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Traffic-related Air Pollution in Relation to Cognitive Function in Older Adults

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Background: Few epidemiologic studies have investigated associations of air pollution with cognition in older adults, and none has specifically compared associations across particle sources. We investigated whether exposure to particulate air pollution, characterized by size and source, was associated with cognitive function and decline in cognitive function.

Methods: We included participants of the Whitehall II cohort who were residents of greater London and who attended the medical examination in study wave 2007–2009 (n = 2867). Annual average concentrations of particulate matter (PM) (PM$_{1.0}$ and PM$_{2.5}$ from all sources and from traffic exhaust) were modeled at resolution of $20 \times 20$ m for 2003–2009. We investigated the relationship between exposure to particles and a cognitive battery composed of tests of reasoning, memory, and phonemic and semantic fluency. We also investigated exposure in relation to decline in these tests over 5 years.

Results: Mean age of participants was 66 (standard deviation = 6) years. All particle metrics were associated with lower scores in reasoning and memory measured in the 2007–2009 wave but not with lower verbal fluency. Higher PM$_{2.5}$ of 1.1 μg/m$^3$ (lag 4) was associated with a 0.03 (95% confidence interval = −0.06 to 0.002) 5-year decline in standardized memory score and a 0.04 (−0.07 to −0.01) decline when restricted to participants remaining in London between study waves.

Conclusions: This study provides support for an association between particulate air pollution and some measures of cognitive function, as well as decline over time in cognition; however, it does not support the hypothesis that traffic-related particles are more strongly associated with cognitive function than particles from all sources.

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Life expectancy has doubled in the last century, leading to considerable aging of populations. Contemporary theories view aging as the result of a gradual, lifelong accumulation of subtle damage to cells and tissues over time, resulting in a finely graded inverse association between age and cognitive performance. Poor cognitive status is perhaps the single most disabling condition at older ages. The large heterogeneity in the cognitive status of older adults suggests that identifying modifiable risk factors that shape cognitive aging trajectories has considerable potential for prevention.

There is limited, but growing, epidemiologic evidence of an association between exposure to particulate air pollution and cognitive function. Epidemiologic studies showing a relationship between distance to high-traffic roadways and cognition suggest that particles from traffic sources, due either to their size or composition, may be particularly harmful. Similarly, toxicological studies provide evidence that ultra-fine particles (diameter of 100 nm or less), which are primarily from traffic exhaust in urban areas, can directly access the central nervous system. Relatively few epidemiologic studies investigating air pollution and cognition or decline over time in cognition have been conducted in older adults, and none has specifically compared associations across particle sources.

We investigated whether long-term exposure to particulate air pollution at residence was associated with cognitive function and decline in cognitive function. We hypothesized that particles from traffic exhaust would have stronger associations than particles from all sources combined.

METHODS

Study Population

Our analysis included a subset of participants of the Whitehall II longitudinal cohort study, which enrolled 10,308 London-based civil servants between 1985 and 1988 to investigate psychosocial and biological risk factors of coronary disease. Participants are invited to a medical examination every 5 years, and a postal questionnaire is sent between...
Exposure to Air Pollution

Annual average concentrations for the years 2003–2009 were modeled at resolution of 20 × 20 m using an approach described in detail elsewhere.14,15 Particulate matter (PM) was modeled according to size and source, including PM_{10} (PM with diameter ≤ 10 μm), PM_{2.5} (PM with diameter ≤ 2.5 μm), and PM_{<2.5} from traffic exhaust only. Briefly, KClurban is a dispersion modeling system based on ADMS dispersion model v.4 and road source model v.2.3,16 which incorporates meteorologic data measured hourly, empirically derived NO–NO_{2}–O_{3} and PM relationships, and emissions from the London Atmospheric Emissions Inventory.17 Model evaluation statistics indicate good agreement between the model and measurements: \( r = 0.78 \) for PM_{10} (year 2008, 76 measurement sites) and \( r = 0.74 \) for PM_{2.5} (year 2008, 15 sites).

Exposure at residence was based on the average concentration at model grid points within 25 m of the residential postcode center. For participants who moved within London between study waves (n = 389), we did not know the date of the move; exposure was assigned as follows. Exposure for years 2003–2006 was based on the address at the 2002–2004 study wave and for years 2007–2009, the address at the 2007–2009 wave (39% moved less than 100 m). Participants who moved outside of Greater London between the study waves (n = 213) were assigned exposure based on their address at the 2002–2004 study wave. Various averaging periods were constructed, including a 1-year average (concentration during the year of the 2007–2009 cognition assessment; yearly lag 0; similarly, yearly lags 1–4 correspond to 1–4 years prior to 2007–2009 assessment; 3-year average (3 years preceding the 2007–2009 assessment: average of yearly lags 1–3) and 5-year average (year of 2007–2009 measurements plus 4 preceding: average of yearly lags 0–4). For example, if a participant’s 2007–2009 cognition assessment took place in 2007, modeled concentrations for the year 2007 were assigned to yearly lag 0, concentrations for the year 2006 were assigned to yearly lag 1, year 2005 assigned to yearly lag 2, and so on. For this person, the 3-year average exposure would be the average of modeled concentrations for 2006, 2005, and 2004, and the 5-year average exposure would be the average of modeled concentrations for 2007, 2006, 2005, 2004, and 2003.

Cognition Measurements

The set of cognitive function tests was chosen to provide a comprehensive assessment of cognition and to be appropriate for the age range in the study population. The tests were administered as part of a medical examination in 2002–2004 and 2007–2009. The tests included in the analysis had good test–retest reliability (range 0.60–0.89)18 and included the following. Reasoning was measured using the Alice Heim 4-I test, which is composed of a series of 65 verbal and mathematic reasoning items of increasing difficulty. The test measures inductive reasoning, the ability to identify patterns and infer principles and rules. Short-term verbal memory was measured with a 20-word free-recall test in which participants were presented a list of 20 or 2 syllable words at 2-second intervals and were then asked to recall them in writing (in any order, within 2 minutes). Two measures of verbal fluency were assessed: semantic and phonemic. To measure semantic fluency, participants were asked to recall in writing as many animal names as they could within 1 minute. To measure phonemic fluency, participants were similarly asked to recall words beginning with “S.” We did not include neurodegenerative diseases in the analysis because numbers are very small given the relatively young age of the cohort at the last follow-up (mean age = 66 years).

Covariates

Data on sociodemographic characteristics, socioeconomic position, and medical conditions were recorded via questionnaire. The following set of covariates based on the 2007–2009 assessment was considered in the analysis. Sociodemographic variables included age (continuous in years), sex, ethnicity (white or nonwhite), marital status (married/cohabiting, single, divorced/separated/widowed), educational achievement (none or lower primary school, lower secondary school, higher secondary school, university, or higher degree), socioeconomic position (using the British civil service grades of employment, high, intermediate, low). Health behaviors included: smoking status (current, past, never); alcohol use (none, moderate, heavy use derived from the number of drinks consumed in the past week); frequency of fruit and vegetable consumption; physical activity categorized as active (≥2.5 hours/week of moderate or 1 hour/week of vigorous physical activity), inactive (<1 hour/week of either moderate or vigorous physical activity), or moderately active (if not active or inactive).19 Health measures included systolic and diastolic blood pressure, serum cholesterol levels, prevalence of stroke, coronary heart disease and diabetes, and frequency of depressive symptoms measured using the Center for Epidemiological Studies Depression Scale.20 In the analysis of cognitive data from 2007 to 2009, models included age, sex, year of screening, and any other covariates that were independent predictors.
of at least one of the cognition tests and also associated with PM$_{2.5}$. In the analysis of cognitive decline, models included age, sex, age-by-time interaction, and any other covariates that were predictive of change in at least one of the cognition tests over time and also associated with PM$_{2.5}$.

**Statistical Analysis**

To allow comparability across cognitive tests, all scores were converted to z-scores (mean = 0, standard deviation = 1), such that a positive score represents better performance. For the analysis of cognitive data assessed in 2007–2009, scores were standardized using distributions at that wave. For the analysis of cognitive decline between 2002–2004 and 2007–2009, scores were standardized using the 2002–2004 distributions. Only participants with complete covariate data were included in the models.

For the analysis of cognitive data from 2007 to 2009, we used linear regression models to estimate the association between pollutants and standardized cognitive scores. To allow comparability across pollutants, associations are reported per interquartile range (IQR) change in 5-year average exposure. The functional form of the exposures and each continuous covariate was explored by fitting a smooth function in a generalized additive model. We then used an analysis-of-deviance approach to test whether a nonlinear function improved the model fit compared with a linear term. Analyses were conducted using R software (2.15.2, R Foundation for Statistical Computing, Vienna, Austria). In sensitivity analyses, participants who moved outside of London between study waves were excluded ($n = 213$).

For the analysis of cognitive decline, linear mixed models were used to estimate the association between exposure to pollutants and cognitive decline between the 2002–2004 and 2007–2009 assessments. We included 2 exposure windows: (1) 5-year average exposure and (2) 4 years prior to the 2007–2009 assessment (yearly lag 4), which was included because residential address was most certain for all participants at that time. We found that the average exposure effect was different across the 4 tests in a model fit with an exposure-by-test interaction term. This suggested our data did not support combining the 4 tests into a single score for global cognition, as has been done in other studies, which can improve statistical power and reduce multiple testing.$^8$ We therefore modeled each test separately. The models included a random intercept for each subject and random slope for time, allowing for differences across individuals in cognition in 2002–2004 and rate of decline. The linear mixed model included terms for time (difference between screening dates in years, divided by 5); age, sex, ethnicity, socioeconomic position, physical activity level, alcohol use, age-by-time interaction, air pollution, and air pollution-by-time interaction. The air pollution-by-time interaction term represents the mean difference in cognition over a 5-year period per IQR change in air pollution. Mixed models were run using SAS software (9.3, SAS Institute, Cary, NC). In sensitivity analyses, we (1) excluded participants who moved outside of London between study waves; (2) adjusted the models for area-level income; and (3) adjusted for education scores from the Index of Multiple Deprivation at the Lower Layer Super Output area level.$^{21}$

**RESULTS**

Participants were predominantly white men retired from work (Table 1); their mean age was 66 years. During the 5 years between 2002–2004 and 2007–2009, average exposure to total

| TABLE 1. Sociodemographic and Clinical Characteristics$^a$ of Participants in 2007–2009, Plus Cognitive Function Scores in 2002–2004 and 2007–2009 |
| Characteristics | No.       |
|-----------------|-----------|
| Age (years); mean (SD) | 2,867 66 (6) |
| Male            | 2,867 65  |
| White           | 2,867 86  |
| Married/cohabiting | 2,807 72  |
| Smoking         | 2,861  |
| Never           | 51       |
| Former smoker   | 42       |
| Current         | 7        |
| Heavy alcohol consumption | 2,782 15 |
| Physically active$^a$ | 2,862 49 |
| Last known employment grade | 2,853  |
| Low             | 15       |
| Intermediate    | 45       |
| High            | 41       |
| Work status     | 2,862  |
| Remaining in civil service | 14 |
| Working outside civil service | 18 |
| Retired/other   | 68       |
| University degree or higher | 2,530 39 |
| Body mass index (kg/m$^2$); mean (SD) | 2,857 26.7 (4.6) |
| Ever diagnosed with stroke or TIA | 2,867 5 |
| Ever diagnosed with diabetes | 2,867 16 |
| Blood pressure (mmHg); mean (SD) | 2,861 123.6 (15.9) |
| Systolic        | 2,861  |
| Diastolic       | 2,861 69.7 (10.0) |
| Cognitive function scores; mean (SD) | 2002–2004 |
| Reasoning       | 2,767 42.7 (12.0) |
| Memory          | 2,762 6.8 (2.5)  |
| Semantic fluency| 2,761 15.4 (4.0) |
| Phonemic fluency| 2,749 15.7 (4.2) |
| 2007–2009 |
| Reasoning       | 2,791 42.0 (12.3) |
| Memory          | 2,785 6.2 (2.3)  |
| Semantic fluency| 2,783 14.9 (3.9) |
| Phonemic fluency| 2,780 15.1 (4.1) |

SD indicates standard deviation; TIA, transient ischemic attack.

$^a$Percent, unless otherwise specified.

$^b$$ > 2.5$ hour/week moderate physical activity or $ > 21$ hour/week vigorous physical activity.
PM$_{10}$ was 23.4 μg/m$^3$ and to total PM$_{2.5}$, 14.9 μg/m$^3$; average exposures from vehicle exhaust were 0.72 μg/m$^3$ for PM$_{10}$ and 0.64 μg/m$^3$ for PM$_{2.5}$ (Table 2). Correlations between pollutants for the same averaging period were very high (0.90–0.99) (eTable 2, http://links.lww.com/EDE/A805). Correlations between averaging periods for the same pollutant were more variable (0.30–0.99) (eTable 3, http://links.lww.com/EDE/A805).

**Association Between Air Pollution and 2007/2009 Cognition**

All particle metrics and all averaging times were associated with lower scores on reasoning (Figure). The strongest associations were observed for total PM$_{2.5}$ for yearly lag 2 (coefficient −0.045 [95% confidence interval (CI) = −0.090 to 0.000]), yearly lag 3 (−0.046 [95% CI = −0.088 to −0.005]), and yearly lag 4 (−0.043 [−0.082 to −0.004]). For comparison, the effect of a 1-year increase in age on reasoning was −0.033 (−0.038 to −0.028). Compared with the other tests, precision was highest for the reasoning test. A similar pattern was observed for memory, where each particle metric and averaging time was consistently associated with lower memory score, with the strongest associations for total PM$_{2.5}$ yearly lags 3 and 4. However, the precision in the estimates was low.

**TABLE 2. Distribution of Exposure to Pollutants over Various Averaging Times (n = 2,867)**

| Pollutant by Averaging Time | Mean (SD) | 25  | 50  | 75  | IQR | Coefficient of Variation |
|----------------------------|----------|-----|-----|-----|-----|--------------------------|
| PM$_{10}$ (μg/m$^3$)       |          |     |     |     |     |                         |
| Total                      |          |     |     |     |     |                         |
| Yearly lag 0               | 21.5 (1.6)| 20.3| 21.1| 22.2| 0.9 | 0.07                     |
| Yearly lag 4               | 24.7 (1.9)| 23.4| 24.3| 25.6| 2.2 | 0.08                     |
| 3-year average             | 24.2 (1.5)| 23.2| 24.0| 25.0| 1.8 | 0.06                     |
| 5-year average             | 23.4 (1.5)| 22.4| 23.2| 24.2| 1.8 | 0.06                     |
| Due to exhaust             |          |     |     |     |     |                         |
| Yearly lag 0               | 0.57 (0.22)| 0.42| 0.53| 0.66| 0.23| 0.39                    |
| Yearly lag 4               | 0.91 (0.36)| 0.67| 0.82| 1.05| 0.38| 0.40                    |
| 3-year average             | 0.78 (0.30)| 0.58| 0.71| 0.90| 0.33| 0.38                    |
| 5-year average             | 0.72 (0.27)| 0.54| 0.66| 0.83| 0.30| 0.38                    |
| PM$_{2.5}$ (μg/m$^3$)      |          |     |     |     |     |                         |
| Total                      |          |     |     |     |     |                         |
| Yearly lag 0               | 13.1 (0.9)| 12.4| 13.0| 13.7| 1.3 | 0.07                    |
| Yearly lag 4               | 16.2 (1.4)| 15.3| 15.8| 16.6| 1.3 | 0.09                    |
| 3-year average             | 15.7 (0.9)| 15.1| 15.6| 16.2| 1.1 | 0.06                    |
| 5-year average             | 14.9 (0.9)| 14.2| 14.7| 15.4| 1.1 | 0.06                    |
| Due to exhaust             |          |     |     |     |     |                         |
| Yearly lag 0               | 0.51 (0.20)| 0.38| 0.47| 0.59| 0.21| 0.39                    |
| Yearly lag 4               | 0.81 (0.32)| 0.60| 0.73| 0.94| 0.34| 0.40                    |
| 3-year average             | 0.70 (0.27)| 0.52| 0.63| 0.81| 0.29| 0.39                    |
| 5-year average             | 0.64 (0.25)| 0.48| 0.59| 0.74| 0.27| 0.39                    |

Three-year average exposure based on average of yearly lags 2, 3, and 4. Five-year average exposure based on yearly lags 0 through 4.

**DISCUSSION**

Our analysis of within-city variation in particulate air pollution in relation to 4 tests of cognition resulted in 3 key findings. First, air pollution was associated with lower scores on reasoning, with stronger associations for the years more distant in time compared with the year of or year before the cognitive assessment. Associations with other cognitive tests were less clear. Second, counter to our hypothesis, there was no indication that particles from traffic exhaust were more strongly associated with cognition compared with total particle mass concentration. Third, when participants who moved out of greater London between study waves were included, we observed associations for decline in memory with exposure 4 years preceding the second assessment. The stronger association after excluding movers is likely due to reduced exposure misclassification.

This analysis included a relatively large population (n = 2867, 94% of whom contributed cognitive data at both waves) residing in Europe’s largest city. Nonetheless, the spatial variation in exposure in this population was relatively limited and resulted in generally imprecise effect estimates. The standard deviation in PM$_{2.5}$ over 5 years was 0.9 μg/m$^3$, considerably lower than in a similar study with participants in multiple US cities (2.8 μg/m$^3$). The coefficient of variation was much higher for PM$_{2.5}$ from exhaust sources compared...
with total PM$_{2.5}$, which resulted in better precision for the estimates related to PM from exhaust (Figure). However, the point estimates for total PM$_{2.5}$ were consistently larger in magnitude compared with those for PM$_{2.5}$ from exhaust sources. One possible explanation for the larger associations for total PM than for PM from exhaust sources is larger error.
in the modeled concentrations for traffic exhaust. No direct evaluation statistics are available for PM by specific sources, but emissions inventories by source type are likely to be more uncertain than for PM mass concentration. Similarly, exposure misclassification may be greater for exhaust PM if penetration indoors is lower than for total PM, or if error from assigning exposure based on postcode rather than address is greater for more spatially variable components of PM. This finding may also be due to chance.

Despite our efforts to adjust for confounding, the pattern of positive associations between particle exposure and verbal fluency measured in the 2007–2009 wave are unlikely to be causal and may be due to residual confounding. The analysis of change in cognitive function over time associated with particle exposure shows a decline in verbal fluency for PM$_{2.5}$ and yearly lag 4 exposure to PM$_{10}$, although small positive associations remain for the traffic exhaust metrics. (eTable 5, http://links.lww.com/EDE/A805, shows minimally and fully adjusted effect estimates for comparison).

Direct comparisons of our results with those from other epidemiologic studies in older adults are complicated by the use of different cognitive tests, reported on different scales, and for different pollutants. Our results for PM$_{2.5}$ exhaust are broadly comparable with findings from other studies investigating the relationship between black carbon (predominantly from traffic sources) at residence and cognition. Power et al. observed 0.054 lower global cognition as a z-score (95% CI = −0.103 to −0.006) for a doubling in black carbon in 680

**TABLE 3.** Five-Year Change in Cognitive Function Per IQR Change in Pollution

| Exposure (IQR, μg/m$^3$) | Reasoning | Memory | Semantic Fluency | Phonemic Fluency |
|---------------------------|-----------|--------|-----------------|-----------------|
| PM$_{10}$ (1.8)           |           |        |                 |                 |
| 5-year average            | $-0.011$  | $-0.023$ | $0.000$         | $0.003$         |
|                           | ($−0.032$ to $0.010$) | ($−0.071$ to $0.025$) | ($−0.035$ to $0.035$) | ($−0.032$ to $0.039$) |
| Yearly lag 4              | $-0.010$  | $-0.029$ | $-0.011$        | $-0.009$        |
|                           | ($−0.026$ to $0.006$) | ($−0.065$ to $0.007$) | ($−0.037$ to $0.016$) | ($−0.036$ to $0.018$) |
| PM$_{10}$ exhaust (0.30)  |           |        |                 |                 |
| 5-year average            | $-0.007$  | $-0.012$ | $0.005$         | $0.004$         |
|                           | ($−0.025$ to $0.011$) | ($−0.053$ to $0.029$) | ($−0.025$ to $0.035$) | ($−0.027$ to $0.034$) |
| Yearly lag 4              | $-0.003$  | $-0.010$ | $0.005$         | $0.010$         |
|                           | ($−0.016$ to $0.011$) | ($−0.041$ to $0.021$) | ($−0.018$ to $0.027$) | ($−0.013$ to $0.033$) |
| PM$_{2.5}$ (1.1)          |           |        |                 |                 |
| 5-year average            | $-0.013$  | $-0.033$ | $-0.006$        | $-0.003$        |
|                           | ($−0.034$ to $0.007$) | ($−0.080$ to $0.015$) | ($−0.040$ to $0.029$) | ($−0.038$ to $0.031$) |
| Yearly lag 4              | $-0.010$  | $-0.030$ | $-0.011$        | $-0.009$        |
|                           | ($−0.024$ to $0.004$) | ($−0.062$ to $0.002$) | ($−0.035$ to $0.012$) | ($−0.033$ to $0.015$) |
| PM$_{2.5}$ exhaust (0.27) |           |        |                 |                 |
| 5-year average            | $-0.007$  | $-0.012$ | $0.005$         | $0.004$         |
|                           | ($−0.025$ to $0.011$) | ($−0.053$ to $0.029$) | ($−0.025$ to $0.035$) | ($−0.027$ to $0.034$) |
| Yearly lag 4              | $-0.003$  | $-0.010$ | $0.005$         | $0.010$         |
|                           | ($−0.016$ to $0.011$) | ($−0.041$ to $0.021$) | ($−0.018$ to $0.028$) | ($−0.013$ to $0.033$) |

Associations adjusted for time, age, sex, ethnicity, socioeconomic position, physical activity level, alcohol use, age × time interaction, and main effect of exposure.

**TABLE 4.** Five-Year Change in Cognitive Function Per IQR Change in Pollution Excluding Participants Who Moved Out of Greater London Between Study Waves

| Exposure (IQR, μg/m$^3$) | Reasoning | Memory | Semantic Fluency | Phonemic Fluency |
|---------------------------|-----------|--------|-----------------|-----------------|
| PM$_{10}$ (1.8)           |           |        |                 |                 |
| 5-year average            | $-0.007$  | $-0.039$ | $-0.004$        | $0.005$         |
|                           | ($−0.029$ to $0.015$) | ($−0.090$ to $0.011$) | ($−0.038$ to $0.037$) | ($−0.033$ to $0.042$) |
| Yearly lag 4              | $-0.010$  | $-0.041$ | $-0.013$        | $-0.010$        |
|                           | ($−0.026$ to $0.007$) | ($−0.079$ to $−0.003$) | ($−0.041$ to $0.015$) | ($−0.038$ to $0.018$) |
| PM$_{10}$ exhaust (0.30)  |           |        |                 |                 |
| 5-year average            | $-0.002$  | $-0.028$ | $0.005$         | $0.008$         |
|                           | ($−0.021$ to $0.017$) | ($−0.073$ to $0.017$) | ($−0.028$ to $0.038$) | ($−0.025$ to $0.041$) |
| Yearly lag 4              | $0.002$   | $-0.022$ | $0.005$         | $0.015$         |
|                           | ($−0.013$ to $0.017$) | ($−0.056$ to $0.012$) | ($−0.019$ to $0.030$) | ($−0.010$ to $0.040$) |
| PM$_{2.5}$ (1.1)          |           |        |                 |                 |
| 5-year average            | $-0.011$  | $-0.048$ | $-0.007$        | $-0.003$        |
|                           | ($−0.032$ to $0.011$) | ($−0.098$ to $0.002$) | ($−0.044$ to $0.029$) | ($−0.040$ to $0.034$) |
| Yearly lag 4              | $-0.010$  | $-0.039$ | $-0.014$        | $-0.010$        |
|                           | ($−0.025$ to $0.004$) | ($−0.073$ to $−0.005$) | ($−0.039$ to $0.011$) | ($−0.035$ to $0.015$) |
| PM$_{2.5}$ exhaust (0.27) |           |        |                 |                 |
| 5-year average            | $-0.002$  | $-0.028$ | $0.005$         | $0.008$         |
|                           | ($−0.021$ to $0.017$) | ($−0.073$ to $0.017$) | ($−0.028$ to $0.038$) | ($−0.025$ to $0.041$) |
| Yearly lag 4              | $0.002$   | $-0.022$ | $0.005$         | $0.015$         |
|                           | ($−0.013$ to $0.017$) | ($−0.056$ to $0.012$) | ($−0.019$ to $0.030$) | ($−0.010$ to $0.040$) |

Associations adjusted for time, age, sex, ethnicity, socioeconomic position, physical activity level, alcohol use, age × time interaction, and main effect of exposure.
men included in the Normative Aging Study. Our results for a
doubling of 5-year average PM$_{2.5}$ exhaust correspond to 0.054 lower reasoning (95% CI = −0.189 to 0.082). Wellenius and colleagues$^{10}$ observed an association between black carbon and lower performance on the Hopkins Verbal Learning Test of immediate recall in 756 older adults; however, there were no clear associations with other tests, including semantic and phonemic fluency. In this same study, closer proximity of residence to major roadways was associated with poorer performance on several cognitive tests, including those measuring executive function and memory, suggesting a link with traffic sources either through air pollution or noise. Similarly, in a cohort of 400 women in the Ruhr area of Germany, a 1 μg/m$^3$ increase in 5-year average PM$_{2.5}$ was associated with 0.6 lower (95% CI = −1.4 to 0.02) total CERAD-Plus score (includes 18 items covering verbal fluency, phonemic fluency, memory, among others). The association for residence 50 m or less from a high traffic roadway was more pronounced: −3.8 (95% CI = −7.8 to 1.1), corresponding to an effect of about one-third the standard deviation of the score.$^{11}$ In a large study of long-term exposure to PM$_{2.5}$ on decline in cognition in older women in the United States, a 10 μg/m$^3$ increase in PM$_{2.5}$ was associated with a 0.014 decline (95% CI = −0.035 to 0.007) in z-score for verbal memory; 0.002 decline (−0.027 to 0.023) in verbal fluency; and 0.032 decline (−0.056 to 0.007) for the digit-span-backwards test over 2 years.$^6$ These associations are comparable with those we observed for a 1.1 μg/m$^3$ increase in 5-year average PM$_{2.5}$ and decline over 5 years. A rough comparison can also be made to the effect of persistent active smoking compared with never smokers in the Whitehall II population. Persistent smokers had a decline of 0.075 in z-score for memory and 0.055 in executive function (reasoning combined with verbal fluency) over 5 years compared with never smokers, which corresponds to about 2–4 times the magnitude of our observed effects for PM$_{2.5}$ on memory and reasoning, respectively.$^{19}$

A relationship between PM and cognitive function may be based on several proposed biological mechanisms, involving cerebral vascular damage, neuroinflammation, and neurodegeneration. Particulate air pollution or exposure to traffic has been associated with measures of arterial structure and function that are inversely associated with cognitive function$^{22}$ including carotid intima media thickness$^{23–25}$ and arterial stiffness.$^{26}$ Particulate air pollution has also been associated with a number of cardiovascular risk factors that may mediate the relationship with cognitive impairment,$^{22}$ including homocysteine,$^{27}$ blood pressure,$^{28}$ and diabetes.$^{29}$ Particle exposure has also been linked to increased systemic inflammation,$^{30}$ which may lead to cellular damage and modification of the reactive oxygen species/cytokine balance in the brain.$^{31}$ Systemic inflammation from air pollution may also contribute to the deterioration of olfactory, respiratory, and blood–brain barriers, enhancing access of particles to the central nervous system.$^{32}$ Toxicological studies indicate that inhaled ultrafine particles and transition metals translocate from the respiratory system directly into the central nervous system via the olfactory nerve.$^{12,32}$ Ultrafine particles have been identified in the brains of highly exposed dogs and humans.$^{33,34}$ However, the precise mechanism of toxicity of particles once they have reached the central nervous system remains unclear.$^{32}$

The strengths of this study include a relatively large cohort with comprehensive data on socioeconomic position and education, which are important confounders of the relationship between air pollution exposure and cognitive function. The detailed exposure information is another strength. Exposure was based on high-spatial resolution data from an established emissions-dispersion model that allowed for breakdown of particles by size and source. Nonetheless, limitations to our exposure assessment should be considered in interpreting the results. Exposure was based at residence and therefore does not take into account the influence of specific activities (eg, commuting) or other locations (eg, workplace) on exposure. Residential stability, penetration of outdoor PM and other pollutants indoors, and indoor sources were also not explicitly accounted for. Nonetheless, the majority of participants did not move in the 5 years prior to the 2002–2004 assessment: for 81% the postcode centre was identical, and for 88% the postcode centre moved less than 100 m. Also, the role of air conditioning in exposure misclassification is likely to be negligible given that less than 3% of residences in England have air conditioning units.$^{35}$ Most of the variability in long-term exposure in this cohort should be from residential exposure, given that the cohort consists of office-based workers, with no significant occupational particle exposures and most worked in central London locations with similar pollution levels. Despite the fine resolution of the exposure model, the gradient in exposures across London was limited, resulting in limited precision in our estimated associations. A further limitation is that we did not have data on exposure to traffic noise, which could have resulted in some residual confounding, particularly for the PM exhaust metrics. Less residual confounding is expected for PM$_{10}$, which is not likely to be as highly correlated with traffic noise. Finally, the analysis of decline in cognitive function was based on 2 assessments roughly 5 years apart. Future analyses using an additional wave of data may be able to improve the precision of our estimates.

In conclusion, this study provides support for an association between particulate air pollution and reasoning and decline over time in memory. The findings in relation to verbal fluency were less conclusive. These results do not support the hypothesis that traffic-related particles are more strongly associated with cognitive function compared with particles from all sources combined. However, the role of particle size and source should be explored in further research with better statistical power to investigate highly correlated exposure metrics. If the relationship between air pollution and cognitive function is causal, interventions to reduce exposure could deliver substantial health benefits given the relatively high global levels and ubiquitous nature of the exposure.
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