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Maternal methylmercury exposure through rice ingestion and offspring neurodevelopment: A prospective cohort study

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ABSTRACT

Background: Dietary methylmercury intake can occur not only through fish ingestion but also through rice ingestion; however, rice does not contain the same beneficial micronutrients as fish.
Objectives: In rural China, where rice is a staple food, associations between prenatal methylmercury exposure (assessed using maternal hair mercury) and impacts on offspring neurodevelopment were investigated.
Methods: A total of 398 mothers were recruited at parturition at which time a sample of scalp hair was collected. Offspring (n = 270, 68%) were assessed at 12 months using the Bayley Scales of Infant Development-II, yielding age-adjusted scores for the Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI).
Results: Among 270 mothers, 85% ingested rice daily, 41% never or rarely ingested fish/shellfish and 11% ingested fish/shellfish at least twice/weekly. Maternal hair mercury averaged 0.41 μg/g (median: 0.39 μg/g, range: 0.079–1.7 μg/g). In unadjusted models, offspring neurodevelopment (both MDI and PDI) was inversely correlated with hair mercury. Associations were strengthened after adjustment for fish/shellfish ingestion, rice ingestion, total energy intake (kcal), and maternal/offspring characteristics for both the MDI [Beta: −4.9, 95% Confidence Interval (CI): −9.7, −0.12] and the PDI (Beta: −2.7, 95% CI: −8.3, 2.9), although confidence intervals remained wide for the latter.
Conclusions: For 12-month old offspring living in rural China, prenatal methylmercury exposure was associated with statistically significant decrements in offspring cognition, but not psychomotor development. Results expose potential new vulnerabilities for communities depending on rice as a staple food.

1. Introduction

Fish consumption is the primary exposure pathway for methylmercury (MeHg), a potent neurotoxin, which impairs fetal brain development (Clarkson and Magos 2006; National Research Council (NRC) 2000). Dietary MeHg intake also occurs through rice ingestion (Rothenberg et al., 2013, 2014); however, less is known concerning the impacts of MeHg exposure from maternal rice ingestion on offspring neurodevelopment.

Fish tissue is a source for MeHg as well as micronutrients that benefit fetal brain development and retinal development, including long-chain polyunsaturated omega-3 (N-3) fatty acids, selenium (Se), choline, iodine and iron (Fe) (Choi et al., 2008; Davidson et al., 2008; Georgieff and Innis 2005; Oken et al., 2005, 2008; Strain et al., 2008). Although rice MeHg concentrations are lower com-

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pared to fish tissue (Rothenberg et al., 2014), rice consumption is substantial in regions of the world where rice is a staple food (Food and Agriculture Organization of the United Nations (FAO), 2015). Furthermore, rice does not contain the same beneficial micronutrients as fish (Rothenberg et al., 2011a). This is partially due to the rice polishing process, which simultaneously removes micronutrients concentrated in the outer bran layer (Villareal et al., 1991). For example, rice-eating communities are often zinc (Zn)-deficient (Allen et al., 2006) because polished white rice contains lower Zn concentrations compared to unpolished brown rice (e.g., 66% less) (Villareal et al., 1991). Conversely, polishing does not reduce MeHg because MeHg accumulates in the rice endosperm and not the outer bran layer (Rothenberg et al., 2011b). Zn deficiency is associated with delays in attention and motor development (Allen et al., 2006) supporting the notion that MeHg exposure from rice may have a different confounding pattern than is characteristic of MeHg exposure from fish ingestion.

Half the world's population subsists on polished rice as a staple food, mostly in Asia (FAO, 2015), where global mercury (Hg) emissions are highest (Zhang et al., 2016), and where locally grown rice may therefore be susceptible to Hg contamination. Atmospheric Hg may be deposited to flooded rice paddies, where anaerobes convert inorganic Hg to MeHg, which is efficiently accumulated in rice grain (Rothenberg et al., 2014).

In 2013, we initiated a prospective birth and child cohort study in rural China, where rice is a staple food, to investigate associations between maternal rice ingestion during pregnancy, biomarkers of MeHg exposure, and offspring neurodevelopment. In this study population, prenatal MeHg exposure during the third trimester (assessed using hair Hg and blood Hg) was similar to other cohorts of pregnant mothers, where fish consumption was the primary MeHg exposure pathway, although dietary MeHg intake was primarily through rice ingestion (average: 71%, median: 87%) and to a lesser extent fish/shellfish ingestion (average: 29%, median: 13%) (Hong et al., 2016).

2. Methods

2.1. Recruitment and Data Collection

Adult women were recruited at parturition at the Maternal and Child Health Hospital in Daxin County, Guangxi, China. Eligible mothers were in good general health, resided in Daxin County during the three previous months, and planned to remain for the next year. The recruitment goal was 400 to ensure sufficient number of children at the follow-up. Residency in Daxin County was important to ensure higher follow-up at 12 months, and consistency in environmental Hg exposures and food consumption patterns. Protocols were reviewed and approved by the Institutional Review Boards at the University of South Carolina (USA) and XinHua Hospital (China). Eligible mothers provided written informed consent prior to enrollment in the study.

After enrollment, ~50 strands of maternal hair (for Hg analyses) were collected from the occipital region and stored at room temperature in a plastic bag. A non-fasting blood sample was collected by venipuncture (6 mL total) into two vials, including one with lithium heparin anticoagulant [for Hg and lead (Pb) analyses], and a second vial for separation of serum by centrifugation [selenium (Se) and Zn analyses]. Whole blood and serum were stored frozen at the hospital at −26 °C for up to 10 months, then transported to Shanghai where samples were archived at −80 °C until analysis.

During their hospital stay, mothers completed a questionnaire eliciting information about demographics, maternal and paternal education and occupation, monthly household income, maternal pregnancy history (including smoke and alcohol exposure), family health history, and child's birth length and weight.

2.2. Food frequencies

Mothers also filled out a modified semi-quantitative 102-item food frequency questionnaire (FFQ) (Cheng et al., 2009), reflecting food intake during the third trimester. Food categories included rice, seven commonly consumed varieties of fish and shellfish (freshwater fish, ocean fish, shrimp, eel, snails, crab, and other shellfish), and other foods (e.g., pork, eggs, tofu, fruits and vegetables). For each food item, the FFQ provided eight options, ranging from "never or rarely" to "≥2 times/day". Food frequencies were converted to servings per day as follows: 0 = never or rarely, 1/30.5 = monthly, 2.5/30.5 = two to three times/month, 1/7 = once per week, 2.5/7 = two to three times/week, 5/7 = four to six times/week, 1 = once per day, and 2.5 = at least two times per day. Servings per day were summed for each food group (e.g., fish/shellfish, pork, tofu, fruits and vegetables). For rice, mothers indicated quantity per serving by selecting one of three bowls from a picture or actual bowls. The daily rice ingestion rate (grams per day) was calculated by multiplying servings per day × quantity per serving. To calculate fish/shellfish ingestion (grams per day), we assumed 170 g/serving for ocean fish and freshwater fish [170 g = 6 ounces, the recommended serving size from the U.S. Food and Drug Administration (USFDA), (2001)], and 100 g/serving for other categories (Cheng et al., 2009). For the remaining food groups, portion sizes were assigned based on previous studies among Chinese pregnant mothers in rural western China (Cheng et al., 2009). Nutrient intakes, including energy and the proportion of calories from fat, carbohydrates and protein, were calculated from the Chinese Food Composition Tables, including 89 foods from 2009 tables (Yang, 2009) and 13 foods from 2005 tables (Yang et al., 2005).

2.3. Offspring Assessment at 12 Months

At the 12-month visit, parents or caregivers provided information on breastfeeding duration and the child's general health. The primary outcome measure was children's cognitive and psychomotor abilities, assessed using the Bayley Scales of Infant Development (BSID)-II, which yields age-adjusted scores for the Mental Developmental Index (MDI) and the Psychomotor Developmental Index (PDI) (Bayley 1993). The BSID-II underwent extensive pre-testing, and a few items were slightly modified to make the BSID-II more culturally appropriate (e.g., image of a Chinese-style home rather than a western-style home), which was consistent with the approach used in other studies in developing countries where the BSID-II was implemented (e.g., India, Pakistan and Zambia, from Carlo et al., 2012). Only one evaluator administered the BSID-II, who spoke the local dialect and completed extensive training in BSID-II administration, and was unaware of the children's prenatal MeHg exposure level. Examiner reliability was assessed throughout the follow-up period by videotaping a subset of children (n = 8, 3.4%). Both MDI and PDI sections were rescored by co-author FJB, a developmental psychologist; the scores were the same 95% of the time and differences in scoring were minor.

2.4. Lab Analyses

Hair total Hg (THg) concentrations corresponding to trimester 3 (proximal 3.4 cm for Asian women, Loussouarn et al., 2005) were analyzed directly without digestion by atomic absorption spectrometry (AAS) using a Lumex Model RA-915+/PYRO-915+ (St. Petersburg, Russia) using U.S. Environmental Protection Agency (USEPA) Method 7473 (USEPA, 2007). Prior to analysis exogenous Hg was removed by washing hair samples in 0.1% 2-