NeuroToxicology 53 (2016) 215–222

Contents lists available at ScienceDirect

NeuroToxicology

Full length article

Associations between prenatal mercury exposure and early child development in the ALSPAC study

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ARTICLE INFO

Article history:
Received 8 October 2015
Received in revised form 1 February 2016
Accepted 10 February 2016
Available online 12 February 2016

Keywords:
ALSPAC
Maternal blood mercury
Child Development
Selenium
Fish
Prenatal exposure

ABSTRACT

Introduction: There is evidence that high levels of mercury exposure to the pregnant woman can result in damage to the brain of the developing fetus. However there is uncertainty as to whether lower levels of the metal have adverse effects on the development of the infant and whether components of fish consumption and/or the selenium status of the woman is protective.

Methods: In this study we analysed data from the Avon Longitudinal Study of Parents and Children (ALSPAC) ($n = 2875–3264$) to determine whether levels of total blood mercury of pregnant women collected in the first half of pregnancy are associated with the development of the offspring at ages 6, 18, 30 and 42 months. The developmental measures used maternal self-reported scales for individual types of development (fine and gross motor, social and communication skills) and total scores. Multiple and logistic regression analyses treated the outcomes both as continuous and as suboptimal (the lowest 15th centile). The statistical analyses first examined the association of prenatal mercury exposure with these developmental endpoints and then adjusted each for a number of social and maternal lifestyle factors; finally this model was adjusted for the blood selenium level.

Results: Total maternal prenatal blood mercury and selenium ranged from 0.17 to 12.76 and 17.0 to 324 μg/L respectively. We found no evidence to suggest that prenatal levels of maternal blood mercury were associated with adverse development of the child, even when the mother had consumed no fish during pregnancy. In general, the higher the mercury level the more advanced the development of the child within the range of exposure studied. For example, the fully adjusted effect sizes for total development at 6 and 42 months were +0.51 [95%CI +0.05, +1.00] and +0.43 [95%CI +0.08, +0.78] points per SD of mercury. For the risk of suboptimal development the ORs at these ages were 0.90 [95%CI 0.80, 1.02] and 0.88 [95%CI 0.77, 1.02]. In regard to the associations between blood mercury and child development there were no differences between the mothers who ate fish and those who did not, thus implying that the benefits were not solely due to the beneficial nutrients in fish.

Conclusions: We found no evidence of adverse associations between maternal prenatal blood mercury and child development between 6 and 42 months of age. The significant associations that were present were all in the beneficial direction.

1. Introduction

In the Minamata tragedy during which a Japanese population consumed seafood (mainly shellfish) contaminated with very high levels of mercury, substantial brain damage resulted, especially to those individuals exposed in utero (Harada, 1968). Subsequently it has been assumed that even low levels of this toxic metal in pregnancy (which crosses the placenta easily) will have deleterious effects on the development of the brain of the offspring.

A number of studies have compared the maternal prenatal levels of mercury, either estimated from maternal hair, umbilical cord tissue or cord blood, with the cognitive development of the child. The results have been mixed, and varied with the type of seafood eaten in the area in which the studies were carried out. For example, in a review of the evidence Myers and Davidson (1998)

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http://dx.doi.org/10.1016/j.neuro.2016.02.006

noted that no adverse associations have been found in the Seychelles cohort study, where exposure to methyl mercury is mainly from fish consumption. In contrast, in the Faroe Islands where seafood exposure is primarily from consumption of whale meat and not fish, adverse associations have been reported (Grandjean et al., 1998); this difference may be because sea mammals are contaminated with multiple other toxicants.

In comparison with studies of school age children, there have been relatively few publications concerning preschool development in association with prenatal mercury exposure. Using the Bayley developmental scales a cohort of 374 children in Poland were examined at 12, 24 and 36 months but only the 12 month measure showed a significant deleterious outcome after adjustment (Jedrychowski et al., 2006, 2007). In the USA, Oken and colleagues reported that at 6 months there was a difference in novelty preference using a test of visual recognition memory (Oken et al., 2005), and at 3 years there were higher scores on tests of child development if the mother had eaten fish in pregnancy (Oken et al., 2008). The World Trade cohort used the Bayley MDI and PDI scales at ages 12, 24 and 36 months but only the 36 month measure showed a significant negative association of mercury with PDI, and only after controlling for fish intake (Lederman et al., 2008). These studies all involved relatively small numbers (<400), and tended to measure different end-points at different ages. They conveyed mixed messages concerning effects which may also have been the result of lack of power.

Not surprisingly there are also mixed messages from advisory bodies with somewhat arbitrary cut-offs for levels of concern of blood mercury levels for adults ranging from 2.0 μg/L in Germany to 5.8 μg/L in the USA (Taylor et al., 2014). However Raymond and Ralston (2004) postulated that "measuring the amount of mercury in the environment or food sources may provide an inadequate reflection of the potential for health risks if the protective effects of selenium are not also considered."

We use a large prenatal birth cohort that includes measures of prenatal fish intake, blood selenium as well as blood mercury—the Avon Longitudinal Study of Parents and Children (ALSPAC). Adjusted analyses of this cohort have already shown that six of the 14 subcomponents of the total development scores showed significant trends with the amount of fish eaten, the less fish the mother ate, the more likely the child to be in the lowest quartile of ability (Hibbeln et al., 2007). This was particularly true of fine motor skills at 18 and 42 months, communication skills at 6 and 18 months and social skills at 30 and 42 months. No analyses of ALSPAC have yet determined whether the prenatal level of blood mercury is associated with these aspects of development, or with the total development scores.

Table 1
Summary of basic statistics relating to child development scores using questionnaire measures.

Age	Score	No. tested	Range	Median	Mean [SD]
6 m	Social skills	11354	0–30	17	17.23 [4.86]
	Fine motor	11359	0–33	21	21.13 [6.36]
	Communication	11355	0–24	16	16.44 [2.97]
	Gross motor	11394	0–39	16	16.42 [5.93]
	Total	11348	6–126	70	71.23 [15.57]
18 m	Social skills	11087	0–28	19	19.15 [3.89]
	Fine motor	11090	0–32	27	26.69 [3.06]
	Communication	11102	0–28	16	15.94 [4.79]
	Gross motor	11087	0–22	20	19.45 [2.88]
	Total	11067	4–110	82	81.25 [10.78]
30 m	Social skills	10260	0–26	19	18.94 [3.76]
	Fine motor	10286	0–32	27	26.37 [3.76]
	Gross motor	10272	0–22	20	19.51 [2.52]
	Total	10244	0–80	66	64.87 [7.82]
42 m	Social skills	10014	0–26	23	22.10 [3.14]
	Fine motor	10019	0–34	31	29.72 [4.06]
	Gross motor	10026	0–30	27	26.35 [3.59]
	Total	10011	0–90	80	78.19 [8.83]

The aims of this study therefore are to provide evidence to help elucidate:

(1) whether maternal prenatal blood mercury levels are associated with adverse preschool development;
(2) whether maternal blood selenium levels modify any associations with pre-school development;
(3) whether maternal fish consumption (with its beneficial levels of omega-3 fatty acids, vitamin D, choline and iodine (Wu et al., 2013) mask any adverse effects of maternal blood mercury on offspring development;
(4) whether the different components of the child development measures (fine and gross motor, communication and social skills) have differential associations.

2. Material and methods

2.1. The ALSPAC cohort

The ALSPAC study aimed to enrol all pregnant women residing in Avon (a geographically defined area that includes the city of Bristol, smaller urban towns, and rural areas about 120 miles west of London, UK) with an expected delivery date between 1 April 1991 and 31 December 1992. The study enrolled 14,541 pregnant women, estimated as about 80% of those eligible. Its stated aims were to evaluate genetic and environmental influences on health and development, including environmental factors measured prospectively during pregnancy (Golding et al., 2001; Boyd et al., 2013). Heavy metals were targeted in the planning for the study, which is why blood samples were obtained in acid-washed vacutainers (which was the advice at the time). In addition, detailed conversations at the planning stage with the late Dr David Horrobin resulted in the collection of dietary information to specifically identify possible effects of prenatal fatty acids (particularly oily fish) on the fetal brain. The study website contains details of all the data that are available through a fully searchable data dictionary: <http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/http://www.bris.ac.uk/alspac/researchers/data-access/data-dictionary/>

2.2. Prenatal trace metal exposures

Blood samples specifically collected in acid-washed containers for determination of trace metals were obtained from 4484 women residing in two of the three Health Authority areas of the recruitment region. Samples were obtained by midwives as early as possible in pregnancy. The sociodemographic characteristics of the women who donated samples were comparable to those of the rest of the ALSPAC study population apart from including a slight excess of older and more educated mothers (Taylor et al., 2013). Gestational age at sample collection [known for 4472 mothers (99.7%)] had a median value of 11 weeks and mode of 10 weeks. The interquartile range (IQR) was 9–13 weeks, and 93% of the samples were collected at <18 weeks gestation. Samples were stored for 0–4 days at 4 °C at the collection site before being sent to the central Bristol laboratory. Samples were transported at room temperature for up to three hours, and stored at 4 °C as whole blood in the original collection tubes for 18–19.5 years before analysis.