Environmental Pollution 239 (2018) 332–341

Contents lists available at ScienceDirect

Environmental Pollution

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

PCBs–high-fat diet interactions as mediators of gut microbiota dysbiosis and abdominal fat accumulation in female mice☆

Yulang Chi [a, b, c, 1], Yi Lin [a, b, 1], Huimin Zhu [a, b], Qiansheng Huang [a, b], Guozhu Ye [a, b], Sijun Dong [a, b, *]

[a] Key Lab of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen, 361021, China
[b] Center for Excellence in Regional Atmospheric Environment, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen, 361021, China
[c] College of Resources and Environment, University of Chinese Academy of Sciences, Beijing, 100049, China

ARTICLE INFO

Article history:
Received 31 January 2018
Received in revised form
21 March 2018
Accepted 1 April 2018

Keywords:
Polychlorinated biphenyls
High-fat diet
Co-exposure
Interaction
Gut microbiota
Obesity

ABSTRACT

Polychlorinated biphenyls (PCBs), one type of lipophilic pollutant, are ubiquitous in daily life. PCBs exposure has been implicated in the alterations of gut microbial community which is profoundly associated with diverse metabolic disorders, including obesity. High-fat diet (H) is a dietary pattern characterized by a high percentage of fat. According to the theory that similarities can be easily solvable in each other, PCBs and H exposures are inevitably and objectively coexistent in a real living environment, prompting great concerns about their individual and combined effects on hosts. However, the effects of PCBs-H interactions on gut microbiota and obesity are still incompletely understood. In the present study, the effects of PCBs and/or H on the gut microbiota alteration and obesity risk in mice were examined and the interactions between PCBs and H were investigated. Obtained results showed that PCBs and/or H exposure induced prominent variations in the gut microbiota composition and diversity. Exposure to PCBs also resulted in higher body fat percentage, greater size of abdominal subcutaneous adipocytes and increased expression of proinflammatory cytokines including TNF-α, iNOS and IL-6. Such PCBs-induced changes could be further enhanced upon the co-exposure of H, implying that obese individuals may be vulnerable to PCBs exposure. Taken together, the present study is helpful for a better understanding of the gut microbiota variation influenced by PCBs and/or H exposure, and furthermore, provides a novel insight into the mechanism of PCBs-H interactions on host adiposity.

1. Introduction

In chemical taxonomy, polychlorinated biphenyls (PCBs) belong to persistent organic pollutants (Orta-Garcia et al., 2014) and lipophilic pollutants (Baker et al., 2015; Bourez et al., 2013). PCBs are recognized as ubiquitous environmental chemical pollutants, are persistent in the environment and bioaccumulative in organisms, have been extensively used for commercial purposes (Boucher et al., 2014; Kohl et al., 2015). Recent evidence indicates that oral exposure to a mixture of environmentally relevant PCB congeners (including PCB153 (P153), PCB138 and PCB180) significantly alters the abundance and diversity of the gut microbiome in mice, primarily by decreasing the levels of Proteobacteria (Choi et al., 2013). Additionally, larval exposure to PCB126 (P126) has been reported to alter the microbial community structure of the amphibian gut (Kohl et al., 2015). In adult zebrafish, exposure to P126 and P153 for 7 days also impaired the dynamics of the gut microbiota (Chen et al., 2018). These potential effects of PCBs exposure on gut microbiota population would further affect the health of different host species. Mounting evidence suggests that dysbiosis of the gut microbiota community is capable of affecting the health status of a host due to the multiple functions performed by the microbiota (Kohl et al., 2015), leading to the development of a variety of physiological disorders, such as obesity, inflammation or oxidative stress (Backhed et al., 2007; Kinross et al., 2011). Exposure to persistent environmental contaminant 2,3,7,8-tetrachlorodibenzofuran induces gut microbiota dysbiosis, as indicated by shifts in the Firmicutes/Bacteroidetes ratio

☆ This paper has been recommended for acceptance by Haidong Kan.

* Corresponding author. Key Lab of Urban Environment and Health, Institute of Urban Environment, Chinese Academy of Sciences, Xiamen, 361021, China.
E-mail address: sjdong@iue.ac.cn (S. Dong).

[1] The authors contributed equally to this work.

https://doi.org/10.1016/j.envpol.2018.04.001
0269-7491/

accompanied by the modulation of many host metabolic pathways involved in hepatic lipogenesis, gluconeogenesis and glycogenolysis, as well as host immune responses in mice (Zhang et al., 2015). P126- and P153-induced alterations in the abundance of Aeromonas species are also positively correlated with the induction of hepatic oxidative stress in zebrafish (Chen et al., 2018). Moreover, a positive correlation between the abundance of three genera (Histophilus, Mannheimia, and Blastococcus) and intestinal permeability has been observed in P126- and P153-exposed zebrafish. Further investigations are still required to explore the adverse impacts of PCBs exposure on the gut microbiota community and host health.

Chemical pollutants exist as intricate environmental mixtures (Chi et al., 2016). A majority of exposure to environmental pollutants occurs via the diet (Zhang et al., 2015). PCBs easily accumulate in adipose tissue because of their lipophilicity (Baker et al., 2015; Bourez et al., 2013). The lipid-rich adipose tissue served as the foremost lipid-storage and reservoir of lipophilic contaminants can also contribute to the accumulation process (Baker et al., 2015; Myre and Imbeault, 2014). Adipose tissues are major targets of PCBs. Higher levels of P126 have been detected in the adipose tissue of patients with deep infiltrating endometriosis (Martínez-Zamora et al., 2015), and exposure to P126 promotes inflammatory gene expression in human preadipocytes and adipocytes, as well as increased inflammatory gene expression in adipose tissue from mice (Kim et al., 2012). Exposure to P126 and PCB77 (P77) also promotes the expression and release of various proinflammatory cytokines from 3T3-L1 adipocytes (Arsenescu et al., 2008). Proinflammatory cytokines secreted by adipose tissue are the key mediators in the pathogenesis of obesity and obesity is often considered as a chronic low-level inflammation state of adipose tissue (Gregor and Hotamisligil, 2011; McNelis and Olefsky, 2014). As a result, one of the adverse metabolic disorder events triggered by PCBs is obesity, and a previous study has confirmed that exposure to P77 increases body weight, adipose mass and adipocyte area (Arsenescu et al., 2008). Remarkably, the lipophilic PCBs are inevitably and objectively coexistent with the so-called lipid-rich diet. P153 has been regarded as a diet-dependent obesogen, which has the ability to worsen nonalcoholic fatty liver disease by dysregulating adipokines and altering hepatic lipid metabolism (Wahlang et al., 2013). High-fat diet (H) characterized by the high proportion of fat and sugar in Western lifestyle can also shifts the diversity of dominant gut bacteria and alters the proportion of gut microbiota composition (Daniel et al., 2014), leading to the development of obesity (Cani et al., 2008). Therefore, PCBs-H interactions are likely important factors in the development of both obesity and gut microbiota dysbiosis.

PCBs include 209 congeners with various structure-related activities, and the toxic effects of PCBs differ depending on their structures. As shown in our previous studies, dioxin-like P126, rather than non-dioxin-like P153, disturbs estrogen metabolism and inflammation in subjects with endometriosis (Huang et al., 2017). In 3T3-L1 adipocytes, adipocyte differentiation and proinflammatory adipokine expression are induced by P77, but not by P153, despite the enhanced lipophilicity of P153 (Arsenescu et al., 2008). However, P153 significantly increases body weight gain in mice fed an H. These differences may be dose-specific or related to differences between *in vitro* and *in vivo* systems, and the roles of PCBs in regulating lipid metabolism require further study.

In the present study, we aimed to identify the effects of different PCB congeners (P77, P126 and P153) and/or H exposure on host obesity and the composition and diversity of the gut microbiota and to investigate the potential relationship between obesity and changes in the gut microbiota in response to PCBs and/or H exposure. We performed 16S rRNA gene sequencing to illuminate the alterations in the host gut microbiota. Measurements of body weight, body fat ratio and adipocyte area were employed to corroborate the occurrence of obesity. Our findings are helpful for obtaining a better understanding of alterations in the gut microbiota induced by PCBs and/or H exposure and provide novel insights into the mechanism of the effects of PCBs-H interactions on host obesity risk.

2. Materials and methods

2.1. Animals and exposure

All animal treatments were conducted on the basis of the protocols approved by the Xiamen University Institutional Committee on the Laboratory Animals Care and Use (XMULAC20150081). Adult female C57BL/6 mice (18–22 g) were housed in a temperature- and humidity-controlled room with a 12:12-h light/dark cycle and provided free access to water and food. Mice were administered six weekly treatments with corn oil (control, CTRL) or PCB congeners dissolved in corn oil (P) via oral gavage. Dioxin-like and non-dioxin-like PCBs were used to examine the physiological impacts of their structural and chemical properties. P153 was chosen as a representative non-dioxin-like congener because it accounts for the majority of PCBs detected in environmental and biological samples and has been regarded as an obesogen (Wahlang et al., 2013). P77 and P126 belong to the dioxin-like PCB congeners. Both chemicals have been reported to be involved in adipocyte dysfunction (Arsenescu et al., 2008; Kim et al., 2012). Moreover, exposure to P126 is also associated with gut microbiota dysbiosis (Kohl et al., 2015). Regarding the exposure dose, lower concentrations of PCBs have been reported to promote adipocyte differentiation, but higher concentrations inhibit adipocyte differentiation. (Arsenescu et al., 2008). Mice exposed to 49 mg/kg of P77 through four intraperitoneal injections during the 6-week study showed an increase in body weight gain and adipocyte surface area (Arsenescu et al., 2008). Mice administered 50 mg/kg of P153 every 2 weeks for a total of 4 exposures also exhibited larger sizes of epididymal adipocytes (Wahlang et al., 2013). As lower doses of PCBs might exert an opposite effect on increasing body weight, mice utilized in the present study were exposed to 5 mg/kg of P77 and P153 once a week for 6 weeks. PCBs have a long half-life (several years); therefore, this dosage was lower than doses previously reported to disrupt lipid metabolism. In addition, because P126 is the most toxic PCB congener, with a toxicity equivalence factor equal to 2,3,7,8-tetrachlorodibenzo-p-dioxin, 50 μg/kg of P126 was chosen in this study. This dose was 100 times lower than the doses of P77 and P153. Structures of these PCB congeners are shown in the Supplementary Data, Fig. S1. Then, some mice in the CTRL and P groups were fed an H containing 40% kcal fat, 20% kcal protein, and 40% kcal carbohydrates for 14 weeks to obtain H and H plus PCB (HP) exposure groups (i.e., HP77, HP126 and HP153). The experimental design of this study is shown in Fig. 1.

2.2. Extraction of genomic DNA

After collection of intestinal contents, the CTAB-SDS method (Panova et al., 2016) was employed to extract the total genomic DNA. One percent agarose gels were utilized to evaluate the concentration and purity of DNA samples. The DNA was then diluted to a final concentration of 1 ng/μL using sterile water, according to the detected concentration.

2.3. Microbial community analysis

The compositions of the microbial communities in the intestinal