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Hearing loss in children with e-waste lead and cadmium exposure

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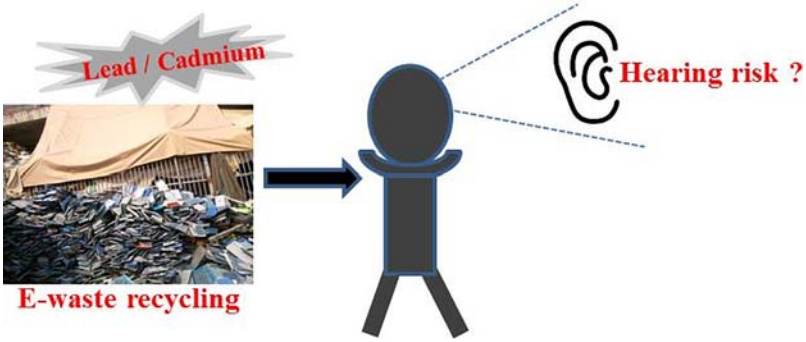
HIGHLIGHTS

- Higher blood Pb but not urinary Cd was found in the e-waste-exposed children.
- Elevated hearing thresholds and hearing loss prevalence in the exposed children were observed.
- Child hand-to-mouth behavior was an important factor for Pb and Cd exposure.
- Pb showed a significant OR for hearing loss in children by adjusting confounding factors.

GRAPHICAL ABSTRACT



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ABSTRACT

Environmental chemical exposure can cause neurotoxicity and has been recently linked to hearing loss in general population, but data are limited in early life exposure to lead (Pb) and cadmium (Cd) especially for children. We aimed to evaluate the association of their exposure with pediatric hearing ability. Blood Pb and urinary Cd were collected form 234 preschool children in 3–7 years of age from an electronic waste (e-waste) recycling area and a reference area matched in Shantou of southern China. Pure-tone air conduction (PTA) was used to test child hearing thresholds at frequencies of 0.25, 0.5, 1, 2, 4 and 8 kHz. A PTA ≥ 25 dB was defined as hearing loss. A higher median blood Pb level was found in the exposed group (4.94 ± 0.20 *vs* 3.85 ± 1.81 μg/dL, $p < 0.001$), while no significance was found for creatinine-adjusted Cd. Compared with the reference group, the exposed group had a higher prevalence of hearing loss (28.8% *vs* 13.6%, $p < 0.001$). The PTA in the left, right and both ears, and hearing thresholds at average low and high frequency, and single frequency of 0.5, 1 and 2 kHz were all increased in the exposed group. Positive correlations of child age and nail biting habit with Pb, and negative correlations of parent education level and child washing hands before dinner with Pb and Cd exposure were observed. Logistic regression analyses showed the adjusted OR of hearing loss for Pb exposure was 1.24 (95% CI: 1.029, 1.486). Our data suggest that early childhood exposure to Pb may be an important risk factor for hearing loss, and the developmental auditory system might be affected in e-waste polluted areas.

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1. Introduction

Hearing loss is one of the most common chronic disabling conditions. Roughly 360 million people around the world suffer from moderate to profound hearing loss due to various causes, and a recent systematic review reports that the incidence of neonatal hearing loss in the U.S. is near 1.1 per 1000 infants and the average prevalence of mild or worse unilateral or bilateral hearing impairment in children and adolescents exceed 3% (Davis et al., 2016; Roland et al., 2016). Many factors are attributable for hearing loss. Studies have shown that modern lifestyles may cause hearing impairment, including smoking, acoustic over-stimulation, drinking alcohol and emotional stress (Canlon et al., 2013; Durusoy et al., 2017; Sumit et al., 2015). For decades, most efforts have been implemented to link the occupational noise or ototoxic drug (*e.g.*, antibiotics) with hearing impairment, and their exposure can initiate a series of pathological changes resulting in damages of spiral ganglion neurons within the cochlea, some of which occur even when the hair cells are not sufficiently injured to undergo degeneration (Caciari et al., 2013; Francis and Cunningham, 2017). Recent studies have shown that heavy metal exposure may also be considered as the risk factors for hearing loss in humans (Hwang et al., 2009; Schaal et al., 2017).

Lead (Pb) is a ubiquitous environmental toxicant that associates with many potential health problems, and nervous system is especially affected with decreasing intelligence quotient and delayed cognitive function during early development in children even at a low-level exposure (Huang et al., 2012; Lee et al., 2017). An early comparison study has been performed to investigate the changes in Pb-induced neurobehavior, finding that the brainstem auditory evoked potentials both in animals and school-age children are deterred (Lilienthal et al., 1990). Then the association of environmental Pb exposure and impaired hearing is also observed among general adult population and workers (Castellanos and Fuente, 2016). Cd is a typical nephrotoxicant that may produce a series of physiological disorders and even cancer potential (Antila et al., 1996; Rango et al., 2015; Zeng et al., 2017). A recent *in vivo* study finds that high Cd exposure may cause an increase in auditory threshold and a decrease in response latency (Low and Higgs, 2015). Upon human epidemiological data of Cd and hearing loss, to date, only 2 studies in a general population have been conducted (Choi et al., 2012; Shargorodsky et al., 2011). Although research on the ototoxic effects of Pb and Cd are not clearly understood, experimental data demonstrate that they can damage cochlea or vestibular function through ROS generation and apoptosis, leading to disorders in auditory nerve conduction and finally significant hearing loss (Kim et al., 2008; Klimpel et al., 2017).

Guiyu, as a typical electrical waste (e-waste) recycling area, has attracted much attention among researchers due to informal dismantling without proper environmental protection measures over the last few decades (Song and Li, 2014; Zeng et al., 2016). In our previous studies, the levels of heavy metals in children and neonates of Guiyu are much higher compared to other areas (Liu et al., 2016; Xu et al., 2015). In perspective of the ototoxic effect of heavy metals and limited epidemiologic studies available for the prevalence of hearing loss in children, especially in an e-waste-polluted area, we therefore attempted to investigate whether environmental chemical pollutant exposure was able to affect hearing abilities of preschool children living in Guiyu, to find out the association of blood Pb and urinary Cd exposure with hearing loss in early childhood.

2. Material and methods

2.1. Study population and questionnaires

A cross-sectional study was performed, with a total of 234 preschool children 3–7 years of age were voluntarily enrolled to participate in a hearing test in 2014. In this, 146 children were from Guiyu town, an e-waste recycling area, and the remaining 88 children were from Haojing area. The reference area is about 31.6 km to the east of Guiyu, Shantou city, in the southeastern coast of Guangdong province in China. Haojiang was selected as the reference area because it lacks of e-waste processing as well as its similarities to Guiyu in population, traffic density, residential lifestyle and socioeconomic status. A questionnaire on lifestyle and residential environment was administrated to parents or guardians of all children participating in the study. Children with otitis media or other hearing impairment problems in medication, family hearing genetic history and chronic diseases such as asthma, or acute cough or cold were excluded. The questionnaire addressed factors that might influence hearing status, including questions related to residence, physical activity, dietary habits, nutrition, behavior habits, whether the parent's occupation was related to e-waste processing, and family member smoking status, education status, and income. Some characteristics for relevant factors were given (Supplemental Table 1). This study protocol was approved by the Human Ethics Committee of Shantou University Medical College, China.

2.2. Sample collection and exposure measurement

A total of 2 mL venous blood from each participant was collected between 7:00 AM and 10:00 AM by trained nurses and stored in a Vacutainer with EDTA-2K as an anticoagulant. Whole blood samples were then transported to lab and stored at −20 °C until measurement of Pb concentration. First morning urine was collected, between 7:00 AM and 8:00 AM, into a polypropylene conical centrifuge tube, divided into two tubes, and frozen at −80 °C until analysis. Blood Pb and urinary Cd levels were both determined by graphite furnace atomic absorption spectrometry (GFAAS, Jena Zeenit 650, Germany). Details for the pretreatment of samples and measurement procedures of instrument were as described previously, which was quite experienced in our laboratory (Huo et al., 2014; Zheng et al., 2008). Another part of urine was diluted tenfold in ultrapure water to detect urinary creatinine. The concentrations of creatinine were determined by a modified Jaffé reaction (Husdan and Rapoport, 1968) and optical density at 490 nm was recorded using a microplate reader (Infinite M200PRO, Tecan, Switzerland).

2.3. Hearing test

In this study, pure-tone air conduction (PTA) has been applied to evaluate the hearing function in children. Audiometric examination was conducted in a quite silent and sound-proofed room in local kindergartens by two audiologists from the affiliated hospitals in Shantou University Medical College and the detailed procedure was based on a clinical protocol (GB/T 16403-1996, China). Before the test, the audiologists did an otoscopic examination on all children to ensure that the ear was free of infection and obstructions, and hearing test procedure was performed using the clinical standard protocol of the hospitals. PTA hearing thresholds were examined in both ears, at frequencies of 0.25, 0.5, 1, 2, 4 and 8 kHz, by a clinical audiometer (model SA203, Entomed AB, Sweden) equipped with headphones (model EF120075, Entomed AB, Sweden). In order to guarantee the quality of participants' responses, we first tested twice at the frequency of 1 kHz in each ear (Choi and Kim, 2014). Hearing loss was defined as a PTA ≥ 25 dB 25 dB (dB) in one or both ears (Austeng et al., 2013).

2.4. Statistical analysis

Normally distributed data was reported as the mean ± standard deviation (SD). The differences between the compared groups were tested using an independent sample *t*-test or analysis of variance (ANOVA). The chi-square test was used for categorical data, such as the ratio of hearing loss. Spearman correlations were used to find the potential risk factors in child exposure to Pb and Cd. Bivariate logistic models