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Persistent organic pollutants and anti-thyroid peroxidase levels in Akwesasne Mohawk young adults

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Abstract

Persistent organic pollutants, such as PCBs, HCB and DDE, have been found to elicit a broad spectrum of biologic, metabolic, and immunologic responses. The potential of these pollutants to impair immune responses and trigger autoimmune disease is of growing concern, given their structural similarity to thyroid hormones and their potential to modulate the mechanisms and interfere with the binding of these hormones. We examine the relationship of different groupings of PCBs, according to chlorination and structure, and of *p,p'*-DDE and HCB to anti-thyroid peroxidase antibody, a useful tool in the evaluation of thyroid dysfunction, among 115 young adults of the Akwesasne Mohawk Nation.

Overall, eighteen participants (15.4%) had TPOAb levels above the normal laboratory reference range (23% of females, 9% of males). Among participants who were breast fed (*n*=47), those with an elevated TPOAb level had significantly higher levels of all PCB groupings, with the exception of levels of non-persistent PCBs which did not differ significantly. Levels of *p,p'*-DDE were also significantly elevated, while HCB and mirex were not higher among those with elevated TPOAb. Also, after stratifying by breast feeding status, participants who were breast fed showed significant, positive relationships between TPOAb levels and all PCB groupings, except groups comprised of non-persistent PCBs, and with *p,p'*-DDE, HCB, and mirex. No effects were evident among non-breastfed young adults.

Further studies are necessary to elucidate the site and mechanism of action of these POPs and to establish thresholds for these effects, especially among populations with background levels of toxicant exposure.

Keywords

PCBs; antithyroid peroxidase; Native American

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Introduction

Polychlorinated biphenyls (PCBs) and other persistent organic pollutants (POPs), such as hexachlorobenzene (HCB), and *p,p'*-dichlorophenyldichloroethylene (*p,p'*-DDE), a metabolite of *p,p'*-DDT, have been found to elicit a broad spectrum of biologic, metabolic, and immunologic responses (ATSDR, 2000; Hagmar, 2003; Safe, 2001; Safe, 2000). The potential of these POPs to impair immune responses and trigger autoimmune disease is of growing concern. Given the structural similarity to thyroid hormones, PCBs (and/or their biphenylol metabolites) may mimic thyroid hormone action and even modulate the mechanisms and interfere with the binding of these hormones (Langer et al., 2007; Meeker et al., 2007; Zoeller, 2007; Zoeller, 2001), potentially leading to thyroid functional disorders and autoimmune thyroid diseases (Barsano, 1981; Murai et al., 1987).

Autoantibodies to thyroid peroxidase (TPOAb) can attack the thyroid and damage thyroid function (Larsen et al., 2003). While not a test of thyroid function, serum TPOAb titers are useful as a biomarker of thyroid dysfunction, as well as a diagnostic tool for many idiopathic autoimmune diseases such as chronic thyroiditis (Langer et al., 1998; Langer et al., 2007), Hashimoto's encephalopathy (Mocellin et al., 2007), Grave's disease (Antonelli et al., 2006), systemic lupus erythematosus (Kohn et al., 1989), and connective tissue disorders such as Sjogren syndrome (Tunc et al., 2004) and rheumatoid arthritis (Lee et al., 2007). The likelihood of damage appears to be greater in females, and increases with age (Antonelli et al., 2006; Lee et al., 2007).

Autoimmune dysfunction is thought to disrupt normal hypothalamic-pituitary-gonadal function and thereby affect reproductive outcomes, such as an increased risk of pregnancy loss (Djursing et al., 1982; Gleicher et al., 1993; Kjaer et al., 1992), and has been linked to the impairment of female fecundity even before the diseases become clinically overt (Nelson et al., 1993). Elevated TPOAb levels have been linked to autoimmune hypo- and hyperthyroidism in pregnancy, immune mediated miscarriages, and an increased risk for postpartum thyroiditis (Adcock et al., 1994; Matarese et al., 2003).

Here we examine the relationship of different PCB groupings, according to chlorination level and substitution pattern, along with *p,p'*-DDE and HCB, to anti-thyroid peroxidase antibody among young adults of the Akwesasne Mohawk Nation.

Methods

Sample

The study was conducted with young adults of the Akwesasne Mohawk Nation (AMN) which is situated on the St. Lawrence River with territory in New York State, Ontario and Quebec, Canada. Residents of the community live within the boundaries of the AMN and in neighboring communities that are part of traditional Mohawk territory, including Bombay, Fort Covington, Hogansburg, Massena, Rooseveltown (NY), and in Cornwall, Ontario. Akwesasne is not a federally censused population; therefore, published estimates of the Akwesasne community's population size vary. Recent reports indicate a population of approximately 12,000–13,000 (Akwesasne Task Force On The Environment, 1997; Fitzgerald et al., 1998; George-Kanentiio, 1995).

Industrial development along the St. Lawrence River began in the 1950s, and several industrial complexes are located near Akwesasne. A National Priority Superfund Site (General Motors Central Foundry Division), and two New York State Superfund Sites (Reynolds Metal Company and Aluminum Company of America) are located upstream of AMN. These three sites, all aluminum foundries, have contaminated the St. Lawrence River and its three

tributaries, and PCBs, *p,p'*-DDE, HCB and mire have entered the local food chain. Some local species of fish, birds, amphibians and mammals were found to have levels exceeding the US Food and Drug administration's tolerance limits for human consumption (Forti et al., 1995; Sloan and Jock, 1990), leading to the issuance of fish and game advisories in the late 1980s and early 1990s (Fitzgerald et al., 1995, 1998). Subsequently, studies of PCB levels in breast milk reported a decrease in levels consistent with adherence to the advisories and reduced fish consumption (Fitzgerald et al., 2001).

This sample is a follow-up of participants in our earlier project, the Mohawk Adolescent Well Being study (MAWBs) conducted between 1995 and 2000, involving 271 youth between the ages of 10 and 16.99 years, with approximately equal numbers of males and females (Schell et al., 2003). Persons were excluded from the MAWBS sample if they were not a singleton birth, had been diagnosed with a psychological or physical impairment or had been diagnosed with fetal alcohol syndrome or effects (related to the cognitive assessment portion of the study and not reported here).

Young adults were eligible for the current study if they had participated in MAWBs, and were now between 17 and 20 years of age. More than half of the participants (51%) were seen within 6 months of their 17th birthday. Participants in MAWBS were not recruited for the current study if they were outside the target age range, were pregnant, had delivered a child, or had lactated in the last 6 months. They could be included 6 months after the last of those events. Of the MAWBs participants who were eligible, 25% were lost to follow-up and 9% refused, leaving 66% who participated in the current study for a sample of 151 individuals. Reasons for refusal included having moved out of the area, being pregnant, having miscarried within the past six months, and did not have time. In addition, we excluded persons from the analysis if they were on any medication that could interfere with normal thyroid function, including medications for thyroid disease and birth control. Thirty four females were on hormonal birth control at the time the blood sample was drawn, and two were currently taking a medication for a diagnosed thyroid disorder; these participants were selected out of the analysis. Additionally, two participants had missing toxicant levels and were also excluded from the analysis for a final sample size of 115.

Data Collection

The University at Albany, State University of New York's Institutional Review Board approved all study protocols and informed consent. Additionally, assent from minors was obtained from all participants.

Members of the Akwesasne community collected all data without prior knowledge of participants' exposure status. Each young adult participant completed interviews and questionnaires, in consultation with their mother, to provide information about their family background including prescription and over-the-counter medicine use, as well as their diet, breastfeeding history (recorded as any or none), sex (males =0, females =1), age (when blood was drawn), educational status (as the highest year of education completed), current cigarette and alcohol use, body mass index, weight (kg), height (cm) and an index of material well-being as a proxy for socioeconomic status, calculated from maternal education, employment and living environment.

Fasting blood specimens were collected at first rising by trained Mohawk staff and provided material for analysis of five toxicants (lead, PCBs, *p,p'*-DDE, HCB, and mirex), and thyroid hormones. PCB and organochlorine pesticide analyses were conducted at the University at Albany's Exposure Assessment Laboratory. Complete details of the current laboratory protocol for PCB analysis and recent data on laboratory performance have been published (DeCaprio et al., 2000,2005). In brief, high resolution, ultratrace, congener-specific analysis was

performed by parallel dual-column (splitless injection) gas chromatography with electron capture detection on an Agilent 6890 instrument. This method quantitates up to 83 individual PCB congeners and 18 PCB congeners as pairs or triplets, as well as *p,p'*-DDE, HCB, and mirex, with detection limits in the low ppt range for individual congeners. Data were expressed on a whole-weight basis (*i.e.*, not lipid-adjusted). Individual chlorinated biphenyl (CB) congeners are identified according to the IUPAC numbering system (Ballschmiter and Zell, 1980; Guitart et al., 1993)

Assessment of TSH, T3, FT3, T4, FT4, and TPOAb levels was performed at the clinical laboratories of the Albany Medical Center in Albany, NY, a New York State and CLIA accredited laboratory meeting all proficiency requirements.

Statistical Analysis

Many of the PCB congeners were detected in only a portion of the sample. Any individual datum of an organochlorine (OC) that was below the minimum detection level (mdl) was substituted with the midpoint value between zero and the mdl of each compound or congener (mdl/2). This substitution approach has been used consistently in our other reports on this sample (Schell et al., 2003). Furthermore, using mdl/sqrt2 instead of mdl/2 for imputing values of the non-detected observations of the congeners used in this analysis changed the mean by no more than 1/1,000 of a ppb. Utilizing the mdl/2 substitution approach, we calculated PCB summary variables for each participant. Fourteen PCB congeners detected in greater than 50% of the sample were grouped into three categories (Table 1): all 14 PCB congeners (Σ PCB50%); nine persistent PCB congeners (Σ PERPCB9) and five non-persistent congeners (Σ NONPER5). Persistent PCBs are congeners with long (years) physiological half lives in humans, which generally are higher chlorinated and substituted at both *para* positions (Brown, Jr., 1994; Hansen, 1998). While some investigators include CB 87 among the persistent congeners (Hansen, 1998), here it is classified as non-persistent since data suggest that it is fairly readily metabolized in humans (Brown, Jr., 1994). From a toxicological view, both the degree of chlorination and chlorination pattern of individual PCB congeners are important. Therefore, we grouped PCB congeners with >20% detection rate according to structure and mechanism using only those congeners (Table 1). The sums of individual levels of mono-*ortho* (Σ MonoPCBs), di-*ortho* (Σ DioPCBs), and tri/tetra-*ortho* (Σ TriPCBs) substituted PCBs were generated according to structure. Three mechanism-based groupings were also created according to Wolff et al. (1997): potentially estrogenic congeners, potentially antiestrogenic, immunotoxic, and dioxin-like congeners, and CYP1A and CYP2B inducers (Σ Wolff1-3). Finally, a UPD-GT inducing-based grouping (Σ EnzPCBs) was generated (Chevrier et al., 2007).

The laboratory protocol for determining TPOAb levels changed once during the course of the study. The change in protocols resulted in two sets of results with different reference ranges for elevated TPOAb level. To standardize the two sets of results, each observation was expressed as a z-score relative to the mean and standard deviation of the values obtained with the relevant laboratory protocol. After standardization the two sets of results were combined. Raw values were not used in any analysis.

All statistical analyses were conducted with SPSS v.15 (SPSS, 2001). Descriptive statistics were calculated to determine the characteristics of the sample; t-tests, and bivariate correlations were examined to determine relationships, if any, between TPOAb and any of the PCB groupings or other toxicants. Finally, multivariate regression analysis was performed to examine the effect of each toxicant on TPOAb while controlling for covariates and stratifying by breastfeeding status. Covariates were chosen on the basis of bivariate associations ($p < 0.1$, t-tests and correlations) with TPOAb and/or PCBs.

Results

The median age of participants was 17.6 years of age; 48% were females (61 males, 57 females). Forty seven participants were breast fed. The mean duration of breast feeding was 2.5 months (sd = 4.4 months). Thyroid hormone levels are described in Table 2. Nineteen participants (16%) had fT3 levels below the laboratory reference range; none had elevated levels. Of these 19, one participant had both fT4 and T4 levels below the laboratory reference range; one participant had elevated T4 and a TSH level below the reference range, and one had elevated TSH and TPOAb levels, and a T4 level below the reference range. Overall, eighteen participants (15.4%) had TPOAb levels above the normal laboratory reference range (23% of females, 9% of males). Levels of thyroid hormones did not differ by breast feeding history. TSH, T3, and fT4 levels did not differ by sex although Akwesasne females had significantly higher levels of T4 ($p < 0.0001$), while males had higher levels of fT3 ($p < 0.0001$).

Toxicant levels did not differ by gender. Breast fed participants ($n=47$) had higher levels of HCB and p,p' -DDE than non-breastfed subjects. All PCB groups (PCB50%, PerPCB9, Σ DioPCBs, Σ EnzPCBs, Σ Wolff1-3) but one (Σ NONPER5) were significantly higher among breastfed youth. Mirex was unrelated to breastfeeding history (Table 3). Among participants who were breast fed, those with an elevated TPOAb level had significantly higher levels of all PCB groupings, with the exception of levels of Σ NONPER5 which did not differ significantly; levels of p,p' -DDE were also significantly elevated (Figure 1). HCB and mirex (not shown in figure) were not higher among those with elevated TPOAb.

We calculated Pearson correlation coefficients to determine the relationship of toxicants to TPOAb among youth (Table 4). When breast fed and non-breast fed participants were combined, no significant relationships were present (the lowest p value equaled 0.44). However, after stratifying by breast feeding status, participants who were breast fed showed significant, positive relationships between TPOAb levels and these PCB groupings: Σ PCB50%, Σ PERPCB9, Σ MonoPCBs, Σ DioPCBs, Σ TriPCBs, Σ Wolff2, Σ Wolff3, and Σ EnzPCBs; but not with Σ NONPER5, p,p' -DDE, HCB, or mirex. Multivariate regression analysis was performed (Table 5), examining the effect of each toxicant while including age, sex, number of years of education completed, and current cigarette use. None of these covariates were significant in the model and the results were not different from those obtained with the bivariate analysis except for p,p' -DDE which was found to be significant ($p=0.05$). Among the non-breast fed group, no significant relationship was found with any of the toxicants in bivariate or multivariate analyses.

Discussion

Our results show that the groups of more persistent PCBs are unambiguously associated with an elevated TPOAb level among late teens and young adults who had been breast fed as infants. Associations with p,p' -DDE are also evident, but these associations are not as consistent. HCB and mirex appear unrelated to elevated TPOAb levels. Consistent with these associations we also observed that within the normal range of TPOAb levels, groups of mono-*ortho* PCBs were positively associated with TPOAb levels. Furthermore, the relationships appeared in both males and females, further supporting the consistency of association between PCBs and TPOAb level. The finding that these relationships were only evident among breast fed youth suggests that perinatal or postnatal exposure to PCBs is influential. Because breast feeding introduces substantial amount of PCBs to the infant (Hooper, et al, 2007; Nagayama et al., 2007; Patandin et al. 1999), one possibility is that the effect is due to the greater exposure itself. Although the PCB levels of the breast fed and non-breast feed youth differ by at most 17% at the age of examination, the difference was likely much greater during infancy depending on the extent of breast feeding and the maternal body burden (Patandin et al. 1999). Another

possibility is that the effect is a matter of timing. When we restricted the analysis of the non-breast fed subsample to those with PCB levels comparable to the breast fed youth, there were no relationships between levels of PCBs and TPOAb. This suggests that the effect on TPOAb may be more one of when exposure occurs rather than how much exposure occurs. It is also possible that breast feeding is associated with other factors that are contributory, but the most likely of these (such as age and gender) were included in the multiple regression analysis and had no effect on the relationship. Unknown, and therefore, unmeasured factors are always a possibility.

The use of multiple groups of congeners was designed to test effects of functionally or structurally defined groups discerned by other investigators even though there is substantial overlap among the congeners contained in several of the groups. It is not possible to discern a clear difference among the PCB groups in terms of the strength of their relationships to elevated TPOAb among breast fed young adults with the exception of the non-persistent PCB congener group and possibly the Σ Wolff1 group. Both groups are largely composed of non-persistent congeners (Wolff et al., 1997). Not including those groups, the average difference in PCB level between elevated and not elevated TPOAb groups is 0.24 ppb while the non-persistent group differs by only 0.04 ppb, and Σ Wolff1 group by 0.05 ppb. Likewise, the r values and β weights describing the relationships of specific PCB groups to TPOAb levels are of similar strength, except again for the two groups of relatively non-persistent congeners. This suggests that the only characteristic of the PCB groups that is relevant to the effect on TPOAb in this sample is relative persistence. This may suggest that current exposure, which is best reflected by the levels of non-persistent congeners, has little effect on TPOAb levels among young adults, whereas earlier exposure, reflected by serum levels of more persistent congeners, does.

We did consider using a TEQ approach but due to insufficient specimen availability from these participants, we could not obtain data for the most potent dioxin-like congeners (126 and 169). Although we could base a measurement on the levels of the dioxin-like CBs 105, 118, and 156, without data for the most potent CBs, the results of such an analysis would be unreliable. We also considered data analyses based on lipid-adjusted PCB values. However, lack of standardization of laboratory methods and the need for considerable technical expertise in conducting total lipid determination can result in bias and variability in these comparisons (Schisterman et al., 2005; Bernert et al., 2007). Consequently, because we were not performing direct comparisons with other investigators' data, and since all of our subjects were fasted prior to blood sampling, we decided not to lipid-adjust our PCB data for this study.

Although the associations reported here support a causal relationship, cause itself is not proven; additional support could come from knowledge of a biological mechanism. However, the mechanism of this effect is not clear. Laboratory studies have not investigated TPOAb levels in relation to PCBs, and this would be an important experimental approach. There are indications that PCBs are associated with frank autoimmune diseases, such as diabetes (Codru et al., 2007; Fierens et al., 2003; Lee et al., 2006), rheumatoid arthritis (Lee et al., 2007), and autoimmune thyroiditis (Langer et al., 2007; Langer et al., 2003). Our results for PCBs agree with those of Langer et al. (2007), who found a relationship between TPOAb levels and levels of several organochlorines (PCBs, HCB and p,p' -DDE) among adults with "long term high exposure." One feature of our study is that levels of PCBs are considerably lower than those found in the study by Langer et al. (2007), and in many other studies of adolescents and young adults (Chevrier et al., 2007; Osius et al., 1999). This suggests that PCB exposures at levels commonly found in the US population and elsewhere could promote autoimmune disease if exposure occurred during a critical window as is suggested here. Considering these findings, we conclude that exposure to background levels of PCBs may in fact increase the risk of acquiring an autoimmune disease. There may be multiple mechanisms involved in the initiation and progression of autoimmune diseases by toxicant exposures as modified by individual

differences in metabolism and lifestyle. Further studies are necessary to elucidate the site and mechanism of action of these POPs and to establish thresholds for these effects, especially among populations with background levels of toxicant exposure.

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Abbreviations

AMN	Akwesasne Mohawk Nation
CB	Chlorinated biphenyl
DDE	<i>p,p'</i> - dichlorophenyldichloroethylene
ΣTotPCBs	

Sum of all PCB congeners tested

Σ PCB50%

Sum of CBs 28,52,74,87,95,99,101[+90],105,110,118,138[+163+164],
153,180,187

Σ PERPCB9

Sum of CBs 28,74,99,105,118,138[+163+164],153,180,187

Σ NONPER5

Sum of CBs 52,87,95,101[+90],110

Σ MonoPCBs

Sum of CBs 28,66,70,105,114,118,156

Σ DioPCBs

Sum of CBs 47,52,87,99,101[+90],110,138[+163+164], 146,153,170,180,190

Σ TriPCBs

Sum of CBs 84,96,123[+149],183,187,196,199

Σ Wolff1

Sum of CBs 52,70,101[+90],187

Σ Wolff2

Sum of CBs 66,74,105,118,138[+163+164],156,170

Σ Wolff3

Sum of CBs 99,153,180,196

Σ EnzPCBs

Sum of CBs 52,99,101[+90],118,153,156,180,183,187,199

fT3

Free Triiodothyronine

fT4

Free Thyroxine

HCB

Hexachlorobenzene

MAWBs

Mohawk Adolescent Well Being study

PCBs

Polychlorinated Biphenyls

T3

Triiodothyronine

TPOAb

Antithyroid Peroxidase Antibodies

TSH

Thyroid Stimulating Hormone

TT4

Total Thyroxine

Abbreviations:

ΣTotPCBs: Sum of all PCB congeners tested

ΣPCB50%: Sum of CBs 28,52,74,87,95,99,101[+90],105,110,118,138[+163+164],153,180,187

ΣPERPCB9: Sum of CBs 28,74,99,105,118,138[+163+164],153,180,187

ΣNONPER5: Sum of CBs 52,87,95,101[+90],110

ΣMonoPCBs: Sum of CBs 28,66,70,105,114,118,156

ΣDioPCBs: Sum of CBs 47,52,87,99,101[+90],110,138[+163+164],146,153,170,180,190

ΣTriPCBs: Sum of CBs 84,96,123[+149],183,187,196,199

ΣWolff1: Sum of CBs 52,70,101[+90],187

ΣWolff2: Sum of CBs 66,74,105,118,138[+163+164],156,170

ΣWolff3: Sum of CBs 99,153,180,196

ΣEnzPCBs: Sum of CBs 52,99,101[+90],118,153,156,180,183,187,199

Figure 1.

The difference of selected toxicant levels between breastfed young adults within and above the laboratory reference range for TPOAb (* $p \leq 0.001$).

Table 1
Congeners used in generating PCB groupings for analysis.

IUPAC#	Σ PCB50%*	Σ PERPCB9*	Σ NONPER5*	Σ MonoPCBs	Σ DioPCBs	Σ TriPCBs	Σ Wolff1	Σ Wolff2	Σ Wolff3	Σ EnzPCBs
28	X	X		X						
47					X					
52	X		X		X		X			X
66				X				X		
70				X			X			
74	X	X						X		
84						X				
87	X		X		X					
95	X		X			X				
99	X	X			X				X	X
101[+90]	X		X		X		X			X
105	X	X		X				X		
110	X		X		X					
114				X						
118	X	X		X				X		X
123[+149]						X				
138[+163+164]	X	X			X			X		
146					X					
153	X	X			X				X	X
156				X				X		X
170					X			X		
180	X	X			X				X	X
183						X				X
187	X	X				X	X			X
190										
196					X				X	
199						X				X

* Congeners found in >50% of the sample. All others found in >20% of the sample.

Table 2
Descriptive statistics of thyroid hormone levels among Akwesasne youth (n=115) ^{*}.

	Mean	Median	SD	Min	Max
T3 (ng/dL)	122.31	118	23.69	9.99	204
FT3 (pg/ml)	3.37	3.30	0.39	2.60	4.70
T4 (µg/dL)	6.96	6.65	1.62	4.20	14.10
FT4 (ng/dL)	1.00	0.98	0.16	0.61	1.49
TSH (IUl)	2.10	1.47	3.77	0.36	40.57
TPOAb (IU/ml)	76.06	13.00	471.32	1.99	5000

^{*} One participant is missing T4.

Table 3

Levels of toxicants among Akwesasne young adults: stratified by breast feeding status (n=115)

Toxicant (ppb)	Breastfed (n=47) GM	Non-breastfed (n=67) GM	t-value
ΣTotPCBs	0.89 [*]	0.78	2.26
Σ PCB50%	0.48 [*]	0.40	2.56
Σ PERPCB9	0.36 [*]	0.28	2.98
ΣNONPER5	0.10	0.11	0.55
ΣMonoPCBs	0.12	0.10	1.85
Σ DioPCBs	0.40 [*]	0.32	2.73
ΣTriPCBs	0.13 [*]	0.05	2.09
ΣWolff1	0.09 [*]	0.08	2.02
ΣWolff2	0.18 [*]	0.15	2.45
ΣWolff3	0.16 [*]	0.12	3.02
ΣEnzPCBs	0.32 [*]	0.25	2.82
p,p'-DDE	0.37 [*]	0.28	1.98
HCB	0.04 [*]	0.03	3.21
Mirex	0.01	0.02	0.76

^{*}
p≤0.05

Data on breast feeding status is missing for one participant.

Table 4

Relationship between TPOAb z-scores and toxicant levels among participants with no hormone or thyroid medication use: All and stratified by breast feeding (* $p \leq 0.01$).

Toxicant (ppb)	Breastfed (n=47)		Non-Breastfed (n=67)		Breastfed and non-breastfed combined (n=115)	
	r	p	r	p	r	p
Σ TotPCBs	0.40*	0.01	-0.06	0.65	-0.04	0.67
Σ PCB50%	0.36*	0.01	-0.06	0.64	-0.05	0.63
Σ PERPCB9	0.35*	0.02	-0.07	0.56	-0.06	0.54
Σ NONPER5	0.11	0.46	0.02	0.86	0.03	0.77
Σ MonoPCBs	0.28*	0.05	-0.09	0.49	-0.07	0.45
Σ DioPCBs	0.35*	0.01	-0.03	0.80	-0.02	0.79
Σ TriPCBs	0.33*	0.02	-0.01	0.95	-0.02	0.82
Σ Wolff1	0.25	0.09	0.00	0.99	-0.01	0.93
Σ Wolff2	0.35*	0.01	-0.07	0.60	-0.05	0.62
Σ Wolff3	0.33*	0.02	-0.05	0.70	-0.04	0.69
Σ EnzPCBs	0.36*	0.01	-0.05	0.70	-0.04	0.69
<i>p,p'</i> -DDE	0.25	0.10	-0.06	0.65	-0.05	0.60
HCb	0.04	0.80	-0.07	0.59	-0.07	0.44
Mirex	0.11	0.47	-0.04	0.73	-0.03	0.75

Abbreviations:

Σ TotPCBs: Sum of all PCB congeners tested
 Σ PCB50%: Sum of CBs 28,52,74,87,95,99,101[+90],105,110,118,138[+163+164],153,180,187
 Σ PERPCB9: Sum of CBs 28,74,99,105,118,138[+163+164],153,180,187
 Σ NONPER5: Sum of CBs 52,87,95,101[+90],110
 Σ MonoPCBs: Sum of CBs 28,66,70,105,114,118,156
 Σ DioPCBs: Sum of CBs 47,52,87,99,101[+90],110,138[+163+164],146,153,170,180,190
 Σ TriPCBs: Sum of CBs 84,96,123[+149],183,187,196,199
 Σ Wolff1: Sum of CBs 52,70,101[+90],187
 Σ Wolff2: Sum of CBs 66,74,105,118,138[+163+164],156,170
 Σ Wolff3: Sum of CBs 99,153,180,196
 Σ EnzPCBs: Sum of CBs 52,99,101[+90],118,153,156,180,183,187,199
 Data on breast feeding status is missing for one participant.

Table 5

Results of the multivariate regression analysis.*

Toxicant (ppb)	Breastfed						Non-breastfed						
	Std.β	t	p	95% CI			r ² (%)	Std.β	t	p	95% CI		r ² (%)
				Lower	Upper	Lower					Upper		
ΣPCB50%	0.43**	2.83	0.01	0.04	0.23		23%	-0.06	-0.47	0.64	-0.77	0.48	5%
ΣPERPCB9	0.40**	2.69	0.01	0.03	0.18		21%	-0.06	-0.50	0.62	-0.70	0.42	5%
ΣNONPER5	0.11	0.67	0.51	-0.06	0.11		7%	-0.01	-0.09	0.93	-0.60	0.55	4%
ΣMonoPCBs	0.27	1.70	0.10	-0.01	0.15		13%	-0.10	-0.73	0.47	-0.64	0.30	5%
ΣDioPCBs	0.45**	2.95	0.01	0.04	0.23		24%	-0.03	-0.23	0.82	-0.67	0.53	4%
ΣTriPCBs	0.40**	2.70	0.01	0.02	0.15		21%	-0.05	-0.38	0.71	-0.42	0.29	4%
ΣWolff1	0.27	1.77	0.09	-0.01	0.18		13%	-0.04	-0.29	0.77	-0.64	0.48	4%
ΣWolff2	0.40**	2.65	0.01	0.02	0.18		21%	-0.07	-0.52	0.60	-0.66	0.39	5%
ΣWolff3	0.40**	2.66	0.01	0.02	0.16		21%	-0.03	-0.24	0.81	-0.56	0.44	4%
ΣEnzPCBs	0.42**	2.84	0.01	0.03	0.19		23%	-0.05	-0.41	0.68	-0.69	0.45	5%
p,p'-DDE	0.34**	2.06	0.05	0.00	0.12		16%	-0.04	-0.27	0.79	-0.40	0.30	4%
HCB	0.05	0.31	0.76	-0.08	0.11		6%	-0.02	-0.11	0.91	-0.75	0.67	4%
Mirex	0.09	0.58	0.56	-0.10	0.18		7%	-0.09	-0.67	0.50	-0.74	0.37	5%

* Model controls for age (yrs), sex (m=0, f=1), educational status, and current cigarette use (any/none)

** p≤0.01; Data on breast feeding status is missing for one participant.