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LETTER

Lifelong exposure to air pollution and cognitive development in young children: the UK Millennium Cohort Study

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Abstract

Evidence about the impact of air pollution on cognitive development of children has been growing but remains inconclusive. To investigate the association of air pollution exposure and the cognitive development of children in the UK Millennium Cohort Study. Longitudinal study of a nationally representative sample of 13 058–14 614 singleton births, 2000–2002, analysed at age 3, 5 and 7 years for associations between exposure from birth to selected air pollutants and cognitive scores for: School Readiness, Naming Vocabulary (age 3 and 5), Picture Similarity, Pattern Construction (age 5 and 7), Number Skills and Word Reading. Multivariable regression models took account of design stratum, clustering and sampling and attrition weights with adjustment for major risk factors, including age, gender, ethnicity, region, household income, parents’ education, language, siblings and second-hand tobacco smoke. In fully adjusted models, no associations were observed between pollutant exposures and cognitive scores at age 3. At age 5, particulate matter (PM 2.5, PM 10), nitrogen dioxide (NO 2), sulphur dioxide (SO 2) and carbon monoxide (CO) were associated with lower scores for Naming Vocabulary but no other outcome except for SO 2 and Picture Similarity. At age 7, PM 2.5, PM 10 and NO 2 were associated with lower scores for Pattern Construction, SO 2 with lower Number Skills and SO 2 and ozone with poorer Word Reading scores, but PM 2.5, PM 10 and NO 2 were associated with higher Word Reading scores. Adverse effects of air pollutants represented a deficit of up to around four percentile points in Naming Vocabulary at age 5 for an interquartile range increase in pollutant concentration, which is smaller than the impact of various social determinants of cognitive development. In a study of multiple pollutants and outcomes, we found mixed evidence from this UK-wide cohort study for association between lifetime exposure to air pollutants and cognitive development to age 7 years.

Abbreviations

| Acronym | Description |
|---------|-------------|
| ASD     | autism spectrum disorder |
| BAS     | British Ability Scales |
| BSRA    | Bracken School Readiness Assessment |
| BREATHE | Brain Development and Air Pollution Ultrafine Particles |
| CI      | confidence interval |
| CO      | carbon monoxide |
| DEFRA   | Department for Environment Food & Rural Affairs |
| EC      | elemental carbons |
| ESCAPE  | European Study of Cohorts for Air Pollution Effects |
| GASPII  | Gene and Environment Prospective Study on Infancy in Italy |
| MAAQ    | Modelling of Ambient Air Quality |
| MCS     | Millennium Cohort Study |
| MOCEH   | Mothers and Children’s Environmental Health |
| MRA     | magnetic resonance imaging |

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1. Introduction

There is accumulating evidence for adverse effects of air pollution on a growing range of health outcomes (Brook et al 2010, Rajagopalan et al 2018, Chen and Hoek 2020, Huangfu and Atkinson 2020, Pope et al 2020), including impacts on cognitive development in children and decline in the elderly (Suades-González et al 2015, Clifford et al 2016, Xu et al 2016, Sram et al 2017, De Prado Bert et al 2018, Costa et al 2020).

Epidemiological evidence for adverse impacts on cognitive development of children has come from studies in the US (Suglia et al 2008, Perera et al 2009, Harris et al 2015), Europe (Guxens et al 2014, Sunyer et al 2015, Porta et al 2016, Lubczynska et al 2017) and Asia (Tang et al 2008, Jung et al 2013, Kim et al 2014, Yorifuji et al 2016). This evidence has been reported in relation to a range of pollutants or proxies, including particle fractions such as particle matters with diameter of 2.5 µm or less (PM2.5) and 10 µm or less (PM10) (Guxens et al 2014, Kim et al 2014, Harris et al 2015, Yorifuji et al 2016, Lubczynska et al 2017), nitrogen dioxide (NO2) (Jung et al 2013, Guxens et al 2014, Kim et al 2014, Suyner et al 2015, Porta et al 2016, Yorifuji et al 2016), PAHs (Tang et al 2008, Edwards et al 2010, Jedrychowski et al 2014, Lovasi et al 2014, Perera et al 2014), lead (Perera et al 2014), proximity to roads and traffic density (Harris et al 2015, Wilker et al 2015). Most of them are cohort studies examining postnatal exposure, except a few studies of prenatal exposure (Tang et al 2008, Perera et al 2009, 2012, Kim et al 2014, Yorifuji et al 2016) and both (Jedrychowski et al 2014). A wide range of cognitive/developmental outcomes were investigated, including verbal and numerical ability (Perera et al 2009, 2012, Jedrychowski et al 2014, Harris et al 2015, Porta et al 2016), psychomotor development (Guxens et al 2014, Kim et al 2014, Lertxundi et al 2015), behavioural development milestones (Perera et al 2012, Newman et al 2013, Gong et al 2017, Mortama et al 2017), working memory and attention processes (Chiu et al 2013, Cowell et al 2015, Sunyer et al 2015) at various ages to 14 years.

Interpretation of this evidence is complex not only because of the range of exposures and outcomes studied but also because of methodological limitations of some studies, including suboptimal control for confounding factors, measurement of exposure only for limited periods or at large spatial scale, and the fact that outcomes have sometimes not been measured using validated or standardized instruments. Only three cohort studies to date have involved more than 1000 people with reasonable controlling for confounding control (Gong et al 2014, Harris et al 2015, Sunyer et al 2015), except two European meta-analysis combining the results from heterogeneous measurements of cognition and psychomotor skills between cities (Guxens et al 2014, Lubczynska et al 2017) and two population-based cohort studies that were based on crude exposure measurement and limited confounding control (Jung et al 2013, Yorifuji et al 2016). Taken as whole, the evidence is suggestive but inconclusive.

We now report an analysis of air pollution and cognitive development based on the UK MCS. Previously the subset of the UK MCS children (n = 8198 MCS in England and Wales) were analysed to assess the association between the Multiple Environmental Deprivation Index (MEDIx) and cognitive ability at age 3 years (Midouhas et al 2018). Their analyses using the MEDIx represented by the national decile groups of annual mean NO2 and green space at less granularity level (ward) did not find significant impact of NO2 or green space on cognition ability at age 3 years. The current study aims to extend the previous analysis by constructing lifelong exposure to several major air pollutants at finer geospatial scale and to analyse its impact on the development of cognitive ability among the all UK MCS children up to 7 years of age by maximising the feature of this valuable national cohort.

2. Methods

2.1. Study population

The UK MCS is a nationally-representative longitudinal study of 18,827 children born in the UK between September 2000 and January 2002 and alive and living in the UK at age 9 months (Connelly and Platt 2014, Joshi and Fitzsimons 2016). The sample is stratified by country and type of electoral ward, with over-sampling of families in areas of socio-economic disadvantage, high proportion of ethnic minority populations and in Scotland, Wales and Northern Ireland (Plewis et al 2007).

To date, seven MCS ‘sweeps’ have been completed in 2001–3, 2003–2005, 2006, 2008, 2012–2013, 2015–16 and 2018–2019, corresponding to follow-up
of cohort members at 9 months and 3, 5, 7, 11, 14 and 18 years of age. Interviewers visited the cohort members’ homes and conducted face-to-face interviews with both resident parents. Parents also answered some questions via self-completion. Collected data include physical, socio-emotional, cognitive and behavioural development, along with individual daily life including physical activities and the families’ socio-economic circumstances, parenting, relationships and lifestyle. Detailed information of available datasets and how the data were collected at each sweep is described elsewhere (Centre for Longitudinal Studies). Data collections used in the current study were listed in supplementary material S1 (available online at stacks.iop.org/ERL/16/055023/mmedia). Briefly, the First to the Fourth Surveys were linked by the cohort member number. Information about the household were added from the Longitudinal Family File. Besides, geographical identifiers (specifically OA) were joined at the time of the First to Fourth survey interview.

In this paper, we report the analysis of follow-up for cognitive outcomes up to age 7 years, using data from sweeps 1–4 for singleton births only with complete data on principal covariates (i.e. sex, birth weight, ethnicity, maternal age at birth, cohort member’s age, household income and region) and cognitive outcomes and successful linkage to air pollution data for all four sweeps (data from the UK Data Archive, University of Essex obtained through the UK Data Service Secure Lab).

2.2. Cognitive measurements

Measurements of cognitive development are described in detail elsewhere (Harris et al. 2015) and summarised in table 1 and supplementary material S2.

The administered tests varied by age. The interviewer conducted age-appropriate cognitive assessments with the cohort member at sweeps 2–4. Most were based on BAS, a battery of individually-administered tests of cognitive ability and educational achievements suitable for use with children from 2 years 6 months to 7 years 11 months. The BAS Naming Vocabulary is a verbal scale for young children that measures expressive language skills, vocabulary knowledge of nouns, ability to attach verbal labels to pictures, general knowledge, retrieval of names from long-term memory and language stimulation. BAS Picture Similarity assesses children’s problem-solving ability and Pattern Construction spatial awareness, dexterity and coordination as well as traits such as perseverance and determination. At age 7, children were assessed by either the BAS Word Reading in English or The Our Adventures in Welsh depending on parents’ choice and also by the UK NFER Number Skills test.

For all BAS batteries, scores were converted to standardized T-scores by reference to age-specific population norms (mean 50, SD 10). We used age-adjusted school readiness composite standard score (mean 100, SD 15) for Bracken School Readiness and the nationally age adjusted standardised score (mean 100, SD 15) for NFER Number Skills. Higher scores on all cognitive tests indicate higher ability.

2.3. Air pollution exposure

Air pollutant exposure was assessed for particles (PM2.5 and PM10), as well as nitrogen dioxide (NO2) and ozone (O3) as the pollutants of primary interest and for SO2 and CO as pollutants of secondary interest. Exposure classification was based on linkage of the child’s place of residence to 1 × 1 km resolution maps of annual average background pollutant concentrations using the Department for Environment Food & Rural Affairs (DEFRA) MAAQ (Ricardo Energy & Environment 2018).

For each cohort member, we constructed a history of residential addresses referring to the reported address at interview and dates of moving residence if they changed from the previous sweep. We assumed the cohort member lived in the same address after birth to age 9 months as no residential information was available before the first survey (sweep MCS1).

Lifelong exposure was quantified by occupancy-time-weighted average of the annual mean concentration for all pollutants except CO (maximum of daily 8 h running mean) and O3 (number of days on which daily maximum of 8 hourly concentration is greater than 120 µg m⁻³). For linkage we used the centroid of the OA of residence (approximately 300 residents per unit in England and Wales and 114 in Scotland) available through the UK Data Service Secure Lab.

2.4. Other major risk factors

Other major risk factors considered in this paper reflect the collective knowledge from previous studies (Chowdry et al. 2010, Côté et al. 2013, Aggio et al. 2016, Midouhas et al. 2018). The individual level risk factors include age (in days), gender and ethnicity (White, Mixed, Indian, Pakistani and Bangladesh, Black or Black British and Others) and low birth weight (< 2500 g or not). The family level risk factors were household income (quintile group), mother’s education (in NVQ), father’s education (in NVQ), maternal age at birth, language spoken in household (English only, Not-English only), number of siblings (1, 2, 3 + ), second-hand tobacco smoke (whether anyone smokes in the same room as the cohort member), chronic illness of the cohort member and breastfeeding (ever tried or not). Areal identification of the region was also included.

2.5. Statistical analysis

First, we conducted a descriptive analysis including examination of missing data and correlations among the key variables. In order to explore possible bias relating to non-response of items in each survey
sweep, we retained observations containing missing data, coding the relevant data item as 'unknown', instead of exclusively fitting the model to observations with complete data or using multiple imputation techniques.

Standardized cognition test scores were analysed in relation to lifelong air pollution exposure using multivariable linear regression model.

The MCS is not a random sample, and its sampling design involved clustering by ward (there are just under 9500 wards in the UK). These clusters were further stratified by deprivation level (and ethnicity in England). There has also been non-random attrition at each successive MCS sweep. Standard errors are adjusted to take account of the survey design and attrition using Stata svyset command (Stata Corp 2017). Analyses were conducted for the whole UK.

The cognitive outcomes analysed at each age are shown in table 1. Each analysis was of a specific measure of cognitive outcome at one specific age only using each of two pre-specified models of confounder control (Model 1 and Model 2). Model 1 included a relatively restricted set of confounder variables: age, gender, low birth weight, ethnicity, maternal age at birth, household income and region; Model 2 included these variables plus additional adjustment for mother’s and father’s education, language, siblings, second-hand tobacco smoke, chronic illness and breast feeding. For the two outcomes where we had more than 1 year of outcome measurement (BAS Naming Vocabulary at ages 3 & 5 and BAS Pattern Construction at 5 & 7), we analysed the change between the two ages in relation to the mean pollution concentration over the life-course from birth with control for confounders measured at the later date. This model specification has the advantage of removing potentially correlated fixed effects via differencing which may impact on consistency in the levels specification. We did not regress change in cognition scores on change in pollution exposure between the two assessments because the DEFRA MAAQ modelling method had been updated over the study period which may introduce bias in estimates of year-to-year changes. All results are expressed as the change in score for an IQR increase in mean pollutant concentration.

Example of Stata codes of the Survey Data analysis and how coefficient standard errors are estimated are shown in supplementary material S3. Non-linearity of the relationship with air pollution was examined by introducing categorical variables, but did not significantly change the results (not shown). Analyses were conducted using Stata version 15.

3. Results

3.1. Study population and lifelong air pollution exposure

The study sample meeting our data completeness and record linkage criteria comprised 13310 children at age 3, 14614 at age 5 and 13058 at age 7 (table 2). The majority were white (88.3% at first follow-up), 90% spoke English only in their household and 6% had low birth weight. Around 12% of children were still the only child in the household by age 7. The number of children exposed to ETS at home decreased over time (17.6% at age 3, 13.5% at age 7). For all pollutants, the estimated lifelong mean concentration was highest at the first follow up (age 3) and declined with age/follow-up (table 3). Correlations between exposure to different air pollutants are reported in the supplementary material (table S4).

3.2. Impacts on cognitive ability

Estimated changes in cognitive test scores for an IQR increase in pollution are shown by age at follow-up in figure 1 and supplementary material table S5.

At first follow-up (age 3), there was no clear evidence of pollution-related differences in scores of cognitive function for either Naming Vocabulary or School Readiness in the fully-adjusted model (Model 2), although there was borderline evidence for School Readiness in relation to SO2 based on the less tightly-controlled Model 1 results: change in percentile score for an IQR increase in pollutant of \(-0.93\) (95%CI \(-1.79, -0.08\))—figure 1(A).

At second follow-up (age 5), there was no clear evidence of pollution-related differences in cognitive function scores for Pattern Construction or Picture Similarity, except for Picture Similarity in relation to SO2. But for Naming Vocabulary, all pollutants except O3 showed evidence of poorer scores in fully-adjusted (Model 2) results. The differences in percentile scores for an interquartile increase in pollutant were: PM2.5: \(-3.92\) (95%CI \(-5.79, -2.06\)), PM10: \(-3.67\) \((-5.25, -2.09\)), NO2: \(-2.33\) \((-3.78, -0.87\)), SO2: \(-1.04\) \((-1.80, -0.28\)) and CO: \(-2.20\) \((-3.44, -0.98\))—figure 1(B).

### Table 1. Summary of measurements used for assessment of cognitive development by age at follow-up.

| Measurement scales used | Age at follow-up |
|-------------------------|------------------|
|                         | 3 years          | 5 years          | 7 years          |
| Bracken School Readiness (Bracken 2002) | BAS Naming Vocabulary | BAS Pattern Construction | BAS Word Reading |
| BAS Naming Vocabulary | BAS Pattern Construction | BAS Picture Similarity | NFER Number Skills |

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Table 2. Characteristics\textsuperscript{a} of the analytic samples of the UK MCS children at age 3, 5 and 7 years.

| Characteristic | MCS2 age 3 years | MCS3 age 5 years | MCS4 age 7 years |
|---------------|------------------|------------------|------------------|
| (n = 13 310)  | (n = 14 614)     | (n = 13 058)     |
| Gender—male   | 6650 (49.6%)     | 7462 (50.9%)     | 6578 (50.9%)     |
| Age in months, mean (s.d.) | 37.7 (2.5) | 62.5 (2.9) | 86.8 (3.0) |
| Ethnicity     |                  |                  |                  |
| White         | 11 410 (88.3%)   | 12 177 (86.6%)   | 10 885 (85.2%)   |
| Mixed         | 373 (3.0%)       | 412 (3.1%)       | 356 (3.2%)       |
| Indian        | 329 (1.8%)       | 372 (1.9%)       | 333 (2.0%)       |
| Pakistani and Bangladesh | 675 (3.4%) | 917 (4.1%) | 840 (4.7%) |
| Black or Black British | 348 (2.2%) | 484 (2.7%) | 423 (3.2%) |
| Others        | 130 (0.9%)       | 201 (1.2%)       | 172 (1.3%)       |
| Unknown       | 45 (0.4%)        | 52 (0.4%)        | 49 (0.4%)        |
| Birth weight  |                  |                  |                  |
| $\geq$ 2.5 kg | 12 223 (91.6%)   | 13 388 (91.4%)   | 12 000 (91.4%)   |
| <2.5 kg       | 766 (5.6%)       | 900 (6.0%)       | 786 (6.0%)       |
| Unknown       | 321 (2.8%)       | 327 (2.6%)       | 272 (2.6%)       |
| Maternal age at birth in years, mean (s.d.) | 28.7 (5.9) | 28.7 (5.9) | 28.4 (5.9) |
| Household income\textsuperscript{b} |                  |                  |                  |
| Lowest quintile | 2701 (18.9%)     | 3212 (19.7%)     | 2652 (19.6%)     |
| Second quintile | 2828 (19.3%)     | 3086 (19.6%)     | 2665 (19.8%)     |
| Third quintile  | 2661 (20.3%)     | 2846 (20.0%)     | 2658 (20.2%)     |
| Fourth quintile | 2551 (20.0%)     | 2812 (20.0%)     | 2544 (19.9%)     |
| Highest quintile | 2474 (20.8%)     | 2576 (20.1%)     | 2526 (20.4%)     |
| Unknown        | 95 (0.7%)        | 83 (0.5%)        | 13 (0.1%)        |
| Mother’s education NVQ\textsuperscript{c} |                  |                  |                  |
| NVQ Level 1    | 1077 (8.3%)      | 1110 (7.6%)      | 894 (7.5%)       |
| NVQ Level 2    | 3787 (29.3%)     | 3966 (28.3%)     | 3426 (27.6%)     |
| NVQ Level 3    | 1995 (14.7%)     | 2158 (14.5%)     | 1985 (14.9%)     |
| NVQ Level 4    | 3894 (30.1%)     | 4257 (30.2%)     | 3984 (29.4%)     |
| NVQ Level 5    | 538 (4.0%)       | 778 (5.3%)       | 871 (6.1%)       |
| Other qualification | 364 (2.4%) | 455 (2.8%) | 386 (2.9%) |
| None of above/Unknown\textsuperscript{d} | 1655 (11.1%)     | 1891 (11.3%)     | 1512 (11.6%)     |
| Father’s education NVQ\textsuperscript{c} |                  |                  |                  |
| NVQ Level 1    | 684 (5.2%)       | 776 (5.4%)       | 715 (5.9%)       |
| NVQ Level 2    | 2885 (21.9%)     | 3170 (22.1%)     | 2833 (21.8%)     |
| NVQ Level 3    | 1614 (12.2%)     | 1760 (12.3%)     | 1653 (12.5%)     |
| NVQ Level 4    | 3113 (24.9%)     | 3314 (24.1%)     | 3081 (23.5%)     |
| NVQ Level 5    | 659 (5.1%)       | 930 (6.5%)       | 1034 (7.4%)      |
| Other qualification | 405 (2.8%) | 506 (3.1%) | 455 (3.1%) |
| None of above (baseline) | 1234 (7.9%) | 1485 (8.7%) | 1290 (9.1%) |
| Unknown        | 2716 (20.1%)     | 2674 (17.7%)     | 1997 (16.8%)     |
| Language spoken in household |                  |                  |                  |
| English only   | 11 518 (90.2%)   | 12 522 (90.4%)   | 11 337 (90.1%)   |
| Mostly or half English | 1725 (0.3%) | 1415 (6.7%) | 1192 (6.8%) |
| Mostly others or others only/Unknown\textsuperscript{d} | 67 (0.5%) | 678 (2.9%) | 529 (3.0%) |
| N of siblings  |                  |                  |                  |
| 0             | 3380 (25.1%)     | 2389 (16.4%)     | 1563 (12.1%)     |
| 1             | 6058 (47.3%)     | 6821 (48.3%)     | 5898 (46.2%)     |
| 2             | 2527 (18.5%)     | 3487 (23.5%)     | 3562 (27.1%)     |
| 3+/Unknown\textsuperscript{d} | 1345 (9.1%)     | 1918 (11.9%)     | 2035 (14.6%)     |
| Second-hand tobacco smoke\textsuperscript{e} |                  |                  |                  |
| Yes           | 2392 (17.6%)     | 2107 (14.3%)     | 1672 (13.5%)     |
| No            | 10 851 (81.8%)   | 12 446 (85.3%)   | 11 330 (86.1%)   |
| Unknown       | 67 (0.5%)        | 62 (0.4%)        | 56 (0.4%)        |

(Continued)
At third follow-up (age 7), there was no evidence of pollution-related association with Number Skills scores, except in relation to SO2 (IQR-related percentile difference $-1.47$, 95%CI $-2.47$, $-0.48$, fully-adjusted model). However, for Pattern Construction, there was evidence of poorer scores in relation to both PM$_{2.5}$ (percentile difference for an IQR pollutant increase $-2.37$, 95%CI $-4.62$, $-0.12$) and PM$_{10}$ ($-2.08$, 95%CI $-3.97$, $-0.19$).

The results for Word Reading showed counter-intuitive mixed results with positive (‘protective’) associations for IQR increases in PM$_{2.5}$ (2.68, 95% CI 0.64, 4.72), PM$_{10}$ (2.36, 95% CI 0.61, 4.10), NO$_2$ (2.33, 95%CI 0.90, 3.76) and CO (1.86, 95%CI 0.61, 3.10); and negative (‘adverse’) associations for O$_3$ ($-2.12$, 95%CI $-3.43$, $-0.81$) and SO$_2$ ($-0.77$, 95%CI $-1.43$, $-0.11$).

Various non-pollutant covariates showed generally stronger associations (larger score differences) with cognitive function than individual pollutants, especially ethnicity, household income, mother’s and father’s education, being a non-English-speaking household and number of siblings (see supplementary material table S7).

### 3.3. Change in cognitive test scores

Change in the Naming Vocabulary test score between age 3 and 5 years was negatively associated with mean lifelong exposure to all air pollutants except O$_3$ (figure 2). For the pollutants of primary interest, the changes in the percentile score for an IQR increase in pollutant concentration were: PM$_{2.5}$ $-3.76$ (95% CI $-6.27$, $-1.26$), PM$_{10}$ $-3.54$ ($-5.73$, $-1.36$) and NO$_2$ $-2.83$ ($-4.82$, $-0.84$). The association with O$_3$ was positive (‘protective’) and of borderline statistical significance—figure 2. Interestingly, whereas in the levels specification, Model 2 estimates were generally lower than Model 1 estimates as expected, in the difference equations estimates were identical in both models suggesting removing unobserved fixed effects was important. More importantly, the results suggest that the Model 2 specification was sufficient to control for correlated fixed effects, with virtually identical results at age 5 for naming vocabulary in the difference and levels specification (remembering no effect was found at age 3).

However, there was no clear pollution association of the change in Pattern Construction scores between age 5 and 7 years (figure 2 and supplementary material table S6) in contrast to the level’s equations.

### 4. Discussion

#### 4.1. Summary

This study, based on the UK nationally-representative MCS, provides further evidence of the associations between lifelong exposure to air pollution and the
cognitive development of children. To our knowledge, it is the first large nationwide analysis of children from birth to age 7 with standardized measures of cognitive ability.

Given the context of assessing multiple pollutants and multiple endpoints at three time points (ages), the results provide somewhat mixed evidence. There was little evidence of any association of air pollution with poorer cognitive ability at age 3. But at age 5, there was evidence of negative (adverse) associations between pollutant concentrations for all pollutants except O$_3$ and cognitive scores for Naming Vocabulary though no clear evidence for either of the other outcomes analysed (except for SO$_2$ in relation
Figure 2. Change in percentile difference (95%CI) in cognitive performance per interquartile range increase in lifelong exposure to neighbourhood air pollution.

Figure 2. Change in percentile difference (95%CI) in cognitive performance per interquartile range increase in lifelong exposure to neighbourhood air pollution.

change in Picture Similarity test scores). At age 7, PM$_{2.5}$, PM$_{10}$ and NO$_2$ were associated with poorer Pattern Construction scores, SO$_2$ with poorer Number Skills and Word Reading scores, and O$_3$ with poorer Word Reading. However, fully-adjusted models also showed PM$_{2.5}$, PM$_{10}$, NO$_2$ and CO to have apparently positive (‘protective’) associations with Word Reading scores measured at age 7. There was also evidence that improvement in Naming Vocabulary between ages 3 and 5 was poorer in higher pollution areas but no association for change in Pattern Construction between ages 5 and 7 years. Although there was diversity in findings by age and different instrument (test) to measure cognition ability, overall results suggested broadly consistent direction of the impacts among generally-correlated pollutants, such as NO$_2$, PM and CO. At age 7, pollution exposure is going to be much more influenced by location of school (not home address) and this may be behind some of the puzzling results observed at that age. Future work should attempt to control for exposure at both home and school. Observed magnitude of the impact from change analysis which accounts for unobserved fixed effects is broadly equivalent to the difference of the two impacts in the level specifications (the second test minus the first test with two years gap) for Model 2 suggesting this specification is robust.

If the observed associations reflect causal effects, they suggest that air pollutants are producing selective deficits of cognitive function of up to around four percentile points (wider if confidence intervals are considered) for an interquartile range increase in pollutant concentrations. These ‘deficits’ would be broadly comparable to those associated with some non-pollutant social factors, but they are generally smaller than the effect of the more important social determinants such as household income, parental education, ethnicity and whether the household is English-speaking, for example. Although the observed air pollution effects are marginal compared with those of other risk factors, given the ubiquity of the exposure, they could be a substantial health burden in the population from early to later stages of life (Power et al 2016, Peters et al 2019). These pollutant associations are observed in populations whose exposure generally falls within national air quality standards but above WHO guideline levels.

4.2. Comparison of the results to other studies
It is difficult to compare evidence across studies directly because of differences in outcome measures and design, but our results are broadly consistent with other published research. An earlier, more limited analysis of the MCS (Midouhas et al 2018) also found little evidence to support cognitive differences due to differences in outdoor NO$_2$ at age 9 months and 3 years, and a European meta-analysis did not observe any impacts of air pollution on cognitive function at age 2.5 years (Guxens et al 2014). This may reflect absence of effect but may also in part be attributed to the methodological challenge of measuring cognitive ability at very young ages.
With regard to specific pollutants, our (mixed) results show selective evidence for adverse associations with all pollutants at ages 5 and 7, specifically including PM$_{2.5}$, PM$_{10}$, NO$_2$, and, for several outcomes/ages, SO$_2$. This is broadly consistent with the finding of the systematic review of Suades-González et al., which supports the hypothesis that pre- and post-natal exposure to ambient pollution, particularly PM$_{2.5}$, nitrogen oxides and PAHs, have a negative impact on neuropsychological development (Suades-González et al. 2015). Cohort studies published after this review also support likely associations between exposure to particles and nitrogen oxides on the one hand and cognitive ability of children on the other (Guxens et al. 2016, Yorifuji et al. 2016, Lubczynska et al. 2017).

4.3. Mechanisms

Possible mechanisms by which air pollution might affect brain function have been described by Block and Calderón-Garciduenas (2009) and may entail the interaction of multiple pathways and mechanisms, including oxidative stress, neuroinflammation, cerebrovascular damage, cell death, which are also common features of neurodegenerative disorders, and genetic and epigenetic mechanisms (Genc et al. 2012, Underwood 2017). Most mechanistic research has been based on animal and post-mortem studies of adults. Precise measurement of the changes occurring in the human brain under real conditions is required to provide biological evidence for the air pollution and cognition link reported in epidemiological studies. Recently, MRI has started to be applied to measure brain structure and functioning in assessing the impacts of urban air pollution on the brain, including comparative studies in Mexico-city (Calderón-Garciduenas et al. 2008, 2011), a birth cohort study in New York (Peterson et al. 2015) and BREATHE studies in Barcelona (Pujol et al. 2016a, 2016b, Mortamais et al. 2017) as summarised in De Prado Bert et al. (2018).

4.4. Strengths and limitations

The advantages of our analyses include the wide contrasts in exposures across the UK, large sample size, the availability of standardized measures of cognitive function and generally good confounder control. In these respects, we believe the study provides fairly robust evidence.

However, the positive correlations between pollutant levels and Word Reading scores at age 7 are counter-intuitive and difficult to interpret as a causal effect of pollution. Some bias is possible from the limitation in capturing pollution exposure only at each child’s residential neighbourhood, not at school or commuting, although only specific forms of misclassification are likely to introduce an appreciable positive association rather than biasing the results towards the null. More likely possibilities are chance or residual confounding from effects such as of school quality, outside-school learning activities and availability of supporting learning resources in (polluted) urban areas that begin to take effect at older ages. It is worth noting that the positive association was observed in only in one of the examined cognitive measures and only at the oldest age examined (7 years). Naming Vocabulary results showed negative correlation at age 5.

The (mixed) results for O$_3$ are largely understandable given its negative or weak correlation with most other air pollutants, especially NO$_2$. O$_3$ is a highly reactive oxidative gas formed by chemical reactions in the atmosphere involving oxides of nitrogen, volatile organic compounds and driven by solar radiation. In urban areas with high traffic density, nitrogen oxides (NO and NO$_2$) are commonly high and often negatively correlated with O$_3$ during daylight hours. Due to complexity of such titration process, it is not unusual to find the impacts of O$_3$ opposite from those of nitrogen oxides in air pollution epidemiology. The tendency for several O$_3$ results to show patterns opposite to NO$_2$ and PM in particular may therefore reflect the fact that it is acting as a negative proxy for such pollutants which might be causally-related to the outcome.

Among our study’s limitations are its reliance on modelled air pollution levels at 1 x 1 km resolution, which will have led to imperfect exposure classification especially for the more spatially-varying pollutants such as NO$_2$. However, this is the optimally best available data to construct the proxy of lifelong exposure to studied air pollution among more than 13 thousands children who reside across the UK. Although we cannot exclude the possibility of misclassification of air pollution exposure, any misclassification would be nondifferential, moving the effect estimates toward the null. In that sense, our estimates of air pollution impacts could be underestimated. Moreover, changes in pollutant modelling methods over time meant that we were unable to analyse changes in cognitive ability specifically in relation to changes in pollutant concentrations (confining analyses instead to spatial differences in cumulative lifetime exposure from birth). We also were unable to construct estimates of prenatal exposure, which is a gap as prenatal exposure may be relatively important for cognitive development (Harris et al. 2015, Porta et al. 2016). Furthermore, we did not have data on other potentially important environmental factors including green space (Dadvand et al. 2015, 2017, 2018), noise (Sunyer et al. 2015) and indoor air quality and/or dampness (Sunyer et al. 2015, Midouhas et al. 2018). Aircraft noise has been shown to be associated with impaired cognitive development of school-aged children (Stansfeld et al. 2005) and it is likely other forms of environmental noise would also be detrimental. Finally, the current paper describes limited sensitivity analysis, apart from exploration of two sets of covariates in a minimum adjusted
model and a further adjusted model by crucial individual and family determinants with relaxed concerns of collinearity based on the empirical evidence (Chowdry et al. 2010), and examination of the potential (but less likely to impact extensively, given marginal environmental impacts in general) effect modification (not reported). Further model identification to disentangle complicated individual, social and environmental factors is expected (Zivin and Neidell 2013, Zhang et al. 2018).

4.5. Conclusions

In conclusion, our results provide further but mixed evidence for the detrimental impact on air pollutants on cognitive development in early childhood, which is broadly consistent with other published research and mechanistic evidence. It adds to the weight to calls for policy action to reduce air pollution exposure, especially for vulnerable groups such as children, but further work is needed to characterize risks with greater certainty, including in relation to specific pollutants and the critical periods of exposure.

Data availability statement

No additional data are available.

The data that support the findings of this study are available upon reasonable request from the authors.

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Ethical approval

This study was approved by the LSHTM Ethics Committee. Data access was covered by Secure Access User Agreement with UK Data Service.

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References

Aggio DJ, Smith L, Fisher A and Hamer M 2016 Context-specific associations of physical activity and sedentary behavior with cognition in children Am. J. Epidemiol. 183 1075–82
Block ML and Calderón-Garcidueñas L 2009 Air pollution: mechanisms of neuroinflammation & CNS disease Trends Neurosci. 32 506–16
Bracken B A 2002 Bracken School Readiness Assessment: Administration Manual (San Antonio, TX: Psychological Corporation)
Brook R D et al 2010 Particulate matter air pollution and cardiovascular disease: an update to the scientific statement from the American Heart Association Circulation 121 2531–78
Calderón-Garcidueñas L et al 2008 Air pollution, cognitive deficits and brain abnormalities: a pilot study with children and dogs Brain Cogn. 68 117–37
Calderón-Garcidueñas L et al 2011 Exposure to severe urban air pollution influences cognitive outcomes, brain volume and systemic inflammation in clinically healthy children Brain Cogn. 77 345–55
Centre for Longitudinal Studies, L.o.E., UCL 2021 Millennium Cohort Study (available at: https://csl.ucl.ac.uk/cs-studies/millennium-cohort-study/) (Accessed 16 February 2021)
Chen J and Hook G 2020 Long-term exposure to PM and all-cause and cause-specific mortality: a systematic review and meta-analysis Environ. Int. 143 105974
Chiu Y-H M et al 2013 Associations between traffic-related black carbon exposure and attention in a prospective birth cohort of urban children Environ. Health Perspect. 121 859–64
Chowdry H et al 2010 Poorer Children's Educational Attainment: How Important are Attitudes and Behaviour? (New York: Joseph Rowntree Foundation)
Clifford A, Lang L, Chen R, Anstey K J and Seaton A 2016 Exposure to air pollution and cognitive functioning across the life course—a systematic literature review Environ. Res. 147 383–98
Connelly R and Platt L 2014 Cohort profile: UK Millennium Cohort Study (MCS) Int. J. Epidemiol. 43 1719–25
Costa L G, Cole T B, Dao K, Chang Y-C, Coburn J and Garrick J M 2020 Effects of air pollution on the nervous system and its possible role in neurodevelopmental and neurodegenerative disorders Pharmacol. Ther. 210 107523
Côté S M, Doyle O, Petitclerc A and Timmins L 2013 Child care in infancy and cognitive performance until middle childhood in the Millennium Cohort Study Child Dev. 84 1191–208
Cowell W J, Bellinger D C, Coull B A, Bennings C, Wright R O and Wright R J 2015 Associations between prenatal exposure to black carbon and memory domains in urban children: modification by sex and prenatal stress PLoS One 10 e014242
Dadvand P et al 2015 Green spaces and cognitive development in primary schoolchildren Proc. Natl Acad. Sci. USA 112 7937–42
Dadvand P et al 2017 Lifelong residential exposure to green space and attention: a population-based prospective study Environ. Health Perspect. 125 097016
Dadvand P et al 2018 The association between lifelong greenspace exposure and 3-dimensional brain magnetic resonance imaging in Barcelona schoolchildren Environ. Health Perspect. 126 027012
De Prado Bert P, Mercader E M H, Pujol J, Sunyer J and Mortaiamis M 2018 The effects of air pollution on the brain: a review of studies interfacing environmental epidemiology and neuroimaging Curr. Environ. Health Rep. 5 351–64
Edwards S C et al 2010 Prenatal exposure to airborne polycyclic aromatic hydrocarbons and children’s intelligence at 5 years of age in a prospective cohort study in Poland Environ. Health Perspect. 118 1326–31
Genc S, Zadeoglulari Z, Fuss S H and Genc K 2012 The adverse effects of air pollution on the nervous system J. Toxicol. 2012 782462

10
Gong T et al 2017 Perinatal exposure to traffic-related air pollution and autism spectrum disorders Environ. Health Perspect. 125 119–26
Gong T, Almqvist C, Bölte S, Lichtenstein P, Anckarsäter H, Lind T, Lundholm C and Pershagen G 2014 Exposure to air pollution from traffic and neurodevelopmental disorders in Swedish twins Twin Res. Hum. Genet. 17 553–62
Guexns M et al 2014 Air pollution during pregnancy and childhood cognitive and psychomotor development: six European birth cohorts Epidemiology 25 636–47
Guexns M et al 2016 Air pollution exposure during pregnancy and childhood autistic traits in four European population-based cohort studies: the ESCAPE project Environ. Health Perspect. 124 133–40
Harris M H et al 2015 Prenatal and childhood traffic-related pollution exposure and childhood cognition in the project viva cohort (Massachusetts, USA) Environ. Health Perspect. 123 1072–8
Huangfu P and Atkinson R 2020 Long-term exposure to NO2 and O3 and all-cause and respiratory mortality: a systematic review and meta-analysis Environ. Int. 144 105998
Jedrychowski W A, Perera F P, Camann D, Spengler J, Butscher M, Huangfu P and Atkinson R 2020 Long-term exposure to NO2 and polycyclic aromatic hydrocarbons and cognitive dysfunction in children Environ. Sci. Pollut. Res. 22 5631–9
Joshi H and Fitzsimons E 2016 The Millennium Cohort Study: the making of a multi-purpose resource for social science and policy Longitud. Life Course Stud. 7 409–22
Jung C R, Lin Y T and Hwang B F 2013 Air pollution and newly diagnosed autism spectrum disorders: a population-based cohort study in Taiwan PLoS One 8 e75510
Kim E et al 2014 Prenatal exposure to PM10 and NO2 and children’s neurodevelopment from birth to 24 months of age: Mothers and Children’s Environmental Health (MOCEH) study Sci. Total Environ. 481 439–45
Lertxundi A et al 2015 Exposure to fine particle matter, nitrogen dioxide and benzene during pregnancy and cognitive and psychomotor developments in children at 15 months of age Environ. Int. 80 33–40
Lovasi G S, Eldred-Skemp N, Quinn J W, Chang H W, Rauh V A, Bundle A, Orjuela M A and Perera F P 2014 Neighborhood social context and individual polycyclic aromatic hydrocarbon exposures associated with child cognitive test scores J. Child Fam. Stud. 23 785–99
Lubczynska M J et al 2017 Exposure to elemental composition of outdoor PM2.5 at birth and cognitive and psychomotor function in childhood in four European birth cohorts Environ. Int. 109 170–78
Middaus E, Kokoski T and Flouri E 2018 Outdoor and indoor air quality and cognitive ability in young children Environ. Res. 161 321–8
Mortanais M et al 2017 Effect of exposure to polycyclic aromatic hydrocarbons on basal ganglia and attention-deficit hyperactivity disorder symptoms in primary school children Environ. Int. 105 1–2
Newman N C et al 2013 Traffic-related air pollution exposure in the first year of life and behavioral scores at 7 years of age Environ. Health Perspect. 121 731–6
Perera F P et al 2012 Prenatal polycyclic aromatic hydrocarbon (PAH) exposure and child behavior at age 6–7 years Environ. Health Perspect. 120 921–6
Perera F P, Li Z, Whyatt R, Hoepner L, Wang S, Camann D and Rauh V 2009 Prenatal airborne polycyclic aromatic hydrocarbon exposure and child IQ at age 5 years Pediatrics 124 e195–202
Perera F, Weiland K, Neidell M and Wang S 2014 Prenatal exposure to airborne polycyclic aromatic hydrocarbons and IQ: estimated benefit of pollution reduction J. Public Health Policy 35 327–36
Peters R, Ee N, Peters J, Booth A, Mudway I and Anstey K J 2019 Air pollution and dementia: a systematic review J. Alzheimers Dis. 70 5145–63
Peterson B S et al 2015 Effects of prenatal exposure to air pollutants (polycyclic aromatic hydrocarbons) on the development of brain white matter, cognition, and behavior in later childhood JAMA Psychiatry 72 531–40
Plewis I, Calderwood L, Hawkes D, Hughes G and Joshi H 2007 The Millennium Cohort Study: Technical Report on Sampling 4th edn (London: Institute of Education, University of London)
Popo C, Arole N, Coleman N, Pond Z A and Burnett R T 2020 Fine particulate air pollution and human mortality: 25+ years of cohort studies Environ. Res. 183 108924
Porta D et al 2016 Air pollution and cognitive development at age 7 in a prospective Italian birth cohort Epidemiology 27 228–36
Power M C, Adar S D, Yanosky J D and Wuebe J 2016 Exposure to air pollution as a potential contributor to cognitive function, cognitive decline, brain imaging, and dementia: a systematic review of epidemiologic research NeuroToxicology 56 235–53
Puojl J et al 2016a Airborne copper exposure in school environments associated with poorer motor performance and altered basal ganglia Brain Behav. 6 e00467
Puojl J et al 2016b Traffic pollution exposure is associated with altered brain connectivity in school children Neuroimage 129 175–84
Rajagopalan S, Al-Kindil S G and Brook R D 2018 Air pollution and cardiovascular disease: JACC state-of-the-art review J. Am. Coll. Cardiol. 72 2054–70
Ricardo Energy & Environment 2018 Technical report on UK policy and practice on India’s climate Action Plan 2018 (Defra)
Sram R J, Veleminsky M Jr, Veleminsky M Sr and Stejskalov J 2017 The impact of air pollution to central nervous system in children and adults Neuro Endocrinol. Lett. 38 389–96
Stansfeld S A et al 2005 Aircraft and road traffic noise and children’s cognition and health: a cross-national study Lancet 365 1492–9
Stata Corp 2017 Stata survey data reference manual, release 15 (College Station, TX) (available at: www.stata.com/manuals15svy.pdf) (Accessed 16 February 2021)
Suades-González E, Gascon M, Guexns M and Sunyer J 2015 Air pollution and neuropsychological development: a review of the latest evidence Endocrinology 156 3473–82
Suglia S F, Gryparis A, Wright R O, Schwartz J and Wright R J 2008 Association of black carbon with cognition among children in a prospective birth cohort study Am. J. Epidemiol. 167 280–8
Sunyer J et al 2015 Association between traffic-related air pollution in schools and cognitive development in primary school children: a prospective cohort study PLoS Med. 12 e1001792
Tang D, Li T Y, Liu J J, Zhou Z J, Yuan T, Chen Y H, Rauh V A, Xie J and Perera F P 2008 Effects of prenatal exposure to coal-burning pollutants on children’s development in China Environ. Health Perspect. 116 674–9
Underwood J A et al 2017 The polluted brain Science 355 342–4
Wilker E H et al 2015 Long-term exposure to fine particulate matter, residential proximity to major roads and measures of brain structure Stroke 46 1161–6
Xu X, Ha S U and Basnet R 2016 A review of epidemiological research on adverse neurological effects of exposure to ambient air pollution Front. Public Health 4
Yoriufi T, Kashima S, Higa Diez M, Kado Y, Sanada S and Doi H 2016 Prenatal exposure to traffic-related air pollution and child behavioral development milestone delays in Japan Epidemiology 27 57–65
Zhang X, Chen X and Zhang X 2018 The impact of exposure to air pollution on cognitive performance Proc. Natl Acad. Sci. USA 115 9193–7
Zivin J G and Neidell M 2013 Environment, health, and human capital J. Econ. Lit. 51 689–730