Environmental Research 166 (2018) 215–222

Contents lists available at ScienceDirect

Environmental Research

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

Maternal selenium status and neuropsychological development in Spanish preschool children

Rubén Amorós[a,b], Mario Murcia[c,d], Llúcia González[d], Marisa Rebagliato[c,d], Carmen Iñiguez[c,d,e], Maria-Jose Lopez-Espinosa[c,d], Jesús Vioque[c,f], Karin Broberg[g], Ferran Ballester[c,d], Sabrina Llop[c,d,*]

[a] Foundation for the Promotion of Health and Biomedical Research in the Valencian Region, FISABIO, Av. Catalunya 21, 46020 Valencia, Spain
[b] School of Mathematics, University of Edinburgh, Peter Guthrie Tait Road, EH9 3FD Edinburgh, United Kingdom
[c] Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Av. Monforte de Lemos, 3-5. Pabellón 11, 28029 Madrid, Spain
[d] Epidemiology and Environmental Health Joint Research Unit, FISABIO-Universitat Jaume I-Universitat de València, Av. Catalunya 21, 46020 Valencia, Spain
[e] Department of Statistics and Operational Research, Universitat de València, Carrer del Dr. Moliner, 50, 46100 Burjassot, Spain
[f] Department of Public Health, Universitat Miguel Hernández, Av. de Alicante KM 87, 03550 Sant Joan d´Alacant, Spain
[g] Institute of Environmental Medicine, Karolinska Institutet, Nobels väg 13, Box 210, 17177 Stockholm, Sweden

ARTICLE INFO

Keywords:
Selenium
Pregnancy
Children
Neurodevelopment
Nutrient

ABSTRACT

Background: The relationship between maternal selenium (Se) status and child neurodevelopment has been scarcely assessed. In a previous study we observed an inverse U-shaped association between maternal Se concentrations and infant neurodevelopment at 12 months of age. In this study, this non-linear association was explored at preschool age. The effect modification by breastfeeding, child's sex and cord blood mercury was also evaluated.

Methods: Study subjects were 490 mother-child pairs from the Spanish Childhood and Environment Project (INMA, 2003–2012). Child neuropsychological development was assessed at around 5 years of age by the McCarthy Scales of Children's Abilities (MSCA). Sociodemographic and dietary characteristics were collected by questionnaire at the first and third trimester of gestation and at 5 years of age. Se was measured in serum samples by ICP-MS at the end of the first trimester of pregnancy (mean ± standard deviation (SD) = 12.4 ± 0.6 weeks of gestation).

Results: The mean ± SD of maternal serum Se concentrations was 79.9 ± 8.1 μg/L. In multivariate analysis, no linear association was found between Se concentrations and the nine MSCA scales. Generalized additive models indicated inverted U-shaped relationships between Se concentrations and the verbal and global memory scales. When assessing the influence of effect modifiers, breastfeeding played a role: the association between Se and neuropsychological development was inverted U-shaped for the quantitative, general cognitive, working memory, fine motor, global motor and executive function scales only for non-breastfed children.

Conclusion: Low and high maternal Se concentrations seem to be harmful for child neuropsychological development, however further studies should explore this non-linear relationship.

1. Introduction

Selenium (Se) is a trace element that is essential for early development since it is incorporated into selenoproteins with a crucial role in preventing damage from oxidative stress during foetal development (Mihailovič et al., 2000; Mistry and Williams, 2011). During pregnancy there is an enhanced demand for Se since it is in part transferred to the foetus (Nandakumaran et al., 2003; Santos et al., 2017); in fact, a decreasing concentration of Se in maternal blood has been reported during this period (Pieczyńska and Grajeta, 2015).

A deficiency of Se during pregnancy has been associated with adverse outcomes, which include miscarriages, preeclampsia, gestational diabetes, premature rupture of membranes and intra-uterine growth restriction (Mistry et al., 2012). In addition, selenoproteins are important for normal brain function, and a lower expression of them can lead to impaired cognitive function and neurological disorders (Pillai

* Corresponding author at: Epidemiology and Environmental Health Joint Research Unit, FISABIO-Universitat Jaume I-Universitat de València, Av. Catalunya 21, 46020 Valencia, Spain.
E-mail address: llop_sab@gva.es (S. Llop).

https://doi.org/10.1016/j.envres.2018.06.002
Received 2 March 2018; Received in revised form 30 May 2018; Accepted 1 June 2018

et al., 2014). However, adverse effects in the nervous system due to a chronic overexposure to Se have also been identified in China, USA or Italy in populations living in high Se content areas (Vinceti et al., 2014).

Se is also present in breast milk as organic compounds and selenoproteins, especially the GPx. In fact, human milk is fundamental for the infant's optimum Se status; thus, a higher plasma Se concentration and glutathione peroxidases (GPx) activity in breastfed infants compared with formula-fed or cow milk-fed infants has been reported (Dorea, 2002). In addition, breast milk has other nutrients, such as fatty acids, that are crucial for development of the nervous system (Innis, 2014).

Very few prospective studies have evaluated the relationship between Se status during pregnancy and child neuropsychological development among populations with intermediate Se levels and the results obtained have been heterogeneous. Thus, positive, negative and null effects on child neuropsychological development have been observed in relationship to prenatal Se levels (Amorós et al., 2018; Kippler et al., 2016; Oken et al., 2016; Polanska et al., 2016; Skröder et al., 2015; Yang et al., 2013) and, in addition, the shape of this association has scarcely been assessed.

In a previous study, we reported an inverted U-shaped relationship between maternal Se status and child neuropsychological development evaluated at around 12 months of age, the turning point for this association being estimated at 86 μg/L (Amorós et al., 2018). The relevance of these findings justifies a further evaluation of Se-related effects at older ages.

The aim of this study was to evaluate the association between maternal Se status and child neuropsychological development evaluated at 5 years of age in the same Spanish population. We also assessed the effect modification by children's sex, breastfeeding, and cord blood mercury.

2. Methods

2.1. Study population

Study subjects were participants in the Valencia region cohort of the INMA Project (Childhood and Environment Project: http://www.proyectoinma.org) – a multicentre birth cohort study that aims to investigate the effects of environmental exposures and diet during pregnancy on foetal and child health in different areas of Spain.

The study protocol has been reported elsewhere (Guxens et al., 2012). Briefly, pregnant women were recruited at the beginning of their pregnancy in the Spanish region of Valencia (n = 855, 2003–2005). A total sample of 787 (92%) women was followed up until delivery. Their children were enrolled at birth and monitored until 5 years of age (n = 536, 63%). The final study population was made up of 490 (57%) mother–child pairs for whom Se concentrations and neuropsychological test scores were available. Informed consent was obtained from all participants in each phase and the study was approved by the Ethics Committee of La Fe Hospital, Valencia, Spain.

2.2. Selenium concentrations

Concentrations of Se were determined in serum samples taken at the end of the first trimester of pregnancy (mean ± standard deviation (SD) = 12.4 ± 0.6 weeks of gestation). The concentrations of serum Se were determined by inductively coupled plasma mass spectrometry with the collision/reaction cell system in hydrogen mode. More information about the methodology used for Se analysis has been reported in detail elsewhere (Amorós et al., 2018) and can be found in the supplementary material.

The limit of detection was 0.03 μg/L and no samples had concentrations below this value. Se concentrations were corrected according to the variations in three daily measures of the Seronorm™ (lot MI0181) reference material. The correction was performed by adding to each measure the difference between the daily mean of the reference measures and the overall mean of the reference measures (Amorós et al., 2018).

2.3. Child neurodevelopment evaluation

The neuropsychological development of the children was assessed at 5 years of age (mean ± SD = 5.8 ± 0.16 years) by using a standardized version of the McCarthy Scales of Children's Abilities (MSCA) adapted to the Spanish population (McCarthy D, 2009).

The MSCA comprise 18 subtests that yield standardized test scores for six conventional domains. The verbal scale refers to cognitive tasks related to the processing of verbal information; the perceptual-performance scale refers to cognitive tasks related to perceptual information processing, including manual performance; the quantitative scale assesses numerical abilities; the global memory scale considers short-term retention of information (verbal, visual or numerical); and the motor scale refers to fine (e.g. drawing) and gross (e.g. balance or accuracy) abilities. The sum of the first three scales provides a general cognitive scale. MCSA's subtests were reorganized into new outcome subarea scores according to those tasks highly associated with a specific neurocognitive function (Julvez et al., 2007, 2011). The new outcome subareas were: working memory, which refers to those cognitive tasks related to temporarily storing and managing the information required to carry out other cognitive tasks such as learning, reasoning and comprehension; executive function, which refers to those cognitive tasks critical to non-routine, goal-oriented situations that are performed by the pre-frontal cortex; and fine motor. Items comprising each of the scales are indicated in Fig. S.1 of the Supplemental material. Testing was conducted by two psychologists using a strict protocol.

2.4. Other variables

The women completed two questionnaires during their pregnancy, one at the first trimester (mean ± SD = 12.6 ± 1.4 weeks of gestation) and the other at the third trimester (mean ± SD = 32.3 ± 1.8 weeks of gestation). The questionnaires were administered by trained interviewers and focused on sociodemographic, dietary, environmental and lifestyle information during pregnancy. The maternal covariates and potential confounders collected were: country of birth, age, body mass index before pregnancy, level of education, parity, area of residence, working status during pregnancy, smoking at the beginning of pregnancy and season of sampling. We also obtained data on paternal age, working status and level of education.

Parental social class was defined from the maternal or paternal occupation during pregnancy with the highest social class, according to a widely used Spanish adaptation of the International Standard Classification of Occupations, approved in 1988 (ISCO88) (Class I + II: managerial jobs, senior technical staff and commercial managers; class III: skilled non-manual workers; and class IV + V: manual and unskilled workers).

Information on diet during pregnancy was collected by using a semiquantitative food frequency questionnaire (FFQ). Maternal intake of bread, eggs and seafood were identified as sources of Se in our study population (Amorós et al., 2018), and for this reason they were tested as possible confounders in the present study.

Information on the children's gestational age, sex, birth weight, breastfeeding (no, yes) and birth size was obtained from clinical records and subsequent interviews. Breastfeeding was defined as receiving breast milk, although it could be supplemented with any other food or liquid, including non-human milk.

Information about maternal and paternal working status, maternal and paternal smoking habit in the presence of the child, and a proxy of the maternal verbal intelligence quotient (IQ) was obtained in an interview at the same time-point as the neuropsychological development assessment. The maternal verbal IQ proxy was assessed using the Similarities Subtest of the Weschler Adult Intelligence-Third Edition