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Circulating levels of persistent organic pollutants are related to retrospective assessment of life-time weight change

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HIGHLIGHTS

- ▶ We examined associations between POP levels in human plasma and body weight.
- ▶ Body weight at age 70 was measured and participants reported their estimated weight at age 20.
- ▶ OC pesticides and less-chlorinated PCBs were associated with an increased estimated weight change over 50 years.
- ▶ The opposite was seen for highly-chlorinated PCBs.
- ▶ The results implicate a complex role of POPs in obesity.

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ABSTRACT

Background: Persistent organic pollutants (POPs) have been suggested to be linked to obesity. We have previously shown that less-chlorinated PCBs were positively related to fat mass, while highly-chlorinated PCBs were inversely related to obesity.
Objective: The aim of the present evaluation is to investigate the relationship between retrospective assessed life-time change in body weight (20–70 years) with circulating POP levels measured at age 70 years.
Methods: 1016 subjects aged 70 years were investigated in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUSs) study. 16 PCBs and 3 OC pesticides were analyzed using HRGC/HRMS. Current body weight was measured and participants self-reported their weight at age 20.
Results: The average estimated weight change over 50 years was 14.4 kg. Both the sum of OC pesticide concentrations (4.3 kg more weight gain in quintile 5 vs. quintile 1, $p < 0.0001$) and the sum of the less-chlorinated PCBs were positively related to the estimated weight change (3.7 kg more weight gain in quintile 2 vs. quintile 1, non-linear relationship $p = 0.0015$). In contrast, the sum of concentrations of highly-chlorinated PCBs were inversely related to estimated weight change (8.4 kg less weight gain in quintile 5 vs. quintile 1, $p < 0.0001$).
Conclusion: High levels of OC pesticides and the less-chlorinated PCBs at age 70 were associated with a pronounced estimated weight change over the previous 50 years. However, the opposite was seen for highly-chlorinated PCBs. Differences in mode of action, toxicokinetics, non-linear relationships and reverse causation might explain these discrepancies.

Abbreviations: BDE, brominated diphenyl ether; BMI, body mass index; DDE, dichlorodiphenyldichloroethylene; DXA, dual-energy X-ray absorptiometry; HCB, hexachlorobenzene; HRGC/HRMS, high resolution chromatography coupled with high resolution mass spectrometry; OC, organochlorine; OCDD, octachlorodibenzo-p-dioxin; PIVUS, prospective Investigation of the Vasculature in Uppsala Seniors; PCBs, polychlorinated biphenyls; POPs, persistent organic pollutants; TNC, transnonachlordane.

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1. Introduction

The prevalence of obesity (BMI $\geqslant$ 30 kg m^{-2}) has risen dramatically in the Western world over the past two decades. In 2007–2008, 32% of adult men and 35.5% of adult women in the US were obese (Flegal et al., 2010). Obesity causes adverse effects on quality of life while also predisposing individuals to a number of diseases including type 2 diabetes and cardiovascular disease. It has recently been shown that the risk of diabetes over a 20 year period was 15-fold increased in obese vs. lean middle-aged subjects (Arnlov et al., 2011). In addition it has also shown that obesity increased the risk of cardiovascular disease even in the absence of diabetes and other metabolic derangements (Arnlov et al., 2011).

Obesity is caused by complex interactions among genetic, behavioral and environmental factors. Many researchers see obesity mainly as an unfavorable balance between a high energy intake and reduced energy expenditure due to inadequate exercise. However, recent research has suggested that environmental contaminants could play an important role in modulating the balance between energy intake and expenditure (Janesick and Blumberg, 2011). It was shown in animal studies that mice exposed prenatally to tributyltin (TBT) showed increased body-weight later in life; therefore, the term "obesogens" was coined (Grun and Blumberg, 2006). This observation supports the emerging hypothesis of fetal programming as a source of certain disorders, such as obesity and diabetes, later in life (Barker et al., 2002). In addition to fetal programming, exposure to certain chemicals in adulthood may also be important. Adult rats given salmon oil contaminated with background levels of persistent organic pollutants (POPs) became obese (Ruzzin et al., 2010), and pharmaceuticals, such as the anti-diabetic drug rosiglitazone (ROSI) acting on the important receptor peroxisome proliferator-activated receptor-gamma (PPAR-γ) increase body fat when given to adult humans (Houtkooper and Auwerx, 2010). Moreover, it was recently shown that thiazide antihypertensive agents induce visceral obesity and insulin resistance (Eriksson et al., 2008). Thus, it is likely that adult as well as early life exposure to environmental contaminants could be important for the development of obesity and diabetes.

We have recently shown that in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUSs) study less-chlorinated PCBs (congeners $\leqslant$ 153) and organochlorine (OC) pesticides were positively related to fat mass, while highly-chlorinated PCBs (congeners $\geqslant$ 156) were inversely related to obesity when evaluated in a cross-sectional fashion (Rönn et al., 2011). Furthermore, the same pattern was found in the same cohort evaluated regarding the predictive power of POPs in relation to the development of abdominal obesity over a 5 year period in the same cohort (Lee et al., 2012). We have speculated that diverging effects of different PCBs could be either due to unique actions of different PCBs, or that the storage of PCBs in fat might differ amongst the PCBs. To investigate this further, the aim of the present evaluation is to investigate the relationship between retrospective assessments in life-time change in body weight (20–70 years) with circulating POP levels measured at age 70 years.

2. Materials and methods

2.1. Subjects

Eligible subjects were all aged 70 who lived in the community of Uppsala, Sweden. The subjects were randomly chosen from the community register. A total of 1016 subjects participated (investigated in between 2001 and 2004), giving a participation rate of 50.1%. The study was approved by the Ethics Committee of the University of Uppsala.

All subjects were investigated in the morning after an overnight fast. No medication or smoking was allowed after midnight. The participants were asked to answer a questionnaire about their medical history, smoking habits and regular medication. Furthermore, they were asked to report their body weight and height at age 20 years. The participants received the questionnaire in advance of the actual investigation, so they had time to go back to prior documents if they wanted.

Lipids were measured by standard laboratory techniques. Body weight was measured by a weight scale.

Basic characteristics are given in Table 1.

Approximately 10% of the cohort reported a history of coronary heart disease, 4% reported stroke, and 9% reported diabetes mellitus. Almost half the cohort reported some sort of cardiovascular medication (45%), with antihypertensive medication being the most prevalent (32%). Fifteen percent reported use of statins, while insulin and oral antiglycemic drugs were reported in 2% and 6%, respectively – see reference (Lind et al., 2005) for details.

2.2. POPs analyses

POPs were measured in stored serum samples collected at baseline. Analyses of POPs were performed using a Micromass Autospec Ultima (Waters, Mildford, MA, USA) high-resolution gas chromatography coupled to high resolution mass spectrometry (HRGC/HRMS) – based on the method by Sandau and co-workers (Sandau et al., 2003) with some modifications. All details on POPs analyses were presented elsewhere (Rönn et al., 2011). A total of 23 POPs were measured: 16 polychlorinated biphenyls (PCBs) congeners, five organochlorine (OC) pesticides, one octachlorodibenzo-*p*-dioxin (OCDD), and one brominated diphenyl ether (BDE) congener.

Table 1
Basic characteristics and major cardiovascular risk factors in the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUSs) study (*N* = 1016, 50.2% females).

Variables	Mean ± SD or *N* (%)	Median (range)
Height (cm)	169 ± 9.1	169 (151–190)
Weight (kg)	77 ± 14	76 (49–116)
Waist circumference (cm)	91 ± 12	90 (67–123)
BMI (kg m^{-2})	27.0 ± 4.3	26.6 (19.1–39)
Waist/hip ratio	0.90 ± 0.075	0.90 (0.73–1.08)
Systolic blood pressure (mmHg)	150 ± 23	148 (105–210)
Diastolic blood pressure (mmHg)	79 ± 10	78 (56–105)
Serum cholesterol (mmol L^{-1})	5.4 ± 1.0	5.4 (3.2–7.8)
LDL-cholesterol (mmol L^{-1})	3.3 ± 0.88	3.3 (1.4–5.6)
HDL-cholesterol (mmol L^{-1})	1.5 ± 0.42	1.4 (0.8–2.9)
Serum triglycerides (mmol L^{-1})	1.3 ± 0.60	1.15 (0.46–3.6)
Fasting blood glucose (mmol L^{-1})	5.3 ± 1.6	5 (3.8–13.5)
Current smokers *N* (%)	107 (11)	
History of myocardial infarction *N* (%)	72 (7)	
History of stroke *N* (%)	37 (4)	
History of diabetes mellitus *N* (%)	88 (9)	
Any cardiovascular medication *N* (%)	461 (45)	
Antihypertensive medication *N* (%)	317 (31)	
Statin treatment *N* (%)	149 (15)	
Insulin therapy *N* (%)	18 (2)	
Oral antiglycemic drug therapy *N* (%)	62 (6)	

BMI = body mass index.