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Exposure to Polyfluoroalkyl Chemicals and Attention Deficit/Hyperactivity Disorder in U.S. Children 12–15 Years of Age

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Polyfluoroalkyl chemicals (PFCs) are a class of highly stable man-made compounds. Composed of a variable-length fluorinated carbon backbone and a carboxylate or sulfonate functional group, PFCs have both hydrophobic and oleophobic portions that enable products to repel both oil and water and resist staining. PFCs are widely used in consumer products containing PFCs, contaminated drinking and surface waters, airborne PFCs, indoor air, and house dust (3M Company 2003; Bollinger et al. 2004; Emmett et al. 2006; Holzer et al. 2008; Martin et al. 2002; Saito et al. 2004; Shoeb et al. 2005; So et al. 2004; Steenland et al. 2009; Stock et al. 2004).

PFCs are absorbed through ingestion and to a lesser extent through inhalation. Once absorbed, PFCs are eliminated from the human body very slowly. Serum half-life estimates in an occupationally exposed cohort ranged from 5.4 years for perfluorooctane sulfonic acid (PFOS) to 8.5 years for perfluorohexane sulfonic acid (PFHxS) (Olsen et al. 2007). In a cohort exposed to drinking water contaminated by perfluorooctanoic acid (PFOA), the serum half-life for PFOA was estimated to be 2.3 years (Bartell et al. 2010). Although the primary producer of PFOS, the 3M Company, discontinued its use in 2002; and U.S. companies have implemented a voluntary emission reduction program for PFOA, > 98% of a 2003–2004 U.S. population sample had detectable serum levels of two perfluorinated carboxylates, PFOA and perfluorononanoic acid (PFNA), and two perfluorinated sulfonates, PFOS and PFHxS (Calafat et al. 2007b).

The ubiquitous presence and persistence of PFCs in the environment and the human body have led to efforts to understand the toxicologic hazards that may be associated with exposure. Early animal studies focused almost exclusively on exposure to PFOS and PFOA and found several potential effects, primarily related to hepatotoxicity, immunotoxicity, and reproductive and developmental toxicity (Lau et al. 2004, 2007). Although assessments are now including other PFCs and examining human populations, data are still limited. Preliminary data suggest that PFCs may be potential developmental neurotoxicants. Using in vitro models, PFCs were shown to affect neuronal cell development in a variety of ways, including changes in cell differentiation (Slotkin et al. 2008). In rat models, in utero exposure to PFOS was linked to reduction in thyroid hormone (circulating thyroxin and triiodothyronine), which is known to regulate brain development (Lau et al. 2003; Luebker et al. 2005). However, in pups exposed to PFOS prenatally, reductions in thyroid hormone did not appear to disrupt...
learning and memory behavior in postnatal evaluations (Lau et al. 2003). Other developmental neurotoxic effects, manifested in changes in motor function and delayed learning, were observed in several animal studies (Fuentes et al. 2007a, 2007b; Johansson et al. 2008). Even at relatively low doses, Johansson et al. (2008) found developmental neurotoxic effects, including changes in spontaneous behavior and habituation ability, associated with PFOA and PFOS exposure in mice, which persisted into adulthood. Neonatal exposure to PFOS and PFOA has also been associated with changes in proteins (tau and synaptophysin) important in normal brain development (Johansson et al. 2009). To our knowledge, a single reported study assessed the human developmental neurotoxic effects of exposure to PFOA and PFOS. Using data for 1,400 pairs of pregnant women and their children randomly selected from the Danish National Birth Cohort, Fei et al. (2008) observed an association between maternal PFOS levels and delayed gross motor development in infancy (maternal report of the age at which a child could sit without support); however, maternal PFOS and PFOS levels were not significantly associated with delays in other developmental milestones, including those related to attention.

Attention deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in children, with an estimated prevalence between 7% and 16% in the United States (Faraone et al. 2003; Froehlich et al. 2007). Data suggest that the underlying prevalence of ADHD is increasing. Children diagnosed with ADHD are a heterogeneous population sharing common symptoms, including inattention, impulsivity, and, in some cases, hyperactivity, or a combination of symptoms. Although the mechanisms that lead to the development of ADHD remain unclear, genetic and environmental factors have been linked to ADHD. Environmental contaminants such as methylmercury and lead have been positively associated with ADHD in children (Braun et al. 2006; Cheuk and Wong 2006).

In the present analyses, we explored the association between ADHD and PFOS, PFOA, PFHxS, and PFNA using cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) 1999–2000 and 2003–2004 cycles. To our knowledge, this is the first study examining the association between PFCs and ADHD.

Methods

Data source. NHANES is a nationally representative, cross-sectional sample of the non-institutionalized U.S. civilian population. The survey combines in-home interviews and physical examinations in a mobile exam unit to collect data on demographics, socioeconomic status (SES), health conditions, and behavioral and environmental risk factors [Centers for Disease Controls and Prevention (CDC) 2008]. Details regarding interviews, examination procedures, and sample collection have been described previously (CDC 2009a, 2009b).

ADHD and PFC exposure assessment. We used parental report of previous ADHD diagnosis as the primary dependent variable. Questionnaires were administered by trained personnel (CDC 2009a, 2009b). The children’s parents or guardians were asked if a doctor or health professional had ever told them that their child had attention deficit disorder. In NHANES, data on ADHD were collected in a target population of children 4–19 years of age.

To improve specificity, we also considered a second definition of ADHD used previously in an assessment of the effects of other environmental exposures on ADHD risk in the NHANES population (Braun et al. 2006). The second case definition included children with a parental report of a previous ADHD diagnosis and a parental report of their child taking medications approved for the treatment of ADHD within the preceding month (e.g., amphetamine aspartate, amphetamine sulfate, dextroamphetamine saccharate, dextroamphetamine sulfate, methylphenidate hydrochloride, or atomoxetine hydrochloride).

The National Center for Environmental Health analyzed serum PFC levels in a one-third sample of all individuals ≥ 12 years of age. Data were available during two nonconsecutive survey cycles, 1999–2000 and 2003–2004. Detailed analytic methods were described previously (Calafat et al. 2007a, 2007b). Briefly, serum samples were analyzed using automated solid-phase extraction coupled to reverse-phase high-performance liquid chromatography/ tandem mass spectrometry. Any subject with a serum PFC concentration below the limit of detection (LOD) was assigned an exposure value of the LOD divided by the square root of 2 (Calafat et al. 2007b).

Covariates. We investigated a number of covariates and potential confounders in the association between PFCs and ADHD. The demographic variables age, sex, and race/ethnicity were included as covariates based on their role in the NHANES selection procedure and previous research on their association with ADHD (Costello et al. 2003; Stevens et al. 2005). Additionally, we included NHANES sample cycle (1999–2000 or 2003–2004) as a covariate. SES was also considered a potential confounder. We used the poverty-income ratio (PIR), which relates the family income to the poverty threshold for each study year as a measure of SES. PIR values < 1.00 are considered living below the poverty level. Having a routine health care provider and health insurance coverage were also considered potential confounders (Stevens et al. 2005).

In addition, we also investigated confounding by other environmental contaminants that have been previously associated with ADHD: lead and environmental tobacco smoke (ETS) indicated by report of living with someone who smokes cigarettes, cigars, or pipes inside the home and by serum cotinine, a metabolite of nicotine (Bellinger et al. 1994; Braun et al. 2006; Fergusson et al. 1988; Weitzman et al. 1992; Williams et al. 1998). We also considered confounding by variables related to conditions during the prenatal and early childhood periods: birth weight, admittance to a neonatal intensive care unit (NICU), maternal smoking during pregnancy, and preschool attendance (Bottig et al. 1997; Braun et al. 2006; Mick et al. 2002a, 2002b; Milberger et al. 1996; National Institute of Child Health and Human Development 2003). NHANES collects different exposure, outcome, and confounder data depending on the age of the individual. Data on ADHD outcomes, confounder information, and PFC measurements were collected for children 12–15 years of age only; consequently, analyses were limited to this age range.

Statistical analyses. We examined the shape of the relationship between the continuous measures of each individual PFC and parent-reported ADHD using a locally weighted regression smoother (LOESS) in S-Plus (version 8.0; Tibbo Software, Inc., Palo Alto, CA). Smoothing allowed us to summarize ADHD odds as a function of PFC exposures without imposing a rigid form of dependence. We selected the optimal span size—the window from which data are drawn to estimate the odds of ADHD—by minimizing Akaike’s information criterion (Hastie and Tibshirani 1990). We visually inspected plots of the smoothed data to inform our decision on how to model exposure.

Logistic regression analyses were performed in SAS (version 9.1; SAS Institute, Inc., Cary, NC) using the Proc SURVEYLOGISTIC procedure, which accounts for stratification and clustering within primary sampling units used to select the NHANES sample. Rather than using NHANES sample weights, we adjusted all models for relevant covariates (age, sex, race/ethnicity, and sample cycle). This method is considered to be a good trade-off between efficiency and bias (Graubard and Korn 1999; Korn and Graubard 1991). Other potential covariates were included if they were strongly associated with ADHD in bivariate analyses (p < 0.10) or if they appreciably altered the association between PFC exposure and ADHD (odds ratio (OR) change > 10%). We included continuous covariates in models as continuous predictors and also explored...
the use of categorization. A p-value of 0.05 was chosen to indicate the statistical significance of the association between each PFC and ADHD.

Our preliminary investigation of PFC data revealed several children with very high serum PFC levels, particularly PFHxS, PFOA, and PFNA. To ensure that individuals with extreme exposure values were not disproportionately influencing results, we conducted sensitivity analyses excluding observations greater than three times the 75th percentile for each compound (PFOS, n = 0; PFOA, n = 2; PFNA, n = 12; PFHxS, n = 26). Additionally, because the range of serum values varied considerably for the PFCs we assessed, we conducted additional analyses to provide ORs standardized to an increase in units equal to the interquartile range (IQR) for each PFC to provide comparable effect estimates.

We also investigated the impact of all four PFCs in the same model. Because PFC levels are correlated (in these data, Spearman correlations ranged from 0.18 between PFOS and PFNA to 0.74 between PFOS and PFOA), we also performed principal component analysis, a systematic method of reducing the number of correlated observed variables into a smaller number of principal components that account for most of the variance in the observed PFC measures (Burstyn 2004).

**Results**

Of the 571 study participants 12–15 years of age with complete data, parents of 48 (8.4%) reported that their child had ADHD. Of those, 21 (3.6% of the study population) also reported using prescription medications approved for the treatment of ADHD within the last month. We included one child reported to be taking prescription medication for ADHD but not reported to have been diagnosed with ADHD in analyses as a noncase. Details regarding the total sample size are displayed in the Supplemental Material, Figure 1 (doi:10.1289/ehp.1001898).

Sex and maternal smoking during pregnancy were significantly associated with parental-report of ADHD in bivariate analyses (Table 1). Compared with non-Hispanic whites, Mexican Americans were less likely to report ADHD diagnosis (OR = 0.28; 95% confidence interval [CI], 0.11–0.72). Associations between ETS and ADHD were similar whether ETS was indicated by categorical serum cotinine levels (data not shown) or report of living with someone who smokes cigarettes, cigars, or pipes inside the home.

We controlled for ETS in models using report of living in a home with a smoker because data were missing less frequently. ETS was not associated with our stricter case definition of ADHD, having a reported diagnosis and taking prescription medication for the treatment of ADHD, which was similar to what Braun et al. (2006) observed. We also observed a positive association between lead and ADHD similar to that reported previously in a larger NHANES sample (Braun et al. 2006).

Table 2 displays the median serum level of each PFC in the study population. Nearly all study participants had detectable serum concentrations of all four PFCs included in our analyses (> 96% for all PFCs). Other PFCs were detected infrequently in this population. Table 3 displays the median serum PFC levels according to categorical covariates. Median serum concentrations were consistently higher in males than females and in children who attended preschool. Similarly, those who lived in a home with a smoker consistently had higher PFC levels. Table 4 displays correlations between continuous covariates and each PFC. With the exception of PFOA, which was weakly correlated with lead, we did not observe evidence of an association between PFCs and lead. Additionally, we observed a small but significant correlation between each PFC and the PIR.

The results of the smoothed analyses suggested that the association between PFC levels and ADHD may be approximately linear over most of the data range; accordingly, we included PFCs in logistic regression models as continuous predictors [see details in Supplemental Material, Figure 2 (doi:10.1289/ehp.1001898)]. We observed a significant (p-value < 0.05) dose–response relationship between PFOS exposure and parent-reported ADHD; the OR for each 1-μg/L increase in serum PFOS was 1.03 (95% CI, 1.01–1.05) (Table 5) after adjusting for confounding by

| Variable                      | Cases Median | Noncases Median | OR (95% CI) |
|-------------------------------|--------------|-----------------|-------------|
| Age [years]                   | 13.4         | 13.4            | 0.93 (0.73–1.18) |
| Sex (n)                       | 41           | 255             | 4.50 (2.17–9.37)  |
| Male                          | 10           | 280             | Reference    |
| Female                        |              |                 |             |
| Race/ethnicity (n)            |              |                 |             |
| Mexican American              | 9            | 206             | 0.28 (0.11–0.72)  |
| Other Hispanic                | 1            | 25              | 0.26 (0.03–2.11)  |
| Non-Hispanic white            | 18           | 116             | Reference    |
| Non-Hispanic black            | 20           | 164             | 0.79 (0.35–1.76)  |
| Other, including multiracial  | 3            | 24              | 0.81 (0.28–2.33)  |
| Birth weight [kg]              |              |                 |             |
| ≤ 5.5 lb (2,500 g)            | 4            | 26              | 1.57 (0.62–4.02)  |
| > 5.5 lb (2,500 g)            | 47           | 481             | Reference    |
| Maternal smoking during pregnancy (n) | | | |
| Yes                           | 13           | 80              | 2.00 (1.04–4.17)  |
| No                            | 35           | 448             | Reference    |
| Preschool attendance (n)      | 37           | 341             | 1.50 (0.84–2.68)  |
| Yes                           | 14           | 193             | Reference    |
| No                            | 43           | 467             | Reference    |
| NICU admittance (n)           |              |                 |             |
| Yes                           | 8            | 60              | 1.45 (0.83–2.53)  |
| No                            | 43           | 467             | Reference    |
| ETS (n)                       |              |                 |             |
| Yes                           | 22           | 117             | 2.68 (1.58–4.53)  |
| No                            | 29           | 413             | Reference    |
| Lead [mean (μg/dL)]           | 1.5          | 1.3             | 1.09 (0.90–1.34)  |
| No                            | 1.8          | 1.9             | 1.00 (0.94–1.23)  |
| Access to health care (n)     |              |                 |             |
| Yes                           | 49           | 495             | 1.98 (0.71–5.49)  |
| No                            | 2            | 40              | Reference    |
| Health insurance coverage (n) |              |                 |             |
| Yes                           | 46           | 427             | 2.15 (0.83–5.57)  |
| No                            | 5            | 100             | Reference    |
| NHANES sample wave (n)        |              |                 |             |
| 1999–2000                     | 20           | 258             | Reference    |
| 2003–2004                     | 31           | 277             | 1.44 (0.84–2.48)  |

**Table 2.** Distribution of PFC levels in the study population (μg/L).

**Variable** | **Median** | **Range** | **IQR** |
|-------------|------------|-----------|---------|
| PFOS        | 22.6       | 2.1–87.2  | 15.9    |
| PFOA        | 4.4        | 0.4–21.7  | 2.7     |
| PFHxS       | 2.2        | ND to 64.1| 2.9     |
| PFNA        | 0.6        | ND to 5.9 | 0.5     |

ND, nondetectable. The LOD in 1999–2000 serum samples was 0.2 μg/L for PFOS, 0.1 μg/L for PFOA, 0.1 μg/L for PFHxS, and 0.1 μg/L for PFNA; in 2003–2004 serum samples, it was 0.4 μg/L for PFOS, 0.1 μg/L for PFOA, 0.3 μg/L for PFHxS, and 0.1 μg/L for PFNA (Calafat et al. 2007b).
NHANES sample cycle, age, race/ethnicity, sex, ETS, and maternal smoking during pregnancy. Crude estimates of the association between PFCs and ADHD were similar to adjusted estimates. The inclusion of other covariates, including the PIR, did not materially alter the association between PFCs and parent-reported ADHD (data not shown). PFOA and PFHxS levels were also positively associated with ADHD (PFOA: OR = 1.12; 95% CI, 1.01–1.23; PFHxS: OR = 1.06; 95% CI, 1.02–1.11). The odds of parent-reported ADHD also increased with PFNA concentrations, although not significantly (OR = 1.32; 95% CI, 0.86–2.02). Results were similar when we used the stricter case definition of ADHD that required both parental report and medication use (Table 5). The same covariates were evaluated for each case definition.

Because the range of serum values varied considerably for the PFCs we assessed, we also calculated ORs standardized to an increase in units equal to the IQR for each PFC. An increase in serum PFOA levels equal to the IQR was associated with 1.60 times the odds of ADHD (95% CI, 1.05–2.31; IQR = 15.9 μg/L). For PFOA, the odds of ADHD increased 1.35 times for an increase equal to the IQR (95% CI, 1.05–1.34). The IQR effect for PFNA increased ADHD odds 1.19 times (95% CI, 0.93–1.42; IQR = 5.5 μg/L). For PFOS, the odds of ADHD increased 1.19 times for an increase equal to the IQR (95% CI, 1.04–1.77; IQR = 2.9 μg/L). A 2.9-μg/L increase in serum PFHxS increased the odds of ADHD 1.19 times (95% CI, 1.05–1.34). The IQR effect for PFNA increased ADHD odds 1.15 times (95% CI, 1.02–1.11; IQR = 0.7 μg/L).

Several children had very high serum PFC levels, particularly PFHxS, PFOA, and PFNA. Estimated ORs were slightly higher than those reported in Table 5 when observations with PFC concentrations more than three times the value of the 75th percentile were excluded (data not shown).

Principal component analyses indicated that PFOS, PFOA, and PFHxS all loaded onto a single component that accounted for 58% of the total variability in all four PFC measures. A second component, which primarily represented PFNA, explained 22% of the total variability. We repeated multiple logistic regression analyses including both PFNA and the principal component that represented the weighted combination of PFOS, PFOA, and PFHxS. A positive association with ADHD remained for the combined PFC variable and for PFNA (data not shown; PFOS, PFOA, and PFHxS component p-value = 0.02; PFNA p-value = 0.72).

Discussion
We observed a positive dose–response relationship between parent-reported ADHD and serum PFOS, PFOA, and PFHxS concentrations modeled as continuous predictors. Including PFC levels modeled as categorical predictors of ADHD produced similar results. The estimated effect of exposure on the population level was similar across these PFCs based on IQR analyses, indicating the importance of extending neurotoxicologic research to PFCs other than PFOS and PFOA, which have historically been the focus of research.

Principal component analyses support evidence of a positive association between ADHD and serum PFCs. Controlling for PFNA levels and other covariates, we observed a significant positive association with the principal component representing PFOS, PFOA, and PFHxS, suggesting that there may be different sources of exposure for PFNA and the other PFCs that we assessed. This is an area for future research.

Our results are consistent with animal data that suggest neurotoxic effects of PFC exposures (Fuentes et al. 2007a, 2007b; Johansson et al. 2008). To our knowledge, the report by Fei et al. (2008) is the only other published study of neurodevelopmental outcomes and PFC exposures. Except for gross motor ability, Fei et al. (2008) did not observe statistically significant differences in maternal reports of developmental milestones in infancy related to PFOS or PFOA exposure. The age of individuals in the study populations may explain differences between our results and those of Fei et al. (2008).

### Table 3. Median serum PFC concentrations (μg/L) by categorical covariates.

| Variable                  | Sex        | PFOS | PFOA | PFHxS | PFNA |
|---------------------------|------------|------|------|-------|------|
|                           | Male       | 256  | 25.7 | 6.8   | 0.7  |
|                           | Female     | 220  | 21.9 | 4.6   | 0.5  |
| Race/ethnicity            | Mexican American | 165 | 20.3 | 4.1   | 1.7  |
|                           | Other Hispanic | 26   | 18.3 | 4.4   | 1.3  |
|                           | Non-Hispanic white | 132 | 26.3 | 4.6   | 3.3  |
|                           | Non-Hispanic black | 184 | 24.1 | 4.6   | 2.4  |
|                           | Other, including multiracial | 27  | 24.6 | 4.1   | 2.7  |
| Birth weight              | ≤ 5.5 lb (2,500 g) | 30  | 22.0 | 3.8   | 2.3  |
|                           | > 5.5 lb (2,500 g) | 528 | 22.7 | 4.4   | 2.2  |
| Maternal smoking during pregnancy | Yes | 93   | 22.8 | 4.4   | 2.6  |
|                           | No | 483  | 22.5 | 4.1   | 2.1  |
| Preschool attendance      | Yes | 378  | 23.5 | 4.5   | 2.4  |
|                           | No | 207  | 21.1 | 4.1   | 1.8  |
| NICU admittance           | Yes | 68   | 22.4 | 4.5   | 2.5  |
|                           | No | 510  | 22.6 | 4.4   | 2.2  |
| ETS*                      | Yes | 139  | 24.7 | 4.5   | 2.3  |
|                           | No | 442  | 22.2 | 4.3   | 2.1  |
| Access to health care     | Yes | 544  | 23.0 | 4.4   | 2.3  |
|                           | No | 42   | 18.4 | 3.5   | 1.4  |
| Health insurance coverage | Yes | 473  | 23.4 | 4.4   | 2.3  |
|                           | No | 105  | 18.8 | 3.9   | 1.6  |
| NHANES sample wave        | 1999–2000 | 278 | 28.2 | 5.3   | 2.2  |
|                           | 2003–2004 | 308 | 18.2 | 3.8   | 2.2  |

*Missing data: low birth weight, n = 28; maternal smoking during pregnancy, n = 10; preschool attendance, n = 1; ETS, n = 5; health insurance coverage, n = 8.

### Table 4. Spearman correlations between continuous covariates and PFCs (p-value).

| Variable                  | PFOS | PFOA | PFHxS | PFNA |
|---------------------------|------|------|-------|------|
| Age (years)               | −0.078 (0.059) | −0.051 (0.220) | −0.052 (0.208) | 0.008 (0.852) |
| Lead‡                     | 0.062 (0.132) | 0.121 (0.003) | 0.033 (0.428) | 0.030 (0.464) |
| PIR‡                      | 0.223 (< 0.001) | 0.172 (< 0.001) | 0.178 (< 0.001) | 0.169 (< 0.001) |

*Missing data: lead, n = 1; PIR, n = 35.

### Table 5. ORs (95% CIs) for 1-μg/L increase in serum level (n = 571).

| Variable | Crude | Adjusted* |
|----------|-------|-----------|
| PFOS     | 1.03 (1.01–1.05) | 1.03 (1.01–1.05) |
| PFOA     | 1.17 (1.07–1.30) | 1.12 (1.01–1.23) |
| PFHxS    | 1.07 (1.01–1.12) | 1.06 (1.02–1.11) |
| PFNA     | 1.76 (1.39–2.23) | 1.32 (0.86–2.02) |

*Adjusted for NHANES sample cycle, age, sex, race, ETS, and maternal smoking during pregnancy.
the difference between our results and those reported by Fei et al. (2008). Because of data availability, we were able to assess only children 12–15 years of age.

Our analyses have a number of limitations. NHANES data are collected cross-sectionally, making it difficult to infer a causal relationship between PFC levels and ADHD. These data do not allow us to speculate on potential development periods of susceptibility to exposure. Although PFCs have a relatively long half-life, there is a lack of information addressing whether current PFC levels are an appropriate surrogate for past levels in the general population (Bartell et al. 2010; Olsen et al. 2007). If the prenatal period and early childhood may be more susceptible, are the critical periods for insult from PFC exposure, then random misclassification error resulting from the use of current PFC levels as proxy measures of etiologically relevant exposures may have biased our results toward the null. These analyses are also potentially limited by our reliance on parental report of ADHD. Previous research indicates parental reports of ADHD are highly reliable (Faraone et al. 1995). Examining the combined outcome of reported ADHD and medication use, we improved the specificity of the outcome and increased the likelihood that children included as ADHD cases had been evaluated and treated by health care professionals. Although we identified a much smaller number of cases using the stricter definition (n = 21), and consequently reduced the precision, the point estimates were similar regardless of which case definition was used. Similarly, although we included a large number of terms in models for a relatively small number of outcomes, crude estimates of the association between PFCs and ADHD were similar to adjusted estimates. Analyses of the NHANES population conducted previously have shown that parental report of ADHD was related to other environmental exposures (e.g., lead and maternal smoking during pregnancy) (Braun et al. 2006).

Detailed questionnaire and laboratory measurement data were available for a number of potential covariates in the NHANES data set, and we able to evaluate the potential for confounding by conditions during the prenatal and early childhood periods and other environmental exposures, such as lead and SES, related to ADHD. Data for potential confounders were generally very complete. However, there may still be residual confounding in the association between PFCs and ADHD. We were unable to assess several potential confounders because they were either not publicly available (i.e., maternal alcohol consumption during pregnancy) or not collected in the NHANES data set (i.e., genetic predisposition for ADHD).

Despite these limitations, our analyses have a number of strengths including the use of a representative sample of the U.S. population. Additionally, we were able to consider the association between PFC levels and ADHD odds over a wide range of exposures. We were also able to estimate associations of PFNA and PFHxS with ADHD; to our knowledge, this is the first assessment of the potential developmental neurotoxicity of these PFCs in children.

Conclusions

To our knowledge, these analyses are the first to assess the association between PFC levels and ADHD. As a whole, our results are consistent with increased ADHD in children with higher serum levels of PFCs. Given the extremely prevalent exposure to PFCs, further investigation into the impact of PFC exposure on ADHD and other neurodevelopmental endpoints is warranted.

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