Science of the Total Environment 714 (2020) 136566

Contents lists available at ScienceDirect

Science of the Total Environment

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

Occupational and dietary differences in hydroxylated and methoxylated PBDEs and metals in plasma from Puget Sound, Washington, USA region volunteers

Irvin R. Schultz *, Li-Jung Kuo, Valerie Cullinan, Sara Cade

Pacific Northwest National Laboratory, Marine Sciences Laboratory, Sequim, WA, USA

HIGHLIGHTS

- Diet and dust are important exposure pathways for PBDEs, OH-PBDEs & MeO-PBDEs.
- E-waste recycling exposes workers to dust with high levels of contaminants.
- We compared E-waste recyclers to workers from other occupations & dietary habits.
- We measured 32 different OH-PBDEs & MeO-PBDEs plus select metals in plasma.
- E-waste workers did not have higher plasma levels relative to non-E-waste workers.

GRAPHICAL ABSTRACT

Diet and occupation as variables contributing to PBDE and metal exposure in volunteers from the Puget Sound region of Western Washington state.

ARTICLE INFO

Article history:
Received 4 October 2019
Received in revised form 3 January 2020
Accepted 5 January 2020
Available online 7 January 2020

Editor: Adrian Covaci

Keywords:
Human
Plasma
Halogenated phenolic
Thyroid

ABSTRACT

Electronic waste (*E*-waste) recycling is a rapidly growing occupation in the USA with the potential for elevated exposure to flame retardants and metals associated with electronic devices. We previously measured polybrominated diphenyl ethers (PBDEs) in plasma from *E*-waste workers and found them similar to non-E-waste workers. This study focused on structurally related PBDE derivatives, the hydroxylated (OH-PBDEs) and methoxylated (MeO-PBDEs) forms along with metals known to occur in *E*-waste. Humans can metabolize PBDEs and some MeO-PBDEs into OH-PBDEs, which is a concern due to greater health risks associated with OH-PBDEs. We measured 32 different OH-PBDEs and MeO-PBDEs in plasma samples provided by 113 volunteers living in the greater Puget Sound region of Washington State, USA. We measured 14 metals in a subset of 10 *E*-waste and 10 non-E-waste volunteers. Volunteers were selected based on occupational and dietary habits: work outdoors and consume above average amounts of seafood (outdoor), electronic waste recycling (*E*-waste) or non-specific indoor occupations (indoor). A two-week food consumption diary was obtained from each volunteer prior to blood sampling. OH-PBDEs were detected in all volunteers varying between 0.27 and 102 ng/g/g-lipid. The MeO-PBDEs were detected in most, but not all volunteers varying between n.d. – 60.4 ng/g/g-lipid. *E*-waste recyclers had OH-PBDE and MeO-PBDE plasma levels that were similar to the indoor group. The outdoor group had significantly higher levels of MeO-PBDEs, but not OH-PBDEs. Comparison of

* Corresponding author at: Northwest Fisheries Science Center, National Marine Fisheries Service, National Oceanic and Atmospheric Administration, 2725 Montlake Blvd E, Seattle, WA 98112, USA.
E-mail address: irvin.schultz@noaa.gov (I.R. Schultz).

https://doi.org/10.1016/j.scitotenv.2020.136566

plasma concentrations of BDE-47 with its known hydroxylated metabolites suggested OH-PBDE levels were likely determined by biotransformation and at least two subpopulations identified differing in their apparent rates of OH-PBDE formation. The metals analysis indicated no significant differences between *E*-waste workers and non-*E*-waste workers. Our results indicate E-waste workers do not have elevated plasma levels of these contaminants relative to non-*E*-waste workers.

1. Introduction

Polybrominated di-phenyl ethers (PBDEs) were used for decades as flame retardants and have become ubiquitous environmental contaminants. Human exposure to PBDEs is a concern due to well-documented impacts on thyroid homeostasis and developmental effects described in animal models and epidemiological studies that found associations between PBDE exposure and thyroid hormone levels (reviewed in Linares et al., 2015). Some PBDEs such as the tetra, penta and hexa bromine substituted forms are known to be biotransformed in animals and human liver tissue, which complicates the assessment of PBDE health risks, as a variety of PBDE derivatives, notably hydroxylated PBDEs (OH-PBDEs) may be formed (Stapleton et al., 2009; Erratico et al., 2012; Liu et al., 2017). Select OH-PBDEs and PBDE-*O*-methyl esters (MeO-PBDEs) are also marine natural products, which are synthesized by certain marine bacteria and algal species (Agarwal et al., 2014; Wiseman et al., 2011). These naturally formed OH- and MeO-PBDEs are known to occur in relatively high levels in some marine organisms including marine mammals (Teuten et al., 2005; Vetter et al., 2002; Nomiyama et al., 2014). Naturally occurring OH- and MeO-PBDEs can also occur in seafood, and it is likely that marine fish and shellfish serve as a vector for human exposure (Cade et al., 2018; Liu et al., 2018a). Growing evidence indicates that OH-PBDEs are the most toxicologically potent form of PBDEs that disturb thyroid function and contribute to neurological effects associated with PBDEs (Dingemans et al., 2011). Demethylation of some MeO-PBDEs has also been demonstrated in vertebrates, including mammals (Wan et al., 2010; Mizukawa et al., 2016). Thus, it is possible that MeO-PBDEs will be converted to OH-PBDEs, increasing concern that consumption of food high in OH-PBDEs or MeO-PBDEs could be a significant source of the more toxicologically active form of PBDEs.

It is generally regarded that the two most important pathways of human exposure to contaminants such as PBDEs are from contaminated food and contact with dust found in households and workplaces (Frederiksen et al., 2009). Some emerging occupations such as electronic waste (*E*-waste) recycling have been recognized as a potential high-exposure occupation due to the high levels of PBDEs measured in dust at these sites (Schecter et al., 2009). The OH-PBDEs have also been detected in particulate matter at *E*-waste sites, likely formed during the dismantling and recycling process (Ren et al., 2013). The generation of E-waste from both residential and commercial use is rapidly increasing in the USA with approximately 40% of the total waste recycled in 2014 (USEPA, 2016). The recycled fraction of domestic *E*-waste is expected to increase, stimulated by legislative actions from 25 states and the District of Columbia, which currently adopt mandatory consumer electronics recycling laws (www.electronicstakeback.com). Electronic equipment contains a complex assortment of potentially hazardous substances that are used in circuit boards, batteries, power supplies, and imaging devices and may be released during the recycling process. Besides flame retardants and other classes of organic chemical additives, *E*-waste can contain relatively high levels of metals such as cadmium, nickel, chromium, beryllium, indium, cobalt, and copper (Robinson, 2009; Grant et al., 2013; Ceballos et al., 2017; NIOSH, 2018a, 2018b). Many of these substances have been identified in workplace dust associated with *E*-waste activities (Julander et al., 2014), however, many E-waste contaminants are also found in food thus making it important for occupational exposure assessments to consider the influence of diet in addition to dust as potential sources of exposure.

In a recent study, we measured PBDE levels in plasma samples from E-waste workers and dust obtained from *E*-waste recycling sites in the greater Seattle, Washington, USA metropolitan area (Kuo et al., 2019). Two important findings were PBDE levels in *E*-waste dust were 32 times that found in homes and other occupational sites and men tended to have higher levels than women, regardless of occupation (Kuo et al., 2019). In the present study, we have expanded our analysis to include 32 different OH-PBDE and MeO-PBDEs in the plasma samples plus 14 metals that were measured in a subset of 20 plasma samples. Our study included 113 volunteers based on three occupational and dietary habits: primarily work outdoors and consume above average amounts of seafood (referred to as outdoor workers), actively employed at an *E*-waste recycling business (E-waste workers), or work in non-specific office occupations (indoor worker). The E-waste recycling and outdoor workers represent occupations that potentially expose individuals to greater quantities of contaminants associated with either electronic goods or seafood. Comparison of exposure levels between these two groups offers an opportunity to gain some insights into the contribution of diet versus dust as a source of exposure. The indoor group was included to provide a reference for indoor dust exposure not associated with E-waste recycling and greater diversity in dietary habits. Each volunteer provided a blood sample and the plasma was archived for chemical analysis. Immediately prior to collection of the blood sample, a two-week dietary history was obtained along with voluntary reporting of sex, age, height, weight and race.

2. Materials and methods

2.1. Human volunteers, collection of plasma samples and analyses

All interactions with volunteers were approved (IRB No.: 2014-02) by the Institutional Review Board (IRB) at Pacific Northwest National Laboratory (PNNL) and informed consent was obtained from all volunteers prior to their participation. A total of 113 adult volunteers participated in the study between December 2013 and August 2015. Specific aspects of the recruitment process were described in Kuo et al., 2019. The 113 male and female volunteers represented 29 *E*-waste workers employed at material recovery or repair/reuse facilities located in the Seattle, WA metropolitan area, 57 office workers (health care and retail sales were the most common occupations), and 27 outdoor workers employed as commercial or subsistence fisherman and day laborers. The latter two groups of volunteers lived in either Seattle or the greater Puget Sound region of Western Washington State. The outdoor group of individuals was interviewed before the study to establish a history of above average seafood consumption, which was defined as five or more 4-oz servings of seafood per week. A blood sample was obtained from each volunteer by a state certified phlebotomist using glass BD vacutainer® tubes with EDTA as an anticoagulant. Plasma was obtained within 30 min of blood collection via centrifugation of whole blood for 15 min at 1500 $\times g$. The plasma samples were initially placed on ice for approximately 2–3 h and then stored in multiple 5-g aliquots at −80 °C until analysis. We initially quantified levels of PBDEs that were previously reported in Kuo et al. (2019). For the present study, we have subsequently quantified OH- and MeO-PBDEs in all 113 samples.

We arbitrarily selected ten plasma samples from *E*-waste volunteers for metal analysis and compared to values measured in ten plasma samples from non-E-waste workers. The latter samples were selected from individuals who consumed relatively high levels of seafood and worked in outdoor or indoor occupations. Monomethylmercury (CH_3Hg) was also measured in 12 of the plasma samples used for metal analysis, six E-waste and six non-E-waste. Dietary history included information on the daily servings and types of seafood consumed in addition to meat and dairy consumption. All volunteers received modest compensation for their time as approved by the PNNL IRB. A summary of demographic information and dietary habits associated with these volunteers is shown in Table 1.

2.2. Chemicals

Authentic standards of all target OH-PBDEs and MeO-PBDEs were purchased from AccuStandard (New Haven, CT, USA) and Wellington Laboratories Inc. (Guelph, ON, Canada). Additional chemicals used as surrogate standards were: 3,3′,4,4′-tetrabromodiphenyl ether (BDE-77), 4-OH-2′,3,3′,4,5,5′-hexachlorobipheny (4-OH-PCB-159) from AccuStandard and 2,2′,4,4′,6-pentabromo-6′-methoxy[13C12] diphenyl ether (13C-6-MeO-BDE-100), which was purchased from Wellington Laboratories Inc. Diazomethane was prepared from *N*-methyl-N-nirosoguanidine, following Aldrich Technical Information Bulletin Number AL-121 and purchased from Sigma Chemical (St. Louis, MO, USA). All other chemicals were of reagent grade or better and were obtained from Fisher Scientific.

2.3. Sample preparation and analysis

OH-, MeO-PBDEs: The extraction protocol for plasma samples was modified from Hovander et al. (2002) and Dahlberg et al. (2014). Briefly, 5 g of plasma was spiked with recovery surrogate standards BDE-77, ^{13}C-6-MeO-BDE-100 and 4-OH-PCB-159 and denatured using 2-propanol and 6 M HCl. Samples were then extracted with Hexane/MTBE (1:1, *v*/v) three times and the organic layers were pooled then washed with 1% KCl solution. The washed extracts were transferred to pre-weighed glass tubes and evaporated under a gentle stream of ultra-high purity nitrogen for lipid weight determination. Next, the sample was reconstituted in 2 mL of hexane and the phenolic fraction (containing the OH-PBDEs) was separated from neutral compounds by adding 2 mL of 0.5 M KOH in 50% ethanol (1:1 v/v). The aqueous layer, which contains phenolic compounds, was transferred to a new tube, acidified with 2 M HCl, and then extracted three times with hexane/MTBE (9:1 v/v). The combined hexane/MTBE extracts, now containing the phenolic compounds, were mixed with ~2 g of sodium sulfate for at least 1 h (to remove traces of water), then volume reduced to 2 mL and mixed overnight with 200 μL of diazomethane for conversion to methyl derivatives. After derivatization, 1 mL of concentrated sulfuric acid was added to the phenolic fraction to remove lipids. The separate extracts containing either the neutral (parent PBDEs, MeO-PBDEs) or derivatized phenolic compounds were further cleaned up using an activated silica-acid silica column (Sjödin et al., 2004) and concentrated to ~200 μL in hexane. The samples were spiked with internal standard (IS) BDE-166 and stored at −20 °C until analysis.

The samples were analyzed by a gas chromatography/mass spectrometry (GC/MS) system (Agilent 7890 GC/5975 MSD, Santa Clara, CA, USA) system fitted with a fused silica column (HP5-MS UI, 30 m, 0.25 mm i.d., 0.25 μm film thickness) and operated in electron capture negative ionization (ECNI) mode. The ion source temperature and the MS quad temperature were set to 200 °C and 150 °C, respectively. Each sample was injected under splitless mode, with helium as the carrier gas (1.5 mL/min). The GC oven was programmed from 80 °C (held for 2 min) to 200 °C at 25 °C/min, 200 °C to 250 °C at 2.5 °C/min, 250 °C to 300 °C at 5 °C/min followed by 300 °C isotemp for 30 min. The GC injector and GC/MS interface were maintained at 285 °C and 300 °C, respectively. The analyses were performed using selected ion monitoring (SIM), scanning for bromine ions 79 and 81 *m/z*. Compound identification was performed using GC retention times by comparison to the commercially available standards.

Calibration curves were made using authentic standards for each analyte. Recoveries for the surrogate standards from all plasma samples were (mean ± SD): 90 ± 18% for ^{13}C-6-MeO-BDE-100 and 64 ± 19% for 4-OH-PCB-159. A procedural blank prepared with deionized water was processed concurrently with each analytical batch. Reported values were not adjusted for surrogate recoveries or blank values. The limit of detection (LOD) was determined for each congener and considered to be three times the background area observed in procedural blanks. Only measurements above the LOD are reported. The LODs for most OH- and MeO-PBDEs ranged from 1.5–4 pg/g (ww) with 2-OH-BDE-28 and 4′-OH-BDE-103 being higher at 9 and 7.5 pg/g respectively.

2.3.1. Metals and methylmercury (CH_3Hg)

Elemental content analysis was performed on ten E-waste, seven outdoor and three indoor plasma samples (the outdoor and indoor results were combined and referred to as non-E-waste) using a Thermo iCap Q inductively coupled plasma mass spectrometer. Samples were volumetrically transferred and digested with trace metal grade nitric acid in polypropylene vials in a heat block for 2 h at 90 °C. The digest was diluted 1:10 with deionzied water in a 15 mL polypropylene trace metal free tube. Instrument calibration was performed daily with quality control samples analyzed every 10 samples. The accuracy of the ICP-MS was verified using NIST standard 1640a, which has previously been used in plasma analysis of metals (Yuan et al., 2018). After calibration a calibration verification sample was run, with the criteria that the recovery must be ±10%. A calibration blank (typically 1% high purity HNO3) was run immediately before the sample run, with the criteria that it must be <3 times the method detection limit.

The CH_3Hg analysis was performed as described by Bloom (1989). Briefly, aliquots of plasma were volumetrically transferred and digested with a 25% (*v*/v) KOH/Methanol solution. The aqueous phase was removed and analyzed after ethylation and separation using isothermal gas chromatography and detection by cold vapour atomic fluorescence spectroscopy. A procedure blank was included in the analysis and there was no detectable CH_3Hg. The recoveries of calibration verification

Table 1
Volunteers characteristics.

		E-waste recyclers	Outdoor worker	Indoor worker	Male	Female
n		29	27	57	61	52
Age (years)		31 ± 9	43 ± 15	33 ± 11	35 ± 13	35 ± 13
Race/ethnicity	White	20	17	38		
	Other	9	10	19		
BMI		27 ± 6	27 ± 6	26 ± 6	27 ± 5	26 ± 7
Gender	Male	26	17	18		
	Female	3	10	39		
Total seafood Consumption	0/week	8	1	15	13	11
	1–10/week	20	9	26	29	26
	>10 week	1	17	16	19	15
Finfish[b]		81	67	75	75	73
Crab/lobster[b]		12	20	20	17	19
Bivalves[b]		7	13	5	8	8
Meat (all non-seafood)	0/week	1	5	18	7	17
	1–10/week	5	7	10	12	10
	>10/week	23	15	29	42	25
Vegetarian[a]		1	0	10	4	7
Dairy	0/week	2	4	5	3	8
	1–10/week	9	6	22	21	16
	>10/week	18	17	30	37	28

Note: Arithmetic mean and SD is shown. Food consumption is based on the number of 4-oz servings (estimated by each volunteer).

[a] These volunteers identified themselves as vegetarian and form part of the sample sizes for 0/week seafood and/or meat categories.

[b] As % of total seafood servings consumed.

samples were 91 ± 8%. The recoveries of matrix (plasma)-spike were 95–118%.

2.4. Data analysis

A general linear model (GLM; $\alpha = 0.05$) was fit to the OH- and MeO-PBDE plasma levels and examined sex, race, and occupation as the main variables and then age, body mass index (BMI), and dietary habits as additional covariates. Plasma results were lipid normalized and transformed to the log10 concentration plus one to reduce within class heterogeneity. The addition of one allowed the log transformation of values less than detection to be included, as they were set to zero. When the interactions between main effects were not significant, Tukey's all pairwise comparison was used to compare levels of main factors. When the interaction between main effects was significant, analysis of variance or the Kruskal-Wallis test followed by all pairwise comparisons was used to compare combined categories such as sex and occupation. The nonparametric Kruskal-Wallis test was used when data transformation did not meet the normal assumptions or when sample sizes were small for categories. For the descriptive statistics, only those values greater than the detection limit were used. Dietary habits (dairy, meat, seafood consumption) were categorized into low (0 servings), moderate (1–10 servings), and high (>10 servings) numbers of servings and the numbers in each category were evaluated for their association with occupation using a Chi-square test ($\alpha = 0.05$). All statistical analyses were conducted using Minitab 17.1.0 (Minitab Inc., 2013).

3. Results and discussion

3.1. Volunteer characteristics

Volunteers in this study ranged in age from 19 to 63 years old with mean ages between 31 and 43 years depending on occupational grouping (Table 1). The overall median age and standard deviation for men and women volunteers was the same, 35 ± 13 years (Table 1). Food consumption patterns summarized in Table 1 indicated the majority of volunteers consumed between one and ten servings of seafood per week. As anticipated, the outdoor group had a greater number of individuals that consumed eleven or more servings of seafood per week. Most *E*-waste workers were men and consumed little or no seafood. The exception was one E-waste worker who reported consuming eleven seafood servings per week. Among all volunteers, meat and dairy consumption was typically greater than ten servings per week. Eleven volunteers indicated they were vegetarian and reported no meat or seafood consumption. Also shown in Table 1 is the percentages of fish and shellfish servings represented in the seafood consumption. We included this information based on our previous market basket study that indicated OH- and MeO-PBDEs were much higher in bivalves (clams and mussels) compared to other types of seafood sold in the Puget Sound region (Cade et al., 2018). In the present study, finfish (typically salmon, canned tuna and various types of whitefish) were the most commonly consumed seafood (Table 1). Shellfish consumption was typically crab and lobster with various types of bivalves (clams, mussels, oysters and scallops) that comprised a much smaller percentage (5–13%) of seafood consumed (Table 1).

3.2. OH- and MeO-PBDEs in plasma

A summary of the most frequently detected OH- and MeO-PBDEs along with their total concentrations based on occupational grouping or sex is listed in Table 2. Supplementary Tables S1-S6 summarize the results for all congeners and group classifications. At least one OH-PBDE congener was detected in all samples while four samples lacked detectable MeO-PBDEs. The most abundant OH-PBDE was 5-OH-BDE-47, which accounted for 40–55% of the total OH-PBDE content. Other frequently detected OH-PBDEs were 4-OH-BDE-17, 6-OH-BDE-47 and 5-OH-BDE-99. Collectively, these four OH-PBDEs typically accounted for approximately 80% of the total OH-PBDE content of the sample. Interestingly, there were no significant differences in the total concentration of OH-PBDEs among the different groups with geometric mean values ranging from 7.37–9.12 ng/g/g-lipid (Table 2). Similarly, ∑MeO-PBDEs did not differ significantly among the groups, varying between 2.30 and 3.50 ng/g/g-lipid (Table 2). Only two MeO-PBDEs, 4′-MeO-BDE-17 and 4′-MeO-BDE-103, were consistently detected in >50% of the samples (Table 2). These two congeners accounted for 48–68% the ∑MeO-PBDEs. Also included in Table 2 is a summary of the ∑PBDEs values that we previously published in Kuo et al. (2019). The mean values are also included in Fig. 1A and B for comparison with the ∑OH- and ∑MeO-PBDEs values measured in the present study. In general, ∑PBDEs were approximately three times greater than ∑OH-PBDEs and nine – ten times greater than ∑MeO-PBDEs. Although mean ∑PBDEs levels are higher, it is interesting to note that in eight volunteers ∑OH-PBDEs were highest and in seven volunteers the ∑MeO-PBDEs were higher than the PBDEs measured (supplemental data). Our previous study indicated three PBDEs, BDE-47, 100 and 153, were routinely detected in nearly every sample and accounted for approximately 90% of the ∑PBDEs in plasma. This differs from the pattern observed for OH-PBDEs and especially MeO-PBDEs, where a greater portion (e.g. 20–50%) of the total concentration of OH-, MeO-PBDEs is comprised of a wider variety of congeners with detection frequencies <50% (Supplemental Tables S1–S6). Thus, measurement of total plasma OH- and MeO-PBDE levels is more challenging compared to PBDEs because more congeners need to be monitored to accurately assess total concentrations.

Subsequent statistical analysis of the ∑OH-PBDE results indicated a lack of association with volunteer occupation, sex, age, race, BMI, or seafood consumption (Table 3). Supplemental figures SF1-SF5 also demonstrate the poor correlation of seafood consumption with OH-PBDEs. The relative similarity in ∑OH-PBDE and ∑MeO-PBDE across the different

Table 2
Summary of plasma OH, MeO-PBDE measurements in human volunteers. Values are Geometric means (GM) adjusted for lipid content (ng/g/g-lipid).

Congener	E-waste		Indoor		Outdoor		Men		Female	
	GM	Range	GM	Range	GM	Range	GM	Range	GM	Range
4-OH-BDE-17	1.72	0.70–6.11	1.24	0.31–10.4	1.89	0.34–9.02	1.46	0.34–10.4	1.17	0.31–9.22
5-OH-BDE-47	4.79	0.27–24.2	3.57	0.23–53.2	4.49	1.10–30.6	4.31	0.27–53.2	3.07	0.23–25.4
6-OH-BDE-47	2.06	0.54–18.0	1.52	0.48–15.3	2.58	0.65–22.6	1.95	0.48–22.6	1.43	0.56–6.66
5-OH-BDE-99	1.52	0.30–7.91	1.50	0.30–11.8	2.06	0.58–8.10	1.61	0.30–11.8	1.37	0.30–10.1
∑OH-PBDEs	8.94	0.27–67.9	9.12	0.54–102	8.11	0.34–54.4	8.87	0.27–102	7.37	0.54–51.3
4-MeO-BDE-17	0.97	0.39–31.7	0.84	0.28–53.2	0.78	0.33–8.63	0.75	0.33–31.7	0.86	0.28–53.2
4-MeO-BDE-103	0.76	0.35–3.17	0.79	0.33–2.30	0.91	0.38–3.01	0.68	0.33–3.17	0.79	0.33–2.30
∑MeO-PBDEs	2.55	0–33.7	2.48	0.32–60.4	3.50	0–26.2	2.30	0.43–33.7	2.78	0.28–60.4
∑PBDEs[a]	26.6	3.6–157.3	27.2	2.1–45.5	50.6	6.6–306	37.4	6.5–292	25.4	2.3–244

Note: Only those congeners identified in at least 50% of the volunteers in a group are shown. Please refer to supplementary Tables S1–S6 for full results.
[a] Values are from Kuo et al. (2019).

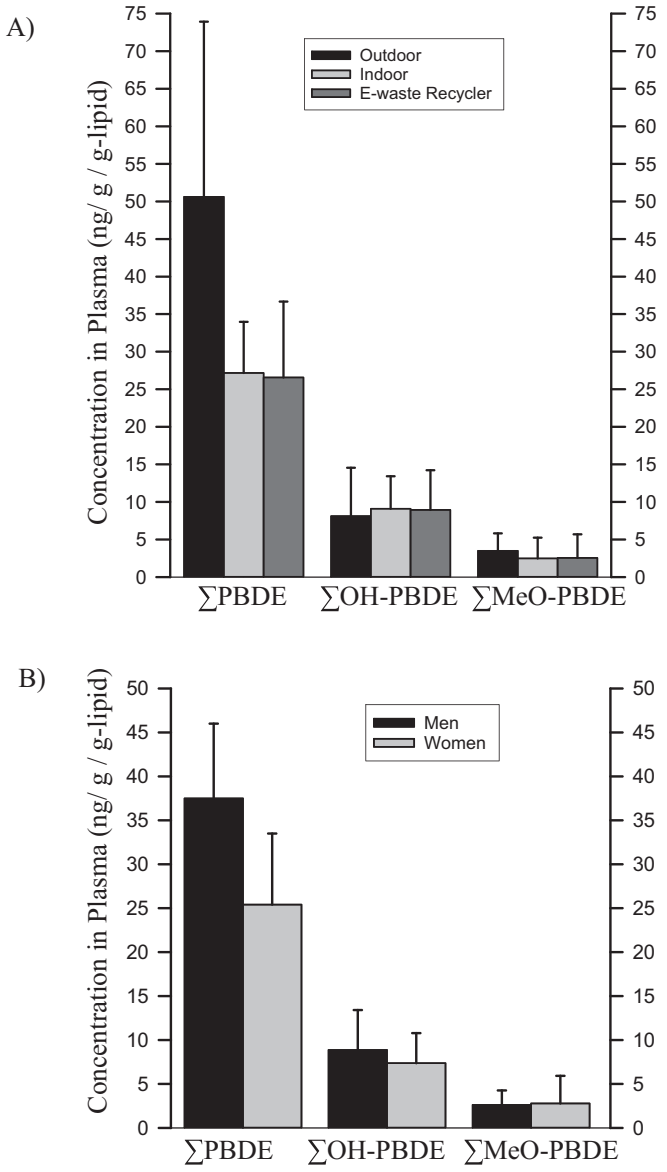

Fig. 1. Geometric mean, upper 95% CI for total concentrations of different classes of PBDEs in plasma from volunteers. A) Results sorted by occupational class. B) Results sorted by sex. Table 2 and Supplementary Tables S1-S6 summarize all individual OH- and MeO-PBDE measurements. PBDE values are from Kuo et al., 2019.

groups was surprising considering the higher levels of PBDE observed in the outdoor group, which was attributed to greater seafood consumption (Kuo et al., 2019). However, ∑MeO-PBDE levels are significantly associated with seafood consumption when seafood intake is high (>10 servings/week; $p<0.012$; Table 3). A good illustration of these results is shown in Fig. 2, which compares ∑PBDEs, ∑OH-PBDEs and ∑MeO-PBDEs among individuals with more extreme differences in dietary habits: the 14 highest seafood consumers (≥14 servings/week) and the 11 vegetarians. High seafood eaters have approximately three times the PBDE and MeO-PBDE levels compared to vegetarians, however ∑OH-PBDEs are nearly the same (Fig. 2). Interestingly, 6-OH-BDE-47, which is known to naturally occur in seafood (Cade et al., 2018) but may also be biotransformed from 6-MeO-BDE-47 (Wan et al., 2010) was greater in high seafood consumers compared to vegetarians (see Fig. 2 inset). This may be an indication that some demethylation of 6-MeO-BDE-47 was occurring in individuals exposed to this MeO-PBDE.

Comparison of our results to previous human monitoring studies is constrained by the number and type of OH/MeO-BDE congeners measured, matrix (plasma, serum or non-blood tissue) and reporting of lipid-adjusted values. However, our results appear to be lower than Athanasiadou et al. (2008) who measured six different OH-BDEs in pools of serum provided by Nicaraguan children living or working at a waste disposal site. The mean plasma OH-BDE concentrations in women reported by Qiu et al. (2009) are similar to our values including the observation that 5-OH-BDE-47 and 5′-OH-BDE-99 are the more abundant congeners. The studies by Eguchi et al. (2012, 2015) are of potentially closer relevance as they reported concentrations of several OH- and MeO-PBDEs in serum provided by volunteers who lived near E-waste disposal sites in India and Vietnam. ∑OH-and ∑MeO-PBDE levels in both studies are lower than our results (comparison made from wet weight values). However, these studies did not include measurement of 5-OH-BDE-47 and 5′-OH-BDE-99 and only two MeO-PBDE congeners were reported, which may have contributed to the observed lower values. Similarly, ∑OH-PBDE levels in serum from Shanghai, China volunteers were lower than our results but 5-OH-BDE-47 and

Table 3
Summary of *p*-values from LM tests.

Characteristic	∑OH-PBDEs	∑MeO-PBDEs
Age	0.31	0.99
BMI	0.49	0.56
Sex	0.28	0.19
Occupation[a]	0.33	0.37
Race	0.19	0.36
Seafood[b]	0.21	0.012
Meat	0.24	0.13
Dairy	0.17	0.26

[a] Test compared differences between E-waste, indoor and outdoor.
[b] Test compared >10 seafood servings vs. <1 serving.

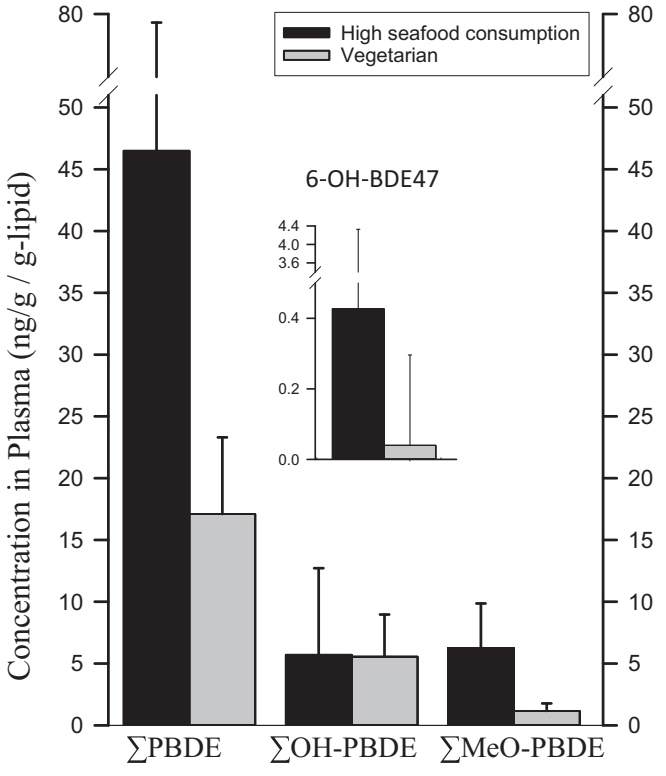

Fig. 2. Geometric mean, upper 95% CI for total concentrations of different classes of PBDEs in plasma from volunteers representing dietary extremes – high seafood consumption (≥28 servings/14 d; $n = 14$) or vegetarian ($n = 11$). Data for PBDEs is from Kuo et al., 2019. Note similarity in total OH-PBDE values.

5′-OH-BDE-99 were not measured (Xu et al., 2018). An interesting study by Wang et al. (2012) measured five OH-PBDEs (including 5-OH-BDE-99) and six MeO-PBDEs in plasma provided by Hong Kong residents. The reported ∑OH-PBDE levels are approximately 100-times lower than our results while the ∑MeO-PBDE levels are twice that of our volunteers. The cause of the wide range in values reported for OH-PBDEs in humans is unclear, but may reflect differences in experimental design, and/or regional differences in exposure or biotransformation among study populations. It is worth noting that when a similar matrix and congener profile is analyzed as in Qiu et al. (2009), results are similar to those reported in this study.

3.3. Biotransformation and OH-PBDEs

An interesting observation made in the present study is the relative similarity in OH-PBDE levels among volunteers with diverse dietary habits. This is surprising considering the association of seafood consumption with ∑PBDE and ∑MeO-PBDE levels (Kuo et al., 2019, Fig. 2, Table 3). Marine shellfish and other types of seafood can contain high levels of OH-PBDEs (Cade et al., 2018) and it was anticipated that high seafood consumers would have higher plasma levels. However, we observed no correlation between ∑OH-PBDEs and seafood consumption (Fig. 3A, Table 3). There was also no apparent correlation

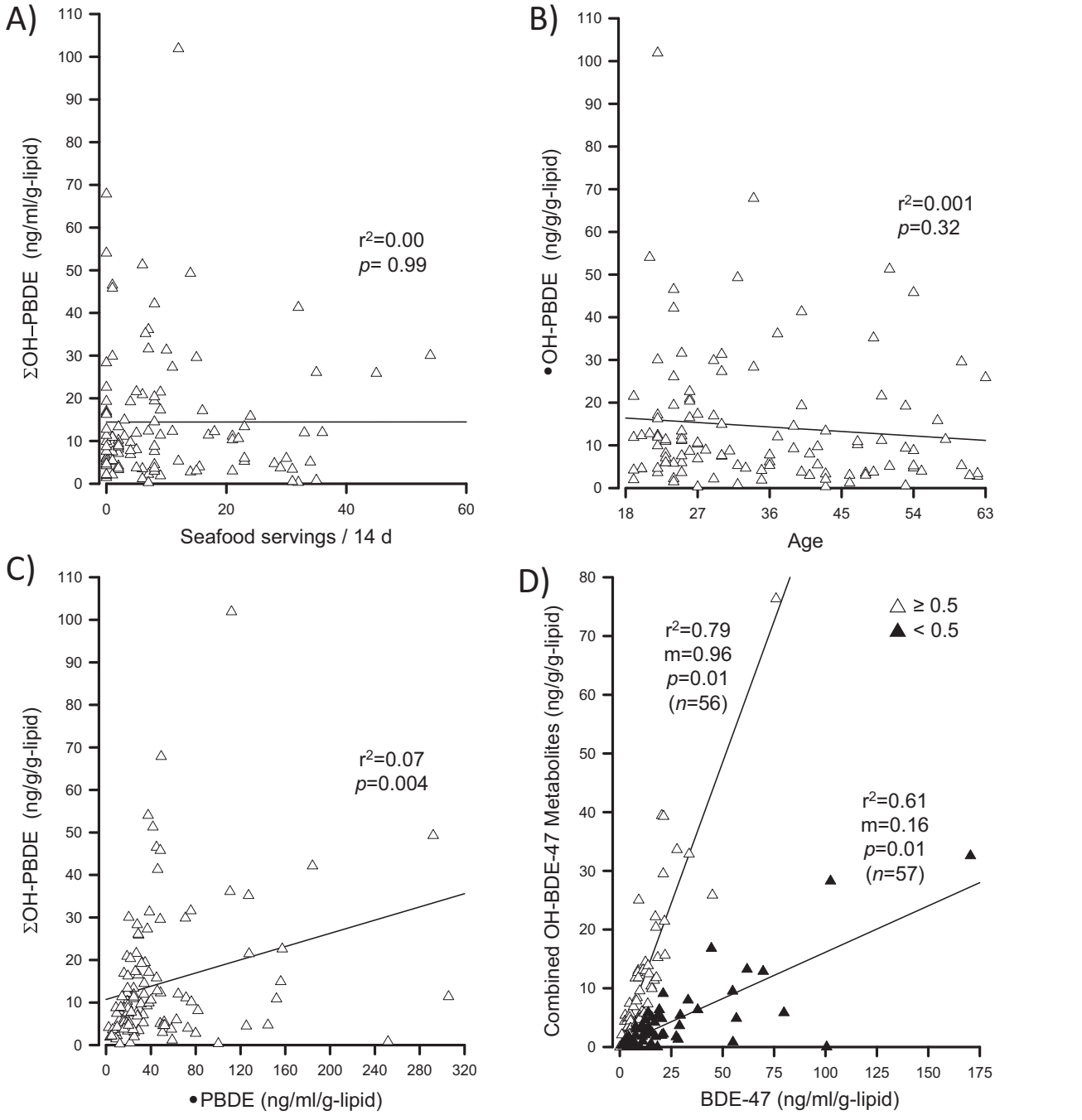

Fig. 3. Scatter plots of OH-PBDEs concentrations against different variables. A) ∑OH-PBDEs vs 14 d seafood consumption. B) ∑OH-PBDEs vs age of volunteer. C) ∑ OH-PBDEs vs ∑ PBDE concentrations. D) Combined OH-BDE-47 metabolites (4-OH-BDE-17, 3-OH-BDE-47, 5-OH-BDE-47, 4-OH-BDE-49 and 4-OH-BDE-42) vs BDE-47. White triangles are volunteers with a combined BDE-47 OH metabolite/BDE-47 ratio greater than or equal to 0.5 and black triangles are volunteers with a ratio <0.5. The solid lines on graphs are the linear regression with the coefficient of determination value listed on each plot. The slope (m) is also included in 3D. ∑PBDE and BDE-47 values are from Kuo et al., 2019.

between ∑OH-PBDEs and volunteer age (Fig. 3B; Supplemental Fig. 5). These findings are in contrast to observations for hydroxylated PCBs (OH-PCBs) where plasma levels have been linked with seafood consumption and increase with a person's age (Eguchi et al., 2012; Rylander et al., 2012, Haraguchi et al., 2016; Dufour et al., 2017). These differences between OH-PBDEs and OH-PCBs appear to be due to the greater persistence of OH-PCBs and importance of dietary intake (Bergman et al., 1994; Oberg et al., 2002; Zhao et al., 2014; Dufour et al., 2017). When ∑OH-PBDEs are plotted against ∑PBDEs, a weak correlation is observed (Fig. 3C), reflecting the wide range in values for the ratio of ∑OH-PBDEs/∑PBDEs (0.003 to 1.8). A similar range of values for this ratio was also reported by Qiu et al. (2009). Closer examination of Fig. 3C suggests at least two sub-populations exist, with one group having proportionally higher levels of OH-PBDEs. The biotransformation of abundant PBDE congeners such as BD*E*-47 into OH-PBDEs has been well characterized in human liver microsomes (Erratico et al., 2012, 2013; Gross et al., 2015). These studies have indicated many of the hydroxylated metabolites are largely formed by a single cytochrome P-450 isoform, *CYP2B6*. We hypothesize that volunteer differences in plasma concentrations of OH-PBDEs are more closely related to a combination of PBDE intake and *CYP2B6* activity. In Fig. 3D, we have restricted the comparison of OH-PBDE and PBDEs to known human hydroxylated metabolites of BD*E*-47. We excluded 6-OH-BDE-47 from this analysis because it is also naturally occurring. We have arbitrarily analyzed the data according to two groups: those individuals with ∑BD*E*-47 metabolites/BDE-47 ratio ≥ 0.5 and those <0.5 (Fig. 3D). This ratio divides the study population into nearly equal halves. Inspection of this graph makes it clearer that for many individuals plasma concentrations of OH-PBDEs sharply increase with BD*E*-47 concentration (slope = 0.96), while in other individuals there is a more gradual increase (slope = 0.16; Fig. 3D). Statistical analysis of individuals in each group indicated there were no significant differences in median age or BMI, or in the number of individuals in each sex or race. However, individuals in the <0.5 group had significantly higher seafood consumption and a higher proportion of volunteers from the outdoor group (Table S7). We hypothesize this difference in slope is primarily due to differences in CYP2B6 activity among the volunteers. This seems plausible given the relationships shown in Fig. 3D, the established polymorphisms of *CYP2B6* and a recent report showing that in a Swedish population, plasma levels of BD*E*-47 are associated with genetic variants of *CYP2B6* (Zanger et al., 2007; Penell et al., 2014). Hepatic CYP2B6 activity in humans is also known to be induced by an expanding list of chemicals (Koudsi and Tyndale, 2010), which may be another contributing factor to the results shown in Fig. 3D. Genotyping volunteers for *CYP2B6* was beyond the scope of the present study but warrants analysis due to the potential for identifying individuals at greater risk for OH-PBDE formation.

3.4. Metals in plasma

A summary of metal concentrations in plasma from *E*-waste and non-E-waste workers is shown in Table 4. These results should be viewed cautiously because of the smaller sample size employed for the analysis ($n = 10$ per group). Also, some metals such as cadmium, mercury, manganese, zinc among others, will preferentially partition into red blood cells. Thus, whole blood is often preferred over plasma or serum for metal monitoring. We believe these results are helpful as an initial survey, to understand the potential for differences among the volunteers. As shown in Table 4, higher geometric mean values were observed in *E*-waste workers for beryllium, indium, gallium, nickel, manganese and molybdenum. However, none of the differences was statistically significant. Measurement of CH_3Hg was primarily done to corroborate dietary history information, as the non-*E*-waste workers selected for CH_3Hg analysis all consumed at least eight servings of seafood per week while the *E*-waste workers consumed little or no seafood. High seafood consumption would be expected to cause increased plasma levels of methyl mercury (Liu et al., 2018b). Consistent with this expectation, we did observe significantly higher CH3Hg levels in the non-E-waste group.

Table 4
Summary of total element concentrations in plasma from select E-waste and non-E-waste workers. Values are Geometric means (GM) ng/ml plasma.

	E-waste		Non-E-waste	
Metal	GM	Range	GM	Range
Antimony	0.36	0.18-0.75	0.67	0.18-0.8.3
Arsenic	0.42	0.20-0.66	0.81	0.33-2.37
Beryllium	0.006	0.002-0.16	0.005	0.002-0.011
Cadmium	0.26	0.062-2.11	0.46	0.087-5.63
Chromium	3.36	1.25-21.2	3.61	2.17-6.88
Cobalt	0.487	0.38-0.66	0.529	0.340-0.741
Copper	935	737-1,230	1,050	870-1,320
Gallium	0.638	0.47-1.04	0.589	0.284-0.945
Indium	0.030	0.018-0.46	0.025	0.013-0.037
Lead	6.45	0.87-39.8	7.24	1.04-29.7
Manganese	2.99	2.00-7.60	2.86	1.97-4.31
Molybdenum	8.49	6.61-16.0	5.95	2.21-11.1
Nickel	6.03	3.05-11.1	4.22	2.32-8.95
Selenium	157	132-175	174	148-230
CH3-Hg[a]	0.012	0.002-0.036	0.090	0.017-0.319

Sample sizes were $n = 10$ or $n = 6$ (CH_3Hg) for each group.
[a] Significantly higher in non-E-waste volunteers ($p = 0.016$).

The interest in monitoring E-waste workers for metal exposure comes in part from studies of workers living in Guiyu and neighboring areas in China, which contain some of the largest accumulations of E-waste. Several studies have documented elevated internal exposure to select metals including lead, chromium, mercury and manganese (reviewed in Grant et al., 2013; Song and Li, 2014). Exposure to these metals is believed to be associated with the dust that is generated from E-waste recycling and is subsequently ingested or inhaled (Song and Li, 2014; Julander et al., 2014). A complete understanding of metals in E-waste is lacking, but some products such as LCD panels may contain up to 40 different elements (Savvilotidou et al., 2014; Premalatha et al., 2014). Increased exposure to more commonly studied metals such as lead, cadmium, and copper have also been reported in E-waste workers from developing countries (Asante et al., 2012; Zheng et al., 2011). A study of Swedish E-waste workers indicated increased exposure to chromium and indium were occurring (Julander et al., 2014). This study highlights the potential for increased exposure of both common and rare metals in E-waste workers even in occupational environments with greater safety controls. There has been little monitoring of U.S. E-waste workers for metal exposure. A recent study of lead and cadmium levels in eight workers at an undisclosed U.S. E-waste site found blood levels to be well below occupational safety limits (NIOSH, 2018a). Direct comparison of metal concentrations measured in the present study with prior studies is complicated by matrix (blood, plasma or urine) and analytical methodology. However, plasma concentrations of indium were approximately four-fold lower, while chromium concentrations were four to six times higher than measured in the Julander et al. (2014) study. For other measured values shown in Table 4, concentrations are similar or within a factor of two to those reported in other plasma based, human monitoring studies (Cesbron et al., 2013; Yuan et al., 2018). Overall, our results from E-waste recyclers working in the Seattle metropolitan area suggest internal exposure to both common and rare metals was similar to individuals from other occupations and living in the greater Puget Sound region.

4. Conclusion

Our combined results indicate E-waste workers who volunteered for this study do not have elevated plasma levels of these contaminants relative to non-E-waste workers. Although mean values for some metals were higher in E-waste volunteers, the differences were not significant. The smaller sample size used for the metal analysis likely hinders

statistical analysis. However, we could still detect differences in CH_3Hg, suggesting any differences in plasma levels of other metals is likely to be low. In addition, our results highlight the complex role that diet plays as a source of these contaminants. High seafood consumption clearly increases exposure to PBDEs, MeO-PBDEs and CH_3Hg, as shown in Fig. 2 and Table 4 but does not influence levels of OH-PBDEs. No sex differences in OH- and MeO-PBDEs were observed in contrast to our previous study on PBDEs. Because biotransformation of PBDEs may be an important source of OH-PBDEs, future human monitoring studies should consider measuring *CYP2B6* genotypes as an explanatory variable for understanding OH-PBDE levels in plasma.

Declaration of competing interest

The other authors declare they have no actual or potential competing financial interests.

Acknowledgements

This work was supported in part by NIOSH Grant 1R21OH010259-01A1 and U.S. Department of Energy under contract DE-AC06-76RLO 1830 with Battelle PNNL. Ms. Cade received support from the U.S. Department of Energy, Office of Science under the Science Undergraduate Laboratory Internship (SULI) program. We thank Jordana Woods for help with the metals analysis and Brenda Lasorsa for CH_3Hg analysis.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2020.136566.

References

Agarwal, V., El Gamal, A.A., Yamanaka, K., Poth, D., Kersten, R.D., Schorn, M., Allen, E.E., Moore, B.S., 2014. Biosynthesis of polybrominated aromatic organic compounds by marine bacteria. Nat. Chem. Biol. 10 (8), 640–647.

Asante, K.A., Agusa, T., Biney, C.A., Agyekum, W.A., Bello, M., Otsuka, M., Itai, T., Takahashi, S., Tanabe, S., 2012. Multi-trace element levels and arsenic speciation in urine of e-waste recycling workers from Agbogbloshie, Accra in Ghana. Sci. Total Environ. 424, 63–73.

Athanasiadou, M., Cuadra, S.N., Marsh, G., Bergman, Å., Jakobsson, K., 2008. Polybrominated diphenyl ethers (PBDEs) and bioaccumulative hydroxylated PBDE metabolites in young humans from Managua, Nicaragua. Environ. Health Perspect. 116, 400–408.

Bergman, A., Klasson-Wehler, E., Kuroki, H., 1994. Selective retention of hydroxylated PCB metabolites in blood. Environ. Health Perspect. 102 (5), 464–469.

Bloom, N.S., 1989. Determination of picogram levels of methylmercury by aqueous phase ethylation, followed by cryogenic gas-chromatography with cold vapor atomic fluorescence detection. Can. J. Fish. Aquat. Sci. 46 (7), 1131–1140.

Cade, S.E., Kuo, L.-J., Schultz, I.R., 2018. Polybrominated diphenyl ethers and their hydroxylated and methoxylated derivatives in seafood obtained from Puget Sound, WA. Sci. Total Environ. 630, 1149–1154.

Ceballos, D., Beaucham, C., Elena, P., 2017. Metal exposures at three US electronic scrap recycling facilities. J. Occup. Environ. Hyg. 14 (6), 401–408.

Cesbron, A., Saussereau, E., Mahieu, L., Couland, I., Guerbet, M., Goulle, J.-P., 2013. Metallic profile of whole blood and plasma in a series of 106 healthy volunteers. J. Anal. Toxicol. 37, 401–405.

Dahlberg, A., Norrgranψa, J., Hovandera, L., Bergman, A., Asplunda, L., 2014. Recovery discrepancies of OH-PBDEs and polybromophenols in human plasma and cat serum versus herring and long-tailed duck plasma. Chemosphere 94, 97–103.

Dingemans, M.M.L., van den Berg, M., Westerink, R.H.S., 2011. Neurotoxicity of brominated flame retardants: (in)direct effects of parent and hydroxylated polybrominated diphenyl ethers on the (developing) nervous system. Environ. Health Perspect. 119 (7), 900–907.

Dufour, P., Pirard, C., Charlier, C., 2017. Determination of phenolic organohalogens in human serum from a Belgian population and assessment of parameters affecting the human contamination. Sci. Total Environ. 599–600, 1856–1866.

Eguchi, A., Nomiyama, K., Devanathan, G., Subramanian, A., Bulbule, K.A., Parthasarathy, P., Takahashi, S., Tanabe, S., 2012. Different profiles of anthropogenic and naturally produced organohalogen compounds in serum from residents living near a coastal area and e-waste recycling workers in India. Environ. Int. 47, 8–16.

Eguchi, A., Nomiyama, K., Nguyen, M.T., Trang, P.T.K., Viet, P.H., Takahashi, S., Tanabe, S., 2015. Residue profiles of organohalogen compounds in human serum from e-waste recycling sites in North Vietnam: association with thyroid hormone levels. Environ. Res. 137, 440–449.

Erratico, C.A., Szeitz, A., Bandiera, S.M., 2012. Oxidative metabolism of BDE-99 by human liver microsomes: predominant role of CYP2B6. Toxicol. Sci. 192, 280–292.

Erratico, C.A., Szeitz, A., Bandiera, S.M., 2013. Biotransformation of 2,2′,4,4′-tetrabromodiphenyl ether (BDE-47) by human liver microsomes: identification of cytochrome P450 2B6 as the major enzyme involved. Chem. Res. Toxicol. 26, 721–731.

Frederiksen, M., Vorkamp, K., Thomsen, M., Knudsen, L.E., 2009. Human internal and external exposure to PBDEs - a review of levels and sources. Internat J Hyg Environ Health 212 (2), 109–134.

Grant, K., Goldizen, F.C., Sly, P.D., Brune, M.N., Neira, M., van den Berg, M., Norman, R.E., 2013. Health consequences of exposure to e-waste: a systematic review. Lancet Glob Heal 1, E350–E361.

Gross, M.S., Butryn, D.M., McGarrigle, B.P., Aga, D.S., Olson, J.R., 2015. Primary role of cytochrome P450 2B6 in the oxidative metabolism of 2,2′,4,4′,6-pentabromodiphenyl ether (BDE-100) to hydroxylated BDEs. Chem. Res. Toxicol. 28, 672–681.

Haraguchi, K., Ito, Y., Takagi, M., Fuji, Y., Harada, K.H., Koizumi, A., 2016. Levels, profiles and dietary sources of hydroxylated PCBs and hydroxylated and methoxylated PBDEs in Japanese women serum samples. Environ. Int. 97, 155–162.

Hovander, L., Malmberg, T., Athanasiadou, M., Athanassiadis, I., Rahm, S., Bergman, A., Wehler, E.K., 2002. Identification of hydroxylated PCB metabolites and other phenolic halogenated pollutants in human blood plasma. Arch. Environ. Contam. Toxicol. 42, 105–117.

Julander, A., Lundgren, L., Skare, L., Grandér, M., Palma, B., Vahter, M., Lidéna, C., 2014. Formal recycling of e-waste leads to increased exposure to toxic metals: an occupational exposure study from Sweden. Environ. Int. 73, 243–251.

Koudsi, N.A., Tyndale, R.F., 2010. Hepatic CYP2B6 is altered by genetic, physiologic, and environmental factors but plays little role in nicotine metabolism. Xenobiotica 40 (6), 381–392.

Kuo, L.-J., Cade, S.E., Cullinan, V., Schultz, I.R., 2019. Polybrominated diphenyl ethers (PBDEs) in plasma from E-waste recyclers, outdoor and indoor workers in the Puget Sound, WA region. Chemosphere 219, 209–216.

Linares, V., Montserrat, B., Domingo, J.L., 2015. Human exposure to PBDE and critical evaluation of health hazards. Arch. Toxicol. 89, 335–356.

Liu, S., Zhaoa, G., Li, J., Zhaob, H., Wanga, Y., Chenb, J., Zhao, H., 2017. Association of polybrominated diphenylethers (PBDEs) and hydroxylated metabolites (OH-PBDEs) serum levels with thyroid function in thyroid cancer patients. Environ. Res. 159, 1–8.

Liu, Y., Liu, J., Yu, M., Zhou, Q., Jiang, G., 2018a. Hydroxylated and methoxylated polybrominated diphenyl ethers in a marine food web of Chinese Bohai Sea and their human dietary exposure. Environ. Pollut. 233, 604–611.

Liu, Y., Buchananb, S., Andersonc, H.A., Xiaob, Z., Perskya, V., Turyk, M.E., 2018b. Association of methylmercury intake from seafood consumption and blood mercury level among the Asian and non-Asian populations in the United States. Environ. Res. 160, 212–222.

Mizukawa, H., Nomiyama, K., Nakatsu, S., Iwata, H., Yoo, J., Kubota, A., Yamamoto, M., Ishizuka, M., Ikenaka, Y., Nakayama, S.M., Kunisue, T., Tanabe, S., 2016. Organohalogen compounds in pet dog and cat: do pets biotransform natural brominated products in food to harmful hydroxlated substances? Environ. Sci. Technol. 50 (1), 444–452.

NIOSH [2018a]. Evaluation of exposure to metals, flame retardants, and nanomaterials at an electronics recycling company. By Beaucham CC, Ceballos D, Page EH, Mueller C, Calafat A, Sjodin A, Ospina M, La Guardia M, Glassford E. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Health Hazard Evaluation Report 2015-0050-3308, https://www.cdc.gov/niosh/hhe/reports/pdfs/2015-0050-3308.pdf.

NIOSH [2018b]. Evaluation of exposure to metals at an electronics recycling facility. By Grimes GR, Beaucham CC, Ramsey JG. Cincinnati, OH: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, Health Hazard Evaluation Report 2016-0242-3315, https://www.cdc.gov/niosh/hhe/reports/pdfs/2016-0242-3315.pdf.

Nomiyama, K., Kanbara, C., Ochai, M., Eguchi, A., Mizukawa, H., Isobe, T., Matsuishi, T., Yamada, T.K., Tanabe, S., 2014. Halogenated phenolic contaminants in the blood of marine mammals from Japanese coastal waters. Mar. Environ. Res. 93, 15–22.

Oberg, M., Sjödin, A., Casabona, H., Nordgren, I., Klasson-Wehler, E., Håkansson, H., 2002. Tissue distribution and half-lives of individual polychlorinated biphenyls and serum levels of 4-hydroxy-2,3,3′,4′,5-pentachlorobiphenyl in the rat. Toxicol. Sci. 70 (2), 171–182.

Penell, J., Lind, L., Fall, T., Syvänen, A.C., Axelsson, T., Lundmark, P., Morris, A.P., Lindgren, C., Mahajan, A., Salihovic, S., van Bavel, B., Ingelsson, E., Lind, P.M., 2014. Genetic variation in the CYP2B6 gene is related to circulating 2,2′,4,4′-tetrabromodiphenyl ether (BDE-47) concentrations: an observational population-based study. Environ. Health 13, 34.

Premalatha, M., Tabassum, A., Abbasi, T., Abbasi, S.A., 2014. The generation, impact, and management of E-waste: state of the art. Crit. Rev. Environ. Sci. Technol. 44, 1577–1678.

Qiu, X., Bigsby, R.M., Hites, R.A., 2009. Hydroxylated metabolites of polybrominated diphenyl ethers in human blood samples from the United States. Environ. Health Perspect. 117, 93–98.

Ren, Z., Bi, X., Bo, H., Liu, M., Sheng, G., Fu, J., 2013. Hydroxylated PBDEs and brominated phenolic compounds in particulate matters emitted during recycling of waste printed circuit boards in a typical e-waste workshop of South China. Environ. Pollut. 177, 71–77.

Robinson, B.H., 2009. E-waste: an assessment of global production and environmental impacts. Sci. Total Environ. 408, 183–191.

Rylander, C., Lund, E., Frøyland, L., Sandanger, T.M., 2012. Predictors of PCP, OH-PCBs, PCBs and chlorinated pesticides in a general female Norwegian population. Environ. Int. 43, 13–20.

Savvilotidou, V., Hahladakis, J.N., Gidarakos, E., 2014. Determination of toxic metals in discarded liquid crystal displays (LCDs). Resour. Conserv. Recy. 92, 108–115.

Schecter, A., Colacino, J.A., Harris, T.R., Shah, N., Brummitt, S.I., 2009. A newly recognized occupational hazard for U.S. electronic recycling facility workers: polybrominated diphenyl ethers (PBDEs). J. Occupat. Environ. Med. 51 (4), 435–440.

Sjödin, A., Jones, R.S., Lapeza, C.R., Focant, J.F., McGahee 3rd, E.E., Patterson, D.G., 2004. Semiautomated high-throughput extraction and cleanup method for the measurement of polybrominated diphenyl ethers, polybrominated biphenyls, and polychlorinated biphenyls in human serum. Anal. Chem. 76, 1921–1927.

Song, Q., Li, J., 2014. A systematic review of the human body burden of e-waste exposure in China. Environ. Int. 68, 82–93.

Stapleton, H.M., Kelly, S.M., Pei, R., Letcher, R.J., Gunsch, C., 2009. Metabolism of polybrominated diphenyl ethers (PBDEs) by human hepatocytes in vitro. Environ. Health Perspect. 117 (2), 20–197.

Teuten, E.L., Xu, L., Reddy, C.M., 2005. Two abundant bioaccumulated halogenated compounds are natural products. Science 307, 917–920.

U.S. EPA, 2016. Electronic Products Generation and Recycling in the United States, 2013 and 2014 U.S. Environmental Protection Agency Office of Resource Conservation and Recovery December 2016.

Vetter, W., Stoll, E., Garson, M.J., Fahey, S.J., Gaus, C., Muller, J.F., 2002. Sponge halogenated natural products found at parts-per-million levels in marine mammals. Environ. Toxicol. Chem. 21, 2014–2019.

Wan, Y., Liu, F., Wiseman, S., Zhang, X., Chang, H., Hecker, M., Jones, P.D., Lam, M.H., Giesy, J.P., 2010. Interconversion of hydroxylated and methoxylated polybrominated diphenyl ethers in Japanese medaka. Environ. Sci. Technol. 44 (22), 8729–8735.

Wang, H.S., Chen, Z.-J., Ho, K.-L., Ge, L.-C., Du, J., Lam, M.H.-W., Giesy, J.P., Wong, M.-H., Wong, C.K.-C., 2012. Hydroxylated and methoxylated polybrominated diphenyl ethers in blood plasma of humans in Hong Kong. Environ. Int. 47, 66–72.

Wiseman, S.B., Wan, Y., Chang, H., Zhang, X., Hecker, M., Jones, P.D., Giesy, J.P., 2011. Polybrominated diphenyl ethers and their hydroxylated/methoxylated analogs: environmental sources, metabolic relationships, and relative toxicities. Mar. Pollut. Bull. 63, 179–188.

Xu, B., Wu, M., Wang, M., Pan, C., Qiu, W., Tang, L., Xu, G., 2018. Polybrominated diphenyl ethers (PBDEs) and hydroxylated PBDEs in human serum from Shanghai, China: a study on their presence and correlations. Environ. Sci. Pollut. Res. 25, 3518–3526.

Yuan, Y., Xiao, Y., Yu, Y., Liu, Y., Feng, W., Qiu, G., Wang, H., Liu, B., Wang, J., Zhou, L., Liu, K., Xu, X., Yang, H., Li, X., Qi, L., Zhang, X., He, M., Hu, F.B., Pan, A., Wu, T., 2018. Associations of multiple plasma metals with incident type 2 diabetes in Chinese adults: the Dongfeng-Tongji Cohort. Environ. Pollut. 237, 917–925.

Zanger, U.M., Klein, K., Saussele, T., Blievernicht, J., Hofmann, M.H., Schwab, M., 2007. Polymorphic CYP2B6: molecular mechanisms and emerging clinical significance. Pharmacogen 8 (7), 743–759.

Zhao, H., Zhang, G., Liu, S., Qu, B., Wang, Y., Hu, D., Jiang, J., Quan, X., Chen, J., 2014. Bioaccumulation and elimination kinetics of hydroxylated polybrominated diphenyl ethers (2′-OH-BDE68 and 4-OH-BDE90) and their distribution pattern in common carp (Cyprinus carpio). J. Hazard. Mater. 274, 16–23.

Zheng, J., Luo, X.-J., Yuan, J.-G., He, L.-Y., Zhou, Y.-H., Luo, Y., Chen, S.-J., Mai, B.-X., Yang, Z.-Y., 2011. Heavy metals in hair of residents in an E-waste recycling area, South China: contents and assessment of bodily state. Arch. Environ. Contam. Toxicol. 61, 696–703.