

ehp

**ENVIRONMENTAL
HEALTH
PERSPECTIVES**

ehponline.org

**Polychlorinated Biphenyl 77 Induces
Adipocyte Differentiation and
Proinflammatory Adipokines and Promotes
Obesity and Atherosclerosis**

**Violeta Arsenescu, Razvan I. Arsenescu, Victoria King,
Hollie Swanson, and Lisa A. Cassis**

**doi:10.1289/ehp.10554 (available at <http://dx.doi.org/>)
Online 6 March 2008**



NIEHS
National Institute of
Environmental Health Sciences

National Institutes of Health
U.S. Department of Health and Human Services

Polychlorinated Biphenyl 77 Induces Adipocyte Differentiation and Proinflammatory
Adipokines and Promotes Obesity and Atherosclerosis

Violeta Arsenescu¹, Razvan I. Arsenescu², Victoria King^{1,3}, Hollie Swanson⁴, Lisa A.
Cassis¹

Graduate Center for Nutritional Sciences¹, University of Kentucky

Division of Digestive Diseases and Nutrition², University of Kentucky

Cardiovascular Research Center³, University of Kentucky

Department of Molecular and Biomedical Pharmacology⁴, University of Kentucky

Lexington, KY

Corresponding Author:

Lisa Cassis, Ph.D.
Professor and Chair
Graduate Center for Nutritional Sciences
Room 521b, Wethington Building
University of Kentucky
900 S. Limestone
Lexington, KY 40536-0200
Phone: 859-323-4933 ext 81400
Fax: 859-257-3646
email: lcassis@uky.edu

Acknowledgments: This work was supported by a grant from NIEHS (P42 ES 007380; LC). There are no competing financial interests to declare.

Running title: PCB77 Promotes Obesity-Associated Atherosclerosis

Keywords: polychlorinated biphenyl, arylhydrocarbon receptor, adipocyte differentiation, ectopic lipid deposition, obesity

Abbreviations:

AhR: Arylhydrocarbon receptor

Ao: Angiotensinogen

aP2: Adipocyte fatty acid binding protein

apolipoprotein E: apoE

DMSO: Dimethyl sulf oxide

GPDH: Glycerol-3-phosphate dehydrogenase

NF: Alpha naphthoflavone

PBS: Phosphate buffered saline

PCB: Polychlorinated biphenyl

PCB77: 3,3',4,4'-Tetrachlorobiphenyl

PCB153: 2,2',4,4,5,5'-Hexachlorobiphenyl

POP: Persistent organic pollutant

PPAR γ : Peroxisome proliferator activated receptor γ

TCDD: 2,3,7,8-tetrachlorodibenzo-p-dioxin

TNF α : Tumor necrosis factor alpha

Outline of section headers:

Abstract: Background, Objectives, Methods, Results, Conclusions

Introduction

Methods: Materials; Cell Culture and Treatment; Oil Red O Staining; Glycerol-3-Phosphate Dehydrogenase Activity; RNA Isolation and Gene Expression Using Real-Time PCR; Measurement of PCBs in Cells, Plasma and Tissue; Measurement of Adipokines in Media from Adipocytes; Animal Treatments, Sample Collection; Serum Cholesterol Measurement; Histology; Quantification of Atherosclerosis; Statistical Analysis

Results: PCB77 promotes 3T3-L1 adipocyte differentiation and the expression of proinflammatory adipokines; The concentration-dependent effects of PCB77 versus TCDD; role of the AhR; In vivo administration of PCB77 increases body weight gain in C57BL/6, but not in AhR^{-/-} mice; In vivo administration of PCB77 results in increased body weight, adipose mass, elevated serum cholesterol concentrations and increased atherosclerosis in apoE^{-/-} mice.

Discussion

References

Table 1

Table 2

Figure Legends

Figures

Abstract

Background. Obesity, an inflammatory condition linked to cardiovascular disease, is associated with expansion of adipose tissue. Highly prevalent coplanar polychlorinated biphenyls (PCBs) such as PCB77 accumulate in adipose tissue due to their lipophilicity, and would increase with obesity. However, the effects of PCBs on adipocytes, obesity and obesity-associated cardiovascular disease are unknown.

Objectives: This study examined *in vitro* and *in vivo* effects of PCB77 on adipocyte differentiation, proinflammatory adipokines, adipocyte morphology, body weight, serum lipids and atherosclerosis.

Methods. PCB77 or PCB153 were incubated with 3T3-L1 adipocytes either during differentiation, or as mature adipocytes. Concentration-dependent effects of PCB77 were contrasted to those of TCDD. For *in vivo* studies, C57BL/6 wild type or arylhydrocarbon receptor (AhR) *-/-* mice were administered vehicle or PCB77 (49 mg/kg, i.p.) and body weight gain examined. In separate studies, apoE *-/-* mice were injected with vehicle or PCB77 over a 6 week period and body weight, adipocyte size, serum lipids and atherosclerosis were examined.

Results. Low concentrations of PCB77 or TCDD increased adipocyte differentiation, GPDH activity and expression of PPAR γ , while higher concentrations inhibited adipocyte differentiation. Effects of PCB77 were abolished by the AhR antagonist, α -naphthoflavone (α -NF). PCB77 promoted the expression and release of various proinflammatory cytokines from 3T3-L1 adipocytes. Administration of PCB77 increased body weight gain in wild type, but not AhR $-/-$ mice. ApoE $-/-$ mice injected with PCB77

exhibited greater body weight, adipocyte hypertrophy, serum dyslipidemia and augmented atherosclerosis.

Conclusions. Our findings suggest that PCB77 may contribute to the development of obesity and obesity-associated atherosclerosis.