Environ Geochem Health
https://doi.org/10.1007/s10653-018-0114-z

ORIGINAL PAPER

Heavy metal exposure has adverse effects on the growth and development of preschool children

Xiang Zeng · Xijin Xu · Qilin Qin · Kai Ye · Weidong Wu · Xia Huo

Received: 26 December 2017 / Accepted: 18 April 2018

Abstract The purpose of this study was to investigate the associations between levels of lead (Pb), cadmium (Cd), chromium (Cr), and manganese (Mn) in the $PM_{2.5}$ and blood and physical growth, and development parameters including birth length and weight, height, weight, body mass index (BMI), head circumference, and chest circumference in preschool children from Guiyu (e-waste exposure area) and Haojiang (the reference area). A total of 470 preschool children from Guiyu and Haojiang located in southeast coast of China were recruited and required to undergo physical examination and blood tests during the study period. Birth length and weight were obtained by birth records and questionnaire. Pb and Cd in both $PM_{2.5}$ and blood were significantly higher in Guiyu than Haojiang. Remarkably, the children of Guiyu had significantly lower birth weight and length, BMI, and chest circumference when compare to their peers from the reference area (all p value < 0.05). Spearman correlation analyses showed that blood Pb was negatively correlated with height ($r = -0.130$, $p < 0.001$), weight ($r = -0.169$, $p < 0.001$), BMI ($r = -0.100$, $p < 0.05$), head circumference ($r = -0.095$, $p < 0.05$), and chest circumference ($r = -0.112$, $p < 0.05$). After adjustment for the potential confounders in further linear regression analyses, blood Pb was negatively associated with

Xiang Zeng and Xijin Xu have contributed equally to this work.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10653-018-0114-z) contains supplementary material, which is available to authorized users.

X. Zeng · X. Xu
Laboratory of Environmental Medicine and Developmental Toxicology and Provincial Key Laboratory of Infectious Diseases and Molecular Immunopathology, Shantou University Medical College, 22 Xinling Road, Shantou 515041, Guangdong, China

X. Zeng · W. Wu
Department of Epidemiology and Health Statistics, School of Public Health, Xinxiang Medical University, 601 Jinsui Road, Xinxiang 453003, Henan, China

X. Zeng
Department of Epidemiology, University Medical Center Groningen, University of Groningen, 1 Hanzeplein, 9700 RB Groningen, The Netherlands

Q. Qin · K. Ye · X. Huo (✉)
Key Laboratory in Environmental Exposure and Health of Guangzhou and Guangdong, School of Environment, Jinan University, Guangzhou 510632, Guangdong, China
e-mail: xhuo@jnu.edu.cn

Published online: 25 April 2018

height ($\beta = -0.066$, $p < 0.05$), weight ($\beta = -0.119$, $p < 0.001$), head circumference ($\beta = -0.123$, $p < 0.01$), and chest circumference ($\beta = -0.104$, $p < 0.05$), respectively. No significant association between blood Cd, Cr, or Mn was found with any of our developmental outcomes. Taken together, lead exposure limits or delays the growth and development of preschool children.

Keywords Heavy metal · Guiyu · Growth · Development · E-waste · Preschool children

Introduction

E-waste refers to all types of electrical or electronic equipment (EEE) nearing the end of their useful life and is regarded as a critical environmental issue as well as a threat to human health (Huo et al. 2007; Ogunseitan et al. 2009; Wang et al. 2016). Approximately, 41.8 and 65.4 million tonnes of e-waste were generated globally in 2014 and in 2017, respectively (Ni et al. 2010; Breivik et al. 2014; Heacock et al. 2016). It was estimated that only 15% of global e-waste were fully recycled (Heacock et al. 2016). China processed about 70% of the e-waste produced worldwide and struggled with e-waste burden due to previous illegal e-waste importation, domestic production and consumption of EEE, and unregulated informal handling and recycling (Gao et al. 2011; Zhang et al. 2012; Xiao et al. 2014). E-waste contains two major types of substances: metals (60%) and plastics (30%) (Widmer et al. 2005; Fujimori and Takigami 2014; Anh et al. 2017). Due to their toxicity and extensive use, heavy metals lead to serious environmental pollution and pose a great threat to human health. In addition, heavy metals are not only a class of non-biodegradable pollutants, but they can also be stored in body tissues or organs via the food chain, causing adverse effects on the body. Moreover, distribution and excretion rate of heavy metals are different in diverse organs of the body. In blood, the half-life of some heavy metals are short. For instance, both blood lead (Pb) and cadmium (Cd) have a half-life of 35 days (US CDC 2008, 2017). However, the half-life of some heavy metals in other tissues or organs of the body is extremely long. For example, the half-life for Pb in bone reaches 30 years (Hu et al. 2007), a half-life for Cd in kidney ranges from 15 to 30 years (Tellez-Plaza et al. 2012), and they can also be released into blood over time.

Exposure to heavy metals can cause toxicity to a variety of tissues, organs, and systems such as circulatory, respiratory, endocrine, immune, nervous, urinary, and reproductive systems (Zeng et al. 2016a, b; Ma et al. 2017; Xu et al. 2017). Metal ions can be combined on a variety of molecules in the body, such as proteins, fats, and polysaccharides in body tissues and organs. In addition, metal ions are also involved in diverse physiological and pathological reactions. Some of the heavy metals themselves are carcinogens such as cadmium, chromium, nickel, and arsenic. In addition, heavy metals can cause toxicity to humans through both direct and indirect mechanisms of promoting oxidative stress and inflammation (Lamas et al. 2016). Exposure to heavy metals can cause adverse effects on human health. A recent study from Taiwan region of China demonstrates that heavy metals are associated with child developmental delays and health status evaluated using the pediatric quality of life (PedsQL) inventory for health-related quality of life (HRQOL) (Hsueh et al. 2017). Another study from South Korea shows that both extreme level of maternal blood Mn level was associated with lower birth weight outcome in a nonlinear fashion (Eum et al. 2014). Previous studies have demonstrated that the concentration of heavy metals in the environment including air, dust, water, soil, and sediment and in blood was higher in Guiyu, an e-waste exposure area, than in areas where e-waste is not processed (Deng and Wong 2006; Yekeen et al. 2016; Zeng et al. 2016a, b, 2017a, b). Early childhood has been recognized as a critical period for cognitive, emotional, and physical growth and development of children (UNICEF 2001). In addition, children are more susceptible and vulnerable to environmental heavy metal exposure when compared to adults, and need widespread concern and protection from the general public, governments, and scientific communities around the world (Gavidia et al. 2011; Leith and Carpenter 2012; Grant et al. 2013). One of our previous studies demonstrated that blood Pb was negatively correlated with height and weight in Guiyu children. However, there was no significant association between blood Pb and height and weight based on the linear regression analysis (Yang et al. 2013). Association between more heavy metals and additional growth and development indicators in children is still unclear and needs to be confirmed.

It was estimated that Guiyu processed around 50% of the e-waste in the world and have to confront extremely serious environmental pollution and health risks (Wu et al. 2010; Zhang et al. 2012). Previous studies have shown that various heavy metals have contaminated the local environment and threaten the health of local residents. However, it has not been studied systematically to investigate the association between blood heavy metals and developmental outcomes in preschool children of e-waste exposed area. The aim of the present study was to assess the level of heavy metals, shed light on the status of physical growth and development of children, and elucidate the relationship between diverse blood heavy metals including Pb, Cd, chromium (Cr), and manganese (Mn) and several physical growth and development parameters such as height, weight, body mass index (BMI), head circumference, and chest circumference in preschool children from an e-waste exposure area and a reference area.

Materials and methods

Study areas and population

A total of 470 preschool children were recruited from a kindergarten in Guiyu (n = 300) and a kindergarten in Haojiang (n = 170). Guiyu and Haojiang are located in Guangdong province in the southeast of China (Fig. 1). We recruited participants who agreed to take part in this study complying with their own wishes and in the absence of any pressure. In the same time, the parents or guardians of all participants gave their written informed consent after being provided detailed explanations of the study and potential consequences prior to enrollment. All participants had no infectious disease within 1 month before sample collection. Self-administered questionnaire surveys were undertaken with the help of parents or guardians of each participant. This study was approved by the medical ethics committee of Shantou University Medical College, China.

$PM_{2.5}$ sample preparations

Two $PM_{2.5}$ monitoring samplers [Harvard-type $PM_{2.5}$ impactors (MS&T Area Sampler; Air Diagnostics, Inc, Harrison, ME)] were used to collect $PM_{2.5}$ samples from Guiyu and Haojiang. $PM_{2.5}$ samples had been continuously collected every 24 h on sunny days in Guiyu (n = 133) and 1 week every quarter in Haojiang (n = 33) from March 2012 to April 2013 by using pre-weighed Teflon membrane filters (2 μm pore apertures; 37 mm diameter; SKC Inc., Eighty-Four, PA). The average flow rate of $PM_{2.5}$ monitoring samplers was set as 10 L/min and was calibrated with a flow meter each 24-h period. The concentrations of Pb, Cd, Cr, and Mn in $PM_{2.5}$ were measured by graphite furnace atomic absorption spectrometry (GFAAS, Jena Zenit 650, Germany).

Physical growth and development test

Birth weight and length were obtained according to the birth records and questionnaire (if the birth records have been lost). Height and weight were measured using a height and weight scale, respectively (TZ120; Yuyao Balance Instrument Factory, Yuyao, China) during the same period of blood sample collection. In addition, head and chest circumference were measured on all preschool children between the ages of 3 and 7. These children were asked to remove their shoes, take off their coat, and stand upright during the process of measurement (Zeng et al. 2017a, b). These physical growth and development test were conducted by two trained physicians. The predicted values of height, weight, head, and chest circumference refer to national standard of China (Li et al. 2009).

Blood sample preparations and heavy metal analyses

Samples of venous blood of preschool children were collected by nurses. All participants were ordered to fast until blood sample collection in the next morning, which is beneficial to compare current and previous data and the normal reference values, and avoid the interference of eating on the results. The main technical parameters for measurement of blood heavy metals by graphite furnace atomic absorption spectrometry (GFAAS) have been described in detail before (Zeng et al. 2016a, b).

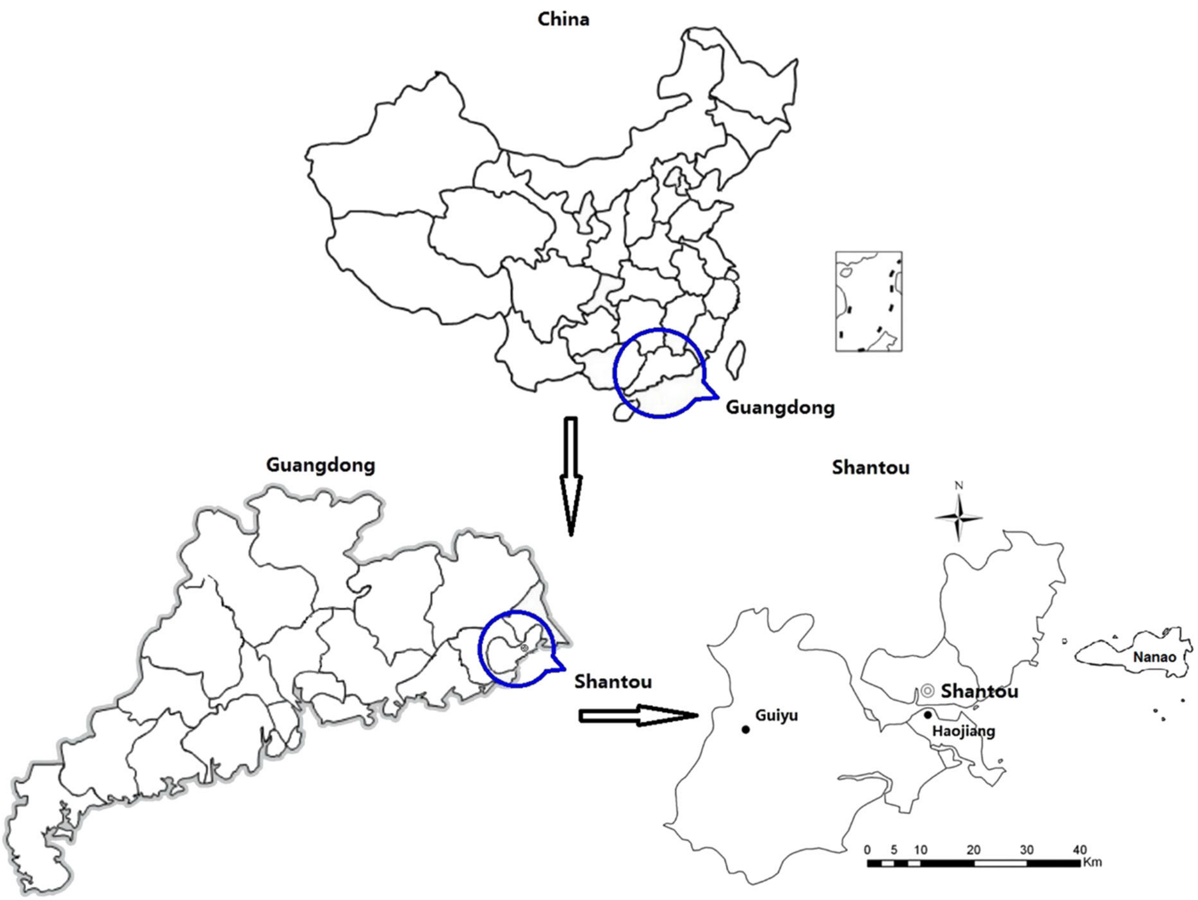

Fig. 1 Location of the sampling sites (Guiyu and Haojiang)

Statistical analysis

Data are presented as mean ± SD for normally distributed data or median (IQR) for non-normal distribution data. The independent sample *t* test was used for two-group comparisons of normally distributed data. The Chi-square test was applied to compare non-normally distributed data among groups. Spearman rank correlation analyses were utilized to examine the correlation between four kinds of blood heavy metals and physical growth and development indicators. Linear regression analyses were adjusted for gender, age, family members smoking, parental education level, and family income level to investigate associations between blood heavy metals and growth and development indicators of preschool children. Analyses were performed using SPSS version 22.0 (IBMCorp, NJ, USA). p values < 0.05 were considered statistically significant (tested two-sided).

Results

Characteristics of the study population

A total of 470 preschool children were enrolled in the study (Table 1). The average age of children from the e-waste exposed Guiyu group was 4.7 years compared to 4.3 years in the reference group from Haojiang ($p < 0.01$). There was no significant difference in the proportion of genders between groups ($p > 0.05$). Smoking frequency of family members of preschool children in Guiyu is higher than that of family members in Haojiang ($p < 0.001$). Parents of children from the exposed group had a lower educational level

Table 1 Study subject and sample characteristics ($n = 470$)

Characteristic	Guiyu ($n = 300$)	Haojiang ($n = 170$)	p value
Gender (M/F) [n (%)]	150(50)/150(50)	97(57)/73(43)	0.141[a]
Age (years)	4.66 ± 1.25	4.34 ± 1.01	0.005[b]
Birth length (cm)	49.87 ± 5.35	51.55 ± 7.04	0.020[b]
Birth weight (kg)	3.10 (3.00–3.40)	3.25 (3.00–3.50)	0.009[c]
Height (cm)	104.43 ± 8.62	103.72 ± 8.10	0.383[b]
Weight (kg)	17.07 ± 3.20	17.46 ± 3.38	0.224[d]
Head circumference (cm)	50.00 (49.16–51.09)	50.20 (49.20–51.40)	0.422[c]
Chest circumference (cm)	51.18 (49.50–53.48)	51.95 (50.00–54.50)	0.025[c]
BMI (kg/m^2)	15.61 ± 1.82	16.12 ± 1.62	0.001[d]
Family member daily smoking [n (%)]			0.000[a]
Non-smoking	62 (20.7)	62 (36.5)	
1–2 cigarettes	62 (20.7)	32 (18.8)	
3–10 cigarettes	67 (22.2)	38 (22.3)	
11–20 cigarettes	68 (22. 7)	27 (15.9)	
> 20 cigarettes	41 (13.7)	11 (6.5)	
Parental education level [n (%)]			0.001[a]
Illiteracy	5 (1.7)	0 (0)	
Primary school	26 (8.7)	4 (2.4)	
Middle school	185 (61.7)	33 (19.4)	
Secondary school	34 (11.3)	33 (19.4)	
High school	22 (7.3)	39 (22.9)	
College/university	28 (9.3)	61 (35.9)	
Family income level per month (¥) [n (%)]			0.167[a]
< 1000	8 (2.7)	5 (2.9)	
1000–1500	27 (9.1)	8 (4.7)	
1500–2000	50 (16.7)	21 (12.4)	
> 2000	215 (71.7)	136 (80.0)	
House close to an e-waste recycling site within 50 m [n (%)]			0.000[a]
No	133 (44.3)	155 (91.2)	
Yes	167 (55.7)	15 (8.8)	

Guiyu: e-waste exposed area; Haojiang: reference area; mean values ± SD, median values with interquartile range (IQR), and ratio value with n (%)

[a]Pearson Chi-Square test

[b]T test

[c]Mann–Whitney U test

[d]T test based on ln-transform

when compared to those from the reference group ($p < 0.01$). There was no significant difference in family income levels between e-waste exposure and reference groups in this study ($p > 0.05$). A significantly higher proportion (56%) of houses belonging to Guiyu participants were located within 50 meters of an e-waste recycling facility than those of the reference group (9%) ($p < 0.001$). Most Guiyu families have been surrounded by e-waste, which is consistent with our previous studies and the actual conditions.

$PM_{2.5}$ heavy metal concentrations in Guiyu and Haojiang

The average concentration of $PM_{2.5}$ was significantly higher in Guiyu (57.73 ± 29.60 $\mu g/m^3$) than that in Haojiang (40.53 ± 17.75 $\mu g/m^3$) ($p < 0.01$). The average concentrations of Pb and Cd in $PM_{2.5}$ from Guiyu were higher than those from Haojiang ($p < 0.01$), while Cr and Mn in $PM_{2.5}$ showed no significant difference between Guiyu and Haojiang ($p > 0.05$, Fig. 2a).

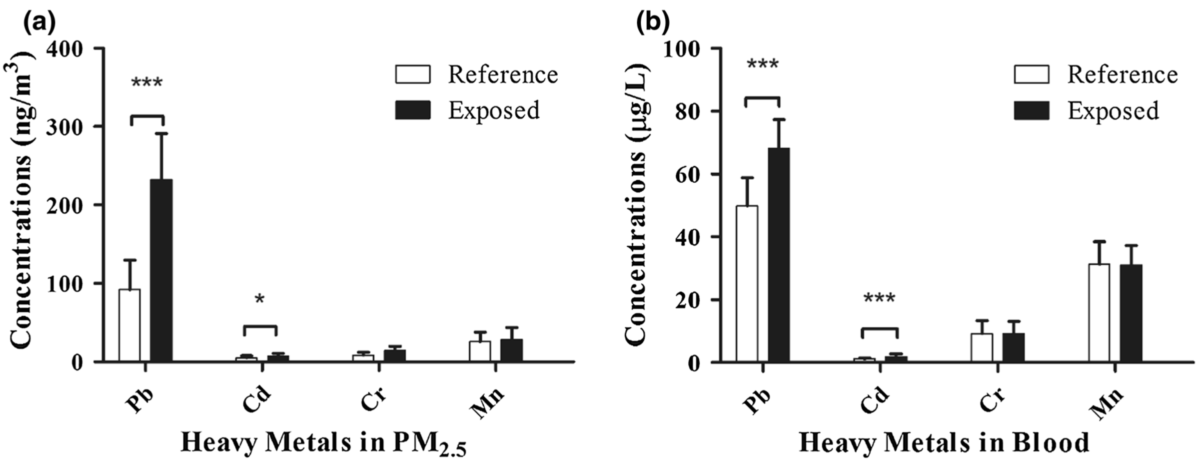

Fig. 2 Heavy metal concentrations in $PM_{2.5}$ and blood from e-waste exposed and reference groups. Pb: lead; Cd; cadmium; Cr: chromium; Mn: manganese; exposed area: Guiyu; reference area: Haojiang. *$p < 0.05$; ***$p < 0.001$

Blood heavy metal concentrations in preschool children

Four heavy metals, Pb, Cd, Cr, and Mn, were measured in the blood of participating children using GFAAS. Both blood Pb (6.81 $\pm$ 1.61 µg/dL) and blood Cd (0.66 $\pm$ 0.37 µg/L) were higher in Guiyu children than those (4.98 $\pm$ 1.56 and 0.54 $\pm$ 0.26 µg/L) in Haojiang ($p < 0.001$, Fig. 2b). However, there was no significant difference in blood Cr and Mn of preschool children between the two groups ($p > 0.05$, Fig. 2b). More than half of the children had blood Pb $\geq$ 5 µg/dL (update threshold) in Guiyu. Excessive rates of blood Pb ($\geq$ 5 µg/dL), blood Cd (> 0.5 µg/L), and blood Cr (> 5 µg/L) in Guiyu were higher than Haojiang ($p < 0.001$). However, neither percentage of blood Mn > 15 µg/L nor percentage of blood Mn > 30 µg/L differed significantly between the between the two groups of children.

Physical growth and development parameters in preschool children

Physical growth and development parameters are shown in Table 1. Birth length and weight of preschool children in Guiyu were lower than Haojiang ($p < 0.05$). Height, weight, and head circumference of children showed no significant differences between the two investigated groups ($p > 0.05$). Guiyu children had a lower BMI (mean BMI males = 15.88 kg/m^2, mean BMI females = 15.35 kg/m^2) than their peers from Haojiang (mean BMI males = 16.28 kg/m^2, mean BMI females = 15.90 kg/m^2) ($p < 0.05$). Height, weight, head circumference, and chest circumference were higher in boys than girls in both study groups (Table S1). The height and weight of preschool children, regardless of study site, were smaller than their predicted values (Table 2). Furthermore, head circumference of Guiyu children (mean = 50.00 cm) were lower than predicted values, while the head circumference of Haojiang children were not significantly different from predicted values (Table 3). Chest circumference was smaller than predicted values both in Guiyu and Haojiang preschool children (Table 3).

The relationship between blood heavy metals and growth and development parameters in preschool children

Spearman rank correlation analyses were performed to evaluate the correlation between four heavy metals in blood and seven physical growth and development parameters (Table 4). We found that height, weight, BMI, head circumference, chest circumference and birth weight were positively correlated with each other (all $p < 0.05$), except for the correlation between height and BMI. All four metals were significantly positively correlated with each other (all $p < 0.05$). Blood Pb was negatively correlated with height ($r = -0.130$, $p < 0.001$), weight ($r = -0.169$, $p < 0.001$), BMI ($r = -0.100$, $p < 0.05$), head

Table 2 Comparison of height and weight of boys and girls in e-waste exposed and reference groups (mean ± SE)

	Height (cm)				Weight (kg)			
	Exposed ($n = 300$)	Predicted of exposed ($n = 300$) ($n = 170$)	Reference ($n = 170$)	Predicted of reference ($n = 170$)	Exposed ($n = 300$)	Predicted of exposed ($n = 300$)	Reference ($n = 170$)	Predicted of reference ($n = 170$)
Boys (247)	$105.3 \pm 9.0^{a***}$ ($n = 150$)	111.2 ± 9.3 ($n = 150$)	$104.0 \pm 7.3^{b***}$ ($n = 97$)	108.5 ± 7.1 ($n = 97$)	$17.6 \pm 3.1^{a***}$ ($n = 150$)	19.2 ± 3.0 ($n = 150$)	$17.7 \pm 3.2^{b*}$ ($n = 97$)	18.3 ± 2.3 ($n = 97$)
Girls (223)	$103.6 \pm 8.2^{a***}$ ($n = 150$)	108.8 ± 8.3 ($n = 150$)	$103.3 \pm 9.1^{b***}$ ($n = 73$)	107.0 ± 7.1 ($n = 73$)	$16.5 \pm 3.2^{a***}$ ($n = 150$)	18.1 ± 2.5 ($n = 150$)	17.1 ± 3.6^{b} ($n = 73$)	17.5 ± 2.1 ($n = 73$)
Total (470)	$104.4 \pm 8.6^{a***}$ ($n = 300$)	110.0 ± 8.8 ($n = 300$)	$103.7 \pm 8.1^{b***}$ ($n = 170$)	107.8 ± 7.1 ($n = 170$)	$17.1 \pm 3.2^{a***}$ ($n = 300$)	18.6 ± 2.8 ($n = 300$)	$17.5 \pm 3.4^{b**}$ ($n = 170$)	18.0 ± 2.2 ($n = 170$)

Exposed: Guiyu (the e-waste exposure area) preschool children; reference: Haojiang (the reference area) preschool children

$*p < 0.05$; $**p < 0.01$; $***p < 0.001$

[a] Comparison between Guiyu and predicted of Guiyu

[b] Comparison between reference areas and predicted of reference areas; the predicted values for each group refer to previous epidemiological survey results (Li et al. 2009)

circumference ($r = -0.095$, $p < 0.05$) and chest circumference ($r = -0.112$, $p < 0.05$), respectively (Table 4).

The association between blood heavy metals and growth and development parameters in preschool children

Linear regression analyses were used to investigate associations between blood heavy metals and growth and development parameters in preschool children (Table 5). We found that blood Pb was negatively associated with height, weight, head circumference, chest circumference both in the bivariate model (height: $\beta = -0.091$, $p < 0.05$; weight: $\beta = -0.135$, $p < 0.01$; head circumference: $\beta = -0.126$, $p < 0.01$; chest circumference: $\beta = -0.112$, $p < 0.05$) and in the full-adjusted models (height: $\beta = -0.066$, $p < 0.05$; weight: $\beta = -0.119$, $p < 0.001$; head circumference: $\beta = -0.123$, $p < 0.01$; chest circumference: $\beta = -0.104$, $p < 0.05$) (Table 5). No other significant associations between Cd, Cr, or Mn with any growth parameters were observed.

Discussion

This study investigated concentrations of heavy metals in blood samples from preschoolers in two Chinese areas in relation to seven physical growth and development indicators. We found that both Pb and Cd concentrations in $PM_{2.5}$ and preschool children blood from Guiyu (the e-waste exposure area) were higher than those from Haojiang (the reference area). Although there was no significant difference in Cr and Mn in $PM_{2.5}$ and blood according to the present study, their concentrations were at high levels exceeding the safe concentration ranges. In addition, almost all of physical growth and developmental parameters were smaller than their predicted values. Birth weight and length, chest circumference, and BMI was lower in Guiyu than Haojiang. However, no significant difference was found in other physical growth and development parameters between the two investigated groups. Height, weight, head circumference, and chest circumference increased with age for all preschool children. In regression analyses, only Pb exposure was significantly associated with decreased growth and development in this population of preschool children.

Table 3 Comparison of head and chest circumference of boys and girls in e-waste exposed and reference groups (mean ± SE)

	Head circumference (cm)				Chest circumference (cm)			
	Exposed (n = 300)	Predicted of exposed (n = 300) (n = 170)	Reference (n = 170)	Predicted of reference (n = 170)	Exposed (n = 300)	Predicted of exposed (n = 300)	Reference (n = 170)	Predicted of reference (n = 170)
Boys (247)	50.5 ± 3.6[a]* (n = 150)	50.9 ± 0.8 (n = 150)	50.7 ± 1.4[b] (n = 97)	50.7 ± 0.6 (n = 97)	52.3 ± 4.5[a]*** (n = 150)	55.0 ± 2.6 (n = 150)	52.9 ± 3.5[b]*** (n = 97)	54.2 ± 2.0 (n = 97)
Girls (223)	49.3 ± 3.2[a]*** (n = 150)	50.8 ± 0.7 (n = 150)	49.6 ± 1.9[b] (n = 73)	49.7 ± 0.6 (n = 73)	50.5 ± 4.0[a]*** (n = 150)	53.0 ± 1.9 (n = 150)	51.7 ± 4.0[b]* (n = 73)	52.6 ± 1.6 (n = 73)
Total (470)	49.9 ± 3.5[a]*** (n = 300)	50.9 ± 0.8 (n = 300)	50.2 ± 1.7[b] (n = 170)	50.3 ± 0.8 (n = 170)	51.4 ± 4.4[a]*** (n = 300)	54.0 ± 2.5 (n = 300)	52.4 ± 3.7[b]*** (n = 170)	53.5 ± 0.2 (n = 170)

Exposed: Guiyu (the e-waste exposure area) preschool children; reference: Haojiang (the reference area) preschool children

*$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

[a]Comparison between Guiyu and predicted of Guiyu

[b]Comparison between reference areas and predicted of reference areas

In the current study, 66% of the children in Guiyu had a blood Pb level of > 5 µg/dL (the update US CDC limit value of blood Pb is ≤ 5 µg/dL) (Betts 2012). Among the preschool children from Guiyu, blood Cd levels exceed the reference value of 0.5 µg/L in 63% of children (Wilhelm et al. 2006). Approximately, 96% of the children in the exposed group had a blood Cr > 5 µg/L (the normal safety range of blood Cr is 1–3 µg/L) (Tiwari et al. 2012). Blood Mn had the highest standard exceeding ratio of 99% (> 15 µg/L) among the four kinds of blood heavy metals in the exposed group (the normal safety range of blood Mn is 4–15 µg/L) (Batterman et al. 2011). In addition, we should not be overlook that blood heavy metal concentrations in the reference group were also at a high level. The average blood heavy metal concentrations of children in this study was higher than their peers in America (Claus et al. 2012), Europe (KutllovciZogaj et al. 2014), and Africa (Hruba et al. 2012). In addition, the average heavy metal concentrations in $PM_{2.5}$ were slightly lower in this study than a previous study conducted in Guiyu in 2004, which may indicate that the concentration of heavy metals in $PM_{2.5}$ has decreased. However, heavy metal concentrations in $PM_{2.5}$ were higher than the most other sites in Asia, which demonstrated that heavy metal pollution state in Guiyu was still a very serious problem. Moreover, the current study showed that heavy metal concentration comparison in external ($PM_{2.5}$) and internal (blood) between the two groups were consistent (Fig. 2). Furthermore, the higher levels of heavy smoking in the exposed group may be due to its lower level of education when compared to the reference group (Table 1).

The levels of physical growth and development parameters in preschool children from the two investigated groups were smaller than their predicted values (Tables 2, 3), which suggested that the physical growth and development of preschool children was severely restricted when compared to their Chinese peers (Li et al. 2009). No significant difference in height and weight between Guiyu and Haojiang was mainly because that Guiyu children were older than those in Haojiang (Table 1). However, the height and weight for age of preschool children in Guiyu were lower than their peers in Haojiang (Table S1). It is worth noting that both height and weight of children in Guiyu are lower when compared to the height and weight of standardized growth charts of their peers from WHO, USA, and China (Bloem 2007; de Onis et al. 2007; Li et al. 2009). As an instance, the average height and weight of children in Guiyu are approximately 5 cm and 2 kg lower than the corresponding Chinese reference value, respectively. It is well known that the physical growth and development parameters such as height and weight are more influenced by environment, nutrition, and healthcare than genetics or ethnics (de Onis et al. 2004). The difference in children's growth between Guiyu and the standardized growth charts demonstrated that the growth and

Table 4 Spearman correlation coefficients between blood heavy metals and physical growth and development parameters in preschool children

	Height	Weight	BMI	HC	CC	BL	BW	lnBPb	lnBCd	lnBCr	lnBMn
Height	1.000										
Weight	0.844***	1.000									
BMI	− 0.105*	0.391***	1.000								
HC	0.541***	0.646***	0.281***	1.000							
CC	0.669***	0.835***	0.419***	0.612***	1.000						
BL	0.043	0.057	0.049	0.060	0.030	1.000					
BW	0.090#	0.176***	0.182***	0.175***	0.194***	0.242***	1.000				
lnBPb	− 0.130***	− 0.169***	− 0.100*	− 0.095*	− 0.112*	0.053	− 0.067	1.000			
lnBCd	0.097*	0.062	− 0.106*	0.027	0.044	− 0.033	− 0.049	0.183***	1.000		
lnBCr	− 0.001	− 0.028	− 0.062	− 0.034	− 0.040	0.007	− 0.010	0.225***	0.083***	1.000	
lnBMn	− 0.169	− 0.045	0.023	− 0.047	− 0.016	0.082	0.018	0.166***	0.128***	0.184***	1.000

BMI body mass index, *HC* head circumference, *CC* chest circumference, *BL* birth length, *BW* birth weight, *lnBPb* ln-transformation of blood lead, *lnBCd* ln-transformation of blood cadmium, *lnBCr* ln-transformation of blood chromium, *lnBMn* ln-transformation of blood manganese

#$0.05 < p < 0.10$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

development of children in Guiyu have been limited or suppressed, and need early intervention without delay.

Head circumference are commonly used as an indicator of neurological development in infancy and early childhood, providing a rapid and cost-effective means to screen for abnormalities such as delayed development or hydrocephalus (Rollins et al. 2010). In addition, head circumference is positively correlated with brain volume and intelligence in groups of healthy children and is often smaller in children with mental retardation (O'Connell et al. 1965; Ivanovic et al. 2004). Based on the fact that Guiyu has been contaminated by e-waste for years, our assumption was that head circumference of Guiyu children was lower than those of reference children. No significant difference was found in head circumference of preschool children between Guiyu and Haojiang in the present study, which mainly because that Guiyu children was older than those in Haojiang (Table 1). However, further investigation demonstrated that head circumference for age of preschool children in Guiyu was lower than their peers in Haojiang (Table S1) and the WHO reference value (Duran et al. 2016). In addition, there was no significant difference between head circumference and predicted head circumference in the reference group. It must be noted that head circumference was smaller than their predicted values in Guiyu preschool children, which may indicate that the growth and development of the nervous system in Guiyu preschool children has been restricted when compared to their peers in the reference and normal Chinese children (Li et al. 2009).

Several studies have pointed out that chest circumference can be a good predictor of early-life respiratory function and nutrition (Whittaker et al. 2005; Silventoinen et al. 2012; Zeng et al. 2017a, b). In this study, chest circumference was smaller than their predicted values both in Guiyu and Haojiang preschool children. Interestingly enough, although Guiyu children was older than those in Haojiang, chest circumference of Guiyu children was still lower than those from Haojiang and the WHO, USA, and China reference value (Bloem 2007; de Onis et al. 2007; Li et al. 2009), which may illustrate that long-term e-waste exposure have an adverse effect on the physical growth and development of respiratory system of children in Guiyu. Our recent study demonstrated that Guiyu preschool children have a lower lung function level when compared with their

Table 5 Association between blood heavy metals and physical growth and development parameters in preschool children

	Height (cm)		Weight (kg)		Head circumference (cm)		Chest circumference (cm)	
	β^a	B^b (95% CI for B)	β^a	B^b (95% CI for B)	β^a	B^b (95% CI for B)	β^a	B^b (95% CI for B)
Bivariate								
Age	0.78	5.40 (4.98, 5.83)***	0.60	1.65 (1.45, 1.85)***	0.28	0.70 (0.49, 0.92)***	0.43	1.51 (1.22, 1.80)***
Gender	− 0.08	− 1.30 (− 2.37, − 0.23)***	− 0.15	− 0.97 (− 1.56, − 0.39)***	− 0.19	− 1.12 (− 1.65, − 0.60)***	− 0.20	− 1.66 (− 2.41, − 0.92)***
lnBPb	− 0.09	− 1.93 (− 3.83, − 0.02)*	− 0.14	− 1.10 (− 1.84, − 0.37)**	− 0.13	− 0.93 (− 1.59, − 0.26)**	− 0.11	− 1.18 (− 2.12, − 0.23)*
lnBCd	0.11	1.87 (0.30, 3.43)*	0.06	0.37 (− 0.24, 0.98)	0.08	0.46 (− 0.09, 1.01)#	0.06	0.48 (− 0.30, 1.26)
lnBCr	0.02	0.434 (− 1.32, 2.18)	0.02	0.12 (− 0.56, 0.80)	− 0.01	− 0.04 (− 0.65, 0.57)	− 0.01	− 0.11 (− 0.98, 0.76)
lnBMn	− 0.05	− 1.31 (− 3.73, 1.11)	− 0.03	− 0.31 (− 1.25, 0.63)	0.02	0.18 (− 0.67, 1.03)	0.01	0.09 (− 1.12, 1.29)
Full								
lnBPb	− 0.07	− 1.39 (− 2.63, − 0.14)*	− 0.12	− 0.97 (− 1.55, − 0.39)***	− 0.12	− 0.90 (− 1.53, − 0.28)**	− 0.10	− 1.09 (− 1.93, − 0.25)*
lnBCd	− 0.02	− 0.336 (− 1.38, 0.71)	− 0.05	− 0.31 (− 0.80, 0.18)	0.03	0.18 (− 0.35, 0.70)	0.02	− 0.14 (− 0.84, 0.57)
lnBCr	0.04	0.836 (− 0.31, 1.98)	0.04	0.27 (− 0.27, 0.81)	0.01	0.06 (− 0.52, 0.64)	0.01	0.06 (− 0.71, 0.83)
lnBMn	0.01	0.32 (− 1.27, 1.91)	0.02	0.16 (− 0.59, 0.91)	0.04	0.34 (− 0.46, 1.15)	0.04	0.47 (− 0.60, 1.54)

Bivariate model: adjusted by age and gender; full model: adjusted by age, gender, family members smoking, parental education level and family income level

lnBPb ln-transformation of blood lead, *lnBCd* ln-transformation of blood cadmium, *lnBCr* ln-transformation of blood chromium, *lnBMn* ln-transformation of blood manganese, *BMI* body mass index, *CI* confidence interval

[a]Standardized coefficients

[b]Unstandardized coefficients

#$0.05 < p < 0.10$; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

peers in the reference area (Zeng et al. 2017a, b). In addition, birth weight and height of Guiyu children was lower than Chinese child standardized growth charts, WHO child growth standards and the CDC 2000 growth charts (Bloem 2007; de Onis et al. 2007; Li et al. 2009). To some extent, these results confirm our hypothesis that physical growth and development of children from e-waste exposure area are restricted or delayed on a degree.

Heavy metal exposure can cause toxicity and damage to diverse organs and tissues in the human body (Zeng et al. 2016a, b). In the current study, height and weight was lower in e-waste exposure group than the reference group, which is consistent to our previous studies (Zheng et al. 2013; Xu et al. 2015a, b; Zeng et al. 2017a, b). To evaluate whether there is an association between heavy metal exposure derived from e-waste and the physical growth and development of children, we measured four kinds of blood heavy metals and investigated seven physical growth and development parameters. We found that blood Pb were negatively associated with height, weight, head circumference, and chest circumference in preschool children, which further confirm the above hypothesis that heavy metal exposure can interfere with physical growth and development of children. The research results were consistent with previous studies. For instances, blood Pb and Cd inhibited the growth and development of children and adults through disturbing the metabolism of calcium and bone (Yang et al. 2013; Xu et al. 2015a, b; Lim et al. 2016). Fleisch et al. (2013) demonstrated that each unit increase in natural log-transformed blood Pb was associated with a 22.2-ng/mL decrease in mean serum IGF-1L. Schell et al. (2009) showed that blood Pb may affect some dimensions of infant growth such as weight, upper arm circumference and head circumference.

The limitation of this study is that samples and data were collected from one epidemiological investigation. In other word, we did not follow-up on these children in the present study, which means that the characteristic of this study, cross-sectional study, prevent us taking a cause-and-effect relationship between heavy metal exposure and the restriction of growth and development of children in e-waste exposure area. In addition, age of the two groups of children was not fully matched. Nevertheless, this was the first study systematically and comprehensively investigating the effect of several blood heavy metals on the various physical growth and development parameters of children from an e-waste-exposed area and the reference area. To confirm causality between heavy metal exposure and physical growth and development of children, an individualized follow-up cohort study will be required in the future.

Conclusion

The current results showed that children from Guiyu have higher levels of blood heavy metals than their peers from America, Europe, and Africa. In addition, physical growth and development of Guiyu children have been restricted compared to WHO and Chinese reference value, and need early prevention and intervention. Furthermore, blood Pb exposure poses adverse effects on the physical growth and development of children. It is imperative to study children throughout their childhood to confirm whether e-waste pollutants such as heavy metals and plastics have a long-term adverse effect on the growth and development of children, and whether early-life Pb exposure is associated with other health outcomes later in childhood or adulthood.

Acknowledgements The authors are grateful to all the recruited children and their guardians for their invaluable involvement and support. We acknowledge the constructive comments of the anonymous reviewers. This work was supported by the Natural Science Foundation of China (21377077, 21577084) and a research grant of Xinxiang Medical University (No. 300/505233).

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