Environment International 80 (2015) 33–40

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Full length article

Exposure to fine particle matter, nitrogen dioxide and benzene during pregnancy and cognitive and psychomotor developments in children at 15 months of age

Aitana Lertxundi [a,b], Michela Baccini [c,d], Nerea Lertxundi [b,e], Eduardo Fano [b,e], Aritz Aranbarri [b,e], Maria Dolores Martínez [b,f], Mikel Ayerdi [b,h], Jon Álvarez [g], Loreto Santa-Marina [b,h,i], Miren Dorronsoro [b,h,i], Jesus Ibarluzea [b,h,i,*]

[a] Faculty of Medicine, University of the Basque Country (UPV/EHU), Leioa, Basque Country, Spain
[b] BIODONOSTIA Health Research Institute, San Sebastian, Basque Country, Spain
[c] Department of Statistics, Informatics and Applications "G. Parenti", University of Florence, Italy
[d] Biostatistics Unit, Cancer Prevention and Research Institute (ISPO), Florence, Italy
[e] Faculty of Psychology, University of the Basque Country UPV/EHU, San Sebastian, Basque Country, Spain
[f] Department of the Environment and Regional Planning, Government of the Basque Country, Vitoria, Spain
[g] Public Health Laboratory, Department of Health, Government of the Basque Country, Bilbao, Spain
[h] Sub-Directorate for Public Health of Guipúzcoa, Department of Health, Government of the Basque Country, San Sebastian, Spain
[i] Biomedical Research Centre Network for Epidemiology and Public Health (CIBERESP), Spain

ARTICLE INFO

Article history:
Received 2 July 2014
Received in revised form 14 February 2015
Accepted 2 March 2015
Available online xxxx

Keywords:
Cognitive development
Psychomotor development
Particle matter
$PM_{2.5}$

ABSTRACT

Background: Prenatal exposure to air pollutants has recently been identified as a potential risk factor for neuropsychological impairment.
Objectives: To assess whether prenatal exposure to fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2) and benzene were associated with impaired development in infants during their second year of life.
Methods: Regression analyses, based on 438 mother–child pairs, were performed to estimate the association between mother exposure to air pollutants during pregnancy and neurodevelopment of the child. The average exposure to $PM_{2.5}$, NO_2 and benzene over the whole pregnancy was calculated for each woman. During the second year of life, infant neuropsychological development was assessed using the Bayley Scales of Infant Development. Regression analyses were performed to estimate the association between exposure and outcomes, accounting for potential confounders.
Results: We estimated that a 1 $\mu g/m^3$ increase during pregnancy in the average levels of $PM_{2.5}$ was associated with a −1.14 point decrease in motor score (90% CI: −1.75; −0.53) and that a 1 $\mu g/m^3$ increase of NO_2 exposure was associated with a −0.29 point decrease in mental score (90% CI: −0.47; −0.11). Benzene did not show any significant association with development. Considering women living closer (≤100 m) to metal processing activities, we found that motor scores decreased by −3.20 (90% CI: −5.18; −1.21) for $PM_{2.5}$ and −0.51 (−0.89; −0.13) for NO_2, while mental score decreased by −2.71 (90% CI: −4.69; −0.74) for $PM_{2.5}$, and −0.41 (9% CI: −0.76; −0.06) for NO_2.
Conclusions: Our findings suggest that prenatal residential exposure to $PM_{2.5}$ and NO_2 adversely affects infant motor and cognitive developments. This negative effect could be higher in the proximity of metal processing plants.

1. Introduction

Few data are available concerning neuropsychological effects of air pollution on children. Indicators of air pollution used in epidemiological studies related to neurodevelopment in children include exposure to polycyclic aromatic hydrocarbons (PAHs) (Edwards et al., 2010; Perera et al., 2006, 2008, 2009; Tang et al., 2008), particulates of less than 10 μm in diameter (PM_{10}) (Kim et al., 2014), nitrogen dioxide (NO_2) (Freire et al., 2010; Guxens et al., 2012a; Guxens et al., 2014; Kim et al., 2014), benzene (Guxens et al., 2012a), and black carbon (Suglia et al., 2007), as well as the distance from their home to the nearest main road with high traffic density (Volk et al., 2013) and the area they live being classified as having a high (versus low) level of pollution (Calderon-Garciduenas et al., 2008; Siddique et al., 2011; Wang et al., 2009).

* Corresponding author at: Avenida de Navarra 4, 20013 Donostia-San Sebastian, Spain.
E-mail address: mambien3-san@ej-gv.es (J. Ibarluzea).

http://dx.doi.org/10.1016/j.envint.2015.03.007
0160-4120/

PAH levels have been found to be inversely related to mental scale scores in 3-year-olds and to full-scale and verbal IQ scores in 5-year-olds in a prospective birth cohort from New York (Perera et al., 2006, 2009) and to non-verbal intelligent quotient (IQ) in 5-year-olds in Poland (Edwards et al., 2010). Further, PAH-DNA adducts used as indicators of traffic-related pollution have been found to be inversely correlated with psychomotor development and full-scale IQ in 2-year-olds living in the zone with the greatest exposure to coal-fired power plant emissions in China (Perera et al., 2008; Tang et al., 2008). Exposure to black carbon estimated on the basis of children's place of residence was analysed in a birth cohort study carried out in Boston. A significant decrease in full-scale IQ, non-verbal IQ, and visual memory was observed in children around 9 years of age (Suglia et al., 2007). Prenatal exposure to PM_{10} may result in delayed cognitive and psychomotor developments in early childhood (Kim et al., 2014).

Delayed psychomotor development was found to be associated with NO_2 levels in children assessed between 1 and 6 years of age in six European birth cohorts; no effect was seen on cognitive development (Guxens et al., 2014). In four Spanish regions, exposures to NO_2 and benzene during pregnancy have been associated with adverse effects on the cognitive development of children of 15 months of age when there was a low maternal intake of fruits and vegetables during pregnancy (Guxens et al., 2012a). Results from a small cohort study in Granada (Spain) analysing exposure to NO_2 also indicated reductions in cognitive and psychomotor developments in 4-year-old children (Freire et al., 2010).

Maternal resources during pregnancy play an important role in the physical and mental health of offspring (Bolton et al., 2013; Hackman et al., 2010). Other factors that have been widely studied in relation to their effect on neuropsychological development include maternal IQ (Der et al., 2006), socioeconomic status (Calderón-Garcidueñas and Torres-Jardón, 2012; Hajat et al., 2013) and breastfeeding (Walfisch et al., 2013). Accordingly, analysis of the impact of air pollutants on neurodevelopment must control for the aforementioned variables.

Little is known about possible neurological effects of particle matter in the air. On the other hand, growing interest is being focused on the first years of life due to the susceptibility of the brain to toxicological insults and the importance of this time window for brain development and the decrease in brain plasticity with age (Grandjean and Landrigan, 2006; Sunyer, 2008).

As previously mentioned, Guxens et al. (2012a) found significant associations of NO_2 and benzene with infant neurodevelopment in the Spanish cohorts participating to the INMA (*INfancia y Medio Ambiente*, the Spanish for Childhood and Environment) Project, while the effect of particulate matter has not been explored. In the present work we focused on the INMA birth cohort of the province of Guipúzcoa (the Basque Country, Spain), for which additional information was gathered about maternal exposure to fine particles with an aerodynamic diameter of up to 2.5 μm ($PM_{2.5}$) during pregnancy. The aims of our study were to examine: 1) the association of cognitive and psychomotor developments at 15 months of age with exposure to $PM_{2.5}$, NO_2 and benzene during pregnancy, 2) the role of distance from place of residence to the main industrial activities and roads, and 3) the possible effect modification by breastfeeding duration and maternal antioxidant intake during pregnancy.

2. Methods

2.1. Study area

The study area covers 519 km^2 in the province of Guipúzcoa and spans three narrow valleys: high Urola-Goierri, mid Urola and high Oria. The area has a population of approximately 88,000 inhabitants, spread across 25 small localities (of up to 14,000 inhabitants). At the time of the pregnancies followed-up, the main economic activities in the region were related to the iron and steel industry, with a total of 11 companies in the sector (listed in the 2006 Spanish Register of Emissions and Pollutant Sources, which is the national Pollutant Release and Transfer Register [PRTR]). While this industry contributed significantly to air pollution, another source that needed to be considered was traffic, given that roads with moderate traffic densities (between 10,000 and 40,000 vehicles/day) run through all three valleys.

2.2. Study design and participants

A population-based birth cohort was established as part of the INMA Project in several regions of Spain following a common protocol (Guxens et al., 2012b). In the analysis reported in this paper, we consider only the INMA cohort of Guipúzcoa, recruited between May 2006 and January 2008. A total of 638 eligible women (≥16 years of age, with intention to deliver at the referral hospital, ability to communicate in Spanish or Basque, singleton pregnancy and non-assisted conception) were recruited during antenatal visits in the first trimester of pregnancy. Cognitive and psychomotor developments of 532 children were assessed at around 15 months of age (range 13–18 months) using the Bayley Scales of Infant Development (BSID) (Bayley, 1977). A total of 9.7% (n = 52) of the test results were excluded from the final analysis due to the poor quality of the child assessments.

Data on exposures, outcomes and potential confounders in this analysis were available for 438 children (73.8% of the children included at birth) (Fig. 1). We included all children living in towns where an air pollution monitor was located, plus 18 children from small towns located in the same valley than Ataun, the so-called "clean town", and having similar air quality profile (towns with no direct influence from any of the sources of pollution). A total of 42 mother–child pairs (8.75%) were excluded from the analysis because they lived in hilly or mountain areas where the $PM_{2.5}$ levels did not correspond to those measured in the valley. There were no statistically significant differences in main characteristics between the mother–child pairs included in the analyses and those excluded (Table S1). The study was approved by the hospital ethics committee and all participating mothers provided informed consent.

2.3. Neuropsychological testing

The mental scale of the BSID consists of 163 items that assessed age-appropriate cognitive development in areas including performance

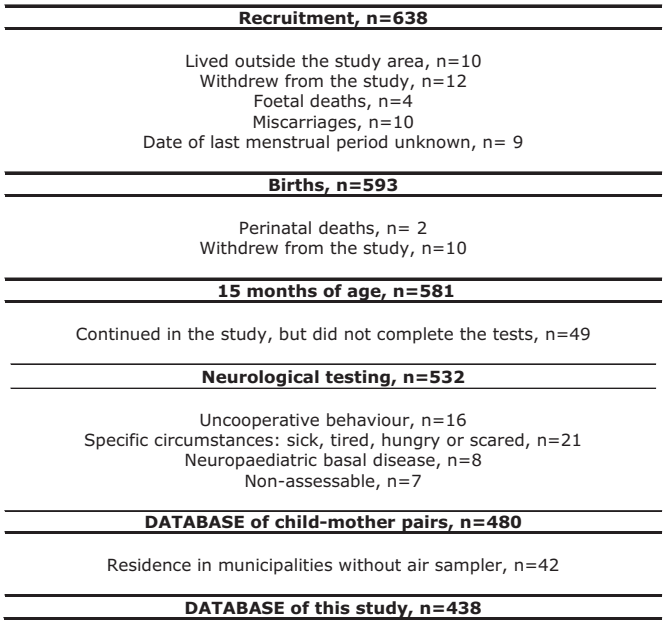

Fig. 1. Follow-up of the cohort of pregnant mothers and their children until a mean of 15 months of age. $PM_{2.5}$, NO_2 and benzene and neuropsychological development.