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Distribution of persistent organic pollutants in two different fat compartments from obese individuals

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ABSTRACT

There are only few studies defining persistent organic pollutant (POP) concentrations in various fat compartments from living obese individuals. The present study has therefore determined the concentrations of various classes of organohalogenated compounds, such as dichlorodiphenyltrichloroethane and its metabolites (DDTs), chlordane compounds (CHLs), hexachlorocyclohexanes (HCHs), hexachlorobenzene (HCB), polychlorinated biphenyls (PCBs), polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDs) in visceral fat (VF: $n = 52$) and subcutaneous abdominal fat (SF: $n = 52$) samples collected in 2010–2012 from obese individuals in Belgium. Organohalogen compounds were detected in all fat samples in the decreasing order of their concentrations: PCBs > DDTs > HCHs > CHLs > HCB > HBCDs > PBDEs, suggesting that Belgians have been widely exposed to these contaminants. The levels and the patterns of POP distribution in VF and SF tissue depots were not significantly different. Concentrations of PCBs (VF/SF; median: 285/275 ng/g lw) and DDTs (VF/SF; median: 150/155 ng/g lw) were the major POPs in all fat samples. Concerning PCBs, PCB 153 (VF/SF: 27/26%) was the most dominant congener, followed by PCB 180 (VF/SF: 17/18%), PCB 138 (VF/SF: 15/14.5%) and PCB 170 (VF/SF: 8.1/8.4%) to the sum PCBs, respectively. Levels of HBCDs (VF/SF; median: 4.0/3.7 ng/g lw) and PBDEs (VF/SF; median: 2.6/2.7 ng/g lw) were 1–2 orders of magnitude lower than those of PCBs and DDTs. Among PBDEs, BDE 153 (VF/SF: 31/34%) was the dominant congener, followed by BDE 47 (VF/SF: 26/23%), BDE 154 (VF/SF: 16/16%), BDE 100 (VF/SF: 10/11%) and BDE 99 (VF/SF: 9/9%). To our knowledge, this is the first report on HBCD concentrations in Belgian human fat tissues. Total PBDE and HBCD levels in human fat samples could not be correlated with age. In agreement with the literature, a significant correlation ($p < 0.05$) between age and the concentration of PCBs ($r = 0.828$), DDTs ($r = 0.640$), HCHs ($r = 0.666$), CHLs ($r = 0.534$) and HCB ($r = 0.754$), was observed in the present study. Levels of DDTs, HCHs, HCB and CHLs were also significantly correlated to each other, suggesting that they share similar exposure routes. Correlation with computed tomography (CT) scan data revealed that VF and VF/SF ratios are positive for most of the POPs, such as PCBs, PBDEs, *p,p′*DDE, CHLs, β-HCH, and HCB. To our knowledge, this study is the first to assess the relationship between POP levels in adipose tissue and markers of abdominal adiposity, determined by CT.

1. Introduction

Persistent organic pollutants (POPs) are highly lipophilic chemicals that bioaccumulate in animal and human adipose tissues (Mullerova and Kopecky, 2007). Concentrations of organochlorines (OCs), including polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs), have generally been decreasing in the environment and in humans during the past few decades due to the decline of their use and production (Jones and de Voogt, 1999). Most studies on the other chemicals, brominated flame retardants (BFRs), have been primarily focused on two groups: polybrominated diphenyl ethers (PBDEs) and hexabromocyclododecanes (HBCDs) (Covaci et al., 2011). In recent years, strict bans have been imposed on the worldwide use of Penta- and Octa-BDE formulations and components of these mixtures have been added to the POP list of the Stockholm Convention (Ashton et al., 2009). HBCDs enter the environment mostly during the use of consumer products and consist mainly of three diastereomers; α-, β-, and γ-HBCD, which have different proportions in the consumer products, environment and organisms (Covaci et al., 2006). HBCD is now regulated in Canada (Canada Gazette, 2010) and U.S. (US EPA, 2010). The POPs Review Committee (POPRC) has just completed reviewing process of the risk profile of HBCDs. Consequently, HBCD is on the candidate POP list of the

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Stockholm Convention (HBCD, 2012 www.pops.int). Despite regulations, BFRs continue to leach from existing products that are in service or have been disposed of in landfills. For the non-occupationally exposed population to BFRs, recent studies have indicated that human exposure occurs mainly via a combination of diet, ingestion of indoor dust, and inhalation of indoor air (Harrad et al., 2010; Roosens et al., 2009). The exact contribution of these pathways varies substantially on a compound-specific basis, between individuals and within national populations (Covaci et al., 2011; Roosens et al., 2009).

Overweight and obesity are defined as abnormal or excessive fat accumulation that may impair health (WHO, 2012). It was also shown that obesity is associated with increased cardiovascular mortality, independent of dyslipidemia, diabetes and hypertension (Calle et al., 1999). The body has several depots of white adipose tissue, of which the major two categories are subcutaneous and visceral fat. It is known that visceral fat correlates better with the development of insulin insensitivity and the metabolic syndrome, most probably related to a greater glucose uptake (Christen et al., 2010) and inflammation (Neels and Olefsky, 2006).

There is increasing evidence that central adiposity is more strongly associated with these metabolic and cardiovascular problems than total adiposity (Folsom et al., 2000). The functional profile of a visceral fat cell differs from that of a subcutaneous fat cell. Whereas visceral adipocytes produce more pro-inflammatory cytokines, subcutaneous adipocytes produce more nutrient-state-sensing cytokines (Wronska and Kmiec, 2012).

Chemicals that are stored in lipid-rich compartments have the potential for long-term disruption of metabolic and endocrine processes and POPs have been proposed to contribute to the obesity epidemic (Dirinck et al., 2011; Yu et al., 2011). Given the evidence that POPs might alter systemic metabolic, endocrine, and immune system functions, it implies that elevated chemical concentrations in abdominal fat may alter function of visceral organs through local chemical signaling (Yu et al., 2011). Obese individuals vary in their body fat distribution, their metabolic profile and the degree of associated cardiovascular and metabolic risks (Van Gaal et al., 2006). Yet, there are only few studies defining POP concentrations in intra-abdominal fat from living humans.

Human specimens, such as breast milk, serum and adipose tissue have been used in biomonitoring the extent of human exposure to organohalogen contaminants (Covaci et al., 2008; Hardell et al., 2006). It is uncertain whether POPs distribute equally to all fat compartments, including visceral and subcutaneous fat. The primary objective of this study was to investigate the current levels of POPs such as PCBs, OCPs, PBDEs and HBCDs in two fat compartments, namely visceral and subcutaneous fat, from living obese individuals in Belgium. Specific objectives include: 1) to enhance the knowledge on these contaminant concentrations, their patterns, distribution profiles, and relationships between age and visceral and subcutaneous abdominal fat samples and 2) to compare for the first time the relationship between POP levels in visceral and subcutaneous adipose tissues and markers of abdominal adiposity, determined by computed tomography (CT) scan.

2. Materials and methods

2.1. Sample collection

We report data on 52 patients who underwent bariatric surgery. These patients were prospectively selected out from a larger cohort participating in a study exploring the role of POPs and endocrine disruption in obesity (ENDORUP trial, registered at clinicaltrials.gov, number NCT01778868). This trial was approved by the Ethical Committee of the Antwerp University Hospital Belgian Registry number B30020097009. All these subjects initially visited the weight management clinic of the Department of Endocrinology, Diabetology and Metabolism of the Antwerp University Hospital between November 2009 and February 2012. The participants gave their written informed consent and agreed to provide adipose tissue samples at the time of bariatric surgery. Patients were all eligible candidates for bariatric surgery according to the following criteria: 1) BMI $\geq$ 40 kg/m^2 with or without co-morbidities; and 2) BMI $\geq$ 35 kg/m^2 with any of these co-morbidities (diabetes mellitus; obstructive sleep apnea; arterial hypertension, insufficiently controlled under three antihypertensive drugs). All patients but one male underwent gastric bypass surgery. One female patient underwent gastric banding. During surgery, paired visceral ($n = 52$) and subcutaneous ($n = 52$) abdominal fat samples were obtained. All age groups were $\geq$18 years (male 18–48; female 18–57). Participant's age, gender, extractable lipids, their demographic characterizes and relevant information's are listed in Table 1.

2.2. Physical measurements

All anthropometric measures were taken in the morning with patients in a fasting state and undressed. At that time, they have also donated serum and urine samples. Height was measured to the nearest 0.5 cm and body weight was measured with a digital scale to the nearest 0.1 kg. Obesity was defined as a BMI $\geq$ 30 kg/m^2. Waist circumference was measured at the mid-level between the lower rib margin and the iliac crest. Hip circumference was measured at the level of the trochanter major and the waist-to-hip ratio was calculated. Body composition was determined by bioimpedance analysis as described by previous methods (Lukaski and Bolonchuk, 1988), and fat mass % was calculated using the formula as described by previous methods (Deurenberg et al., 1989). A computed tomography (CT) scan at the L4–L5 level was performed to measure the amount of total visceral abdominal adipose tissue, and subcutaneous adipose tissue according to previously described methods (Van der Kooy and Seidell, 1993).

2.3. Chemical analysis

The following OCs were targeted: 28 PCB congeners (IUPAC nrs. 28, 52, 74, 95, 99, 101, 105, 118, 149, 146, 153, 138, 187, 183, 128, 167, 174, 177, 171, 172, 156, 180, 170, 199, 196/203, 194, 206 and 209), dichlorodiphenyltrichloroethane (DDT) and its metabolites, two chlordanes (oxychlordane (OxC) and transnonachlor (TN)), three hexachlorocyclohexane isomers (α-, β-, and γ-HCH), hexachlorobenzene (HCB), PBDEs (BDE 28, 47, 99, 100, 153, 154 and 183) and HBCDs (α-, β-, and γ-HBCD isomers). Analyses of OCs in visceral and subcutaneous abdominal fat samples were performed according to the methods described elsewhere (Covaci et al., 2008; Roosens et al., 2010), with

Table 1
General demographic characteristics of the subjects.

N	Men[a]	Women[a]
	18	34
Age	40 (18–58)	39 (18–57)
Height (m)	1.8 (1.6–1.9)	1.6 (1.5–1.8)
Weight (kg)	132 (108–170)	113 (91–154)
BMI (kg/m^2)	42 (36–48)	42 (36–51)
Waist (cm)	131 (117–148)	119 (98–150)
Hip (cm)	123 (110–145)	129 (106–150)
Waist-to-hip ratio	1.1 (1.0–1.2)	0.93 (0.73–1.1)
Total fat mass (%)	45 (32–54)	54 (46–62)
Total adipose tissue (cm^2)	913 (540–1151)	889 (657–1334)
CT — visceral fat (%)	26 (7.9–43)	22 (6.6–47)
CT — subcutaneous fat (%)	74 (57–92)	78 (53–93)
Visceral fat/subcutaneous fat ratio	0.39 (0.086–0.76)	0.31 (0.071–0.90)

[a] The results are presented as median with minimal and maximum values.