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THE ARCTIC UNIVERSITY OF NORWAY

Faculty of Biosciences, Fisheries and Economics
Department of Arctic and Marine Biology

Effect of body condition on tissue distribution of perfluoroalkylated substances (PFASs) in Arctic fox (*Vulpes lagopus*)

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Camilla Bakken Aas

Master thesis in Biology, BIO-3950, May 2014

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Front page photo: Eva Fuglei

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Camilla

Abstract

The effect of body condition on the distribution and composition of 16 perfluoroalkylated substances (PFASs) in liver, blood, kidney, adipose tissue and muscle of Arctic fox (*Vulpes lagopus*) from Svalbard was investigated. Quantifiable concentrations of the PFASs were found in all samples (n=18). Overall, PFASs concentrations were highest in liver, followed by blood and kidney, while lowest concentrations were found in adipose tissue and muscle. Lean foxes had higher concentrations of ∑PFASs and several individual compounds in adipose tissue. Higher concentrations of perfluorodecanoic acid and perfluoroheptane sulfonic acid in liver, kidney and blood were found in lean foxes, and perfluorononanoic acid concentrations in liver and blood increased with decreasing body condition. The lowest ratio between perfluorooctane sulfonamide and its metabolite perfluorooctane sulfonic acid (PFOS) was in liver, muscle and kidney while significantly higher proportions were found in adipose tissue and blood. Kidney was the organ containing most branched PFOS (32 % of sum linear and branched PFOS), while the remaining tissues had ~20 % of branched PFOS. Arctic mammals have large variability in fat content, and increased concentration of PFASs in target organs of individuals with poor body condition may increase the possibility of metabolic disruption.

Contents

Introduction

Perfluoroalkylated substances (PFASs) are synthetic chemicals used since the 1950's for commercial and industrial purposes. In 2009, perfluorooctane sulfonic acid (PFOS), its salts and perfluorooctane sulfonyl fluoride were defined as persistent organic pollutants (POPs) in the Stockholm convention (listed in Part III of Annex B of the Convention). This was due to their persistence in the environment, ability for long-range transport, bioaccumulative character and toxic potential. Nevertheless, the production and use of PFOS and related compounds is only heavily restricted and not completely banned like many other POPs. So far PFOS, its salts and perfluorooctane sulfonyl fluoride are the only PFASs defined as a POP, though other PFASs have the same persistent and toxic qualities [1].

As a result of substantial persistence in the environment and long-range transportation, PFASs are now found in the Arctic [2]. Moreover, modeled ocean water concentrations in the Arctic showed that PFASs concentration are expected to increase until 2030, even if emissions are substantially reduced or eliminated in near future [3]. Certain PFASs, such as PFOS, have similar biomagnifying capacity as the well-known legacy POPs such as, polychlorinated biphenyls (PCBs), dichlorodiphenyltrichloroethane (DDTs) and polybrominated diphenyl ethers (PDBEs) [4]. In fact, PFOS has been reported at higher concentrations than legacy POPs (PCBs, DDTs and PDBEs) in polar bears (*Ursus maritimus*) [5] and Arctic foxes (*Vulpes lagopus*) [6]. These high concentrations of PFASs in Arctic top predators are of great concern due to increased possibility of health issues.

Arctic mammals, especially the Arctic fox, have large seasonal variability of fat content and rely heavily on regulation of lipid metabolism [7]. They are therefore sensitive to the effects of POPs due to release and redistribution of POPs stored in adipose tissue [8]. Wildlife reports have mainly focused on PFASs in liver and blood due to high accumulation in the enterohepatic system [9]. Reports on tissue distribution of PFASs in mammals are

limited, though there have been done studies on harbor seals (*Phoca vitulina*) [10, 11], Baikal seals (*Pusa sibirica*)[12], polar bears [13] and mice [14]. These previous studies show species-specificity in tissue distribution[15]. Nevertheless, only one of these studies has examined tissue distribution of PFASs on Arctic mammals [13]. Knowledge of tissue distribution in different species is crucial in order to map all potential harmful effects PFASs can give.

Chronic exposure to PFASs are correlated with potential health effects, such as metabolic disruption [16] , developmental toxicity [17], thyroid disruption [18], and liver-and pancreas carcinogenicity [19], in both animals and humans. Metabolic disruption and liver-and pancreas carcinogenicity are associated with PFASs' ability to mediate the peroxisome proliferator-activated receptor (PPAR) pathway [16, 19]. PPARs, are found in three isoforms which all take part in regulating target genes involved in fatty acid metabolism, in addition to moderate the effect of peroxisome proliferators [20]. PPARs are activated by fatty acids, as well as PFAS, which are structurally similar to fatty acids, having a strong hydrophobic body and polar head group [21]. Previous in vitro and epidemiological studies suggest that PFASs exposure is associated with metabolic disruption, obesity and diabetes [22, 23]. Uncertainties evolve around if variation of body condition further affects concentration of PFASs in tissues and may amplify the effects of PFASs.

The aim for this study is to examine concentrations and patterns of PFASs within and between tissues of the Arctic fox and the effect body condition have on it. The large fluctuations in adipose tissue of Arctic foxes indicate that this species is a good reference model to look at the implications how body condition affects distribution of contaminants. As far as I know this is the first study reporting the effect of body condition on distribution and concentration of PFASs.

Methods and materials

Sample collection

Arctic foxes were collected on Spitsbergen, Svalbard, mainly around Isfjorden area (77-79^{o}N, 13-18^{o}E). Baited traps were used to collect the foxes during the annual harvest between 1st of November and 15th of March in 2010/2011 (n=13) and 2011/2012 (n=5). All foxes were weighted, sex-determined, and skinned before shipped frozen to Tromsø for the final dissection.

Samples of liver, kidney, abdominal adipose tissue and muscle were wrapped in aluminum foil and stored at -20^{o}C until further use. Samples of whole blood were taken from the heart and stored with the other tissues. Individual body condition was also assessed during the dissection, and was defined as either lean or fat. The age of the Arctic foxes was determined by counting the annuli in the cementum of a sectioned canine tooth [24]. All foxes used in this study were between one and three years old. The females (n=7) were not expected to have given birth since Svalbard vixens do not reach maximum pregnancy rates before the age of four [25]. Also, there were no marks from reproduction on the uterus of the vixens used in this study.

PFASs analyses

The PFASs analysis was conducted at the Norwegian Institute for Air Research (NILU). All solvents used in this experiment were of Lichrosolv® grade and were purchased from Merck-Schuchardt (Hohenbrunn, Germany). The method used for preparing the samples for analysis has previously been described by Powley, et al. [26]. In short, all samples (1 g) were added 0.1 ng/µl isotopically-labeled internal standards, which were used to calculate PFASs concentrations. Isotopically-labeled compounds used as internal standard were of >98% purity and were obtained from Wellington Laboratories Inc. The internal standard contained: MPFHxS (PFHxS$^{18}O_2$), MPFOS ($^{13}C_4$PFOS), MPFOA ($^{13}C_4$PFOA), MPFNA ($^{13}C_5$PFNA),

MPFHxA ($^{13}C_2$PFDA), MPFUnDA ($^{13}C_2$PFUnDA) and MPFDoDA ($^{13}C_2$PFDoDA). Acetonitrile was blended in with the samples followed by ultrasonic bath and centrifuged for sedimentation (2000 rpm). The supernatant was concentrated to 1 ml using a RapidVap (Rapid Vap; Labconco corp., Kansas city, MO, USA). 25 mg ENVI-Carb 120/400 (Supelco, PN, USA) and glacial acetic acid was prepared and mixed with the supernatant. The mixture was centrifuged (10 000 rpm), and the supernatant solution was transferred to an auto injector vial where recovery standard (RSTD) was added. The RSTD, which were used to measure percentage recovery, contained 3,7-dimethyl-branched perfluorodecanoic acid (bPFDA). It was of 97 % purity and was obtained from ABCR (Karlsruhe, Germany). Prior to the ultrahigh pressure liquid chromatography triple-quadruple mass-spectrometry (UHPLC-MS/MS) analysis the extract was added in a liquid chromatography-vial with 2 mM ammonium acetate in HLB-water (NH4OAc, ≥ 99%, Sigma-Aldrich, St. Louis, MO, USA) in a 50/50 mixture. PFASs were analyzed by UHPLC-MS/MS as previously described by Hanssen, et al. [27]. The atomic mass of the sulfonate anions were taken into account for all the concentration calculations.

Stable isotope analysis (SIA) of $\delta^{13}C$ and $\delta^{15}N$

To assess the possible confounding effect of diet on PFASs exposure, stable isotope ratios of nitrogen ($\delta^{15}N$) and carbon ($\delta^{13}C$) in muscle were analysed [28]. Muscle SIA is expected to provide dietary information from the previous one to two months in the Arctic fox[28].

Approximately 1 g (cm^3) of muscle tissue was dried for 2-3 days at 60°C before it was grounded into a fine powder in a bread-mill homogenizer (TissueLyzerll, Qiagen Gmbh, Hilden, Germany) and 0.4 mg (±0.05 mg) fine powder was put into a tin container. Stable isotope analysis was performed at the Stable Isotopes in Nature Laboratory (SINLAB), New Brunswick, Canada as previously described by Ehrich, et al. [29]. In short, samples were

combusted in a Carlo Erba NC2500 Elemental Analyzer before delivery to a Finnigan MatDelta Pluss mass spectrometer (Thermo Finnigan, Bremen, Germany). Stable isotope signatures are expressed as parts per thousand (‰) relative to a standard as follows $[(R_{sample}/R_{standard})-1] \times 1000$, where R is the fractions of heavy to light isotopes ($^{13}C/^{12}C$ and $^{15}N/^{14}N$). As standards for $\delta^{13}C$ and $\delta^{15}N$, Peedee belemnite carbonate and atmospheric nitrogen were used, respectively [30]. As $\delta^{13}C$ reflects the lipid content of the tissue sample, the model based normalisation for muscular tissue was used to correct the value of $\delta^{13}C$ for lipid content in the samples with a C/N ratio between 3.5 and 7 [29].

Quality control

Quality control was assessed according to Hansen et al [27]. In order to reduce background interference, a blank was run with every 10 samples. The blank was treated identically to the other samples, except that no tissue was added. None of the blanks in this study had contamination. Recovery of the mass labeled internal standards ranged for liver between 45-125 %, for adipose tissue 35-125 % and for blood, kidney and muscle between 50-115 %. A certified reference material was run with every 10 samples to assure quality of the analysis. This was used to minimize the fluctuations between samples made at different times. The control used for liver, kidney, muscle and adipose tissue, was pike IRMM-427, sample ID 0119. For the blood sample, a blood/serum control was used (SRM 1958, NIST, Gaithersburg, MD, USA).

Data analysis

Statistical analyses were carried out by using the statistical program R, version 3.0.2 (R Core Team, 2013).

Compounds detected in >60% of the samples in a given tissue were used for statistical analyses. Non-detected values of the compounds used in the analysis were set to be half the limit of detection (LOD). LOD is expressed as the concentration derived from the lowest

measure that can be detected with reasonable certainty for a given analytical procedure [31]. The tissues with detected samples of less than 60 % were removed from the mixed models for the given compounds. Furthermore, the whole compound was removed from the ∑PFASs analyses, and for the analyses of the two subgroups, ∑perfluorocarboxylic acids (PFCAs) and ∑perfluoroalkylated sulfonic acid (PFSAs).

Linear mixed-effects models was applied using the R-library lme4 [32], which were used to analyze the effect of explanatory variables on distribution of PFASs in Arctic fox tissues. The most parsimonious model for summed and individual PFASs was selected using ∑PFASs as a response variable. The possible explanatory variables included in the global model, applied as fixed effects were tissue (liver, blood, kidney, adipose tissue and muscle), body condition (lean and fat), $\delta^{15}N$ and $\delta^{13}C$, while individual was applied as a random effect. Age and gender were not included as explanatory variables since almost all the foxes were between 1-2 years old (two foxes were 3) and none of the females were expected to have reproduced. As our study is based on planned comparisons of tissue and body condition the interaction between them were kept in all models. From the pool of models we selected the most parsimonious model with the lowest value of Akaike's Information Criterion corrected for small sample size (AICc)[33]. The most parsimonious model was further applied for individual PFASs, ∑PFASs, ∑PFCAs and ∑PFSAs, the ratios of PFOS:PFOSA and the ratio of branched and linear PFOS. One outlier was removed in the analysis of PFOS:PFOSA, however, removing this value did not change the estimates. PFOS used in the models for individual compounds, ∑PFASs and ∑PFSAs was based on the sum of branched and linear PFOS.

The MCMCglmm (MCMCglmm, Marcov chain Monte Carlo Sampler simulations for Bayesian estimations of Generalized Linear Mixed Models) package [34] were used to calculate

the 95 % confidence intervals of the effect. 500 000 MCMC iterations were used, retaining every fifth values in the chain.

Assumptions of constant variance and approximate normal distribution of residuals were determined through plots of residuals against fitted values and normal-and quantile-quantile plots [35]. To meet the assumptions, all PFASs concentrations were log-transformed prior to the analyses. Additionally, a constant (0.05) was added to take the few non-detected compounds into account and the constant was chosen when residuals were approximately normally distributed.

Results and discussion

Model selection

The result from the model selection showed that the most parsimonious model explaining the variation of ΣPFASs contained $\delta^{15}N$, tissue and body condition as fixed factors and individual as random variable (see Supporting Information).

The relationship between body condition and tissue showed great evidence to explain the variation of PFASs, while variation was weakly explained by $\delta^{15}N$, respectively.

Tissue concentrations of PFASs

PFOS was the dominating PFASs in all Arctic fox tissues, while perfluorononanoic acid (PFNA) was the most dominating PFCAs followed by perfluoroundecanoic acid (PFUnA) and perfluorotridecanoic acid (PFTrA) (Table 1). PFTrA was observed at similar concentrations as PFUnA in all tissues except adipose tissue where PFTrA was detected in less than 60 % of samples. These findings are consistent with previous studies on Arctic predators, where PFOS is the dominating PFASs, while in the PFCAs group, PFNA, PFUnA and PFTrA are found to have among the highest concentrations [6, 13, 36]. Perfluorohexane sulfonic acid (PFHxS) and perfluorooctanoic acid (PFOA) were detected in all tissues although at lower concentrations than PFOS, PFNA and PFUnA (Figure 1, Table 1). Perfluorodecanoic acid (PFDcA), perfluorododecanoic acid (PFDoA), perfluorotetradecanoic acid (PFTeA), PFOSA and perfluoroheptane sulfonic acid (PFHpS) were detected in most samples, though not detected over 60 % of samples in adipose tissue, and additionally PFTeA were not detected in blood samples.

Table 1. Geometric mean concentrations (ng/g wet weight), standard error (SE) for all detected compounds* and range for all PFASs in tissues of the Arctic fox from Svalbard.

		Liver	Blood	Kidney	Adipose Tissue	Muscle
			Perfluorocarboxylic acids			
PFOA	Mean±SE Range	2.7 ± 0.49 (0.81 - 7.45)	1.35 ± 0.24 0.47 - 3.5)	0.23 ± 0.05 (0.01 - 0.64)	0.10 ± 0.06 (0.01 - 0.88)	0.26 ± 0.01 (0.01 – 0.15)
PFNA	Mean±SE Range	14 ± 3.2 (3.95 - 55)	3.8 ± 0.7 (1.4 - 13)	1.9 ± 0.62 (0.53 - 9.8)	0.33 ± 0.26 (0.09 - 4.4)	0.41 ± 0.55 (0.22 – 1.2)
PFDcA	Mean±SE Range	4.15 ± 0.79 (1.2 - 12.5)	0.82 ± 0.13 (0.32 – 2)	0.46 ± 0.11 (0.15 - 1.9)	n.d (0.01 - 0.65)	0.13 ± 0.02 (0.05 – 0.4)
PFUnA	Mean±SE Range	5.2 ± 1.5 (1.2 - 26)	1.3 ± 0.37 (0.34 - 6.4)	0.79 ± 0.28 (0.26 - 4.9)	0.09 ± 0.08 (0.004 - 1.1)	0.25 ± 0.06 (0.07 – 0.95)
PFDoA	Mean±SE Range	0.72 ± 0.21 (0.21 - 4.05)	0.175 ± 0.06 (0.05 - 1.15)	0.1 ± 0.06 (0.003 - 1.0)	n.d. (0.004 - 0.23)	0.04 ± 0.015 (0.002 – 0.25)
PFTrA	Mean±SE Range	6.0 ± 1.79 (1.55 - 33)	1.4 ± 0.63 (0.30 - 12)	0.42 ± 0.21 (0.14 - 4.1)	n.d. (0.01 - 1.3)	0.18 ± 0.06 (0.03 – 1.0)
PFTeA	Mean±SE Range	2.3 ± 0.62 (0.45 - 10)	n.d. (47 - 47)	0.1 ± 0.02 (0.03 - 0.49)	n.d (0.034 - 0.71)	0.04 ± 0.01 (0.01 – 0.18)
∑PFCAs	Mean±SE Range	2.7 ±0.66 (0.21 - 55)	0.69 ± 0.25 (0.05 – 13)	0.3 ± 0.11 (0.003 - 9.8)	0.065 ± 0.04 (0.004 - 4.4)	0.07 ± 0.02 (0.002 – 1.2)
			Perfluoroalkylated sulfonamides			
PFOSA	Mean±SE Range	0.38 ± 0.53 (0.01 - 9.8)	0.84 ± 1.5 (0.08 – 28.5)	0.1 ± 0.16 (0.005 - 2.8)	n.d. (0.034 - 1.5)	n.d. (0.001 – 0.44)
			Perfluoroalkylated sulfonic acid			
PFHxS	Mean±SE Range	5.2 ± 2.2 (0.75 – 36)	4.6 ± 2.2 (0.54 - 29)	3.0 ± 1.6 (0.27 - 27)	0.47 ± 0.24 (0.04 - 3.9)	0.745 ± 0.34 (0.09 - 5.4)
PFHpS	Mean±SE Range	1.3 ± 0.3 (0.12 - 5.45)	0.305 ± 0.08 (0.05 - 1.4)	0.23 ± 0.05 (0.005 - 0.68)	n.d. (0.02 - 0.155)	0.02 ± 0.01 (0.002 – 0.16)
PFOS	Mean±SE Range	80 ± 15 (9.7 – 275)	10 ± 2.1 (1.1 - 29)	8.6 ± 2.1 (0.74 - 35)	0.79 ± 0.46 (0.09 - 7.8)	2.0 ± 0.36 (0.20 - 5.5)
∑PFSAs	Mean±SE Range	8.1 ± 8.2 (0.12 - 275)	2.4 ± 1.2 (0.05 - 29)	1.9 ± 1.07 (0.005 - 35)	0.2 ± 0.19 (0.02 - 7.8)	0.30 ± 0.22 (0.002 - 5.46)
∑PFASs	Mean±SE Range	3.7 ± 2.50 (0.01 – 275)	0.97 ± 0.42 (0.05 - 29)	0.49 ± 0.34 (0.003 - 35)	0.09 ± 0.06 (0.004 - 7.8)	0.11 ± 0.07 (0.002 - 5.5)

*All compounds found above the detection limit in at least 60 % of the samples for a given tissue.
n.d.= not detected

Odd-numbered PFCAs were found in greater amount than the even-numbered in all tissues, and concentrations of odd-numbered PFCAs decreased with increasing chain length (Table 1). These trends are in agreement with previous findings on Arctic foxes, polar bears and seabirds [6, 13, 37, 38]. Perfluorobutane sulfonic acid (PFBS), Perfluorodecane sulfonic acid (PFDcS), perfluorohexanoic acid (PFHxA) and perfluoroheptanoic acid (PFHpA) were not detected in any of the tissue samples of Arctic foxes, which is consistent with previous literature [39]. PFBS, PFHxA and PFHpA are neither considered bioaccumulative nor biomagnifying, and are usually not detected in wildlife samples [39]. PFDcS has been detected in sea birds [37, 40, 41] and polar bears [13], though at low concentrations (e.g 1.8 ng/g ww in blood of polar bears). Polar bears, have in general five to ten times higher concentrations of PFASs than Arctic foxes [6], which may explain why PFDcS were detected in polar bears but not Arctic foxes.

The concentrations of PFASs differed between Arctic fox tissues (Table 1). The highest concentrations of PFASs were found in the liver, followed by blood and kidney. The lowest concentrations were found in adipose tissue and muscle. These findings are in accordance with previous literature on mammalian predators [11, 13, 42]. It is well established that PFASs go through extensive uptake from enterohepatic circulation, and accumulate mostly in the liver [1]. Furthermore, the distribution of PFASs is affected by localized proteins [43, 44]. In detail, PFASs have great affinity to liver fatty acid-binding protein (L-FABP), which partly explains their high concentration in the liver [1, 21, 43, 45]. Additionally, recent modeled studies suggest that PFASs have great affinity towards phospholipids [44, 46]. These are found in large quantities in the liver, and may contribute to the high concentrations of PFASs in this organ [44, 46]. Blood had the second highest concentration of PFASs. This is due to their affinity to albumin [43, 44, 47-49]. Reabsorption of PFASs from the gut and urine by passive diffusion and organic anion transporters (OATs) into the blood probably plays a significant role in high

concentrations and the long half-life of PFASs in blood[50]. Phospholipids, L-FABPs and OATs are found in the kidney, which may explain the high concentration of PFASs in this organ [44]. Furthermore, the high concentrations of PFASs in the kidney may also indicate excretion of these compounds through urine [51], or simply reflect the high flow of blood through this organ[9].

PFASs composition was similar between Arctic fox tissues (Figure 1a, 1b). These findings are in agreement with studies on harbor seals, where the same composition was seen [10]. However, these results are not in agreement with the PFASs composition in polar bears, in which longer-chained PFCAs are found in adipose tissue while shorter-chained PFCAs are found in liver and blood [13].

Effect of body condition

Concentrations of summed and individual PFASs differed between lean and fat foxes (Figure 2). For ∑PFASs, adipose tissue was the only body compartment affected by body condition, where the lean foxes had four times [95% Cl: 2.0, 10] higher concentrations of ∑PFASs than the fat foxes. The same trend was seen for ∑PFSAs, where lean foxes had seven times [95% Cl: 2.6, 19] higher concentration of ∑PFSAs in adipose tissue than fat foxes. This similar trend in ∑PFASs and ∑PFSAs is explained by the large concentration and contribution of PFSAs in ∑PFASs. The trend for ∑PFCAs was different, as lean foxes had over two times [95% Cl: 1.1, 4.4] higher concentrations of ∑PFCAs in liver, blood and kidney. Adipose tissue of lean individuals had fivefold [95% Cl: 2.4, 9.4] higher concentrations of ∑PFCAs than fat foxes. Muscle were not significantly affected by body condition, as lean individuals only had 0.3 times [95% Cl: -0.6, 2.6] higher concentrations of ∑PFCAs than fat foxes.

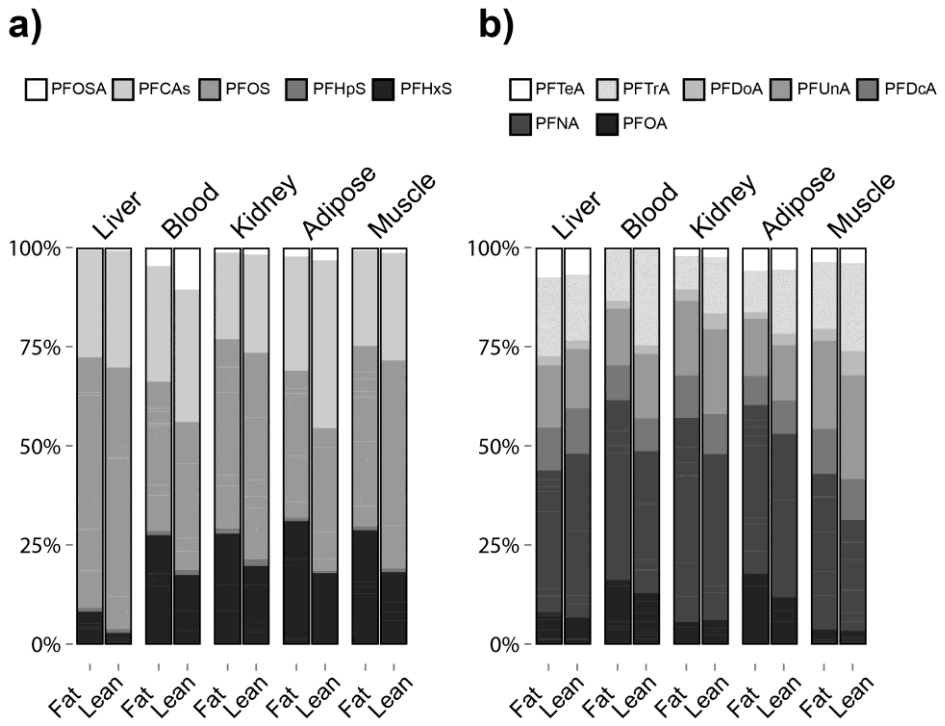

Figure 1. Percent composition of PFASs (a) and PFCAs (B) within each tissue in lean and fat Arctic foxes from Svalbard (n=18). The values are based on arithmetic mean.

Analysis on individual compounds showed that medium chain length PFCAs (C_9-C_{11}) and short chain length PFSAs (C_6-C_7) were the compounds affected by decreased body condition. Lean foxes had twice as high [95% Cl: 1.2, 4.5] concentrations of PFNA in liver, blood and adipose tissue compared to fat foxes. Concentrations of PFDcA were two times [95% Cl: 1.2, 3.7] higher in liver, kidney and blood of lean individuals compared to the fat foxes. Eight times [95% Cl: 3.4, 20] higher concentration of PFUnA was found in adipose tissue of the lean foxes compared to the fat individuals. For PFHxS, adipose tissue was the only tissue affected by body condition, with lean foxes having three times [95% Cl: 1.0, 10] higher concentration of PFHxS than fat foxes. Liver, kidney and blood of lean foxes had two times [Cl: 1.1, 4.0] higher concentrations of PFHpS than fat foxes.

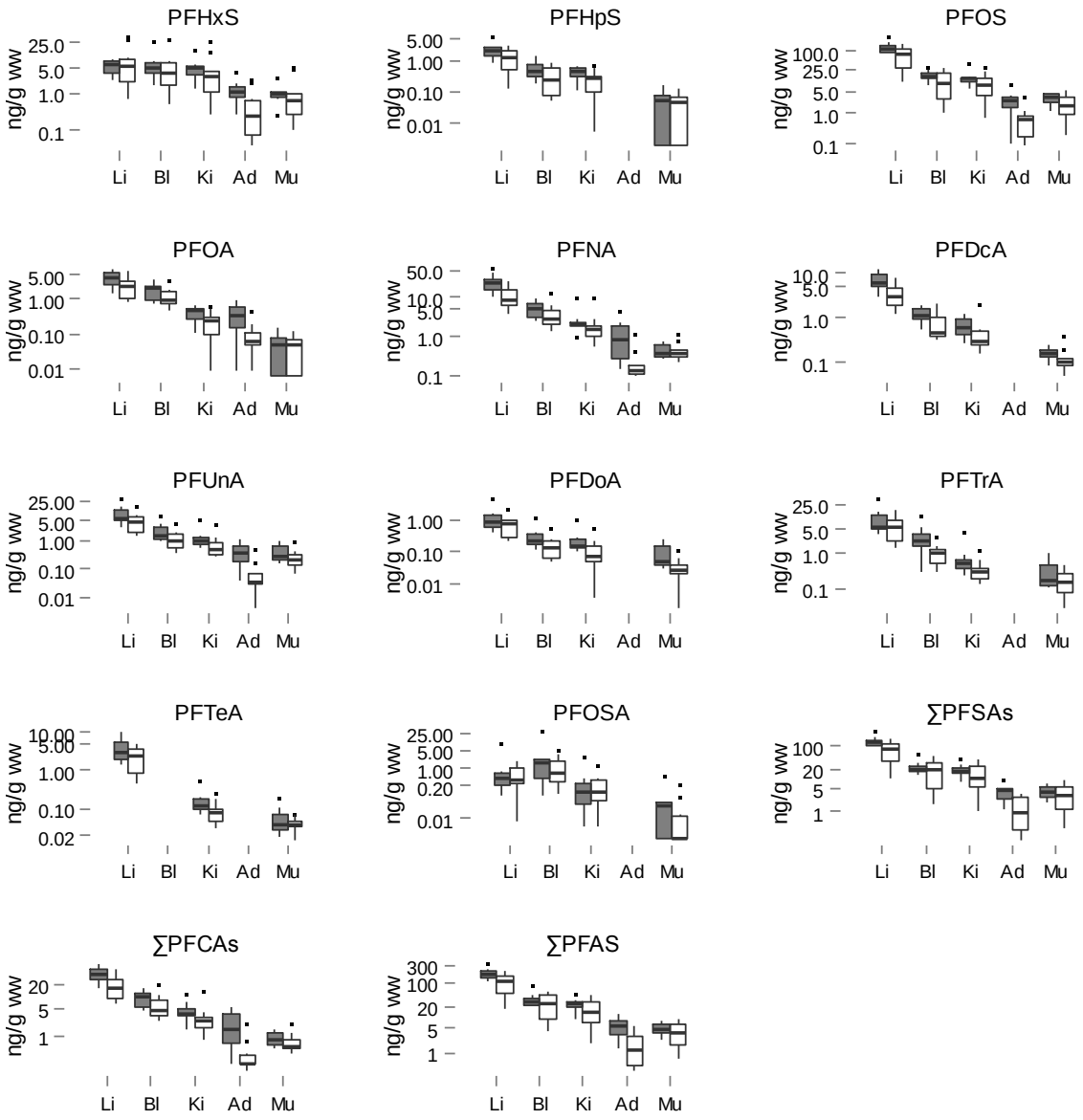

Figure 2. Concentrations (ng/g wet weight) of individual and sum (Σ) PFSAs, PFCAs and PFASs, in liver (Li), blood (Bl), kidney (Ki), adipose tissue (Ad) and muscle (Mu) of lean (dark grey) and fat (white) Arctic foxes form Svalbard (n=18). Y-axis is on a logarithmic scale.

Concentrations of PFOSA, PFOS, PFOA, PFDoA, PFTrA and PFTeA were not affected by body condition in any tissue analyzed in our study. Similarly, studies on sea otter (*Enhydra lutris nereis*) and harbor seals showed that PFOS and PFOA measured in liver were not affected by body condition [52, 53]. This is further supported in a study on male mink (*Neovison vison*) where it was found that concentrations of PFHxS, PFOS, PFOA, PFUnA,

PFDoA, PFTrA in the liver was not affected by body condition [54]. However, in the same study PFNA and PFDcA were also found not to differ between body condition in the liver, while in this study these compounds were found at higher concentration in that organ of lean foxes.

The results from this study clearly show that adipose tissue concentrations of most PFASs vary with nutritional status. This may be explained by a concentration effect of the compound within the adipose tissue i.e. the reduction of adipose tissue in lean foxes lead to PFASs being stored in a smaller total lipid mass. A possible explanation for the increased concentrations in kidney, liver and blood may be explained by the lowered intake of food during fasting [55]. Fasting leads to reduced resting metabolic rate [55] and reduced excretion of contaminants, which by its turn gives increased half-life and increased accumulation of contaminants [56]. This may further, explain why medium chain length PFCAs are more affected by decreased body condition than the short chain length PFCAs. The short chain length PFCAs are water-soluble [57] and are highly eliminated through urine [58, 59]. Medium chain length PFCAs, which are more hydrophobic, favor biliary enterohepatic recirculation [58, 59]. This means that reduced excretion and food intake will affect medium chain length PFCAs, more than short chain length PFCAs. Other mechanism may explain why shorter chained length PFSAs are affected by body condition while PFOS is not.

PFOSA and PFOS concentration

The estimated ratio between PFOSA and its metabolite PFOS were 0.0037 [CI: 0.001, 0.013] in liver, muscle and kidney, while significantly higher ratios were found in adipose tissue and blood, 0.042 [CI: 0.004; 0.40] and 0.068 [CI: 0.007, 0.66], respectively. Body condition had no effect on the ratio between PFOSA and PFOS (Figure 3a). The low PFOSA:PFOS ratio in liver of Arctic foxes may be related to the metabolism of

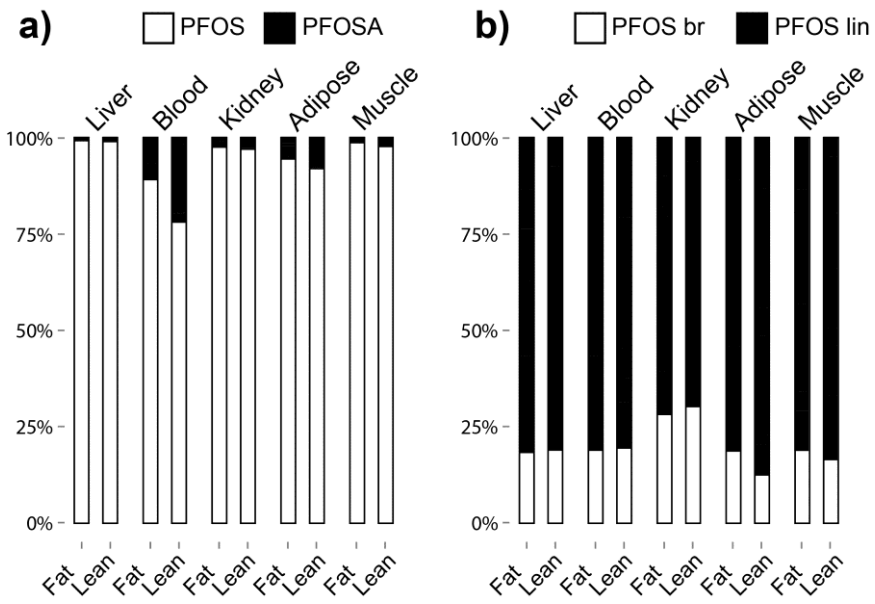

Figure 3. Percent compositions of PFOSA and PFOS (a) and composition between linear and branched PFOS (b) within each tissue in lean and fat Arctic foxes from Svalbard (n= 18). The values are based on arithmetic mean.

N-ethyl perfluorooctanesulfonamido ethanol (N-EtFOSA) via PFOSA to PFOS [60]. This process is mainly catalyzed by cytochrome P450 enzymes (CYP2C9 and CYP2C19 in humans), which is expressed in liver [61]. The higher proportion of PFOSA in blood and adipose tissue may be due to the absence or low activity of CYP enzymes in these body compartments resulting in slower degradation of PFOSA to PFOS.

Branched and Linear PFOS concentration

Kidney was the organ containing most branched PFOS (32 %), while the remaining tissues contained ~20 % of branched PFOS. Nevertheless, the branched and linear PFOS composition did not differ significantly between tissues (Figure 3b). Body condition did not have an effect on the proportion either. Branched PFOS were found in much higher proportion in Arctic foxes compared to polar bears, where branched PFOS varied between ~0 % to 25 % depending on tissue [62]. Moreover, the composition of branched and linear PFOS varied between tissues in polar bears [62], whereas no difference between tissues was

observed in the Arctic foxes of the present study. Inter-species variation in metabolism of branched and linear PFOS may explain the contrasting effect in this study compared the previous literature [63-65].

Implications

In this study there was found that decreased body condition (lean foxes) increases the concentrations of PFASs in adipose tissue in Arctic foxes. Additionally, higher concentrations of PFDcA and PFHpS in liver, kidney and blood, and higher PFNA concentrations in liver and blood where found to increase with decreasing body condition. In general, Arctic mammals have large seasonal variability in fat content [7, 66-68], which affects concentration of PFASs in tissues and may amplify the its effects. The effects are not only related to the increased concentration of PFASs, but are also related to increased concentration of other POPs in target organs during decreased body condition which may further increase toxicity [8]. Essentially, PFASs interfere with the PPAR-pathway by binding to the PPAR, and by binding to liver-FABPs which is directly involved in the transportation of fatty acids to the PPAR [69]. Interference with the PPAR-pathway is related to metabolic disruption [70, 71]. Future studies should focus on toxicity in animals in relation to body condition in order to map if decreased body condition amplify the possible effects of PFASs. The results also suggest that these large annual changes in body condition must be taken into account when performing time-trend analyses and other studies on PFASs.

References

1. Lau, C.; Anitole, K.; Hodes, C.; Lai, D.; Pfahles-Hutchens, A.; Seed, J., Perfluoroalkyl Acids: A Review of Monitoring and Toxicological Findings. *Toxicological Sciences* **2007,** *99*, (2), 366-394.
2. Butt, C. M.; Berger, U.; Bossi, R.; Tomy, G. T., Levels and trends of poly- and perfluorinated compounds in the arctic environment. *Science of The Total Environment* **2010,** *408*, (15), 2936-2965.
3. Armitage, J.; Cousins, I. T.; Buck, R. C.; Prevedouros, K.; Russell, M. H.; MacLeod, M.; Korzeniowski, S. H., Modeling Global-Scale Fate and Transport of Perfluorooctanoate Emitted from Direct Sources. *Environmental Science & Technology* **2006,** *40*, (22), 6969-6975.
4. Haukås, M.; Berger, U.; Hop, H.; Gulliksen, B.; Gabrielsen, G. W., Bioaccumulation of per- and polyfluorinated alkyl substances (PFAS) in selected species from the Barents Sea food web. *Environmental Pollution* **2007,** *148*, (1), 360-371.
5. Smithwick, M.; Mabury, S. A.; Solomon, K. R.; Sonne, C.; Martin, J. W.; Born, E. W.; Dietz, R.; Derocher, A. E.; Letcher, R. J.; Evans, T. J.; Gabrielsen, G. W.; Nagy, J.; Stirling, I.; Taylor, M. K.; Muir, D. C. G., Circumpolar Study of Perfluoroalkyl Contaminants in Polar Bears (Ursus maritimus). *Environmental Science & Technology* **2005,** *39*, (15), 5517-5523.
6. Martin, J. W.; Smithwick, M. M.; Braune, B. M.; Hoekstra, P. F.; Muir, D. C. G.; Mabury, S. A., Identification of Long-Chain Perfluorinated Acids in Biota from the Canadian Arctic. *Environmental Science & Technology* **2004,** *38*, (2), 373-380.
7. Prestrud, P.; Nilssen, K., Fat Deposition and Seasonal Variation in Body Composition of Arctic Foxes in Svalbard. *The Journal of Wildlife Management* **1992,** *56*, (2), 221-233.
8. Helgason, L. B.; Wolkers, H.; Fuglei, E.; Ahlstrøm, Ø.; Muir, D.; Jørgensen, E. H., Seasonal emaciation causes tissue redistribution and an increased potential for toxicity of lipophilic pollutants in farmed arctic fox (Vulpes lagopus). *Environmental Toxicology and Chemistry* **2013,** *32*, (8), 1784-1792.
9. Martin, J. W.; Mabury, S. A.; Solomon, K. R.; Muir, D. C. G., Bioconcentration and tissue distribution of perfluorinated acids in rainbow trout (Oncorhynchus mykiss). *Environmental Toxicology and Chemistry* **2003,** *22*, (1), 196-204.
10. Van de Vijver, K. I.; Hoff, P.; Das, K.; Brasseur, S.; Van Dongen, W.; Esmans, E.; Reijnders, P.; Blust, R.; De Coen, W., Tissue Distribution of Perfluorinated Chemicals in Harbor Seals (Phoca vitulina) from the Dutch Wadden Sea. *Environmental Science & Technology* **2005,** *39*, (18), 6978-6984.
11. Ahrens, L.; Siebert, U.; Ebinghaus, R., Total body burden and tissue distribution of polyfluorinated compounds in harbor seals (Phoca vitulina) from the German Bight. *Marine Pollution Bulletin* **2009,** *58*, (4), 520-525.
12. Ishibashi, H.; Iwata, H.; Kim, E.-Y.; Tao, L.; Kannan, K.; Amano, M.; Miyazaki, N.; Tanabe, S.; Batoev, V. B.; Petrov, E. A., Contamination and Effects of Perfluorochemicals in Baikal Seal (Pusa sibirica). 1. Residue Level, Tissue Distribution, and Temporal Trend. *Environmental Science & Technology* **2008,** *42*, (7), 2295-2301.
13. Greaves, A. K.; Letcher, R. J.; Sonne, C.; Dietz, R.; Born, E. W., Tissue-Specific Concentrations and Patterns of Perfluoroalkyl Carboxylates and Sulfonates in East Greenland Polar Bears. *Environmental Science & Technology* **2012,** *46*, (21), 11575-11583.

14. Bogdanska, J.; Borg, D.; Sundstrom, M.; Bergstrom, U.; Halldin, K.; Abedi-Valugerdi, M.; Bergman, A.; Nelson, B.; Depierre, J.; Nobel, S., Tissue distribution of (3)(5)S-labelled perfluorooctane sulfonate in adult mice after oral exposure to a low environmentally relevant dose or a high experimental dose. *Toxicology* **2011,** *284*, (1-3), 54-62.
15. Galatius, A.; Bossi, R.; Sonne, C.; Rigét, F.; Kinze, C.; Lockyer, C.; Teilmann, J.; Dietz, R., PFAS profiles in three North Sea top predators: metabolic differences among species? *Environ Sci Pollut Res* **2013,** *20*, (11), 8013-8020.
16. Ikeda, T.; Aiba, K.; Fukuda, K.; Tanaka, M., The Induction of Peroxisome Proliferation in Rat Liver by Perfluorinated Fatty Acids, Metabolically Inert Derivatives of Fatty Acids. *Journal of Biochemistry* **1985,** *98*, (2), 475-482.
17. Shi, X.; Du, Y.; Lam, P. K. S.; Wu, R. S. S.; Zhou, B., Developmental toxicity and alteration of gene expression in zebrafish embryos exposed to PFOS. *Toxicology and Applied Pharmacology* **2008,** *230*, (1), 23-32.
18. Cheng, Y.; Cui, Y.; Chen, H.-m.; Xie, W.-p., Thyroid disruption effects of environmental level perfluorooctane sulfonates (PFOS) in Xenopus laevis. *Ecotoxicology* **2011,** *20*, (8), 2069-2078.
19. USEPA, Science Advisory Board SAB Review of EPA's Draft Risk Assessment of Potential Human Health Effects Associated with PFOA and Its Salts. In Agency, U. S. E. P., Ed. EPA-SAB-06-006: Washington DC, May 30, 2006.
20. Barger, P. M.; Kelly, D. P., PPAR Signaling in the Control of Cardiac Energy Metabolism. *Trends in Cardiovascular Medicine* **2000,** *10*, (6), 238-245.
21. Luebker, D. J.; Hansen, K. J.; Bass, N. M.; Butenhoff, J. L.; Seacat, A. M., Interactions of flurochemicals with rat liver fatty acid-binding protein. *Toxicology* **2002,** *176*, (3), 175-185.
22. Halldorsson, T. I.; Rytter, D.; Haug, L. S.; Bech, B. H.; Danielsen, I.; Becher, G.; Henriksen, T. B.; Olsen, S. F., Prenatal exposure to perfluorooctanoate and risk of overweight at 20 years of age: a prospective cohort study. *Environmental health perspectives* **2012,** *120*, (5), 668.
23. Lind, L.; Zethelius, B.; Salihovic, S.; van Bavel, B.; Lind, P. M., Circulating levels of perfluoroalkyl substances and prevalent diabetes in the elderly. *Diabetologia* **2013**, 1-7.
24. Grue, H.; Jensen, B., Annual cementum structures in canine teeth in arctic foxes (Alopex lagopus L.) from Greenland and Denmark. *Danish Rev. Game Biol* **1976,** *10*, 1-12.
25. Eide, N. E.; Stien, A.; Prestrud, P.; Yoccoz, N. G.; Fuglei, E., Reproductive responses to spatial and temporal prey availability in a coastal Arctic fox population. *Journal of Animal Ecology* **2012,** *81*, (3), 640-648.
26. Powley, C. R.; George, S. W.; Ryan, T. W.; Buck, R. C., Matrix Effect-Free Analytical Methods for Determination of Perfluorinated Carboxylic Acids in Environmental Matrixes. *Analytical Chemistry* **2005,** *77*, (19), 6353-6358.
27. Hanssen, L.; Dudarev, A. A.; Huber, S.; Odland, J. Ø.; Nieboer, E.; Sandanger, T. M., Partition of perfluoroalkyl substances (PFASs) in whole blood and plasma, assessed in maternal and umbilical cord samples from inhabitants of arctic Russia and Uzbekistan. *Science of The Total Environment* **2013,** *447*, (0), 430-437.
28. Lecomte, N.; Ahlstrøm, Ø.; Ehrich, D.; Fuglei, E.; Ims, R. A.; Yoccoz, N. G., Intrapopulation Variability Shaping Isotope Discrimination and Turnover: Experimental Evidence in Arctic Foxes. *PLoS ONE* **2011,** *6*, (6), e21357.
29. Ehrich, D.; Tarroux, A.; Stien, J.; Lecomte, N.; Killengreen, S.; Berteaux, D.; Yoccoz, N. G., Stable isotope analysis: modelling lipid normalization for muscle and eggs from arctic mammals and birds. *Methods in Ecology and Evolution* **2011,** *2*, (1), 66-76.

30. Kelly, J. F., Stable isotopes of carbon and nitrogen in the study of avian and mammalian trophic ecology. *Canadian Journal of Zoology* **2000,** *78*, (1), 1-27.
31. McNaught, A. D.; Wilkinson, A., *Compendium of chemical terminology*. Blackwell Science Oxford: 1997; Vol. 1669.
32. Bates, D.; Maechler, M.; Bolker, B., lme4: Linear mixed-effects models using S4 classes. R package version 0.999375-39. *R Foundation for Statistical Computing, Vienna, Austria* **2011**.
33. Burnham, K. P.; Anderson, D. R., *Model selection and multimodel inference: a practical information-theoretic approach*. Springer: 2002.
34. Hadfield, J.; Nakagawa, S., General quantitative genetic methods for comparative biology: phylogenies, taxonomies and multi-trait models for continuous and categorical characters. *Journal of evolutionary biology* **2010,** *23*, (3), 494-508.
35. Zuur, A. F.; Ieno, E. N.; Elphick, C. S., A protocol for data exploration to avoid common statistical problems. *Methods in Ecology and Evolution* **2010,** *1*, (1), 3-14.
36. Bytingsvik, J.; van Leeuwen, S. P. J.; Hamers, T.; Swart, K.; Aars, J.; Lie, E.; Nilsen, E. M. E.; Wiig, Ø.; Derocher, A. E.; Jenssen, B. M., Perfluoroalkyl substances in polar bear mother–cub pairs: A comparative study based on plasma levels from 1998 and 2008. *Environment International* **2012,** *49*, (0), 92-99.
37. Verreault, J.; Berger, U.; Gabrielsen, G. W., Trends of Perfluorinated Alkyl Substances in Herring Gull Eggs from Two Coastal Colonies in Northern Norway: 1983–2003. *Environmental Science & Technology* **2007,** *41*, (19), 6671-6677.
38. Rigét, F.; Bossi, R.; Sonne, C.; Vorkamp, K.; Dietz, R., Trends of perfluorochemicals in Greenland ringed seals and polar bears: Indications of shifts to decreasing trends. *Chemosphere* **2013,** *93*, (8), 1607-1614.
39. Conder, J. M.; Hoke, R. A.; Wolf, W. d.; Russell, M. H.; Buck, R. C., Are PFCAs Bioaccumulative? A Critical Review and Comparison with Regulatory Criteria and Persistent Lipophilic Compounds. *Environmental Science & Technology* **2008,** *42*, (4), 995-1003.
40. Bustnes, J. O.; Borgå, K.; Erikstad, K. E.; Lorentsen, S.-H.; Herzke, D., Perfluorinated, brominated, and chlorinated contaminants in a population of lesser black-backed gulls (Larus fuscus). *Environmental Toxicology and Chemistry* **2008,** *27*, (6), 1383-1392.
41. Gebbink, W. A.; Letcher, R. J., Comparative tissue and body compartment accumulation and maternal transfer to eggs of perfluoroalkyl sulfonates and carboxylates in Great Lakes herring gulls. *Environmental Pollution* **2012,** *162*, (0), 40-47.
42. Kelly, B. C.; Ikonomou, M. G.; Blair, J. D.; Surridge, B.; Hoover, D.; Grace, R.; Gobas, F. A. P. C., Perfluoroalkyl Contaminants in an Arctic Marine Food Web: Trophic Magnification and Wildlife Exposure. *Environmental Science & Technology* **2009,** *43*, (11), 4037-4043.
43. Ng, C. A.; Hungerbühler, K., Bioconcentration of Perfluorinated Alkyl Acids: How Important Is Specific Binding? *Environmental Science & Technology* **2013,** *47*, (13), 7214-7223.
44. Ng, C. A.; Hungerbühler, K., Bioaccumulation of Perfluorinated Alkyl Acids: Observations and Models. *Environmental Science & Technology* **2014,** *48*, (9), 4637-4648.
45. Zhang, L.; Ren, X.-M.; Guo, L.-H., Structure-Based Investigation on the Interaction of Perfluorinated Compounds with Human Liver Fatty Acid Binding Protein. *Environmental Science & Technology* **2013,** *47*, (19), 11293-11301.

46. Armitage, J. M.; Arnot, J. A.; Wania, F.; Mackay, D., Development and evaluation of a mechanistic bioconcentration model for ionogenic organic chemicals in fish. *Environmental Toxicology and Chemistry* **2013,** *32*, (1), 115-128.
47. Jones, P. D.; Hu, W.; De Coen, W.; Newsted, J. L.; Giesy, J. P., Binding of perfluorinated fatty acids to serum proteins. *Environmental Toxicology and Chemistry* **2003,** *22*, (11), 2639-2649.
48. Chen, Y.-M.; Guo, L.-H., Fluorescence study on site-specific binding of perfluoroalkyl acids to human serum albumin. *Arch Toxicol* **2009,** *83*, (3), 255-261.
49. Hebert, P. C.; MacManus-Spencer, L. A., Development of a Fluorescence Model for the Binding of Medium- to Long-Chain Perfluoroalkyl Acids to Human Serum Albumin Through a Mechanistic Evaluation of Spectroscopic Evidence. *Analytical Chemistry* **2010,** *82*, (15), 6463-6471.
50. Yang, C. H.; Glover, K. P.; Han, X., Characterization of cellular uptake of perfluorooctanoate via organic anion-transporting polypeptide 1A2, organic anion transporter 4, and urate transporter 1 for their potential roles in mediating human renal reabsorption of perfluorocarboxylates. *Toxicological sciences : an official journal of the Society of Toxicology* **2010,** *117*, (2), 294-302.
51. Zhang, Y.; Beesoon, S.; Zhu, L.; Martin, J. W., Biomonitoring of Perfluoroalkyl Acids in Human Urine and Estimates of Biological Half-Life. *Environmental Science & Technology* **2013,** *47*, (18), 10619-10627.
52. Van de Vijver, K. I.; Hoff, P. T.; Das, K.; Van Dongen, W.; Esmans, E. L.; Jauniaux, T.; Bouquegneau, J.-M.; Blust, R.; De Coen, W., Perfluorinated Chemicals Infiltrate Ocean Waters: Link between Exposure Levels and Stable Isotope Ratios in Marine Mammals. *Environmental Science & Technology* **2003,** *37*, (24), 5545-5550.
53. Kannan, K.; Perrotta, E.; Thomas, N. J., Association between Perfluorinated Compounds and Pathological Conditions in Southern Sea Otters. *Environmental Science & Technology* **2006,** *40*, (16), 4943-4948.
54. Persson, S.; Rotander, A.; Kärrman, A.; van Bavel, B.; Magnusson, U., Perfluoroalkyl acids in subarctic wild male mink (Neovison vison) in relation to age, season and geographical area. *Environment International* **2013,** *59*, (0), 425-430.
55. Fuglei, E.; Øritsland, N. A., Seasonal trends in body mass, food intake and resting metabolic rate, and induction of metabolic depression in arctic foxes (Alopex lagopus) at Svalbard. *J Comp Physiol B* **1999,** *169*, (6), 361-369.
56. Polischuk, S. C.; Norstrom, R. J.; Ramsay, M. A., Body burdens and tissue concentrations of organochlorines in polar bears (Ursus maritimus) vary during seasonal fasts. *Environmental Pollution* **2002,** *118*, (1), 29-39.
57. Jing, P.; Rodgers, P. J.; Amemiya, S., High Lipophilicity of Perfluoroalkyl Carboxylate and Sulfonate: Implications for Their Membrane Permeability. *Journal of the American Chemical Society* **2009,** *131*, (6), 2290-2296.
58. Goecke-Flora, C. M.; Reo, N. V., Influence of Carbon Chain Length on the Hepatic Effects of Perfluorinated Fatty Acids. A 19F- and 31P-NMR Investigation. *Chemical Research in Toxicology* **1996,** *9*, (4), 689-695.
59. Kudo, N.; Suzuki, E.; Katakura, M.; Ohmori, K.; Noshiro, R.; Kawashima, Y., Comparison of the elimination between perfluorinated fatty acids with different carbon chain length in rats. *Chemico-Biological Interactions* **2001,** *134*, (2), 203-216.
60. Giesy, J. P.; Kannan, K., Peer Reviewed: Perfluorochemical Surfactants in the Environment. *Environmental Science & Technology* **2002,** *36*, (7), 146A-152A.

61. Nishimura, M.; Yaguti, H.; Yoshitsugu, H.; Naito, S.; SATOH, T., Tissue Distribution of mRNA Expression of Human Cytochrome P450 Isoforms Assessed by HighнSensitivity RealнTime Reverse Transcription PCR. *Age* **2003,** *15*, (35), 23_40.
62. Greaves, A. K.; Letcher, R. J., Linear and branched perfluorooctane sulfonate (PFOS) isomer patterns differ among several tissues and blood of polar bears. *Chemosphere* **2013,** *93*, (3), 574-580.
63. Hundley, S. G.; Sarrif, A. M.; Kennedy, G. L., Absorption, distribution, and excretion of ammonium perfluorooctanoate (APFO) after oral administration to various species. *Drug and Chemical Toxicology* **2006,** *29*, (2), 137-145.
64. Olsen, G. W.; Burris, J. M.; Ehresman, D. J.; Froehlich, J. W.; Seacat, A. M.; Butenhoff, J. L.; Zobel, L. R., Half-Life of Serum Elimination of Perfluorooctanesulfonate, Perfluorohexanesulfonate, and Perfluorooctanoate in Retired Fluorochemical Production Workers. *Environmental Health Perspectives* **2007,** *115*, (9), 1298-1305.
65. O'Brien, J. M.; Kennedy, S. W.; Chu, S.; Letcher, R. J., Isomer-specific accumulation of perfluorooctane sulfonate in the liver of chicken embryos exposed in ovo to a technical mixture. *Environmental Toxicology and Chemistry* **2011,** *30*, (1), 226-231.
66. Reimers, E.; Ringberg, T.; Sørumgård, R., Body composition of Svalbard reindeer. *Canadian Journal of Zoology* **1982,** *60*, (8), 1812-1821.
67. Mortensen, A.; Unander, S.; Kolstad, M.; Blix, A. S., Seasonal Changes in Body Composition and Crop Content of Spitzbergen Ptarmigan Lagopus mutus hyperboreus. *Ornis Scandinavica* **1983,** *14*, (2), 144-148.
68. Atkinson, S. N.; Ramsay, M. A., The Effects of Prolonged Fasting of the Body Composition and Reproductive Success of Female Polar Bears (Ursus maritimus). *Functional Ecology* **1995,** *9*, (4), 559-567.
69. Hostetler, H. A.; McIntosh, A. L.; Atshaves, B. P.; Storey, S. M.; Payne, H. R.; Kier, A. B.; Schroeder, F., L-FABP directly interacts with PPARα in cultured primary hepatocytes. *Journal of Lipid Research* **2009,** *50*, (8), 1663-1675.
70. Grün, F.; Blumberg, B., Environmental Obesogens: Organotins and Endocrine Disruption via Nuclear Receptor Signaling. *Endocrinology* **2006,** *147*, (6), s50-s55.
71. Grün, F.; Blumberg, B., Endocrine disrupters as obesogens. *Molecular and Cellular Endocrinology* **2009,** *304*, (1–2), 19-29.

Supporting Information

Table S1. Result of model selection based on log-transformed ∑PFASs as response variable. Tissue (liver, blood, kidney, muscle and adipose tissue), body condition (lean and fat), $\delta^{15}N$ and $\delta^{13}C$, were applied as fixed effects, while individual was applied as a random effect. BC = Body condition, Df = Degrees of freedom, logLIK = logarithmic likelihoods of the fitted model, AICc = Akaike's Information Criterion corrected for small sample size.

Model	Intercept	Df	logLik	AICc	Delta	Weight
BC+ Tissue + $\delta^{15}N$	3.07400	8	-101.969	221.7	0.0	0.473
BC + Tissue + $\delta^{13}C$+ $\delta^{15}N$	6.37700	9	-101.401	223.1	1.33	0.243
BC + Tissue	1.21200	7	-104.847	225.1	3.34	0.089
BC * Tissue + $\delta^{15}N$	3.49600	12	-98.678	225.4	3.69	0.075
BC + Tissue + $\delta^{13}C$	-0.41030	8	-103.974	225.7	4.01	0.064
BC * Tissue + $\delta^{13}C$ + $\delta^{15}N$	6.79900	13	-98.066	226.9	5.20	0.035
BC * Tissue	1.63400	11	-101.767	228.9	7.20	0.013
BC * Tissue + $\delta^{15}N$	0.01213	12	-100.831	229.7	8.00	0.009
Tissue + $\delta^{13}C$ + $\delta^{15}N$	9.39500	8	-109.842	237.5	15.74	0.00
Tissue + $\delta^{15}N$	2.45400	7	-111.995	239.4	17.64	0.00
Tissue	0.80350	6	-113.854	240.7	19.00	0.00
Tissue + $\delta^{13}C$	0.33750	7	-113.794	243.0	21.24	0.00
BC	2.97200	3	-169.608	345.5	123.78	0.00
BC + $\delta^{15}N$	4.83400	4	-168.942	346.4	124.64	0.00
BC + $\delta^{13}C$	1.35000	4	-169.403	347.3	125.56	0.00
-	2.56400	2	-171.913	348.0	126.25	0.00
BC + $\delta^{13}C$ + $\delta^{15}N$	8.13700	5	-168.814	348.3	126.63	0.00
$\delta^{15}N$	4.21400	3	-171.409	349.1	127.38	0.00
$\delta^{13}C$	2.09800	3	-171.896	350.1	128.36	0.00
$\delta^{13}C$ + $\delta^{15}N$	11.16000	4	-170.844	350.2	128.44	0.00