

Supplemental Digital Content 7: Primary analysis for all scores, including study-specific composites.

Test	N	P*	Single exposure, estimate (95% CI) of difference from unexposed	P**	Multiple exposures, estimate (95% CI) of difference from unexposed	P**	Unexposed, estimate (95%) CI of mean†
Psychometrist-administered							
WASI: Full Scale IQ Score	993	0.599	-0.46 (-2.78, 1.87)	0.701	-1.27 (-3.75, 1.21)	0.315	106.0 (104.2, 107.8)
WASI: Matrix Reasoning subtest (TS)	993	0.136	-0.96 (-2.38, 0.46)	0.184	-1.59 (-3.17, 0.00)	0.049	53.4 (52.3, 54.5)
WASI: Vocabulary subtest (TS)	992	0.856	0.47 (-1.27, 2.20)	0.598	0.08 (-1.72, 1.87)	0.933	53.5 (52.3, 54.7)
WASI: Matrix – Vocabulary subtests (TS)	992	0.111	-1.43 (-3.11, 0.25)	0.095	-1.67 (-3.45, 0.11)	0.066	-0.11 (-1.23, 1.01)
WASI: Proportion with Full Scale Score <85	993	0.399	-0.36 (-1.42, 0.69)	0.498	0.26 (-0.76, 1.28)	0.615	4.3% (1.9%, 9.2%)
WRAML-2: Attention/Concentration Index (StdS)	926	0.404	0.59 (-2.34, 3.53)	0.692	-1.58 (-4.57, 1.40)	0.299	104.0 (102.1, 105.8)
CPT-II: # Commissions (TS)	981	0.742	-0.17 (-2.49, 2.15)	0.886	0.63 (-1.36, 2.61)	0.538	50.6 (49.1, 52.0)
CPT-II: # Omissions (TS)	981	0.196	-1.77 (-4.55, 1.00)	0.211	0.64 (-2.50, 3.78)	0.690	53.5 (51.3, 55.7)
CPT-II: Hit Reaction Time (TS)	981	0.504	0.20 (-1.89, 2.29)	0.853	1.09 (-0.84, 3.03)	0.268	51.6 (50.2, 53.0)
CPT-II: Hit Reaction Time Std Error (TS)	981	0.472	-0.29 (-2.23, 1.65)	0.768	0.85 (-1.20, 2.89)	0.417	50.1 (48.6, 51.7)
CPT-II: Variability (TS)	981	0.619	-0.51 (-2.46, 1.44)	0.610	0.48 (-1.47, 2.43)	0.627	50.3 (48.9, 51.7)
CPT-II: Detectability (TS)	981	0.077	-0.80 (-3.03, 1.43)	0.482	1.48 (-0.29, 3.26)	0.102	51.4 (50.1, 52.7)
WRAML-2: Verbal Memory Index (StdS)	993	0.269	1.27 (-1.08, 3.63)	0.289	-0.82 (-3.23, 1.60)	0.507	105.7 (104.1, 107.2)
WRAML-2: Story Memory Delay Recall subtest (SS)***	995	0.018	0.33 (-0.10, 0.76)	0.133	-0.35 (-0.79, 0.08)	0.115	11.4 (11.1, 11.7)
WRAML-2: Verbal Learning Delay Recall subtest (SS)	994	0.759	0.12 (-0.41, 0.65)	0.648	0.19 (-0.33, 0.71)	0.469	10.4 (10.1, 10.8)
WRAML-2: Delayed Verbal Recall composite (StdS)††	994	0.340	1.13 (-0.84, 3.11)	0.261	-0.40 (-2.40, 1.60)	0.697	104.5 (103.2, 105.8)
WRAML-2: Story Memory Recognition subtest (SS)	995	0.081	0.12 (-0.32, 0.55)	0.591	-0.40 (-0.87, 0.07)	0.092	11.7 (11.4, 12.0)
WRAML-2: Verbal Learning Recognition subtest (SS)	993	0.897	0.11 (-0.34, 0.56)	0.645	0.06 (-0.39, 0.51)	0.797	10.6 (10.3, 10.9)
WRAML-2: Verbal Recognition Composite (StdS)	992	0.343	0.78 (-1.46, 3.02)	0.495	-1.02 (-3.27, 1.24)	0.378	106.5 (105.0, 107.9)

Test	N	P*	Single exposure, estimate (95% CI) of difference from unexposed	P**	Multiple exposures, estimate (95% CI) of difference from unexposed	P**	Unexposed, estimate (95%) CI of mean†
WRAML-2: Design Memory subtest (SS)‡‡	995	0.037	0.11 (-0.37, 0.60)	0.648	-0.54 (-1.03, -0.05)	0.030	8.9 (8.6, 9.2)
WRAML-2: Design Recognition subtest (SS)	995	0.828	0.17 (-0.38, 0.71)	0.550	0.12 (-0.44, 0.68)	0.678	9.9 (9.5, 10.2)
D-KEFS Trail Making Test: Condition 1 (SS)	996	0.009	-0.13 (-0.69, 0.43)	0.653	-0.79 (-1.32, -0.27)	0.003	10.9 (10.5, 11.2)
D-KEFS Trail Making Test: Condition 2 (SS)	996	0.004	0.02 (-0.39, 0.43)	0.935	-0.76 (-1.25, -0.27)	0.002	11.5 (11.2, 11.8)
D-KEFS Trail Making Test: Condition 3 (SS)	995	0.005	0.26 (-0.27, 0.79)	0.335	-0.73 (-1.33, -0.13)	0.017	11.1 (10.7, 11.5)
D-KEFS Trail Making Test: Condition 4 (SS)	994	0.194	0.22 (-0.37, 0.80)	0.469	-0.33 (-0.99, 0.33)	0.323	10.0 (9.5, 10.5)
D-KEFS Trail Making Test: Condition 5 (SS)	996	0.022	-0.34 (-0.69, 0.01)	0.056	-0.45 (-0.80, -0.11)	0.011	11.7 (11.5, 11.9)
D-KEFS Tower Test: Total Achievement Score(SS)	996	0.350	0.02 (-0.42, 0.46)	0.939	-0.29 (-0.76, 0.17)	0.216	10.1 (9.8, 10.4)
Wisconsin Card Sort: Perseverative Responses (TS)	958	0.104	1.46 (-0.92, 3.85)	0.229	-1.40 (-3.97, 1.17)	0.286	55.4 (53.8, 57.0)
Wisconsin Card Sort: Perseverative Errors (TS)***	958	0.036	1.58 (-0.60, 3.76)	0.156	-1.58 (-3.96, 0.80)	0.193	54.6 (53.1, 56.1)
CTOPP: Rapid Naming Composite Score (StdS)	995	0.047	-2.03 (-4.78, 0.72)	0.147	-3.51 (-6.32, -0.70)	0.014	97.8 (95.9, 99.8)
Boston Naming Test (StdS) ‡	882	0.506	0.45 (-3.06, 3.97)	0.801	-1.56 (-5.13, 2.02)	0.394	100.0 (97.4, 102.5)
D-KEFS Verbal Fluency: Category Fluency (SS)	996	0.205	0.30 (-0.32, 0.92)	0.340	-0.29 (-0.89, 0.31)	0.340	11.5 (11.1, 11.9)
Expressive language composite (StdS)††	882	0.202	1.31 (-1.21, 3.83)	0.309	-1.13 (-3.75, 1.49)	0.398	103.6 (101.9, 105.3)
Beery: Motor Coordination (StdS)	995	0.047	-0.10 (-2.58, 2.39)	0.939	-3.06 (-5.72, -0.39)	0.025	87.4 (85.7, 89.1)
Grooved Pegboard dominant hand (StdS)‡‡‡	988	0.001	-2.25 (-6.18, 1.69)	0.264	-7.76 (-11.94, -3.57)	<.001	99.6 (97.1, 102.2)
Grooved Pegboard other hand (StdS)	988	<.001	-3.70 (-7.81, 0.41)	0.078	-11.52 (-16.46, -6.58)	<.001	99.4 (96.3, 102.6)
Fine motor composite (StdS)††	988	<.001	-1.34 (-3.91, 1.23)	0.306	-5.53 (-8.42, -2.64)	<.001	93.7 (92.0, 95.4)
Beery: Visual-Motor Integration (StdS)	990	0.148	-2.48 (-5.00, 0.04)	0.054	-1.40 (-3.77, 0.97)	0.246	89.4 (87.6, 91.1)
Beery: Visual Perception (StdS)	995	0.472	-0.62 (-2.70, 1.46)	0.561	-1.36 (-3.53, 0.81)	0.221	99.5 (98.0, 101.0)
Judgment of Line Orientation (StdS)‡	529	0.350	-2.71 (-6.53, 1.11)	0.164	-0.36 (-4.26, 3.54)	0.856	96.8 (94.4, 99.3)

Test	N	P*	Single exposure, estimate (95% CI) of difference from unexposed	P**	Multiple exposures, estimate (95% CI) of difference from unexposed	P**	Unexposed, estimate (95%) CI of mean†
Visual-spatial abilities composite (StdS)††,‡	529	0.490	-1.73 (-4.61, 1.15)	0.239	-0.95 (-3.73, 1.84)	0.506	99.4 (97.5, 101.2)
Parent report							
BRIEF: Global Executive Composite (TS)	840	<.001	4.64 (2.36, 6.92)	<.001	3.23 (0.89, 5.57)	0.007	46.3 (44.9, 47.8)
Proportion with score > 60	840	0.062	0.86 (0.14, 1.58)	0.020	0.69 (-0.03, 1.42)	0.061	10.0% (5.7%, 17.1%)
CBCL: Internalizing Problems (TS)	829	0.038	1.16 (-1.25, 3.57)	0.347	2.94 (0.68, 5.20)	0.011	47.5 (46.0, 49.1)
Proportion with score > 60	829	0.175	0.37 (-0.33, 1.07)	0.297	0.63 (-0.04, 1.29)	0.064	11.8% (7.1%, 18.9%)
CBCL: Externalizing Problems (TS)	829	<.001	2.03 (-0.24, 4.30)	0.080	3.91 (1.90, 5.92)	<.001	43.2 (41.9, 44.6)
Proportion with score > 60	829	0.003	1.43 (0.59, 2.27)	<.001	1.11 (0.29, 1.92)	0.008	3.4% (1.8%, 6.4%)
CBCL: Total Problems (TS)	828	0.001	2.10 (-0.68, 4.88)	0.139	4.75 (2.23, 7.27)	<.001	43.8 (41.9, 45.6)
Proportion with score > 60	828	0.113	0.49 (-0.39, 1.36)	0.277	0.86 (0.02, 1.69)	0.045	7.7% (3.8%, 14.9%)
CBCL: ADHD Problems (TS)	828	0.026	1.41 (-0.05, 2.86)	0.058	1.97 (0.51, 3.44)	0.008	52.6 (51.5, 53.7)
Proportion with score > 60	828	0.115	0.54 (-0.29, 1.37)	0.206	0.84 (0.03, 1.65)	0.041	8.1% (4.1%, 15.2%)
CLDQ: Math Scale (ZS)	894	0.210	0.17 (-0.09, 0.43)	0.204	0.23 (-0.04, 0.50)	0.089	0.04 (-0.15, 0.23)
CLDQ: Reading Scale (ZS)	895	<.001	0.24 (0.07, 0.42)	0.005	0.44 (0.24, 0.64)	<.001	-0.29 (-0.39, -0.19)

Also included are analyses planned *a priori* for those variables with an available clinical cut-off score indicating an abnormality (< 85 for the WASI full scale IQ and >60 for the BRIEF and CBCL). These results are reported as log-odds ratio (so that 0 represents no effect and the results match the scale of other outcomes). Exponentiating produces the odds ratio (such that odds ratio = 1 is no effect, because $\exp(0)=1$).

* 2 degrees of freedom test for overall difference, significance indicated in bold for $p < 0.05$

** Pairwise comparisons of single or multiple exposures versus no exposure, significance indicated in bold for $p < 0.025$ (Bonferroni adjustment).

***Note that the significant difference noted for the 2 degrees of freedom test reflects the opposite signs and similar absolute values for single and multiple exposure effect size estimates.

†Estimate for unexposed children (95% CI)

††In addition to scores derived from the test developers, 4 study-specific composite scores were defined *a priori* from individual tests to increase the ability to detect effects when more than one instrument assessed a particular domain. Individual test scores were first converted to standard-scores using available normative data from either the test developers or available scientific literature. The individual standard-scores were then averaged to create an overall composite domain score.

‡Because normative data was not available for the Judgement of Line Orientation for older subjects, standard scores could not be calculated and these older children are excluded from this analysis. In addition, normative data was also not available for the Boston Naming Test for subjects aged 19 or 20, who were excluded from analysis.

‡‡The WRAML-2 Design Memory task requires drawing figures by pencil, thus motor coordination.

‡‡‡8%, 10%, and 15% of the unexposed, singly-exposed, and multiply-exposed children were left handed, respectively (p=0.029, Pearson Chi-squared)

N indicated number of children completing a given test. TS, T score (mean = 50, standard deviation = 10); SS, Scaled score (mean = 10, standard deviation = 3); StdS, Standard score (mean = 100, standard deviation = 15); ZS, Z score (mean = 0, standard deviation = 1). D-KEFS, Delis-Kaplan Executive Function System; WASI, Wechsler Abbreviated Scale of Intelligence; WRAML-2, Wide Range Assessment of Memory and Learning- Second Edition; CPT II, Connor's Continuous Performance Test II; CTOPP, Comprehensive Test of Phonological Processing; ADHD, attention deficit hyperactivity disorder; BRIEF, Behavior Rating Inventory of Executive Function; CLDQ, Colorado Learning Difficulties Questionnaire; CBCL, Child Behavior Checklist.