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Polybrominated Diphenyl Ethers and Their Hydroxylated Analogues in Ringed Seals (*Phoca hispida*) from Svalbard and the Baltic Sea

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The present study investigated the concentrations and patterns of PBDEs and hydroxylated (OH) PBDE analogues in two ringed seal populations: less contaminated Svalbard and more contaminated Baltic Sea. Mean concentration of hepatic Σ-PBDE, which was dominated by BDE47, was six times higher in the ringed seals from the Baltic Sea compared to the seals from Svalbard. BDE47/Σ-PBDE was higher in the seals from Svalbard compared to that for Baltic seals, while the trend was opposite for BDE153 and 154. The geographical difference in contaminant pattern of PBDEs in ringed seals could be explained by biotransformation via oxidative metabolism and/or by dietary differences. OH-PBDEs were detectable in the majority of plasma samples from both locations, and dominated by bioaccumulation of naturally occurring congeners. Low levels of 3-OH-BDE47 and 4′-OH-BDE49 in the Baltic ringed seals suggested minor oxidative biotransformation of BDE47. In the Baltic seals, BDE153/Σ-PBDEs and BDE154/Σ-PBDEs increased and BDE28/Σ-PBDE decreased with increasing Σ-POP concentration, which suggests BDE153 and 154 are more persistent than BDE28. Contrasting diets of the ringed seals in these two locations may influence the PBDE congener pattern due to selective long-range transport and direct effluent emissions to Svalbard and the Baltic, respectively.

Introduction

Polybrominated diphenyl ethers (PBDE), manufactured and used as flame retardants, are used in large quantities worldwide (*1*). PBDEs have been detected throughout the marine food web including species at high trophic levels such as seals (*2*). In Greenland, Canadian Arctic, and St. Lawrence regions, PBDE levels have been rising rapidly in ringed seals and beluga whales during recent decades (*2, 3*), while ringed seals from Svalbard show a decreasing trend since the late 1990s (*4*). In the Baltic, the levels of PBDEs in guillemot eggs have been decreasing since 1980s, but the decline has slowed since then (*5*).

Toxic effects, including endocrine disruption and neurotoxicity, have been observed and reported for PBDE-exposed laboratory rodents (*1*). Possible effects of PBDEs, particularly via the formation of hydroxylated (OH) metabolites, on endocrine system have recently received much attention (*6, 7*). Results have shown that the potency of PBDEs to disrupt thyroid and estrogen systems significantly increases after biotransformation of PBDEs to hydroxy (OH) PBDEs by enzymes in liver microsomes (*7*−*9*).

Biotransformation of PBDEs may involve several processes including debromination and oxidation that is mediated by phase I (cytochrome P450, i.e., CYP) and/or conjugating phase II enzyme systems (*10*). In rodents, PBDE biotransformation is congener and species specific, and a wide range of metabolites have been detected including OH-, thiol-, glutathione-, and glucuronide-metabolites (*11*−*13*).

Recent in vitro studies suggested that *ortho*−*meta* unsubstituted PBDEs are partly metabolized in beluga whales (*14*), although initial in vitro models on marine mammals did not show any indication of PBDE biotransformation (*15*). OH-PBDEs have been detected in marine mammals including beluga and minke whales, ringed seals, and polar bears (*16*−*19*). *Ortho*-OH-substituted PBDEs detected in marine predators may be bioaccumulated via natural sources because they have been detected, for example, in algae, cyanobacteria, and marine sponges including locations such as the Baltic Sea (*20, 21*). However, some of these OH-PBDEs may also be products of CYP-mediated biotransformation of bioaccumulated PBDEs as has been shown in studies with BDE47-exposed laboratory rodents (*8, 22*).

High levels of persistent organic pollutants (POPs) in ringed seals (*Phoca hispida*) from the Baltic Sea have been associated with adverse health effects including endocrine disruption and reproductive problems (*23, 24*), but the underlying toxic mechanisms remain unknown. High concentrations of polychlorinated biphenyls (PCBs) have been related to elevated CYP activities in ringed seals, leading to formation of OH-PCBs (*25*). Therefore, it is supposed that elevated xenobiotic-metabolizing enzyme activities in ringed seals may also lead to biotransformation of PBDEs to endocrine-disruptive OH-PBDEs. The aim of the present study is to investigate the levels and patterns of PBDEs and OH-PBDEs in two contrasting ringed seal populations, those from more contaminated Baltic Sea and from the less contaminated Svalbard area.

Experimental Section

Sample Collection and Preparation. The Ministry of Forestry and Agriculture in Finland granted the Finnish Game and Fisheries Research Institute special permission to sample Baltic ringed seals in April 2002, 2006, and 2007 (65°10′ N, 24°20′ E). The seal samples from Svalbard, Norway (77°47′ N to 78°23′ N, 17°00′ E) were obtained in May and June 2007. At Svalbard, the seals were sampled with special permission granted to the Norwegian Polar Institute by the Governor of Svalbard and during the local hunting season under local hunting law of Svalbard. All the samples were collected after the weaning period during the molting season of the seals. The mean age of the seals from Svalbard was 11.4 years [95% confidence interval (CI): 8.1, 14.8] and from the Baltic Sea 9.2 years [95% CI: 7.3, 11.1], respectively. The sex distribution

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TABLE 1. Concentrations (Geometric Mean [95% Confidence Intervals] and Range ng/g Wet Weight) of the Polybrominated Diphenyl Ethers (PBDEs) and the OH-PBDEs in Ringed Seals from the Baltic and Svalbard and the Percentage of Samples above Minimum Level of Quantification (MLOQ)[a]

	Svalbard				Baltic			
	n	mean	min−max	>MLOQ	*n*	mean	min−max	>MLOQ
liver								
lipid%		3.2 [2.9, 3.6]	2.7−6.4			3.7 [3.4, 4.0]	2.5−6.4	
BDE28	0				22	0.032 [0.027, 0.038]	0.014−0.074	100
BDE47	18	0.90 [0.62, 1.3]	0.28−3.9	100	31	4.4 [3.4, 5.7]	0.62−26	100
BDE66	18		<0.001−0.004	11	31	0.037 [0.022, 0.062]	0.001−0.33	100
BDE85	18	0.007 [0.003, 0.014]	<0.001−0.059	67	30	0.098 [0.072, 0.13]	0.009−0.46	100
BDE99	18	0.041 [0.027, 0.061]	0.009−0.16	100	26	0.57 [0.46, 0.71]	0.21−1.4	100
BDE100	18	0.051 [0.035, 0.076]	0.014−0.26	100	31	0.55 [0.45, 0.66]	0.21−2.0	100
BDE138	18		<0.001−0.006	17	31	0.032 [0.016, 0.062]	<0.001−0.27	90
BDE153	11	0.010 [0.006, 0.015]	<0.003−0.046	91	30	0.40 [0.29, 0.55]	0.076−1.8	100
BDE154	18	0.014 [0.007, 0.030]	<0.001−0.13	83	30	0.48 [0.34, 0.68]	0.052−3.1	100
BDE183	0				22	0.013 [0.009, 0.018]	0.003−0.075	100
Σ-PBDE[b]	18	1.1 [0.73, 1.5]	0.33−4.5		31	7.1 [5.8, 8.8]	2.8−35	
plasma								
lipid %		0.68 [0.61, 0.77]	0.42−1.13			0.65 [0.59, 0.72]	0.24−1.0	
Σ-PBDE[b]	18	0.17 [0.13, 0.24][c]	0.067−0.80	100	27	0.69 [0.57, 0.83] [d]	0.25−2.1	100
2′-OH-BDE68	19		<0.02	0	28	0.079 [0.055, 0.11]	<0.02−0.29	89
6-OH-BDE47	19	0.019 [0.013, 0.027]	<0.02−0.11	74	28	0.074 [0.052, 0.10]	<0.02−0.39	93
3-OH-BDE47	19		<0.02−0.077	21	28	0.066 [0.047, 0.093]	<0.02−0.22	86
6-OH-BDE90	19		<0.02	0	28	0.070 [0.042, 0.12]	<0.02−0.36	79
4′-OH-BDE49	19		<0.02	0	28	0.026 [0.018, 0.036]	<0.02−0.18	68
Σ-OH-PBDE[b]	19	0.019 [0.013, 0.027]	<0.02−0.11		28	0.36 [0.27, 0.49]	0.041−1.06	

[a] BDE17, 28, 49, 66, 85, 138, 183, and 190, BB101, HBCDD, 4′-OH-BDE17, 6′-OH-BDE17, 4-OH-BDE42, 5-OH-BDE47, 6′-OH-BDE49, 6-OH-BDE85, 6-OH-BDE99, and 2-OH-BDE123 were detected in <44% of the plasma samples. [b] Sum of congeners detected in >60% of the samples. [c] Sum of BDE47, 99 and 100. [d] Sum of BDE47, 99, 100, 153 and 154/BB153.

was similar between the areas (males/females ratio for Svalbard 13/6 and for the Baltic Sea 19/13). Samples for chemical analysis were stored at −20 °C until analyzed.

PBDEs in Liver. The method of extraction and cleanup for analysis of PBDEs in liver samples, which is similar to that for analysis of PCBs, has been previously described (*25*). However, for more detail, please refer to the Supporting Information. All the analyses for PBDEs in liver samples were carried out at the MTM Research Centre, Örebro University (Sweden). The internal standards (IS) used were $^{13}C_{12}$-labeled BDE 77 and BDE 139. The mixture of recovery standards (RS) contained $^{13}C_{12}$-labeled PCB 178 for PBDEs. Ten PBDE congeners were monitored and they are listed in Table 1. For liver samples, PBDEs were determined by gas chromatography (GC) (Agilent 6890, Agilent, Waldorff, Germany) coupled with low-resolution mass spectrometry (MS) (Agilent 5973) with electron capture negative impact ionization (ECNI) mode monitoring m/z 79/81.

In accordance with routine QA/QC measures, a standard reference material (SRM, human adipose tissue) and a laboratory blank sample were run with each batch of samples. Laboratory blank samples ($n = 6$) did not contain the reported target compounds at levels >15% of the levels found in the seal samples reported in Table 1. The reported seal sample size was reduced for BDE28, 85, 99, 153, and 154 due to contamination in blank samples. In some batches the levels of these congeners in the blank were >15% of the levels found in the samples, which resulted in the elimination of these samples for a given congener. Detailed information of the sample elimination is given in the Supporting Information. All PBDE levels of the SRM were within 2× the RSD which was less than 20% for all individual congeners. IS recoveries were 73% [95% CI: 63, 84] for $^{13}C_{12}$−BDE77 and 74% for [95% CI: 64, 84] $^{13}C_{12}$−BDE139. Using the isotope dilution /internal standards, all data were automatically adjusted for recovery. The minimum level of quantification (MLOQ) was defined as a signal-to-noise ratio of 3. The variance of individual BDE congeners of the SRM (human adipose tissue) was less than 20%. The laboratory participates regularly part in international interlaboratory comparison studies with good results (z-scores <2) and is currently a reference laboratory for POP analysis for the UN within the UNEP program. The lipid content in liver was determined gravimetrically.

OH-PBDEs and PBDEs in Plasma. The extraction method for analysis of OH-PBDEs in plasma sample, similar to that of OH-PCBs, has been described elsewhere (*25*). However, for more detail, please refer to the Supporting Information. Brominated compounds monitored in plasma are listed in Table 1. All the analyses for the present plasma samples were carried out at the NWRC (Environment Canada, Carleton University, Ottawa, ON, Canada). The neutral fraction, which contained PBDEs, was obtained after the extraction of phenols. This fraction was cleaned up with LC-Si solid phase extraction (SPE) cartridge (500 mg, 6 mL, J.T. Baker, USA). After the sample was loaded on the cartridge PBDEs were eluted with dichlormethane/hexane (5:95). The collected fractions were then concentrated and translated the solvent to isooctane for GC-MS analysis.

The IS used was 2′-OH-BDE28 for OH-PBDEs and BDE30 for PBDEs. The methoxy-derivatized phenolic, containing OH-PBDEs, and the neutral, containing PBDEs, fractions from samples were analyzed by GC-MS (Agilent 6890 and 5973; Agilent Technologies, CA) with ECNI source in the SIM mode. Two columns with different polarities were used. First, GC separation was performed using a silica DB-5 capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness) (J&W Scientific, Folsom, CA) with the GC conditions described elsewhere (*26*). The oven temperature was programmed as follows: 80 °C, hold for 2 min, then increase at 10 °C/min to 290 °C, hold for 20 min. The injector temperature was 300 °C and the purge time was 1 min after injection. Second, the OH-PBDEs were separated on a polar SP-2331 column (30

m × 0.25 mm i.d., 0.2 μm film thickness) (Supelco, Bellefonte, WA) using the same GC conditions as described previously (*27*).

The mean IS recovery for OH-PBDEs was 43% [95% CI: 37, 49] and for PBDEs in plasma 165% [95% CI: 149, 180]. All data were adjusted for recovery. No OH-PBDE residues were detected in method blank samples ($n = 5$). Traces of the BDE47, 99, and 100 were observed at levels <10% of the levels found in the reported samples. Results for BDE99 for three seals and those of BDE100 for two seals were eliminated, because the blank samples run with these seal samples contained these congeners >10% of the levels detected in these seal samples. The replicate determination ($n = 4$) of a polar bear plasma pool, used at NWRC as an in-house plasma reference material, showed 32% variation in the Σ-PBDE concentrations. The minimum level of quantification (MLOQ) was defined as a signal-to-noise ratio of 10. The lipid content in plasma was determined by sulfo-phospho-vanillin reaction using pure olive oil as a calibrant.

Data Analysis. Sum concentrations of PBDEs and their metabolites include congeners/metabolites detected in 60% or more of the samples for each population. For these congeners/metabolites, the samples with concentrations below the minimum level of quantification (MLOQ) were replaced by randomly generated normally distributed data, assuming 1/2 of the MLOQ as the mean, with 40% variation. Statistical analyses were carried out using R version 2.8.1 (*28*). The eliminated values (see Experimental Section) were replaced by population mean for calculation of Σ-PBDE. Possible impacts of geographical area on PBDEs were investigated using linear models. All the continuous variables were ln-transformed. Diagnostic plots of residuals were used to verify that the model assumptions were met (most importantly constant variance between residuals). Hepatic lipid concentrations were more elevated in the high than in the low contaminated seal population (*25*) (Table 1). To avoid the confounding effect of lipid concentration with area, hepatic Σ-PBDE concentrations were lipid normalized for the geographical comparison. Parameter estimates for linear models (β) and mean values are given in the text with 95% confidence intervals.

Principal component analyses (PCA) were used to investigate hepatic PBDE pattern (*29*). As we dealt with proportions summing up to one, PCA derived from the covariance matrix of centered log-ratio of proportions ($\ln(BDE_x/\Sigma\text{-PBDE})$) (*30*). Congeners showing high uncertainty were not included in the PCA (BDE28, 66, 85, 138, 183). Consequently, 1.6% of the data included in the PCAs were < MLOQ. Eliminated values replaced by population mean accounted 5.7% of the data included in the PCA.

Pearson correlation coefficients (r) are given in the text with 95% confidence intervals. The replaced eliminated values were not included in the correlations. One outlier was removed for calculating the Pearson correlation coefficients for BDE_x/Σ-PBDE and Σ-POPs. The removal of this individual did not result in changes of the significance of the results.

Results and Discussion

Geographical Differences of PBDEs. Concentrations of Σ-PBDEs in liver and in plasma were clearly higher in the ringed seals from the Baltic Sea compared to the seals from Svalbard ($\beta = 1.26$ [1.00, 1.52]; $\beta = 0.97$ [0.71, 1.23], respectively) (Table 1). In both seal populations, BDE47 was the dominant congener followed by BDE100, 99, 154, and 153 (Table 1). Σ-PBDEs comprised 2.0% [1.3, 2.6] of the total hepatic Σ-POP (Σ-PCB (*25*), sum of organochlorine pesticides (*31*) and Σ-PBDEs) burden in the ringed seals from Svalbard, and 1.0% [0.9, 1.2] in the Baltic ringed seals, respectively. The results of PCA on hepatic PBDEs indicate that concentrations of BDE153 and 154 relative to Σ-PBDEs were higher in the seals from the Baltic compared to the seals from Svalbard, while the trend was opposite for BDE47 (Figure 1). PBDE pattern shifted more toward BDE153 and 154 ($r = 0.73$ [0.54, 0.85] and $r = 0.73$ [0.56, 0.84], respectively) and less toward BDE47 ($r = -0.73$ [−0.85, −0.58]) with increasing hepatic Σ-POP concentrations. Observed difference in PBDE pattern between seals from high- and low-contaminated areas may be explained by biotransformation via oxidative metabolism and/or via debromination, and/or via different dietary exposure.

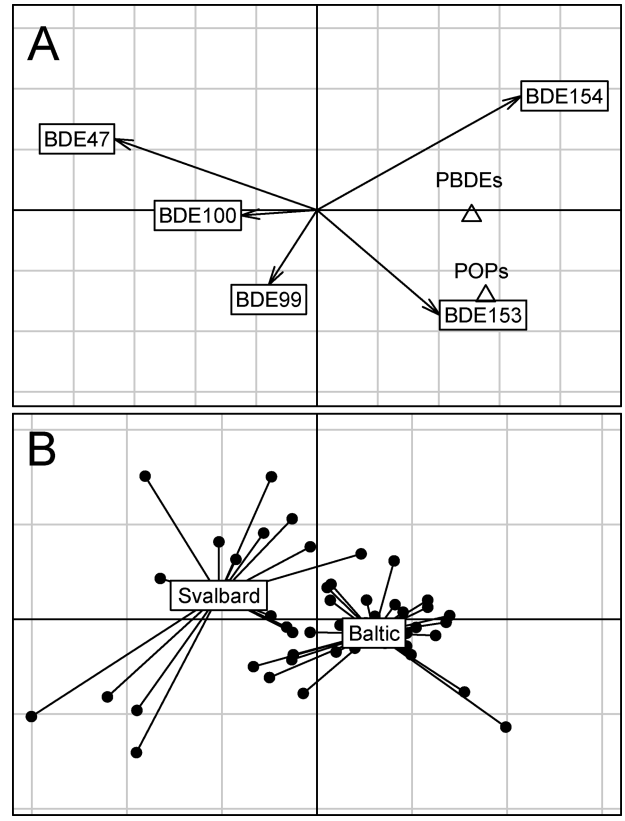

FIGURE 1. (A) PBDE pattern shown as ordination plot from PCA based on covariance matrix of log-ratio PBDEs congeners in ringed seal liver from Svalbard and the Baltic Sea. Hepatic Σ-PBDEs and Σ-POPs are shown as supplementary variables. (B) Sample scores are grouped by geographical area. The first axis explains 64% of the variation of PBDEs and the second axis explains 21%.

OH-PBDEs and Oxidative Metabolism. A very responsive (m/z 79 and 81) peak coeluted at the same retention time as 3-MeO-BDE47 on the DB-5 column for the plasma samples of the seals from Svalbard (Figure S1A, Supporting Information). Therefore all the samples, including the samples from Baltic Sea, were reanalyzed with SP-2331 column to confirm the results (Figure S1B). No further identification of this 3-MeO-BDE47 interfering compound could be made due to the lack of authentic standard. All OH-PBDE concentrations presented were dependent on the results from the chromatographic analysis using the SP-2331 column.

Concentrations of OH-PBDEs in ringed seals from Svalbard and the Baltic Sea are presented in Table 1. OH-PBDE levels and patterns in the ringed seals from Svalbard and the Baltic Sea suggest that formation and/or plasma retention of OH-PBDE metabolites in ringed seals is low.

In the Baltic ringed seals, the concentrations of the five major OH-PBDEs were close to the MLOQ and the Σ_5-OH-PBDE pattern was dominated by *ortho* OH-substituted PBDEs (71% [67, 75]), 2′-OH-BDE68, 6-OH-BDE47, and 6-OH-BDE90, which have been reported to occur as natural products in the Baltic Sea. These three *ortho*-OH-PBDEs have been

detected in several species at lower trophic levels in the Baltic ecosystem including cyanobacteria, red algae, blue mussel, and salmon (*20, 27, 32*). The presence of the *ortho*-OH-substituted PBDEs through the food web indicates that the ortho-OH-PBDEs detected in the Baltic ringed seals result from natural origin. However, a metabolic origin of the *ortho*-OH-PBDEs cannot be completely excluded. For example, 6-OH-BDE47 metabolite has been detected in small quantities in rats exposed to BDE47 in vivo (*22*) and in vitro (*8*).

In the ringed seals from Svalbard 6-OH-BDE47 was the most often detected OH-PBDE, and the concentrations were close to the MLOQ. 6-OH-BDE47 has also been detected in Glaucous gulls from Svalbard (*19*) and in polar bears from East Greenland (*26*). Both natural sources and metabolic formation have been suggested to be the origin for 6-OH-BDE47 detected in the Arctic biota.

Small amounts of 3-OH-BDE47 were detected in the Baltic seals and in a few individuals from Svalbard. In addition, low concentrations of 4′-OH-BDE49 were detected in the majority of the Baltic seals. These compounds are suggested to originate from biotransformation, since *meta* and *para* substituted OH-PBDEs have not been detected in algae, cyanonobacteria, or mussels from the Baltic Sea (*20*). This hypothesis is further supported by experimental studies in rodents. In phenobarbital-induced rat microsomes, 3-OH-BDE47 has been reported to be the main OH-metabolite of BDE47 (*8*). 4′-OH-BDE49 was the major OH-PBDE in addition to 4-OH-BDE42 in the feces of rats exposed to BDE47 (*22*). However, bioaccumulation of 4′-OH-BDE49 cannot be excluded, because it has been detected in Baltic salmon (*27*) and in fish from the Detroit river suggesting formation of OH-PBDEs in fish (*33*).

Correlations between hepatic PBDE congener ratios (BDE_x/Σ-PBDEs) and Σ-POPs concentrations also suggest that some PBDE biotransformation occurs in the Baltic ringed seals. Relative concentrations of BDE28 to Σ-PBDEs decreased with increasing Σ-POP concentration while BDE153 and 154 showed the opposite trend (Figure 2), which indicates BDE153 and 154 are more persistent than BDE28 in the Baltic ringed seals. The results are supported by the hypothesis of McKinney et al. (*14*), who suggested that, similar to PCBs, metabolic capacity of beluga whales is greater toward congeners with increasing number of *ortho*−*meta* bromine-unsubstituted sites. BDE28 has three pairs of vicinal *ortho*−*meta* hydrogen pairs, whereas BDE153 and 154 have no vicinal hydrogen atoms. Persistence of BDE153 relative to BDE28 has also been observed in phenobarbital-induced rat liver microsomes in vitro (*34*).

Metabolism of PBDEs has been suggested to be catalyzed by CYP enzymes. Elevated CYP2B induction has been shown following PBDE exposure in rodents (*35*−*37*). In rats, administration of PBDEs has also been reported to result to elevated CYP3A gene expressions (*35, 37*) and protein levels (*35*). In the present study, formation of 3-OH-BDE47 and 4′-OH-BDE49 may be related to CYP enzyme mediation, which are more highly induced in the present ringed seals from the Baltic Sea compared to the animals from Svalbard (*25*).

Debromination. Biotransformation via debromination is suggested to have a minor influence on the geographical differences in PBDE patterns and in the correlations between the relative concentrations of BDE153 and 154 and the levels of Σ-POPs observed in the present ringed seals. Although fish studies have demonstrated debromination of higher brominated compounds to lower brominated BDEs as a result of endogenous enzyme function (CYPs and deiodinase) and intestinal microflora (*38*−*40*), simple debromination has not been observed in mice administered to different PBDE congeners (*13*). In addition, the levels of BDE183 and 209 are low in the Baltic herring compared to hexa-BDEs (*41, 42*).

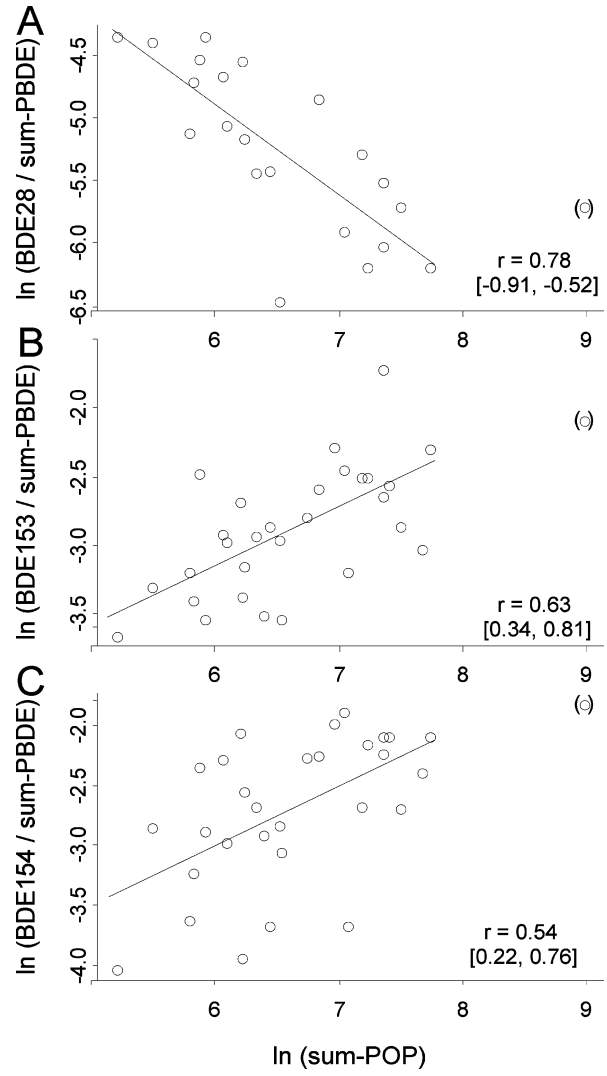

FIGURE 2. Relationships between hepatic ratios of BDE28 (A), BDE153 (B), and BDE154 (C) and Σ-POP (ng/g wet weight) in the Baltic ringed seals. Pearson correlations coefficients with 95% confidence intervals are shown. Observation in parentheses is considered as an outlier.

Dietary Exposure. Dietary exposure of PBDE congeners in the ringed seals of the present study is difficult to assess because the differences in PBDE congener ratios between the Baltic and the Svalbard seal populations are similar to the differences in PBDE congener ratios between polar cod collected from eastern (*43*) and northeastern Svalbard (*44*). However, possible differences in dietary exposure of PBDEs between the seals from the northern Europe and from the Arctic could result from global fractioning of PBDE congeners. Lower-brominated PBDEs have been suggested to have higher long-range transport potential compared to higher-brominated compounds (*45*). The relative presence of lower-brominated PBDEs compared to higher-brominated congeners has been observed to be greater in ringed seals from the Canadian Arctic compared to gray and harbor seals from lower latitudes of Canada (*46*), which is consistent with the results from the present study.

The usage of BDE mixtures has recently changed from lower-brominated BDEs to higher-brominated BDEs, which may also have an influence on the geographical difference in congener pattern observed in the present ringed seals. The penta- and octa-BDE formulations have been banned from use in the European Union since 2004 (*47*). In contrast, the deca-BDE mixture has been partly banned in European

countries as of July 2008 (*48*) although no such restriction exists as yet in North America and Asia (*47*). A decreasing trend of BDE47 and BDE99, and an increasing trend of BDE153, have been reported in human milk from Swedish women during the period 1996−2004 (*49*). Possibly, the temporal change in PBDE pattern may also have occurred in the Baltic seals while the biota in the remote Arctic may take longer to respond to the changes in usage of PBDE-mixtures in industrialized areas.

Toxicological Implications. There is growing evidence that OH-PBDEs have a potential to disrupt the endocrine system. Recent results suggest that at least thyroid, androgen, and estrogen hormone pathways can be affected by OH-PBDEs (*6*). PBDEs show higher affinity to human transthyretin (TTR) in vitro than its natural ligand, thyroxine, only after metabolic conversion by liver microsomes (*9*). In vitro studies suggest that in humans *meta* and *para* OH-substituted PBDEs (*8*), and in gulls also *ortho* substituted OH-PBDEs (*50*), have higher relative binding potencies toward TTR than their natural ligands. OH-PCBs have also reported to have higher binding affinity toward human TTR relative to its natural ligands (*50, 51*). In vitro studies have reported that OH-PBDEs inhibit estradiol-sulfotranseferase (*8*) and have weak affinity to estrogen receptor compared to its natural ligand (*7*). Also OH-PCBs have been reported to inhibit estradiol-sulfotranseferase in vitro (*52*).

Thyroid is vulnerable to endocrine-disrupting effects in seals (*24, 53, 54*) and reproductive failures have been common in highly contaminated seals (*23*). In vitro studies suggest that OH-PBDEs and OH-PCBs may have a common mechanism of action toward the endocrine system. Currently, OH-PCBs may cause higher risk than OH-PBDEs to ringed seals from the Baltic Sea and Svalbard, because OH-PCBs have been detected at 23 [17, 31] times higher concentrations than OH-PBDEs in the present seals (*25*). Future studies should primarily focus on underlying mechanisms of OH-PCBs on endocrine disruption in ringed seals.

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Supporting Information Available

Methods for analysis of PBDEs and OH-PBDEs. Mass chromatograms of OH-PBDEs separated using DB-5 and SP-2331 column. This material is free of charge via the Internet at http://pubs.acs.org.

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