Supplementary information

The role of air pollution and lung function on cognitive impairment

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Table S1: Comparison of baseline characteristics of participants lost to follow-up and participants included in the analyses. Differences in the continuous variables were tested with the two-sample t-test and differences in the categorical variables were tested with Fisher's exact test at the 5% significance level.

	Lost between baseline and follow-up investigation (N=2785 with lung function at baseline)			**Lost due to selection of complete cases used in analysis (N=834 at follow-up investigation)**		
	Lost	**Available**	**p-value**	**Lost**	**Available**	**p-value**
N	1951	834		314	520	
BMI [kg/m^2], Mean (SD)	28.0 (4.8)	26.7 (3.9)	<0.001	26.9 (3.7)	26.6 (4.0)	0.209
Educational level, n/N (%)						
<10 years	569/1948 (29.2%)	144/813 (17.7%)	<0.001	52/293 (17.7%)	92/520 (17.7%)	0.481
=10 years	957/1948 (49.1%)	396/813 (48.7%)		150/293 (51.2%)	246/520 (47.3%)	
>10 years	422/1948 (21.7%)	273/813 (33.6%)		91/293 (31.1%)	182/520 (35.0%)	
Smoking, n/N (%)						
Active smoker	298/1872 (15.9%)	85/833 (10.2%)	<0.001	29/313 (9.3%)	56/520 (10.8%)	0.731
Ex-smoker	144/1872 (7.7%)	84/833 (10.1%)		30/313 (9.6%)	54/520 (10.4%)	
Never smoker	1430/1872 (76.4%)	664/833 (79.7%)		254/313 (81.2%)	410/520 (78.8%)	
Passive smoking, n/N (%)	965/1919 (50.3%)	390/828 (47.1%)	0.134	145/308 (47.1%)	245/520 (47.1%)	1.000
Urban area, n/N (%)	993/1951 (50.9%)	439/834 (52.6%)	0.408	209/314 (66.6%)	230/520 (44.2%)	<0.001
Rural area, n/N (%)	958/1951 (49.1%)	395/834 (47.4%)		105/314 (33.4%)	290/520 (55.8%)	
$PM_{2.5}$, (µg/m^3), Median (IQR)	33.4 (3.8)	33.3 (4.7)	<0.001	33.6 (4.2)	33.0 (4.9)	0.004
PM_{10}, (µg/m^3), Median (IQR)	51.3 (5.0)	50.2 (6.8)	<0.001	50.7 (5.4)	49.8 (8.0)	0.002
NO_2, (µg/m^3), Median (IQR)	36.1 (17.4)	34.7 (14.7)	<0.001	37.9 (14.5)	33.5 (13.8)	<0.001
GLI z-score FEV1, Mean (SD)	-0.6 (1.1)	-0.3 (1.0)	<0.001	-0.3 (1.1)	-0.2 (1.0)	0.531
GLI z-score FVC, Mean (SD)	-0.3 (1.0)	0.0 (0.9)	<0.001	-0.1 (1.0)	0.0 (0.9)	0.276
GLI z-score FEV1/FVC, Mean (SD)	-0.5 (0.9)	-0.4 (0.8)	0.046	-0.4 (0.9)	-0.4 (0.8)	0.445

Table S2: Mediation analysis (exposure: air pollution; mediator: lung function; outcome: visuo-construction performance (figure copying)) in all participants (N=520). Indirect, direct and total effects (95% confidence intervals and p-values).

			Indirect effects		Direct effects		Total effects	
	Mediator	**Exposure**	**β-estimate (95%-CI)**	**p-value**	**β-estimate (95%-CI)**	**p-value**	**β-estimate (95%-CI)**	**p-value**
Without exposure x mediator interaction	FEV_1	PM_{10}	-0.02 (-0.05;0.00)	0.068	-0.30 (-0.47;-0.13)	<0.001	-0.31 (-0.49;-0.15)	<0.001
		$PM_{2.5}$	-0.02 (-0.04;0.00)	0.062	-0.22 (-0.38;-0.07)	0.008	-0.24 (-0.40;-0.09)	0.004
		NO_2	-0.02 (-0.05;0.00)	0.104	-0.23 (-0.45;0.00)	0.046	-0.24 (-0.47;-0.02)	0.032
	FVC	PM_{10}	-0.01 (-0.04;0.01)	0.160	-0.30 (-0.47;-0.14)	<0.001	-0.32 (-0.49;-0.15)	<0.001
		$PM_{2.5}$	-0.01 (-0.04;0.01)	0.164	-0.23 (-0.38;-0.07)	0.008	-0.24 (-0.40;-0.09)	0.004
		NO_2	-0.02 (-0.05;0.01)	0.188	-0.23 (-0.45;-0.01)	0.044	-0.24 (-0.46;-0.02)	0.034
	FEV_1/FVC	PM_{10}	0.01 (-0.01;0.04)	0.312	-0.32 (-0.49;-0.14)	<0.001	-0.30 (-0.47;-0.14)	<0.001
		$PM_{2.5}$	0.01 (-0.01;0.03)	0.376	-0.24 (-0.40;-0.08)	0.004	-0.23 (-0.39;-0.08)	0.004
		NO_2	0.01 (-0.01;0.03)	0.532	-0.24 (-0.46;-0.02)	0.034	-0.23 (-0.46;-0.01)	0.032
With exposure x mediator interaction	FEV_1	PM_{10}	-0.02 (-0.04;0.00)	0.046	-0.28 (-0.45;-0.09)	<0.001	-0.30 (-0.46;-0.11)	<0.001
		$PM_{2.5}$	-0.01 (-0.04;0.00)	0.056	-0.20 (-0.35;-0.03)	0.016	-0.21 (-0.37;-0.04)	0.008
		NO_2	-0.02 (-0.06;0.00)	0.070	-0.23 (-0.44;-0.02)	0.032	-0.25 (-0.46;-0.04)	0.026
	FVC	PM_{10}	-0.01 (-0.03;0.00)	0.184	-0.29 (-0.45;-0.11)	<0.001	-0.30 (-0.46;-0.12)	<0.001
		$PM_{2.5}$	-0.01 (-0.03;0.00)	0.188	-0.21 (-0.36;-0.04)	0.014	-0.22 (-0.37;-0.06)	0.008
		NO_2	-0.02 (-0.05;0.01)	0.206	-0.23 (-0.44;-0.02)	0.030	-0.25 (-0.46;-0.03)	0.028
	FEV_1/FVC	PM_{10}	0.01 (-0.01;0.03)	0.466	-0.33 (-0.50;-0.15)	<0.001	-0.32 (-0.49;-0.15)	<0.001
		$PM_{2.5}$	0.01 (-0.01;0.03)	0.582	-0.25 (-0.41;-0.09)	0.006	-0.25 (-0.40;-0.08)	0.006
		NO_2	0.01 (-0.01;0.03)	0.500	-0.22 (-0.44;-0.01)	0.036	-0.22 (-0.43;0.00)	0.042

Approach utilizing exposure and mediator averages with interaction.
All models were adjusted for age, height, body mass index (BMI), socioeconomic status, current and former smoking, exposure to second hand smoke (SHS), living in an urban vs. rural area, APOE ε4, physical activity and depression.

Table S3: Mediation analysis (exposure: air pollution; mediator: lung function; outcome: visuo-construction performance (figure copying)) in never-smokers (N=410). Indirect, direct and total effects (95% confidence intervals and p-values).

			Indirect effects		Direct effects		Total effects	
	Mediator	**Exposure**	**β-estimate (95%-CI)**	**p-value**	**β-estimate (95%-CI)**	**p-value**	**β-estimate (95%-CI)**	**p-value**
Without exposure x mediator interaction	FEV_1	PM_{10}	-0.02 (-0.05;0.00)	0.064	-0.34 (-0.53;-0.15)	0.002	-0.36 (-0.55;-0.17)	<0.001
		$PM_{2.5}$	-0.02 (-0.05;0.00)	0.068	-0.26 (-0.43;-0.08)	0.004	-0.27 (-0.45;-0.10)	0.002
		NO_2	-0.02 (-0.05;0.01)	0.156	-0.16 (-0.41;0.09)	0.198	-0.18 (-0.43;0.07)	0.150
	FVC	PM_{10}	-0.02 (-0.04;0.00)	0.114	-0.34 (-0.53;-0.16)	<0.001	-0.36 (-0.54;-0.17)	<0.001
		$PM_{2.5}$	-0.02 (-0.04;0.00)	0.112	-0.26 (-0.43;-0.08)	0.004	-0.27 (-0.44;-0.10)	0.002
		NO_2	-0.02 (-0.06;0.01)	0.188	-0.16 (-0.41;0.09)	0.204	-0.18 (-0.42;0.07)	0.152
	FEV_1/FVC	PM_{10}	0.00 (-0.01;0.02)	0.674	-0.35 (-0.54;-0.16)	<0.001	-0.34 (-0.54;-0.16)	<0.001
		$PM_{2.5}$	0.00 (-0.01;0.02)	0.756	-0.26 (-0.44;-0.09)	0.002	-0.26 (-0.44;-0.09)	0.002
		NO_2	0.00 (-0.01;0.02)	0.880	-0.17 (-0.42;0.08)	0.182	-0.17 (-0.41;0.08)	0.190
With exposure x mediator interaction	FEV_1	PM_{10}	-0.02 (-0.04;0.00)	0.118	-0.32 (-0.51;-0.14)	0.004	-0.33 (-0.52;-0.15)	0.002
		$PM_{2.5}$	-0.01 (-0.04;0.00)	0.126	-0.23 (-0.41;-0.07)	0.012	-0.25 (-0.42;-0.08)	0.012
		NO_2	-0.02 (-0.06;0.01)	0.182	-0.17 (-0.41;0.07)	0.172	-0.19 (-0.43;0.05)	0.116
	FVC	PM_{10}	0.00 (-0.02;0.02)	0.982	-0.37 (-0.56;-0.19)	<0.001	-0.37 (-0.56;-0.18)	<0.001
		$PM_{2.5}$	0.00 (-0.02;0.02)	0.962	-0.28 (-0.45;-0.11)	0.004	-0.28 (-0.45;-0.11)	0.006
		NO_2	0.00 (-0.01;0.02)	0.942	-0.16 (-0.39;0.07)	0.208	-0.15 (-0.39;0.08)	0.206
	FEV_1/FVC	PM_{10}	-0.02 (-0.04;0.00)	0.118	-0.32 (-0.51;-0.14)	0.004	-0.33 (-0.52;-0.15)	0.002
		$PM_{2.5}$	-0.01 (-0.04;0.00)	0.126	-0.23 (-0.41;-0.07)	0.012	-0.25 (-0.42;-0.08)	0.012
		NO_2	-0.02 (-0.06;0.01)	0.182	-0.17 (-0.41;0.07)	0.172	-0.19 (-0.43;0.05)	0.116

Approach utilizing exposure and mediator averages with interaction.
All models were adjusted for age, height, body mass index (BMI), socioeconomic status, exposure to second hand smoke (SHS), living in an urban vs. rural area, APOE ε4, physical activity and depression.

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Table S4: Mediation analysis (exposure: air pollution; mediator: lung function; outcome: visuo-construction performance (figure copying)) in non-APOEε4 carriers (N=369). Indirect, direct and total effects (95% confidence intervals and p-values).

			Indirect effects		Direct effects		Total effects	
	Mediator	**Exposure**	**β-estimate (95%-CI)**	**p-value**	**β-estimate (95%-CI)**	**p-value**	**β-estimate (95%-CI)**	**p-value**
Without exposure x mediator interaction	FEV_1	PM_{10}	-0.02 (-0.06;0.00)	0.032	-0.19 (-0.38;-0.01)	0.034	-0.21 (-0.40;-0.03)	0.020
		$PM_{2.5}$	-0.02 (-0.06;0.00)	0.038	-0.15 (-0.32;0.02)	0.070	-0.17 (-0.35;0.00)	0.046
		NO_2	-0.02 (-0.06;0.00)	0.124	-0.11 (-0.34;0.11)	0.334	-0.13 (-0.36;0.09)	0.240
	FVC	PM_{10}	-0.01 (-0.04;0.01)	0.254	-0.20 (-0.39;-0.03)	0.022	-0.21 (-0.40;-0.04)	0.016
		$PM_{2.5}$	-0.01 (-0.04;0.01)	0.254	-0.16 (-0.33;0.01)	0.058	-0.17 (-0.34;-0.01)	0.044
		NO_2	-0.01 (-0.06;0.02)	0.376	-0.12 (-0.35;0.10)	0.286	-0.13 (-0.36;0.09)	0.246
	FEV_1/FVC	PM_{10}	0.01 (-0.02;0.04)	0.506	-0.21 (-0.40;-0.04)	0.018	-0.20 (-0.39;-0.03)	0.026
		$PM_{2.5}$	0.01 (-0.02;0.03)	0.564	-0.17 (-0.35;0.00)	0.046	-0.16 (-0.33;0.00)	0.054
		NO_2	0.00 (-0.02;0.03)	0.674	-0.13 (-0.36;0.09)	0.260	-0.12 (-0.36;0.10)	0.278
With exposure x mediator interaction	FEV_1	PM_{10}	-0.02 (-0.06;0.00)	0.046	-0.19 (-0.38;0.01)	0.066	-0.21 (-0.40;-0.02)	0.032
		$PM_{2.5}$	-0.02 (-0.05;0.00)	0.060	-0.14 (-0.31;0.04)	0.118	-0.16 (-0.33;0.02)	0.088
		NO_2	-0.02 (-0.07;0.01)	0.128	-0.13 (-0.36;0.10)	0.296	-0.15 (-0.38;0.08)	0.204
	FVC	PM_{10}	-0.01 (-0.04;0.01)	0.272	-0.20 (-0.39;-0.01)	0.040	-0.21 (-0.40;-0.02)	0.030
		$PM_{2.5}$	-0.01 (-0.04;0.01)	0.278	-0.15 (-0.33;0.03)	0.096	-0.16 (-0.34;0.02)	0.076
		NO_2	-0.01 (-0.05;0.02)	0.376	-0.13 (-0.36;0.10)	0.270	-0.14 (-0.38;0.08)	0.218
	FEV_1/FVC	PM_{10}	0.01 (-0.02;0.04)	0.596	-0.24 (-0.42;-0.04)	0.014	-0.23 (-0.42;-0.04)	0.014
		$PM_{2.5}$	0.00 (-0.02;0.03)	0.718	-0.19 (-0.36;-0.01)	0.038	-0.19 (-0.36;-0.01)	0.042
		NO_2	0.01 (-0.01;0.04)	0.560	-0.12 (-0.35;0.10)	0.298	-0.12 (-0.35;0.11)	0.332

Approach utilizing exposure and mediator averages with interaction.
All models were adjusted for age, height, body mass index (BMI), socioeconomic status, current and former smoking, exposure to second hand smoke (SHS), living in an urban vs. rural area, , physical activity and depression.

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