HEI

ADDITIONAL MATERIALS AVAILABLE ON THE HEI WEBSITE

Research Report 209

Associations of Air Pollution on the Brain in Children: A Brain Imaging Study

Mònica Guxens et al.

Additional Materials 1: Appendix

These Additional Materials were not formatted or edited by HEI. This document was part of the HEI Review Committee's review process.

Correspondence may be addressed to Dr. Mònica Guxens, Barcelona Institute for Global Health (ISGlobal), Doctor Aiguader, 88, 08003 Barcelona, Spain; e-mail: *monica.guxens@isglobal.org*.

Although this document was produced with partial funding by the United States Environmental Protection Agency under Assistance Award CR–83467701 to the Health Effects Institute, it has not been subjected to the Agency's peer and administrative review and therefore may not necessarily reflect the views of the Agency, and no official endorsement by it should be inferred. The contents of this document also have not been reviewed by private party institutions, including those that support the Health Effects Institute; therefore, it may not reflect the views or policies of these parties, and no endorsement by them should be inferred.

APPENDIX

Associations of Air Pollution on the Brain in Children: A Brain Imaging Study

Mònica Guxens et al.

Correspondence may be addressed to Dr. Mònica Guxens, Barcelona Institute for Global Health (ISGlobal), Doctor Aiguader 88, 08003 Barcelona, Spain; email: *monica.guxens@isglobal.org*

Table of contents

Figure A1. Distribution of measurement sites within the Netherlands/Belgium study area....3

Table A1. Description of the land use regression models..... 4

Table A2. R2 cross-validation of the land use regression models....6

Figure A2. Direct acyclic graph....7

Table A3. Adjusted associations between exposure to air pollutants during pregnancy and childhood and global brain volumes (mm^3) in preadolescents....8

Table A4. Adjusted associations between exposure to air pollutants during pregnancy and childhood and region-specific brain volumes in preadolescents – Deletion/Substitution/Addition approach*....10

Table A5. Adjusted associations between exposure to air pollutants during pregnancy and childhood simultaneously and hippocampus and corpus callosum in preadolescents....11

Figure A3. Association between age at MRI scanning session and region-specific brain volumes in preadolescents....12

Table A6. Adjusted associations between exposure to air pollutants during pregnancy and childhood and global fractional anisotropy and mean diffusivity in preadolescents – Deletion/Substitution/Addition approach*....13

Table A7. Adjusted associations between exposure to air pollutants during pregnancy and childhood simultaneously and global fractional anisotropy and mean diffusivity in preadolescents....14

Table A8. Adjusted associations between exposure to $PM_{2.5}$ during pregnancy and to NO_x during childhood and fractional anisotropy in the twelve individual white matter tracts in preadolescents....15

Table A9. Adjusted associations between exposure to Si during pregnancy and to Zn and OP^{DTT} during childhood and mean diffusivity in the twelve individual white matter tracts in preadolescents....16

Table A10. Adjusted associations between exposure to air pollutants during pregnancy and childhood and global fractional anisotropy with and without accounting for measurement error....17

Table A11. Adjusted associations between exposure to air pollutants during each time period and brain functional connectivity in preadolescents....18

Figure A1. Distribution of measurement sites within the Netherlands/Belgium study area

To cover the geographical spread of several cohort studies, the study area of the Netherlands and Belgium comprised a large geographical area, involving eight major cities. We monitored 80 sites as two campaigns of each 40 sites were joined. Twenty regional background monitoring sites were selected in small villages and countryside settings, to capture regional differences resulting from long-range transport. Ten sites were selected in the larger cities of Amsterdam, Rotterdam, Utrecht and Antwerp (300,000-800,000 inhabitants), while in the smaller cities of Amersfoort, Groningen, Doetinchem and Maastricht (50,000-200,000 inhabitants) only 6 or 4 sites were selected. Both urban background and street sites were sampled in each of these towns. The Dutch & Belgian study area is characterized by minor altitude differences and an overall high population density. Major sea ports are present near both Rotterdam and Antwerp (based on Cyrys J, Eeftens M, Heinrich J, Ampe C, Armengaud A, Beelen R, et al. 2012. Variation of NO2 and NOx concentrations between and within 36 European study areas: Results from the ESCAPE study. Atmos Environ 62:374–390)

Table A1. Description of the land use regression models

Air Pollutant	LUR model	Reference
NOx	-7.80 +1.18*REG_EST_NO2+2.30*10^- 5*POPEEA_5000+2.46*10^- 6*TRAFLOAD_50+ 1.06*10^- 4*ROADLENGTH_1000+ 9.84*10^- 5*HEAVYTRAFLOAD_25+ 12.19* DISTINVNEARC1+4.47*10^- 7 *HEAVYTRAFLOAD_25_500	Beelen R et al. 2013. Atmos Environ 72:10–23
NO_2	3.25 + 0.74*REG_EST_NOx + 4.22*10^- 6*TRAFLOAD_50+ 6.36*10^- 4*POPEEA_1000 + 2.39*10^- 6 *HEAVYTRAFLOAD_500+ 71.65*DISTINVMAJOR1+ 0.21*MAJORROADLENGTH_25	Beelen R et al. 2013. Atmos Environ 72:10–23
PM_{10}	23.71 + 2.16*10^-8 * TRAFMAJORLOAD_500 + 6.68*10^- 6 * POPEEA_5000 + 0.02 * MAJORROADLENGTH_50	Eeftens M et al. 2012. Environ Sci Technol 46:11195–11205
PM_{COARSE}	7.59 + 5.02*10^- 9 * TRAFLOAD_1000 + 1.38*10^- 7 * PORT_5000 + 5.38*10^- 5 * TRAFNEAR	Eeftens M et al. 2012. Environ Sci Technol 46:11195–11205
$PM_{2.5}$	9.46 + 0.42 * REG_EST_PM25 + 0.01 * MAJORROADLENGTH_50 + 2.28*10^- 9 * TRAFMAJORLOAD_1000	Eeftens M et al. 2012. Environ Sci Technol 46:11195–11205
$PM_{2.5}$absorbance	0.07 + 2.95*10^- 9 * TRAFLOAD_500 + 2.93*10^- 3 * MAJORROADLENGTH_50 + 0.85 * REG_EST_PM25abs + 7.90*10^- 9 * HDLDRES_5000 + 1.72*10^- 6 * HEAVYTRAFLOAD_50	Eeftens M et al. 2012. Environ Sci Technol 46:11195–11205
PAHs	1.621 + 0.0061 * MAJORROADLENGTH_50 - 5.429*(10^- 8) * UGNL_5000	Jedynska A et al. 2014. Environ Sci Technol 48:14435–14444
OC	0.480 + 4.798*10^- 7 * LDRES_1000 + 0.00397 * ROADLENGTH_25	Jedynska A et al. 2014. Environ Sci Technol 48:14435–14444
Cu	6.5 + 4.8*10^- 8 * HDLDRES_5000 + 5.0*10^- 7 * TRAFMAJORLOAD_50 + 1.0*10^- 2 * MAJORROADLENGTH_50 - 6.7*10^- 6 * (XCOORD + YCOORD)	de Hoogh K et al. 2013. Environ Sci Technol 47:5778–5786
Fe	149.0 + 1.4*10^- 6 * HDLDRES_5000 + 1.9*10^- 3 * TRAFNEAR + 8.7*10^- 6 * TRAFMAJORLOAD_50 - 1.5*10^- 4 * (XCOORD + YCOORD)	de Hoogh K et al. 2013. Environ Sci Technol 47:5778–5786
Si	146.0 + 2.6*10^- 3 * TRAFNEAR - 1.1*10^- 4 * (XCOORD + YCOORD)	de Hoogh K et al. 2013. Environ Sci Technol 47:5778–5786
Zn	85.6 + 2.0*10^- 7 * TRAFMAJORLOAD_300 + 2.0*10^- 4 * (XCOORD - YCOORD)	de Hoogh K et al. 2013. Environ Sci Technol 47:5778–5786
OP^{DTT}	0.08096 + 0.76684 * REG_EST_OPdtt + 2.364*10^- 5 * ROADLENGTH_500 + 6.977*10^- 5 * INTMAJORINVDIST - 2.65222*10^- 7 * NATURAL_1000	Yang A et al. 2015. Environ Health Perspect 123:1187–1192
OP^{ESR}	326.53554 + 0.56805 * REG_EST_OPesr + 2.0309*10^- 4 * TRAFLOAD_50 + 8.1288*10^- 4 * POPEEA_5000	Yang A et al. 2015. Environ Health Perspect 123:1187–1192

Cu, copper; DISTINVMAJOR1, Distance to the nearest major road (m^{-1}); DISTINVNEARC1, inverse of distance to the nearest road (m^{-1}); Fe, iron; HDLDRES, sum of high density and low density residential land in a buffer (m^2); HEAVYTRAFLOAD, Total heavy-duty traffic load of all roads in a buffer (sum of (heavy-duty traffic intensity*length of all segments)) (vehicles day^{-1} m); INTMAJORINVDIST Product of traffic intensity on nearest major road and inverse of distance to the nearest major road (vehicles day^{-1} m^{-1}); LDRES, Low density residential land in a buffer (m^2); MAJORROADLENGTH, Road length of major roads in a buffer (m); NATURAL, Semi-natural and forested areas in a buffer (m^2); NO_2, nitrogen dioxide; NOx, nitrogen oxides; OC, organic carbon; OP^{DTT}, oxidative potential using dithiothreitol; OP^{ESR} , oxidative potential using electron spin resonance; PAHs, polycyclic aromatic hydrocarbons; $PM_{2.5}$, particulate matter with aerodynamic

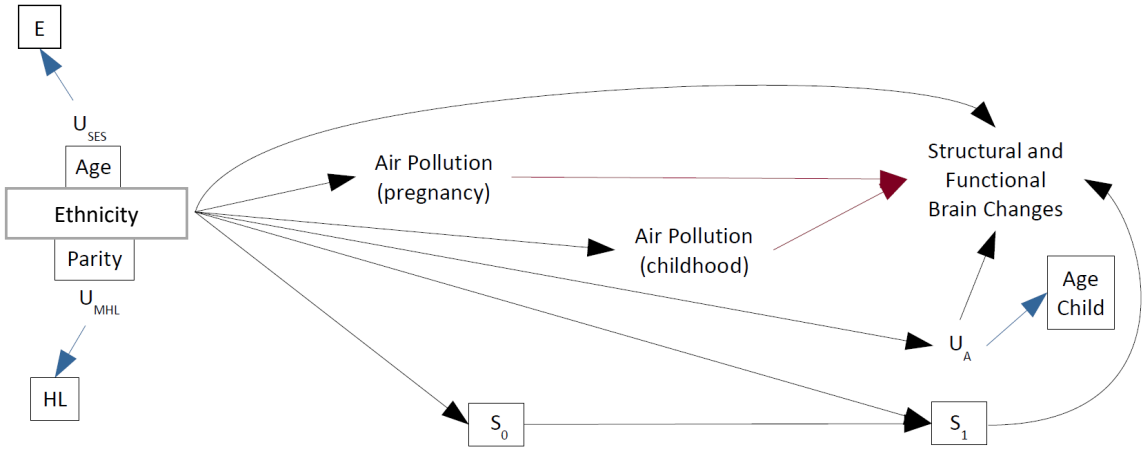
diameter less than 2.5µm, $PM_{2.5}$absorbance, absorbance of $PM_{2.5}$ filters; PM_{10}, particulate matter with aerodynamic diameter less than 10µm; PM_{COARSE}, particulate matter with aerodynamic diameter between 10µm and 2.5µm; POPEEA, Number of inhabitants in a buffer (N); PORT, Port in a buffer (m^2) ; REG_EST, Regional estimate of a specific air pollutant; ROADLENGTH, Road length of all roads in a buffer (m); Si, silicon; TRAFLOAD, Total traffic load of all roads in a buffer (sum of (traffic intensity*length of all segments)) (vehicles day^{-1} m); TRAFMAJORLOAD, Total traffic load of major roads in a buffer (sum of (traffic intensity*length of all segments)) (vehicles day^{-1} m); TRAFNEAR, Traffic intensity on nearest road (vehicles day^{-1}); UGNL, Combined urban green and natural land in a buffer (m^2); XCOORD, X coordinate (m); YCOORD, Y coordinate (m); Zn, zinc.

Table A2. R2 cross-validation of the land use regression models

	R^2 cross-validation
NOx	82
NO_2	81
PM_{10}	60
PM_{COARSE}	38
$PM_{2.5}$	61
$PM_{2.5}$absorbance	89
PAHs	31
OC	71
Cu	81
Fe	73
Si	39
Zn	58
OP^{DTT}	47
OP^{ESR}	60

Cu, copper; CV, cross-validation; Fe, iron; NO_2, nitrogen dioxide; NOx, nitrogen oxides; OC, organic carbon; OP^{DTT}, oxidative potential using dithiothreitol; OP^{ESR} , oxidative potential using electron spin resonance; PAHs, polycyclic aromatic hydrocarbons; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5µm, $PM_{2.5}$absorbance, absorbance of $PM_{2.5}$ filters; PM_{10}, particulate matter with aerodynamic diameter less than 10µm; PM_{COARSE}, particulate matter with aerodynamic diameter between 10µm and 2.5µm; Si, silicon; Zn, zinc.

Figure A2. Direct acyclic graph



E: proxy variables for unmeasured socioeconomic status of the parents (e.g. parental education level, household income, family status); HL: proxy variables for unmeasured parental health and life-style (e.g. maternal smoking and alcohol use during pregnancy, body mass index and height, psychological distress during pregnancy, maternal IQ); S: selection into the case-control study; S_0: selection into the cohort; S_1: selection into the brain imaging study; U: unmeasured variables; U_A: unmeasured variables related to the time the child comes to the brain imaging assessment; U_{MHL}: unmeasured variables related to parental health and life-style; U_{SES}: unmeasured variables related to socioeconomic status
The box indicates the conditioning on the variables. Solid black arrows represent existing pathways indicating thereby the direction of the associations.

Table A3. Adjusted associations between exposure to air pollutants during pregnancy and childhood and global brain volumes (mm^3) in preadolescents

		Pregnancy exposure		Childhood exposure	
Global brain volumes	Air pollutants	Coef	(95% CI)	Coef	(95% CI)
Total brain	NOx (Δ 20 µg/m^3)	2,051	(-2,265; 6,368)	-908	(-5,625; 3,809)
	PM_{10} (Δ 10 µg/m^3)	12,590	(-6,760; 31,940)	-3,766	(-25,982; 18,450)
	PAHs (Δ 1 ng/m^3)	1,412	(-7,885; 10,710)	2,918	(-8,175; 14,012)
	OC (Δ 1 µg/m^3)	298	(-8,176; 8,771)	-4,134	(-12,677; 4,408)
	Cu (Δ 5 ng/m^3)	6,045	(-12,136; 24,226)	-4,909	(-25,386; 15,567)
	Fe (Δ 100 ng/m^3)	9,963	(-5,776; 25,703)	-3,425	(-18,140; 11,291)
	Si (Δ 100 ng/m^3)	7,325	(-11,687; 26,337)	1,792	(-17,842; 21,426)
	Zn (Δ 10 ng/m^3)	2,643	(-5,180; 10,467)	4,117	(-3,182; 11,416)
	OP^{DTT} (Δ 1 nmol DTT/min/m^3)	11,571	(-15,015; 38,157)	-14,159	(-40,905; 12,587)
	OP^{ESR} (Δ 1,000 units/m^3)	9,249	(-8,089; 26,588)	5,354	(-12,770; 23,477)
Cortical gray matter	NOx (Δ 20 µg/m^3)	762	(-1,382; 2,906)	-924	(-3,265; 1,417)
	PM_{10} (Δ 10 µg/m^3)	4,211	(-5,402; 13,825)	-4,777	(-15,797; 6,243)
	PAHs (Δ 1 ng/m^3)	-1,024	(-5,635; 3,588)	-345	(-5,848; 5,158)
	OC (Δ 1 µg/m^3)	200	(-3,998; 4,398)	-1,786	(-6,023; 2,450)
	Cu (Δ 5 ng/m^3)	303	(-8,719; 9,324)	-5,508	(-15,672; 4,655)
	Fe (Δ 100 ng/m^3)	4,562	(-3,244 12,369)	-3,857	(-11,152; 3,438)
	Si (Δ 100 ng/m^3)	3,575	(-5,859; 13,009)	-2,022	(-11,756; 7,712)
	Zn (Δ 10 ng/m^3)	1,161	(-2,723; 5,045)	2,282	(-1,337; 5,901)
	OP^{DTT} (Δ 1 nmol DTT/min/m^3)	2,893	(-10,305; 16,090)	-10,981	(-24,256; 2,293)
	OP^{ESR} (Δ 1,000 units/m^3)	2,689	(-5,917; 11,294)	846	(-8,140; 9,833)
Subcortical gray matter	NOx (Δ 20 µg/m^3)	58	(-75; 191)	42	(-103; 187)
	PM_{10} (Δ 10 µg/m^3)	140	(-457; 738)	62	(-622; 746)
	PAHs (Δ 1 ng/m^3)	30	(-257; 317)	-181	(-525; 163)
	OC (Δ 1 µg/m^3)	-56	(-315; 204)	-122	(-385; 141)
	Cu (Δ 5 ng/m^3)	-133	(-693; 427)	-170	(-801; 461)
	Fe (Δ 100 ng/m^3)	-69	(-555; 418)	84	(-367; 535)
	Si (Δ 100 ng/m^3)	-17	(-604; 569)	305	(-295; 905)
	Zn (Δ 10 ng/m^3)	42	(-199; 284)	75	(-148; 299)
	OP^{DTT} (Δ 1 nmol DTT/min/m^3)	103	(-718; 924)	-371	(-1,201; 459)
	OP^{ESR} (Δ 1,000 units/m^3)	-31	(-567; 505)	27	(-525; 579)
Total white matter	NOx (Δ 20 µg/m^3)	501	(-1,499; 2,501)	-285	(-2,469; 1,898)
	PM_{10} (Δ 10 µg/m^3)	4,145	(-4,827; 13,118)	-1,147	(-11,439; 9,145)
	PAHs (Δ 1 ng/m^3)	1,148	(-3,165; 5,460)	2,260	(-2,895; 7,414)
	OC (Δ 1 µg/m^3)	-21	(-3,948; 3,906)	1,899	(-5,861; 2,063)
	Cu (Δ 5 ng/m^3)	3,085	(-5,343; 11,512)	228	(-9,260; 9,715)
	Fe (Δ 100 ng/m^3)	3,354	(-3,945; 10,653)	656	(-6,151; 7,463)
	Si (Δ 100 ng/m^3)	2,013	(-6,801; 10,827)	3,657	(-5,511; 12,646)
	Zn (Δ 10 ng/m^3)	263	(-3,367; 3,893)	605	(-2,772; 3,983)
	OP^{DTT} (Δ 1 nmol DTT/min/m^3)	8,301	(-4,026; 20,628)	1,460	(-13,875; 10,956)
	OP^{ESR} (Δ 1,000 units/m^3)	3,944	(-4,090; 11,979)	3,385	(-4,980; 11,749)

CI, confidence interval; Coef, coefficient; Cu, copper; Fe, iron; NOx, nitrogen oxides; OC, organic carbon; OP^{DTT}, oxidative potential using the dithiothreitol method; OP^{ESR} , oxidative potential using the electron spin resonance method; PAHs, polycyclic aromatic hydrocarbons; PM_{10}, particulate matter with aerodynamic diameter less than 10μm; Si, silicon; Zn, zinc.
Coefficients and 95% confidence intervals from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, and age at the scanning session. Subcortical gray matter was additionally adjusted by intracranial volume.

Table A4. Adjusted associations between exposure to air pollutants during pregnancy and childhood and region-specific brain volumes (mm^3) in preadolescents – Deletion/Substitution/Addition approach*

Pregnancy exposure			Childhood exposure		
	Coef	(95% CI)		Coef	(95% CI)
Hippocampus					
Model 1 (27%)			Model 1 (20%)		
PAHs (Δ 1 ng/m^3)	**-69**	**(-129; -9)**	OP^{DTT} (Δ 1 nmol DTT/min/m^3)	**-198**	**(-371; -25)**
Amygdala					
Model 1 (61%)			---		
OC (Δ 1 µg/m^3)	**-34**	**(-62; -5)**			
PAHs (Δ 1 ng/m^3)	**-36**	**(-70; -2)**			
Si (Δ 100 ng/m^3)	**111**	**(41; 181)**			
Nucleus accumbens					
---			Model 1 (60%)		
			Zn (Δ 10 ng/m^3)	**17**	**(3; 30)**
Corpus callosum					
Model 1 (44%)			Model 1 (63%)		
OP^{ESR} (Δ 1,000 units/m^3)	**-101**	**(-185; -16)**	OC (Δ 1 µg/m^3)	**-56**	**(-97; -14)**
Model 2 (13%)					
PAHs (Δ 1 ng/m^3)	52	(-1; 105)			
Si (Δ 100 ng/m^3)	119	(-1; 240)			
OP^{ESR} (Δ 1,000 units/m^3)	**-222**	**(-340; -104)**			
Cerebellum					
Model 1 (28%)			---		
PM_{COARSE} (Δ 5 µg/m^3)	**2,501**	**(447; 4,555)**			
Zn (Δ 10 ng/m^3)	642	(-321; 1,606)			
OP^{DTT} (Δ 1 nmol DTT/min/m^3)	**-4,102**	**(-7,488; -715)**			

Coefficients and 95% CI from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, age at the scanning session, and intracranial volume.

CI, confidence interval; Coef, coefficient; Fe, iron; NO_2, nitrogen dioxide; OC, organic carbon; OP^{DTT}, oxidative potential using dithiothreitol; OP^{ESR} , oxidative potential using electron spin resonance; PAHs, polycyclic aromatic hydrocarbons; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5µm; PM_{coarse}, particulate matter with aerodynamic diameter between 10µm and 2.5µm; Si, silicon; Zn, zinc.

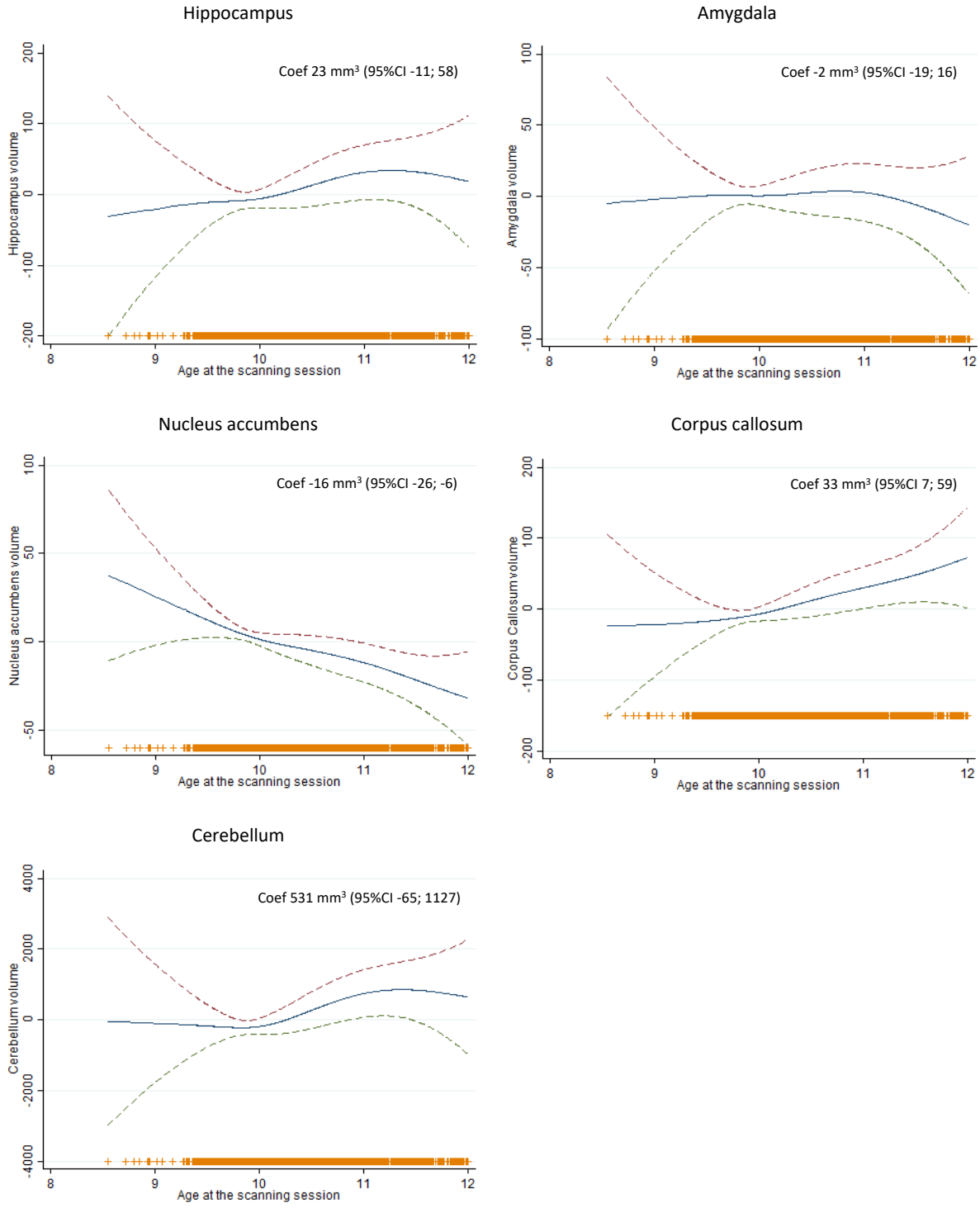
*The Deletion/Selection/Addition approach is an iterative selection method that selects the variables that better predict the outcome by cross-validation (see section 'Statistical Methods and Data Analysis'). Since it is subject to random variations, we ran each model 200 times and we considered as final model the combination of pollutants that were selected at least 10% of the runs. The percentage shown in the table for each model reflects the times that the model occurred within the 200 times and it is an indicator of the stability of the results.

Table A5. Adjusted associations between exposure to air pollutants during pregnancy and childhood simultaneously and hippocampus and corpus callosum volume (mm^3) in preadolescents

	Coef	(95% CI)
Corpus callosum		
OP^{ESR} pregnancy (Δ 1,000 units/m^3)	-87	(-172; -3)
OC childhood (Δ 1 μg/m^3)	-50	(-91; -8)
Hippocampus		
PAHs pregnancy (Δ 1 ng/m^3)	-62	(-121; -2)
OP^{DTT} childhood (Δ 1 nmol DTT/min/m^3)	-176	(-349; -3)

Coefficients and 95% CI from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, age at the scanning session, and intracranial volume.
CI, confidence interval; Coef, coefficient; OC, organic carbon; OP^{DTT}, oxidative potential using dithiothreitol; OP^{ESR} , oxidative potential using electron spin resonance; PAHs, polycyclic aromatic hydrocarbons.

Figure A3. Association between age at MRI scanning session and region-specific brain volumes in preadolescents



CI, confidence interval; Coef, coefficient.

Table A6. Adjusted associations between exposure to air pollutants during pregnancy and childhood and global fractional anisotropy and mean diffusivity in preadolescents – Deletion/Substitution/Addition approach*

Pregnancy exposure			Childhood exposure		
	Coef	(95% CI)		Coef	(95% CI)
Global fractional anisotropy					
Model 1 (25%)			Model 1 (23%)		
$PM_{2.5}$ (Δ 5 μg/m^3)	**-1.49**	**(-2.25; -0.73)**	NOx (Δ 20 μg/m^3)	**-0.14**	**(-0.23; -0.04)**
PAHs (Δ 1 ng/m^3)	**0.33**	**(0.06; 0.59)**	Model 2 (11%)		
OP^{DTT} (Δ 1 nmol DTT/min/m^3)	0.50	(-0.07; 1.07)	NOx (Δ 20 μg/m^3)	**-0.13**	**(-0.24; -0.03)**
Model 2 (20%)			OP^{DTT} (Δ 1 nmol DTT/min/m^3)	0.46	(-0.19; 1.12)
$PM_{2.5}$ (Δ 5 μg/m^3)	**-1.32**	**(-2.06; -0.58)**	OC (Δ 1 μg/m^3)	-0.19	(-0.40; 0.01)
PAHs (Δ 1 ng/m^3)	**0.33**	**(0.06; 0.60)**			
Model 3 (13%)					
$PM_{2.5}$ (Δ 5 μg/m^3)	**-0.71**	**(-1.26; -0.16)**			
Global mean diffusivity					
Model 1 (14%)			Model 1 (47%)		
Si (Δ 100 ng/m^3)	**0.06**	**(0.01; 0.11)**	Zn (Δ 10 ng/m^3)	**0.03**	**(0.01; 0.04)**
OP^{DTT} (Δ 1 nmol DTT/min/m^3)	0.05	(-0.02; 0.11)	OP^{DTT} (Δ 1 nmol DTT/min/m^3)	**0.07**	**(0.00; 0.14)**
			Model 2 (23%)		
			Zn (Δ 10 ng/m^3)	**0.02**	**(0.01; 0.04)**
			OP^{DTT} (Δ 1 nmol DTT/min/m^3)	0.06	(-0.01; 0.13)
			Si (Δ 100 ng/m^3)	0.04	(-0.02; 0.09)

Coefficients and 95% CI from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, and age at the scanning session.

CI, confidence interval; Coef, coefficient; NO_X, nitrogen oxides; OC, organic carbon; OP^{DTT}, oxidative potential using dithiothreitol; PAHs, polycyclic aromatic hydrocarbons; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5μm, Si, silicon; Zn, zinc.

* The Deletion/Selection/Addition approach is an iterative selection method that selects the variables that better predict the outcome by cross-validation (see section 'Statistical Methods and Data Analysis'). Since it is subject to random variations, we ran each model 200 times and we considered as final model the combination of pollutants that were selected at least 10% of the runs. The percentage shown in the table for each model reflects the times that the model occurred within the 200 times, and it is an indicator of the stability of the results.

Table A7. Adjusted associations between exposure to air pollutants during pregnancy and childhood simultaneously and global fractional anisotropy and mean diffusivity in preadolescents

	Coef	(95% CI)
Global fractional anisotropy		
$PM_{2.5}$ pregnancy (Δ 5 µg/m^3)	-0.48	(-1.07; 0.10)
NOx childhood (Δ 20 µg/m^3)	-0.10	(-0.21; 0.00)
Global mean diffusivity		
Si pregnancy (Δ 100 ng/m^3)	**0.06**	**(0.01; 0.11)**
Zn childhood (Δ 10 ng/m^3)	**0.02**	**(0.01; 0.04)**
OP^{DTT} childhood (Δ 1 nmol DTT/min/m^3)	0.06	(-0.01; 0.13)

Coefficients and 95% CI from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, age at the scanning session.

CI, confidence interval; Coef, coefficient; NOx, nitrogen oxides; OP^{DTT}, oxidative potential using the dithiothreitol method; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5µm; Si, silicon; Zn, zinc.

Table A8. Adjusted associations between exposure to $PM_{2.5}$ during pregnancy and to NO_x during childhood and fractional anisotropy in the twelve individual white matter tracts in preadolescents

	Fractional anisotropy			
	$PM_{2.5}$ during pregnancy		NO_x during childhood	
	Coef	(95% CI)	Coef	(95% CI)
Uncinate fasciculus left hemisphere	-0.009	(-0.018; 0.000)	**-0.002**	**(-0.003; -0.000)**
Uncinate fasciculus right hemisphere	-0.005	(-0.013; 0.003)	**-0.002**	**(-0.003; -0.000)**
Cingulate gyrus part of cingulum left hemisphere	-0.010	(-0.023; 0.003)	-0.002	(-0.004; 0.001)
Cingulate gyrus part of cingulum right hemisphere	-0.006	(-0.018; 0.006)	0.000	(-0.002; 0.002)
Superior longitudinal fasciculus left hemisphere	-0.006	(-0.013; 0.009)	-0.001	(-0.002; 0.001)
Superior longitudinal fasciculus right hemisphere	**-0.009**	**(-0.016; -0.002)**	**-0.002**	**(-0.003; -0.000)**
Forceps minor	**-0.013**	**(-0.023; -0.003)**	-0.002	(-0.003; 0.000)
Forceps major	-0.003	(-0.014; 0.008)	-0.000	(-0.002; 0.002)
Inferior longitudinal fasciculus left hemisphere	-0.003	(-0.009; 0.004)	-0.001	(-0.002; 0.000)
Inferior longitudinal fasciculus right hemisphere	-0.002	(-0.009; 0.005)	**-0.001**	**(-0.003; -0.000)**
Corticospinal tract left hemisphere	**-0.008**	**(-0.014; -0.001)**	**-0.001**	**(-0.002; -0.000)**
Corticospinal tract right hemisphere	**-0.008**	**(-0.014; -0.002)**	-0.001	(-0.002; 0.000)

CI, confidence interval; Coef, coefficient; NOx, nitrogen oxides; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5µm.

Coefficients and 95% CI from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, and age at the scanning session.

In bold, association with a p-value < 0.05.

Table A9. Adjusted associations between exposure to Si during pregnancy and to Zn and OP^{DTT} during childhood and mean diffusivity in the twelve individual white matter tracts in preadolescents

	Mean diffusivity*					
	Si during pregnancy		Zn during childhood		OP^{DTT} during childhood	
	Coef	(95% CI)	Coef	(95% CI)	Coef	(95% CI)
Uncinate fasciculus left hemisphere	0.003	(-0.003; 0.008)	**0.002**	**(0.000; 0.004)**	0.004	(-0.003; 0.011)
Uncinate fasciculus right hemisphere	0.004	(-0.002; 0.009)	**0.002**	**(0.001; 0.004)**	0.002	(-0.004; 0.009)
Cingulate gyrus part of cingulum left hemisphere	**0.009**	**(0.002;0.016)**	**0.004**	**(0.002; 0.007)**	**0.010**	**(0.001; 0.019)**
Cingulate gyrus part of cingulum right hemisphere	**0.008**	**(0.001;0.014)**	**0.004**	**(0.001; 0.006)**	0.007	(-0.001; 0.016)
Superior longitudinal fasciculus left hemisphere	**0.009**	**(0.004;0.014)**	**0.003**	**(0.001; 0.004)**	0.003	(-0.004; 0.010)
Superior longitudinal fasciculus right hemisphere	0.006	(-0.000;0.012)	**0.003**	**(0.001; 0.005)**	0.005	(-0.003; 0.013)
Forceps minor	**0.017**	**(0.009;0.024)**	**0.005**	**(0.002; 0.007)**	0.008	(-0.002; 0.018)
Forceps major	-0.001	(-0.016; 0.015)	0.000	(-0.005; 0.006)	0.008	(-0.012; 0.028)
Inferior longitudinal fasciculus left hemisphere	**0.007**	**(0.000;0.014)**	**0.002**	**(0.000; 0.005)**	0.007	(-0.001; 0.016)
Inferior longitudinal fasciculus right hemisphere	0.007	(-0.001;0.014)	**0.003**	**(0.000; 0.005)**	0.006	(-0.004; 0.015)
Corticospinal tract left hemisphere	0.002	(-0.009;0.013)	0.001	(-0.003; 0.005)	0.006	(-0.008; 0.020)
Corticospinal tract right hemisphere	-0.001	(-0.011;0.009)	0.002	(-0.001; 0.006)	0.002	(-0.011; 0.015)

CI, confidence interval; Coef, coefficient; OP^{DTT}, oxidative potential using dithiothreitol; Si, silicon; Zn, zinc.
Coefficients and 95% CI from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, and age at the scanning session.
In bold, association with a p-value < 0.05.
*Values of mean diffusivity were multiplied by 10^9.

Table A10. Adjusted associations between exposure to air pollutants during pregnancy and childhood and global fractional anisotropy with and without accounting for measurement error

	Global fractional anisotropy							
	Pregnancy exposure				Childhood exposure			
	Original results		With measurement error		Original results		With measurement error	
	(95% CI)	SE	(95% CI)	SE	(95% CI)	SE	(95% CI)	SE
NOx (Δ 20 μg/m^3)	(-0.20; -0.02)	0.045	(-0.19; -0.01)	0.046	(-0.23; -0.04)	0.049	(-0.23; -0.04)	0.050
NO_2 (Δ 10 μg/m^3)	(-0.25; 0.03)	0.068	(-0.24; 0.02)	0.068	(-0.25; -0.01)	0.059	(-0.25; -0.02)	0.060
PM_{10} (Δ 10 μg/m^3)	(-0.90; -0.08)	0.205	(-0.99; -0.03)	0.245	(-0.91; 0.01)	0.232	(-1.12; -0.04)	0.275
PM_{COARSE} (Δ 5 μg/m^3)	(-0.37; 0.27)	0.161	(-0.38; 0.26)	0.164	(-0.63; 0.04)	0.169	(-0.65; 0.00)	0.167
$PM_{2.5}$ (Δ 5 μg/m^3)	(-1.26; -0.16)	0.277	(-0.99; -0.11)	0.224	(-1.14; 0.21)	0.340	(-1.06; 0.14)	0.306
$PM_{2.5}$absorbance (Δ 10^{-5}m^{-1})	(-0.51; -0.07)	0.113	(-0.51; -0.05)	0.119	(-0.51; -0.02)	0.122	(-0.51; -0.03)	0.122
Cu (Δ 5 ng/m^3)	(-0.71; 0.06)	0.193	(-0.69; 0.05)	0.189	(-0.65; 0.21)	0.217	(-0.66; 0.18)	0.215
Fe (Δ 100 ng/m^3)	(-0.54; 0.14)	0.172	(-0.55; 0.14)	0.175	(-0.53; 0.09)	0.156	(-0.55; 0.06)	0.155
Si (Δ 100 ng/m^3)	(-0.70; 0.15)	0.214	(-0.73; 0.15)	0.225	(-0.66; 0.19)	0.216	(-0.34; 0.06)	0.102
Zn (Δ 10 ng/m^3)	(-0.28; 0.04)	0.081	(-0.48; 0.20)	0.174	(-0.27; 0.02)	0.075	(-0.18; 0.00)	0.047
	Global mean diffusivity							
	Pregnancy exposure				Childhood exposure			
	Original results		With measurement error		Original results		With measurement error	
	(95% CI)	SE	(95% CI)	SE	(95% CI)	SE	(95% CI)	SE
NOx (Δ 20 μg/m^3)	(0.00; 0.02)	0.005	(0.00; 0.02)	0.006	(0.01; 0.03)	0.006	(0.01; 0.03)	0.007
NO_2 (Δ 10 μg/m^3)	(0.00; 0.04)	0.008	(0.00; 0.04)	0.009	(0.00; 0.03)	0.007	(0.01; 0.03)	0.006
PM_{10} (Δ 10 μg/m^3)	(0.00; 0.10)	0.025	(0.00; 0.11)	0.030	(0.01; 0.12)	0.028	(0.01; 0.14)	0.032
PM_{COARSE} (Δ 5 μg/m^3)	(-0.01; 0.07)	0.020	(-0.02; 0.06)	0.019	(0.00; 0.09)	0.021	(0.00; 0.08)	0.021
$PM_{2.5}$ (Δ 5 μg/m^3)	(0.02; 0.15)	0.034	(0.01; 0.12)	0.028	(0.03; 0.20)	0.041	(0.02; 0.18)	0.040
$PM_{2.5}$absorbance (Δ 10^{-5}m^{-1})	(0.01; 0.06)	0.014	(0.01; 0.06)	0.015	(0.01; 0.07)	0.015	(0.01; 0.07)	0.015
Cu (Δ 5 ng/m^3)	(0.01; 0.10)	0.023	(0.01; 0.10)	0.024	(-0.02; 0.09)	0.026	(-0.02; 0.09)	0.027
Fe (Δ 100 ng/m^3)	(0.01; 0.09)	0.021	(0.01; 0.09)	0.021	(-0.01; 0.07)	0.019	(0.00; 0.07)	0.018
Si (Δ 100 ng/m^3)	(0.02; 0.12)	0.026	(0.01; 0.13)	0.031	(0.00; 0.11)	0.026	(0.00; 0.11)	0.027
Zn (Δ 10 ng/m^3)	(-0.01; 0.03)	0.010	(-0.02; 0.06)	0.022	(0.01; 0.05)	0.009	(0.01; 0.06)	0.013

CI, confidence interval; Coef, coefficient; Cu, copper; Fe, iron; NO_2, nitrogen dioxide; NOx, nitrogen oxides; $PM_{2.5}$, particulate matter with aerodynamic diameter less than 2.5μm; $PM_{2.5}$absorbance, absorbance of $PM_{2.5}$ filters; PM_{10}, particulate matter with aerodynamic diameter less than 10μm; PM_{COARSE}, particulate matter with aerodynamic diameter between 10μm and 2.5μm; SE, standard error; Si, silicon; Zn, zinc.

Coefficients and 95% confidence intervals from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, and age at the scanning session.

Table A11. Adjusted associations between exposure to air pollutants during each time period and brain functional connectivity in preadolescents

	Pregnancy		Childhood 0-2y		Childhood 2-5y		Childhood 5-9y	
Air pollutant – Brain regions*	Coef	(95% CI)	Coef	(95% CI)	Coef	(95% CI)	Coef	(95% CI)
NOx (Δ 20 µg/m³)								
Auditory association cortex - Ventral DC area								
Left STSd posterior area - Left Ventral DC area	---	---	0.06	(0.04; 0.09)	---	---	---	---
Left STSd posterior area - Right Ventral DC area	---	---	0.06	(0.03; 0.09)	---	---	---	---
Right STSv posterior area - Left Ventral DC area	---	---	0.06	(0.04; 0.09)	---	---	---	---
Dorsal Stream Visual Cortex - Superior Parietal Cortex								
Left V3A area - Right ventral intraparietal complex area	---	---	0.07	(0.04; 0.09)	---	---	---	---
Dorsal Stream Visual Cortex - MT+ Complex and Neighboring Visual Areas								
Left V3A area - Right Lateral Occipital 3 area	---	---	0.06	(0.03; 0.09)	---	---	---	---
Premotor cortex - Inferior Parietal Cortex								
Left Rostral Area 6 - Right PFt area	---	---	0.06	(0.03; 0.09)	---	---	---	---
Orbital and Polar Frontal Cortex - Orbital and Polar Frontal Cortex								
Left Orbital Frontal area - Right posterior 47r area	---	---	0.06	(0.04; 0.09)	---	---	---	---
Temporo-Parieto-Occipital Junction - Early Auditory Cortex								
Left TemporoParietoOccipital Junction 3 area - Right RetroInsular Cortex	---	---	0.06	(0.04; 0.09)	---	---	---	---
Premotor cortex - Premotor cortex								
Right Premotor Eye Field - Right Ventral Area 6	---	---	0.06	(0.04; 0.09)	---	---	---	---
Inferior Frontal Cortex - Posterior Opercular Cortex								
Right IFSa area - Right Area 43	---	---	0.06	(0.04; 0.09)	---	---	---	---
Posterior cingulate cortex - Inferior Parietal Cortex								
Left Parieto-Occipital Sulcus Area 1 - Right Area PGi	---	---	---	---	0.07	(0.04; 0.09)	---	---
Right Area dorsal 23 a+b - Right Area PGi	---	---	---	---	0.07	(0.04; 0.09)	---	---
Posterior Cingulate Cortex - Posterior Cingulate Cortex								
Right Area dorsal 23 a+b - Right Area 7m	---	---	---	---	0.06	(0.04; 0.09)	---	---
Inferior Frontal Cortex - MT+ Complex and Neighboring Visual Areas								
Right Area IFJp - Right Lateral Occipital 3 Area	---	---	---	---	0.07	(0.05; 0.10)	---	---
Insular and Frontal Opercular Cortex - MT+ Complex and Neighboring Visual Areas								
Right Area Frontal Opercular 5 - Right Lateral Occipital 3 Area	---	---	---	---	0.07	(0.04; 0.10)	---	---

Table A11 (continued).

Air pollutant – Brain regions*	Pregnancy Coef	Pregnancy (95% CI)	Childhood 0-2y Coef	Childhood 0-2y (95% CI)	Childhood 2-5y Coef	Childhood 2-5y (95% CI)	Childhood 5-9y Coef	Childhood 5-9y (95% CI)
NO_2 (Δ 10 μg/m³)								
Posterior cingulate cortex - Dorsal Stream Visual Cortex								
Left prostriate area - Left V3A area	0.08	(0.04; 0.11)	---	---	---	---	---	---
Auditory association cortex - Ventral DC area								
Left STSd posterior area - Right ventral DC area	0.08	(0.04; 0.10)	0.10	(0.06; 0.14)	---	---	---	---
Left STSd posterior area - Left ventral DC area	---	---	0.10	(0.06; 0.13)	---	---	---	---
Ventral Stream Visual Cortex - Dorsal Stream Visual Cortex								
Left Posterior InferoTemporal area - Right V6A area	0.08	(0.05; 0.10)	---	---	---	---	---	---
Posterior cingulate cortex - Dorsal Stream Visual Cortex								
Left superior 6-8 transitional area - Right area 2	0.07	(0.04; 0.10)	---	---	---	---	---	---
Somatosensory and Motor Cortex - Insular and Frontal Opercular Cortex								
Right primary motor cortex area - Right posterior insular 1 area	0.07	(0.04; 0.10)	---	---	---	---	---	---
Right primary sensory cortex area - Right posterior insular 1 area	0.06	(0.03; 0.09)	---	---	---	---	---	---
Anterior Cingulate and Medial Prefrontal Cortex - Dorsal Stream Visual Cortex								
Left s32 area - Right V6A area	0.07	(0.04; 0.11)	---	---	---	---	---	---
Somatosensory and Motor Cortex - Somatosensory and Motor Cortex								
Right primary sensory cortex area - Right area 2	0.07	(0.04; 0.10)	---	---	---	---	---	---
Paracentral Lobular and Mid Cingulate Cortex - DorsoLateral Prefrontal Cortex								
Right supplementary and cingulate eye field -Right posterior 9-46v area	0.07	(0.04; 0.11)	---	---	---	---	---	---
Anterior Cingulate and Medial Prefrontal Cortex - Orbital and Polar Frontal Cortex								
Right p32 prime area - Right posterior 10p area	0.07	(0.04; 0.11)	---	---	---	---	---	---
Inferior Frontal Cortex - Anterior Cingulate and Medial Prefrontal Cortex								
Right IFJa area - Right s32 area	0.07	(0.03; 0.10)	---	---	---	---	---	---
DorsoLateral Prefrontal Cortex - Posterior Opercular Cortex								
Right posterior 9-46v area - Right area 43	0.07	(0.04; 0.10)	---	---	---	---	---	---
Dorsal Stream Visual Cortex - Superior Parietal Cortex								
Left V3A area - Right ventral intraparietal complex area	---	---	0.11	(0.07; 0.15)	---	---	---	---
Posterior Opercular Cortex - Early Auditory Cortex								
Left PFcm area - Right medial belt complex area	---	---	0.09	(0.05; 0.13)	---	---	---	---

Table A11 (continued).

Air pollutant – Brain regions*	Pregnancy Coef	(95% CI)	Childhood 0-2y Coef	(95% CI)	Childhood 2-5y Coef	(95% CI)	Childhood 5-9y Coef	(95% CI)
NO_2 (Δ 10 μg/m^3)								
Temporo-Parieto-Occipital Junction - Posterior Cingulate Cortex								
Left TemporoParietoOccipital Junction 1 area -Right area 31pd	---	---	0.10	(0.06; 0.14)	---	---	---	---
Auditory association cortex - Insular and Frontal Opercular Cortex								
Left TA2 area - Left Insular granular complex area	---	---	0.11	(0.07; 0.15)	---	---	---	---
Somatosensory and Motor Cortex - Early Auditory Cortex								
Right primary motor cortex area - Right Parabelt complex	---	---	0.10	(0.06; 0.14)	---	---	---	---
Premotor cortex - Premotor cortex								
Right premotor eye field area - Right Ventral 6 area	---	---	0.09	(0.05; 0.13)	---	---	---	---
PM_{COARSE} (Δ 5 μg/m^3)					---	---	---	---
Anterior Cingulate and Medial Prefrontal Cortex - MT + Complex and Neighboring Visual Areas								
Right lateral occipital 1 area - Right s32 area	---	---	---	---	0.25	(0.15; 0.34)	0.23	(0.14; 0.33)
$PM_{2.5}$absorbance (Δ $10^{-5}m^{-1}$)								
Amygdala - Somatosensory and Motor Cortex								
Left Amygdala - Left Area 3a	---	---	0.15	(0.08; 0.22)	---	---	---	---
Ventral DC - Auditory association cortex								
Left Ventral DC - Left Area STSd posterior	---	---	0.15	(0.08; 0.22)	---	---	---	---
Left Ventral DC - Right Area STSd anterior	---	---	0.16	(0.08; 0.24)	---	---	---	---
Left Ventral DC -Right Area STSv posterior	---	---	0.15	(0.08; 0.23)	---	---	---	---
Caudate - Lateral Temporal Cortex								
Right Caudate - Left Area TE1 posterior	---	---	0.16	(0.08; 0.23)	---	---	---	---
Premotor Cortex - MT+Complex and Neighboring Visual Areas								
Left Area 55b - Left Area Lateral Occipital	---	---	0.15	(0.08; 0.23)	---	---	---	---
Ventral DC - Lateral Temporal Cortex								
Left Ventral DC - Left Area TG Ventral	---	---	0.16	(0.08; 0.23)	---	---	---	---
Accumbens Area - Lateral Temporal Cortex								
Right Accumbens Area - Left Area TG Ventral	---	---	0.15	(0.08; 0.23)	---	---	---	---
Somatosensory and Motor Cortex - Auditory Association Cortex								
Left Primary Motor Cortex - Left Auditory 4 Complex	---	---	0.14	(0.07; 0.21)	---	---	---	---
Premotor Cortex - Auditory Association Cortex								
Left Area 55b - Left Auditory 4 Complex	---	---	0.15	(0.08; 0.22)	---	---	---	---
Dorsal Stream Visual Cortex - Superior Parietal Cortex								
Left Area V3A - Right Lateral Area 7A	---	---	0.15	(0.08; 0.22)	---	---	---	---
Left Area V3A - Right Ventral IntraParietal Complex	---	---	0.18	(0.11; 0.25)	---	---	---	---

Table A11 (continued).

Air pollutant – Brain regions*	Pregnancy Coef	(95% CI)	Childhood 0-2y Coef	(95% CI)	Childhood 2-5y Coef	(95% CI)	Childhood 5-9y Coef	(95% CI)
$PM_{2.5}$absorbance (Δ $10^{-5}m^{-1}$)								
Posterior Cingulate Cortex - Superior Parietal Cortex								
Left Parieto-Occipital Sulcus Area 2 - Right Area 7PC	---	---	0.15	(0.09; 0.22)	---	---	---	---
Dorsal Stream Visual Cortex - Auditory Association Cortex								
Left Area V6 - Right Area STGa	---	---	0.16	(0.09; 0.23)	---	---	---	---
Somatosensory and Motor Cortex - Early Auditory Cortex								
Left Primary Motor Cortex - Right Parabelt complex	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right Primary Motor Cortex - Right ParaBelt Complex	---	---	0.16	(0.09; 0.23)	---	---	---	---
Dorsal Stream Visual Cortex - Lateral Temporal Cortex								
Left Area V6 -Right Area PHT	---	---	0.17	(0.09; 0.24)	---	---	---	---
MT+ Complex and Neighboring Visual Areas - Temporo-Parieto-Occipital Junction								
Left Area Lateral Occipital 1 - Right Area TemporoParietoOccipital Junction 3	---	---	0.18	(0.10; 0.26)	---	---	---	---
Dorsal Stream Visual Cortex - MT+ Complex and Neighboring Visual Areas								
Left Area V3A - Right Area Lateral Occipital 3	---	---	0.19	(0.11; 0.26)	---	---	---	---
MT+ Complex and Neighboring Visual Areas - Early Auditory Cortex								
Left Middle Temporal Area - Right Area PFcm	---	---	0.16	(0.08; 0.23)	---	---	---	---
MT+ Complex and Neighboring Visual Areas - Posterior Opercular Cortex								
Left Middle Temporal Area - Right Area OP1/SII	---	---	0.15	(0.08; 0.22)	---	---	---	---
Somatosensory and Motor Cortex - Somatosensory and Motor Cortex								
Left Area 3a - Right Area 2	---	---	0.15	(0.08; 0.22)	---	---	---	---
Paracentral Lobular and Mid Cingulate Cortex - Premotor Cortex								
Left Dorsal Area 24d - Right Frontal Eye Fields	---	---	0.16	(0.09; 0.24)	---	---	---	---
Paracentral Lobular and Mid Cingulate Cortex - Temporo-Parieto-Occipital Junction								
Left Area 5m - Left TemporoParietoOccipital Junction 1 area	---	---	0.16	(0.09; 0.24)	---	---	---	---
Auditory Association Cortex - Insular and Frontal Opercular Cortex								
Left Area TA2 - Left Insular granular complex area	---	---	0.15	(0.08; 0.22)	---	---	---	---
Orbital and Polar Frontal Cortex -Ventral Stream Visual Cortex								
Left Area 47m - Right Posterior InferoTemporal	---	---	0.17	(0.10; 0.24)	---	---	---	---
Insular and Frontal Opercular Cortex - Inferior Frontal Cortex								
Left Middle Insular Area - Right Area IFJp	---	---	0.16	(0.08; 0.23)	---	---	---	---

Table A11 (continued).

Air pollutant – Brain regions*	Pregnancy Coef	(95% CI)	Childhood 0-2y Coef	(95% CI)	Childhood 2-5y Coef	(95% CI)	Childhood 5-9y Coef	(95% CI)
$PM_{2.5}$absorbance (Δ $10^{-5}m^{-1}$)								
DorsoLateral Prefrontal Cortex - Superior Parietal Cortex								
Left Area 44 - Right Medial Area 7P	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right Area anterior 9-46v - Right Anterior Area IntraParietal	---	---	0.16	(0.08; 0.23)	---	---	---	---
Premotor Cortex - Inferior Parietal Cortex								
Left Rostral Area 6 - Right Area PFt	---	---	0.16	(0.09; 0.23)	---	---	---	---
Early Auditory Cortex - Inferior Parietal Cortex								
Left Area 52 - Right Area PFt	---	---	0.15	(0.08; 0.22)	---	---	---	---
Auditory Association Cortex - Anterior Cingulate and Medial Prefrontal Cortex								
Left Area STSv posterior - Right Area posterior 24	---	---	0.17	(0.10; 0.25)	---	---	---	---
Left Area STSd posterior - Right Area dorsal 32	---	---	0.16	(0.08; 0.23)	---	---	---	---
Left Area STSv posterior - Right Area dorsal 32	---	---	0.16	(0.09; 0.24)	---	---	---	---
Insular and Frontal Opercular Cortex - Posterior Cingulate Cortex								
Left Anterior Agranular Insula Complex - Right Area 31pd	---	---	0.15	(0.08; 0.22)	---	---	---	---
Temporo-Parieto-Occipital Junction - Posterior Cingulate Cortex								
Left TemporoParietoOccipital Junction 1 area - Right Area 31pd	---	---	0.17	(0.10; 0.25)	---	---	---	---
Left TemporoParietoOccipital Junction 1 area - Right Area 7m	---	---	0.16	(0.09; 0.24)	---	---	---	---
Left TemporoParietoOccipital Junction 1 area - Right Area ventral 23 a+b	---	---	0.17	(0.09; 0.25)	---	---	---	---
Temporo-Parieto-Occipital Junction - Inferior Parietal Cortex								
Left TemporoParietoOccipital Junction 1 area - Right Area PGi	---	---	0.16	(0.09; 0.24)	---	---	---	---
Medial Temporal Cortex - Auditory Association Cortex								
Left PreSubiculum - Right Area STSv posterior	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right Entorhinal Cortex - Right Area STSv posterior	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right PreSubiculum - Right Area STGa	---	---	0.16	(0.09; 0.23)	---	---	---	---
Auditory Association Cortex - Medial Temporal Cortex								
Left Area STSd posterior - Right Entorhinal Cortex	---	---	0.15	(0.08; 0.22)	---	---	---	---
Temporo-Parieto-Occipital Junction - Early Auditory Cortex								
Left Area TemporoParietoOccipital Junction 3 - Right RetroInsular Cortex	---	---	0.16	(0.09; 0.23)	---	---	---	---
Auditory Association Cortex - Somatosensory and Motor Cortex								
Left Auditory 4 Complex - Right Primary Motor Cortex	---	---	0.15	(0.08; 0.22)	---	---	---	---

Table A11 (continued).

Air pollutant – Brain regions*	Pregnancy Coef	(95% CI)	Childhood 0-2y Coef	(95% CI)	Childhood 2-5y Coef	(95% CI)	Childhood 5-9y Coef	(95% CI)
$PM_{2.5}$absorbance (Δ $10^{-5}m^{-1}$)								
MT+ Complex and Neighboring Visual Areas - Early Auditory Cortex								
Left Area Lateral Occipital 3 - Right Primary Auditory Cortex	---	---	0.17	(0.10; 0.24)	---	---	---	---
Left Area Lateral Occipital 3 - Right RetroInsular Cortex	---	---	0.18	(0.10; 0.25)	---	---	---	---
Anterior Cingulate and Medial Prefrontal Cortex - Temporo-Parieto-Occipital Junction								
Left Area 25 - Right Superior Temporal Visual Area	---	---	0.16	(0.09; 0.24)	---	---	---	---
Somatosensory and Motor Cortex - Somatosensory and Motor Cortex								
Right Primary Motor Cortex - Right Area 2	---	---	0.18	(0.10; 0.25)	---	---	---	---
Right Area 2 - Right Area 3a	---	---	0.15	(0.08; 0.22)	---	---	---	---
Premotor Cortex - Premotor Cortex								
Right Premotor Eye Field - Right Ventral Area 6	---	---	0.17	(0.10; 0.24)	---	---	---	---
Premotor Cortex - Posterior Opercular Cortex								
Right Premotor Eye Field - Right Area OP4/PV	---	---	0.15	(0.08; 0.23)	---	---	---	---
Temporo-Parieto-Occipital Junction - Insular and Frontal Opercular Cortex								
Right PeriSylvian Language Area - Right Area PHT	---	---	0.17	(0.09; 0.24)	---	---	---	---
Premotor Cortex - Insular and Frontal Opercular Cortex								
Right Ventral Area 6 - Right Area PHT	---	---	0.16	(0.09; 0.23)	---	---	---	---
Posterior Cingulate Cortex - Anterior Cingulate and Medial Prefrontal Cortex								
Right Parieto-Occipital Sulcus Area 1 - Right Area a24	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right Area 31pd - Right area a24	---	---	0.15	(0.08; 0.22)	---	---	---	---
DorsoLateral Prefrontal Cortex - Inferior Parietal Cortex								
Right Area anterior 9-46v - Right Area IntraParietal 2	---	---	0.16	(0.09; 0.24)	---	---	---	---
Posterior Opercular Cortex - Lateral Temporal Cortex								
Right Area 43 - Right Area PHT	---	---	0.16	(0.09; 0.23)	---	---	---	---
Auditory Association Cortex - Dorsal Stream Visual Cortex								
Right Area TA2 - Right Area V6A	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right Area STGa - Right Area V6A	---	---	0.17	(0.10; 0.24)	---	---	---	---
Dorsal Stream Visual Cortex - Auditory Association Cortex								
Left Area V6 - Right Area STGa	---	---	---	---	0.17	(0.10; 0.24)	---	---
Right Area V6 - Right Area STGa	---	---	---	---	0.17	(0.10; 0.24)	---	---
Posterior Cingulate Cortex - Superior Parietal Cortex								
Left Parieto-Occipital Sulcus Area 2 - Right Area 7PC	---	---	---	---	0.16	(0.09; 0.22)	---	---

Table A11 (continued).

Air pollutant – Brain regions*	Pregnancy Coef	(95% CI)	Childhood 0-2y Coef	(95% CI)	Childhood 2-5y Coef	(95% CI)	Childhood 5-9y Coef	(95% CI)
$PM_{2.5}$absorbance (Δ $10^{-5}m^{-1}$)								
Anterior Cingulate and Medial Prefrontal Cortex - Posterior Cingulate Cortex								
Left Area 10r - Right Area 7m	---	---	---	---	0.16	(0.09; 0.22)	---	---
Right Area a24 - Right Area 31pd	---	---	---	---	0.16	(0.09; 0.23)	---	---
Right Area 10r - Right Area 31pd	---	---	---	---	0.16	(0.09; 0.23)	---	---
Right Area 10r - Right RetroSplenial Complex	---	---	---	---	0.16	(0.09; 0.23)	---	---
Right Area p32 - Right Area 31p ventral	---	---	---	---	0.17	(0.10; 0.24)	---	---
Right Area 10r - Right Area 31p ventral	---	---	---	---	0.18	(0.11; 0.25)	---	---
Posterior Cingulate Cortex - Inferior Parietal Cortex								
Right Area dorsal 23 a+b - Right Area PGi	---	---	---	---	0.16	(0.09; 0.23)	---	---
Superior Parietal Cortex - MT + Complex and Neighboring Visual Areas								
Left Area Lateral IntraParietal dorsal - Right Area Lateral Occipital 1	---	---	---	---	0.18	(0.10; 0.25)	---	---
Left Area Lateral IntraParietal dorsal - Right Area Lateral Occipital 1	---	---	0.16	(0.09; 0.24)	---	---	---	---
Right Ventral IntraParietal Complex - Left Area V3CD	---	---	0.16	(0.08; 0.23)	---	---	---	---
Insular and Frontal Opercular Cortex - Lateral Temporal Cortex								
Right Area Frontal Opercular 4 - Right Area PHT	---	---	---	---	0.17	(0.10; 0.25)	---	---
Left Middle Insular Area - Right Area PHT	---	---	0.16	(0.09; 0.24)	---	---	---	---
Right Area Frontal Opercular 5 - Right Area PHT	---	---	0.16	(0.09; 0.24)	---	---	---	---
Right Posterior Insular Area 2 - Right Area PHT	---	---	0.18	(0.11; 0.26)	---	---	---	---
Right Frontal OPercular Area 4 - Right Area PHT	---	---	0.18	(0.11; 0.25)	---	---	---	---
Right Middle Insular Area - Right Area PHT	---	---	0.17	(0.11; 0.25)	---	---	---	---
Right Pirform Cortex - Right Area PHT	---	---	0.15	(0.08; 0.22)	---	---	---	---
Right Frontal OPercular Area 4 - Right Area TE1 posterior	---	---	0.17	(0.09; 0.25)	---	---	---	---
Right Pirform Cortex - Right Area TG dorsal	---	---	0.15	(0.08; 0.21)	---	---	---	---
Insular and Frontal Opercular Cortex - MT+ Complex and Neighboring Visual Areas								
Right Area Frontal Opercular 5 - Right Area Lateral Occipital 3	---	---	---	---	0.17	(0.10; 0.24)	---	---

CI, confidence interval; Coef, coefficient; NO_x, nitrogen oxides; NO_2, nitrogen dioxide; $PM_{2.5}$absorbance, absorbance of $PM_{2.5}$ filters; PM_{COARSE}, particulate matter with aerodynamic diameter between 10 µm and 2.5µm.
Coefficients and 95% confidence intervals from linear regression models adjusted for maternal and paternal education, ethnicity, age, height, body mass index, and psychological distress during pregnancy, maternal smoking and alcohol use during pregnancy, parity, and intelligence quotient, family status, household income, and child's genetic ancestry, gender, and age at the scanning session. All brain regions survived the correction for multiple testing using false discovery rating.
The expected direction of the association was higher air pollution exposure during pregnancy and altered brain functional connectivity, without *a priori* hypothesis on the direction of the association.

*For organizational purposes, the cortical areas of parcellation were grouped into 22 regions based on several criteria: each region includes a set of geographically contiguous areas that can be seen in their entirety from a single viewing perspective

on the inflated cortical surface or in some cases on a flatmap. In addition, the areas within a region often share common properties, based on architecture, task-fMRI profiles, and/or functional connectivity (based on Glasser MF, Coalson TS, Robinson EC, Hacker CD, et al. A multi-modal parcellation of human cerebral cortex. Nature. 2016;536(7615):171-178)