**Supporting Information**

# Perfluorochemical (PFC) Exposure in Children: Associations with Impaired Response Inhibition

Brooks B. Gump[1], PhD, MPH, Qian Wu[2], BS, Amy K. Dumas[3], MSEd, and Kurunthachalam Kannan[2], PhD

[1] Syracuse University, Syracuse NY 13244
[2] Wadsworth Center, New York State Department of Health and Department of Environmental Health Sciences, School of Public Health, State University of New York, Albany, New York 12201-0509, USA
[3]State University of New York College at Oswego, Oswego, NY 13126

Corresponding Author
Brooks B. Gump, PhD, MPH
426 Ostrom Ave
Department of Public Health, Food Studies, and Nutrition
Syracuse University
Syracuse, NY 13244
Ph: 315-443-2208
Fax: 315-342-2046
Email: bbgump@syr.edu

**Summary Information**

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Measurement methods for potential confounds

A parent questionnaire assessed the child's age (converted from date of birth), child's gender, child's race (using checklist as well as write-in), mother's age (continuous variable), father's age (continuous variable), family income (using a 9-point scale ranging from "< $5,000" to "$65,000 or greater"), parent's education (using a 8-point scale ranging from "Less than 7$^{th}$ grade" to "Graduate Degree" averaged across parents), parent's occupation (using self-reported occupation and subsequent conversion to a scale value based on the Hollingshead's classification scheme (*1)*, averaged across parents), and family history for a number of diseases (namely diabetes, heart disease, high cholesterol, high blood pressure, stroke, and asthma; used as a categorical variable – 0=No, 1=Yes). Most children self-identified as Anglo-American/White (84.81%) and other races were not represented in sufficient numbers for meaningful analysis of specific races (e.g., 2 identified as African American and 8 identified as multi-ethnic); therefore, race was treated as a dichotomous variable (0=Anglo-American/White; 1=Other). Children were considered to have a family history if the reporting parent noted a history of any disease for themselves, their spouses, a maternal grandparent, or a paternal grandparent. Parent's BMI (based on height and weight; BMI = weight (kg)/height (m)$^2$) and age were assessed via self-report (and entered in models as continuous variables). The child's height and weight were measured upon arrival at the laboratory and converted to BMI (and entered in models as a continuous variable). Finally, skinfold thickness was measured at the biceps, triceps, subscapular, and suprailiac sites using a Lange skinfold caliper on the right side of all subjects. Percent body fat in the present study was calculated using Durnin's regression equation (*2)*: Percent body fat = (.265 x sum of skinfolds) + 13.08, for females, and Percent body fat = (.2608 x sum of skinfolds) + 5.27, for males.

Blood metals (Pb and Hg) were measured in a separate whole blood specimen (2-mL) collected into a Vacutainer tube during the blood draw. Blood specimens are refrigerated pending shipment to the Lead Poisoning/Trace Elements Laboratory at the New York State Department of Health's Wadsworth Center, Albany, NY, New York State's principal reference laboratory for the measurement of trace metals in blood. The analysis for Pb and mercury in whole blood was carried out using a Perkin-Elmer ELAN DRC Plus ICP-MS according to a standard operating procedure (SOP) that has been certified and approved for use in NY State (*3)*. Details regarding these methods have been published previously (*4)*.

The selection of these potential confounds was based on prior research suggesting associations of behavioral inhibition and impulsivity with the following variables: socioeconomic status (e.g., income, (*5)*), age (*6)*, obesity (*7)*, maternal age (*8)*, and blood metal exposure (*9)*. Some variables such as maternal BMI and family history are designed to control for confounding by underlying unmeasured variables that might affect impulsivity (e.g., serum ω-3 fatty acids; (*10)*).

Alternative method of covariate selection

A SAS macro (*11)* was employed to conduct a change-in-estimate approach to covariate selection. Using this macro, an initial model included all potential covariates, the specific predictor variable (e.g., PFOS), and the specific outcome (e.g., median IRT for 0 – 5 min). Using this macro, each covariate is removed (and returned) to determine the change

in estimate for the association between the predictor and outcome produced by that particular covariate. The covariate producing the least change-in-estimate is then permanently removed from this pool. This backward elimination is continued until all covariates are removed. We selected those covariates from this backward elimination list that produced a change-in-estimate of 5%. Table S6 shows the associations between median IRTs and PFC blood levels using this alternative covariate selection method.

Alternative Nonparametric Regression

Using data without transformation, a locally weighted scatterplot smoother (Lowess) method (*12)* using PROC LOWESS is shown in Figure S1 (with a smoothed predicted curve as well as raw data shown). The y-axis is truncated to avoid an overrepresentation of outlying data points. Similar to the results of the linear regressions using log-transformed data, these figures suggest that increasing PFC blood levels are associated with shorter IRTs, particularly for the 6 – 10 minute and 11 – 15 minute intervals.

**Table S1**. Relationship of PFC blood levels to median IRTs within each time period of the DRL task and money earned (standardized β; $N = 79$).

| | Median IRTs (within time period) | | | | Money |
|---|---|---|---|---|---|
| PFC | 0 – 5 | 6 – 10 | 11 – 15 | 16 – 20 | Earned |
| PFHpA | -0.11 | -0.11 | -0.01 | -0.05 | -0.22 # |
| PFDoDA | 0.08 | 0.04 | -0.04 | 0.06 | -0.04 |

Note: # $p < 0.10$; * $p < .05$

**Table S2**. Cardiovascular measures acquired before the DRL task correlated with DRL performance (mean IRT within each 5 minute period)) and PFC levels (log-transformed). Cardiovascular measures include systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), cardiac output (CO; the quantity of blood pumped from heart each minute), and total peripheral resistance (TPR; the vascular resistance to blood flow). CO and TPR measured with impedance cardiography is considered reliable for measuring changes across time but is not acceptable for the measurement of absolute (baseline) levels. Details regarding these measures can be found in Gump et al. (*22*).

| | DRL IRTs (within time period) | | | | Perfluorochemicals (PFCs) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Measure | 0 – 5 | 6 – 10 | 11 – 15 | 16 – 20 | PFOS | PFOA | PFNA | PFDA | PFHxS | PFOSA |
| Baseline | | | | | | | | | | |
| SBP (mmHg) | -0.21 # | 0.04 | -0.01 | -0.06 | 0.05 | 0.02 | -0.03 | -0.09 | 0.13 | 0.15 |
| DBP (mmHg) | -0.20 # | 0.05 | -0.04 | -0.14 | 0.06 | 0.04 | 0.01 | -0.02 | 0.09 | 0.16 |
| Heart Rate (beats/min) | -0.10 | 0.11 | 0.19 # | 0.01 | 0.01 | -0.09 | -0.20 # | -0.19 # | -0.01 | 0.02 |
| Response to stress (tasks-baseline) | | | | | | | | | | |
| SBP (mmHg) | 0.26 * | 0.13 | 0.17 | 0.17 | 0.05 | 0.15 | -0.05 | -0.04 | -0.13 | -0.19 # |
| DBP (mmHg) | 0.22 * | 0.11 | 0.19 # | 0.27 * | 0.03 | 0.11 | -0.04 | -0.10 | -0.09 | -0.16 |
| HR (beast/min) | -0.01 | -0.08 | -0.07 | -0.13 | -0.03 | 0.06 | 0.28 * | 0.11 | -0.08 | -0.16 |
| Cardiac Output (l/min) | 0.16 | 0.10 | 0.16 | 0.24 * | -0.08 | -0.02 | 0.07 | -0.05 | -0.05 | -0.04 |
| Total Peripheral Resistance (dyne-s/cm$^5$) | 0.02 | -0.03 | -0.02 | -0.03 | 0.13 | 0.12 | -0.06 | 0.04 | 0.07 | -0.04 |

# $p < .10$; * $p < .05$

**Table S3**. Bivariate associations between DRL task performance measures (outcomes) and potential covariates (Pearson r reported for all variables with the exception of point biserial correlations reported for gender and family history variables).

| | Median IRTs (within time period) | | | | Money |
|---|---|---|---|---|---|
| Potential Covariate | 0 – 5 | 6 – 10 | 11 – 15 | 16 – 20 | Earned |
| Child age (yrs) | 0.05 | -0.03 | -0.02 | -0.02 | -0.04 |
| Mother's age | **0.25** * | 0.08 | 0.04 | 0.08 | -0.04 |
| Father's age (yrs) | 0.10 | 0.04 | **0.16** | **0.18** | **0.17** |
| Family Income (score) | -0.04 | -0.13 | -0.03 | 0.06 | -0.01 |
| Parent's Education (score) | 0.08 | **0.19** | **0.18** | **0.24** * | **0.16** |
| Parent's Occupation (score) | 0.12 | 0.06 | 0.09 | 0.12 | 0.02 |
| Child's BMI (kg/m$^2$) | **-0.21** # | 0.00 | -0.08 | -0.11 | -0.10 |
| Child's Body Fat (%) | -0.07 | **0.18** | 0.11 | 0.01 | 0.09 |
| Mother's BMI (kg/m$^2$) | -0.03 | 0.05 | 0.08 | 0.06 | -0.05 |
| Father's BMI (kg/ m$^2$) | **-0.25** * | -0.12 | -0.12 | **-0.18** | -0.04 |
| Child's height (inches) | 0.00 | 0.06 | 0.01 | 0.06 | 0.07 |
| Gender (0=male; 1=female) | **0.23** * | **0.32** ** | **0.27** * | 0.09 | 0.03 |
| Family History (0=No; 1=Yes) | | | | | |
| Diabetes | **-0.19** # | -0.07 | **-0.17** | **-0.20** # | **-0.19** |
| Heart Disease | 0.08 | -0.09 | 0.00 | **0.18** | 0.13 |
| Cholesterol | -0.12 | 0.02 | 0.14 | **0.18** | -0.07 |
| High blood pressure | 0.00 | **-0.16** | -0.08 | 0.06 | -0.12 |
| Stroke | 0.00 | 0.04 | 0.02 | **0.15** | 0.10 |
| Asthma | 0.04 | **0.20** # | 0.09 | -0.03 | -0.14 |
| Blood Pb (mg/dL) | -0.07 | **-0.21** # | -0.07 | -0.12 | 0.08 |
| Blood Hg (mg/dL) | 0.07 | -0.04 | -0.01 | -0.04 | 0.04 |

# $p < .10$; * $p < .05$; ** $p < .01$

Note. Those associations that are shown in bold were associated at $p < .20$ and therefore included as covariates in analytic models.

**Table S4**. Characteristics of Participants ($N = 83$) as a Function of Blood PFC Levels with Pearson *r* Correlations (for continuous variables) or point biserial correlations (for Categorical Variables) reported.

| Measure | PFOS | PFOA | PFNA | PFDA | PFHxS | PFOSA |
|---|---|---|---|---|---|---|
| Child age (yrs) | 0.00 | 0.07 | 0.12 | 0.27 * | -0.13 | -0.21 # |
| Mother's age (yrs) | 0.11 | 0.10 | -0.24 * | -0.05 | 0.19 # | -0.01 |
| Father's age (yrs) | 0.13 | 0.07 | -0.13 | 0.04 | 0.23 * | -0.15 |
| Family Income (score) | 0.10 | 0.09 | -0.12 | -0.15 | 0.00 | 0.12 |
| Parent's Education (score) | 0.03 | -0.03 | -0.32 ** | -0.23 * | 0.16 | 0.14 |
| Parent's Occupation (score) | 0.05 | 0.11 | -0.08 | -0.15 | 0.04 | 0.07 |
| Child's BMI ($kg/m^2$) | -0.10 | -0.09 | 0.04 | -0.02 | -0.12 | -0.14 |
| Child's Body Fat (%) | 0.01 | -0.02 | -0.18 | -0.17 | 0.03 | -0.03 |
| Mother's BMI ($kg/m^2$) | -0.17 | -0.17 | -0.05 | -0.10 | -0.11 | -0.22 * |
| Father's BMI ($kg/m^2$) | 0.01 | 0.04 | 0.08 | -0.17 | 0.02 | 0.18 |
| Child's height (inches) | -0.15 | -0.21 # | -0.23 * | -0.33 ** | 0.14 | 0.10 |
| Gender (0=male; 1=female) | -0.08 | -0.14 | -0.06 | -0.08 | -0.06 | 0.05 |
| Mean PFC (Male, Female) | (10.10, 9.77) | (3.34, 2.92) | (0,78, 0.84) | (0.25, 0.25) | (6.54, 5.57) | (0.70, 0.79) |
| Family History (0=no; 1=yes) | | | | | | |
| Diabetes | -0.13 | -0.09 | -0.04 | -0.10 | 0.07 | 0.02 |
| Heart Disease | -0.04 | -0.05 | 0.01 | 0.05 | -0.02 | 0.08 |
| Cholesterol | 0.02 | 0.01 | -0.05 | 0.04 | -0.04 | -0.03 |
| High Blood Pressure | 0.13 | 0.25 * | 0.04 | 0.06 | -0.11 | -0.05 |
| Stroke | -0.21 # | -0.23 * | -0.12 | -0.11 | 0.02 | -0.02 |
| Asthma | 0.06 | 0.07 | -0.01 | 0.04 | -0.01 | 0.11 |
| Blood Pb (mg/dL | 0.05 | 0.03 | 0.19 # | 0.08 | 0.19 | -0.12 |
| Blood Hg (mg/dL) | 0.36 ** | 0.27 * | 0.08 | 0.28 * | 0.17 | -0.03 |

# $p < .10$; * $p < .05$; ** $p < .01$

**Table S5**. Partial correlations between fasting blood lipid levels and PFCs (controlling for gender, family history of high cholesterol, and family income).

| | Perfluorochemicals (PFCs) | | | | | |
|---|---|---|---|---|---|---|
| Measure | PFOS | PFOA | PFNA | PFDA | PFHxS | PFOSA |
| Total Cholesterol | 0.17 | 0.20 # | 0.15 | 0.26 * | -0.07 | -0.02 |
| High density lipoprotein (HDL) | 0.21 # | 0.22 # | -0.01 | 0.07 | 0.08 | 0.07 |
| Low density lipoprotein (LDL) | 0.10 | 0.13 | 0.16 | 0.24 * | -0.11 | -0.06 |
| Triglycerides | 0.03 | 0.05 | 0.12 | 0.17 | -0.06 | 0.01 |

# $p < .10$; * $p < .05$

Table S6. Relationship of PFC blood levels to median IRTs within each time period of the DRL task (standardized β and 95% confidence intervals are shown; $N = 79$) using change-in-estimate approach to covariate selection

| | DRL Time Period | | | |
|---|---|---|---|---|
| PFC | 0 – 5 minutes [1] | 6 – 10 minutes [2] | 11 – 15 minutes [3] | 16 – 20 minutes [4] |
| Total | -0.10 [-0.34, 0.14] [1] | -0.35** [-0.58, -0.12] [2] | -0.37** [-0.59, -0.14] [3] | -0.17 [-0.40, 0.05] [4] |
| PFOS | -0.04 [-0.29, 0.20] [5] | -0.24 # [-0.48, 0.01] [6] | -0.35 ** [-0.57, -0.13] [7] | -0.15 [-0.37, 0.08] [8] |
| PFOA | -0.01 [-0.23, 0.22] [9] | -0.08 [-0.30, 0.13] [10] | -0.21 # [-0.43, 0.01] [11] | -0.10 [-0.32, 0.12] [12] |
| PFNA | -0.10 [-0.33, 0.13] [13] | -0.18 [-0.42, 0.05] [14] | -0.16 [-0.39, 0.08] [15] | -0.01 [-0.23, 0.22] [16] |
| PFDA | -0.13 [-0.35, 0.09] [17] | -0.28* [-0.50, -0.06] [18] | -0.22* [-0.44, -0.01] [19] | -0.12 [-0.35, 0.10] [20] |
| PFHxS | -0.13 [-0.36, 0.09] [21] | -0.40 *** [-0.61, -0.20] [22] | -0.24 * [-0.50, -0.02] [23] | -0.10 [-0.32, 0.13] [24] |
| PFOSA | -0.14 [-0.36, 0.09] [25] | -0.24* [-0.47, -0.01] [26] | -0.15 [-0.37, 0.08] [27] | -0.21 # [-0.43, 0.01] [28] |

# p < .10; * p < .05; ** p < .01; *** p < .001

Covariates in models: [1] blood Hg; [2] blood Hg, child BMI, child's body fat, father age; [3] father age, child's body fat child BMI, family stroke; [4] no covariates; [5] blood Hg; [6] blood Hg, family history of high blood pressure and CVD; [7] child BMI, child's body fat, family history of stroke, family history of diabetes, father age; [8] no covariates; [9] no covariates; [10-] gender; [11] no covariates; [12] no covariates; [13] mother's age; [14] child's body fat, child BMI, mother's BMI, family history of high blood pressure, mother's age; [15] race, parent's education; [16] race, parent's education; [17] father's BMI; [18] no covariates; [19] no covariates; [20] no covariates; [21] blood Hg, child's BMI; [22] parent's education, family history of CVD, father's age, child's body fat, child's BMI; [23] father's age, child's body fat, child's BMI; [24] parent's education; [25] no covariates; [26] blood lead, child's age; [27] no covariates; [28] parent's education

Figure 1S. Smoothed Nonparametric Regressions using PROC LOESS