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Longitudinal association between air pollution exposure at school and cognitive development in school children over a period of 3.5 years

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ABSTRACT

Introduction: Recently, we showed that exposure to traffic-related air pollutants (TRAPs) at school was negatively associated with cognitive development, specifically working memory and inattentiveness, in primary schoolchildren during a course of 12 months. The persistence of such associations over longer periods remains as an open question.
Objective: To study the longitudinal association between TRAPs at school and cognitive development over a period of 3.5 years.
Methods: Indoor and outdoor levels of TRAPs (elemental carbon (EC), dioxide nitrogen (NO_2), particulate matter ($PM_{2.5}$) from traffic sources and ultrafine particles (UFP)) were measured at 39 schools across Barcelona during 2012/2013. Working memory, as a measure of cognitive development, was evaluated 4 times in 2012/2013 assessment and was re-evaluated one more time in 2015 using computerized n-back test (3-back d′ as main outcome). Linear mixed effects models were used to test the association between TRAPs and 3-back d′, adding child and school as random effects to account for the multilevel nature of the data, and school air pollutants levels (one at a time) as predictor.
Results: We found detrimental associations between all TRAPs and annual change in 3-back d′ (working memory) (i.e. slower development of working memory in children attending schools with higher levels of air pollution). The associations (per one interquartile range increase in exposure) were strongest for outdoor NO_2 (Coefficient (Coef) = − 4.22, 95% confidence interval (CI), − 6.22, − 2.22) and indoor UFP (Coef = − 4.12, 95%CI, − 5.68, − 1.83). These reductions were equivalent to − 20% (95%CI, − 30.1, − 10.7) and − 19.9% (95%CI, − 31.5, − 8.4) change in annual working memory development associated with one interquartile range increase in outdoor NO_2 and indoor UFP, respectively.
Conclusion: Our findings suggest the persistence of the negative association between TRAPs exposure at school and cognitive trajectory measured by n-back test over a period of 3.5 years.

1. Introduction

The city of Barcelona (Spain) presents high levels of air pollution, partly attributed to high traffic density due to the high prevalence of diesel-powered vehicles, but also is attributed to high population density, urban design, and low precipitation average, among other factors. In 2015, the annual average from background station in Barcelona for NO_2 was 34 $\mu g/m^3$ and 17 $\mu g/m^3$ for $PM_{2.5}$ (Amato et al., 2014, p. 200; Generalitat de Catalunya, 2016). The quality of the air around the schools is becoming a public health concern not only because of its potential adverse impacts on child respiratory health (McConnell et al., 2010), but also because of the growing evidence implicating air pollution as a developmental neurotoxicant (Grandjean and Landrigan, 2014). Such evidence suggests that cognitive development could be delayed due to the exposure to pre- and postnatal traffic-related air pollutants at home (Guxens and Sunyer, 2012). However, in a recent

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literature review, we concluded that the available evidence is suggestive for the association of exposure to polycyclic aromatics hydrocarbons (PAHs) with reduced cognitive development in humans (Suades-González et al., 2015). For the rest of TRAPs, the available evidence still remains limited.

The available evidence on the association between TRAPs exposure at school and neuropsychological development is still very scarce (Mohai et al., 2011; Sunyer et al., 2015; van Kempen et al., 2012; Wang et al., 2009). In a study conducted in Michigan (USA), the authors reported lower scores in the standard educational tests and lower attendance in those children from highly polluted schools (Mohai et al., 2011). Lower performance in a number of computerized cognitive tests measuring several cognitive functions was reported, including sustained attention and speed processing, in children attending schools from a polluted area compared to children from less polluted schools in a study conducted in China (Wang et al., 2009). In another study conducted in The Netherlands, the authors reported a negative association between NO_2 at schools and memory span in a sample of 553 from primary school (van Kempen et al., 2012). Recently, we studied, for the first time, the association between TRAP levels at school and cognitive development over a course of 12 months in a sample of ~ 2500 primary schoolchildren within the context of the BRain dEvelopment and Air polluTion ultrafine particles in scHool childrEn (BREATHE) project (Sunyer et al., 2015). First, we have measured several TRAPs (elemental carbon (EC), dioxide nitrogen (NO_2), particulate matter ($PM_{2.5}$) from traffic sources and ultrafine particles (UFP)) in two different periods of 2012. Secondly, cognitive development (working memory and attention) was measured 4 times in the same year using the same computerized tests (n-back and Attention Network task (ANT)) in order to study cognitive trajectories instead of cognitive status. We found that in children exposed to higher levels of TRAPs at school, working memory and attention functions did not have the expected development during the 12-month study period. These findings were supported by those of another study based on the functional magnetic resonance brain imaging of a subsample of BREATHE participants showing slower brain maturation in children exposed to higher levels of TRAPs, characterized by lower functional integration and segregation in some of the key brain networks (Pujol et al., 2016).

In our previous study, we demonstrated a longitudinal negative association between air pollution exposure at schools and trajectories of cognitive development over a course of 12 months. As such, our previous study provided a novel perspective over the effect of air pollution on cognitive development in children; however, given the relatively modest size of the association, it was not able to answer a critical question which has very important implications for both researchers and policymakers: would these modest associations remain over longer periods or they would be counterbalanced and disappear by “catching up” of affected children. This was the very reason we decided to conduct another campaign of cognitive tests 2.5 years after the initial study to evaluate how this effect would remain over a longer period (i.e. 3.5 years in total compared to 1 year of previous study) covering some of the most important years of school period (which make such an effect having important educational implications).

2. Methods

2.1. Study population

The BREATHE project was a longitudinal study conducted in Barcelona (Spain) from 2012 to 2013. Barcelona (Spain) is a city placed on the North-East of the Iberian Peninsula and has a Mediterranean climate with hot and dry summers and mild winters. Barcelona has high levels of air pollution with large exposure contrast over the city (Dadvand et al., 2013). In total, 2897 children who were recruited from 39 schools across Barcelona participated in the 2012/2013 assessments of the BREATHE project. Further details on study settings and school

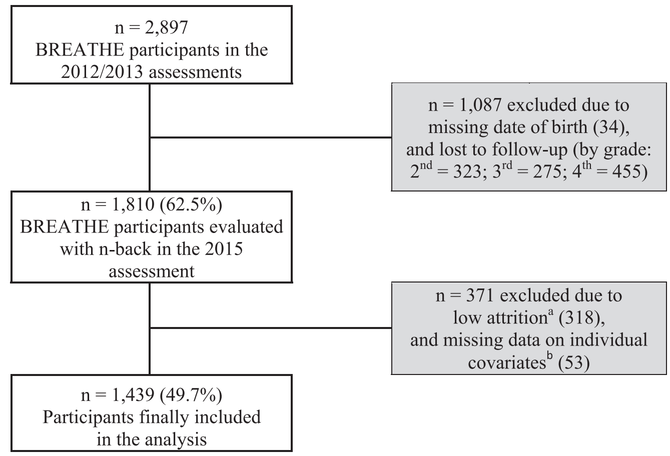

Fig. 1. Flowchart of participants in the study: a Children at 4th grade during 2012/2013 assessment were a priori excluded. The reason of exclusion was the low attrition of these children because the Spanish primary school ends up at 6th grade, therefore, at the time of new assessment these children had already left the primary school. b confounders used in main analysis: maternal education, Urban Vulnerability Index and NO_2 exposure at home address.

selection process have been previously published (Dadvand et al., 2015; Forns et al., 2014; Sunyer et al., 2015). In 2015, a single round of cognitive assessment of children was conducted. In total, 1810 (62.5% of the children recruited) children were assessed during this last follow-up (Fig. 1). The present study was limited to 1439 (49.7% of the children recruited for the BREATHE project) children attending the 2nd and 3rd grade at baseline who also participated in the new round of assessments conducted in 2015. Children in the 4th grade at baseline were *a priori* excluded because the Spanish primary school ends up at 6th grade, therefore, at the time of new assessment these children had already left the primary school and the attrition among this group was high. All parents or guardians signed the informed consent form approved by the Clinical Research Ethical Committee (No. 2010/41221/I) of the Institut Hospital del Mar d'Investigacions Mèdiques.

2.2. Air pollution measurement

For the present analysis, we used the air pollution measurement performed in the 2012/2013 assessment. Briefly, TRAPs were measured twice during one-week sampling campaigns separated by six months (one week in cold season and one week in warm season). In each campaign week, we measured TRAP indoor (in a classroom) and outdoor (in the school playground) levels in two schools simultaneously: one located in an area with high levels of pollution, and one in area with low levels. We selected EC, NO_2, $PM_{2.5}$ from traffic sources and UFP given their relation to road traffic emissions in Barcelona (Amato et al., 2014; Reche et al., 2014; Rivas et al., 2014).

The pollutants measured during class time in schools were real-time concentrations of UPF and black carbon (BC). UFP number (from 10 to 700 nm in the BREATHE project) concentrations were measured using the DiSCmini (Matter Aerosol). Black carbon (BC) concentrations were measured using the MicroAeth AE51 (AethLabs). For the present study, we only included EC in the analyses due to the high correlation ($r = 0.95$) between EC and BC in the $PM_{2.5}$ filters. $PM_{2.5}$ was measured by installing High-Volume samplers (MCV SA, Spain) during 8 h (09:00 to 17:00 h) from Monday to Thursday. Details of $PM_{2.5}$ filter chemical analysis are described elsewhere (Amato et al., 2014). Among the nine sources identified, we selected $PM_{2.5}$ from traffic sources (exhaust and non-exhaust contributions).

EC and NO_2 were adjusted for temporal variability in order to achieve a better spatial long-term average of these TRAPs. Seasonalized levels were obtained by multiplying the daily concentration at each