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PCBs and ADHD in Mohawk adolescents



NEUROTOXICOLOGY TERATOLOGY

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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 breastfeeding history was examined but dismissed.

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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, 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 the 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 the 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 breastfeeding. Because PCBs are lipophilic, they are stored in breast milk and may be transmitted to infants during breastfeeding.

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 the recent decades, and assessment instruments have been developed and

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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, 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., 2001; 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 and 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 and 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 at al., 2012, but only for boys; Stewart et al., 2003, 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 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 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 breastfeeding 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 and 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 breastfeeding. 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 h. Blood was allowed to clot at room temperature for 20 min and then centrifuged at $800 \times g$ for 15 min. 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

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