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## Environmental Pollution

journal homepage: [www.elsevier.com/locate/envpol](http://www.elsevier.com/locate/envpol)Elevated lead levels from e-waste exposure are linked to decreased olfactory memory in children<sup>☆</sup>Bo Zhang<sup>a,1</sup>, Xia Huo<sup>c,1</sup>, Long Xu<sup>a</sup>, Zhiheng Cheng<sup>a</sup>, Xiaowei Cong<sup>a</sup>, Xueling Lu<sup>a</sup>, Xijin Xu<sup>a,b,\*</sup><sup>a</sup> Laboratory of Environmental Medicine and Developmental Toxicology, and Guangdong Provincial Key Laboratory of Infectious Diseases, Shantou University Medical College, Shantou 515041, Guangdong, China<sup>b</sup> Department of Cell Biology and Genetics, Shantou University Medical College, Shantou 515041, Guangdong, China<sup>c</sup> School of Environment, Guangzhou Key Laboratory of Environmental Exposure and Health, Guangdong Key Laboratory of Environmental Pollution and Health, Jinan University, Guangzhou, Guangdong, 510632, China

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## ABSTRACT

Lead (Pb) is a developmental neurotoxicant and can cause abnormal development of the nervous system in children. Hence, the aim of this study was to investigate the effect of Pb exposure on child olfactory memory by correlating the blood Pb levels of children in Guiyu with olfactory memory tests. We recruited 61 preschool children, 4- to 7-years of age, from Guiyu and 57 children from Haojiang. The mean blood Pb level of Guiyu children was 9.40 µg/dL, significantly higher than the 5.04 µg/dL mean blood Pb level of Haojiang children. In addition, approximately 23% of Guiyu children had blood Pb levels exceeding 10.00 µg/dL. The correlation analysis showed that blood Pb levels in children highly correlated with e-waste contact ( $r_s = 0.393$ ). Moreover, the mean concentration of serum BDNF in Guiyu children (35.91 ng/ml) was higher than for Haojiang (28.10 ng/ml) and was positively correlated with blood Pb levels. Both item and source olfactory memory tests at 15 min, 5 h and 24 h after odor exposure showed that scores were lower in Guiyu children indicative of reduced olfactory memory in Guiyu children. Olfactory memory tests scores negatively correlated with blood Pb and serum BDNF levels, but were positively associated with parental education levels. At the same time, scores of both tests on children in the high blood Pb level group (blood Pb levels > 5.00 µg/dL) were lower than those in the low blood Pb level group (blood Pb levels ≤ 5.00 µg/dL), implying that Pb exposure decreases olfactory memory in children. Our findings suggest that Pb exposure in e-waste recycling and dismantling areas could result in an increase in serum BDNF level and a decrease in child olfactory memory, in addition, BDNF might be involved in olfactory memory impairment.

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## 1. Introduction

With the advance of science and technology around the world, the quality and performance of electronic equipment has continued to improve. Satisfying consumer needs, the continual updating of high-tech equipment at the same time has resulted in the accumulation electronic waste (e-waste), whose components have

become major contaminants. E-waste includes the end-of-life electronics or electrical equipment for home or office, such as computers, printers, television sets, mobile phones, refrigerators, washing machines, and even large electrical products such as medical equipment and telecommunication equipment (Chen et al., 2011; Grant et al., 2013). To date, e-waste has become the fastest-growing stream of solid waste, the accumulation of which has caused serious environmental pollution and has become one of the most significant environmental health concerns (Heacock et al., 2016; Li et al., 2015; Tansel, 2017). Approximately 80% of the world's e-waste is imported into Asia, with as much as 90% being deposited in China (Chen et al., 2011; Hicks et al., 2005; LaDou and Lovegrove, 2008).

E-waste contamination mainly occurs in less developed

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countries, such as Nigeria or Ghana, and developing countries as India and China (LaDou and Lovegrove, 2008; Suk et al., 2016). In Guiyu, a small town in southern China and the biggest e-waste recycling and dismantling area in the world, the irregular disposal or recycling processes with e-waste is a major concern, for example the burning, acid leaching, roasting, dismantling and dumping of e-waste, resulting the release of heavy metals and organic pollutants to the surrounding air, water, and soil environment, contaminating food and threatening the health of local residents (Heacock et al., 2016; LaDou and Lovegrove, 2008; Lin et al., 2017; Ogunseitan et al., 2009; Schmidt, 2006; CS Wong et al., 2007; MH Wong et al., 2007; Wu et al., 2011; L Xu et al., 2015; Xu et al., 2013; X Xu et al., 2015; Yekeen et al., 2016; Yu et al., 2006; Zeng et al., 2016b).

As one of the major pollutants in e-waste recycling and dismantling, lead (Pb) is released by the dumping, roasting, burning and acid leaching of scrap electronic equipment such as Pb-contained circuit boards, batteries, and TVs, resulting in the liberation of pollutants into air, soil and water (Bi et al., 2015; CS Wong et al., 2007). The main routes of exposure for Pb are inhalation and ingestion (X Xu et al., 2015). Due to differences in physiology and habits, children are more susceptible to the adverse effects of Pb exposure than adults (Bellinger, 2004; Chen et al., 2011; Lidsky and Schneider, 2003; Zeng et al., 2016a). Previous studies showed that 1- to 6-year-old children living in primitive e-waste recycling areas have a higher burden of Pb compared to other toxicants, with mean blood Pb levels of 15.3  $\mu\text{g}/\text{dL}$ , much higher than children from non-e-waste recycling and dismantling areas (Huo et al., 2007; Zhang et al., 2016; Zheng et al., 2008). The percentage of children with blood Pb levels exceeding 10  $\mu\text{g}/\text{dL}$  is approximately 81.8%, which is much higher than the 37.7% found in non-e-waste recycling and dismantling areas, and continues to rise with age (Huo et al., 2007; Zheng et al., 2008). Several studies show that Pb impacts the nervous system of children who are at the critical period for neurodevelopment. Lower IQ performance, neuropsychological dysfunction, attention deficit hyperactivity disorder and impaired cognitive function as memory, language and executive function have all been demonstrated in Pb-exposed children. A prior study showed that 6- to 10-year-old children with blood Pb levels of 5–10  $\mu\text{g}/\text{dL}$  exhibit mental decline, accompanied with attention disorders, and decreased memory and executive function (Bellinger, 2004, 2008, 2011; Lidsky and Schneider, 2003; Zhang et al., 2015). An increasing number of studies revealed that even Pb-exposed children with blood Pb levels less than 5  $\mu\text{g}/\text{dL}$  are associated with intellectual impairment (Canfield et al., 2003; Chandramouli et al., 2009; Lanphair et al., 2005; Lucchini et al., 2012; Mazumdar et al., 2011; Miranda et al., 2007).

Brain derived neurotrophic factor (BDNF) has been shown to play an important role in nervous system development and synaptic plasticity, and the BDNF signaling system has been implicated in the processes of hippocampus-dependent learning and memory formation (Ninan, 2014; Zagrebelsky and Korte, 2014), which also can be observed in the induction and formation of olfactory memory (Tong et al., 2014). The production and release of BDNF have been shown to be activity-dependent, which can be modulated by N-methyl-D-aspartate (NMDA) receptors through the  $\text{Ca}^{2+}$  signaling pathway (Matsuda et al., 2009; Shieh et al., 1998; West et al., 2001). Modulating glutamate receptors by BDNF is thought to play an important role in hippocampal plasticity and memory formation (Fortin et al., 2012; Slipczuk et al., 2009). Deficiency of serum BDNF is associated with a reduction in spine density and dendritic complexity and in hippocampus volume (Erickson et al., 2010; von Bohlen und Halbach 2010). The insulin-like growth factor 1 (IGF-1) is a member of the insulin superfamily of peptides and is mainly produced by hepatocytes, contributing to circulating IGF-

1 (Fernandez and Torres-Aleman, 2012). Serum IGF-1 entries into brain through brain vessels in an activity-dependent manner and affects neuronal plasticity and cognition (Nishijima et al., 2010). In addition, reduction of serum IGF-1 levels results in decreased hippocampal size and learning deficits (Lopez-Lopez et al., 2004; Trejo et al., 2007).

Olfactory memory is based on the recollection of odor in the associated context. Olfactory epithelium perceives the odor signal and *via* olfactory bulb projects inputs onto the piriform cortex, amygdala, and entorhinal cortex. Simultaneously, with the information from visual senses, olfactory information converges onto the orbitofrontal cortex, thalamus, hippocampus and insula cortex, allowing for the representation of the odor memory in the context in which it was experienced (Saive et al., 2014). Long-term potentiation (LTP), synaptic plasticity and neurogenesis mediated by NMDA receptors are involved in the molecular basis for formation and development of olfactory memory (du Bois and Huang, 2007; Tolia et al., 2005; Tong et al., 2014; Wang et al., 2011). Olfactory memory can be divided into two types: odor recognition memory (item memory) and odor associative memory (source memory) (Pirogovsky et al., 2006; Saive et al., 2014). Item memory is about the fact or content of an event, but source memory is the process of remembering the source or connection of events through specific projects or facts (Pirogovsky et al., 2006). According to the differences in storage time, olfactory memory can also be divided into short-term memory (STM), intermediate-term memory (ITM) and long-term memory (LTM) (Grimes et al., 2011; Tong et al., 2014).

To date, studies on the effects of lead on olfactory memory are few, and only in animal experiments. A recent study showed that Pb induces olfactory recognition memory impairment in rats (Flores-Montoya et al., 2015). There have been no epidemiological studies concerning the impairment of olfactory memory caused by Pb exposure. However it is clear that the relationship between lead exposure and impaired children's nervous system development is closely related. During the critical period of development, even low levels of Pb exposure may have adverse effects on mental development, and adverse effects on memory caused by low level Pb exposure may have profound effects on the health of a child's brain (Flores-Montoya et al., 2015). Pb blocks NMDA receptors which are essential for hippocampus-mediated learning and memory (Baranowska-Bosiacka et al., 2012; Gavazzo et al., 2008; Guilarte et al., 1995; Morris et al., 1982, 1986; Neal and Guilarte, 2013; Tsien et al., 1996). Therefore, we hypothesize that olfactory memory, which also depends on NMDA receptors, may be altered as a result of Pb-mediated neurotoxicity.

The aim of this study is to detect the level of Pb exposure and the olfactory memory in children from an e-waste recycling and dismantling area, to explore the effects of Pb exposure on children's olfactory memory, and to provide scientific basis for further study concerning the effect of lead exposure on both child nervous system development and the neurotoxicity of Pb.

## 2. Materials and methods

### 2.1. Study population

We recruited 118 preschool children approximately 6 years of age from Guiyu ( $n = 61$ ) and Haojiang ( $n = 57$ ), which was selected as the reference area for the similarities to Guiyu in population, cultural background and socioeconomic status, and furthermore without e-waste pollution. All children's parents or guardians gave written informed consent prior to enrollment. To collect the information as the general characteristics, health physiological, living and eating habits of children as well as dwelling environments, parental education level and jobs whether related to e-waste, a

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