.21)	.99	3.00 (0.98, 5.01)	.004	.050	
RAVLT								
Learning	0.06 (-0.11, 0.23)	.47	-0.42 (-0.91, 0.07)	.09	0.14 (-0.09, 0.38)	.24	.144	
Immediate delay	0.07 (-0.19, 0.33)	.59	-0.53 (-1.28, 0.22)	.17	0.20 (-0.16, 0.57)	.27	.100	
Long (30 min) delay	0.19 (-0.09, 0.46)	.19	-0.67 (-1.46, 0.13)	.10	0.18 (-0.20, 0.57)	.35	.101	
Brain Structure								
<i>Volume</i>								
Cerebrum	9352.00 (656.26, 18047.73)	.04	24635.00 (40.81, 49229.23)	.05	15876.20 (4162.20, 27590.29)	.008	.323	
Inferior parietal L	323.23 (101.08, 545.38)	.02	903.49 (271.87, 1535.10)	.03	130.89 (-169.62, 431.39)	.39	.130	
Supramarginal R	213.99 (21.57, 406.41)	.17	286.49 (-258.33, 831.31)	.30	325.93 (65.66, 586.18)	.08	.112	
Inferior temporal L	357.24 (165.48, 549.00)	<.001	130.87 (-414.95, 676.69)	.64	335.42 (75.96, 594.88)	.03	.160	
Middle temporal L	124.99 (-40.11, 290.09)	.84	176.03 (-291.57, 643.64)	.46	160.92 (-62.17, 384.02)	.16	.163	
	R	125.11 (-45.34, 295.56)	.90	118.81 (-363.73, 601.35)	.63	142.86 (-87.53, 373.25)	.22	.200
Lateral occipital L	213.64 (39.75, 387.53)	.10	612.93 (117.37, 1108.49)	.09	303.41 (68.06, 538.75)	.07	.209	
<i>Surface area</i>								
Precuneus R	72.69 (20.69, 124.70)	.02	140.18 (-8.87, 289.24)	.20	59.04 (-11.47, 129.56)	.30	.186	
Inferior temporal L	98.18 (48.91, 147.44)	<.001	47.62 (-91.45, 186.69)	.50	100.82 (34.25, 167.40)	.009	.163	
Lateral occipital L	63.51 (4.53, 122.48)	.10	213.62 (47.20, 380.05)	.04	117.85 (38.13, 197.57)	.01	.190	
Functional connectivity								
Sensorimotor hand – salience	0.01 (-0.03, 0.05)	.31	-0.02 (-0.06, 0.02)	.30	0.02 (0.00, 0.04)	.02	.009	
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.04	0.00 (-0.04, 0.04)	.89	0.00 (-0.02, 0.01)	.42	.007	

^aUnstandardized regression coefficients and associated 95% confidence interval, p-value/false discovery rate adjusted p-value (for brain ROIs) and *R*² value are presented for generalized additive model results for common patterns of alcohol exposure during pregnancy, when compared to unexposed youth. Only brain ROIs identified from first series of analyses are presented. These generalized additive mixed models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, school grade) and random (family, scanner/site) effects. N= 1908.

Multilevel Mediation Analysis: Cross-sectional baseline analysis to examine associations between PAE, brain structure, and psychological, behavioral, and cognitive outcomes. (Tables S17-S31).

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade), and random (family, scanner/site) effects.

Table S17: Mediation Analyses – CBCL Total Problems

	PAE → Brain (A)		Brain → Total Problems (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Total Problems (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
Volume										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.002 (-0.003, -0.001)	<.001	-0.08 (-0.12, -0.04)	<.001	1.53 (1.20, 2.12)	<.001	1.44 (1.11, 2.05)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.05 (-0.09, -0.02)	<.001	1.50 (1.18, 2.09)	<.001	1.44 (1.11, 2.05)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.02 (-0.04, -0.01)	<.001	-0.05 (-0.09, -0.02)	<.001	1.50 (1.18, 2.09)	<.001	1.44 (1.11, 2.05)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.03 (-0.04, -0.01)	<.001	-0.06 (-0.09, -0.02)	<.001	1.50 (1.18, 2.10)	<.001	1.44 (1.11, 2.05)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.03 (-0.07, -0.01)	<.001	1.48 (1.16, 2.08)	<.001	1.44 (1.11, 2.05)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.02 (-0.04, -0.02)	<.001	-0.05 (-0.9, -0.02)	<.001	1.50 (1.18, 2.09)	<.001	1.44 (1.11, 2.05)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.02 (-0.04, -0.01)	<.001	-0.04 (-0.07, -0.01)	<.001	1.49 (1.17, 2.08)	<.001	1.44 (1.11, 2.05)	<.001
Surface area										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.06 (-0.12, -0.02)	<.001	-0.05 (-0.09, -0.02)	<.001	1.50 (1.17, 2.09)	<.001	1.44 (1.11, 2.05)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.07 (-0.12, -0.04)	<.001	-0.06 (-0.11, -0.03)	<.001	1.52 (1.19, 2.11)	<.001	1.44 (1.11, 2.05)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.07 (-0.12, -0.04)	<.001	-0.04 (-0.08, -0.01)	<.001	1.49 (1.17, 2.08)	<.001	1.44 (1.11, 2.05)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.09 (-2.27, 2.15)	.48	0.00 (-0.02, 0.02)	.48	1.35 (0.99, 2.01)	<.001	1.35 (0.98, 2.02)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	-0.50 (-2.50, 1.11)	.28	0.01 (-0.02, 0.03)	.28	1.34 (0.98, 2.00)	<.001	1.36 (1.00, 2.00)	<.001

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S18: CBCL Externalizing Psychopathology

	PAE → Brain (A)		Brain → Externalizing Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Externalizing Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.95 (25.39, 51.6)	<.001	-0.002 (-0.003, -0.001)	<.001	-0.08 (-0.12, -0.05)	<.001	1.13 (0.84, 1.67)	<.001	1.05 (0.74, 1.60)	<.001
Inferior temporal L	2.93 (1.99, 3.68)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.06 (-0.10, -0.03)	<.001	1.11 (0.82, 1.65)	<.001	1.05 (0.74, 1.60)	<.001
Middle temporal L	2.20 (1.37, 2.87)	<.001	-0.03 (-0.04, -0.02)	<.001	-0.06 (-0.10, -0.03)	<.001	1.12 (0.83, 1.66)	<.001	1.05 (0.74, 1.60)	<.001
Middle temporal R	2.23 (1.37, 2.91)	<.001	-0.03 (-0.05, -0.02)	<.001	-0.07 (-0.11, -0.04)	<.001	1.13 (0.83, 1.67)	<.001	1.04 (0.74, 1.60)	<.001
Lateral occipital L	2.10 (1.23, 2.79)	<.001	-0.02 (-0.04, -0.01)	<.001	-0.04 (-0.08, -0.02)	<.001	1.10 (0.81, 1.64)	<.001	1.05 (0.75, 1.60)	<.001
Inferior parietal L	2.12 (1.06, 2.97)	<.001	-0.02 (-0.03, -0.02)	<.001	-0.05 (-0.08, -0.02)	<.001	1.10 (0.81, 1.64)	<.001	1.05 (0.75, 1.60)	<.001
Supramarginal R	1.88 (0.96, 2.61)	<.001	-0.02 (-0.04, -0.02)	<.001	-0.04 (-0.8, -0.02)	<.001	1.10 (0.81, 1.64)	<.001	1.05 (0.75, 1.60)	<.001
<i>Surface area</i>										
Inferior temporal L	0.79 (0.55, 0.99)	<.001	-0.09 (-0.13, -0.51)	<.001	-0.07 (-0.11, -0.03)	<.001	1.12 (0.83, 1.66)	<.001	1.05 (0.74, 1.60)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.08 (-0.12, -0.52)	<.001	-0.07 (-0.12, -0.04)	<.001	1.13 (0.83, 1.67)	<.001	1.05 (0.74, 1.60)	<.001
Precuneus R	0.60 (0.34, 0.81)	<.001	-0.07 (-0.12, -0.04)	<.001	-0.05 (-0.08, -0.02)	<.001	1.10 (0.81, 1.64)	<.001	1.05 (0.75, 1.60)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	-0.85 (-2.98, 1.02)	.16	-0.01 (-0.02, 0.01)	.18	1.07 (0.74, 1.67)	<.001	1.06 (0.73, 1.67)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.43 (-1.38, 1.89)	.34	-0.01 (-0.03, 0.02)	.34	1.10 (0.74, 1.67)	<.001	1.08 (0.75, 1.65)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S19: CBCL Internalizing Psychopathology

	PAE → Brain (A)		Brain → Internalizing Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Internalizing Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.001 (-0.002, 0.000)	.010	-0.03 (-0.07, 0.00)	.010	0.99 (0.68, 1.56)	<.001	0.95 (0.64, 1.54)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.02, 0.00)	.140	-0.01 (-0.06, 0.01)	.140	0.98 (0.66-1.55)	<.001	0.95 (0.64, 1.54)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.01 (-0.02, 0.00)	.120	-0.01 (-0.5, 0.01)	.120	0.97 (0.66-1.55)	<.001	0.95 (0.64, 1.54)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.01 (-0.02, 0.00)	.060	-0.02 (-0.5, 0.01)	.060	0.98 (0.67-1.55)	<.001	0.95 (0.64, 1.54)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (-0.02, 0.01)	.280	-0.01 (-0.04, 0.01)	.280	0.97 (0.66-1.54)	<.001	0.95 (0.64, 1.54)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.03 (-0.06, -0.01)	<.001	0.99 (0.68-1.56)	<.001	0.95 (0.64, 1.54)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.01 (-0.02, 0.00)	.030	-0.02 (-0.04, 0.00)	.030	0.98 (0.67-1.55)	<.001	0.95 (0.64, 1.53)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.01 (-0.06, 0.03)	.250	-0.01 (-0.05, 0.02)	.250	0.97 (0.66-1.54)	<.001	0.95 (0.64, 1.54)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.03 (-0.07, 0.00)	.020	-0.03 (-0.07, 0.00)	.020	0.99 (0.67-1.56)	<.001	0.95 (0.64, 1.54)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.04 (-0.08, 0.00)	.020	-0.02 (-0.05, 0.00)	.020	0.98 (0.67-1.55)	<.001	0.95 (0.64, 1.54)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.12 (-2.15, 2.10)	.47	0.00 (-0.02, 0.02)	.49	0.82 (0.47, 1.45)	<.001	0.81 (0.46, 1.46)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	-0.58 (-2.51, 0.97)	.22	0.01 (-0.01, 0.04)	.22	0.81 (0.46, 1.45)	<.001	0.83 (0.48, 1.44)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S20: CBCL Anxious and Depressive Symptoms

	PAE → Brain (A)		Brain → Anxiety Depression Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Anxiety Depression Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	0.00 (-0.001, 0.000)	.010	-0.02 (-0.04, 0.00)	.010	0.23 (0.05, 0.55)	.010	0.21 (0.02, 0.54)	.010
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.012, 0.001)	.050	-0.01 (-0.04, 0.00)	.050	0.22 (0.04, 0.55)	.010	0.20 (0.02, 0.54)	.010
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.01 (-0.01, 0.00)	.060	-0.01 (-0.03, 0.00)	.060	0.22 (0.04, 0.55)	.010	0.21 (0.02, 0.54)	.010
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.01 (-0.02, 0.00)	.010	-0.02 (-0.04, 0.00)	.010	0.22 (0.05, 0.55)	.010	0.21 (0.02, 0.54)	.010
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (-0.01, 0.01)	.490	0.00 (-0.02, 0.01)	.490	0.21 (0.03, 0.54)	.010	0.20 (0.03, 0.54)	.010
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.01 (-0.02, -0.004)	<.001	-0.02 (-0.04, -0.01)	<.001	0.23 (0.05, 0.56)	.010	0.21 (0.02, 0.54)	.010
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.01 (-0.01, 0.00)	.030	-0.01 (-0.03, 0.00)	.030	0.22 (0.04, 0.55)	.010	0.21 (0.03, 0.54)	.010
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.01 (-0.04, 0.01)	.140	-0.01 (-0.03, 0.01)	.140	0.22 (0.04, 0.55)	.010	0.20 (0.02, 0.54)	.010
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.01 (-0.03, 0.01)	.110	-0.01 (-0.03, 0.01)	.110	0.22 (0.04, 0.55)	.010	0.20 (0.02, 0.54)	.010
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.01 (-0.04, 0.01)	.110	-0.01 (-0.02, 0.00)	.110	0.22 (0.04, 0.54)	.010	0.21 (0.03, 0.54)	.010
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.04 (-1.24, 1.15)	.48	0.00 (-0.01, 0.01)	.48	0.15 (-0.05, 0.51)	.06	0.15 (-0.05, 0.51)	.08
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	-0.43 (-1.52, 0.44)	.14	0.01 (-0.01, 0.02)	.14	0.15 (-0.05, 0.50)	.08	0.16 (-0.04, 0.50)	.06

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S21: CBCL Withdrawn/Depressed

	PAE → Brain (A)		Brain → Withdrawal Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Withdrawal Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.001 (-0.001, 0.000)	<.001	-0.03 (-0.05, -0.01)	<.001	0.29 (0.11, 0.60)	<.001	0.25 (0.08, 0.57)	.010
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.02, 0.00)	<.001	-0.03 (-0.05, -0.01)	<.001	0.28 (0.11, 0.59)	<.001	0.25 (0.08, 0.57)	.010
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.01 (-0.02, 0.00)	<.001	-0.02 (-0.04, -0.01)	<.001	0.28 (0.11, 0.59)	<.001	0.25 (0.08, 0.57)	.010
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.01)	<.001	0.28 (0.11, 0.60)	<.001	0.25 (0.08, 0.57)	.010
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (-0.01, 0.00)	.230	-0.01 (-0.02, 0.01)	.230	0.26 (0.09, 0.58)	<.001	0.25 (0.08, 0.57)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.28 (0.11, 0.59)	<.001	0.25 (0.08, 0.57)	.010
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.28 (0.11, 0.59)	<.001	0.25 (0.08, 0.57)	.010
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.03 (-0.05, -0.01)	.010	-0.02 (-0.04, 0.00)	.010	0.28 (0.11, 0.59)	<.001	0.25 (0.08, 0.57)	.010
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.01 (-0.03, 0.01)	.260	-0.01 (-0.03, 0.01)	.260	0.26 (0.09, 0.58)	<.001	0.25 (0.08, 0.57)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.04 (-0.06, -0.02)	<.001	-0.02 (-0.04, -0.01)	<.001	0.28 (0.11, 0.59)	<.001	0.25 (0.08, 0.57)	.010
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.36 (-0.84, 1.41)	.26	0.00 (-0.01, 0.01)	.28	0.18 (0.00, 0.52)	.03	0.18 (-0.01, 0.52)	.03
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	-0.42 (-1.44, 0.40)	.13	0.01 (-0.01, 0.02)	.13	0.18 (-0.01, 0.51)	.04	0.19 (0.00, 0.52)	.02

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S22: CBCL Somatic Complaints

	PAE → Brain (A)		Brain → Somatic Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Somatic Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	0.00 (-0.001, 0.000)	.150	-0.01 (-0.03, 0.01)	.150	0.41 (0.23, 0.75)	<.001	0.40 (0.22, 0.74)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	0.00 (-0.01, 0.01)	.500	0.00 (-0.02, 0.02)	.500	.041 (0.22, 0.74)	<.001	0.40 (0.22, 0.74)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.01 (-0.01, 0.00)	.060	-0.01 (-0.03, 0.00)	.060	0.42 (0.24, 0.75)	<.001	0.40 (0.22, 0.74)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.01 (-0.01, 0.00)	.060	-0.01 (-0.03, 0.00)	.060	0.42 (0.24, 0.75)	<.001	0.40 (0.22, 0.74)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (-0.01, 0.00)	.280	0.00 (-0.02, 0.01)	.280	0.41 (0.23, 0.74)	<.001	0.40 (0.22, 0.74)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	0.00 (-0.01, 0.00)	.110	-0.01 (-0.02, 0.00)	.110	0.41 (0.23, 0.75)	<.001	0.40 (0.22, 0.74)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.01 (-0.01, 0.00)	.030	-0.01 (-0.03, 0.00)	.030	0.42 (0.24, 0.75)	<.001	0.40 (0.22, 0.74)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	0.01 (-0.02, 0.03)	.280	0.01 (-0.02, 0.03)	.280	0.40 (0.22, 0.74)	<.001	0.40 (0.22, 0.74)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.01 (-0.04, 0.00)	.070	-0.01 (-0.04, 0.00)	.070	0.42 (0.24, 0.76)	<.001	0.40 (0.24, 0.76)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.02 (-0.05, 0.00)	.010	-0.01 (-0.03, 0.00)	.010	0.42 (0.24, 0.75)	<.001	0.40 (0.22, 0.74)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	-0.36 (-1.67, 0.78)	.28	0.00 (-0.01, 0.01)	.30	0.32 (0.12, 0.68)	<.001	0.31 (0.11, 0.68)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.56 (-0.55, 1.45)	.12	-0.01 (-0.02, 0.01)	.12	0.32 (0.12, 0.69)	<.001	0.32 (0.12, 0.68)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S23: CBCL Thought

	PAE → Brain (A)		Brain → Thought Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Thought Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.001 (-0.001, 0.000)	<.001	-0.02 (-0.05, -0.01)	<.001	0.39 (0.22, 0.71)	<.001	0.37 (0.19, 0.69)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.015, -0.003)	<.001	-0.02 (-0.05, -0.01)	<.001	0.39 (0.22, 0.71)	<.001	0.37 (0.19, 0.9)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.01 (-0.02, 0.00)	.010	-0.02 (-0.04, 0.00)	.010	0.39 (0.21, 0.70)	<.001	0.37 (0.19, 0.69)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.01 (-0.01, 0.00)	.020	-0.01 (-0.03, 0.00)	.020	0.38 (0.21, 0.70)	<.001	0.37 (0.19, 0.69)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (-0.01, 0.01)	.410	0.00 (-0.02, 0.01)	.410	0.37 (0.20, 0.69)	<.001	0.37 (0.19, 0.69)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.39 (0.22, 0.71)	<.001	0.37 (0.19, 0.69)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.01 (-0.01, 0.00)	.010	-0.01 (-0.03, 0.00)	.010	0.38 (0.21, 0.70)	<.001	0.37 (0.19, 0.69)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.03 (-0.06, -0.01)	.010	-0.02 (-0.04, -0.01)	.010	0.39 (0.22, 0.71)	<.001	0.37 (0.19, 0.69)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.01 (-0.04, 0.00)	.100	-0.01 (-0.03, 0.00)	.100	0.38 (0.21, 0.70)	<.001	0.37 (0.19, 0.69)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.03 (-0.06, 0.01)	<.001	-0.02 (-0.03, 0.00)	<.001	0.39 (0.22, 0.70)	<.001	0.37 (0.19, 0.69)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.49 (-0.73, 1.56)	.18	0.00 (-0.01, 0.01)	.20	0.30 (0.11, 0.64)	<.001	0.30 (0.11, 0.65)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.17 (-0.87, 1.00)	.38	0.00 (-0.02, 0.01)	.38	0.30 (0.12, 0.65)	<.001	0.31 (0.12, 0.64)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S24: CBCL Attention Problems

	PAE → Brain (A)		Brain → Attention Deficits (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Attention Deficits (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.001 (-0.002, -0.001)	<.001	-0.05 (-0.08, -0.03)	<.001	0.43 (0.25, 0.75)	<.001	0.37 (0.19, 0.71)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.01)	<.001	0.41 (0.23, 0.73)	<.001	0.37 (0.19, 0.71)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.01)	<.001	0.40 (0.23, 0.73)	<.001	0.37 (0.19, 0.71)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.04 (-0.06, -0.02)	<.001	0.41 (0.24, 0.74)	<.001	0.37 (0.19, 0.71)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.01)	<.001	0.40 (0.22, 0.73)	<.001	0.37 (0.19, 0.71)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.40 (0.22, 0.73)	<.001	0.37 (0.19, 0.71)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.02 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.02)	<.001	0.41 (0.23, 0.73)	<.001	0.37 (0.19, 0.71)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.04 (-0.07, -0.02)	<.001	-0.03 (-0.6, -0.01)	<.001	0.41 (0.23, 0.74)	<.001	0.37 (0.19, 0.71)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.04 (-0.06, -0.02)	<.001	-0.04 (-0.06, -0.02)	<.001	0.41 (0.23, 0.74)	<.001	0.37 (0.19, 0.71)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.05 (-0.08, -0.03)	<.001	-0.03 (-0.05, -0.01)	<.001	0.41 (0.23, 0.73)	<.001	0.37 (0.19, 0.71)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.58 (-0.67, 1.67)	.12	0.00 (0.00, 0.01)	.14	0.33 (0.14, 0.68)	<.001	0.33 (0.14, 0.69)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	-0.21 (-1.26, 0.64)	.29	0.00 (-0.01, 0.02)	.29	0.33 (0.14, 0.68)	<.001	0.34 (0.15, 0.68)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S25: CBCL Rule Breaking

	PAE → Brain (A)		Brain → Rule Breaking Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Rule Breaking Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.001 (-0.001, -0.001)	<.001	-0.04 (-0.06, -0.02)	<.001	0.26 (0.12, 0.51)	<.001	0.22 (0.08, 0.48)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.02)	<.001	0.25 (0.12, 0.50)	<.001	0.22 (0.08, 0.48)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.02 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.02)	<.001	0.26 (0.12, 0.51)	<.001	0.22 (0.08, 0.48)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.02 (-0.02, -0.01)	<.001	-0.04 (-0.06, -0.02)	<.001	0.26 (0.12, 0.51)	<.001	0.22 (0.08, 0.48)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.04, -0.01)	<.001	0.25 (0.11, 0.50)	<.001	0.22 (0.08, 0.48)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.24 (0.11, 0.49)	<.001	0.22 (0.08, 0.48)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.02 (0.02, -0.01)	<.001	-0.03 (-0.05, -0.01)	<.001	0.25 (0.11, 0.50)	<.001	0.22 (0.08, 0.48)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.04 (-0.06, -0.03)	<.001	-0.03 (-0.05, -0.02)	<.001	0.25 (0.12, 0.51)	<.001	0.22 (0.08, 0.48)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.03 (-0.05, -0.02)	<.001	-0.03 (-0.05, -0.01)	<.001	0.25 (0.11, 0.50)	<.001	0.22 (0.08, 0.48)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.03 (-0.05, -0.02)	<.001	-0.02 (-0.03, -0.01)	<.001	0.24 (0.10, 0.49)	<.001	0.22 (0.08, 0.48)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	-0.66 (-1.62, 0.17)	.05	0.00 (-0.01, 0.00)	.07	0.26 (0.11, 0.52)	<.001	0.25 (0.10, 0.52)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.16 (-0.65, 0.81)	.36	0.00 (-0.01, 0.01)	.36	0.25 (0.11, 0.52)	<.001	0.25 (0.11, 0.51)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S26: CBCL Aggressive Symptoms

	PAE → Brain (A)		Brain → Aggressive Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Aggressive Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	-0.001 (-0.001, -0.001)	<.001	-0.04 (-0.07, -0.02)	<.001	0.36 (0.20, 0.65)	<.001	0.31 (0.15, 0.61)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.05, -0.01)	<.001	0.35 (0.19, 0.34)	<.001	0.31 (0.15, 0.61)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	-0.02 (-0.02, -0.01)	<.001	-0.03 (-0.06, -0.02)	<.001	0.35 (0.19, 0.64)	<.001	0.31 (0.15, 0.61)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	-0.02 (-0.02, -0.01)	<.001	-0.04 (-0.06, -0.02)	<.001	0.35 (0.20, 0.64)	<.001	0.31 (0.15, 0.61)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	-0.01 (-0.02, 0.00)	<.001	-0.02 (-0.04, -0.01)	<.001	0.34 (0.18, 0.63)	<.001	0.31 (0.15, 0.61)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.34 (0.18, 0.63)	<.001	0.31 (0.15, 0.61)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, -0.01)	<.001	0.34 (0.18, 0.63)	<.001	0.31 (0.15, 0.61)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	-0.05 (-0.07, -0.03)	<.001	-0.04 (-0.06, -0.02)	<.001	0.35 (0.19, 0.64)	<.001	0.31 (0.15, 0.61)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	-0.04 (-0.06, -0.02)	<.001	-0.03 (-0.06, -0.02)	<.001	0.35 (0.19, 0.64)	<.001	0.31 (0.15, 0.61)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	-0.04 (-0.06, -0.02)	<.001	-0.02 (-0.04, -0.01)	<.001	0.34 (0.18, 0.63)	<.001	0.31 (0.15, 0.61)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	-1.03 (-2.14, -0.07)	.02	-0.01 (-0.02, 0.00)	.04	0.30 (0.13, 0.61)	<.001	0.29 (0.12, 0.60)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.36 (-0.58, 1.11)	.23	-0.01 (-0.02, 0.01)	.23	0.30 (0.13, 0.61)	<.001	0.30 (0.13, 0.60)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S27: UPPS-P Lack of Planning

	PAE → Brain (A)		Brain → Lack Planning (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Lack Planning (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	0.00 (0.00, 0.00)	.360	0.00 (-0.01, 0.01)	.360	0.19 (0.11, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	0.00 (0.00, 0.00)	.400	0.00 (-0.01, 0.01)	.400	0.18 (0.11, 0.31)	<.001	0.18 (0.11, 0.32)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	0.00 (0.00, 0.00)	.410	0.00 (-0.01, 0.01)	.410	0.19 (0.12, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	0.00 (0.00, 0.00)	.380	0.00 (-0.01, 0.00)	.380	0.19 (0.12, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (0.00, 0.00)	.410	0.00 (-0.01, 0.01)	.410	0.19 (0.11, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	0.00 (0.00, 0.00)	.400	0.00 (-0.01, 0.00)	.400	0.19 (0.12, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	0.00 (0.00, 0.00)	.290	0.00 (-0.01, 0.00)	.290	0.19 (0.12, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	0.00 (-0.01, 0.01)	.350	0.00 (-0.01, 0.01)	.350	0.19 (0.12, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	0.00 (-0.01, 0.01)	.310	0.00 (-0.01, 0.01)	.310	0.18 (0.11, 0.31)	<.001	0.18 (0.11, 0.32)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	0.00 (-0.01, 0.01)	.450	0.00 (-0.01, 0.00)	.450	0.19 (0.12, 0.32)	<.001	0.18 (0.11, 0.32)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.21 (-0.30, 0.65)	.16	0.00 (0.00, 0.01)	.18	0.20 (0.12, 0.34)	<.001	0.20 (0.12, 0.34)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.02 (-0.41, 0.36)	.48	0.00 (-0.01, 0.01)	.48	0.20 (0.12, 0.34)	<.001	0.20 (0.12, 0.34)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S28: UPPS-P Sensation Seeking

	PAE → Brain (A)		Brain → Sensation Seeking (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Sensation Seeking (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	0.00 (0.00, 0.00)	.050	0.01 (0.00, 0.02)	.050	0.22 (0.14, 0.36)	<.001	0.22 (0.14, 0.37)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	0.00 (0.00, 0.01)	.060	0.01 (0.00, 0.02)	.060	0.22 (0.14, 0.36)	<.001	0.22 (0.14, 0.37)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	0.00 (0.00, 0.01)	.050	0.01 (0.00, 0.01)	.050	0.22 (0.14, 0.36)	<.001	0.22 (0.14, 0.37)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	0.00 (0.00, 0.01)	.030	0.01 (0.00, 0.02)	.030	0.22 (0.14, 0.36)	<.001	0.22 (0.14, 0.37)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.00 (0.00, 0.01)	.040	0.01 (0.00, 0.01)	.040	0.22 (0.14, 0.36)	<.001	0.22 (0.14, 0.37)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	0.00 (0.00, 0.00)	.130	0.00 (0.00, 0.01)	.130	0.22 (0.14, 0.37)	<.001	0.22 (0.14, 0.37)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	0.00 (0.00, 0.01)	.090	0.00 (0.00, 0.01)	.090	0.22 (0.14, 0.37)	<.001	0.22 (0.14, 0.37)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	0.01 (-0.01, 0.02)	.100	0.01 (0.00, 0.01)	.100	0.22 (0.14, 0.37)	<.001	0.22 (0.14, 0.37)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	0.00 (-0.01, 0.01)	.230	0.00 (-0.01, 0.01)	.230	0.22 (0.14, 0.37)	<.001	0.22 (0.14, 0.37)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	0.01 (0.00, 0.02)	.070	0.00 (0.00, 0.01)	.070	0.22 (0.14, 0.37)	<.001	0.22 (0.14, 0.37)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	0.19 (-0.39, 0.69)	.25	0.00 (0.00, 0.01)	.27	0.19 (0.10, 0.35)	<.001	0.19 (0.10, 0.35)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.44 (-0.04, 0.83)	.03	-0.01 (-0.02, 0.00)	.03	0.20 (0.11, 0.36)	<.001	0.19 (0.10, 0.35)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S29: NIH Flanker Task

	PAE → Brain (A)		Brain → Flanker (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Flanker (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	39.43 (24.62, 51.22)	<.001	0.003 (0.002, 0.003)	<.001	0.10 (0.05, 0.16)	<.001	1.07 (0.66, 1.81)	<.001	1.15 (0.77, 1.91)	<.001
Inferior temporal L	2.87 (1.91, 3.63)	<.001	0.02 (0.004, 0.033)	.010	0.05 (0.01, 0.10)	.010	1.11 (0.70, 1.86)	<.001	1.15 (0.76, 1.92)	<.001
Middle temporal L	2.23 (1.39, 2.90)	<.001	0.03 (0.01, 0.04)	<.001	0.06 (0.02, 0.11)	<.001	1.10 (0.70, 1.85)	<.001	1.15 (0.76, 1.92)	<.001
Middle temporal R	2.30 (1.44, 2.99)	<.001	0.03 (0.01, 0.04)	<.001	0.06 (0.02, 0.11)	<.001	1.11 (0.70, 1.85)	<.001	1.15 (0.76, 1.92)	<.001
Lateral occipital L	2.18 (1.29, 2.88)	<.001	0.03 (0.01, 0.04)	<.001	0.06 (0.03, 0.12)	<.001	1.10 (0.70, 1.85)	<.001	1.15 (0.77, 1.91)	<.001
Inferior parietal L	2.22 (1.15, 3.08)	<.001	0.01 (-0.002, 0.02)	.05	0.02 (-0.01, 0.06)	.05	1.11 (0.74, 1.89)	<.001	1.15 (0.76, 1.91)	<.001
Supramarginal R	1.94 (1.01, 2.69)	<.001	0.01 (-0.004, 0.03)	.06	0.02 (-0.01, 0.05)	.06	1.14 (0.74, 1.89)	<.001	1.16 (0.76, 1.91)	<.001
<i>Surface area</i>										
Inferior temporal L	0.77 (0.53, 0.97)	<.001	0.11 (0.05, 0.16)	<.001	0.08 (0.04, 0.14)	<.001	1.08 (0.68, 1.83)	<.001	1.15 (0.76, 1.92)	<.001
Lateral occipital L	0.93 (0.63, 1.17)	<.001	0.10 (0.06, 0.14)	<.001	1.07 (0.67, 1.82)	<.001	1.07 (0.67, 1.82)	<.001	1.15 (0.76, 1.92)	<.001
Precuneus R	0.57 (0.31, 0.78)	<.001	0.11 (0.05, 0.15)	<.001	0.06 (0.02, 0.11)	<.001	1.11 (0.70, 1.86)	<.001	1.15 (0.77, 1.91)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.02	-0.43 (-3.36, 2.13)	.37	0.00 (-0.02, 0.02)	.37	1.18 (0.73, 2.00)	<.001	1.17 (0.71, 2.00)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, -0.01)	<.001	0.68 (-1.80, 2.68)	.31	-0.01 (-0.04, 0.02)	.31	1.19 (0.73, 2.01)	<.001	1.19 (0.74, 1.98)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S30: KSADS Oppositional Defiant Disorder

	PAE → Brain (A)		Brain → ODD (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → ODD (C)		Total Effect	
	B (SE)	p	B (SE)	p	B (SE)	p	B (SE)	p	B (SE)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	38.711 (20.530, 53.418)	<.001	-0.0001 (-0.0002, 0.0000)	.03	-0.004 (-0.009, 0.000)	.03	0.164 (0.078, 0.239)	<.001	0.160 (0.077, 0.234)	<.001
Inferior temporal L	2.734 (1.554, 3.689)	<.001	-0.002 (-0.004, 0.000)	<.001	-0.006 (-0.012, -0.002)	<.001	0.167 (0.081, 0.241)	<.001	0.160 (0.077, 0.234)	<.001
Middle temporal L	2.214 (1.174, 3.054)	<.001	-0.002 (-0.004, 0.000)	.04	-0.004 (-0.009, 0.000)	.04	0.164 (0.079, 0.240)	<.001	0.160 (0.077, 0.235)	<.001
Middle temporal R	2.200 (1.136, 3.061)	<.001	-0.001 (-0.003, 0.000)	.06	-0.003 (-0.009, 0.000)	.06	0.162 (0.079, 0.238)	<.001	0.159 (0.077, 0.234)	<.001
Lateral occipital L	1.949 (0.864, 2.827)	<.001	-0.001 (-0.002, 0.001)	.23	-0.001 (-0.005, 0.003)	.23	0.161 (0.076, 0.236)	<.001	0.159 (0.077, 0.234)	<.001
Inferior parietal L	2.372 (1.044, 3.446)	<.001	-0.002 (-0.004, 0.000)	.005	-0.005 (-0.001, -0.001)	.005	0.164 (0.080, 0.241)	<.001	0.160 (0.077, 0.235)	<.001
Supramarginal R	2.016 (0.853, 2.957)	<.001	-0.002 (-0.003, 0.000)	.03	-0.003 (-0.008, 0.001)	.03	0.162 (0.078, 0.238)	<.001	0.159 (0.077, 0.235)	<.001
<i>Surface area</i>										
Inferior temporal L	7.336 (4.291, 9.799)	<.001	-0.001 (-0.002, 0.000)	<.001	-0.007 (-0.013, -0.002)	<.001	0.167 (0.081, 0.243)	<.001	0.160 (0.077, 0.235)	<.001
Lateral occipital L	0.871 (0.500, 1.171)	<.001	-0.003 (-0.009, 0.003)	.12	-0.003 (-0.008, 0.002)	.12	0.163 (0.077, 0.239)	<.001	0.160 (0.077, 0.235)	<.001
Precuneus R	0.570 (0.215, 0.804)	<.001	-0.008 (-0.015, -0.001)	.02	-0.004 (-0.009, 0.000)	.02	0.163 (0.078, 0.238)	<.001	0.160 (0.076, 0.233)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.007 (0.000, 0.012)	.01	-0.166 (-0.538, 0.183)	.17	-0.001 (-0.005, 0.001)	.18	0.159 (0.076, 0.235)	<.001	0.159 (0.076, 0.235)	<.001
Auditory – right ventral diencephalon	-0.015 (-0.023, -0.008)	<.001	-0.123 (-0.399, 0.136)	.23	0.002 (-0.002, 0.006)	.23	0.157 (0.075, 0.233)	<.001	0.159 (0.073, 0.239)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S31: KSADS Separation Anxiety

	PAE → Brain (A)		Brain → Separation Anxiety (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Separation Anxiety (C)		Total Effect	
	B (SE)	p	B (SE)	p	B (SE)	p	B (SE)	p	B (SE)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	38.71 (20.53, 53.42)	<.001	0.00 (0.00, 0.00)	.12	0.00 (-0.01, 0.00)	.12	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.03
Inferior temporal L	2.73 (1.55, 3.69)	<.001	0.00 (0.00, 0.00)	.29	0.00 (-0.01, 0.01)	.29	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.02
Middle temporal L	2.21 (1.17, 3.05)	<.001	0.00 (0.00, 0.00)	.20	0.00 (-0.01, 0.00)	.20	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.02
Middle temporal R	2.20 (1.14, 3.06)	<.001	0.00 (0.00, 0.00)	.28	0.00 (-0.01, 0.00)	.28	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.03
Lateral occipital L	1.95 (0.86, 2.83)	<.001	0.00 (0.00, 0.00)	.32	0.00 (-0.01, 0.00)	.32	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.03
Inferior parietal L	2.37 (1.04, 3.45)	<.001	0.00 (0.00, 0.00)	.12	0.00 (-0.01, 0.00)	.12	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.03
Supramarginal R	2.02 (0.85, 2.96)	<.001	-0.003 (-0.005, -0.001)	<.001	-0.005 (-0.011, -0.001)	<.001	0.10 (0.00, 0.18)	.02	0.10 (0.00, 0.17)	.03
<i>Surface area</i>										
Inferior temporal L	7.34 (4.29, 9.80)	<.001	0.00 (0.00, 0.00)	.42	0.00 (-0.01, 0.01)	.42	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.02
Lateral occipital L	0.87 (0.50, 1.17)	<.001	0.00 (-0.01, 0.00)	.30	0.00 (-0.01, 0.00)	.30	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.03
Precuneus R	0.57 (0.22, 0.80)	<.001	-0.01 (-0.01, 0.00)	.06	0.00 (-0.01, 0.00)	.06	0.10 (0.00, 0.17)	.03	0.10 (0.00, 0.17)	.03
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.01	-0.14 (-0.55, 0.27)	.23	0.00 (0.00, 0.00)	.24	0.10 (0.00, 0.17)	.03	0.09 (0.00, 0.17)	.03
Auditory – right ventral diencephalon	-0.02 (-0.02, -0.01)	<.001	-0.10 (-0.41, 0.20)	.30	0.00 (0.00, 0.01)	.30	0.10 (0.00, 0.17)	.03	0.0 (-0.01, 0.17)	.03

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Longitudinal Multilevel Mediation Analysis: Examining associations between PAE, baseline brain structure, and one-year follow-up psychological outcomes. (Tables S31-S42).

Table S32: Mediation Analyses – CBCL Total Problems At One-Year Follow-Up

	PAE → Brain (A)		Brain → Total Problems (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Total Problems (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	0.00 (0.00, 0.00)	.11	-0.03 (-0.10, 0.01)	.11	1.69 (1.21, 2.58)	<.001	1.65 (1.16, 2.56)	<.001
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.01 (-0.03, 0.00)	.06	-0.03 (-0.10, 0.01)	.06	1.70 (1.22, 2.58)	<.001	1.65 (1.16, 2.56)	<.001
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.03, 0.01)	.31	-0.01 (-0.05, 0.03)	.31	1.67 (1.19, 2.55)	<.001	1.66 (1.17, 2.55)	<.001
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.01 (-0.03, 0.01)	.19	-0.02 (-0.08, 0.02)	.19	1.68 (1.20, 2.56)	<.001	1.65 (1.16, 2.55)	<.001
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.01 (-0.03, 0.01)	.11	-0.02 (-0.06, 0.01)	.13	1.69 (1.20, 2.56)	<.001	1.66 (1.17, 2.55)	<.001
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.02 (-0.04, -0.01)	<.001	-0.03 (-0.07, 0.00)	.05	1.69 (1.21, 2.57)	<.001	1.66 (1.16, 2.55)	<.001
Supramarginal R	1.34 (-0.08, 2.44)	.05	-0.01 (-0.03, 0.01)	.15	-0.01 (-0.04, 0.01)	.20	1.68 (1.20, 2.55)	<.001	1.66 (1.17, 2.55)	<.001
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.04 (-0.11, 0.02)	.10	-0.03 (-0.10, 0.02)	.10	1.70 (1.21, 2.58)	<.001	1.65 (1.17, 2.56)	<.001
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.04 (-0.10, 0.01)	.06	-0.04 (-0.12, 0.01)	.06	1.70 (1.22, 2.59)	<.001	1.65 (1.17, 2.56)	<.001
Precuneus R	0.77 (0.37, 1.08)	<.001	-0.01 (-0.08, 0.05)	.43	0.00 (-0.06, 0.04)	.43	1.67 (1.18, 2.55)	<.001	1.65 (1.17, 2.55)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-0.27 (-3.88, 2.81)	.41	0.00 (-0.02, 0.01)	.40	1.52 (1.00, 2.46)	<.001	1.51 (0.98, 2.47)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-2.20 (-5.27, 0.28)	.04	0.02 (-0.01, 0.06)	.06	1.49 (0.97, 2.44)	<.001	1.52 (0.99, 2.45)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S33: CBCL Internalizing Psychopathology At One-Year Follow-Up

	PAE → Brain (A)		Brain → Internalizing Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Internalizing Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	0.00 (0.00, 0.00)	.32	0.01 (-0.05, 0.06)	.32	1.07 (0.60, 1.93)	<.001	1.07 (0.60, 1.94)	<.001
Inferior temporal L	2.88 (1.46, 3.97)	<.001	0.00 (-0.02, 0.01)	.29	-0.01 (-0.07, 0.03)	.29	1.10 (0.63, 1.95)	<.001	1.07 (0.60, 1.95)	<.001
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.02, 0.02)	.35	0.01 (-0.04, 0.04)	.35	1.08 (0.61, 1.93)	<.001	1.07 (0.61, 1.94)	<.001
Middle temporal R	2.48 (1.19, 3.47)	<.001	0.01 (-0.02, 0.02)	.31	0.01 (-0.04, 0.06)	.31	1.07 (0.60, 1.92)	<.001	1.07 (0.60, 1.94)	<.001
Lateral occipital L	1.78 (0.48, 2.79)	.02	0.01 (-0.02, 0.02)	.31	0.01 (-0.03, 0.04)	.33	1.08 (0.61, 1.93)	<.001	1.08 (0.61, 1.94)	<.001
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.03, 0.00)	.03	-0.02 (-0.05, 0.01)	.08	1.10 (0.64, 1.95)	<.001	1.08 (0.60, 1.94)	<.001
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.00 (-0.02, 0.02)	.44	0.00 (-0.03, 0.03)	.47	1.08 (0.62, 1.93)	<.001	1.08 (0.61, 1.94)	<.001
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	0.02 (-0.06, 0.07)	.34	0.02 (-0.05, 0.07)	.34	1.07 (0.60, 1.92)	<.001	1.07 (0.61, 1.95)	<.001
Lateral occipital L	1.15 (0.70, 1.51)	<.001	0.02 (-0.04, 0.07)	.24	0.02 (-0.05, 0.08)	.24	1.06 (0.59, 1.92)	<.001	1.07 (0.61, 1.95)	<.001
Precuneus R	0.77 (0.37, 1.08)	<.001	0.02 (-0.05, 0.07)	.34	0.01 (-0.05, 0.06)	.34	1.07 (0.60, 1.93)	<.001	1.07 (0.60, 1.94)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-0.08 (-3.59, 2.92)	.46	0.00 (-0.02, 0.02)	.43	1.03 (0.52, 1.95)	<.001	1.02 (0.51, 1.95)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-2.61 (-5.59, -0.20)	.02	0.02 (0.00, 0.07)	.04	1.00 (0.49, 1.92)	<.001	1.04 (0.52, 1.94)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S34: CBCL Externalizing Psychopathology At One-Year Follow-Up

	PAE → Brain (A)		Brain → Externalizing Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Externalizing Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	-0.001 (-0.002, -0.001)	<.001	-0.07 (-0.14, -0.02)	<.001	1.31 (0.88, 2.11)	<.001	1.24 (0.80, 2.05)	<.001
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.03 (-0.04, -0.01)	<.001	-0.07 (-0.13, -0.02)	<.001	1.32 (0.89, 2.11)	<.001	1.24 (0.79, 2.05)	<.001
Middle temporal L	1.92 (0.67, 2.88)	<.001	-0.01 (-0.03, 0.01)	.09	-0.02 (-0.06, 0.01)	.09	1.27 (0.84, 2.06)	<.001	1.24 (0.80, 2.04)	<.001
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.02 (-0.04, -0.01)	<.001	-0.05 (-0.11, -0.01)	<.001	1.30 (0.87, 2.09)	<.001	1.24 (0.79, 2.05)	<.001
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.02 (-0.04, 0.00)	.01	-0.03 (-0.08, 0.00)	.03	1.28 (0.85, 2.07)	<.001	1.24 (0.80, 2.04)	<.001
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.02 (-0.03, -0.01)	<.001	-0.02 (-0.07, 0.00)	.05	1.28 (0.85, 2.06)	<.001	1.24 (0.80, 2.04)	<.001
Supramarginal R	1.34 (-0.08, 2.44)	.05	-0.01 (-0.03, 0.00)	.02	-0.02 (-0.05, 0.00)	.07	1.27 (0.84, 2.05)	<.001	1.25 (0.80, 2.04)	<.001
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.10 (-0.17, -0.05)	<.001	-0.08 (-0.15, -0.03)	<.001	1.33 (0.90, 2.12)	<.001	1.24 (0.80, 2.05)	<.001
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.06 (-0.11, -0.02)	<.001	-0.06 (-0.13, -0.02)	<.001	1.31 (0.88, 2.10)	<.001	1.23 (0.80, 2.05)	<.001
Precuneus R	0.77 (0.37, 1.08)	<.001	-0.02 (-0.09, 0.02)	.16	-0.02 (-0.07, 0.02)	.16	1.27 (0.84, 2.06)	<.001	1.24 (0.80, 2.05)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-1.39 (-4.62, 1.36)	.13	0.00 (-0.03, 0.01)	.24	1.19 (0.72, 2.03)	<.001	1.18 (0.70, 2.03)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.88 (-3.62, 1.33)	.22	0.01 (-0.01, 0.04)	.22	1.17 (0.71, 2.02)	<.001	1.19 (0.72, 2.02)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S35: CBCL Somatic Complaints At One-Year Follow-Up

	PAE → Brain (A)		Brain → Somatic Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Somatic Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	0.00 (0.00, 0.00)	.37	0.01 (-0.03, 0.03)	.37	0.39 (0.12, 0.87)	.01	0.39 (0.12, 0.88)	<.001
Inferior temporal L	2.88 (1.46, 3.97)	<.001	0.00 (-0.01, 0.01)	.31	-0.01 (-0.04, 0.02)	.31	0.40 (0.14, 0.88)	.01	0.39 (0.12, 0.88)	.01
Middle temporal L	1.92 (0.67, 2.88)	<.001	-0.01 (-0.02, 0.00)	.14	-0.01 (-0.04, 0.01)	.14	0.41 (0.14, 0.89)	<.001	0.39 (0.12, 0.88)	.01
Middle temporal R	2.48 (1.19, 3.47)	<.001	0.00 (-0.02, 0.01)	.18	-0.01 (-0.04, 0.01)	.18	0.41 (0.14, 0.89)	<.001	0.39 (0.12, 0.88)	.01
Lateral occipital L	1.78 (0.48, 2.79)	.02	0.00 (-0.01, 0.01)	.46	0.00 (-0.02, 0.02)	.46	0.40 (0.13, 0.88)	.01	0.39 (0.13, 0.88)	<.001
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, 0.00)	.05	-0.01 (-0.03, 0.00)	.10	0.41 (0.14, 0.88)	<.001	0.39 (0.13, 0.88)	.01
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.00 (-0.02, 0.00)	.15	-0.01 (-0.02, 0.01)	.20	0.40 (0.14, 0.88)	<.001	0.39 (0.13, 0.88)	.01
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	0.01 (-0.03, 0.04)	.35	0.01 (-0.03, 0.04)	.35	0.39 (0.13, 0.87)	.01	0.39 (0.13, 0.88)	<.001
Lateral occipital L	1.15 (0.70, 1.51)	<.001	0.01 (-0.03, 0.03)	.32	0.01 (-0.03, 0.04)	.32	0.38 (0.12, 0.87)	.01	0.39 (0.13, 0.88)	<.001
Precuneus R	0.77 (0.37, 1.08)	<.001	-0.02 (-0.05, 0.01)	.15	-0.01 (-0.04, 0.01)	.15	0.41 (0.14, 0.89)	<.001	0.39 (0.12, 0.88)	.01
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	0.40 (-1.58, 2.08)	.34	0.00 (-0.01, 0.01)	.47	0.40 (0.12, 0.92)	.01	0.40 (0.11, 0.92)	.01
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.48 (-2.16, 0.87)	.24	0.01 (-0.01, 0.03)	.24	0.40 (0.11, 0.91)	.01	0.40 (0.12, 0.91)	.01

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S36: CBCL Attention Problems At One-Year Follow-Up

	PAE → Brain (A)		Brain → Attention Deficits (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Attention Deficits (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	0.00 (0.00, 0.00)	.05	-0.02 (-0.06, 0.00)	.05	0.33 (0.08, 0.79)	.01	0.30 (0.05, 0.77)	.01
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.01 (-0.02, 0.00)	.09	-0.01 (-0.05, 0.01)	.09	0.33 (0.08, 0.78)	.01	0.30 (0.05, 0.77)	.01
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.02, 0.01)	.19	-0.01 (-0.03, 0.01)	.19	0.32 (0.07, 0.77)	.01	0.31 (0.05, 0.77)	.01
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.01 (-0.02, 0.00)	.05	-0.02 (-0.05, 0.00)	.05	0.33 (0.08, 0.78)	.01	0.30 (0.05, 0.77)	.01
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.01 (-0.02, -0.001)	.01	-0.01 (-0.04, 0.00)	.03	0.33 (0.08, 0.78)	.01	0.31 (0.05, 0.77)	.01
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, 0.00)	.01	-0.01 (-0.04, 0.00)	.06	0.32 (0.08, 0.78)	.01	0.31 (0.05, 0.77)	.01
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.00 (-0.02, 0.00)	.13	-0.01 (-0.02, 0.00)	.18	0.32 (0.07, 0.77)	.01	0.31 (0.06, 0.77)	.01
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.02 (-0.06, 0.01)	.11	-0.01 (-0.05, 0.01)	.11	0.33 (0.08, 0.78)	.01	0.30 (0.05, 0.77)	.01
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.03 (-0.06, -0.01)	.01	-0.03 (-0.07, -0.01)	.01	0.34 (0.09, 0.80)	.01	0.30 (0.05, 0.77)	.01
Precuneus R	0.77 (0.37, 1.08)	<.001	-0.01 (-0.05, 0.01)	.18	-0.01 (-0.04, 0.01)	.18	0.32 (0.07, 0.77)	.01	0.30 (0.05, 0.77)	.01
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-0.62 (-2.42, 0.91)	.21	0.00 (-0.01, 0.01)	.30	0.20 (-0.06, 0.67)	.07	0.19 (-0.08, 0.67)	.09
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.74 (-2.27, 0.49)	.11	0.01 (-0.01, 0.03)	.13	0.19 (-0.07, 0.66)	.10	0.20 (-0.07, 0.66)	.10

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S37: CBCL Anxious and Depressive Symptoms At One-Year Follow-Up

	PAE → Brain (A)		Brain → Anxiety Depression Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Anxiety Depression Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	-0.01 (-0.05, 0.03)	.29	-0.01 (-0.04, 0.02)	.29	0.26 (-0.02, 0.78)	.04	0.25 (-0.04, 0.77)	.04
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.01 (-0.02, 0.00)	.12	-0.01 (-0.04, 0.01)	.12	0.27 (-0.01, 0.78)	.04	0.25 (-0.04, 0.77)	.04
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.01, 0.01)	.33	0.00 (-0.02, 0.03)	.35	0.25 (-0.03, 0.76)	.04	0.26 (-0.03, 0.77)	.04
Middle temporal R	2.48 (1.19, 3.47)	<.001	0.00 (-0.01, 0.01)	.42	0.00 (-0.03, 0.02)	.42	0.26 (-0.02, 0.77)	.04	0.25 (-0.04, 0.77)	.04
Lateral occipital L	1.78 (0.48, 2.79)	.02	0.00 (-0.01, 0.01)	.42	0.00 (-0.02, 0.01)	.43	0.26 (-0.02, 0.77)	.04	0.26 (-0.03, 0.77)	.04
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, 0.00)	.04	-0.01 (-0.03, 0.00)	.09	0.27 (-0.01, 0.78)	.04	0.25 (-0.04, 0.77)	.04
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.00 (-0.01, 0.01)	.26	0.00 (-0.01, 0.02)	.29	0.25 (-0.03, 0.76)	.04	0.26 (-0.03, 0.77)	.04
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.01 (-0.05, 0.02)	.28	-0.01 (-0.04, 0.02)	.28	0.26 (-0.02, 0.78)	.04	0.25 (-0.03, 0.77)	.04
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.01 (-0.04, 0.02)	.29	-0.01 (-0.04, 0.02)	.29	0.26 (-0.02, 0.78)	.04	0.25 (-0.03, 0.77)	.04
Precuneus R	0.77 (0.37, 1.08)	<.001	0.02 (-0.02, 0.05)	.10	0.01 (-0.01, 0.04)	.10	0.24 (-0.04, 0.75)	.04	0.25 (-0.03, 0.77)	.04
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	0.29 (-1.65, 1.94)	.37	0.00 (-0.01, 0.01)	.48	0.26 (-0.02, 0.76)	.04	0.26 (-0.03, 0.77)	.04
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-1.24 (-2.88, 0.09)	.03	0.01 (0.00, 0.04)	.05	0.24 (-0.04, 0.75)	.04	0.26 (-0.02, 0.76)	.04

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S38: CBCL Withdrawn/Depressed At One-Year Follow-Up

	PAE → Brain (A)		Brain → Withdrawal Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Withdrawal Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	0.00 (0.00, 0.00)	.48	0.00 (-0.04, 0.03)	.48	0.25 (-0.04, 0.78)	.04	0.25 (-0.05, 0.78)	.05
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.01 (-0.02, 0.00)	.11	-0.01 (-0.04, 0.01)	.11	0.26 (-0.03, 0.79)	.04	0.25 (-0.05, 0.78)	.05
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.01, 0.01)	.45	0.00 (-0.02, 0.02)	.45	0.25 (-0.04, 0.78)	.04	0.25 (-0.05, 0.78)	.05
Middle temporal R	2.48 (1.19, 3.47)	<.001	0.00 (-0.01, 0.01)	.41	0.00 (-0.03, 0.03)	.41	0.25 (-0.04, 0.78)	.04	0.25 (-0.05, 0.78)	.05
Lateral occipital L	1.78 (0.48, 2.79)	.02	0.00 (-0.01, 0.01)	.44	0.00 (-0.02, 0.01)	.45	0.25 (-0.04, 0.78)	.04	0.25 (-0.04, 0.78)	.04
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, 0.00)	.02	-0.01 (-0.04, 0.00)	.07	0.26 (-0.03, 0.79)	.04	0.25 (-0.05, 0.78)	.05
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.01 (-0.01, 0.02)	.12	0.00 (-0.01, 0.03)	.15	0.24 (-0.05, 0.77)	.05	0.25 (-0.04, 0.78)	.04
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.01 (-0.05, 0.03)	.35	-0.01 (-0.04, 0.02)	.35	0.26 (-0.04, 0.78)	.04	0.24 (-0.05, 0.78)	.05
Lateral occipital L	1.15 (0.70, 1.51)	<.001	0.01 (-0.03, 0.04)	.30	0.01 (-0.03, 0.04)	.30	0.24 (-0.05, 0.77)	.05	0.25 (-0.05, 0.78)	.05
Precuneus R	0.77 (0.37, 1.08)	<.001	0.01 (-0.03, 0.04)	.35	0.01 (-0.02, 0.03)	.35	0.24 (-0.04, 0.77)	.04	0.25 (-0.05, 0.78)	.05
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	0.11 (-1.89, 1.80)	.47	0.00 (-0.01, 0.01)	.46	0.25 (-0.04, 0.78)	.04	0.25 (-0.04, 0.78)	.04
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.03 (-1.73, 1.34)	.48	0.00 (-0.02, 0.02)	.48	0.25 (-0.04, 0.78)	.04	0.26 (-0.03, 0.77)	.04

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S39: CBCL Thought At One-Year Follow-Up

	PAE → Brain (A)		Brain → Thought Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Thought Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	0.00 (0.00, 0.00)	.08	-0.02 (-0.06, 0.01)	.08	0.58 (0.30, 0.18)	<.001	0.55 (0.27, 1.06)	<.001
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.01 (-0.02, 0.00)	.09	-0.02 (-0.04, 0.01)	.09	0.57 (0.30, 1.07)	<.001	0.56 (0.27, 1.06)	<.001
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.02, 0.01)	.24	-0.01 (-0.03, 0.01)	.24	0.56 (0.29, 1.06)	<.001	0.56 (0.28, 1.06)	<.001
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.00 (-0.02, 0.01)	.32	0.00 (-0.03, 0.02)	.32	0.56 (0.29, 1.06)	<.001	0.56 (0.28, 1.06)	<.001
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.01 (-0.02, 0.00)	.06	-0.01 (-0.03, 0.00)	.13	0.57 (0.30, 1.06)	<.001	0.56 (0.28, 1.06)	<.001
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, 0.00)	.06	-0.01 (-0.03, 0.00)	.11	0.57 (0.30, 1.06)	<.001	0.56 (0.28, 1.06)	<.001
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.00 (-0.01, 0.01)	.25	0.00 (-0.01, 0.02)	.28	0.55 (0.28, 1.05)	<.001	0.56 (0.28, 1.06)	<.001
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.03 (-0.07, 0.01)	.06	-0.02 (-0.06, 0.01)	.06	0.58 (0.30, 1.08)	<.001	0.55 (0.28, 1.06)	<.001
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.03 (-0.06, 0.00)	.01	-0.03 (-0.06, 0.00)	.01	0.58 (0.30, 1.08)	<.001	0.55 (0.27, 1.06)	<.001
Precuneus R	0.77 (0.37, 1.08)	<.001	0.00 (-0.04, 0.03)	.48	0.00 (-0.03, 0.02)	.48	0.56 (0.29, 1.06)	<.001	0.56 (0.28, 1.06)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-0.88 (-2.77, 0.72)	.12	0.00 (-0.02, 0.01)	.23	0.56 (0.29, 1.06)	<.001	0.56 (0.28, 1.06)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.52 (-2.13, 0.77)	.22	0.01 (-0.01, 0.02)	.22	0.55 (0.28, 1.05)	<.001	0.56 (0.29, 1.05)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S40: CBCL Rule Breaking At One-Year Follow-Up

	PAE → Brain (A)		Brain → Rule Breaking Symptoms (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → Rule Breaking Symptoms (C)		Total Effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	-0.001 (-0.001, -0.001)	<.001	-0.04 (-0.08, -0.02)	<.001	0.46 (0.25, 0.82)	<.001	0.41 (0.20, 0.79)	<.001
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.02 (-0.02, -0.01)	<.001	-0.04 (-0.07, -0.01)	<.001	0.45 (0.25, 0.82)	<.001	0.41 (0.20, 0.79)	<.001
Middle temporal L	1.92 (0.67, 2.88)	<.001	-0.01 (-0.02, 0.00)	.01	-0.01 (-0.04, 0.00)	.03	0.43 (0.23, 0.80)	<.001	0.41 (0.20, 0.79)	<.001
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.06, -0.01)	<.001	0.44 (0.24, 0.81)	<.001	0.41 (0.20, 0.79)	<.001
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.02 (-0.03, -0.01)	<.001	-0.02 (-0.05, 0.01)	.07	0.43 (0.23, 0.80)	<.001	0.42 (0.20, 0.78)	<.001
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, 0.00)	.05	0.43 (0.23, 0.80)	<.001	0.41 (0.20, 0.78)	<.001
Supramarginal R	1.34 (-0.08, 2.44)	.05	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, 0.00)	.03	0.43 (0.23, 0.80)	<.001	0.41 (0.20, 0.78)	<.001
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.05 (-0.08, -0.02)	<.001	-0.04 (-0.07, -0.01)	<.001	0.45 (0.25, 0.82)	<.001	0.41 (0.20, 0.79)	<.001
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.04 (-0.06, -0.02)	<.001	-0.04 (-0.07, -0.01)	<.001	0.45 (0.25, 0.82)	<.001	0.41 (0.20, 0.79)	<.001
Precuneus R	0.77 (0.37, 1.08)	<.001	-0.03 (-0.06, -0.01)	.01	-0.02 (-0.04, 0.00)	.01	0.43 (0.23, 0.80)	<.001	0.41 (0.20, 0.79)	<.001
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-0.85 (-2.23, 0.34)	.08	0.00 (-0.01, 0.00)	.21	0.42 (0.22, 0.78)	<.001	0.41 (0.21, 0.78)	<.001
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	0.07 (-1.11, 1.03)	.47	0.00 (-0.01, 0.01)	.47	0.42 (0.22, 0.78)	<.001	0.42 (0.22, 0.78)	<.001

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S41: CBCL Aggressive Symptoms At One-Year Follow-Up

	PAE → brain (a)		Brain → aggressive symptoms (b)		Overall indirect effect (a*b)		Direct effect: PAE → aggressive symptoms (c)		Total effect	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	-0.001 (-0.001, 0.000)	<.001	-0.03 (-0.07, -0.01)	<.001	0.18 (-0.05, 0.59)	.06	0.14 (-0.10, 0.56)	.14
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.06, -0.01)	<.001	0.17 (-0.06, 0.58)	.07	0.14 (-0.10, 0.56)	.14
Middle temporal L	1.92 (0.67, 2.88)	<.001	-0.01 (-0.02, 0.00)	.01	-0.02 (-0.04, 0.00)	.03	0.16 (-0.07, 0.57)	.10	0.14 (-0.10, 0.56)	.13
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.01 (-0.02, -0.01)	<.001	-0.03 (-0.06, -0.01)	<.001	0.17 (-0.06, 0.58)	.07	0.14 (-0.10, 0.56)	.14
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.04, 0.00)	.07	0.16 (-0.07, 0.57)	.10	0.14 (-0.10, 0.56)	.14
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.01 (-0.02, -0.01)	<.001	-0.02 (-0.05, 0.00)	.05	0.16 (-0.06, 0.57)	.10	0.14 (-0.10, 0.56)	.14
Supramarginal R	1.34 (-0.08, 2.44)	.05	-0.01 (-0.02, 0.00)	.04	-0.01 (-0.03, 0.00)	.07	0.15 (-0.07, 0.56)	.13	0.14 (-0.10, 0.56)	.14
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.05 (-0.08, -0.02)	<.001	-0.03 (-0.07, -0.01)	<.001	0.18 (-0.05, 0.59)	.06	0.14 (-0.09, 0.56)	.14
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.03 (-0.06, -0.01)	<.001	-0.03 (-0.06, -0.01)	<.001	0.17 (-0.06, 0.58)	.06	0.14 (-0.10, 0.56)	.14
Precuneus R	0.77 (0.37, 1.08)	<.001	-0.01 (-0.04, 0.01)	.20	-0.01 (-0.03, 0.01)	.009	0.15 (-0.05, 0.59)	.06	0.14 (-0.10, 0.56)	.14
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-1.39 (-2.95, -0.07)	.02	0.00 (-0.02, 0.01)	.19	0.15 (-0.08, 0.56)	.13	0.14 (-0.09, 0.56)	.14
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.47 (-1.80, 0.60)	.17	0.00 (-0.01, 0.02)	.17	0.14 (-0.09, 0.55)	.16	0.15 (-0.08, 0.55)	.14

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

Association of Prenatal Alcohol Exposure and Associated Outcomes

Table S42: KSADS Oppositional Defiant Disorder At One-Year Follow-Up

	PAE → Brain (A)		Brain → ODD (B)		Overall Indirect Effect (A*B)		Direct Effect: PAE → ODD (C)		Total Effect	
	B (SE)	p	B (SE)	p	B (SE)	p	B (SE)	p	B (SE)	p
Brain Structure										
<i>Volume</i>										
Cerebrum	50.27 (28.25, 67.27)	<.001	-0.0002 (-0.0004, -0.00002)	.03	-0.01 (-0.02, 0.00)	.02	0.11 (0.00, 0.20)	.03	0.10 (-0.01, 0.19)	.05
Inferior temporal L	2.88 (1.46, 3.97)	<.001	-0.004 (-0.008, -0.001)	<.001	-0.01 (-0.02, 0.00)	<.001	0.11 (0.00, 0.20)	.03	0.10 (-0.01, 0.19)	.05
Middle temporal L	1.92 (0.67, 2.88)	<.001	0.00 (-0.01, 0.00)	.09	0.00 (-0.01, 0.00)	.10	0.11 (-0.01, 0.20)	.04	0.10 (-0.01, 0.19)	.05
Middle temporal R	2.48 (1.19, 3.47)	<.001	-0.003 (-0.006, 0.000)	.01	-0.01 (-0.02, 0.00)	.01	0.11 (-0.01, 0.20)	.05	0.10 (-0.01, 0.19)	.06
Lateral occipital L	1.78 (0.48, 2.79)	.02	-0.003 (-0.007, 0.000)	.01	0.00 (-0.01, 0.00)	.10	0.11 (-0.01, 0.20)	.04	0.10 (-0.01, 0.19)	.05
Inferior parietal L	1.51 (-0.10, 2.75)	.05	-0.004 (-0.007, -0.002)	<.001	-0.01 (-0.01, 0.00)	.07	0.11 (-0.01, 0.20)	.03	0.10 (-0.01, 0.19)	.04
Supramarginal R	1.34 (-0.08, 2.44)	.05	0.00 (0.00, 0.00)	.22	0.00 (-0.01, 0.00)	.26	0.10 (-0.01, 0.19)	.05	0.10 (-0.01, 0.19)	.05
<i>Surface area</i>										
Inferior temporal L	0.86 (0.50, 1.14)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.02 (-0.03, -0.01)	<.001	0.12 (0.00, 0.21)	.01	0.10 (-0.01, 0.19)	.05
Lateral occipital L	1.15 (0.70, 1.51)	<.001	-0.02 (-0.03, -0.01)	<.001	-0.02 (-0.03, -0.01)	<.001	0.12 (0.00, 0.21)	.01	0.10 (-0.01, 0.19)	.05
Precuneus R	0.77 (0.37, 1.08)	<.001	0.00 (-0.02, 0.01)	.17	0.00 (-0.01, 0.00)	.17	0.11 (-0.01, 0.20)	.04	0.10 (-0.01, 0.19)	.05
Functional connectivity										
Sensorimotor hand – salience	0.01 (0.00, 0.01)	.19	-0.04 (-0.64, 0.42)	.46	0.00 (0.00, 0.00)	.48	0.10 (-0.01, 0.19)	.05	0.10 (-0.01, 0.19)	.05
Auditory – right ventral diencephalon	-0.01 (-0.02, 0.00)	.02	-0.19 (-0.60, 0.18)	.19	0.00 (0.00, 0.01)	.19	0.10 (-0.01, 0.19)	.05	0.10 (-0.01, 1.19)	.04

All multilevel mediation models controlled for fixed (age, sex, race/ethnicity, birthweight, premature birth, maternal age at birth, highest parent education, maternal depression, other prenatal substance use, school grade) and random (family, scanner/site) effects.

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