Published in final edited form as:

Neurotoxicol Teratol. 2014 ; 42: 25–34. doi:10.1016/j.ntt.2014.01.005.

PCBs and ADHD in Mohawk adolescents

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Abstract

The present study examines the relationship between the levels of persistent polychlorinated biphenyls (PCBs) in adolescents' blood serum and concurrent measures of their ADHD-like behavior derived from ratings provided by parents and teachers. Two measures with demonstrated diagnostic validity, the Conners and ADDES scales, are used. The study was conducted in partnership with the Mohawk Nation at Akwesasne where the St. Lawrence River and surrounding waterways have been contaminated with PCBs that have entered the food chain. This study examines a subset of the data derived from the Mohawk Adolescent Well-Being Study (MAWBS), which was designed to investigate psychosocial and health related outcomes of 271 adolescents aged 10 years to 17 years and whose mothers were likely to have consumed PCB-contaminated fish and wild game before and during their pregnancy. No evidence of negative effects of adolescent blood PCB levels on ADHD-like behavior was found, and indeed occasional findings were in the unexpected direction. The possibility of negative confounding by SES and breast-feeding history was examined but dismissed.

Keywords

Polychlorinated biphenyls (PCBs); ADHD; Adolescents; Native American

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Conflict of Interest Statement

The authors have no conflicts of interest to report.

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1. Introduction

The current paper involves adolescents from Akwesasne, a community concerned about industrial pollution of its waterways and consequent toxic contamination of the local food chain. Previous publications (Newman et al., 2006; Newman et al., 2009) reported a negative association between the body burden of polychlorinated biphenyls (PCBs) and measures of long-term memory in the adolescent sample. The current paper examines potential relationships of PCBs and concurrent measures of ADHD gained from behavioral ratings completed by the participants' parents and teachers.

1.1. Akwesasne studies

Akwesasne is a community of approximately 12,000 people of the Mohawk Nation (Akwesasne Task Force on the Environment, 1997; Fitzgerald, et al., 1998) located along the St. Lawrence River adjacent to Quebec, Ontario and New York State. Industrial development upstream, upwind and up-gradient of the Akwesasne community has contaminated the waterways with PCBs, which have subsequently entered the food chain in this region. The community is concerned about effects of past and ongoing exposure to PCBs and other toxicants. The Mohawk Adolescent Wellbeing Study (MAWBS) was carried out in partnership with the people of Akwesasne to examine psychosocial and various health related outcomes of Akwesasne adolescents who have grown up in the contaminated environment and whose mothers were likely to have ingested fish from the PCB-polluted waterways before and during their pregnancy until the publication of fish advisories.

1.2 Polychlorinated biphenyls and human exposure

Because of increasing knowledge of negative human health effects, the production of PCBs has been banned in most countries for some years, but these chemicals persist in the environment (World Health Organization, 1993), although the persistence of the different PCB congeners varies. Humans bioaccumulate PCBs through the consumption of contaminated food. In addition, children can be exposed both prenatally during gestation and postnatally through breast-feeding. Because PCBs are lipophilic, they are stored in breast milk and may be transmitted to infants during breast-feeding.

1.3. ADHD

Attention Deficit Disorder (ADHD) is a syndrome of behaviors involving hyperactivity and problems in focusing and maintaining attention. The conceptualization of ADHD has varied somewhat in recent decades, and assessment instruments have been developed and modified in parallel. However, the essential features of hyperkinesis, impulsivity and lack of sustained attentional focus have remained part of the conceptualization (American Psychiatric Association, 2000). The prevalence of the condition is of concern, as the behavioral components of ADHD underlie much social behavior and as such can seriously affect children's learning and school performance. Adults may also display ADHD and experience negative job and social consequences.

1.4. PCBs and behavior

There are numerous studies examining the impact of PCB exposure (mostly prenatal) on global measures of development, cognitive functioning or memory (see Ribas-Fito et al., 2001; Schantz et al., 2003; Schantz et al., 2004, for a review of many studies), but findings are not consistent (Stewart et al., 2012) and range from no observed effects to negative effects. A smaller number of studies have focused on measures of behavior, despite their importance in adaptive functioning.

There is substantial animal research suggesting a relationship between PCB exposure and behaviors such as hyperactivity and response inhibition (Berger et al., 2002; Sable et al., 2006). In addition, concerns have been raised that PCBs may disrupt endocrine activity. PCB exposure has been linked to a reduction of dopamine processes in rats (Seegal et al., 1997; 2005), and thyroid hormones in rats (Miller et al., 2012) and humans (Porterfield & Hendry, 1998; Schell et al., 2008). This further demonstrates the need for research on behavioral effects of PCB exposure because thyroid hormones are implicated in the regulation of attentional processes (Zoeller et al., 2000). Animals exposed to PCBs exhibit some of the characteristics found in children with attention deficit disorder (Rice, 2000). Note however that one study (Johansen et al., 2011) found that rats exposed to two PCB congeners (CBs 153 and 180) demonstrated reduced activity.

Some of those human studies that have investigated behavioral outcomes of PCB exposure report that individuals so exposed have deficits in aspects of attention (Jacobson & Jacobson, 1996, 2003; Peper et al., 2005; Sagiv et al., 2010) but other studies do not show this relationship (Boucher et al., 2012; Grandjean et al., 2012; Jacobson et al., 1992; Lee et al., 2007; Vermeir et al., 2005), or show it only for boys (Sagiv et al., 2012). It has also been reported that PCB measures are related to reduced response inhibition/impulsivity (Sagiv et al., 2012, but only for boys; Stewart, Fitzgerald et al., 2003; Stewart et al., 2005; Till et al., 2001) which is a deficit of executive functioning, one component of ADHD. In addition, poorer ability to maintain attention may result in slower processing speed, which has been associated with PCB exposure (Vreugdenhil et al., 2004). Both higher (Chen, Yu et al., 1994) and lower activity levels (Huisman et al., 1995; Jacobson et al., 1990) have been associated with PCB exposure. A small number of behavior rating studies (Chen, Yu et al., 1994; Sagiv et al., 2010) suggest that children's PCB exposure may be associated with behavior patterns consistent with ADHD. Further research is clearly needed.

Study design differences may contribute to some inconsistency in reported findings. In most of the human studies cited above, PCB measures have been based on prenatal or perinatal exposure, and related to later developmental functioning. A few of the studies have employed a cross sectional design in which PCBs and behavioral outcomes are measured concurrently. Using this design, Boucher et al. (2012), Lee et al., (2007) and Vermeir et al., (2005), found that serum PCBs in older children were not related to ADHD-related behaviors, whereas adults in Peper et al., (2005) showed subtle negative effects on attention associated with chronic PCB exposure. While this design does not allow conclusions about the specific timing of any negative effect, it provides useful information about the ongoing effects of cumulative exposure, some of which may have occurred prenatally.

Some inconsistency in the literature about the effects of PCBs on developmental outcomes may occur because of negative confounding in populations where PCB exposure is associated with factors that influence functioning positively (Stewart et al., 2012). One example is the situation when elevated PCB levels result from breast-feeding which may have a positive influence on aspects of children's development (Anderson et al., 1999; Borra et al., 2012; Kramer et al., 2008; McCrory & Layte, 2011). Such confounding may mask negative effects of PCBs, or even indicate that more highly exposed individuals have better developmental outcomes.

The current study uses ecologically valid measures of ADHD to investigate the relationship between current PCB body burden of the Akwesasne adolescents and behavior ratings provided by parents and teachers. As in the study by Sagiv et al. (2010) who investigated prenatal PCB exposure and ADHD-like behaviors in school aged children, the measures used in the current study have demonstrable validity as measures of ADHD. The PCB measure in our study represents the accumulation of lifetime exposure, originating from ongoing postnatal sources as well as prenatal and perinatal exposure when the child's brain is very plastic. Mothers of the Akwesasne adolescent participants would very likely have eaten local fish before the publication of fish advisories, and so have contributed PCBs to their children in utero and by breast-feeding. The cross sectional design will restrict conclusions about causality, but the inclusion of multiple covariates will allow control of most obvious competing hypotheses to explain the results. A similar reliance on cross sectional designs occurs in other areas of investigation such as the role of lead exposure in ADHD-related behaviors where the design has allowed substantial contributions (see Eubig, et al., 2010 for a review). Any evidence of negative confounding in the results will be examined.

2. Methods

2.1. Participants and procedures

The MAWBS sample included 271 Mohawk adolescents aged 10 years to 16.9 years (mean age 13.2 years). Many children of this age were born to mothers who had likely been fish consumers before advisories were issued. The participants were also of an age when considerable cognitive and physical developmental change occurs (Giedd et al., 1996). Members of the research team identified households with residents between the ages of 10 and 17 years, visited each home, and explained the goals and procedures of the study. If the family met criteria for inclusion in the study and consented, one of the 10 to 17 year olds from the household was randomly selected to participate in the study along with her/his mother. Children with the following health history were excluded from participation in the study: hospitalization for brain injury, serious organic or psychological pathology, or diagnosis of Fetal Alcohol Syndrome or Fetal Alcohol Effects.

Interviewers were members of the Mohawk Nation of Akwesasne who had received training. Each participant's mother was interviewed and completed two behavior rating scales. In addition, a teacher who had ongoing contact with the participant was given both rating scales to complete. The behavior rating scales were sent to the University at Albany to be checked by trained school psychology graduate students. Written feedback regarding differential

strengths on the various tests and behavior measures was provided to parents in addition to some written practical guidance to address behavioral issues revealed on the measures. Parents were given the opportunity to discuss the individual test results of their child with the first author from the University at Albany.

2.2. Independent variable: PCB body burden

PCBs in the adolescents were measured from current blood draws taken in the homes of the participants after they had fasted for 8 hours. Blood was allowed to clot at room temperature for 20 minutes and then centrifuged at $800 \times g$ for 15 minutes. Complete details of the protocol for PCB analysis and data on laboratory performance are presented in DeCaprio et al., (2000) and Schell et al. (2003). Analyses conducted at the University at Albany Exposure Assessment Laboratory yielded data for 83 individual PCB congeners and 18 additional congeners co-eluting as pairs or triplets.

The PCB summary measure (hereafter termed Persistent PCBs) for each participant was created from those congeners that may have been active throughout much of the adolescents' lives or even prenatally. The persistent congeners included in our measure were those found in at least 50% of the participants. Including congeners found in a smaller percentage of the participants would have necessitated many substituted values. Values below the detection level were substituted by $mdl/2$. The congeners included in this measure were IUPAC numbers 118, 138[+163+164], 153, 180, 74, 99, 187, 105. For the 271 adolescent participants, the mean level of Persistent PCBs was 0.43 ppb (SD 0.26), ranging from a minimum of 0.10 ppb, to a maximum of 2.45 ppb. Several of these persistent congeners exceeded the 90th percentile as reported by the Centers for Disease Control for 12 to 19 year old adolescents (Gallo et al., 2011), but lower than levels reported for other European cohorts of similar or younger age ranges (Schell et al., 2003).

2.3. Dependent variables: Ratings of ADHD-like behavior

Rating scales provide a standardized format for describing and interpreting an individual's behavior, and can be completed by different people who have observed the individual's behavior in various settings. This is important because different settings place distinctive demands on an individual's demonstration of attention. Furthermore, rating scales provide information about categories of behavior, some of which are consistent with those employed by clinicians and are codified in professional publications such as the various editions of the Diagnostic Manual of Mental Disorders (DSM-IV-TR, American Psychiatric Association, 2000). In this study, ADHD was measured by two behavior rating questionnaires, the Attention Deficit Disorders Evaluation Scale: Second Edition hereafter termed the ADDES, and the Conners Rating Scales. The former provides scores that fit the ADHD diagnostic categories whereas the latter allows replication of other studies (Sagiv et al., 2010). Both the ADDES and the Conners scales have diagnostic validity and correlate positively with other instruments designed for the same purpose including each other. Both provide continuous measures of component behaviors and so allow sensitive analysis of outcomes. These scales have good psychometric properties, and are derived from two informants (parents and teachers) who based judgment on ecologically valid behavior. As responses for the full

sample were not available for all measures, the sample characteristics were slightly different for each of the dependent measures used in the various analyses performed.

2.3.1. ADDES—The ADDES Home Version (McCarney, 1995a) and the ADDES School Version (McCarney, 1995b) both have subscales measuring the two major components of ADHD, namely inattention and hyperactivity-impulsivity. The participant's parent and a teacher were asked to rate the frequency that each listed behavior (e.g. 'grabs things away from others') occurs on a 5-item scale.

The ADDES scales have been examined with regard to reliability and validity and judged to be psychometrically sound instruments (Koutnik, 1992; Olejnik, 1995). The manuals for the Home and School Versions (McCarney, 1995a, 1995b) provide the following psychometric summaries. Test-retest reliabilities for the various age groups of the ADDES Inattentive Scale range from .88 to .91 for the Home Version, and .91 to .96 for the School Version. Measures of inter-rater reliability range from .80 to .84 (for the Home Version) and .84 to .91 (for the School Version). Internal consistency of .96 for the Home Version and .98 for the School Version is reported. Reports in the manuals of the scales' content and construct validity further support the technical merits of the ADDES as a valid instrument.

2.3.2. Conners Rating Scales—The Conners Parent and Teacher scales yield scores on a wide range of behaviors that can be problematic, and include those suggestive of hyperactivity (Conners, 1990). The Conners Parent Rating Scale (CPRS-48) includes the subscale of Impulsive-Hyperactivity, and an overall Hyperactivity Index score based on items from subscales concerning conduct problems, learning problems, and impulsive-hyperactive behavior. The Conners Teacher Scale (CTRS-28) has subscales of Hyperactive, Inattentive-Passive, and a Hyperactive Index Score based on items from the other scales as well as conduct problems. To complete items on the Conners scale, teachers were asked to consider the adolescent's behavior (e.g. 'Easily distracted or lacks adequate attention span') in the last month and consider how much of a problem certain behaviors had been on a 4-item scale ranging from "Not at all" to "Very much".

Although currently revised, the Conners Scales used in MAWBS were appropriate measures at the time the study was designed and have good psychometric properties. The test-retest reliability on the Conners scales ranges from .72 to .91 over a one month period (Conners, 1990). Several studies evaluating the inter-rater reliability of the Conners scales report coefficients ranging from .39 to .94 on different subscales (Epstein & Nieminen, 1983; Homatidis & Konstantareas, 1981; Kazdin et al., 1983). Internal consistency for the Conners scales is approximately .94 on the various scales (Edelbrock et al., 1985). Studies have assessed the discriminant validity of the Conners scales and found that they adequately distinguish between clinical and non-clinical populations on the various scales (King & Young, 1982). The scales have also been found to have good concurrent and construct validity (Edelbrock et al., 1985; Campbell & Steinert, 1978). We selected the subscales of the Conners Behavior Rating Scales that were indicative of ADHD and which have been shown to correlate most highly with the ADDES hyperactivity scale (McCarney, 1995a, 1995b).

2.3.3 Participants' scores on the ADHD measures—Some teachers did not provide ratings, so the sample sizes for teacher ratings are smaller than those for parent ratings. For the ADDES standardization sample, scores have a mean of 10 and a standard deviation of 3. Scores falling within the range of 7–13 are considered to be statistically average, while those scores falling at least two standard deviations below the mean, that is less than 4, suggest significant problem behavior. For the Conners standardization sample, scores have a mean of 50 and a standard deviation of 10. Scores falling between 40–60 are considered to be in the average range, while those scores that are two or more standard deviations above the mean, that is greater than 70, indicate an area of significant concern. Descriptive analyses of the standardized scores of the participants in the current study for the dependent measures relating to attention are shown on Table 1. Overall, the scores of the participants as a group fell within the average range on all behavioral measures.

2.4. Covariates

Data on numerous variables that could have contributed to the outcome measures were available. Descriptive data on those variables that were measured continuously are listed on Table 2, as well as their correlations with Persistent PCB levels.

In addition, measures on two dichotomous variables ('yes' or 'no') were available for all 271 adolescents about current usage of cigarettes and alcohol. For cigarettes, 235 adolescents said they did not currently smoke whereas 36 did smoke, and 246 said they currently did not use alcohol whereas 25 said that they did. Responses to neither question were related to PCB levels.

Bivariate correlations were carried out between all potential covariates and each outcome measure (see Table 3). A liberal inclusion rule was used to select variables as covariates; for each ADHD measure, those correlations that reached the criterion of $p < .2$ are bolded, and covariates that correlated to this extent were used in analyses of that particular ADHD measure.

2.5. Data screening

Independent and covariate variables with skewed distributions were log transformed (lead, mercury, PCBs, p,p' -DDE, HCB, breast-feeding duration (weeks), and number of cigarettes mothers smoked per day during pregnancy). The distributions of the dependent variables, although slightly skewed, did not warrant transformation.

3. Results

3.1. PCBs and ADHD

All data were analyzed using SPSS 17. The results of a multiple regression (Table 4), taking into account any effects of empirically derived covariates, show that the PCB level was significantly related only to the Conners Impulsive-Hyperactive (IHPT) measure derived from the parent's report. The negative relationship indicates that higher PCB levels were related to lower IHPT scores, which indicated fewer problems. These and subsequent analyses were repeated using the raw scores of the dependent variables, as recommended by

Rice (2005). All results were unchanged substantively, so only the analyses using standardized dependent measures are reported below.

ADHD scores of adolescents in the upper and lower quartiles of Persistent PCBs were compared with t-tests, and were significantly different only for the Conners HIPT. The mean score (54.87) for adolescents in the lowest quartile was greater (that, is more problematic) than the mean score (50.07) of adolescents at the upper quartile ($t(133 \text{ df}) = 2.296, p < .023$).

In our multiple regressions (Table 4 and subsequent regression tables) we included three cognitive variables (RPM, TOMAL and WJR) that qualified empirically as covariates to be controlled statistically. None of these three variables were related to PCB levels. However, it is possible that performance on the cognitive tests was influenced by the ADHD-like behaviors, as well as the reverse. Because of this, we repeated all of our multiple regressions excluding these three covariates and found that few of our results were changed and none substantially, and the pattern of findings and conclusions derived did not change from those reported.

3.2. Sex differences

The multiple regression summarized in Table 4 was repeated separately for boys ($n = 131$) and girls ($n = 140$). Our data provide no evidence of gender related patterns. Persistent PCBs were not related to any of the ADHD scores for males or for females.

3.3. Negative confounding

Table 4 shows that PCBs were significantly related to less problematic Conners hyperactive scores (IHPT) when adjusted for covariates. When the same multiple regression was done without any covariates, PCBs were not significantly related to any scores (including IHPT). Because this one example may indicate negative confounding by at least one of the covariates, we examined our findings to identify any variables that were positively related to PCB measures, and also related to the reduced occurrence of ADHD behaviors. We used a criterion of $p < .05$ to identify covariates with a positive contribution to the adolescents' behavior that were also associated with increased PCBs. We found that two variables in our data set were candidates for this role; SES and breast-feeding.

3.3.1. SES—The SES index score was positively related to PCB measures (Table 2) and to less problematic scores on most ADHD behaviors (Table 3). Adolescents in our sample of higher SES experienced several benign factors (Table 5) which may have outweighed any putative negative effects of PCBs, and account for their less problematic ADHD behaviors. SES was associated with higher scores on the WJR and TOMAL, fewer ADHD behaviors on the Conners scales, (but more problems on one ADDES score, the APHIS), and with mothers with higher WJR scores, who had smoked less and breast-fed longer. We carried out separate multiple regressions for adolescents whose SES index score was above and below the mean SES level (Table 6).

If SES was functioning as a negative confounder and masking any negative effects of PCBs, we would expect to observe PCBs associated with fewer problematic scores in the

participant group receiving the protection of high SES. Conversely we would expect to observe PCBs associated with more problematic scores in the low SES participant group that lacked the protection of high SES. This was not observed. As shown on Table 6, in the low SES group, increasing PCBs were associated with decreased (i.e. less problematic) IHPT scores, whereas in the high SES group PCBs were no longer associated with IHPT scores. These findings are opposite to what one would expect if SES was functioning as a negative confounder. Also inconsistent with negative confounding is the finding that PCBs were associated with increased (more problematic) HATT scores in this high SES subgroup, but not in the low SES group. Only one ADHD subtest provides possible support for the role of SES as a negative confounder; increasing PCBs were associated with decreased (less problematic) HIPT scores in the high SES group, but not in the low SES group.

In summary, findings concerning SES provide very limited support for its role as a negative confounder.

3.3.2. Breast-feeding—Breast-feeding was the second variable in our data set that could have functioned as a negative confounder and masked any putative effects of PCBs on ADHD scores. Adolescents in our study who had been breast-fed for longer durations had higher PCB levels (Table 2). Adolescents who had been breast-fed, compared to those who had not, had more PCBs, and had mothers with higher WJR cognitive scores ($t = 3.954$, 247, $p < .001$), and higher SES ($t = 3.321$, 269, $p < .001$). We therefore examined the relationship of PCBs to ADHD-like behaviors separately in those adolescents who had been breast-fed ($n = 122$) and those who had not ($n = 149$). The breast-fed group had been breast-fed for an average of 26 weeks (range .28 weeks to 120 weeks).

Multiple regression was carried out in each breast-fed group separately to examine relationships between PCBs and the ADHD outcome measures, using the same covariates as in previous analyses. No relationships were significant in either breast-feeding group. Because there is no difference in the relationship of PCBs and ADHD behaviors in the two groups differentiated by breast-feeding history, we conclude that breast-feeding was not functioning as a negative confounder in our data.

4. Discussion

4.1. Overall findings

Despite some previous research showing that greater PCB levels were associated with more problematic ADHD-like behavior, this was not the case for the adolescent Mohawk participants of the present study, albeit based on a relatively small sample size. Almost no measures of their attention and behavior provided by parents and teachers were associated with their current blood serum PCB levels. In addition, the ADHD-like behavior scores in the lowest and highest quartiles of PCB burdens were not different. There were two isolated inconsistent findings and both were in the unexpected direction; two parent-reported measures of hyperactive behavior showed fewer problems for their adolescent children who had higher PCB levels.

It is hard to know what to conclude about this, but the findings should be known and added to those of other researchers who have unexpected findings. In particular, Sagiv et al. (2012) found sex differences in the effects of cord serum PCBs and DDE on a computerized measure of deficits in attention and impulsivity. Results for girls were either null or in the unpredicted direction. We did not find any sex differences in relationships between PCBs and our measures. Some other investigators have also reported a lack of association between PCBs and measures of attention and impulsivity in children (Boucher et al., 2012; Grandjean et al., 2012; Jacobson et al., 1992; Lee et al., 2010; Vermeir et al., 2005), or even findings in the unexpected direction for humans (Huisman et al., 1995; Jacobson et al., 1990; Sagiv et al., 2012, for girls) and animals (Johansen et al., 2011).

Although not a particular focus of the present study, cigarette use by mothers during their pregnancy and currently by the adolescents themselves was related to higher scores on almost all measures of problem behavior. This finding was not surprising in view of previous research indicating that maternal smoking during pregnancy was related to inattention as well as hyperactivity in youth (Kotimaa et al., 2003; Leech et al., 1999; Mick et al., 2002).

4.2. Negative confounding

Because our results did not show that PCB exposure was related to ADHD-like behaviors, and were at times in the opposite direction to expectations, we examined our analyses and findings carefully to determine if any characteristics of our data set could have created negative confounding and so interfered with our ability to observe PCB effects. In the current study, our PCB measure was significantly related to two factors that were likely to benefit children's social behavior, namely SES and breast-feeding.

Stewart et al. (2012) reported that individuals from higher SES backgrounds had higher levels of PCBs. These authors attribute this finding to the greater contribution of PCBs from mothers who have less body fat and who bear fewer children. In our data, adolescents from families of higher SES also had higher levels of PCBs. On the other hand, a number of benign factors were also associated with SES. If the combined factors associated with SES were responsible for the paucity of putative negative PCB effects on the ADHD measures in our study, we would expect that any PCB effects would have been more evident for adolescents of lower SES levels (who lack the beneficent features of higher SES). For all but one of nine ADHD subtests, findings were lacking or were opposite to what negative confounding would lead us to predict.

Another potential negative confounding variable was breast-feeding. However, when we carried out separate analyses of the relationship between PCBs and ADHD behaviors in groups differentiated by breast-feeding history, we found no differences. If breast-feeding was masking any negative PCB effects, we would expect to see more PCB effects in the group which had not been breast-fed. As this was not the case, apparently breast-feeding was not functioning as a negative confounder.

In summary, analyses focused on the possibility of negative confounding revealed almost no evidence for this process. Our data indicate that neither SES nor breast-feeding history were functioning as negative confounds.

4.3. Study design

Unlike the majority of studies in the literature, the present study employed a cross sectional design. Most studies have reported longitudinal findings relevant to ADHD based on prenatal PCB exposure of participants (e.g., Grandjean et al., 2012; Jacobson & Jacobson, 2003; Sagiv et al., 2010; Sagiv et al., 2012; Stewart et al., 2005). There are a few cross-sectional studies of older children in which concurrent levels of PCBs have been employed (Boucher et al., 2012; Lee et al., 2007; Peper et al., 2005; Vermeir et al. 2005). In the present cross sectional study, current body burden measured exposure accumulated from prenatal and postnatal sources. It was not possible to isolate the role of prenatal exposure as any effects observed in the current participants could derive from prenatal or post-natal exposure, or both.

Despite the findings of the current study that were discrepant from those of some others, there were strengths in the methodology of this study to allow for valid findings to emerge. The statistical control of multiple covariates compensated for the restricted causality allowed by the cross sectional design, and lack of evidence for negative confounding provided no reason to conclude that any PCB effects were being masked.

There was careful selection of instruments to identify ecologically valid behaviors. We used two instruments, both validated for the purpose of identifying ADHD behaviors, with norms for the age range of the participants. We had ratings from two informants (parents and teachers) who observed the participants over considerable time in different settings. Children are likely to display different behavior in different settings and parents and teachers are likely to interpret it differently (Achenbach et al., 1987; Edwards et al., 1995). The use of rating scales was viewed as a strength of the current study in that they provide measures that are more comparable to 'real life' outcomes for participants. Both rating scales used in the current study provided measures of several facets of ADHD (attention, impulsivity and hyperactivity), thus allowing investigation of any specific PCB-behavior links.

The PCB measure used in our study was chosen to represent the persistent PCBs that were likely to have been present during critical periods of brain development. It is likely that ADHD related behaviors would have resulted largely from neurological development in the prenatal and early childhood periods (Curatolo, 2005).

In light of these considerations, the results of this study are likely to provide valid information with respect to the relationship between accumulated PCBs and ADHD-like behaviors. Our results show no such relationship, or isolated negative relationships, between persistent PCBs and behavior ratings of ADHD in the adolescent participants.

4.4. Explanation of inconsistency with previous findings

Several factors should be taken into account when the results of the present study are compared with those of previous studies.

Differences in the age of participants and hence timing of exposure assessment may account for differences in the results. The participants in the current study were adolescents whereas much of the previous research in the field has involved preschoolers or those who were

under the age of 11 years. Moreover, the findings of some cohort studies have changed as the children have grown older. Several examples of this are found in the research from the Michigan cohort where no relationship was found between PCB exposure and attention in participants at 4-years old (Jacobson et al. 1992), but did find a relationship when the sample was retested at 11-years old (Jacobson & Jacobson, 1996). Similarly, in the Oswego cohort (Stewart, Fitzgerald et al., 2003) and the German cohort (Winneke et al., 2005), effects found in the preschool years were no longer evident in the early school years. Thus it is clear that researchers still have much to understand regarding the trajectory of effects from PCB exposure, as of other neurotoxic exposure (Spear, 2007). Findings from this and other studies must be interpreted with knowledge that effects may be differently evident at different ages.

ADHD and its component behaviors have been operationalized and measured variously in different human studies. It is likely that there are different neurological and physical underpinnings for the behaviors operationalized in each way, and these may have been impacted differently by PCB exposure. For example, Eubig et al., (2010) reviewed findings about ADHD and executive functioning and concluded that PCBs may have different effects on response inhibition and attention.

Different studies may have included different covariates in their analyses and hence yielded different findings (Stewart et al., 2012). Also, different populations may experience actual differences in their situations, and these differences may modify the impact of PCBs. For example, some groups of mothers are more likely to breast-feed their infants, or to smoke during pregnancy, or to live in polluted environments and be exposed to other toxicants. Whether or not these variables are measured and included in analyses, they are likely to have important effects on the children's development.

Variables of potential impact do not occur in isolation, and may cluster consistently in terms of favorability for children's development. In certain situations, the individual or combined effect of such beneficent variables may mask PCB effects which may in fact be there, and make study results appear less consistent with those of others studies. Each study's covariate set may modify differently any PCB effects.

It may be that our results differ from those of some previous studies because of differences in the level of exposure to PCBs (represented in this study by body burden), or differences in the particular PCB congeners included in the measured PCB level. There are considerable differences in the exposure measures and levels across studies (Longnecker et al., 2003). Divergent findings in the various studies of the effects of PCB exposure must be interpreted with attention given to the methods of grouping and measuring PCBs as well as the differing levels of exposure of the participants in the study.

4.5. Future research

The present study did not find that exposure to the PCBs in the environment had impacted the ADHD-like behavior of the Akwesasne adolescents. Nevertheless, care must be taken to establish the generality of this finding. It is important to show the extent to which this conclusion is limited to the age group of the participants, their context, and the particular

measures of behavior employed. Furthermore, the contribution of other possibly harmful toxicants in the environment should be investigated.

Future research should examine other behavioral outcomes in relation to PCB exposure. Computerized measures of attention and vigilance are more sensitive and rely less on subjective judgments of observers than do behavior ratings, although they have less ecological validity. Another approach would be to examine 'real life' outcomes such as school grades, disciplinary records, and school drop out data.

As behavior patterns may be more evident in some periods of children's development, longitudinal study is needed to show fluctuations in behavior patterns. There is some evidence that ADHD prevalence changes throughout development (Biedeman et al., 2000; Conners, 1990), so longitudinal study is most able to capture such change.

More research with adolescent populations is needed. PCBs have been associated with disruption of thyroid or endocrine pathways, which are implicated in various aspects of growth and development (Porterfield & Hendry, 1998; Schell, 1999). Because adolescence is a period of considerable brain development (Giedd et al., 1996; Spear, 2000) as well as a time of many developmental changes and new skill acquisitions, it is possible that some variations in brain functioning would not be apparent until this time period. Some researchers (Chen & Hsu, 1994; Rogan & Gladen, 1991) have argued for this reason that effects of PCB exposure may be delayed. Thus, in light of the findings from this study and the developmental considerations mentioned, examination of the negative outcomes that have been associated with PCB exposure in previous research must be revisited with adolescent populations.

An important goal for future research is to investigate the unpredicted findings of the current study, namely the relationship of PCBs to two indicators of less problematic impulsivity and hyperactivity in our data. The large body of existing research on PCB effects demonstrates that it is very unlikely that PCB exposure would reduce ADHD-like behaviors. Systematic investigation of the concurrent influences of many factors in children's developmental contexts, will establish if the current unpredicted findings are chance happenings, or the result of some interaction of positive and negative influences on development. Comparison of PCB effects in populations with contrasting maternal, social and toxicological characteristics will allow clarification of any systematic confounding that is occurring in particular populations.

Finally, future research can determine the role of the particular PCB congeners selected and grouped to represent PCB exposure. More theoretical and toxicological work is needed to formulate congener profiles to allow more sensitive study of associations between PCB exposure and outcomes.

4.6. Conclusion

The current study did not find that the body burden of PCBs in the participating adolescents was related to their ADHD-like behavior, although previous studies showed that PCB levels are related to memory functioning in this cohort. Further research is necessary to establish

whether the conclusions hold for individuals of a different age, or whose exposure to PCBs is greater, or who experience different social environments, or when different PCB analytic categories are used.

Acknowledgments

We would like to acknowledge and thank the Akwesasne Mohawk community, and in particular we would like to thank Maxine Cole, Alice Tarbell, Dawn David, Agnes Jacobs, Priscilla Worswick, Ken Jock, and Craig Arquette for their many contributions, cooperation and participation in the research we have done together on this topic. This work was supported by grants from the National Institute of Environmental Health Sciences (NIEHS-ESO4913; ES10904), and the National Institute on Minority Health and Health Disparities, National Institutes of Health (grant number 1 P20 MD003373). The content is solely the responsibility of the authors and does not represent the official views of the National Institute on Minority Health and Health Disparities or the National Institutes of Health.

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Highlights

- Persistent PCBs in the blood serum of 271 Mohawk adolescents were measured.
- Two rating scales of ADHD-like behavior were completed by parents and teachers.
- PCB levels were not related to ratings of ADHD-like behavior.
- There was no evidence of negative confounding by SES or breastfeeding history.

Table 1

Descriptive statistics for the ADHD scores

Dependent Variables	n	Mean	SD	Minimum	Maximum
ADDES Parent Standard Scores					
Inattentive (APINS)	269	9.24	3.04	0.00	15.00
Hyperactive-Impulsive (APHIS)	269	9.95	2.90	0.00	15.00
ADDES Teacher Standard Scores					
Inattentive (ATINS)	232	9.81	2.60	2.00	14.00
Hyperactive-Impulsive (ATHIS)	232	10.09	2.52	0.00	13.00
Conners Parent T-scores					
Impulsive-Hyperactive (IHPT)	269	50.68	11.43	35.00	94.00
Hyperactivity Index Score (HIPT)	269	52.90	13.19	35.00	99.00
Conners Teacher T-scores					
Hyperactive (HATT)	231	53.45	13.30	41.00	100.00
Inattentive-Passive (IPTT)	231	54.11	12.04	38.00	99.00
Hyperactivity Index Score (HITT)	231	55.59	14.03	40.00	100.00

Note. ADDES: Scores from 7–13 are considered average; low scores indicate more problems.

Conners: Scores from 40–60 are considered average; high scores indicate more problems.

Table 2

Descriptive statistics for potential covariates and correlation with PCBs

Covariates						Correlation with PCBs	
	n	Mean	SD	Minimum	Maximum	r	p
Adolescent							
Age (years)	271	13.23	1.96	10.00	16.99	-0.03	0.66
BMI (kg/m ²)	270	24.15	5.29	13.65	43.49	-0.15	0.01
Triglyceride level (mg/dL)	259	87.19	44.20	25.00	259.00	0.07	0.24
Cholesterol level (mg/dL)	259	159.48	28.93	100.00	251.00	0.09	0.16
Ravens: RPM	268	54.15	26.48	1.00	99.00	-0.04	0.57
TOMAL: CMIS	269	100.26	10.36	65.00	137.00	-0.04	0.51
WJ-R: BCAE	236	100.66	12.41	66.00	135.00	0.00	0.98
Maternal							
Maternal BMI (kg/m ²)	269	29.52	6.07	16.34	55.96	0.01	0.83
Maternal Broad Cognitive Ability (WJ-R: BCAS)	249	95.27	10.74	70.00	126.00	0.06	0.34
Socioeconomic Status Index	271	24.46	5.61	9.00	37.00	0.12	0.05
Number of Social Problems Reported	269	0.45	0.80	0.00	4.00	0.07	0.23
Pregnancy Order	269	2.17	1.39	1.00	8.00	0.17	0.01
Cigarette Use during Pregnancy (#/day)	269	3.70	6.55	0.00	40.00	-0.07	0.27
Breast-feeding Duration (weeks)	269	11.80	21.09	0.00	120.00	0.43	<0.001
Toxicants							
HCb (ppb)	271	0.04	0.02	0.01	0.19	0.27	<0.001
p,p'-DDE (ppb)	271	0.43	0.34	0.09	3.08	0.62	<0.001
Blood Lead (µg/dL)	265	1.43	0.83	0.50	4.80	0.06	0.33
Total Mercury (µg/dL)	265	0.12	0.96	0.02	0.58	0.07	0.25

Abbreviations. ppb = parts per billion; BMI= body mass index; Ravens: RPM = Ravens Progressive Matrices; TOMAL: CMIS = The Test of Memory and Learning: Composite Memory Index; WJ-R: BCAE = Woodcock Johnson-Revised Tests of Cognitive Ability; Broad Cognitive Ability Extended; WJ-R: BCAS = Woodcock Johnson-Revised Tests of Cognitive Ability Broad Cognitive Ability Standard.

SES index is a composite variable including maternal education, maternal employment, marital status, and various assets.

Table 3

Correlation of potential covariates with each ADHD variable

	APINS (n=269)		APHIS (n=269)		ATINS (n=232)		ATHIS (n=232)		IHPT (n=269)		HIPT (n=269)		HATT (n=234)		IPTT (n=234)		HITT (n=234)	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
Adolescent																		
Sex (M/F)	-0.06	0.36	-0.08	0.19	0.04	0.52	0.02	0.74	0.11	0.07	0.08	0.20	-0.18	0.01	-0.05	0.42	-0.12	0.06
Age (years)	-0.01	0.84	-0.08	0.21	-0.06	0.35	-0.16	0.02	0.14	0.02	0.07	0.26	0.14	0.04	0.02	0.82	0.09	0.18
BMI (kg/m ²)	-0.06	0.36	-0.10	0.10	0.06	0.37	0.01	0.83	-0.09	0.17	-0.04	0.52	-0.03	0.61	-0.02	0.74	-0.06	0.39
Triglyceride level (mg/dL)	-0.02	0.81	0.05	0.43	0.07	0.33	0.11	0.11	-0.11	0.09	-0.07	0.28	-0.15	0.03	0.00	0.98	-0.12	0.07
Cholesterol level (mg/dL)	-0.02	0.81	0.03	0.64	0.09	0.19	0.13	0.06	-0.05	0.44	-0.07	0.24	-0.16	0.02	-0.03	0.68	-0.11	0.11
Ravens: RPM	0.26	<0.001	0.19	<0.001	0.17	0.01	0.03	0.71	-0.08	0.20	-0.19	<0.001	-0.09	0.19	-0.20	<0.001	-0.15	0.03
TOMAL: CMIS	0.26	<0.001	0.20	<0.001	0.27	<0.001	0.07	0.31	-0.13	0.03	-0.24	<0.001	-0.19	0.01	-0.29	<0.001	-0.27	<0.001
WJ-R: BCAE	0.20	<0.001	0.17	0.01	0.13	0.06	-0.04	0.53	-0.11	0.10	-0.21	<0.001	-0.06	0.37	-0.14	0.06	-0.11	0.11
Currently consumes cigarettes (n/y)	-0.17	0.01	-0.17	0.01	-0.16	0.02	-0.24	<0.001	0.14	0.03	0.25	<0.001	0.22	<0.001	0.11	0.11	0.16	0.01
Currently consumes alcohol (n/y)	-0.14	0.03	-0.13	0.03	-0.05	0.41	-0.17	0.01	0.17	0.01	0.14	0.02	0.15	0.02	0.03	0.65	0.07	0.29
Maternal																		
Maternal BMI (kg/m ²)	-0.05	0.47	-0.02	0.72	0.00	0.98	0.06	0.33	-0.03	0.64	-0.01	0.87	-0.08	0.21	0.03	0.70	-0.04	0.55
WJ-R: BCAS	0.02	0.77	0.06	0.37	0.12	0.09	0.04	0.60	-0.11	0.10	-0.15	0.02	-0.08	0.25	-0.13	0.05	-0.13	0.07
Socioeconomic Status Index	0.05	0.44	0.13	0.04	0.05	0.49	0.05	0.46	-0.14	0.02	-0.16	0.01	-0.16	0.01	-0.14	0.03	-0.15	0.02
Number of Social Problems Reported	-0.27	<0.001	-0.25	<0.001	-0.02	0.81	0.04	0.59	0.19	<0.001	0.26	<0.001	0.06	0.37	0.05	0.46	0.04	0.55
Pregnancy Order	-0.02	0.80	-0.06	0.29	-0.14	0.04	-0.12	0.08	0.01	0.82	0.07	0.23	0.12	0.07	0.17	0.01	0.16	0.01
Cigarette Use during Pregnancy (#/day)	-0.20	<0.001	-0.28	<0.001	-0.17	0.01	-0.03	0.66	0.20	<0.001	0.24	<0.001	0.14	0.03	0.21	<0.001	0.15	0.02
Breastfeeding Duration (weeks)	0.05	0.38	0.11	0.08	0.02	0.75	0.06	0.40	-0.10	0.09	-0.12	0.05	-0.02	0.81	0.00	0.98	-0.01	0.90
Toxicants																		
ΣParPCB50%	0.02	0.82	0.06	0.31	-0.05	0.48	-0.01	0.87	-0.10	0.12	-0.11	0.08	0.06	0.41	0.05	0.47	0.09	0.20
HCB (ppb)	-0.02	0.71	-0.02	0.80	-0.11	0.09	-0.16	0.02	0.07	0.26	0.08	0.21	0.20	<0.001	0.08	0.22	0.20	<0.001
p,p'-DDE (ppb)	0.06	0.34	0.04	0.57	-0.10	0.14	-0.09	0.17	0.02	0.78	-0.05	0.40	0.11	0.09	0.09	0.17	0.14	0.03

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	APINS (n=269)		APHIS (n=269)		ATINS (n=232)		ATHIS (n=232)		IHPT (n=269)		HIPT (n=269)		HATT (n=234)		IPTT (n=234)		HITT (n=234)	
	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p	r	p
<i>Blood Lead (µg/dL)</i>	-0.04	0.55	-0.05	0.47	-0.07	0.28	-0.10	0.13	0.10	0.11	0.08	0.20	0.17	0.01	0.06	0.38	0.13	0.06
<i>Total Mercury (µg/dL)</i>	0.00	1.00	0.01	0.84	0.07	0.31	0.15	0.02	0.00	0.98	0.03	0.57	-0.13	0.05	-0.10	0.16	-0.10	0.15

Abbreviations: ppb, parts per billion; BMI= body mass index; Ravens: RPM = Ravens Progressive Matrices; TOMAL: CMIS = The Test of Memory and Learning; Composite Memory Index; WJ-R: BCAS = Woodcock Johnson-Revised Tests of Cognitive Ability Extended; WJ-R: BCAS = Woodcock Johnson-Revised Tests of Cognitive Ability Broad Cognitive Ability Standard; APINS= ADDES Parent Inattentive Standard Score; APHIS = ADDES Parent Hyperactive-impulsive Standard Score; ATINS = ADDES Teacher Inattentive Standard Score; ATHIS = ADDES Teacher Hyperactive-impulsive Standard Score; IHPT = Conners Parent Impulsive-hyperactive; HIPT = Conners Parent Hyperactivity Index; HATT = Conners Teacher Hyperactive; IPTT = Conners Teacher Inattentive-impulsive; HITT = Conners Teacher Hyperactivity Index

ΣPerPCB%= IUPAC#s 118,138[+163+164],153,180,74,99,187,105.

Bold denotes $p < 0.2$.

Italic denotes log transformed.

Note: For ADDES, low scores indicate more problems; for Conners, high scores indicate more problems.

Table 4

Multiple regression between sum of Persistent PCBs and each ADHD score

Measures	Unstd. β	SE	Std. β	<i>p</i>
ADDES Parent Standard Scores				
Inattentive (APINS)	0.22	0.39	0.04	0.57
Hyperactive-impulsive (APHIS)	0.45	0.43	0.07	0.29
ADDES Teacher Standard Scores				
Inattentive (ATINS)	0.17	0.48	0.03	0.72
Hyperactive-impulsive (ATHIS)	-0.02	0.43	0.00	0.97
Conners Parent T-scores				
Impulsive-hyperactive (IHPT)	-3.84	1.84	-0.16	0.04
Hyperactivity Index Score (HIPT)	-3.02	1.94	-0.11	0.12
Conners Teacher T-scores				
Hyperactive (HATT)	0.52	2.30	0.02	0.82
Inattentive-Passive (IPTT)	-0.02	2.20	0.00	0.99
Hyperactivity Index Score (HITT)	-0.68	2.62	-0.02	0.80

Σ PerPCB50% = IUPAC#s 118, 138[+163+164], 153, 180, 74, 99, 187, 105.

* Covariates included in the analysis are: Sex; age (yrs); adolescent BMI (kg/m²); adolescent triglyceride and cholesterol levels; Ravens Progressive Matrices; TOMAL: CMIS = The Test of Memory and Learning: Composite Memory Index; WJ-R: BCAS = Woodcock Johnson-Revised Tests of Cognitive Ability: Broad Cognitive Ability Extended; adolescent's current cigarettes and alcohol use; maternal WJ-R: BCAS = Woodcock Johnson-Revised Tests of Cognitive Ability Broad Cognitive Ability Standard; SES; # reported social problems; pregnancy order, cigarette use during pregnancy; breast-feeding duration (wks); HCB; *p,p'*-DDE; Pb; Hg.

Note: For ADDES, low scores indicate more problems; for Conners, high scores indicate more problems.

Table 5

Correlation between socio-economic index scores and covariates

	SES		
	<i>r</i>	<i>p</i>	<i>n</i>
Adolescent			
Sex (M/F)	0.08	0.18	271
Age (years)	0.03	0.64	271
BMI (kg/m ²)	−0.02	0.81	270
Triglyceride level (mg/dL)	0.00	1.00	259
Cholesterol level (mg/dL)	−0.04	0.52	259
Ravens: RPM	0.06	0.32	268
TOMAL: CMIS	0.16	0.01	269
WJ-R: BCAE	0.15	0.03	236
Currently consumes cigarettes (n/y)	−0.05	0.40	271
Currently consumes alcohol (n/y)	−0.008	0.90	271
Maternal			
Maternal BMI (kg/m ²)	−0.01	0.86	269
WJ-R: BCAS	0.37	<0.01	249
Number of Social Problems Reported	−0.03	0.67	269
Pregnancy Order	−0.05	0.41	269
<i>Cigarette Use during Pregnancy (#/day)</i>	−0.22	<0.01	269
<i>Breast-feeding Duration (weeks)</i>	0.25	<0.01	268
Toxicants			
<i>ΣPerPCB50%</i>	0.12	0.05	271
<i>HCB (ppb)</i>	−0.01	0.81	271
<i>p,p'-DDE (ppb)</i>	0.16	0.01	271
<i>Blood Lead (μg/dL)</i>	−0.14	0.02	265
<i>Total Mercury (μg/dL)</i>	0.11	0.08	265

Table 6

Multiple regression of PCBs and ADHD in adolescents below and above the mean of SES

Measures	Low SES				High SES			
	Unstd. β	SE	Std. β	p	Unstd. β	SE	Std. β	p
ADDES Parent Standard Scores								
Inattentive (APINS)	-0.15	0.60	-0.02	0.80	0.66	0.52	0.11	0.21
Hyperactive-impulsive (APHIS)	0.53	0.72	0.08	0.46	0.56	0.53	0.10	0.29
ADDES Teacher Standard Scores								
Inattentive (ATINS)	0.74	0.85	0.14	0.39	-0.21	0.55	-0.04	0.70
Hyperactive-impulsive (ATHIS)	-0.02	0.72	0.00	0.98	-0.50	0.52	-0.12	0.34
Conners Parent T-scores								
Impulsive-hyperactive (IHPT)	-7.01	3.23	-0.27	0.03	-1.68	2.33	-0.08	0.47
Hyperactivity Index Score (HIPT)	-2.17	3.59	-0.07	0.55	-4.52	2.19	-0.19	0.04
Conners Teacher T-scores								
Hyperactive (HATT)	-2.36	4.48	-0.07	0.60	4.72	2.36	0.24	0.05
Inattentive-Passive (IPTT)	-3.35	4.09	-0.12	0.42	1.62	2.54	0.07	0.53
Hyperactivity Index Score (HITT)	-4.63	5.01	-0.14	0.36	3.44	3.01	0.14	0.26

 $\Sigma \text{PerPCB50\%} = \text{IUPAC\#s } 118, 138[+163+164], 153, 180, 74, 99, 187, 105.$

* Covariates included in the analysis are: Sex; age (yrs); adolescent BMI (kg/m^2); adolescent triglyceride and cholesterol levels; Ravens Progressive Matrices; TOMAL: CMIS = The Test of Memory and Learning; Composite Memory Index; WJ-R: BC/AE = Woodcock Johnson-Revised Tests of Cognitive Ability; Broad Cognitive Ability Extended; adolescent's current cigarettes and alcohol use; maternal WJ-R: BCAS = Woodcock Johnson-Revised Tests of Cognitive Ability Broad Cognitive Ability Standard; SES; # reported social problems; pregnancy order, cigarette use during pregnancy; breast-feeding duration (wks); HCB; p,p' -DDE; Pb; Hg.

Note: For ADDES, low scores indicate more problems; for Conners, high scores indicate more problems.