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Impact of low-level mercury exposure on intelligence quotient in children via rice consumption

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ABSTRACT

Wanshan is a city in southwest China that has several inactive mercury (Hg) mines. The local population are exposed to methylmercury (MeHg) due to the consumption of Hg contaminated rice. The relationship between Hg exposure and the cognitive functions of local children is unknown. This study investigated the relationship between hair Hg concentrations and the intelligence quotient (IQ) of 314 children aged 8–10 years, recruited from three local primary schools in Wanshan area in 2018 and 2019. IQ was evaluated using Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV). The average THg concentration in children's hair samples was 1.53 μg g^{-1} (range: 0.21–12.6 μg g^{-1}), and 65.6% exceeded the United States Environment Protection Agency (USEPA) recommended value of 1 μg g^{-1}. Results of logistic regression analysis showed that children with hair Hg ≥ 1 μg g^{-1} were 1.58 times more likely to have an IQ score < 80, which is the clinical cut-off for borderline intellectual disability ($R^2 = 0.20$, $p = 0.03$). Increasing of 1 μg g^{-1} hair Hg resulted in 1 point of IQ loss in Wanshan children, which was.much higher than that via fish consumption. The economical cost due to Hg exposure was estimated to be $69.8 million (9.43% of total GDP) in the Wanshan area in 2018.

1. Introduction

Methylmercury (MeHg) is a toxic mercury (Hg) compound and the developing central nervous system is particularly vulnerable to MeHg (Johansson et al., 2007; Grandjean and Herz, 2011; Santos et al., 2016). The brain has a high affinity for MeHg, and MeHg concentrations in the brain can be 3–6 times higher than that in the blood (Santos et al., 2016). MeHg entered the brain in the form of cysteine complex and accumulated in the astrocytes (Farina et al., 2011). MeHg interferes the uptake of glutamate and aspartate in astrocytes and increases glutamate concentration in the synaptic cleft, which is toxic to neurons (Santos et al., 2016). MeHg can enter fetal brain tissue by crossing the blood-placental barrier, causing damage to the fetal brain (Ha et al., 2017; Basu et al., 2018). Therefore, the neurotoxic effects of MeHg on the sensitive population (such as newborns and children) are the primary health concern (Hong et al., 2016; Rothenberg et al., 2016; Nišević et al., 2019).

Minamata disease in Japan has caused severe health damages on local population (Clarkson and Magos, 2006; Mergler et al., 2007). Currently, more attentions were paid on the effect of low-dose long-term Hg exposure on the population with fish consumption (Myers et al., 2009; Driscoll et al., 2013; Wang et al., 2014b; Jeong et al., 2017; Golding et al., 2017). Three major epidemiological studies on children's cognitive ability have been carried out in the Faroe Islands (Grandjean et al., 1997), New Zealand (Kjellstrom et al., 1989; Crump et al., 1998), and Seychelles (Davidson et al., 1998; Myers et al., 2003). Axelrad et al. (2007) conducted a meta-analysis based on the results of these three regional studies and found a decrease of 0.18 Intelligence Quotient (IQ) points for each part per million (ppm) increase in maternal hair Hg. However, the observed relationship was not consistent between the three individual studies. Studies in the Faroe Islands (Grandjean et al., 1997) and New Zealand (Kjellstrom et al., 1989; Crump et al., 1998) showed that Hg negatively affects IQ scores, but there was no significant correlation between maternal Hg and infant development scores in the Seychelles (Davidson et al., 1998; Myers et al., 2003). The co-intake of nutrients from fish consumption that are beneficial to brain development, *e.g.*, n-3 fatty acids, is thought to be the main reason (Grandjean et al., 1997; Golding et al., 2017). The n-3 fatty acids may

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be beneficial for brain development and may hide the toxic effects of MeHg (Strain et al., 2008; Nišević et al., 2019). Therefore, Balancing the risks and benefits of fish consumption has become an increasingly important goal of fish consumption advisories (Ginsberg and Toal, 2009).

Generally, fish consumption is considered as the main exposure pathway of human MeHg exposure (Mergler and Anderson, 2007). However, recent studies have confirmed that rice can be another source of MeHg exposure. Rice cultivated in Wanshan Hg mining area can bioaccumulate MeHg (Meng et al., 2010) and the MeHg concentrations in rice grain were found to be as high as 174 ng g^{-1} (Qiu et al., 2008). Rice consumption can be the main pathway of MeHg exposure for local populations, which contributed > 95% MeHg intake (Feng et al., 2008; Zhang et al., 2010). Hair total Hg (THg) concentrations in Wanshan children averaged at 1.4 μg g^{-1} (with a range of 0.50–6.0 μg g^{-1}), which indicated health risks of Hg exposure via rice consumption (Du et al., 2016). The toxicokinetic model of MeHg exposure based on fish consumption underestimated the human hair MeHg levels (Li et al., 2015). As well, rice grain does not have the beneficial nutrients such as n-3 fatty acids found in fish tissues, the relationship between MeHg exposure from rice consumption and the cognitive functions also may be different from that observed in the fish eating populations.

Both hair Hg and blood Hg concentrations are effective biomarkers for MeHg exposure (Mergler and Anderson, 2007). Hg in whole blood provides information about the exposure in the last 1–2 half-lives and the half-life of MeHg in blood is about 50–70 days. The hair Hg represents the average exposure level for the whole growing period and the growth rate of hair is estimated to be 1 cm/month (Mergler and Anderson, 2007). As the convenient and non-invasive characteristics, the hair Hg is considered as good biomarker to detect MeHg exposure in most studies (Basu et al., 2018). MeHg is the main form of Hg in hair, constituting from 80% to 98% of hair total Hg in non-occupational population (Mergler and Anderson, 2007). Previous studies also found that the hair THg concentrations were significantly correlated with hair MeHg concentrations even in the Hg contaminated areas (Li et al., 2011; Du et al., 2016).

In this study, we evaluated Hg exposure in Wanshan children by hair THg analysis and investigated the relationship between hair Hg concentrations and the IQ loss in children. The annual economic costs of IQ loss due to Hg exposure were also calculated in Wanshan area. The obtained results can provide scientific evidence for risk assessment and risk control of children Hg exposure via rice consumption in Hg contaminated areas worldwide.

2. Materials and methods

2.1. Study area

Wanshan is located in the east of the Guizhou province, southwest China, and it has the largest Hg mine in China (Qiu et al., 2005). There are four rivers passing through the Wanshan Hg mine area, and all the mining sites are situated upstream of local farmers who use the river water for irrigation, leading to Hg accumulation in rice grain (Fig. 1).

The economy of Wanshan is undeveloped, and the per capita gross domestic product (40,183 RMB, US$5,843) was about two-thirds of the national average in China in 2018. The Wanshan population was 270,000 in 2018. There were 11,561 primary school students (5–14 years old) in 2018 and 54% were male. These data were from the local government's website.

2.2. Sample collection

This study was granted ethics approval from the Affiliated Hospital of Guizhou Medical University. The guardians of the participants in this study all signed informed consent forms.

Wanshan has six township-level primary schools. According to the distance from the Hg mine, primary schools A, B, and C were selected for this study (Fig. 1). Hair sample collection, IQ tests, and questionnaires were carried out for pupils (8–10 years old) in these three schools between September 2018 and March 2019. The criteria to select the participants included: 1) local students who had not left their home during the previous 3 months; 2) the ability to complete IQ tests (no communication impairment, hand disability, etc.); and 3) parents have no history of mental illness. In total, 322 volunteer participants were recruited into this study. After excluding children who could not complete the IQ test, 314 children were analyzed in this study. Among them, 11.1%, 67.2%, and 21.7% are the proportions of 8, 9 and 10 years old of the study population, respectively.

A total of 314 hair samples were collected in this study. The hair samples were cut with stainless-steel scissors from the occipital region of the scalp, wrapped in paper, put in polyethylene bags, and then stored at room temperature for Hg measurement.

The children's guardians completed the questionnaire. The questionnaires provided information about potential confounding factors (Sun et al., 2015; Taylor et al., 2017; Gustin et al., 2018; Pan et al., 2018) including children's basic information (gender, age, ethnicity, primary school grade, and school); socioeconomic and lifestyle factors of the family (parents' education, parents' marriage, number of siblings, annual per capita income (RMB), whether parents were migrant workers, passive smoking at home, maternal drinking, and house decoration within 1 year); newborn situation of children (breastfeeding and birth weight); child's diet (frequency of consuming fish); presence of child social adaptability disorder; cram school attendance; summer school attendance. Among these, the question on social adaptability disorder was adopted from the mental health rating scale for primary school students (Chinese version; MHRSP) (Chen, 2000).

Epidata (version 3.1) software was used to establish the database for the questionnaire and double-entry was used to reduce information bias when the questionnaire data were input into the database.

2.3. Hg analysis

Hair samples were wrapped with wettable paper towels and placed in an ultrasonic cleaning instrument with frequency of 30 kHz. The hair samples were ultrasonically cleaned in non-ionic detergent (alkylphenol ethoxylate, APEO), distilled water, and acetone for 3 times successively and each produce lasted 30 min. The washed hair samples were then dried overnight in a 60 °C oven and preserved at 4 °C (Du et al., 2016). After the hair was cut into pieces, the THg concentrations in hair samples were measured by DMA-80 (Direct mercury analyzer, Milestone, Italy). DMA-80 is an atomic absorption spectrophotometer that can directly analyze THg concentration in solid and liquid matrices (EPA 7473). The experimental work was completed in the State Key Laboratory of Environmental Geochemistry, Institute of Geochemistry, Chinese Academy of Sciences.

Quality control for hair Hg analysis included method blanks, certified reference materials (CRM), and duplicates. When the blank of the machine was < 0.1 ng, the experiment was started. The limit of detection for hair THg was 0.5 ng g^{-1} (Wang et al., 2014a). The human hair CRM GBW09010b produced by Geophysical and Geochemical Exploration Institute, Chinese Academy of Geological Sciences (IGGE) was used for the THg analysis, and the recoveries averaged at 103%. The precision (relative standard deviation, RSD) was 4.6%, which was obtained from duplicate analyses of every ten samples.

2.4. Cognitive assessment

The IQ test followed the Wechsler Intelligence Scale for Children – Fourth Edition, Chinese version (WISC-IV). The Wechsler intelligence scale is internationally recognized as the most reliable and widely applicable diagnostic intelligence test (Whitaker, 2008; Nuovo et al., 2012). WISC-IV is composed of 10 subtests, from which children's total

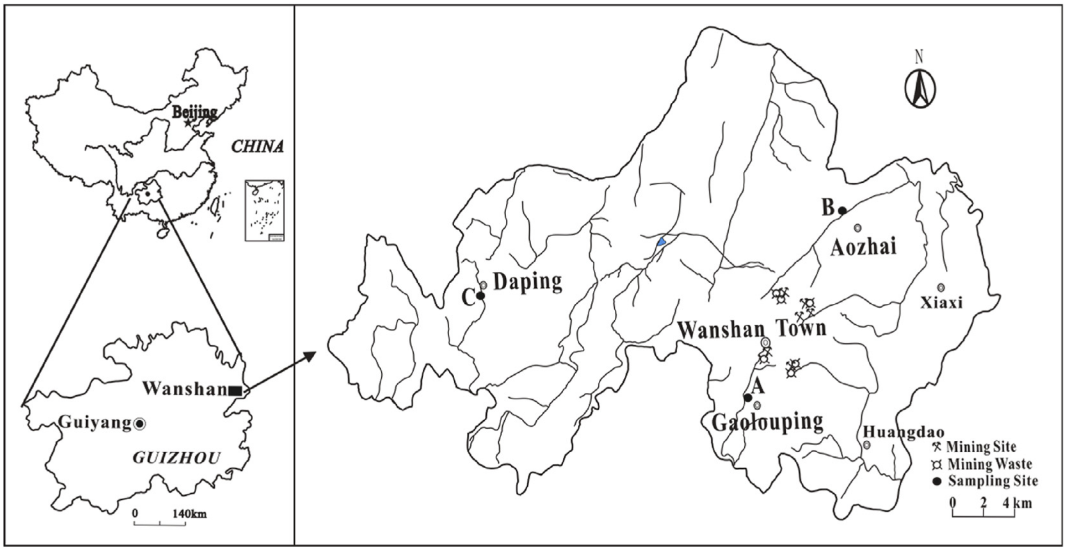

Fig. 1. Spatial locations of the study sites in the Wanshan area. School A, B, and C were 3 km, 7 km, and 24 km away from the Hg mine, respectively.

IQ scores and four ability scores (verbal comprehension, perceptual reasoning, working memory, and processing speed) can be obtained. All testers were trained by a professional before the test. We provided separate rooms for one-to-one, face-to-face interviews for the IQ test. A total IQ score of 80 is considered as the upper bound cut-off for borderline intellectual disability (Jacobson et al., 2015) and a total IQ score of 100 is the average level of Chinese children (Wechsler and Zhang, 2008).

2.5. Economic loss calculation

In order to assess the costs due to MeHg exposure, the economic loss calculation model in this study was adopted from Trasande et al. (2005). The calculated approach was initially developed by Institute of Medicine (IOM , 1981) to assess the costs of environmental and occupational disease. It also used to estimate the environmental costs of lead poisoning and neurodevelopmental disabilities in American children (Landrigan et al., 2002; Trasande et al., 2005). We used hair Hg concentrations in children for the calculation as follows:

$$\text{Costs} = \text{EAF} \times \text{population size} \times \text{cost per case} \quad (1)$$

Costs refer to the cost of Hg exposure in every year's birth cohort; population size refers to the number of births in a year; cost per case refers to each person loss of money in their lifetime under Hg exposure; EAF refers to environmentally attributable fraction. This study concerned estimation of the costs caused by anthropogenic sources of Hg, EAF means the portion of Hg that can be attributed to human activities. The anthropogenic sources of Hg was set at 70% of the total global Hg pool (Mason and Sheu, 2002).

Trasande et al. (2005) used the method described by Salkever (1995) to assess the economic cost of Hg exposure based on IQ scores. When the IQ fell by one point, a person's lifetime earnings were reduced by 1.9% for men and 3.2% for women, respectively. The USEPA (2000) used a participation-weighted average of 2.379% per IQ point for the combined lifetime earnings, which was adopted in this study. Therefore, cost per case can be calculated as the following:

$$\text{Cost per case} = 2.379\,\% \times \sum \$ \times (1 + n\%)^{k} \quad (2)$$

$ refers to annual income; n% refers to the annual growth rate of income; k refers to the average number of years of work in a person's life.

2.6. Statistical analysis

SPSS 24.0 was used for statistical analysis in this study. The normal distribution of the data was determined using the Kolmogorov–Smirnov test. Since the hair Hg data was not normally distributed, a non-parametric test was used in the following analysis. Arithmetic means were used to describe the hair Hg concentrations and IQ scores. The correlation between hair Hg and IQ was tested by Spearman's correlation, and the mean value was compared in different sites using the Kruskal–Wallis H rank-sum test. Binary logistic regression was used to assess the relationship between hair Hg and IQ < 80 (IQ < 80 regarded as $y = 1$). Children's age was considered as a qualitative variable. Initially, univariable logistic regression analysis was performed. Then, the confounders were added into the model to adjust the logistic regression analysis. Multiple linear regression analysis was used to assess the relationship between IQ and hair Hg. To make sure the regression coefficient (B value) range, the multivariable-adjusted linear regressions of models 5 and 6 were analyzed. The confounders were used in the model due to the model R-squared value and previous relevant research (Sun et al., 2015; Taylor et al., 2017; Gustin et al., 2018; Pan et al., 2018). If $p < 0.05$, the statistical test results were considered as significantly different.

3. Results

3.1. Characteristics of participants

The basic information of primary school students in Wanshan is shown in Table 1. A total of 314 (97.5%, 314/322) children were analyzed. In this study, 51.9% of the participants were boys, and 86.6% of the participants were the Dong minority. Less than 15% of parents attended senior school. Of all the households, 26.7% had a per capita annual income lower than 4,080 RMB (about $574), which is the minimum standard of living allowances for rural residents in Guizhou in 2019. A majority of students (76.4%) ate fish less than once a week.

3.2. Hair Hg level

Hair Hg concentrations in the participants are shown in Fig. 2. The mean hair Hg concentration was 1.53 μg g^{-1} (range: 0.21–12.6 μg g^{-1}), and 65.6% (206/314) exceeded the reference value of 1 μg g^{-1} set by the USEPA (USEPA, 1997); while 12.4% (39/314) exceeded the reference value of 2.3 μg g^{-1} suggested by the Joint

Table 1
Characteristics of primary school students in the Wanshan area.

Variable		n	%
Total		314	100
Gender			
	Boys	163	51.9
Age			
	8	35	11.1
	9	211	67.1
	10	68	21.6
Ethnicity			
	Han	19	6.00
	Dong	272	86.6
	Others	22	6.80
School			
	A	218	69.4
	B	47	14.9
	C	49	15.6
Number of siblings			
	0	35	11.1
Father's education			
	≤Junior school	257	81.7
	≥Senior school	33	10.4
Mother's education			
	≤Junior school	244	77.6
	≥Senior school	35	11.0
Parents' marriage			
	cohabitation or married	252	80.1
	others	41	12.9
Annual per capital income (RMB)			
	< 3900	84	26.7
	3900-29999	135	42.5
	≥30000	37	11.7
Passive smoking at home			
	Yes	191	60.8
Maternal drinking			
	Yes	30	9.30
Frequency of consuming fish			
	< 1/week	240	76.4
	≥1/week	44	13.9
Breastfeeding			
	< 4 month	94	29.8
	4–6 month	36	11.4
	≥6 month	132	42.0
House decoration within 1 year			
	Yes	82	26.1
Summer school attendance			
	Yes	27	8.50
IQ score			
	< 80	42	13.4
	80-99	198	67.8
	≥100	74	18.8
Hair Hg concentration ($\mu g{\cdot}g^{-1}$)			
	< 1	108	34.4
	1-1.99	149	47.5
	2-5.99	53	16.9
	≥6	4	1.27

Expert Committee on Food Additives (JECFA, 2003). Significant differences were found for the children's hair Hg concentrations between different schools ($p < 0.05$). School A was closest to the Wanshan Hg mine and showed the highest hair Hg concentrations in children. Hair Hg concentrations in students from school A averaged 1.73 $\mu g\ g^{-1}$, and 77.6% exceeded the USEPA reference value and 16.0% exceeded the JECFA reference value.

3.3. Cognitive test results

The mean value of the total IQ scores was 91.0 (range: 51–122) in the children, which is much lower than the average intelligence level (100) of Chinese children (Fig. 3). Of note, 13.4% (42/314) of children's IQ values were lower than 80, which is the upper bound cut-off for borderline intellectual disability. The means of the IQ scores in children from schools A, B, and C were 91.7, 88.9, and 90.3 points, respectively. There was no significant difference in the total IQ scores between the students from the three schools.

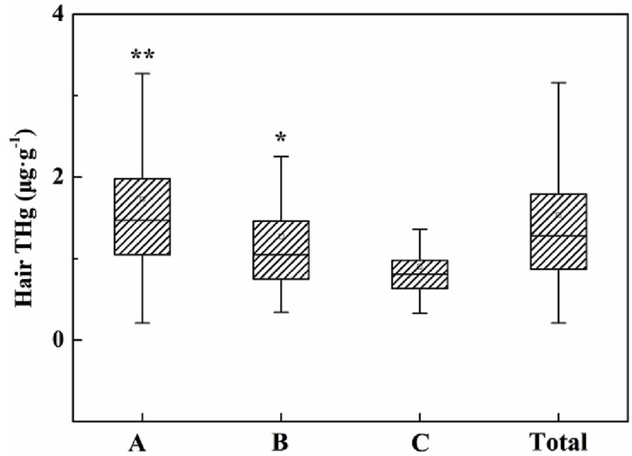

Fig. 2. Hair THg in children of the Wanshan Hg mining area. *, $p < 0.05$, compared with C; **$p < 0.05$ compared with B and C, Kruskal–Wallis H test. Each box represents interquartile range (25th and 75th percentile), the band near the middle of the box is the 50th percentile (the median), the whisker represents 5th and 95th percentile, and the squares in the box represent the mean value.

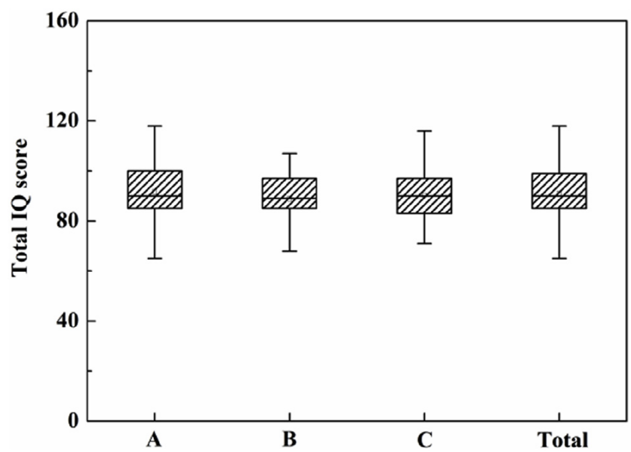

Fig. 3. Total IQ in children of the Wanshan Hg mining area. Total IQ = 100 is the average IQ level of Chinese children. Each box represents interquartile range (25th and 75th percentile), the band near the middle of the box is the 50th percentile (the median), the whisker represents 5th and 95th percentile, and the squares in the box represent the mean value.

3.4. Hair Hg and IQ

The correlation between hair Hg and IQ was negative but not significant ($r = -0.054$, $p > 0.05$). In logistic regression analysis, there was no significant association between hair Hg and IQ (< 80 or ≥ 80) without adjusting for confounders in model 1 ($R^2 = 0.002$, $p > 0.05$; Table 2a). However, after adjusting for confounders in models 3 and 4, statistically significant associations were found between hair Hg and IQ < 80. The odds of children having IQ < 80 increased by 1.58 times when the hair Hg increased by 1 $\mu g\ g^{-1}$ in model 4 ($R^2 = 0.20$, $p = 0.03$).

As more confounders were adjusted, the regression coefficients between IQ and hair Hg were stable between −0.9 and −1.1 in multiple linear regression analysis but there was no significant association between hair Hg and IQ (Table 2b). Attending summer school, parents' marriage, and the age of children were the most important confounders

Table 2a
Logistic regression analysis of hair mercury and the children's total IQ.

Model	IQ < 80				
	n	OR	95% (CI)	R^2	*p*
Model 1	314	1.106	(0.883,1.385)	0.002	0.379
Model 2	314	1.116	(0.891,1.397)	0.018	0.341
Model 3	297	1.421	(1.012,1.995)	0.139	0.043
Model 4	295	1.580	(1.043,2.394)	0.195	0.031

Table 2b
Linear regression analyses of hair mercury and the children's total IQ scores.

Model	n	B	95%(CI)	R^2	*p*
Model 1	314	-0.294	(-1.226, 0.637)	0.001	0.535
Model 2	314	-0.254	(-1.182, 0.675)	0.019	0.591
Model 3	296	-0.957	(-2.057, 0.144)	0.077	0.088
Model 4	295	-1.035	(-2.121, 0.050)	0.106	0.062
Model 5	297	-0.999	(-2.114, 0.115)	0.045	0.079
Model 6	297	-1.041	(-2.156, 0.740)	0.066	0.067

Model 2: Adjusted for child gender and age.
Model 3: Adjusted for child gender, age, ethnicity, school, father's education, mother's education, parents' marriage, annual per capita income (RMB), number of siblings, breastfeeding, frequency of consuming fish and house decoration within 1 year.
Model 4: Adjusted for child gender, age, ethnicity, school, father's education, mother's education, parents' marriage, annual per capita income (RMB), number of siblings, breastfeeding, frequency of consuming fish, house decoration within 1 year, passive smoking at home, maternal drinking and summer school attendance.
Model 5: Adjusted for child gender, age, ethnicity, school, father's education, mother's education, annual per capita income (RMB), frequency of consuming fish, house decoration within 1 year and whether parents were migrant workers (more than half year).
Model 6: Adjusted for child gender, age, ethnicity, school, father's education, mother's education, annual per capita income (RMB), frequency of consuming fish, house decoration within 1 year, whether parents were migrant workers (more than half year), primary school grade, passive smoking at home, maternal drinking and child social adaptability disorder.

Table 3
The contribution of each factor to IQ in multiple linear regression in model 4.

Factor	R^2	Adjusted R^2
Father's education	0	-0.003
Passive smoking at home	0	-0.003
Mother's education	0.001	-0.003
Hair Hg	0.001	-0.002
Maternal drinking	0.004	0.001
Ethnicity	0.004	0.001
House decoration within 1 year	0.005	0.001
Frequency of consuming fish	0.005	0.002
Annual per capita income	0.006	0.002
Gender	0.005	0.002
Number of siblings	0.006	0.004
School	0.009	0.005
Breastfeeding	0.010	0.006
Age	0.013	0.010
Parents' marriage	0.016	0.013
Summer school attendance	0.021	0.018

affecting IQ in multiple linear regression model 4 (Table 3).

3.5. Economic costs of IQ loss

Based on the multiple linear analysis, the regression coefficients between IQ and hair Hg were stable between −0.9 and −1.1. Therefore, we propose that an increase in hair Hg of 1 μg g^{-1} would result in a one-point decrease in the child population's IQ on average. According to the USEPA reference value of 1 μg g^{-1} (USEPA, 1997) and our previous study also carried out in this area (Du et al., 2016), we chose Wanshan, Gaolouping, Aozhai, Xiaxi, and Huangdao town (Fig. 1) to calculate the economic cost of Hg exposure. We studied the Hg exposure of 237 children at eight primary schools in Wanshan Hg mining area in 2013 (Du et al., 2016). The school A and B in this study were primary school A2 and D2 studied by Du et al. (2016), but the children involved in this study are not the same group with children in Du et al. (2016).

Wanshan area had serious environmental Hg pollution in previous studies (Li et al., 2009, 2015). Combined with the results obtained in this study and previous results from Du et al. (2016), we set 1.64 μg g^{-1} (n = 482) as the mean hair Hg concentration of children in WMMA. The total population of WMMA was 84,624 in 2012. According to the local birth rate of 10.7‰, there were 905 newborns in WMMA annually. The GDP and the per capita GDP of Wanshan town were 5.06 billion RMB (US$0.74 billion) and 40,183 RMB (US$5843) in 2018, respectively. These data were from the local government's website. We assumed that the average number of years of work in a person's life was 39 years, because the age of 16, 50, and 60 are the legal minimum working age, female retirement age, and male retirement age in China, respectively.

We estimated that the total cost of IQ loss due to Hg exposure was US$69.8 million per year in Wanshan. If the hair Hg in Wanshan people was reduced to 0.1 μg g^{-1} by pollution control and remediation, the economic value was estimated to be US$4.25 million per year in the Wanshan area (Table 4).

4. Discussion

Hair Hg concentrations in Wanshan children averaged at 1.53 μg g^{-1}. This is consistent with the THg concentration (1.4 μg.g^{-1}) in children's hair in our previous study (Du et al., 2016). The comparison of hair Hg concentrations in children from different studies is shown in Table 5. For comparison of Hg levels between different biological materials measured in different studies, we assumed a ratio of 250:1 for Hg in hair to blood (WHO, 1990). Notably, hair Hg concentrations in Wanshan children were much higher than those in Zhoushan, China who ate 32.2 kg fish per person in 2013 (Gao et al., 2007). Furthermore, the hair Hg concentrations in Wanshan children were higher than those of children from the USA (0.22 μg g^{-1}) and Canada (1.43 μg g^{-1}) (McDowell et al., 2004; Tian et al., 2011). However, the hair Hg concentrations in Wanshan children were much lower than those in children of the Faroe Islands (2.99 μg g^{-1}), Seychelles (6.50 μg g^{-1}), and Hong Kong (Grandjean et al., 1997; Davidson et al., 1998; Lam et al., 2013). The median of cord blood Hg in Hong Kong (n = 608) was 9.18 μg L^{-1}, which is equivalent to 2.30 μg g^{-1} for hair Hg (Lam et al., 2013). Fok et al. (2007) thought that the high consumption of fish during pregnancy caused high hair Hg concentrations in Hong Kong people. In summary, the hair Hg concentrations in Wanshan children were at a low or medium level.

The mean of the total IQ scores (91.0 points) in Wanshan children

Table 4
Economic costs of IQ loss in the Wanshan Hg mining area.

Variable	Wanshan Hg mining area
Population	84624
Birth rate (‰)	10.7
The number of births in a year	905
Per capita GDP ($)	5,843
Grown rate of per capita GDP (%)	10.7
Per capita lifetime income ($)	2,822,852.7
Costs of hair Hg of 1.64 μg g^{-1} ($)	69,770,707.6
Costs of hair Hg of 0.1 μg g^{-1} ($)	4,254,311.4

Table 5
Comparison of hair/blood mercury and cord blood mercury level in children from different study areas.

Reference	Study area	Exposure source	N	Age	Hg level		
					Hair ($\mu g \cdot g^{-1}$)	Cord blood ($\mu g \cdot L^{-1}$)	Blood ($\mu g \cdot L^{-1}$)
This study	Wanshan	Rice	314	8-10	1.53		
McDowell et al. (2004)	USA	Fish	838	1-5	0.22		
Yan et al. (2017)	Shanghai	Fish	1982		0.30		
Gao et al. (2018)	China	Fish	14202	0-6			1.39
Ou et al. (2015)	North China	Fish	42	0	0.62	2.93	
Gao et al. (2007) *	Zhoushan	Marine fish	408	0		5.58	
Tian et al. (2011)	Canada	Fish, whale meat, Seal meat	361	3-5	1.43		
Lam et al. (2013)[#]	Hong Kong	Marine fish	608	6-10		9.18	
Grandjean et al. (1997) *	Faroe Island	Whale meat	903	7	2.99	22.9	
Davidson et al. (1998)	Seychelles	Fish	708	5	6.50		

Note: *, represent the average category of data was geometric mean, #, represent the average category of data was median. And the rest is mean value.

obtained by the WISC-IV method was much lower than that of average children in China (100 points). The mean total IQ of children in the ALSPAC study (n = 2217) using the WISC-III method in the UK was 104 points (Golding et al., 2017). The means of the IQ values by WISC-IV test for Italian and Canadian children were 106 (n = 299) and 101 (n = 259), respectively (Tian et al., 2011; Lucchini et al., 2019). The IQ points of children living in the Wanshan area were much lower than these populations, which may due to socio-economic factors such as low family income and undeveloped school education level. Wanshan County is an undeveloped district, and the studied schools were township-level schools. In comparison, the effects of Hg exposure on IQ scores may be relatively low. This may be the main reason that we found no significant associations between IQ score and hair Hg in the multiple linear regression analysis in this study (p = 0.062). In addition, low IQ score in children will not only affect the level of education and personal income, but also affect the speed of technological progress and productivity. Many studies have found that small decreases in IQ will result in lower income (USEPA et al., 1985; Salkever, 1995; Bellanger et al., 2013). Generally speaking, a lower average of IQ value in the population will increase the number of people who have low IQ (IQ < 80 or 70) and who may be considered as retarded. It also reduce the number of talented and highly gifted people with high IQ (IQ > 130) who may contribute to the development of society (Muir and Zegarac, 2001).

We found that the odds of children having an IQ < 80 increased 1.58 times when hair Hg increased by 1 $\mu g\ g^{-1}$. The regression coefficients between IQ and hair Hg were stable from −0.9 to −1.1 in multiple linear regression analyses. This means that children's IQ scores will drop by about one point when hair Hg increased by 1 $\mu g\ g^{-1}$. We compared this relationship with that reported by Axelrad et al. (2007) who estimated that children IQ would decrease by 0.18 points with each increase of 1 $\mu g\ g^{-1}$ in maternal hair Hg from fish consumption. Previous studies showed that rice consumption is the main pathway of MeHg exposure (> 95%) for our studied populations living in the Hg mining area (Feng et al., 2008; Zhang et al., 2010). Our results suggest that the effects of Hg exposure via rice consumption on children's IQ development may be much higher than that via fish consumption.

In this study, we found that attending summer school, parents' marriage and children's age were the most important contributing factors to IQ scores in model 4 of the multiple linear regression. These factors may be part reason that children's average IQ in Wanshan area is lower than the average of Chinese children. We found that 9.8% and 8.5% of the students had attended cram schools' and summer schools, respectively. Attending summer school is a factor that reflects the family economy condition and the guardians' attention to education. Family economics, parents' attitudes towards education, and family harmony are important factors in IQ (Ali et al., 2013; Hanson et al., 2015; Buckley et al., 2019). The average total IQ score in children whose parents were married or cohabiting was 91.3 points, while the total IQ score in children whose parents were divorced or widowed was 90.3 points, but without significant difference. Several large longitudinal studies found that children whose parents were divorced had symptoms such as conduct disorders, antisocial behaviour, difficulty with peers and authority figures, depression, and academic and achievement problems (Cherlin et al., 1991; Elliott and Richards, 1991; Kelly, 2000). Parents' divorce has been associated with lower academic performance and achievement test scores (Kelly, 2000). We selected the children with age of 9-year-old for study and this age group were the majority (67.1%) of the studied population. The 8-year-old students (n = 36) came from the third grade of primary school and 97.1% of the 10-year-old students (66/68) came from the fourth grade. The averages of IQ scores in children with ages of 8, 9, and 10 were 93.0 ± 9.94, 91.4 ± 10.2, and 88.8 ± 9.99 points, respectively, but without significant difference between different age groups.

Based on the multiple linear analysis, we assumed that a hair Hg increase of 1 $\mu g\ g^{-1}$ would result in a one-point decrease in IQ. According to this result, the economic losses caused by Hg exposure in Wanshan area were US$69.8 million in 2018, which accounted for 9.43% of the Wanshan total GDP in 2018. This cost will occur each year with every new birth cohort without Hg pollution control. We also found that when hair Hg drops by 0.1 $\mu g\ g^{-1}$, the economic loss will decline by US$4.25 million per year in 2018. These results can provide a theoretical basis for Hg pollution control and remediation for the local government.

This is the first study to evaluate the relationship between Hg exposure and cognition function in children who are exposed to MeHg via rice consumption rather than fish consumption. Second, the mean total IQ scores in Wanshan children obtained by the WISC-IV approach was much lower than the children in China. However, we still observed an adverse effect on children's cognition resulting from Hg exposure. However, a limitation of this study is the sample size, which may restrict the observation of significant relationship between hair Hg and IQ. In addition, the hair Hg concentrations in this study ranged from 0.21 to 12.6 $\mu g\ g^{-1}$, with an average of 1.53 $\mu g\ g^{-1}$. This indicates that the range of hair Hg concentration in children of Wanshan is large, which poses a challenge for dose-response analyses. The results obtained in this study may not be applicable to other populations whose range of hair Hg concentrations are different from this study. Lastly, this study is a cross-sectional study, which only shows an association but not a cause-effect relationship between Hg exposure and children's IQ.

5. Conclusions

The average hair THg concentration in Wanshan children was 1.53 $\mu g\ g^{-1}$, which indicated health risks of children Hg exposure in this area. The mean value of the total IQ scores was 91.0 (range: 51–122) in Wanshan children, which is much lower than the average

(100) of Chinese children. We found that the odds of children having an IQ < 80 increased by 1.58 times when hair Hg increased by 1 μg g^{-1}. The total cost of IQ loss due to Hg exposure was estimated to be 69.8 million USD per year in the Wanshan area in 2018. The results obtained in this study indicated that Hg pollution control actions (such as soil remediation) are urgently needed to reduce Hg bioaccumulation in rice and health risks of human Hg exposure in Wanshan area.

Credit Author Statement

Lin Feng: Data curation, Formal analysis, Investigation, Roles/Writing - original draft, Writing - review & editing. Chanchan Zhang: Data curation, Investigation. Haohao Liu: Formal analysis, Investigation. Ping Li: Conceptualization, Funding acquisition, Investigation, Supervision, Writing - review & editing. Xuefeng Hu: Data curation, Methodology. Huiqun Wang: Supervision. Hing Man Chan: Methodology, Supervision, Writing - review & editing. Xinbin Feng: Conceptualization, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ecoenv.2020.110870.

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