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## Association between Outdoor Air Pollution Exposure and Handgrip Strength: Findings from the French CONSTANCES Study

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### Introduction

Hand grip strength (HGS) is a powerful predictor of disability, morbidity, and mortality in middle-age and elderly subjects. Available evidence on the link between poor HGS and cigarette smoking<sup>1</sup> suggests the potential for a similar association for air pollution due to shared mechanisms.<sup>2</sup> Furthermore, evidence of a reduction in dopamine production in the brain following exposure to diesel exhaust particles<sup>3</sup> supports the hypothesized association between air pollution and HGS. We aimed to evaluate whether exposure to outdoor air pollution is associated with poor HGS in a large study on adults from all over mainland France.

### Materials and Methods

We used data on 51,845 out of 85,612 participants over 45 y old from the enrollment phase of the French CONSTANCES study until December 2017 (approved by the institutional review board of the Inserm: institutional review board de l’Inserm IRB00003888, IORG0003254, FWA00005831).<sup>4</sup> These participants were asked to attend physical and cognitive assessments, including three repeated HGS measurements in standing position for the dominant hand with a JAMAR portable Hand Dynamometer. Because a sex difference has been reported for HGS values, the sex-specific z-score of the maximum measurement (HGS<sub>max</sub>) was used as the outcome. Annual mean exposure for the year 2010 was assigned from a hybrid land-use regression model (LUR) at a fine spatial resolution (100 × 100 m) for western Europe for particulate matter (PM) with an aerodynamic diameter <2.5 μm (PM<sub>2.5</sub>), black carbon (BC), and nitrogen dioxide (NO<sub>2</sub>) (see supporting information: [https://github.com/mjzare/AP\\_HGS\\_CONSTANCES/blob/main/Air\\_pollution\\_HGS\\_CONSTANCES\\_Supporting\\_Information\\_20220326.docx?raw=true](https://github.com/mjzare/AP_HGS_CONSTANCES/blob/main/Air_pollution_HGS_CONSTANCES_Supporting_Information_20220326.docx?raw=true)).<sup>5</sup> The estimated concentrations for 2010 were assigned to each participant’s residential address at enrollment; participants’ residential history before enrollment could not be accounted for in the exposure assessment.

We used linear mixed models with a random intercept per recruitment center separately for each sex (and both sexes together for the interaction test) and reported adjusted regression coefficients (β) and 95% confidence intervals (CIs) for each pollutant

separately. We used multiple imputed data sets for missing covariates; exposures and outcome were neither imputed nor included in the imputation process. We defined two models: *a*) model 1 adjusted for covariates selected based on univariate analysis and *b*) model 2 additionally adjusted for possible mediators. For sensitivity analysis, we included women and men together in the same single-pollutant model (for models 1 and 2). We also tested the interaction by sex with inclusion of an interaction term between each pollutant and sex and checked the interaction term’s *p*-value. We conducted stratified analyses based on selected personal and contextual variables and conducted additional analyses using the z-scores of average HGS (HGS<sub>average</sub>). For these variables, we tested the interaction by including an interaction term between each pollutant and variable of interest and checked the significance of interaction by the likelihood-ratio test *p*-value.

### Results

The study sample included 51,845 participants (mean age: 57.4 ± 7.2 y); 50.3% (*n* = 26,092) were women, educated (49% more than 12 y of education), currently nonsmokers (58.4%), and residing in urban and suburban areas (75.5%). The average HGS<sub>max</sub> in men was significantly higher than in women (44.09 ± 8.72 and 27.01 ± 5.85 kg, respectively). The average exposure to PM<sub>2.5</sub>, BC, and NO<sub>2</sub> was 16.79 ± 3.12 μg/m<sup>3</sup>, 1.76 ± 0.54 10<sup>-5</sup>/m, and 25.09 ± 11.55 μg/m<sup>3</sup>, respectively.

Significant negative associations were found between exposure to all three pollutants (PM<sub>2.5</sub>, BC, and NO<sub>2</sub>) and HGS<sub>max</sub> in both men and women (Table 1). The associations with BC and NO<sub>2</sub> were weaker for women in comparison with those for men. Further adjustment for potential mediators in model 2 did not substantially change the size and direction of the estimates from model 1. Exposure–response analyses showed a linear and monotonic decrease in HGS<sub>max</sub> with increasing exposure to all pollutants in men (likelihood-ratio test *p*-values were as follows: 0.12 for PM<sub>2.5</sub>; 0.76 for BC; 0.74 for NO<sub>2</sub>). The findings for women suggested nonlinear trends for NO<sub>2</sub>, using models with spline term (likelihood-ratio test *p*-values: 0.67 for PM<sub>2.5</sub>; 0.24 for BC; 0.03 for NO<sub>2</sub>).

A significant interaction between pollutant and sex was found for all pollutants (Table 1). For men living in urban or suburban areas, all three air pollutants were significantly associated with poorer HGS<sub>max</sub>. We found stronger associations in men age 65 y and older, with low and middle education, and nonsmokers in comparison with the rest of the study participants. For women, we found no significant interaction with age. The findings were similar using average HGS (Table 2).

### Discussion

Our study adds to the scarce literature on the association between air pollution and HGS.<sup>2</sup> We found that an increase in PM<sub>2.5</sub>, BC,

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The authors declare they have nothing to disclose.

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**Table 1.** Association between exposure to outdoor air pollution and maximum HGS in the French CONSTANCES study participants (*n* = 51,845).

Pollutant	Model	Men	Women	All	<i>p</i> -Value for sex interaction
PM <sub>2.5</sub>	Model 1 <sup>a</sup>	-0.069 (-0.105, -0.033)	-0.077 (-0.115, -0.040)	-0.076 (-0.102, -0.050)	< 0.001
	Model 2 <sup>b</sup>	-0.067 (-0.103, -0.032)	-0.077 (-0.115, -0.040)	-0.075 (-0.101, -0.049)	< 0.001
Black carbon	Model 1 <sup>a</sup>	-0.088 (-0.117, -0.059)	-0.052 (-0.081, -0.022)	-0.072 (-0.093, -0.051)	< 0.001
	Model 2 <sup>b</sup>	-0.087 (-0.116, -0.058)	-0.050 (-0.079, -0.021)	-0.071 (-0.092, -0.050)	< 0.001
NO <sub>2</sub>	Model 1 <sup>a</sup>	-0.081 (-0.108, -0.054)	-0.053 (-0.080, -0.025)	-0.069 (-0.088, -0.049)	< 0.001
	Model 2 <sup>b</sup>	-0.079 (-0.106, -0.053)	-0.052 (-0.080, -0.024)	-0.068 (-0.087, -0.048)	< 0.001

Note: HGS, hand grip strength; PM<sub>2.5</sub>, particulate matter with an aerodynamic diameter <2.5 μm.

<sup>a</sup>Regression coefficients and 95% confidence intervals; all estimates are based on an interquartile range increase in exposure (3.86 μg/m<sup>3</sup> for PM<sub>2.5</sub>; 0.73 10<sup>-5</sup>/m for black carbon; and 13.80 μg/m<sup>3</sup> for NO<sub>2</sub>) in the linear mixed model. Model 1: adjusted for age (year), education (<5 y; 5–12 y; more than 12 y), height (centimeters), household income (below and 2,100 euros/month; above 2,100 euros/month), marital status (unmarried; married or in a civil partnership; separated or divorced; widow), country of origin (France; other countries), smoking status (nonsmoker; ex-smoker; smoker), alcohol drinking (abstinent; no abuse or dependence; abuse; dependence), body mass index (in four groups; <18.5; 18.5–25; 25–30; >30), nonoccupational physical activity (scored from 0 to 6), socio-occupational status (farmer or craftsman; executive or intellectual profession; middle-level professional; employee; blue-collar worker), perceived health status (scored from 1 to 8), classification of the commune of residence (urban; suburban; isolated city; rural), and area-level deprivation index (categorized on tertiles), and center as a clustering variable.

<sup>b</sup>Model 2: In addition to the variables in model 1, further adjusted for depressive symptoms (yes; no), hypertension (yes; no), type 2 diabetes (yes; no), hypercholesterolemia (yes; no), hypertriglyceridemia (yes; no), neurological disorders (yes; no), respiratory disorders (yes; no), cardiovascular disorders (yes; no).

and NO<sub>2</sub> was associated with weaker HGS; estimates were higher in men for NO<sub>2</sub> and BC, but not for PM<sub>2.5</sub>. Because PM<sub>2.5</sub> contains many different hazardous components that cannot be distinguished by using the total mass of PM<sub>2.5</sub>, the effect of all these components may affect HGS differently than specific components such as BC. Considering the previously reported hazard ratio of 1.2 (95% CI: 1.17, 1.23) for all-cause mortality per 5 kg lower HGS,<sup>6</sup> estimated effect sizes for an interquartile range increase in the air pollutants included in our study would be roughly equivalent to 2.2%–2.8% and 1.1%–1.6% increase in all-cause mortality in men and women, respectively (from Celis-Morales et al.<sup>6</sup> study estimates). Direct evidence to compare our findings for BC and NO<sub>2</sub> is not available; however, considering a degree of analogy between air pollution and exposure to cigarette smoke, pesticides, solvents, and heavy metals (shares some chemical components)

and reported associations for exposure to these compounds and impaired HGS,<sup>1,7</sup> the observed associations in our study seem physiologically plausible. Sex differences have been reported in the risk factors of the HGS decline, and air pollution epidemiology studies also justify our findings on men and women.<sup>8,9</sup> A higher level of deprivation in rural areas could be an explanation for our findings on women residing in rural areas.<sup>10</sup>

The study benefits from a large sample size, good spatial variation in exposure from a validated LUR model, the inclusion of a wide range of personal and area-level covariates, and from being the first to provide results on BC and NO<sub>2</sub>. However, the cross-sectional study design limited us to drawing a cause–effect association. Exposure allocation with the LUR models from a single year assigned to the residential address at the time of enrollment may have introduced some nondifferential exposure misclassification. We excluded participants

**Table 2.** Regression coefficients (and 95% CI) from the linear mixed models between maximum HGS and an interquartile range increase in pollutants concentrations (3.86 μg/m<sup>3</sup> for PM<sub>2.5</sub>; 0.73 10<sup>-5</sup>/m for black carbon; and 13.80 μg/m<sup>3</sup> for NO<sub>2</sub>) in the French CONSTANCES study participants (the last line of the results of each pollutant is based on average HGS).

Group	Men ( <i>n</i> = 25,753)			Women ( <i>n</i> = 26,092)		
	<i>n</i>	Regression coefficient (95% CI)	<i>p</i> -Value for interaction	<i>n</i>	Regression coefficient (95% CI)	<i>p</i> -Value for interaction
PM <sub>2.5</sub>	—	—	0.03	—	—	0.69
Age	—	—	—	—	—	—
<65 y	4,891	-0.061 (-0.135, 0.012)	—	4,327	-0.051 (-0.131, 0.029)	—
>65 y	20,862	-0.070 (-0.110, -0.029)	—	21,765	-0.075 (-0.117, -0.033)	—
Education	—	—	0.04	—	—	0.95
Low and middle	13,696	-0.082 (-0.129, -0.034)	—	12,813	-0.097 (-0.148, -0.046)	—
High	12,057	-0.047 (-0.101, 0.006)	—	13,279	-0.048 (-0.102, 0.005)	—
BMI (kg/m <sup>2</sup> )	—	—	0.12	—	—	0.33
<25	9,989	-0.097 (-0.151, -0.042)	—	15,614	-0.068 (-0.116, -0.021)	—
25–30	11,800	-0.041 (-0.094, 0.012)	—	7,102	-0.066 (-0.137, 0.004)	—
>30	3,964	-0.071 (-0.161, 0.018)	—	3,376	-0.082 (-0.180, 0.015)	—
Smoking	—	—	0.12	—	—	0.84
Nonsmoker	9,904	-0.091 (-0.147, -0.034)	—	13,530	-0.083 (-0.134, -0.032)	—
Ex-smoker	12,353	-0.041 (-0.092, 0.010)	—	9,151	-0.072 (-0.134, -0.010)	—
Smoker	3,496	-0.095 (-0.189, -0.001)	—	3,411	-0.033 (-0.129, 0.062)	—
CVDs	—	—	0.55	—	—	0.01
No	22,671	-0.057 (-0.096, -0.019)	—	24,115	-0.075 (-0.114, -0.037)	—
Yes	3,082	-0.149 (-0.246, -0.051)	—	1,977	-0.059 (-0.183, 0.065)	—
Type 2 diabetes	—	—	0.23	—	—	0.93
No	23,568	-0.061 (-0.099, -0.024)	—	25,161	-0.075 (-0.113, -0.037)	—
Yes	2,185	-0.127 (-0.235, -0.019)	—	931	-0.020 (-0.175, 0.136)	—
Depression	—	—	0.97	—	—	0.04
No	21,957	-0.065 (-0.104, -0.027)	—	19,412	-0.085 (-0.127, -0.042)	—
Yes	3,796	-0.103 (-0.197, -0.009)	—	6,680	-0.041 (-0.114, 0.033)	—
Neurological disorders	—	—	0.97	—	—	0.23
No	24,750	-0.072 (-0.109, -0.036)	—	25,055	-0.078 (-0.116, -0.040)	—
Yes	1,003	-0.044 (-0.188, 0.099)	—	1,037	0.017 (-0.172, 0.207)	—
Urbanicity	—	—	0.35	—	—	0.01
Rural	4,617	-0.005 (-0.080, 0.070)	—	4,322	-0.108 (-0.192, -0.025)	—
Isolated cities	1,935	-0.059 (-0.190, 0.072)	—	1,836	0.012 (-0.118, 0.142)	—
Suburban	9,630	-0.066 (-0.122, -0.011)	—	9,768	-0.099 (-0.156, -0.042)	—
Urban	9,571	-0.087 (-0.158, -0.016)	—	10,166	-0.031 (-0.102, 0.040)	—

**Table 2.** (Continued.)

Group	Men (n = 25,753)			Women (n = 26,092)		
	n	Regression coefficient (95% CI)	p-Value for interaction	n	Regression coefficient (95% CI)	p-Value for interaction
Other analyses						
Average HGS	25,753	-0.072 (-0.108, -0.036)		26,092	-0.079 (-0.116, -0.042)	
Age	—	—	0.002	—	—	0.19
<65 y	4,891	-0.036 (-0.096, 0.023)		4,327	-0.101 (-0.167, -0.035)	
>65 y	20,862	-0.108 (-0.141, -0.074)		21,765	-0.049 (-0.082, -0.016)	
Education	—	—	0.08	—	—	0.59
Low and middle	13,696	-0.102 (-0.143, -0.060)		12,813	-0.029 (-0.071, 0.014)	
High	12,057	-0.071 (-0.112, -0.031)		13,279	-0.069 (-0.109, -0.028)	
BMI (kg/m <sup>2</sup> )	—	—	0.74	—	—	0.17
<25	9,989	-0.116 (-0.159, -0.073)		15,614	-0.062 (-0.099, -0.025)	
25–30	11,800	-0.059 (-0.103, -0.016)		7,102	0.000 (-0.057, 0.058)	
>30	3,964	-0.107 (-0.187, -0.027)		3,376	-0.083 (-0.167, 0.000)	
Smoking	—	—	0.02	—	—	0.76
Nonsmoker	9,892	-0.116 (-0.163, -0.070)		13,530	-0.052 (-0.094, -0.011)	
Ex-smoker	12,367	-0.059 (-0.101, -0.017)		9,151	-0.051 (-0.100, -0.003)	
Smoker	3,494	-0.101 (-0.177, -0.025)		3,411	-0.043 (-0.121, 0.036)	
CVDs	—	—	0.79	—	—	0.06
No	22,671	-0.079 (-0.109, -0.048)		24,115	-0.050 (-0.080, -0.019)	
Yes	3,082	-0.156 (-0.238, -0.074)		1,977	-0.044 (-0.146, 0.059)	
Type 2 diabetes	—	—	0.32	—	—	0.41
No	23,568	-0.082 (-0.112, -0.051)		25,161	-0.044 (-0.074, -0.014)	
Yes	2,185	-0.134 (-0.229, -0.040)		931	-0.136 (-0.283, 0.011)	
Depression	—	—	0.41	—	—	0.21
No	21,957	-0.072 (-0.103, -0.041)		19,412	-0.050 (-0.083, -0.016)	
Yes	3,796	-0.182 (-0.258, -0.106)		6,680	-0.049 (-0.108, 0.010)	
Neurological disorders	—	—	0.51	—	—	0.50
No	24,750	-0.091 (-0.121, -0.062)		25,055	-0.058 (-0.088, -0.028)	
Yes	1,003	-0.058 (-0.187, 0.070)		1,037	0.140 (-0.020, 0.300)	
Urbanicity	—	—	0.35	—	—	0.01
Rural	4,617	0.063 (-0.072, 0.198)		4,322	-0.124 (-0.282, 0.034)	
Isolated cities	1,935	0.139 (-0.056, 0.334)		1,836	0.020 (-0.178, 0.218)	
Suburban	9,630	-0.098 (-0.146, -0.050)		9,768	-0.067 (-0.115, -0.019)	
Urban	9,571	-0.095 (-0.136, -0.053)		10,166	-0.032 (-0.073, 0.010)	
Other analyses						
Average HGS	25,753	-0.087 (-0.116, -0.058)		26,092	-0.051 (-0.081, -0.022)	
NO <sub>2</sub>	—	—	0.003	—	—	0.31
Age	—	—		—	—	
<65 y	4,891	-0.038 (-0.093, 0.017)		4,327	-0.089 (-0.150, -0.027)	
>65 y	20,862	-0.097 (-0.127, -0.066)		21,765	-0.049 (-0.080, -0.018)	
Education	—	—	0.12	—	—	0.80
Low and middle	13,696	-0.098 (-0.136, -0.061)		12,813	-0.042 (-0.082, -0.003)	
High	12,057	-0.055 (-0.094, -0.017)		13,279	-0.060 (-0.098, -0.021)	
BMI (kg/m <sup>2</sup> )	—	—	0.58	—	—	0.30
<25	9,989	-0.102 (-0.142, -0.061)		15,614	-0.060 (-0.095, -0.025)	
25–30	11,800	-0.056 (-0.096, -0.016)		7,102	-0.012 (-0.066, 0.041)	
>30	3,964	-0.092 (-0.164, -0.020)		3,376	-0.081 (-0.158, -0.005)	
Smoking	—	—	0.03	—	—	0.84
Nonsmoker	9,904	-0.106 (-0.149, -0.062)		13,530	-0.059 (-0.098, -0.021)	
Ex-smoker	12,353	-0.054 (-0.093, -0.016)		9,151	-0.052 (-0.098, -0.006)	
Smoker	3,496	-0.089 (-0.161, -0.017)		3,411	-0.015 (-0.089, 0.058)	
CVDs	—	—	0.71	—	—	0.02
No	22,671	-0.068 (-0.097, -0.040)		24,115	-0.053 (-0.081, -0.024)	
Yes	3,082	-0.160 (-0.235, -0.084)		1,977	-0.034 (-0.130, 0.062)	
Type 2 diabetes	—	—	0.30	—	—	0.55
No	23,568	-0.074 (-0.102, -0.046)		25,161	-0.048 (-0.076, -0.020)	
Yes	2,185	-0.111 (-0.197, -0.024)		931	-0.094 (-0.229, 0.042)	
Depression	—	—	0.39	—	—	0.21
No	21,957	-0.066 (-0.095, -0.037)		19,412	-0.051 (-0.082, -0.019)	
Yes	3,796	-0.158 (-0.228, -0.087)		6,680	-0.052 (-0.107, 0.003)	
Neurological disorders	—	—	0.94	—	—	0.79
No	24,750	-0.081 (-0.108, -0.054)		25,055	-0.061 (-0.089, -0.033)	
Yes	1,003	-0.079 (-0.199, 0.041)		1,037	0.149 (0.005, 0.294)	
Urbanicity	—	—	0.35	—	—	0.01
Rural	4,617	0.032 (-0.057, 0.121)		4,322	-0.103 (-0.203, -0.003)	
Isolated cities	1,935	0.042 (-0.086, 0.170)		1,836	0.054 (-0.077, 0.185)	
Suburban	9,630	-0.094 (-0.137, -0.050)		9,768	-0.083 (-0.127, -0.039)	
Urban	9,571	-0.088 (-0.130, -0.047)		10,166	-0.024 (-0.066, 0.018)	
Other analyses						
Average HGS	25,753	-0.080 (-0.107, -0.053)		26,092	-0.052 (-0.079, -0.024)	

Note: All the estimates are based on the models adjusted for age (year), education (<5 y; 5–12 y; more than 12 y), height (centimeters), household income (below 2,100 euros/month; above 2,100 euros/month), marital status (unmarried; married or in a civil partnership; separated or divorced; widow), country of origin (France; other countries), smoking status (nonsmoker; ex-smoker; smoker), alcohol drinking (abstinent; no abuse or dependence; abuse; dependence), BMI (in four groups: <18.5, 18.5–25, 25–30, >30), nonoccupational physical activity (scored from 0 to 6), socio-occupational status (farmer or craftsman, executive or intellectual professional; middle-level professional, employee, blue-collar worker), perceived health status (scored from 1 to 8), classification of the commune of residence (urban, suburban, isolated city, rural), and area-level deprivation index (categorized on tertiles), depressive symptoms (yes, no), hypertension (yes, no), type 2 diabetes (yes, no), hypercholesterolemia (yes, no), hypertriglyceridemia (yes, no), neurological disorders (yes, no), respiratory disorders (yes, no), cardiovascular disorders (yes, no), and center as a clustering variable. —, no data; BMI, body mass index; CI, confidence interval; CVDs, cardiovascular disorders; HGS, hand grip strength; PM<sub>2.5</sub>, particulate matter (PM) with an aerodynamic diameter <2.5 μm.

without suitable HGS data, which could potentially result in healthier and more resilient retained participants. Even with these limitations, we found a significant association between air pollution exposure and lower HGS, which highlights the importance of evaluating frailty in relation to air pollution.

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