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Supplemental Material

Prenatal Mancozeb Exposure, Excess Manganese, and Neurodevelopment at One Year of Age in the Infants' Environmental Health (ISA) Study

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Table S8. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations with BSID-III standardized composite scores at 1 year of age for all children and stratified by child sex (all exposures in the same model), **with additional adjustment for prenatal lead concentrations**, ISA study.

Figure S1. Smoothed associations of prenatal mancozeb exposure and excess Mn with child neurodevelopment. Generalized additive models were fit using penalized splines with smoothing parameters estimated by generalized cross-validation [*gam()* function in the R package *mgcv*]. Models were stratified by child sex, and adjusted simultaneously for prenatal log_{10}-transformed and specific-gravity adjusted urinary ETU, log_{10}-transformed hair Mn, blood Mn concentrations, maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit. (A) Prenatal blood manganese; (B) prenatal log_{10}-transformed hair Mn; (C) prenatal log_{10}-transformed and specific-gravity adjusted urinary ETU. *p*-values correspond to smoothed splines (i.e., exposure-outcome associations). *Abbreviations*: edf, estimated degrees of freedom; ETU, ethylenethiourea; Mn, manganese.

Figure S2. Adjusted associations of prenatal mancozeb exposure and excess Mn during pregnancy and by halves of pregnancy with child neurodevelopment. Models were stratified by child sex and adjusted simultaneously for prenatal log_{10}-transformed and specific-gravity adjusted urinary ETU, log_{10}-transformed hair Mn, blood Mn concentrations, maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit. (A) Prenatal log_{10} urinary ETU with cognitive composite scores; (B) prenatal log_{10} urinary ETU with socio-emotional composite scores; (C) prenatal log_{10}-transformed hair Mn with cognitive composite scores; and (D) prenatal log_{10}-transformed hair Mn with socio-emotional composite scores. *Abbreviations*: ETU, ethylenethiourea; Mn, manganese.

Table S1. Distribution of prenatal biomarkers of exposure and child neurodevelopmental outcomes stratified by child sex, ISA study.

Exposures and outcomes	Boys		Girls		*p*-value[a]
	n	**Median (P25-P75) or mean ± SD**	***n***	**Median (P25-P75) or mean ± SD**	
Prenatal biomarkers of exposure					
Urinary ETU_{SG} (μg/L)	178	3.3 (2.4-4.9)	177	3.5 (2.4-4.9)	0.70
Hair Mn (μg/g)	178	1.8 (1.0-4.2)	177	1.7 (0.9-3.7)	0.42
Blood Mn (μg/L)	174	23.6 (19.2-27.7)	175	24.3 (21.2-28.6)	0.15
Neurodevelopmental outcomes[b]					
BSID-III composite scores					
Cognitive	178	98.2 ± 9.4	177	98.3 ± 9.7	0.94
Language	173	88.6 ± 6.8	173	91.7 ± 7.1	<0.01
Motor	166	96.6 ± 8.5	172	98.0 ± 9.2	0.15
Social-emotional	177	88.8 ± 11.6	175	91.7 ± 12.2	0.02
BSID-III z-scores					
Cognitive	178	-0.04 ± 1.02	177	0.04 ± 0.98	0.49
Receptive language	175	-0.19 ± 1.01	174	0.19 ± 0.96	<0.01
Expressive language	173	-0.20 ± 1.04	173	0.20 ± 0.92	<0.01
Fine motor	166	-0.14 ± 1.00	173	0.14 ± 0.99	0.01
Gross motor	177	0.00 ± 1.00	175	0.00 ± 1.00	0.95
Social-emotional	177	-0.08 ± 0.98	175	0.09 ± 1.02	0.12

Abbreviations: *n*, number of children; ETU_{SG}, specific-gravity adjusted ethylenethiourea; Mn, manganese; BSID-III, Bayley Scales of Infant and Toddler Development, Third Edition.

[a]p-values are for Kruskal-Wallis tests or t-tests comparing boys and girls.

[b]Not all 355 infants were administered all four BSID scales. For example, only 346 infants were administered the language scale, whereas only 338 were administered the motor scale.

Table S2. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations with BSID-III composite scores at 1 year of age for all children, stratified by child sex and with **interaction terms between exposures** (all exposures in the same model), ISA study.

Neurodevelopmental	**All children**		**Boys**		**Girls**	
outcomes	***n***	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**
Cognitive						
LogETU_{SG}	349	7.9 (-7.0, 22.7)	174	-1.3 (-21.9, 19.3)	175	15.0 (-10.6, 40.6)
LogMnH	349	0.0 (-5.0, 5.1)	174	-0.9 (-8.4, 6.6)	175	1.2 (-6.0, 8.4)
MnB	349	0.3 (-0.1, 0.6)	174	0.2 (-0.2, 0.6)	175	0.3 (-0.3, 0.9)
LogETU_{SG}*LogMnH	349	-0.6 (-8.9, 7.7)	174	5.8 (-6.1, 17.8)	175	-8.1 (-20.5, 4.3)
p_{INT}		0.89		0.33		0.20
LogETU_{SG}*MnB	349	-0.4 (-1.0, 0.2)	174	-0.1 (-1.0, 0.7)	175	-0.6 (-1.6, 0.5)
p_{INT}		0.21		0.77		0.28
Language						
LogETU_{SG}	340	-0.3 (-12.2, 11.5)	169	-1.0 (-17.4, 15.4)	171	5.7 (-14.4, 25.8)
LogMnH	340	1.5 (-2.5, 5.5)	169	0.2 (-5.7, 6.2)	171	3.1 (-2.5, 8.7)
MnB	340	0.0 (-0.3, 0.3)	169	0.0 (-0.4, 0.3)	171	0.2 (-0.3, 0.7)
LogETU_{SG}*LogMnH	340	-2.7 (-9.2, 3.9)	169	0.9 (-8.6, 10.4)	171	-6.9 (-16.4, 2.6)
p_{INT}		0.43		0.85		0.16
LogETU_{SG}*MnB	340	0.0 (-0.4, 0.5)	169	0.0 (-0.7, 0.6)	171	-0.1 (-0.9, 0.7)
p_{INT}		0.90		0.94		0.72
Motor						
LogETU_{SG}	332	7.2 (-8.2, 22.5)	162	5.9 (-15.4, 27.3)	170	1.5 (-25.7, 28.7)
LogMnH	332	0.1 (-5.2, 5.3)	162	-3.1 (-10.9, 4.7)	170	3.5 (-4.1, 11.1)
MnB	332	0.2 (-0.2, 0.5)	162	0.2 (-0.2, 0.7)	170	0.0 (-0.6, 0.7)
LogETU_{SG}*LogMnH	332	0.8 (-7.8, 9.4)	162	5.8 (-6.7, 18.2)	170	-4.0 (-16.9, 8.9)
p_{INT}		0.86		0.36		0.54
LogETU_{SG}*MnB	332	-0.3 (-0.9, 0.3)	162	-0.3 (-1.2, 0.5)	170	-0.1 (-1.2, 1.0)
p_{INT}		0.29		0.47		0.84
Socio-emotional						
LogETU_{SG}	346	11.3 (-8.3, 30.9)	173	12.0 (-15.5, 39.4)	173	11.9 (-22.0, 45.8)
LogMnH	346	-0.1 (-6.7, 6.6)	173	-2.1 (-12.0, 7.9)	173	1.0 (-8.6, 10.6)
MnB	346	0.4 (0.0, 0.9)	173	0.3 (-0.3, 0.9)	173	0.5 (-0.3, 1.3)
LogETU_{SG}*LogMnH	346	-4.2 (-15.1, 6.8)	173	-4.5 (-20.4, 11.3)	173	-2.4 (-18.8, 14.0)
p_{INT}		0.45		0.57		0.77
LogETU_{SG}*MnB	346	-0.6 (-1.4, 0.2)	173	-0.5 (-1.6, 0.6)	173	-0.8 (-2.1, 0.6)
p_{INT}		0.14		0.40		0.27

Models were adjusted for maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit.

Abbreviations: *n*, number of participants; LogETU_{SG}, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

Table S3. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations with BSID-III standardized composite scores at 1 year of age for all children and stratified by child sex (models simultaneously adjusted for all three biomarkers), **using complete cases only**, ISA study.

Neurodevelopmental outcomes[a]	All children		Boys		Girls		p_{INT}
	n	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**	
Cognitive							
LogETU_{SG}	330	-1.1 (-5.2, 2.9)	167	-1.9 (-7.2, 3.5)	163	-1.4 (-7.8, 5.0)	0.62
LogMnH	330	0.1 (-2.0, 2.3)	167	2.6 (-0.4, 5.7)	163	-2.5 (-5.7, 0.7)	0.02
MnB	330	0.1 (-0.1, 0.2)	167	0.1 (-0.1, 0.3)	163	-0.1 (-0.3, 0.2)	0.20
Language							
LogETU_{SG}	321	-0.5 (-3.7, 2.7)	162	-0.9 (-5.0, 3.2)	159	-0.3 (-5.2, 4.6)	0.93
LogMnH	321	0.1 (-1.6, 1.7)	162	1.0 (-1.3, 3.3)	159	-0.3 (-2.8, 2.1)	0.43
MnB	321	0.0 (-0.1, 0.2)	162	-0.0 (-0.2, 0.1)	159	0.1 (-0.1, 0.3)	0.29
Motor							
LogETU_{SG}	313	-0.0 (-4.1, 4.0)	155	1.3 (-4.2, 6.7)	158	-1.5 (-8.0, 5.0)	0.43
LogMnH	313	0.9 (-1.3, 3.1)	155	0.1 (-3.0, 3.2)	158	2.4 (-0.8, 5.6)	0.65
MnB	313	0.0 (-0.1, 0.1)	155	0.1 (-0.1, 0.3)	158	-0.1 (-0.3, 0.2)	0.39
Socio-emotional							
LogETU_{SG}	329	-4.3 (-9.7, 1.1)	167	-0.3 (-7.4, 6.7)	162	-7.9 (-16.5, 0.7)	0.11
LogMnH	329	-1.9 (-4.8, 0.9)	167	-4.9 (-8.8, -0.9)	162	1.1 (-3.2, 5.5)	0.08
MnB	329	0.1 (-0.1, 0.3)	167	0.1 (-0.2, 0.3)	162	0.1 (-0.2, 0.4)	0.80

Models were adjusted for maternal education, parity, gestational age at birth, and child age, HOME score, location of assessment at 1-year visit, and all three biomarkers of exposure.

Abbreviations: *n*, number of samples; LogETU_{SG}, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

[a]Sample sizes vary between neurodevelopmental domains and with respect to Table 2 because not all infants completed all four BSID-III scales and not all of their mothers contributed urine, hair, and blood samples during pregnancy. For instance, 355 infants completed the administration of the BSID-III cognitive scale, and all of them had a maternal urine sample collected during pregnancy (see Table 2), but only 349 of these infants had maternal hair and blood samples.

Table S4. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations with BSID-III composite scores at 1 year of age for all children and stratified by child sex (exposures in **separate models**), ISA study.

Neurodevelopmental outcomes	All children		Boys		Girls		p_{INT}
	n	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**	
Cognitive							
LogETU_{SG}	355	-1.3 (-5.0, 2.4)	178	-1.5 (-6.5, 3.4)	177	-1.9 (-7.7, 4.0)	0.83
LogMnH	355	-0.2 (-2.2, 1.8)	178	2.2 (-0.5, 4.9)	177	-2.9 (-5.9, 0.1)	0.01
MnB	349	0.1 (-0.1, 0.2)	174	0.1 (-0.1, 0.3)	175	0.0 (-0.2, 0.2)	0.34
Language							
LogETU_{SG}	346	-0.8 (-3.8, 2.2)	173	-0.5 (-4.4, 3.3)	173	-0.6 (-5.2, 4.0)	0.90
LogMnH	346	-0.2 (-1.8, 1.4)	173	0.5 (-1.6, 2.6)	173	-0.7 (-3.0, 1.7)	0.53
MnB	340	0.0 (-0.1, 0.1)	169	0.0 (-0.2, 0.1)	171	0.1 (-0.1, 0.3)	0.27
Motor							
LogETU_{SG}	338	-0.2 (-4.1, 3.7)	166	0.9 (-4.2, 6.1)	172	-2.1 (-8.1, 4.0)	0.37
LogMnH	338	0.5 (-1.6, 2.5)	166	0.1 (-2.7, 3.0)	172	1.3 (-1.8, 4.4)	0.98
MnB	332	0.0 (-0.1, 0.2)	162	0.1 (-0.1, 0.3)	170	0.0 (-0.3, 0.2)	0.57
Socio-emotional							
LogETU_{SG}	352	-4.7 (-9.7, 0.2)	177	-2.3 (-9.0, 4.3)	175	-7.2 (-14.8, 0.5)	0.24
LogMnH	352	-2.8 (-5.4, -0.2)	177	-4.8 (-8.3, -1.2)	175	-0.7 (-4.7, 3.3)	0.22
MnB	346	0.1 (-0.1, 0.3)	173	0.1 (-0.1, 0.4)	173	0.1 (-0.2, 0.4)	0.98

Models were adjusted for maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit.

Abbreviations: *n*, number of participants; LogETU_{SG}, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

Table S5. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations with BSID-III subtest **z-scores** at 1 year of age for all children and stratified by child sex (all exposures in the same model), ISA study.

Neurodevelopmental outcomes	All children		Boys		Girls		p_{INT}
	n	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**	
Cognitive							
LogETU_{SG}	349	-0.07 (-0.46, 0.32)	174	-0.26 (-0.80, 0.28)	175	0.04 (-0.55, 0.64)	0.20
LogMnH	349	-0.08 (-0.29, 0.13)	174	0.22 (-0.08, 0.52)	175	-0.40 (-0.70, -0.09)	0.01
MnB	349	0.01 (-0.01, 0.02)	174	0.01 (-0.01, 0.03)	175	0.00 (-0.02, 0.02)	0.41
Receptive language							
LogETU_{SG}	349	0.06 (-0.32, 0.43)	171	-0.22 (-0.78, 0.34)	172	0.40 (-0.11, 0.91)	0.19
LogMnH	349	0.02 (-0.18, 0.22)	171	0.13 (-0.19, 0.44)	172	-0.08 (-0.34, 0.18)	0.29
MnB	343	0.01 (-0.01, 0.02)	171	0.00 (-0.02, 0.02)	172	0.01 (-0.01, 0.03)	0.23
Expressive language							
LogETU_{SG}	346	-0.09 (-0.44, 0.27)	169	-0.03 (-0.52, 0.46)	171	-0.19 (-0.71, 0.32)	0.73
LogMnH	346	-0.13 (-0.32, 0.06)	169	-0.05 (-0.32, 0.23)	171	-0.19 (-0.45, 0.08)	0.65
MnB	340	0.00 (-0.01, 0.01)	169	0.00 (-0.02, 0.02)	171	0.00 (-0.02, 0.02)	0.90
Fine motor							
LogETU_{SG}	339	-0.03 (-0.35, 0.30)	162	0.10 (-0.37, 0.56)	171	-0.14 (-0.60, 0.33)	0.41
LogMnH	339	0.04 (-0.13, 0.21)	162	-0.08 (-0.34, 0.18)	171	0.19 (-0.05, 0.43)	0.19
MnB	333	0.00 (-0.01, 0.01)	162	0.00 (-0.02, 0.02)	171	-0.01 (-0.03, 0.01)	0.56
Gross motor							
LogETU_{SG}	352	0.03 (-0.29, 0.35)	173	0.10 (-0.36, 0.55)	173	-0.11 (-0.58, 0.36)	0.62
LogMnH	352	-0.01 (-0.19, 0.16)	173	0.11 (-0.14, 0.37)	173	-0.13 (-0.37, 0.11)	0.08
MnB	346	0.00 (-0.01, 0.01)	173	0.01 (-0.01, 0.02)	173	0.00 (-0.02, 0.02)	0.73
Socio-emotional							
LogETU_{SG}	352	-0.15 (-0.48, 0.18)	173	0.02 (-0.43, 0.48)	173	-0.28 (-0.78, 0.22)	0.21
LogMnH	352	-0.15 (-0.32, 0.03)	173	-0.31 (-0.57, -0.06)	173	0.02 (-0.23, 0.28)	0.13
MnB	346	0.01 (-0.01, 0.02)	173	0.01 (-0.01, 0.02)	173	0.00 (-0.02, 0.02)	0.95

Models were adjusted for maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit.

Abbreviations: *n*, number of participants; LogETU_{SG}, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

Table S6. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), MnB (μg/L) concentrations during the **second** half of pregnancy with BSID-III composite scores at 1 year of age stratified by child sex (all exposures in the same model), ISA study.

Neurodevelopmental	**All children**		**Boys**		**Girls**		p_{INT}
outcomes	***n***	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**	
Cognitive							
LogETU_{SG}	280	-1.6 (-5.6, 2.3)	145	-1.1 (-6.4, 4.3)	135	-2.5 (-8.7, 3.7)	0.77
LogMnH	280	0.0 (-2.1, 2.2)	145	2.1 (-0.8, 5.0)	135	-2.3 (-5.7, 1.1)	0.05
MnB	280	0.0 (-0.1, 0.2)	145	0.1 (-0.1, 0.3)	135	-0.1 (-0.3, 0.2)	0.20
Language							
LogETU_{SG}	274	-0.3 (-3.4, 2.8)	140	0.2 (-3.9, 4.2)	134	-0.5 (-5.3, 4.3)	0.60
LogMnH	274	0.9 (-0.7, 2.6)	140	1.2 (-1.0, 3.4)	134	1.3 (-1.3, 4.0)	0.91
MnB	274	0.0 (-0.1, 0.1)	140	-0.1 (-0.2, 0.1)	134	0.1 (-0.1, 0.3)	0.17
Motor							
LogETU_{SG}	266	0.8 (-3.1, 4.7)	133	0.8 (-4.6, 6.3)	133	1.2 (-4.6, 7.1)	0.74
LogMnH	266	-0.1 (-2.3, 2.0)	133	-0.2 (-3.2, 2.8)	133	0.1 (-3.1, 3.3)	0.74
MnB	266	0.1 (-0.1, 0.2)	133	0.1 (-0.1, 0.3)	133	0.1 (-0.2, 0.3)	0.90
Socio-emotional							
LogETU_{SG}	279	-3.7 (-8.8, 1.5)	145	-2.9 (-9.7, 3.9)	134	-2.7 (-10.9, 5.6)	0.87
LogMnH	279	-2.0 (-4.8, 0.8)	145	-3.9 (-7.6, -0.2)	134	-0.3 (-4.8, 4.3)	0.30
MnB	279	0.2 (0.0, 0.4)	145	0.2 (-0.1, 0.5)	134	0.2 (-0.2, 0.5)	0.86

Models were adjusted for maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit.

Abbreviations: *n*, number of participants; LogETU_{SG}, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

Table S7. Adjusted associations of prenatal logETU_{SG} (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations during the **first** half of pregnancy with BSID-III composite scores at 1 year of age for all children and stratified by child sex (all exposures in the same model), ISA study.

Neurodevelopmental	**All children**		**Boys**		**Girls**		p_{INT}
outcomes	***n***	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**	
Cognitive							
LogETU_{SG}	161	-2.2 (-7.2, 2.8)	77	-3.9 (-11.0, 3.2)	84	1.2 (-6.6, 9.0)	0.20
LogMnH	161	-0.3 (-2.9, 2.4)	77	-0.2 (-4.5, 4.1)	84	-0.7 (-4.4, 3.1)	0.82
MnB	161	0.1 (-0.1, 0.3)	77	0.1 (-0.2, 0.4)	84	0.2 (-0.2, 0.5)	0.66
Language							
LogETU_{SG}	158	-1.3 (-5.0, 2.3)	76	-1.6 (-6.8, 3.7)	82	-1.8 (-7.2, 3.6)	0.82
LogMnH	158	0.0 (-2.0, 1.9)	76	0.3 (-2.9, 3.4)	82	0.2 (-2.4, 2.8)	0.67
MnB	158	0.0 (-0.1, 0.2)	76	0.1 (-0.2, 0.3)	82	0.0 (-0.2, 0.3)	0.78
Motor							
LogETU_{SG}	154	-5.4 (-10.6, -0.1)	72	-4.9 (-12.2, 2.4)	82	-5.3 (-13.4, 2.7)	0.81
LogMnH	154	3.6 (0.8, 6.4)	72	1.2 (-3.3, 5.7)	82	5.8 (1.9, 9.6)	0.32
MnB	154	-0.2 (-0.4, 0.1)	72	-0.1 (-0.4, 0.2)	82	-0.3 (-0.7, 0.1)	0.68
Socio-emotional							
LogETU_{SG}	159	-2.8 (-9.9, 4.4)	76	2.8 (-6.5, 12.0)	83	-8.6 (-20.5, 3.3)	0.07
LogMnH	159	-1.2 (-5.1, 2.6)	76	-2.5 (-8.1, 3.1)	83	-0.6 (-6.4, 5.1)	0.75
MnB	159	0.1 (-0.2, 0.4)	76	0.0 (-0.4, 0.4)	83	0.0 (-0.5, 0.6)	0.69

Models were adjusted for maternal education, parity, gestational age at birth, and child age, HOME z-scores, and location of assessment at 1-year visit.

Abbreviations: *n*, number of participants; LogETU_{SG}, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

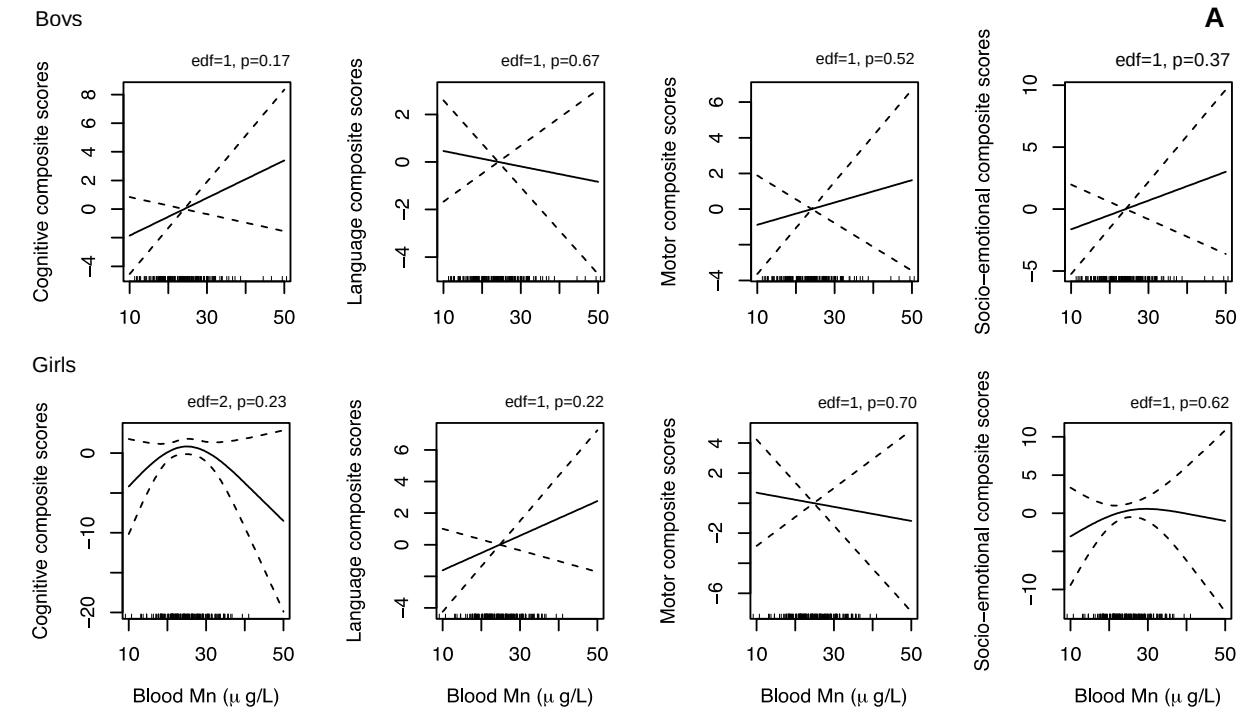
Table S8. Adjusted associations of prenatal $logETU_{SG}$ (μg/L), logMnH (μg/g), and MnB (μg/L) concentrations with BSID-III standardized composite scores at 1 year of age for all children and stratified by child sex (all exposures in the same model), **with additional adjustment for prenatal lead concentrations**, ISA study.

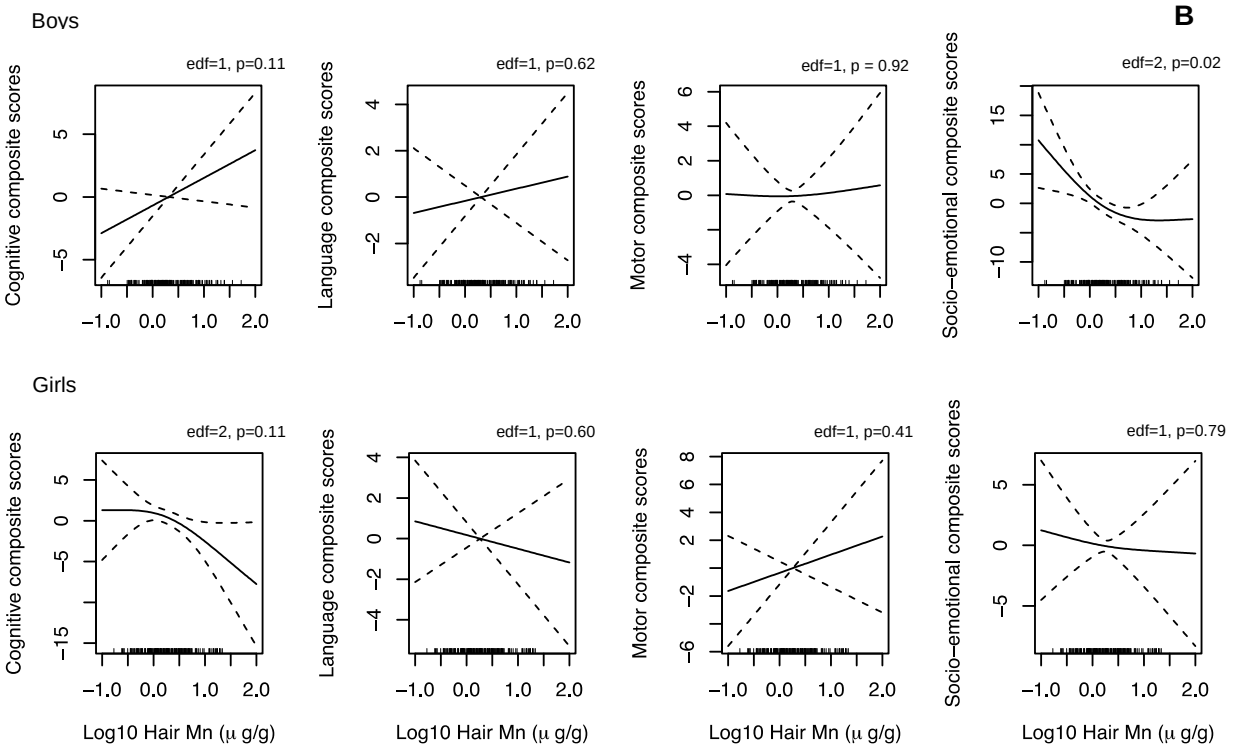
Neurodevelopmental outcomes[a]	All children		Boys		Girls		p_{INT}
	n	**β (95% CI)**	***n***	**β (95% CI)**	***n***	**β (95% CI)**	
Cognitive							
$LogETU_{SG}$	349	-1.1 (-4.9, 2.8)	174	-1.7 (-7.0, 3.6)	175	-1.2 (-7.2, 4.9)	0.60
LogMnH	349	-0.2 (-2.3, 1.8)	174	2.5 (-0.5, 5.4)	175	-3.1 (-6.2, 0.0)	0.01
MnB	349	0.1 (-0.1, 0.2)	174	0.1 (-0.1, 0.3)	175	0.0 (-0.2, 0.2)	0.33
Language							
$LogETU_{SG}$	340	-0.6 (-3.7, 2.5)	169	-1.2 (-5.4, 3.1)	171	0.2 (-4.4, 4.9)	0.79
LogMnH	340	-0.0 (-1.7, 1.6)	169	0.7 (-1.6, 3.1)	171	-0.6 (-3.0, 1.8)	0.47
MnB	340	0.0 (-0.1, 0.1)	169	-0.0 (-0.2, 0.1)	171	0.1 (-0.1, 0.3)	0.27
Motor							
$LogETU_{SG}$	332	-0.2 (-4.2, 3.8)	162	1.9 (-3.6, 7.4)	170	-2.5 (-8.7, 3.8)	0.28
LogMnH	332	0.6 (-1.6, 2.7)	162	0.1 (-3.0, 3.1)	170	1.4 (-1.8, 4.6)	0.92
MnB	332	0.0 (-0.1, 0.2)	162	0.1 (-0.1, 0.3)	170	0.0 (-0.3, 0.2)	0.56
Socio-emotional							
$LogETU_{SG}$	346	-3.9 (-9.1, 1.2)	173	0.0 (-7.1, 7.1)	173	-7.8 (-15.8, 0.1)	0.10
LogMnH	346	-2.3 (-5.0, 0.5)	173	-4.6 (-8.5, -0.7)	173	-0.1 (-4.1, 4.0)	0.17
MnB	346	0.1 (-0.1, 0.3)	173	0.1 (-0.2, 0.4)	173	0.1 (-0.2, 0.4)	0.88

Models were adjusted for maternal education, parity, gestational age at birth, prenatal blood lead concentrations, and child age, HOME score, location of assessment at 1-year visit, and all three biomarkers of exposure.

Abbreviations: *n*, number of samples; $LogETU_{SG}$, log_{10}-transformed and specific-gravity adjusted urinary ethylenethiourea; LogMnH, log_{10}-transformed hair manganese; MnB, blood manganese; BSID-III, Bayley Scales of Infant and Toddler Development, 3rd edition.

[a]Sample sizes vary between neurodevelopmental domains and with respect to Table 2 because not all infants completed all four BSID-III scales and not all of their mothers contributed urine, hair, and blood samples during pregnancy. For instance, 355 infants completed the administration of the BSID-III cognitive scale, and all of them had a maternal urine sample collected during pregnancy (see Table 2), but only 349 of these infants had maternal hair and blood samples.


A
Bovs
Girls
Cognitive composite scores
Language composite scores
Motor composite scores
Socio–emotional composite scores
edf=1, p=0.17
edf=1, p=0.67
edf=1, p=0.52
edf=1, p=0.37
edf=2, p=0.23
edf=1, p=0.22
edf=1, p=0.70
edf=1, p=0.62
Blood Mn (μ g/L)


B
Bovs
Girls
Cognitive composite scores
Language composite scores
Motor composite scores
Socio–emotional composite scores
edf=1, p=0.11
edf=1, p=0.62
edf=1, p = 0.92
edf=2, p=0.02
edf=2, p=0.11
edf=1, p=0.60
edf=1, p=0.41
edf=1, p=0.79
Log10 Hair Mn (μ g/g)

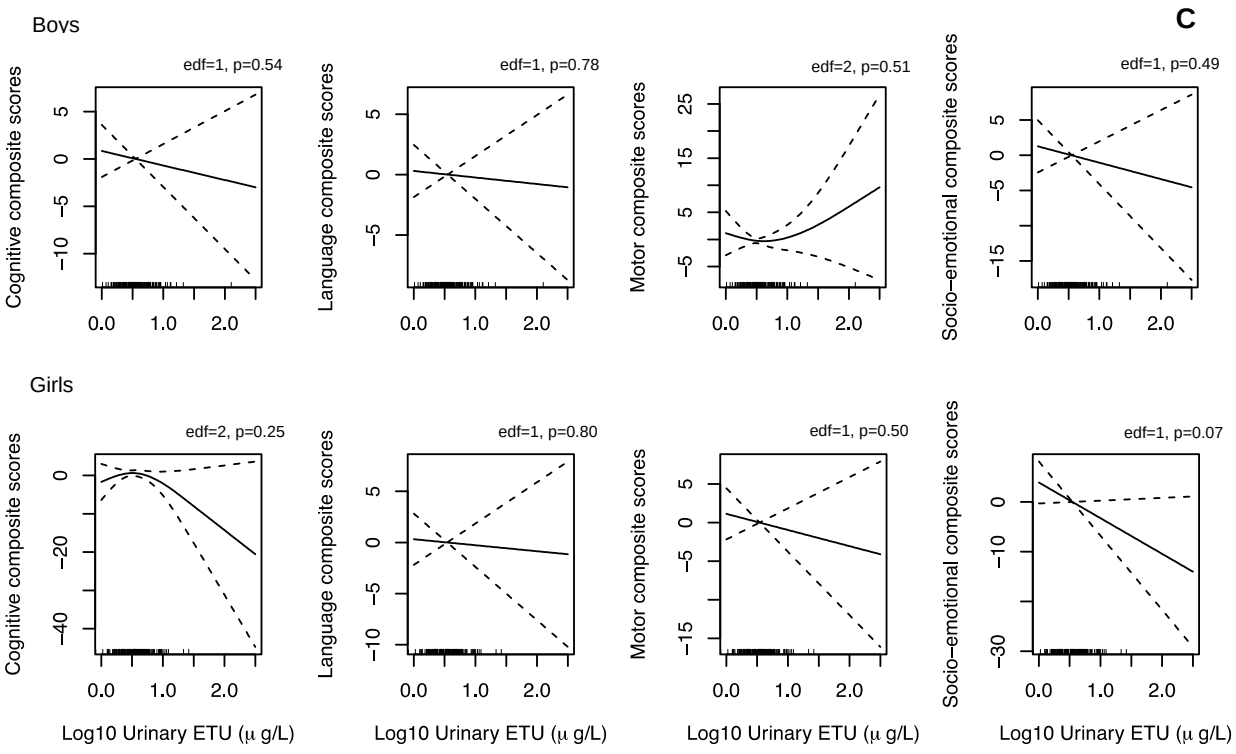


Figure S1. Smoothed associations of prenatal mancozeb exposure and excess Mn with child neurodevelopment. Generalized additive models were fit using penalized splines with smoothing parameters estimated by generalized cross-validation [*gam()* function in the R package *mgcv*]. Models were stratified by child sex, and adjusted simultaneously for prenatal $\log_{10}$-transformed and specific-gravity adjusted urinary ETU, $\log_{10}$-transformed hair Mn, blood Mn concentrations, maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit. (A) Prenatal blood manganese; (B) prenatal $\log_{10}$-transformed hair Mn; (C) prenatal $\log_{10}$-transformed and specific-gravity adjusted urinary ETU. *p*-values correspond to smoothed splines (i.e., exposure-outcome associations). *Abbreviations*: edf, estimated degrees of freedom; ETU, ethylenethiourea; Mn, manganese.

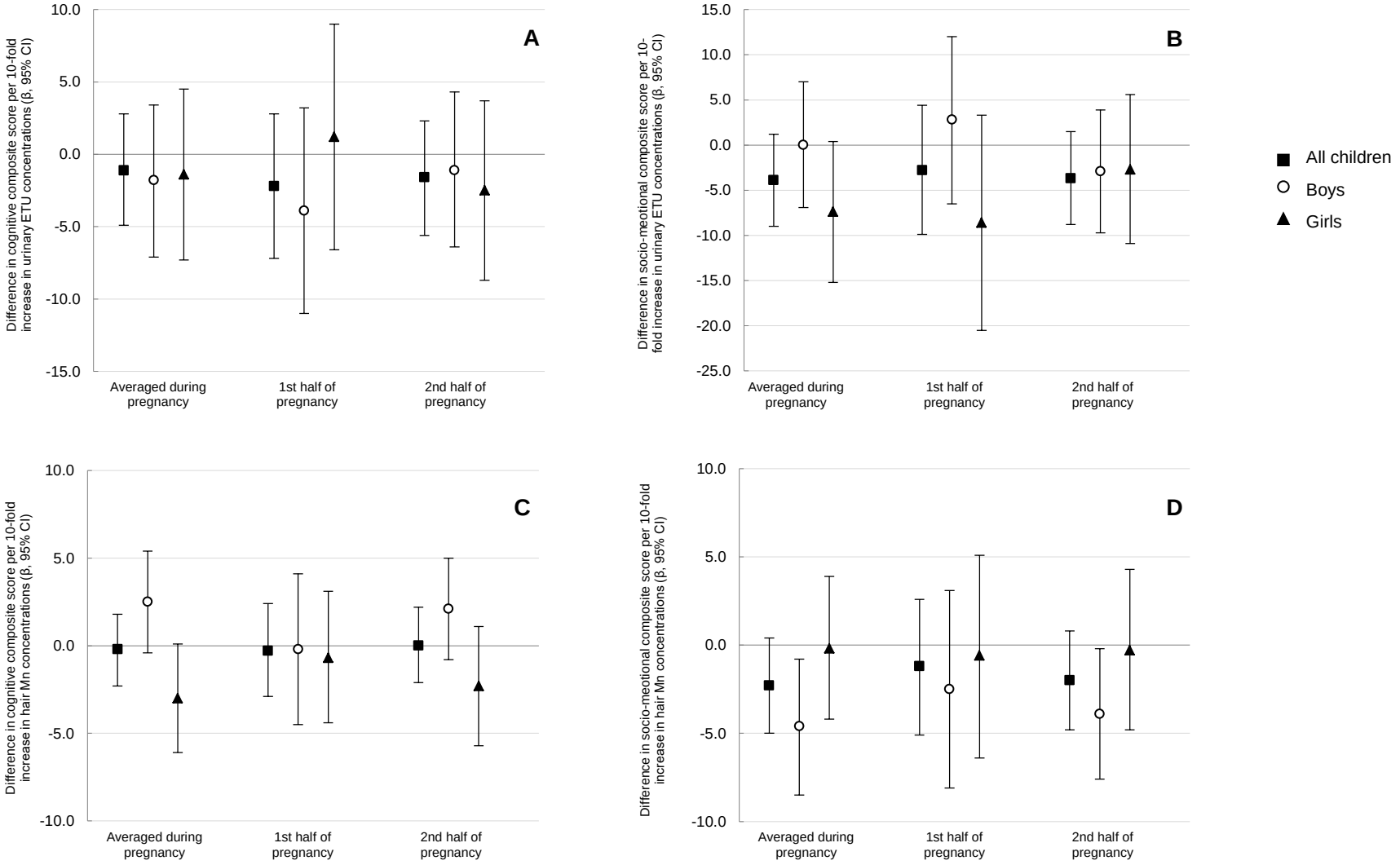


Figure S2. Adjusted associations of prenatal mancozeb exposure and excess Mn during pregnancy and by halves of pregnancy with child neurodevelopment. Models were stratified by child sex and adjusted simultaneously for prenatal log_{10}-transformed and specific-gravity adjusted urinary ETU, log_{10}-transformed hair Mn, blood Mn concentrations, maternal education, parity, gestational age at birth, and child age, HOME score, and location of assessment at 1-year visit. (A) Prenatal log_{10} urinary ETU with cognitive composite scores; (B) prenatal log_{10} urinary ETU with socio-emotional composite scores; (C) prenatal log_{10}-transformed hair Mn with cognitive composite scores; and (D) prenatal log_{10}-transformed hair Mn with socio-emotional composite scores. *Abbreviations*: ETU, ethylenethiourea; Mn, manganese.