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Total mercury exposure in early pregnancy has no adverse association with scholastic ability of the offspring particularly if the mother eats fish

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ABSTRACT

There is a public perception that relatively low doses of mercury found in seafood are harmful to the fetal brain but little consistent evidence to support this. In earlier publications we have shown no adverse associations between maternal total blood mercury levels and child behaviour, early development or cognitive function as measured by IQ. However, for IQ the lack of adverse association was conditional upon the mother being a fish eater.

In this paper we analyse further data from the Avon Longitudinal Study of Parents and Children (ALSPAC), this time examining whether prenatal exposure to total mercury is associated with the child's scholastic abilities in reading, spelling, phoneme awareness, mathematics and science; the number of participants with prenatal mercury and relevant test results varied from 1500 to 2200. Multiple regression was used to assess relationships between prenatal total blood mercury concentrations and 16 different test results, after taking account of a variety of potential confounders; in parallel, logistic regression was used to determine associations with the risk of the child being in the lowest 15% of each score. Analyses were repeated stratifying for fish consumption and sex of the child.

There was no evidence of harm associated with the level of total mercury, provided the mother ate fish during pregnancy. This was particularly true for tests of mathematics and science. We conclude that women should be confident that eating fish in pregnancy is beneficial for their unborn child.

1. Introduction

Very high doses of total mercury in pregnancy have a harmful effect on the development of offspring, with increased risks of cerebral palsy and cognitive impairment (Snyder, 1971). Such deleterious exposures have been found, for example, when spillages of pollutants into water have undergone bioaccumulation by fish and shellfish, with subsequent consumption by the population (such as in Minamata in Japan), or when grain treated with mercury was unintentionally put into the human food chain (such as happened in Iraq) (Amin-Zaki et al., 1976). Such adverse events have understandably raised concerns about all levels of exposure to mercury during pregnancy.

There have been several studies measuring maternal prenatal exposure to low levels of mercury and subsequent child development, with results that are sometimes reported erroneously as causing problems to the offspring (e.g. Myers et al., 2015). Such studies necessitate collecting data during pregnancy and then following the offspring into childhood (and beyond). Using a large population cohort in the UK, we have found that early child development and IQ measured at age 8 years were not affected by the mother's total mercury level if she ate fish (Golding et al., 2016a, 2016b, 2017).

The most important outcome of mercury exposure from the point of view of the future economic success of a country lies in the ability of its workforce, particularly regarding their literacy and numeracy. However, to our knowledge, only two studies appear to have considered these outcomes: the Seychelles Child Development Study (Davidson

Abbreviations: ALSPAC, Avon Longitudinal Study of Parents & Children; CDC, Centers for Disease Control & Prevention; LOD, Level of detection; IQR, Interquartile range; NARA, Neale Analysis of Reading Ability; TOWRE, Test of Word Reading Ability; WISC, Wechsler Intelligence Scale for Children; WORD, Wechsler Objective Reading Dimension; WPPSI, Wechsler Preschool and Primary Scale of Intelligence

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et al., 2010, 2011) and a study in New Zealand (Gearhart et al., 1995).

The New Zealand study is little known; details of the methodology used are scanty, and it is not clear that all the publications arising from it have been peer-reviewed. The study started in the North Island of New Zealand with a birth survey of 10,970 pregnancies. A small group of women with high hair mercury levels who were relatively high fish consumers (> 3 times per week) were identified and each was matched with three controls of differing mercury levels and fish consumption. The offspring of 57 matched sets were followed up at 6 years of age and given a battery of 26 tests which included reading and mathematics. Although the authors did not give the results for each test, they did claim that none showed an association between maternal mercury level and outcome. However, if an outlier of over 50 ppm higher than the rest of the cohort was removed, there were six of the outcomes that were associated at the 10% level, but it is unclear which test results were implicated (Crump et al., 1998).

In comparison, the longitudinal study undertaken in the Seychelles is very well documented and well designed. A study of 643 unselected children in this cohort had results from their national standardised examinations at ages 9 and 17 years linked to their mother's prenatal mercury level (as estimated from maternal hair). The subjects of the examinations undertaken at 9 years of age comprised English, French, Creole, mathematics, science and social studies; at 17 years geography and history were added but Creole and social studies were excluded. None of these outcomes showed any adverse relationship with prenatal mercury exposure, and there was a beneficial association with one of the math tests at 17 years (Davidson et al., 2010, 2011).

The study in the Seychelles was undertaken because the population of the archipelago consumed a large quantity of fish on average and therefore, if there were adverse effects of such a diet, particularly regarding the consequent increased levels of mercury, this study should have sufficient statistical power to reveal it. However, despite a large variety of measures over the years, there have been no significant adverse outcomes attributable to mercury. Indeed comparison of the scholastic abilities of the Seychelles children with other countries in Africa and the Indian Ocean shows them to be among the most advanced in ability (Leste and Davidson, 2004).

Nevertheless, it is important that similar studies be undertaken in areas where less fish is consumed, and where any adverse effects of prenatal mercury exposure may be masked by beneficial effects of fish but revealed in the offspring of women who have not eaten fish. We therefore used the comprehensive data collected on a population of pregnant women in the UK in 1991–2, whose total blood mercury level is available for the first half of pregnancy and whose offspring have been followed throughout childhood and adolescence.

2. Material and methods

2.1. The study design

The Avon Longitudinal Study of Parents and Children (ALSPAC) aimed to study all births to women resident in a geographic area (Avon) in the UK, whose expected date of delivery lay between the 1st April 1991 and 31st December 1992. It recruited 14,541 women who completed at least one questionnaire. Of these initial pregnancies, there was a total of 14,676 fetuses, resulting in 14,062 live births and 13,988 children who were alive at one year of age. The study's stated aims were to determine ways in which the individual's genotype combines with environmental pressures to influence health and development. It recognised the need to identify environmental factors prospectively during pregnancy. The advantage of an area-based study concerned the relative ease of contacting the pregnant women, collecting biological samples and providing facilities for hands-on examination of the study children under controlled circumstances. (Boyd et al., 2013; Golding et al., 2001). For full details of all the data collected see the study website: www.bristol.ac.uk/alspac/researchers/data-access/data-dictionary/. Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees.

2.2. The exposures

2.2.1. Measurement of total blood mercury

This has been described in detail elsewhere (Golding et al., 2013). In brief, blood samples were collected in acid-washed vacutainers provided by ALSPAC to midwives who were collecting blood for clinical purposes on the first occasion on which they saw the pregnant women. Samples were kept as whole blood in the original tubes for long-term storage at 4 °C. After approximately 19 years, the samples were sent to the Centers for Disease Control and Prevention (CDC) for analysis of whole blood mercury, lead, selenium, and cadmium (CDC method 3009.1). Of the 4484 samples collected, 4131 had valid results for total mercury. Only three samples had total mercury values below the assay limit of detection (LOD) (0.24 μg/L); they were assigned the LOD value divided by the square root of 2.

Gestational age at sample collection ranged from 1 to 42 weeks, with a median value of 11 weeks and mode of 10 weeks. The IQR (interquartile range) was 9 to 13 weeks, and 93% of the samples were collected at < 18 weeks of gestation.

2.2.2. Maternal consumption of fish

The pregnant woman was sent a questionnaire at 32 weeks gestation, which included a food frequency questionnaire. This enquired about the frequency with which she ate white fish and oily fish. We used these two questions to identify women who ate no fish, as previously described (Golding et al., 2016a, 2016b, 2017).

2.3. The outcome measures

A total of 15 different scholastic tests have been used in this paper, covering spelling, reading, phoneme understanding, mathematics and science; 11 of these tests were administered in the ALSPAC clinics in a one-to-one situation, and the three mathematics reasoning and the one scientific reasoning tests were administered in a school setting. Details of the tests used are described in the Supplementary Information.

2.4. The analyses

Ways in which the total blood mercury varies with demographic and lifestyle factors is shown in Appendix Table 1. Because of these and other associations we therefore took account of maternal age at the child's birth, parity of the mother at the birth (no. previous births: 0 v 1 +); maternal education level (in five levels of achievement); housing tenure (owner occupied; public housing; other rented); level of household crowding (no. persons in the household divided by the number of living rooms and bedrooms); no. of stressful life events during the first half of pregnancy; whether the mother smoked at mid-pregnancy (yes; no); whether any alcohol was drunk mid-pregnancy (yes; no); whether the infant was breast fed (yes; no); and the family adversity index (a score comprised of a number of adverse features present during pregnancy including presence of maternal depression and anxiety). Because the educational ability of the child depends on the length of time he/she has attended school, we took account of that rather than age when tested.

We mainly employed regression analyses, treating both mercury and the scholastic measures as continuous variables; results for the adjusted and unadjusted outcomes are presented as β coefficients (i.e. the change in value per SD of total mercury). The analyses were repeated according to whether the mother had eaten fish or not prenatally, and whether the child was a boy or girl.

To determine whether the children who had low results on the scholastic tests were at especial risk, we used logistic regression to