Title: Long-term Exposure to Outdoor Air Pollution and Cognitive Performance: Findings from the Harmonised Cognitive Assessment Protocol Sub-Study of the English Longitudinal Study of Ageing (ELSA-HCAP)

Abstract

Background – Although air pollution has been associated with worse cognitive performance, whether these relationships differ by cognitive domain, and which sources of air pollution are particularly detrimental for cognition remains understudied. This study examined associations between 8-10 years of exposure to air pollutants (NO_2, total $PM_{2.5}$, and $PM_{2.5}$ from different emission sources) and cognitive scores across three cognitive domains in older adults.

Methods – We used data from the 2018 Harmonized Cognitive Assessment Protocol (HCAP) sub-study of the English Longitudinal Study of Ageing (N=1,127). Outdoor concentrations of each pollutant for all HCAP respondents' residences were estimated for 2008/10-2017 and summarised using means and group-based trajectory modelling. Linear regression models were used to assess the relationships of long-term air pollution exposure with memory, executive function, language, and global cognitive function after adjustment for key individual and neighbourhood-level confounders.

Results – The associations between outdoor air pollution trajectories and cognition are mostly inverted j-shaped, suggesting that respondents exposed to the highest residential levels of NO_2 and total $PM_{2.5}$ had worse performance for global cognition [β=-0.241; 95%CI=(-0.46,-0.02) and β=-0.334; 95%CI=(-0.55,-0.12) respectively] than those exposed to average levels of pollution. Similar associations were also found for executive function and memory ($PM_{2.5}$ only), whereas more compelling dose-response evidence was found for language. Higher emissions from industry and residential combustion as well as biofuel, coal, oil and natural gas combustion were associated with worse language scores.

Conclusions – Older people's cognitive performance might benefit from continued efforts to reduce air pollution, particularly where levels are the highest.

Keywords – NO_2; $PM_{2.5}$, Emission sources; Cognition; Pollution

Introduction

Ageing-related decline in cognitive function contributes to reductions in life expectancy, quality of life, and social participation [1-5]. With a rapidly ageing global population, identifying drivers of heterogeneity in cognitive function during ageing is therefore a pressing public health issue. Among the modifiable factors associated with cognitive health, a growing body of evidence supports the link between exposure to outdoor air pollutants and worse cognitive function [6-10]. In their report, Livingston and colleagues estimate the population-attributed fraction for air pollution for dementia at 2.6%, higher than the one calculated for hypertension and physical inactivity [11]. In particular, exposure to nitrogen dioxide (NO_2) and particulate matter with aerodynamic diameters less than 2·5 μm ($PM_{2.5}$) are most implicated for cognitive health [8, 9, 12]. Although the biological pathways underlying associations between air pollution and cognitive function are not yet fully understood and specific air pollutants may affect the brain and cognitive health differently, it is hypothesised that air pollution adversely affects both the central nervous system and the circulatory system, leading to increased cognitive decline and risk of dementia [13, 14]. It is also understood that there may be direct impacts to the brain since the smallest particles can travel to the brain through the olfactory bulb and cross the blood-brain barrier[15].

Several knowledge gaps in this area of research remain. First, despite evidence that associations between air pollution and cognitive function may differ by cognitive domain, few studies have investigated the links between air pollution and specific cognitive domains, with findings inconsistent in direction and magnitude depending on the type of pollutant and the cognitive domain considered [16-23]. For instance, Gatto et al. [19] reported no association between exposure to NO_2 and executive function but found increasing exposure to $PM_{2.5}$ associated with lower verbal learning among healthy residents living in the Los Angeles, California area of the United States (US). Tonne et al [20], however, found that increased exposure to $PM_{2.5}$ was associated with reduced reasoning ability among Whitehall II study residents of Greater London, United Kingdom (UK). Using the UK Biobank, Cullen et al [21] found that exposure to NO_2 was associated with better reasoning scores but lower visuospatial memory. Second, $PM_{2.5}$ originates from many sources in the environment including traffic, coal-fired power plants, and agricultural emissions, and each source can emit $PM_{2.5}$ with distinct physical and chemical characteristics. For example, components such as black carbon (BC) and nitrates are more common in $PM_{2.5}$ from traffic-related sources, whereas ammonium is often in $PM_{2.5}$ from agriculture. However, to date, few studies have examined associations between specific constituents of $PM_{2.5}$ and cognitive function, with most focusing on BC and traffic-related exposures [23-26]. The only study so far that has considered broader sources of $PM_{2.5}$ emissions has focused on dementia, and found that $PM_{2.5}$ from agriculture and wildfires were particularly detrimental for incident dementia in the US [27]. Finally, although it is common practice to examine the association between air pollutants and cognitive function by taking the mean concentration of air pollutants over the study period, this approach might not account for different patterns and levels of exposures to air pollutants over time.

In this study, we attempt to fill these gaps in knowledge by examining associations of long-term exposure to NO_2, total $PM_{2.5}$, and source-specific $PM_{2.5}$ measured over a period of up to 10-years with cognitive function. Cognitive function is assessed using the Harmonised Cognitive Assessment Protocol (HCAP), a detailed set of neuropsychological assessments designed to measure key cognitive domains affected by cognitive aging (including memory, executive function, and language) and facilitate cross-national comparisons between national cohort studies of ageing. We examine long-term exposure to air pollution using both mean air pollution concentration during the study period, as well as by classifying participants into 10-year trajectories of air pollution concentrations.

Method

Study Population

Our study population was adults aged 65 years and over living in private households in England in 2018. We used data from wave 4 (2008-09) of the English Longitudinal Study of Ageing (ELSA) and wave 1 (2018) of the Harmonized Cognitive Assessment Protocol (HCAP) sub-study of ELSA (ELSA-HCAP). ELSA is a nationally representative cohort study of adults aged 50 years and above, living in private households in England [28]. ELSA started in 2002 and data are collected biennially using face-to-face personal interviews and self-completion questionnaires; more than 18,000 people have taken part in the study since its inception. Refreshment samples of new participants have been recruited regularly to maintain the age profile and ensure that the study remains representative of the English population aged 50 years and over.

The HCAP was implemented in a subset of ELSA participants to examine mild cognitive impairment and dementia using more detailed assessments of cognitive function than possible in the main interviews of ELSA [29]. A probability sample of ELSA participants who did not use a proxy for their core ELSA interview, were aged 65 years or older in January 2018, and had completed an ELSA interview in person at either wave 8 (2016–17) or wave 7 (2014–15) were invited to participate in ELSA-HCAP interviews that took place between January and April 2018. To ensure adequate sample sizes of participants with dementia, participants with low cognitive scores (assessed using telephone interview cognitive screening and/or Alzheimer's disease or dementia previously self-reported in ELSA interviews) were oversampled. Of the 1,684 eligible respondents invited to the study, 1,272 completed the face-to-face HCAP interview (response rate 76%). More details of ELSA and ELSA-HCAP surveys' sampling frame, methodology, and questionnaires can be found at www.elsa-project.ac.uk. ELSA was approved by the London Multicentre Research Ethics Committee (MREC/01/2/91) and the ELSA-HCAP sub-study received ethical approval from the South Central-Berkshire National Health Services (NHS) Research Ethics Committee. Informed consent was obtained from all participants or their guardians. All ELSA data are available through the UK Data Service (SN 5050 and 8502).

In the present study, demographic and socioeconomic characteristics of ELSA-HCAP participants were drawn from ELSA core interviews. Though most ELSA-HCAP participants first participated in ELSA during wave 1 (2002), 257 (20%) were first interviewed in wave 4 (2008-09); to retain these individuals, we therefore considered ELSA wave 4 (2008-09) as the baseline wave in the analyses.

Exposure Assessment

Environmental exposome data are drawn from the Gateway to Global Aging Data (https://exposome.g2aging.org). Full details on the environmental exposome data, their spatial and temporal resolutions, and links to the original source information are presented by D'Souza and colleagues [30] and can be found at the Gateway exposome site. Briefly, spatiotemporal prediction models were used to estimate annual average estimates of total NO_2 concentrations and $PM_{2.5}$ levels for each ELSA-HCAP participant based on their residential addresses. Estimates for NO_2 were predicted at a resolution of 50m x 50m from 2005 to 2019 and were generated using models that included remote sensing from the Ozone Monitoring Instrument, road networks, built environments, and meteorological variables [31]. Annual mean concentrations of total $PM_{2.5}$ were available at a 1 km^2 resolution from 2010 to 2019 and were created using the Data Integration Model for Air Quality that combines information from satellite remote sensing and chemical transport models, meteorological information, correlations over space, and ground-based monitoring data [32]. As ELSA wave 4 (2008-09) was the baseline wave for this study, we considered air pollution data recorded between 2008 and 2017 for NO_2 and between 2010 and 2017 for $PM_{2.5}$.

Source-specific $PM_{2.5}$ concentrations were derived by multiplying the yearly average $PM_{2.5}$ concentration at each address by local fractions of $PM_{2.5}$ attributable to different emission sources. These fractions were generated at a resolution of 0.5° × 0.625° (~55km × ~70km) by serially running an atmospheric chemistry-transport model (GEOS-Chem) with all sources but one to isolate the unique contribution of that source to the total $PM_{2.5}$ mixture [33]. Although these emission-specific fractions were generated using data from 2017, prior evidence suggests that these estimates are representative for previous years as well [27]. In this study, we focused on agriculture, energy production, industry, residential combustion, and road traffic as sector-specific sources of $PM_{2.5}$. Altogether, these sources accounted for ~61% of the total $PM_{2.5}$ emissions. We also considered fuel-specific sources with primary emissions including solid biofuel, coal, and liquid oil and natural gas combustion. These sources and the percentage of total $PM_{2.5}$ they account for are described in Supplementary Table S1.

Cognitive function

The HCAP battery was designed to assess key cognitive domains affected by cognitive ageing, including memory, executive function, and language. In ELSA-HCAP, respondents were administered a range of cognitive tests adapted from the original battery by Langa and colleagues [34]; these included well-established neurocognitive assessments such as the "East Boston Memory Test" and the "Wechsler Memory Scale", immediate and delayed recall, backwards counting tasks, and shape drawing. Details of cognitive testing protocols and tests used (with relevant references) are available in the ELSA-HCAP Technical Report [35] and its profile description [29]. Cognitive scores for each cognitive domain were produced using the procedure described by Gross et al [36]. These scores have been shown to have high reliability and be useful for population-based research on cognition. Scores for executive function, language, and memory were derived using factor analysis of cognitive tests relevant to each domain, with a similar procedure also used for general cognition. The derived cognitive scores were normally distributed (Supplementary Figure S1); to facilitate their interpretation, scores were standardised using the mean and standard deviation of the analytic sample, with positive scores representing above-the-average scores.

Covariates

Potential confounders of the relationship between long-term exposure to outdoor air pollution and cognitive function were drawn from ELSA wave 4 (2008-09) and included age, sex, age at which participants completed their highest education qualification, and total wealth, defined as the sum of financial, physical, and housing wealth (divided into quintiles). We also included a summary measure of cognitive function (based on tests of immediate and delayed recall and verbal fluency administered in ELSA wave 4). Based on each participant's residential location, we also included urbanicity, measured according to the 2001 Census Urban/Rural Indicator, and neighbourhood socioeconomic status (in quintiles) measured using the 2007 Index of Multiple Deprivation that accounts for area dimensions including income, employment, living environment, and crime [37].

Statistical Analysis

We adopted two strategies to summarise long-term exposure to air pollution. First, for each of the air pollutants (NO_2, total $PM_{2.5}$, and source-specific $PM_{2.5}$), we calculated mean-centred average concentrations and interquartile range (IQR) over the period under study (2008-2017 for NO_2; 2010-2017 for $PM_{2.5}$), in line with previous literature on long-term exposure to outdoor air pollution. Second, we applied group-based trajectory modelling [38] to investigate if there were distinctive trajectory patterns of exposure to different air pollutants over time and understand how these trajectories relate to cognitive function.

A group-based trajectory modelling framework takes into account the dependency of observations and assumes a mixture of subpopulations with different individual trajectories within the target population and identifies distinctive groups within which individuals share similar trajectories [39, 40]. Both linear and nonlinear trajectories can be captured by introducing higher-order polynomial growth parameters into the model. For each subject, the model provides the probability of belonging to each of the identified trajectory groups and assigns the subject to the trajectory group based on the highest probability. To determine the optimal number of trajectory groups within our sample, we fitted unconditional group-based trajectory models using up to ten years of data (2008-2017) on outdoor air pollution, with missing data for air pollutants handled using full information maximum likelihood estimation. We tested 1-7 trajectory groups, with the optimal number of groups selected using a wide range of criteria including the Akaike Information Criterion (AIC), the Bayesian Information Criterion (BIC), and its sample size-corrected version (c-BIC). For each of these, lower scores indicate (relatively) better fitting models. We also considered the following criteria: overall average posterior probabilities of group membership as a measure of classification quality (APPA is an entropy index, with values approaching 1.0 indicating a favourable classification); group size (no trajectory groups should include <5% of participants to ensure reproducibility of the results); the usefulness of the number of groups in terms of the similarities/differences in their trajectory shapes; and the interpretability of these distinctive trajectories [38, 39]. After determining the optimal number of trajectory groups, we established the optimal shape of the trajectory by testing growth parameters for each trajectory group up to the fifth degree. Higher order growth parameters (quadratic to quintic) were dropped if not statistically significant ($p<0.05$). Trajectories were estimated for NO_2, $PM_{2.5}$, and each of the source-specific $PM_{2.5}$ concentrations.

We used linear regression models to estimate associations between air pollution and cognitive performance for NO_2 and total $PM_{2.5}$, then for source-specific $PM_{2.5}$. These models first included mean air pollution during the study period (2005-2017 for NO_2; 2010-2017 for $PM_{2.5}$)

fitted as continuous exposures. We then fitted models including the air pollution trajectory group as categorical exposure; we chose as the reference trajectory group the one with the trajectory closest to the mean concentration of that pollutant during the study period (as this level was used for the continuous exposures). For both continuous and categorical exposures, we fitted basic models (Model 1), where we adjusted for age and sex and fully-adjusted models (Model 2), where we further adjusted for education, wealth, urbanicity, area-level deprivation, and the summary cognitive function measure assessed at baseline. All models were weighted to account for differential probability of selection into ELSA-HCAP, non-response (especially for the low cognition group, which had the lowest response rate), and the ELSA study design [35]. Data management, trajectories, and statistical analyses were performed using Stata/MP 18.0 (and the *traj* plugin) [41, 42].

Results

Sample descriptives; NO_2 and $PM_{2.5}$ pollution mean and trajectories

For this study, we selected all HCAP-ELSA respondents with no missing data on the exposure, outcome, or key confounders described above, with a final analytical sample of 1,172 respondents. At ELSA wave 4, respondents were aged 65 years on average (SD=7); 54% were female and 77% were living in an urban area, with 25% in the highest wealth quintile and 14% living in the most deprived area quintile (Table 1). The mean (SD) 10-year average NO_2 concentration between 2008 and 2017 was 22.89 (6.36) μg/m^3 and it was 11.89 (1.53) μg/m^3 for total $PM_{2.5}$ between 2010 and 2017.

Over the years under study, there was a general decline in both levels of NO_2 and $PM_{2.5}$, with the mean levels of NO_2 reducing from 24.18 μg/m^3 in 2008 to 21.36 μg/m^3 in 2017, and for $PM_{2.5}$ from 13.52 μg/m^3 in 2010 to 10.33 μg/m^3 in 2017 (Figure 1, Supplementary Table S2). As shown in Figure 1, we identified five NO_2 exposure trajectories (Supplementary Table S3), and four $PM_{2.5}$ trajectories (Supplementary Table S4). Although the slopes of the trajectory groups were statistically different and the changes in absolute values of air pollutants over time were not equal across groups, substantially the trajectory groups were largely parallel and are labelled in descending order of average exposure (groups 1-5 for NO_2 and groups 1-4 for $PM_{2.5}$). For instance, 20% of the respondents were exposed to a mean level of 9.71 μg/m^3 of $PM_{2.5}$ (with values reducing by 2.38 μg/m^3 from 10.92 in 2010 to 8.53 μg/m^3 in 2017) compared to 7% of the sample who were exposed to higher levels of $PM_{2.5}$ (an average of 15.16 μg/m^3, reducing by 4.43 μg/m^3 from 17.43 μg/m^3 in 2010 to 13.00 μg/m^3 in 2017). Source-specific and fuel-specific $PM_{2.5}$ values are presented in Table 1 and their trajectories are presented in Supplementary Figures S2 and S3.

Outdoor air pollution and cognitive performance

Table 2 shows the associations between cognitive performance and NO_2 and total $PM_{2.5}$ for each cognitive domain. When we considered air pollution as a continuous exposure, in models only adjusted for age and sex (Model 1), higher NO_2 concentrations were generally associated with lower overall cognitive performance [β=-0.013; 95%CI=(-0.02;-0.00)], executive function [β=-0.016; 95%CI=(-0.03,-0.01)], and language [β=-0.016; 95%CI=(-0.03,-0.01)]. However, adjustment for other covariates weakened these associations and the main model findings (Model 2) remained statistically significant only for language [β=-0.013; 95%CI=(-0.02,-0.00)]. When we considered groups of exposure to NO_2, results suggest that even accounting for key personal and neighbourhood confounders, compared to those who experienced an average level of NO_2 between 2008 and 2017 of 24.07 μg/m^3, respondents in the group of highest exposure (at an average level of 36.34 μg/m^3) had worse performance for overall cognitive function [β=-0.241; 95%CI=(-0.46,-0.02)], executive function [β=-0.291; 95%CI=(-0.54,-0.04)], and language [β=-0.328; 95%CI=(-0.59,-0.07)]. Regardless of whether NO_2 exposure was considered as a continuous or categorical variable, no associations between memory and NO_2 were found although the direction of association generally suggested lower scores of cognitive performance on average with higher exposure.

For total $PM_{2.5}$, when we assessed the relationship between 8-year mean exposure and cognitive performance, we only found an association with the cognitive domain related to language [β=-0.039; 95%CI=(-0.08,-0.00)]. However, when trajectory groups were considered, we found that those exposed to the highest levels of $PM_{2.5}$ (at an average level of 15.16 μg/m^3) had consistently worse cognitive scores than those who experienced an average level of exposure to $PM_{2.5}$ (11.48 μg/m^3) in the years under study. This relationship was observed for both overall cognitive function [β=-0.334; 95%CI=(-0.55,-0.12)] as well as executive function [β=-0.292; 95%CI=(-0.57,-0.01)], language [β=-0.222; 95%(CI=-0.44,-0.01)], and memory [β=-0.376; 95%CI=(-0.58,-0.17)] though there was no clear evidence of a compelling concentration-response function across the groups.

Tables 3 and 4 report fully adjusted associations between source-specific and fuel-specific $PM_{2.5}$ and cognitive function (with basic Models 1 available in Supplementary Tables S5 and S6). Overall, we observed weak or no associations between source-specific $PM_{2.5}$ and cognitive performance, with the exception that $PM_{2.5}$ from industry and residential combustion were associated with worse language scores [β=-0.364; 95%CI=(-0.64,-0.09) and β=-0.321; 95%CI=(-0.54,-0.11) respectively]; a similar direction and strength of associations was found when industry and residential combustion were examined using trajectory groups. Agriculture and road traffic also demonstrated similar trends though these could not be distinguished from no associations. The only cognitive domain associated with fuel-specific emissions was language where overall, lower levels of $PM_{2.5}$ derived from solid biofuel, coal, as well as liquid oil and natural gas combustion were all associated with better performance (Table 5). Analysis using IQR change in air pollutions, that account for differences across the observed ranges in concentrations, are available in Supplementary Table S7.

Discussion

In this population-based study of English respondents aged 65 and older, air pollution exposure was associated with poorer cognitive performance, both overall and in the specific domains of executive function, language, and to some extent memory. However, we found some differences in the magnitude and direction of these associations depending on whether we used continuous or categorical measurements of the cumulative past exposure of the participants to outdoor air pollution. On the one hand, when we analysed the average concentration during the period of exposure as a linear term (i.e., cognitive function vs. a unit change from the mean), our results reached the conventional threshold level of 5% for statistical significance only for language, for both NO_2 and $PM_{2.5}$. Partly, this could be caused by power issues as the sample was relatively small and the estimated 95% confidence intervals just overlapped zero, with the direction of associations as expected. On the other hand, when we considered these exposures as categorical groups based on their levels and trends, we found that older adults experiencing the highest levels of outdoor air pollution had consistently poorer cognitive performance than those exposed to average levels of NO_2 and $PM_{2.5}$, with especially compelling associations for language and $PM_{2.5}$. Although the percentage of respondents classified in the group exposed to the highest levels of NO_2 (at an average of 36.34 $\mu g/m^3$) and $PM_{2.5}$ (at an average of 15.16 $\mu g/m^3$) is relatively small at 6-7%, this represents more than half a million people aged 65 and older in England. Efforts made to reduce air pollution concentration in the past decades should therefore continue, with a specific focus on those residential areas where outdoor pollution levels are the highest.

Our findings are broadly in line with associations found in previous studies that have assessed the links between exposure to outdoor air pollution and cognitive performance. However, the direction of associations are not always consistent with previous findings. For instance, the association between exposure to highest levels of NO_2 and poorer cognitive performance (overall as well as executive function and language domains) was in line with Zare Sakhvidi et al [23] but not with other studies that found links with dimensions of memory or even higher scores of cognition for higher exposure to NO_2 [19, 21, 22]. Similarly, exposure to highest levels of $PM_{2.5}$ was associated with lower cognitive scores overall and in all three domains of cognition studied, but these findings are not always in line with previous studies that have found associations for some but not all domains of cognition [16-22]. Moreover, it is worth mentioning that in our analyses based on trajectory groups, results are suggestive of a consistent monotonic concentration-response only for language and $PM_{2.5}$. For the other air pollutants and cognitive domains, the associations are inverted j-shaped, similarly to findings reported elsewhere [12, 43, 44]. The suggestion that older people exposed to the lowest level of air pollution have lower cognitive scores than those exposed to average levels contradicts our initial hypothesis. Although our study adjusts for key individual and neighbourhood-level characteristics, it is still possible that the advantages for cognition of living in an area with lower levels of pollution are offset by other factors such as economic development, access to medical insurance and health services, or housing characteristics. Future research should explore this issue with different data source(s) that allow the inclusion of a wider range of potential confounders.

Some of the inconsistencies between our findings and previous studies are also likely driven by the apparent differences across study designs and settings. For example, outdoor air pollution in previous studies was collected between 2000 and 2017 with exposure ranging between one to ten years prior to cognitive testing; its operationalisation included mostly continuous but also categorical (tertiles or quartiles) measures; and the median values of exposures ranged from 9.9 to 25.1 $\mu g/m^3$ for $PM_{2.5}$, and from 25.5 to 48.1 $\mu g/m^3$ for NO_2,, reflecting different levels of exposure to air pollution in different geographical settings. Additionally, and more importantly, the tests used to assess global and domain-specific cognitive scores as well as the methods used to construct and operationalise them were different from one study to another. Finally, the sample characteristics themselves were quite different – as an illustration, the mean age of the study participants ranged from 57 to 76 years old, and this range might well influence the scores in the cognitive tests, the exposure to air pollution, and the selectivity of the sample.

Our study also extends the existing literature by examining associations of cognitive performance with sector- and fuel-specific $PM_{2.5}$ emissions. We found that higher levels of $PM_{2.5}$ from the industry and residential sectors and fuel combustion were consistently negatively associated only with the language domain. This was the case both for both continuous and categorical exposures, with the latter suggesting also a dose-response in their association between sector- and fuel-specific $PM_{2.5}$ emissions and language. Previous studies have mostly investigated associations BC emissions and global cognitive performance as well as memory, language, and executive function with inconsistent findings [23-26, 45]. More research is needed to disentangle the links between source-specific $PM_{2.5}$ emissions and cognitive health as well as potential mechanisms that might affect cognitive domains differently.

Strengths and limitations

Strengths of this study include the use of a representative sample of the general population of older people living in private households in England and the use of an extensive battery of cognitive tests designed to assess key cognitive domains affected by cognitive ageing, including memory, executive function, and language. Moreover, we had long-term exposure data measured up to ten years before the cognitive performance tests administered in the ELSA-HCAP study and we were able to account for changes in the residential address of the participants during this time reducing therefore potential exposure misclassification. Also, in this study we accounted for a range of different sources of $PM_{2.5}$, and these were isolated by removing each source individually from a chemical-transport dispersion model, leading to better specificity. The ability to investigate long-term exposure to NO_2 and $PM_{2.5}$, including source-specific $PM_{2.5}$, increases our understanding of the neurotoxicity of air pollutants even though further studies are needed to explore the role of components of particulate matter on cognitive performance. A novel aspect of this study is also the use of group-based trajectory modelling to identify groups of older people exposed to different levels (and trends) of outdoor air pollution which is less common in air pollution epidemiology. In this work, the population under study largely experienced similar decreases in exposure to air pollution and we failed to find distinct trajectories (such as increasing, decreasing, and consistently high or low levels of exposure to air pollution). However, other studies in different geographical settings (with more heterogeneity and contrasting changes in concentrations of air pollutants or where regulations impact air pollution across different populations [46, 47]) may find this method useful to differentiate trajectories of exposure to air pollutants. Furthermore, by using group trajectories of pollutants we were able to capture more heterogeneity in exposure levels than when modelling the mean exposure. Also, unlike quartiles, tertiles, or other splits of the data based on arbitrary cut-offs of the data, group-based trajectory modelling identifies homogenous groups that share similar trajectories. Other strengths of this work include the availability of detailed individual and area-level information on key factors that could confound our associations, including a measure of baseline cognition. Finally, ELSA is part of a harmonized group of studies initially developed to facilitate cross-national comparisons (with more than 40 countries around the world using the family of Health and Retirement Studies, HRS). In this study, we used data on cognitive performance based on the HCAP (conducted in dozens of countries in the HRS-style ageing surveys) and long-term exposure to outdoor air pollution that currently is being harmonised for up to eight countries of the HRS family. Future studies should exploit this data harmonisation effort by repeating these analyses in different geographical and social contexts (and possibly meta-analysing findings). Given the current diversity of study designs, exposures, and end-points, the availability of comparable measures will provide stronger insights into the links between outdoor air pollution exposure and cognitive ageing research.

Despite these advantages, our study has some limitations. First, although air pollutant data were measured over 10 years pre-HCAP assessment, these years might not be representative of exposures over longer terms (and ideally across an individual's entire lifetime or at different stages of the life course). Therefore, we might be unable to capture the true magnitude of the association between long-term exposure to air pollution and cognitive performance. Second, previous studies have suggested that the duration of exposure at different levels of intensity is as important as the overall intensity of exposure [43, 48]. In our study, however, we use yearly averages of exposures, failing to account for the duration of exposure to high NO_2 and $PM_{2.5}$ concentrations (measured, for instance, as the number of days or months where concentrations are above certain thresholds) and therefore to elucidate on the role of (cumulative) short-term impacts of air pollutants on cognition. Third, as with all observational studies, we cannot completely rule out the possibility that the associations we observed are attributable to unmeasured confounding. Also, although we used survey weights to minimise selection bias and non-response, it is probable that those who survived for the duration of the study and who agreed to participate in HCAP were a selected sample to some extent (with higher probability of response among those with higher cognitive scores). If this population was healthier and more immune to the long-term exposures to air pollution, this might underestimate the effect sizes observed. Moreover, it is worth noting that HCAP did not include respondents living in long-term care or other institutional settings and was predominantly of White European ancestry.

In summary, air pollution has been suggested as a modifiable risk factor for cognitive impairment. In our study, we found associations between exposure to NO_2 and $PM_{2.5}$ and poor cognitive performance, particularly at higher levels of concentration. Our data further indicate that key emission sources might be important particularly for the domain of language, although more research is needed to confirm these findings. Older people's cognitive performance might benefit from continued efforts to reduce levels of exposure to air pollution, particularly where outdoor pollution levels are the highest.

Conflict of interest: The authors have no relevant financial or non-financial interests to disclose.

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Consent to participate: Informed consent was obtained from all ELSA participants or their guardians.

Data availability. All ELSA data are available through the UK Data Service (SN 5050 and 8502).

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Table 1 – Characteristics of the study population

ELSA characteristics	
Mean age at baseline in years (SD)	65.37 (7.13)
Sex	
Male	46.3% (533)
Female	53.7% (639)
Wealth Quintiles	
Lowest wealth	16.3% (N=186)
Second	18.5% (N=232)
Middle	22.2% (N=261)
Fourth	18.5% (N=222)
Highest wealth	24.5% (N=271)
Age at completion of highest education qualification	
14 or under	12.7% (N=177)
15	40.5% (N=474)
16	19.6% (N=228)
17	8.1% (N=81)
18	4.7% (N=57)
19 or older	14.4% (N=155)
Urbanicity	
Urban	77.3% (N=880)
Rural	22.7% (N=292)
Quintile Index of Multiple Deprivation Score	
0.37 - 8.32 [least deprived]	21.7% (N=268)
8.32 - 13.74	25.2% (N=295)
13.74 - 21.22	20.6% (N=248)
21.22 - 34.42	18.4% (N=209)
34.42 - 85.46 [most deprived]	14.1% (N=152)
Cognitive function (Range of scores)	
Overall cognition	-2.84; 2.42
Executive function	-2.77; 2.30
Language	-2.12; 3.77
Memory	-2.81; 1.89
Mean air pollutants pre-HCAP interview (SD)	
Nitrogen Dioxide (NO_2)	22.89 (SD=6.36)
Total fine particulate matter ($PM_{2.5}$), $\mu g/m^3$	11.89 (SD=1.53)
Agriculture	3.21 (SD=0.46)
Energy	1.07 (SD=0.26)
Industry	0.96 (SD=0.21)
Residential	1.04 (SD=0.26)
Road traffic	1.05 (SD=0.17)
Biofuel	1.24 (SD=0.33)
Coal	0.65 (SD=0.14)
Oil and Gas	3.18 (SD=0.43)

Sources: English Longitudinal Study of Ageing (ELSA) and Gateway to Global Aging Environmental Exposome Data for England. The sample is restricted to participants of the Harmonised Cognitive Assessment Protocol (HCAP) Sub-Study of ELSA (N=1,127). Weighted ELSA data. Notes: Data are reported as percentages (numbers) unless otherwise indicated. SD=Standard Deviation

Figure 1. Trajectories of outdoor air pollution and characteristics of the groups

Sources: Gateway to Global Aging Environmental Exposome Data for England. The sample is restricted to participants of the Harmonised Cognitive Assessment Protocol Sub-Study of the English Longitudinal Study of Ageing (ELSA-HCAP, N=1,127). NO_2 ($\mu g/m^3$) = Nitrogen dioxide; $PM_{2.5}$ ($\mu g/m^3$) = Particulate matter with aerodynamic diameters less than 2.5 µm. SD=Standard Deviation. Best-fitting trajectory groups were obtained using group-based trajectory modelling – See Supplementary Tables S3 and S4 for details.

Table 2 – Associations (95% confidence intervals) between outdoor air pollution concentrations (NO_2 and total $PM_{2.5}$) and cognitive performance in the ELSA-HCAP (2018)

	Overall Cognition		Executive Function		Language		Memory	
NO_2	**Model 1**	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Mean NO_2 (centred)	-0.013** (-0.02,-0.00)	-0.007 (-0.02,0.00)	-0.016** (-0.03,-0.01)	-0.010 (-0.02,0.00)	-0.016** (-0.03,-0.01)	-0.013* (-0.02,-0.00)	-0.005 (-0.01,0.00)	-0.002 (-0.01,0.01)
Group 1 (*mean 13.7 μg/m³*)	-0.006 (-0.18,0.16)	-0.117 (-0.28,0.05)	-0.017 (-0.19,0.16)	-0.152 (-0.32,0.02)	0.005 (-0.19,0.20)	-0.044 (-0.25,0.16)	-0.001 (-0.17,0.17)	-0.069 (-0.25,0.11)
Group 2 (*mean 19.7 μg/m³*)	0.062 (-0.07,0.20)	-0.002 (-0.12,0.11)	0.052 (-0.09,0.19)	-0.006 (-0.12,0.11)	0.082 (-0.08,0.24)	0.030 (-0.12,0.18)	0.039 (-0.10,0.17)	-0.013 (-0.14,0.11)
Group 3 (*mean 24.1 μg/m³*)	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Group 4 (*mean 28.9 μg/m³*)	-0.055 (-0.21,0.10)	-0.014 (-0.14,0.11)	-0.115 (-0.27,0.04)	-0.061 (-0.19,0.07)	-0.056 (-0.25,0.13)	-0.019 (-0.19,0.15)	0.029 (-0.12,0.18)	0.037 (-0.10,0.17)
Group 5 (*mean 36.3 μg/m³*)	-0.267* (-0.53,-0.01)	-0.241* (-0.46,-0.02)	-0.333* (-0.62,-0.04)	-0.291* (-0.54,-0.04)	-0.369** (-0.64,-0.10)	-0.328* (-0.59,-0.07)	-0.148 (-0.39,0.09)	-0.143 (-0.37,0.08)
Total $PM_{2.5}$	**Model 1**	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**	**Model 1**	**Model 2**
Mean $PM_{2.5}$ (centred)	-0.025 (-0.06,0.01)	-0.008 (-0.04,0.03)	-0.027 (-0.07,0.02)	-0.005 (-0.05,0.04)	-0.048* (-0.09,-0.01)	-0.039* (-0.08,-0.00)	-0.016 (-0.05,0.02)	-0.010 (-0.05,0.03)
Group 1 (*mean 9.7 μg/m³*)	-0.050 (-0.21,0.11)	-0.065 (-0.20,0.07)	-0.020 (-0.18,0.15)	-0.049 (-0.19,0.09)	0.060 (-0.11,0.23)	0.075 (-0.07,0.22)	-0.097 (-0.25,0.06)	-0.103 (-0.24,0.05)
Group 2 (*mean 11.5 μg/m³*)	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Group 3 (*mean 12.8 μg/m³*)	0.058 (-0.06,0.18)	0.059 (-0.05,0.17)	0.059 (-0.06,0.18)	0.065 (-0.04,0.17)	0.012 (-0.14,0.16)	0.021 (-0.12,0.16)	0.063 (-0.06,0.18)	0.060 (-0.05,0.17)
Group 4 (*mean 15.2 μg/m³*)	-0.460*** (-0.71,-0.21)	-0.334** (-0.55,-0.12)	-0.434** (-0.74,-0.13)	-0.292* (-0.57,-0.01)	-0.332** (-0.55,-0.11)	-0.222* (-0.44,-0.01)	-0.442*** (-0.66,-0.23)	-0.376*** (-0.58,-0.17)

Sources – English Longitudinal Study of Ageing (ELSA), Harmonised Cognitive Assessment Protocol (HCAP) Sub-Study of ELSA, and Gateway to Global Aging Environmental Exposome Data for England (N=1,127). Notes: For all scores, negative β indicates worse cognitive performance. Model 1 is adjusted for age and sex. Model 2 is further adjusted for age at completion of highest education qualification, wealth quintiles, urbanicity, deprivation index quintiles, and cognitive function at baseline. All covariates were drawn from ELSA Wave 4 (2008-09). NO_2 (μg/m³) =nitrogen dioxide; $PM_{2.5}$ (μg/m³) =particulate matter with aerodynamic diameters less than 2.5 μm. Values in brackets represent 95% confidence intervals. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Weighted data.

Table 3 – Results of multiple linear regression for the association between sector-specific sources of $PM_{2.5}$ and cognitive performance

		Overall Cognition	Executive Function	Language	Memory
Agriculture	**Mean $PM_{2.5}$ (centred)**	0.005 (-0.11,0.12)	0.030 (-0.09,0.15	-0.106 (-0.22,0.01)	0.003 (-0.12,0.13)
	Group 1 (*mean 2.4 µg/m³*)	-0.052 (-0.21,0.11)	-0.046 (-0.21,0.12)	0.165 (-0.02,0.35)	-0.056 (-0.24,0.13)
	Group 2 (*mean 2.9 µg/m³*)	Ref	Ref	Ref	Ref
	Group 3 (*mean 3.4 µg/m³*)	0.021 (-0.09,0.13)	0.033 (-0.08,0.14)	-0.037 (-0.18,0.11)	0.059 (-0.07,0.18)
	Group 4 (*mean 3.9 µg/m³*)	-0.011 (-0.17,0.15)	0.014 (-0.16,0.19)	-0.045 (-0.22,0.13)	-0.005 (-0.16,0.15)
Industry	**Mean $PM_{2.5}$ (centred)**	-0.093 (-0.35,0.16)	-0.068 (-0.36,0.22)	-0.364* (-0.64,-0.09)	-0.084 (-0.36,0.19)
	Group 1 (*mean 0.5 µg/m³*)	-0.020 (-0.22,0.18)	0.016 (-0.19,0.22)	0.095 (-0.12,0.31)	-0.053 (-0.28,0.17)
	Group 2 (*mean 0.8 µg/m³*)	Ref	Ref	Ref	Ref
	Group 3 (*mean 1.0 µg/m³*)	-0.047 (-0.06,0.15)	0.079 (-0.03,0.19)	-0.011 (-0.15,0.12)	0.051 (-0.06,0.16)
	Group 4 (*mean 1.3 µg/m³*)	-0.003 (-0.14,0.15)	-0.005 (-0.16,0.15)	-0.151 (-0.33,0.02)	0.020 (-0.13,0.17)
Energy	**Mean $PM_{2.5}$ (centred)**	0.009 (-0.18,0.20)	0.087 (-0.10,0.28)	-0.090 (-0.35,0.17)	-0.055 (-0.27,0.16
	Group 1 (*mean 0.8 µg/m³*)	-0.007 (-0.12,0.11)	0.019 (-0.10,0.14)	0.083 (-0.06,0.23)	-0.056 (-0.18,0.07)
	Group 2 (*mean 1.0 µg/m³*)	Ref	Ref	Ref	Ref
	Group 3 (*mean 1.3 µg/m³*)	-0.061 (-0.19,0.06)	0.031 (-0.10,0.16)	-0.117 (-0.26,0.03)	-0.098 (-0.22,0.03)
	Group 4 (*mean 1.6 µg/m³*)	-0.028 (-0.18,0.13)	0.021 (-0.16,0.20)	0.084 (-0.13,0.30)	-0.148 (-0.31,0.01)
Residential	**Mean $PM_{2.5}$ (centred)**	-0.096 (-0.30,0.11)	-0.079 (-0.31,0.15)	-0.321** (-0.54,-0.11)	-0.079 (-0.30,0.14)
	Group 1 (*mean 0.7 µg/m³*)	-0.131 (-0.26,0.00)	-0.129 (-0.27,0.01)	-0.011 (-0.15,0.13)	-0.138 (-0.28,0.00)
	Group 2 (*mean 1.0 µg/m³*)	Ref	Ref	Ref	Ref
	Group 3 (*mean 1.2 µg/m³*)	-0.073 (-0.18,0.04)	-0.032 (-0.14,0.08)	-0.144* (-0.29,-0.00)	-0.063 (-0.18,0.05)
	Group 4 (*mean 1.5 µg/m³*)	-0.121 (-0.27,0.02)	-0.136 (-0.29,0.02)	-0.210* (-0.39,-0.03)	-0.102 (-0.26,0.05)
Road Traffic	**Mean $PM_{2.5}$ (centred)**	0.102 (-0.21,0.41)	0.039 (-0.30,0.38)	0.025 (-0.30,0.35)	0.051 (-0.29,0.40)
	Group 1 (*mean 0.8 µg/m³*)	-0.091 (-0.21,0.03)	-0.094 (-0.22,0.03)	0.075 (-0.06,0.21)	-0.114 (-0.24,0.02)
	Group 2 (*mean 1.0 µg/m³*)	Ref	Ref	Ref	Ref
	Group 3 (*mean 1.1 µg/m³*)	-0.027 (-0.14,0.09)	-0.029 (-0.15,0.09)	-0.018 (-0.17,0.14)	-0.036 (-0.15,0.08)
	Group 4 (*mean 1.3 µg/m³*)	-0.101 (-0.27,0.07)	-0.156 (-0.34,0.03)	-0.021 (-0.19,0.15)	-0.095 (-0.27,0.08)

Sources – English Longitudinal Study of Ageing (ELSA), Harmonised Cognitive Assessment Protocol (HCAP) Sub-Study of ELSA, and Gateway to Global Aging Environmental Exposome Data for England (N=1,127). Notes: For all scores, negative β indicates worse cognitive performance. All results presented in this Table are adjusted for age, sex, age at completion of highest education qualification, wealth quintiles, urbanicity, deprivation index quintiles, and cognitive function at baseline (Model 2). All covariates were drawn from ELSA Wave 4 (2008-09). Results from Model 1 (that adjusted for age and sex) are available in the Supplementary Table 5. $PM_{2.5}$ (µg/m³) = Particulate matter with aerodynamic diameters less than 2.5 µm. Values in brackets represent 95% confidence intervals. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Weighted data.

Table 4 – Results of multiple linear regression for the association between fuel-specific sources of $PM_{2.5}$ and cognitive performance

		Overall Cognition	Executive Function	Language	Memory
Biofuel	**Mean $PM_{2.5}$ (centred)**	-0.058 (-0.22,0.10)	-0.033 (-0.21,0.14)	-0.236** (-0.41,-0.07)	-0.059 (-0.23,0.11)
	Group 1 (*mean 0.7 µg/m³*)	-0.106 (-0.29,0.08)	-0.057 (-0.26,0.14)	0.044 (-0.16,0.25)	-0.140 (-0.35,0.07)
	Group 2 (*mean 1.0 µg/m³*)	*Ref*	*Ref*	*Ref*	*Ref*
	Group 3 (*mean 1.3 µg/m³*)	-0.034 (-0.15,0.08)	0.030 (-0.09,0.15)	-0.074 (-0.21,0.06)	-0.058 (-0.18,0.06)
	Group 4 (*mean 1.7 µg/m³*)	-0.031 (-0.16,0.10)	0.023 (-0.11,0.16)	-0.159* (-0.31,-0.01)	-0.059 (-0.20,0.08)
Coal	**Mean $PM_{2.5}$ (centred)**	-0.125 (-0.47,0.22)	0.017 (-0.34,0.37)	-0.525** (-0.91,-0.14)	-0.155 (-0.54,0.23)
	Group 1 (*mean 0.4 µg/m³*)	-0.080 (-0.27,0.11)	-0.075 (-0.27,0.12)	-0.012 (-0.20,0.18)	-0.067 (-0.27,0.14)
	Group 2 (*mean 0.6 µg/m³*)	*Ref*	*Ref*	*Ref*	*Ref*
	Group 3 (*mean 0.7 µg/m³*)	0.041 (-0.06,0.15)	0.036 (-0.07,0.15)	-0.081 (-0.22,0.05	0.075 (-0.04,0.19)
	Group 4 (*mean 0.9 µg/m³*)	-0.127 (-0.27,0.01)	-0.078 (-0.23,0.08)	-0.238** (-0.39,-0.08)	-0.103 (-0.24,0.04)
Oil and Gas	**Mean $PM_{2.5}$ (centred)**	0.013 (-0.14,0.11)	-0.019 (-0.16,0.12)	-0.133* (-0.26,-0.00)	-0.002 (-0.15,0.14)
	Group 1 (*mean 2.5 µg/m³*)	-0.086 (-0.23,0.06)	-0.115 (-0.26,0.03)	0.212* (0.05,0.37)	-0.124 (-0.29,0.03)
	Group 2 (*mean 3.0 µg/m³*)	*Ref*	*Ref*	*Ref*	*Ref*
	Group 3 (*mean 3.4 µg/m³*)	0.065 (-0.04,0.17)	0.021 (-0.09,0.13)	0.099 (-0.04,0.23)	0.070 (-0.04,0.18)
	Group 4 (*mean 4.0 µg/m³*)	-0.098 (-0.28,0.09)	-0.150 (-0.35,0.05)	-0.019 (-0.22,0.18)	-0.099 (-0.29,0.08)

Sources – English Longitudinal Study of Ageing (ELSA), Harmonised Cognitive Assessment Protocol (HCAP) Sub-Study of ELSA, and Gateway to Global Aging Environmental Exposome Data for England (N=1,127). Notes: For all scores, negative β indicates worse cognitive performance. All results presented in this Table are adjusted for age, sex, age at completion of highest education qualification, wealth quintiles, urbanicity, deprivation index quintiles, and cognitive function at baseline (Model 2). All covariates were drawn from ELSA Wave 4 (2008-09). Results from Model 1 (that adjusted for age and sex) are available in the Supplementary Table 6. $PM_{2.5}$ (µg/m³) = Particulate matter with aerodynamic diameters less than 2.5 µm. Values in brackets represent 95% confidence intervals. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Weighted data.