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Exposure to elemental composition of outdoor $PM_{2.5}$ at birth and cognitive and psychomotor function in childhood in four European birth cohorts

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ABSTRACT

Background: Little is known about developmental neurotoxicity of particulate matter composition. We aimed to investigate associations between exposure to elemental composition of outdoor $PM_{2.5}$ at birth and cognitive and psychomotor functions in childhood.
Methods: We analyzed data from 4 European population-based birth cohorts in the Netherlands, Germany, Italy and Spain, with recruitment in 2000–2006. Elemental composition of $PM_{2.5}$ measurements were performed in each region in 2008–2011 and land use regression models were used to predict concentrations at participants' residential addresses at birth. We selected 8 elements (copper, iron, potassium, nickel, sulfur, silicon, vanadium and zinc) and used principal component analysis to combine elements from the same sources. Cognitive (general, verbal, and non-verbal) and psychomotor (fine and gross) functions were assessed between 1 and 9 years of age. Adjusted cohort-specific effect estimates were combined using random-effects meta-analysis.
Results: 7246 children were included in this analysis. Single element analysis resulted in negative association between estimated airborne iron and fine motor function (− 1.25 points [95% CI − 2.45 to − 0.06] per 100 ng/m^3 increase of iron). Association between the motorized traffic component, derived from principal component analysis, and fine motor function was not significant (− 0.29 points [95% CI − 0.64 to 0.06] per unit increase). None of the elements were associated with gross motor function or cognitive function, although the latter estimates were predominantly negative.

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Conclusion: Our results suggest that iron, a highly prevalent element in motorized traffic pollution, may be a neurotoxic compound. This raises concern given the ubiquity of motorized traffic air pollution.

1. Introduction

Air pollution is a serious threat to human health. The potential effects of air pollution on human brain are an active area of research (Block et al., 2012). Particulate matter (PM), highly prevalent in traffic related air pollution, could reach the brain and other organs by translocation to the systemic circulation following a deposition in the pulmonary region after inhalation (Block et al., 2012). The brain of a fetus could be reached via an indirect path as the placenta and the blood-brain barrier grant only a partial protection against entry of environmental toxicants to which the mother is exposed. As the brain is in the process of development and the detoxification mechanisms are relatively immature, the potential adverse effects of exposure to air pollution during pregnancy are of particular concern (Block et al., 2012; Grandjean and Landrigan, 2014).

Although the precise biological mechanisms are yet to be clarified, there is some evidence for a negative association between pre- and postnatal exposure to outdoor PM and children's cognition, psychomotor development, and behavioral problems (Guxens and Sunyer, 2012; Guxens et al., 2014, 2015; Suades-González et al., 2015). It has been hypothesized that traffic-related PM might be neurotoxic mainly through some of its components such as polycyclic aromatic hydrocarbons (PAHs), black carbon, and trace elements, potentially leading to increased oxidative stress and increased activation of brain microglia, the primary regulators of neuroinflammation (Block et al., 2012). Studies focusing on PAHs found negative association with children's cognition and behavioral problems (Edwards et al., 2010; Lovasi et al., 2014; Perera et al., 2006, 2009, 2013; Wang et al., 2010). Moreover, a recent study using magnetic resonance imaging found preliminary evidence for reduction in the white matter surface of the left hemisphere of the brain in childhood with increased prenatal concentrations of PAHs, associated with slower information processing speed (Peterson et al., 2015). Studies with focus on pre- and postnatal exposure to black carbon also found a negative association with cognitive and/or psychomotor development (Chiu et al., 2013; Suglia et al., 2008), although these findings were inconsistent.

To date, developmental neurotoxicity has been documented for only a small selection of existing trace elements (Grandjean and Landrigan, 2014). Studies addressing the association between pre- and/or postnatal exposure to trace elements in outdoor air and children's brain development are very limited in number. The few existing studies have linked higher levels of several airborne elements including arsenic, cadmium, chromium, lead, manganese, mercury, nickel, selenium, and vanadium, to elevated prevalence of autism spectrum disorder (Lam et al., 2016). Additionally, the only study to date that focused on airborne elements and cognition, found evidence for a negative association between childhood exposure at schools to airborne elements originating from motorized traffic sources and specific cognitive functions in school aged children (Basagaña et al., 2016). However, for many elements, sparse evidence of neurotoxicity is possibly a consequence of limited amount of research addressing the topic rather than absence of an association (Grandjean and Herz, 2015).

Therefore, the aim of this study was to analyze the association between exposure at birth to a set of elements measured in outdoor PM with aerodynamic diameter of < 2.5 μm ($PM_{2.5}$) and cognitive and psychomotor function in childhood using data from four European cohorts. The elemental components examined in this study were copper, iron, potassium, nickel, sulfur, silicon, vanadium and zinc, selected based on their reflection of major anthropogenic emission sources. This study builds on a previous epidemiological study that investigated the association between air pollution and neuropsychological development in 6 European cohorts (Guxens et al., 2014). In that study, the authors found a negative association between prenatal exposure to NO_2 and PM - latter borderline significant - and psychomotor function in childhood. The cohorts included in the current study are a subset of the cohorts studied previously due to the availability of elemental composition data. Also, in the current study we used additional neuropsychological domains and some of the tests included were carried out at older ages.

2. Methods

2.1. Population and study design

This study is part of the ESCAPE (European Study of Cohorts for Air Pollution Effects; www.escapeproject.eu) project. The aim of the project was to investigate the association between exposure to outdoor air pollution and health within prospective cohort studies. In the current study, we included 4 European population-based birth cohorts: GENERATION R (The Netherlands) (Kooijman et al., 2016), DUISBURG (Germany) (Wilhelm et al., 2008), GASPII (Italy) (Porta et al., 2007), and INMA-Sabadell (Spain) (Guxens et al., 2012), a selection based on the availability of elemental composition of $PM_{2.5}$ and neuropsychological data. Mother-child pairs were recruited between 2000 and 2006. A total of 7246 children aged between 1 and 9 years was included in this analysis and had data on exposures and at least one of the neuropsychological outcomes (Table 1). Local authorized Institutional Review Boards granted the ethical approval for the studies and all participants provided signed informed consent.

2.2. Exposure to elemental composition of outdoor $PM_{2.5}$ at birth

The exposure of each participant to the elemental composition of $PM_{2.5}$ at birth was estimated using standardized procedure based on land use regression (LUR) methodology (de Hoogh et al., 2013). A number of studies have shown that LUR models provide a cost-effective methodology to capture the spatial contrasts of air pollution (Hoek et al., 2008; Marshall et al., 2008). The locations of the measuring stations were based on the specific characteristics of each study area including a large diversity of potential sources of air pollution variability, and were selected in a manner to maximise the representativeness of the residential addresses of the cohort participants (Eeftens et al., 2012). We focused on fine particles rather than coarse, due to their higher potential to translocate to the systemic circulation because of the smaller size (Phalen et al., 2010). $PM_{2.5}$ concentrations in outdoor air were measured at 40 sites in the Netherlands/Belgium and Catalunya, and 20 sites in Ruhr area and Rome three times over a year (in summer, winter, and an intermediate season) during a two-week period each time to capture seasonal variations (Eeftens et al., 2012). The campaigns took place between 2008 and 2011. The filters were sent to Cooper Environmental Services (Portland, Oregon, USA) to analyze their elemental composition using X-Ray Fluorescence (XRF) (de Hoogh et al., 2013; Tsai et al., 2015). The results of the three measurements were then averaged, adjusting for temporal trends using data from a continuous reference site, resulting in one mean annual concentration for each element identified in the composition of $PM_{2.5}$.

Following previous ESCAPE studies on elemental components (de Hoogh et al., 2013; Pedersen et al., 2016; Wang et al., 2014) we selected 8 elements based on their reflection of major anthropogenic emission sources and on data availability determined by (i) the coefficient of variation acquired from duplicate samples, (ii) the percentage