Environmental Pollution 229 (2017) 168–176

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Serum metabolome biomarkers associate low-level environmental perfluorinated compound exposure with oxidative /nitrosative stress in humans☆

Xiaofei Wang [a, b, 1], Liangpo Liu [b, 1], Weibing Zhang [a, *], Jie Zhang [b, **], Xiaoyan Du [b], Qingyu Huang [b], Meiping Tian [b], Heqing Shen [b, ***]

[a] *Shanghai Key Laboratory of Functional Materials Chemistry, School of Chemistry & Molecular Engineering, East China University of Science and Technology, Shanghai 200237, China*
[b] *Key Lab of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, China*

A R T I C L E I N F O

Article history:
Received 5 December 2016
Received in revised form
22 March 2017
Accepted 29 April 2017

Keywords:
Perfluorinated compound
Serum
Metabolome
Oxidative stress
Nitrosative stress

A B S T R A C T

Previous *in vivo* and *in vitro* studies have linked perfluorinated compound (PFC) exposure with metabolic interruption, but the inter-species difference and high treatment doses usually make the results difficult to be extrapolated to humans directly. The best strategy for identifying the metabolic interruption may be to establish the direct correlations between monitored PFCs data and metabolic data on human samples. In this study, serum metabolome data and PFC concentrations were acquired for a Chinese adult male cohort. The most abundant PFCs are PFOA and PFOS with concentration medians 7.56 and 12.78 nM, respectively; in together they count around 81.6% of the total PFCs. PFC concentration-related serum metabolic profile changes and the related metabolic biomarkers were explored by using partial least squares-discriminant analysis (PLS-DA). Respectively taking PFOS, PFOA and total PFC as the classifiers, serum metabolome can be differentiated between the lowest dose group (1st quartile PFCs) and the highest PFC dose group (4th quartile PFCs). Ten potential PFC biomarkers were identified, mainly involving in pollutant detoxification, antioxidation and nitric oxide (NO) signal pathways. These suggested that low-level environmental PFC exposure has significantly adverse impacts on glutathione (GSH) cycle, Krebs cycle, nitric oxide (NO) generation and purine oxidation in humans. To the best of our knowledge, this is the first report investigating the association of environmental PFC exposure with human serum metabolome alteration. Given the important biological functions of the identified biomarkers, we suggest that PFC could increase the metabolism syndromes risk including diabetes and cardiovascular diseases.

© 2017 Elsevier Ltd. All rights reserved.

1. Introduction

Perfluorinated compounds (PFCs) have been widely used in industry and human daily life over the past few decades. The concerns regarding PFC exposure have risen in recent years due to their ubiquitous presence and high persistency (Lindstrom et al., 2011; Giesy and Kannan, 2001). PFC exposure has been linked to a number of adverse health outcomes, including metabolic and immune system disorders (Nelson and Webster, 2010; Grandjean et al., 2012), hepatotoxicity (Lau et al., 2007), developmental toxicity (Rogers, 2004) and neurotoxicity (Mariussen, 2012). Previous toxicity studies suggested that perfluorooctanoic acid (PFOA) exerted genotoxic effects (Yao and Zhong, 2005), induced apoptosis *via* the p53-dependent mitochondrial pathway (Huang et al., 2013) and genes expression alteration (Guruge et al., 2006), but most of the PFC toxicities were evaluated based on cell or animal models rather than population study. Moreover, most studies usually adopted high-dose and short-time treatment for the sake of

☆ This paper has been recommended for acceptance by Prof. von Hippel Frank A.

* Corresponding author. East China University of Science and Technology, Meilong Road 130, 200237 Shanghai, China.
** Corresponding author. Institute of Urban Environment, Chinese Academy of Sciences, 1799 Jimei Road, Xiamen 361021, China.
*** Corresponding author. Institute of Urban Environment, Chinese Academy of Sciences, 1799 Jimei Road, Xiamen 361021, China.
E-mail addresses: weibingzhang@ecust.edu.cn (W. Zhang), jzhang@iue.ac.cn (J. Zhang), hqshen@iue.ac.cn (H. Shen).
[1] Contribute equally to this article.

http://dx.doi.org/10.1016/j.envpol.2017.04.086
0269-7491/© 2017 Elsevier Ltd. All rights reserved.

significant toxic effect (Qazi et al., 2009a, 2009b; Yang et al., 2000, 2001). In contrast, the study regarding to the mode of actions of PFCs in humans are very limited. Most preliminary PFCs toxic information on human was from the traditional epidemiological investigation (Lau et al., 2007). The best strategy for identifying PFC induced effects is to set up the human study following the epidemiological approach, and then discover the potential exposure-associated biomarkers.

PFCs can be generally detected in human serum samples, thus the serum is commonly used as biomonitoring matrix in epidemiology study (Lau et al., 2007). On the other hand, metabolic alterations induced by the external stressors are the most abundant and commonly investigated phenomena in body fluids, as the global metabolic response to the changing individual environment (Zhang et al., 2016; Wang et al., 2015). Therefore, serum metabolic biomarkers might be the most practical indicators for exploring the molecular hints behind human exposure to PFCs. Like other omics (i.e. genomics, transcriptomics and proteomics), metabolomics has been widely used in exploring the mechanisms of organism responses to internal and external stressors such as disease, environmental exposure and nutritional imbalances (Nicholson et al., 1999; Bundy et al., 2009). Due to its high throughput capacity, metabolomics approach may address the metabolic changes responding to ambient stimulation in individuals (Ravenzwaay et al., 2007; Zhang et al., 2014a). More importantly, these endogenous changes can indicate the true metabolic toxic effects induced by PFCs. Finally, the endogenous metabolic changes that describe the direct biological response to the define stimulation can play the important role in accurate risk assessment of environmental pollutants.

As we have observed in arsenic (Zhang et al., 2014a) and phthalates (Zhang et al., 2016), the pollution related metabolic alterations could be sensitively detected in humans. By adopting metabolomics technologies in the studies of low-level environmental pollutant exposure in human body, our work identified the metabolic alterations that related to no obviously pathological change. Therefore, this approach was effective in investigating the general population to make up for the deficiency of animal and cell toxicity analyses. Finally, the toxicity mechanism of pollutants on humans could be directly elucidated through investigating the metabolic alteration.

In this study, we explored the influence of low-level environmental PFC exposure on serum metabolome in a general population. Since PFCs are suspected as endocrine disruptors (De Coster and van Larebeke, 2012; White et al., 2011; Jensen and Leffers, 2008) beyond human liver toxicity (Peng et al., 2013; Tian et al., 2012), male subjects were selected in this study to avoid the endocrine change that could confound the metabolic changes, i.e., their endocrine-metabolism regulation may be more sensitive to PFCs. Serum samples from 181 Chinese male adults were investigated for PFC concentrations and metabolome changes. Considering the possible toxicity difference of PFCs with different molecular structures (Gorrochategui et al., 2016), the serum exposure levels of different PFCs were measured, and PFC species-related serum biomarkers were screened based on their internal doses. We also illustrated the biological network behind the PFC-associated metabolic responses.

2. Materials and methods

2.1. Subject demographics and sample collection

The research was approved by Ethics Committees of the Maternal and Child Care Center of Zaozhuang, Shandong, China. Male subjects (n = 181) were recruited from this center during their annual physical examination. Prior to blood sample collection, the consent was acquired from each volunteer. A questionnaire was administered by medical doctors or trained nurses, which includes the information of age, weight, height, smoking and drinking status. Only men without metabolic diseases were enrolled to avoid any ambiguity. To analyze PFC levels and obtain the metabolic profile, approximately 10 mL of blood were collected from each volunteer. The serum samples were stored at −80 °C immediately. Then the samples were transported in dry ice to the analytical laboratory and stored at −80 °C again prior to analysis. The same samples were used for PFC measurement and metabolic profile acquisition to avoid any possible sampling uncertainties.

2.2. Serum PFCs analysis

Eleven serum perfluorinated compounds, including perfluorooctanoic acid (PFOA), perfluorooctane sulfonate (PFOS), perfluorobutanoic acid (PFBA), perfluorobutane sulfonate (PFBS), perfluorodecanoic acid (PFDA), perfluoroheptanoic acid (PFHpA), perfluorohexanoic acid (PFHxA), perfluorohexane sulfonate (PFHxS), perfluorononanoic acid (PFNA), perfluoroundecanoic acid (PFUnA) and perfluorododecanoic Acid (PFDoA), were determined using liquid chromatography/quadrupole-mass spectrometry (LC-MS). Perfluorooctanoic acid ($^{13}C_8$) and perfluorooctane sulfonate ($^{13}C_4$) were used as internal standards. The details of sample preparation and instrumental analysis have been described previously (Liu et al., 2015). Briefly, the samples were thawed at 4 °C, then 0.5 mL distilled water and 10 ng internal standards were added into 0.5 mL serum. The spiked samples were equilibrated overnight at room temperature (26 °C). Then 1 mL of 0.5 M tetra-*n*-butylammonium hydrogen sulfate and 2 mL of sodium carbonate (0.25 M, pH 10) were added in each spiked samples. After mixing, 5 mL of methyl-*tert*-buty ether was added, and the mixture was shaken for 15 min at 250 rpm. Obtaining the organic layer by centrifugation for 15 min (3000 rpm, 4 °C). The extraction procedure was repeated twice. Extracts were combined and evaporated to dryness under a gentle stream of nitrogen at 45 °C. Before analysis, the dried residue was resuspended in 0.5 mL of methanol/water (50:50, v/v). The limits of detection (LODs) for PFOA, PFOS, PFBA, PFBS, PFDA, PFHpA, PFHxA, PFHxS, PFNA, PFUnA and PFDoA were 0.07, 0.14, 0.08, 0.10, 0.09, 0.09, 0.06, 0.12, 0.10, 0.11 and 0.10 μg/L, respectively. In the spiked recovery experiments (tested at 5 μg/L, n = 6), the relative standard deviations (RSDs) of peak area for these PFCs ranged from 2.8 to 14.9%, the recoveries of 11 PFCs ranged from 66.8 to 111.9%.

2.3. Serum metabolome analysis

Details of sample preparation, metabolic profiling, data processing, biomarker screening and identification, quality control procedures were described in Supporting Information. Briefly, to prepare serum samples, 600 μL cold methanol was added to 200 μL serum and shaken vigorously. The mixture was stored for 10 min and then centrifuged at 12,000 g for 10 min at 4 °C. The supernatant was filtered through a 0.22 μm syringe-filter before analysis. From each sample, 20 μL of serum were pooled together and mixed well before dividing into several aliquots and used as quality control (QC) samples. The serum metabolic profiles were acquired using a liquid chromatography/obitrap-mass spectrometry system (Thermo, USA). Due to more and higher ion abundance of metabolites were detected under the negative ion mode, the mass spectrometer was operated in the full-scan negative ion mode in the range of 100–1000 m/z. The chromatographic separations were performed on a Kinetex C18 column (2.6 μm i.d., 2.1 mm × 150 mm), using mobile phase A (water containing 0.1%

Download English Version:

https://daneshyari.com/en/article/5748764

Download Persian Version:

https://daneshyari.com/article/5748764

Daneshyari.com