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Supplemental Material

A Genome-Wide Analysis of DNA Methylation and Fine Particulate Matter Air Pollution in Three Study Populations: KORA F3, KORA F4, and the Normative Aging Study

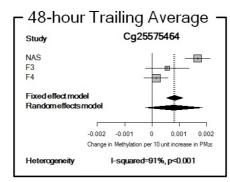
Tommaso Panni, Amar J. Mehta, Joel D. Schwartz, Andrea A. Baccarelli, Allan C. Just, Kathrin Wolf, Simone Wahl, Josef Cyrys, Sonja Kunze, Konstantin Strauch, Melanie Waldenberger, and Annette Peters

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Supplemental Code and Data Zip File

Excel File S1. FDR significant CpG sites for 28-day PM_{2.5}



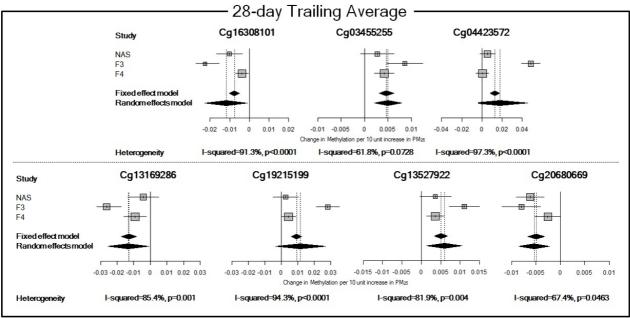


Figure S1. Forest plots for the eight CpG sites that showed Bonferroni genome-wide significance but results heterogeneous (I^2 p-value<0-05 or $I^2 > 0.5$).

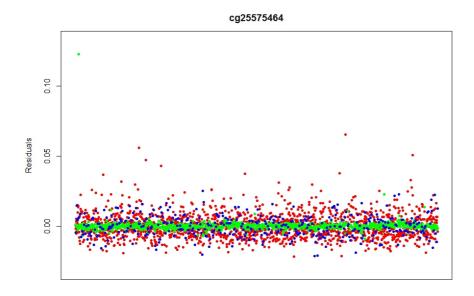


Figure S2. Residual plot for FDR significant CpG at 2-day average (F3=blue, F4=red, NAS=green).

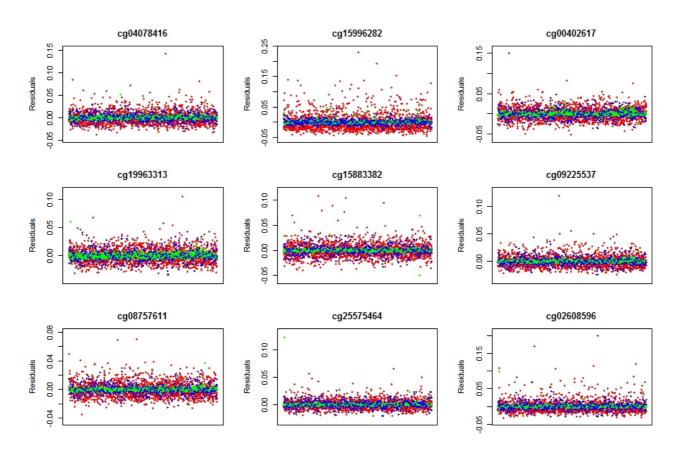


Figure S3. Residual plot for FDR significant CpG at 7-day average (F3=blue, F4=red, NAS=green).

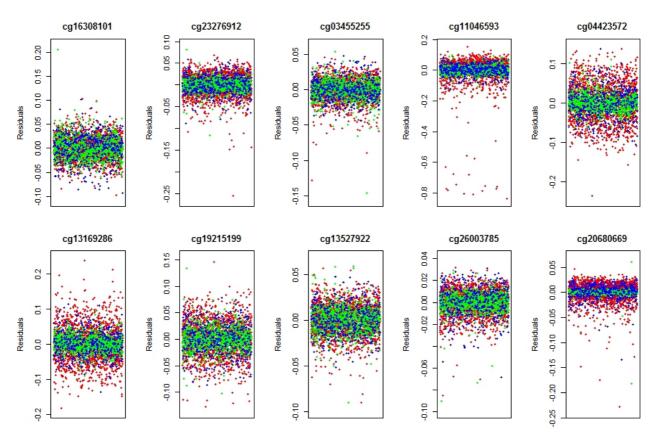


Figure S4. Residual plot for Bonferroni significant CpG at 28-day average (F3=blue, F4=red, NAS=green). For cg11046593, 21 methylation values were excluded and re-run the models and the meta-analysis. New p-value resulted 5.48E-08, still Bonferroni significant.

Table S1. Study specific regression coefficients of FDR (2- and 7-day average) and Bonferroni (28-day average) significant CpGs.

СрG	NAS		F3		F4			
	ß*	P-value	ß	P-value	ß	P-value		
2-day Trailing Average								
cg25575464†	0.00167	6.83E-12	5.58E-04	0.17597	1.51E-04	0.502384		
7-day Trailing Average								
cg00402617	0.00169	0.01372	0.00422	2.65E-05	0.00174	0.002803		
cg02608596	0.00204	5.02E-07	0.0012	0.138056	0.00106	0.096751		
cg04078416	0.00129	0.000277	8.52E-04	0.266829	0.00184	0.000476		
cg08757611	9.30E-04	5.95E-05	6.43E-04	0.279705	0.00122	0.001554		
cg09225537	0.00116	9.71E-05	0.00148	0.02347	9.22E-04	0.020167		
cg15883382	0.00295	4.15E-06	0.00105	0.181377	0.00125	0.013804		
cg15996282	0.0023	3.34E-05	0.00183	0.008537	0.00108	0.279726		
cg19963313†	0.00183	0.000141	0.00249	0.005548	0.00147	0.001984		
cg25575464	0.00248	7.86E-10	4.82E-04	0.390485	5.65E-04	0.07276		
28-day Trailing Average								
cg03455255	0.00271	0.140615	0.00857	1.81E-05	0.0042	7.24E-05		
cg04423572	0.00564	0.15232	0.04859	4.58E-22	5.25E-04	0.872754		
cg11046593	0.01191	0.007323	0.02234	5.85E-07	0.01072	0.072973		
cg13169286	-0.0043	0.360508	-0.0263	6.31E-09	-0.0092	0.009082		
cg13527922	0.0036	0.081134	0.01107	7.09E-08	0.00359	0.001815		
cg16308101	-0.0101	0.002248	-0.0225	1.13E-09	-0.0038	0.020929		
cg19215199	0.0027	0.49826	0.0283	5.52E-14	0.00441	0.04335		
cg20680669	-0.0061	2.95E-05	-0.008	7.67E-05	-0.0026	0.053071		
cg23276912	0.00639	0.038665	0.01122	5.64E-05	0.00596	0.000643		
cg26003785	0.00378	0.012775	0.00635	0.000282	0.00319	6.62E-05		

^{*} β express change in %5mC associated with a 10 µg/m³ increase in PM_{2.5}

[†] Bonferroni Significant

Table S2. Sensitivity analysis, comparison of fixed-effect regression coefficients (β) and p-values of fully-adjusted models in 28-day significant hits with and without yearly PM_{2.5} exposure adjustment.

	With lo	ng-term	Without long-term		
	ß*	P-value	ß*	P-value	
cg16308101	-0.0070	4.64E-07	-0.0076	2.86E-08	
cg23276912	0.0079	8.85E-09	0.0073	4.56E-08	
cg03455255	0.0050	5.37E-09	0.0047	1.86E-08	
cg11046593	0.016	1.28E-07	0.016	1.12E-08	
cg04423572	0.013	1.23E-08	0.013	7.26E-09	
cg13169286	-0.014	5.97E-08	-0.013	6.21E-08	
cg19215199	0.0095	4.32E-08	0.0093	3.66E-08	
cg13527922	0.0056	2.09E-09	0.0051	1.54E-08	
cg26003785	0.0033	1.10E-06	0.0038	9.53E-09	
cg20680669	-0.0020	2.36E-03	-0.0049	2.09E-08	

^{*} ß express change in %5mC associated with a 10 μ g/m³ increase in PM_{2.5}

Covariates: age, personal income (education years for NAS, in which information on income was not available), alcohol intake, BMI, temperature (moving average always matching with the PM exposure window) and the proportion of five white blood cell types: monocytes, B Cells, CD8 T cells, CD4 T cells, NK as continuous and sex, smoking status (never, former, current and passive only for KORA - smokers), day of the week and season as categorical