



# Elevated biomarkers of sympatho-adrenomedullary activity linked to e-waste air pollutant exposure in preschool children



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## ABSTRACT

Air pollution is a risk factor for cardiovascular disease (CVD), and cardiovascular regulatory changes in childhood contribute to the development and progression of cardiovascular events at older ages. The aim of the study was to investigate the effect of air pollutant exposure on the child sympatho-adrenomedullary (SAM) system, which plays a vital role in regulating and controlling the cardiovascular system. Two plasma biomarkers (plasma epinephrine and norepinephrine) of SAM activity and heart rate were measured in preschool children ( $n = 228$ ) living in Guiyu, and native ( $n = 104$ ) and non-native children ( $n = 91$ ) living in a reference area (Haojiang) for  $> 1$  year. Air pollution data, over the 4-months before the health examination, was also collected. Environmental  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ ,  $NO_2$  and CO, plasma norepinephrine and heart rate of the e-waste recycling area were significantly higher than for the non-e-waste recycling area. However, there was no difference in plasma norepinephrine and heart rate between native children living in the non-e-waste recycling area and non-native children living in the non-e-waste recycling area.  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$  and  $NO_2$  data, over the 30-day and the 4-month average of pollution before the health examination, showed a positive association with plasma norepinephrine level.  $PM_{2.5}$ ,  $PM_{10}$ ,  $SO_2$ ,  $NO_2$  and CO concentrations, over the 24 h of the day of the health examination, the 3 previous 24-hour periods before the health examination, and the 24 h after the health examination, were related to increase in heart rate. At the same time, plasma norepinephrine and heart rate on children in the high air pollution level group ( $\leq 50$ -m radius of family-run workshops) were higher than those in the low air pollution level group. Our results suggest that air pollution exposure in e-waste recycling areas could result in an increase in heart rate and plasma norepinephrine, implying e-waste air pollutant exposure impairs the SAM system in children.

## 1. Introduction

Air pollution is an important global environmental problem and associated with many health burdens in many parts of the world. It is estimated that the vast majority of global population (89%) lives in unhealthy levels of outdoor air pollution exceeding World Health Organization (WHO) air quality standards [fine particulate matter ( $PM_{2.5}$ ) annual mean of  $10 \mu\text{g}/\text{m}^3$ ] (Brauer et al., 2012; WHO, 2016). A growing body of evidence linking outdoor air pollution with morbidity and mortality of cardiovascular and respiratory disease, cancer and all-cause has been found (Cao et al., 2011; Kan et al., 2008; Wang et al.,

2018; Zhang et al., 2013). The health effects of outdoor air pollution will further escalate in the future, approximately 3.3 million premature deaths per year is attributed to outdoor air pollution in both cities and rural areas in 2010, increasing to about 6.6 million in 2050 (Lelieveld et al., 2015).

With the rapid development of technology and science and increases in consumer needs, the requisite continual improvement and updating of electronic equipment has resulted in the accumulation of electronic waste (e-waste), including the end-of-life electrical and electronic products for homes and offices, and even large electrical equipment, such as telecommunication equipment and medical equipment (Chen

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et al., 2011; Grant et al., 2013; Zhang et al., 2017). It is estimated that global e-waste will be 65.4 million tons by 2017 (Breivik et al., 2014; Baldé et al., 2014). However, its poor management is an important environmental health problem (Chen et al., 2011). Based on the Basel Convention regulations, the flow of hazardous materials across national borders is prohibited (LaDou and Lovegrove, 2008; Lundgren, 2012). In 2006, the Nairobi Declaration on the Environmentally Sound Management of Electrical and Electronic Waste was adopted by the Basel Convention's eighth meeting of COP and launched on a global scale (Lundgren, 2012). In addition, in order to better manage e-wastes, a series of tools have also been designed and developed, including Extended Producer Responsibility, Material Flow Analysis, Multi-Criteria Analysis and Life Cycle Assessment (Kiddee et al., 2013). Unfortunately, approximately 70% of the world's e-waste is still deposited and processed in China every year (Robinson, 2009; Chen et al., 2011; Hicks et al., 2005; LaDou and Lovegrove, 2008). Recent studies revealed that the lion's share of global e-waste still be received in China, and some scarce mineral resources are acquired from e-waste to continue economic and social development (Dai et al., 2017; Bakhiyi et al., 2018). E-waste contains many toxic organic pollutants and metals, and the informal recycling and dismantling processes can lead to air pollution and the release of toxicants into the environment, especially in developing countries (Huo et al., 2007; Liu et al., 2008; Lu et al., 2016; Wang et al., 2016; Wu et al., 2012; Xu, L. et al., 2015b).

Emission of air pollutants from e-waste recycling and dismantling activities in China is known. Studies indicate that combustion of e-waste can cause the emission of air pollution. For example, the process of coal burning for the melting of circuit boards will release pollutants into the atmosphere; moreover, some processes used within the informal e-waste recycling and dismantling sectors, including grinding and melting, also release dust, fumes and smoke into the air (Dai et al., 2017; Huo et al., 2007; Zeng et al., 2016; Zhang et al., 2017; Zheng et al., 2016). Guiyu, a town in Shantou, Guangdong Province, China, is one of the largest e-waste recycling and dismantling locations in the world, and has a > 30-year history of e-waste recycling and dismantling (Huo et al., 2007; Lundgren, 2012), and air pollution has become prevalent as a result of informal e-waste recycling and dismantling activity. Previous studies show that the geometric mean concentration of PM<sub>2.5</sub> (49.9 µg/m<sup>3</sup>) in Guiyu is higher than the reference group (37.6 µg/m<sup>3</sup>), and PM air samples of Guiyu contain potentially carcinogenic and highly toxic pollutants such as Pb (geometric mean: 160 µg/m<sup>3</sup>), Cd (geometric mean: 5.7 µg/m<sup>3</sup>), Cr (geometric mean: 4.5 µg/m<sup>3</sup>), Mn (geometric mean: 17 µg/m<sup>3</sup>), PBDEs (mean ± SD: 16575 ± 13,286 pg/m<sup>3</sup>), PCDD/F (64.9–2365 pg/m<sup>3</sup>) and PBDD/Fs (8.124–61 pg/m<sup>3</sup>) (Li et al., 2007; Deng et al., 2007; Zeng et al., 2016; Zheng et al., 2016). Air pollutants of e-waste dismantling areas have raised public concern in recent years (Zheng et al., 2016; Zeng et al., 2016). At the same time, the risks for developing cardiovascular disease (CVD) and cancer are significantly elevated in e-waste recycling and dismantling workers and people living in e-waste recycling areas (Lu et al., 2017; Lu et al., 2016; Guo et al., 2013; Wang et al., 2012).

Although an increasing number of studies show that air pollution is a risk factor for CVD, the mechanisms by which air pollution leads to CVD is not fully understood (Brook et al., 2010; Dehbi et al., 2017; Zhang et al., 2014; Mustafic et al., 2012; Day et al., 2017). Assessment of sympatho-adrenomedullary (SAM) function in humans is one of the major fields in cardiovascular disease research (Grassi and Esler, 1999; Grassi et al., 2015; Guyenet, 2006; Malpas, 2010). Prior studies show that plasma epinephrine and norepinephrine and heart rate are reliable biomarkers of assessment of SAM activity (Chang et al., 1991; Esler et al., 1985; Kawada et al., 2006; Miyamoto et al., 2003; Peronnet et al., 1982; van den Meiracker et al., 1989). Generally, the SAM system transduces biological information either primarily through adrenergic receptors to regulate and control cardiovascular system, such as β1-adrenergic receptors, α1-adrenergic receptors and β2-adrenergic receptors (Masuo et al., 2005; Osei-Owusu and Scrogin, 2004; Rohrer

et al., 1998). In mammals, epinephrine and norepinephrine are the signaling hormones of the SAM system (Roy and Rai, 2008). In addition, among the numerous cardiovascular physiology parameters, heart rate is also an independent risk factor for CVD and a key vital sign to assess the physiological status in the clinical settings (Cooney et al., 2010; Fleming et al., 2011; Palatini, 2007).

To date, toxicological studies have shown that although the SAM system is not typically viewed as a primary target of numerous pollutants, pollutants can cause SAM dysfunction (Geraldés et al., 2016). The mechanisms underlying pollutant-induced SAM dysfunction could involve some central mechanisms and pathways, such as impairment of cholinergic and dopaminergic transmission and environmental pollutant-induced oxidative stress (Bielarczyk et al., 1996; Bourjeily and Suszkiw, 1997; Brockel and Cory-Slechta, 1999). A previous study showed that pollutant exposure can promote the autonomic nervous system dysfunction and increase chemoreceptor sensitivity in rats (Geraldés et al., 2016). Either short-term or long-term exposure to cigarette smoke, in either active or passive smoking, affects the balance of the autonomic nervous system, leading to predominance of sympathetic nervous activity (Middlekauff et al., 2014). A recent study shows that long-term PM<sub>2.5</sub> exposure increases blood pressure in rats, abnormal sympathetic nervous system activation and inflammation of the hypothalamus play an important role in this process (Ying et al., 2014). There have been no epidemiological studies concerning SAM dysfunction of preschool children by ambient air pollutant exposure. However, it is clear that the relationship between air pollution and exposure to some chemical contaminants and impaired nervous system development of children is closely related. Interaction of air pollution and heavy metals with the nervous system can lead to nervous system dysfunction and alter the balance of neurotransmitters, and some pollutant-induced neurobehavioral disorders can continue through youth (Annarapu and Kathi, 2016; Geraldés et al., 2016; Kioumourtoglou et al., 2016; Needleman, 1990; Valciukas et al., 1978). At the same time, it is worth noting that cardiovascular regulatory changes in childhood could contribute to the development and progression of cardiovascular events at older ages (Feinstein and Quivers, 1997). Therefore, we predict that the SAM system in children living in e-waste recycling areas may be affected as a result of air pollutant exposure.

The aim of this study is to investigate changes in the SAM system of children living in an e-waste recycling area, and explore the effect of air pollutant exposure on the SAM system by measuring plasma epinephrine and norepinephrine, and heart rate in children as a function of air pollutant data in a typical e-waste recycling area. We hope to provide a scientific basis for further study concerning the effect of air pollutant exposure on development of the child cardiovascular system.

## 2. Materials and methods

### 2.1. Sample collection

423 of the 591 children (3- to 6-years of age) from two different kindergartens in Guiyu and Haojiang, from November to December 2016, were recruited and had blood samples taken (Fig. 1). The response rate was 71.6% (Guiyu: 67.5%/Haojiang: 77.1%). Guiyu and Haojiang are both small rural towns in Shantou. There are many similarities between Haojiang (the non-e-waste recycling area) and Guiyu (the e-waste recycling area) in population, cultural background, living habits, climate conditions socioeconomic status, but there is no e-waste pollution in Haojiang (Zhang et al., 2017). For the purpose of this study, non-native children are defined as children who were not born in Shantou, and neither of their parents was a native of Shantou. All participants and guardians of children consented to participate, and signed informed consent. This study was also approved by the Human Ethics Committee of Shantou University Medical College, China. Self-administered questionnaire surveys were completed by each participant (or guardian), covering their personal information about age, gender,

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