Prenatal exposure to persistent organic pollutants and changes in infant growth and childhood growth trajectories

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\textbf{HIGHLIGHTS}

- Multi-pollutant approach is advocated in chemical risk assessment.
- Prenatal PCB-153 exposure might be related to increased infant growth.
- Prenatal \textit{p,p}'-DDE exposure might be associated with decreased infant growth.
- Longitudinal data are useful for investigating the persistent effects of environmental pollutants.

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\textbf{ABSTRACT}

\textbf{Background:} Children are born with a burden of persistent organic pollutants (POPs) which may have endocrine disrupting properties and have been postulated to contribute to the rise in childhood obesity. The current evidence is equivocal, which may partly because many studies investigate the effects at one time point during childhood. We assessed associations between prenatal exposure to POPs and growth during infancy and childhood.

\textbf{Methods:} We used data from two Belgian cohorts with cord blood measurements of five organochlorines [(dichlorodiphenyldichloroethylene (\textit{p,p}'-DDE), hexachlorobenzene (HCB), polychlorinated biphenyls (PCB-138, -150, -180)] (N = 1418) and two perfluoroalkyl substances [perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS)] (N = 346). We assessed infant growth, defined as body mass index (BMI) z-score change between birth and 2 years, and childhood growth, characterized as BMI trajectory from birth to 8 years. To evaluate associations between POP exposures and infant growth, we applied a multi-pollutant approach, using penalized elastic net regression with stability selection, controlling for covariates. To evaluate associations with childhood growth, we used single-pollutant linear mixed models with random effects for child individual, parametrized using a natural cubic spline formulation.

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1. Introduction

Childhood obesity has become a serious public health problem (Sahoo et al., 2015). The prevalence of overweight and obesity among children has risen sharply in both high-income and low- and middle-income countries over the past 50 years (World Health Organization, 2021). Long-term consequences of childhood obesity include an increased risk of obesity in adulthood, co-morbidities and premature mortality (Geserick et al., 2018; Reilly and Kelly, 2011). Although elucidating the etiology of obesity has been focused on diet, both overnutrition and poor quality food, and insufficient physical activity, concerns about widespread exposure to endocrine disrupting chemicals (EDCs) and their potential effects on fetal and childhood growth have been increasingly raised (Heindel et al., 2015).

The term “metabolism disrupting chemicals” (MDCs) was first coined in 2017 and refers to a subgroup of EDCs that disrupt metabolic functions and can eventually result in obesity, type-2 diabetes, and/or non-alcoholic fatty liver disease (Heindel et al., 2017). A variety of persistent organic pollutants (POPs) are suspected MDCs, including specific organochlorines (OCs) [including dichlorodiphenylchloroethene (p, p’-DDE), polychlorinated biphenyls (PCBs), and hexachlorobenzene (HCB)] and poly- and perfluoroalkyl substances (PFAS) [including perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS)]. Although the use of these specific POPs has been banned or restricted (Stockholm Convention, 2019), humans continue to be exposed due to their pervasiveness in the environment and human food chain and their long half-life in the body (Cooke, 2014; Rovira et al., 2019). These chemicals are transmitted to the fetus through the placenta of pregnant women (Vizcaino et al., 2014), and breastfeeding contributes to substantial exposure in early life (Haddad et al., 2015).

Toxicological studies have identified that MDCs can be obesogenic through various mechanisms, for example by altering the differentiation and function of white adipose tissue, leading to modifications in serum levels of insulin, leptin and fatty acids that regulate energy homeostasis (Heindel et al., 2017). Exposure of rodents to MDCs during the prenatal period can permanently alter mesenchymal stem cells and cause dysfunction of adipocytes (Blumberg, 2011; Diamanti-Kandarakis et al., 2013). The fetus is sensitive to MDCs because of its dependency on hormones for development, and it is important to ascertain if effects observed in animal studies are translated to humans.

To date, most epidemiological studies focusing on the impact of POP exposures on obesity are cross-sectional. Of the limited set of longitudinal studies on prenatal POPs and childhood obesity, perhaps due to data availability, most have examined only infant growth up to the first two years of life, which is a well-known risk factor for obesity later in life (Monteiro and Victora, 2005; Ong et al., 2000; Zheng et al., 2018). However, many of these studies implemented single-pollutant models, hampering the interpretability, and the findings have been discrepant. Some studies reported positive associations with OCs (Izatt et al., 2015; Mendez et al., 2011; Valvi et al., 2014; Verhalst et al., 2009) and negative associations with PFAS (Andersen et al., 2010; Shoaff et al., 2018), but others reported null associations (Alkhalawi et al., 2016; Chen et al., 2017; Garced et al., 2012). Furthermore, knowledge about whether the possible perturbations are persistent across childhood is scarce.

The European GOLIATH project strives to better understand the role of prenatal exposure to MDCs in obesity, including underlying mechanisms (Legler et al., 2020). Therefore, in this study we focused on seven POPs (p,p’-DDE, HCB, PCB-138, -153, –180, PFOA, PFOS) which are abundant and which are among the suspected MDCs. We examined longitudinal data from a Belgian cohort to assess the relationships between prenatal POP exposures and child growth by assessing changes in infant growth and childhood growth trajectories.

2. Methods

2.1. Study design and population

We used data from two birth cohorts of the Flemish Environment and Health Studies (FLEHS). The two cohorts (FLEHS I: 2002–2004, FLEHS II: 2008–2009) enrolled 1196 and 255 mother-child pairs from Flanders, Belgium, respectively. Details of recruitment protocols have been reported elsewhere (Den Hond et al., 2009; Schoeters et al., 2012). Briefly, in FLEHS I, participants were recruited from eight geographical areas, including urban, industrial, fruit-growing, and rural areas, covering 20% of the Flemish population. In FLEHS II, participants were recruited from the general population in all five Flemish provinces using a two-stage sampling procedure, with province as the primary sampling unit and municipality as the secondary sampling unit. The distribution of participants across provinces was proportional to the number of residents in that province. The human biomonitoring studies were approved by the Ethics Committee of the University of Antwerp and participating maternity units. The present study was restricted to singletons for whom cord blood samples were available, resulting in a total of 1171 (FLEHS I) and 247 (FLEHS II) mother-child pairs available for the analysis. PFAS were not originally assessed in FLEHS I, but in 2020 PFAS levels were assessed in 99 subjects that were randomly selected from 182 participants whose biobank samples were retained. We pooled data from two cohorts and created an OCs-specific pooled dataset (FLEHS_OC, N = 1418) and a PFAS-specific pooled dataset (FLEHS_PFAS, N = 346).

2.2. Exposure assessment

Cord blood samples were collected immediately after birth and stored at –80 °C until the measurements. POPs measured in cord blood with more than 50% of measurements above the limits of quantification (LOQs) were included in the analysis, i.e. five OCs (p,p’-DDE, HCB, PCB-138, PCB-153, PCB-180) and two PFAS (PFOA, PFOS) (Table S1). The measurement and quality control methods for OCs in both cohorts as well as for PFAS in FLEHS II were described in detail in previous studies (Collins et al., 2020; Govarts et al., 2020). Briefly, OC concentrations in FLEHS I and II were measured using gas chromatography-electron capture negative ionization mass spectrometry by the same laboratory of the University of Antwerp and PFAS concentrations in FLEHS II were measured using high-performance liquid chromatography with tandem mass spectrometry detection. More recently, PFAS concentrations in FLEHS I were measured in 15-year stored biobank samples by ultra-performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) using Waters Acquity UPLC H-class system (Waters, Milford, MA, USA).

POP concentrations which were lower than the LOQs were singly imputed per cohort using maximum likelihood estimation, assuming a censored log-normal distribution for values over the LOQ conditional on the observed values for other biomarkers (Lubin et al., 2004; Ottenbros et al., 2021). Considering that the concentrations of lipophilic biomarkers vary depending on lipid levels, the concentrations of OCs after
lipid standardization was calculated and expressed in ng/g lipid for subsequent analyses.

2.3. Outcome assessment

Anthropometric data of children at birth were collected from maternity medical records. Data for the next three years were obtained from child and family registration records (Kind en Gezin, 2022), followed by data for ages 4–8 years through school physical examination (CLB, 2022). Based on weight (kg) and height (m) the body mass index (BMI) (kg/m²) was calculated and expressed in ng/g lipid for subsequent analyses.

We identified the minimally sufficient adjustment set of covariates using a directed acyclic graph (DAG) (Fig. S2): maternal education (low, median, high), maternal age at delivery (years), maternal pre-pregnancy BMI (kg/m²), parity (0, 1, ≥2), maternal smoking during pregnancy (non-smoking, smoking), cohort (FLEHS I, II; representing multiple populations (Table 1). Mothers were a median of 30 years of age at pregnancy. The majority were nulliparous, highly educated, and did not smoke during pregnancy. More than 95% children were full-term. The distributions of BMI measurements by child age are presented in Table S3. Registered BMI data of more than half of study population was available at the later period (6 years of age), and then more data available at the later period (6–8 years of age). POP levels decreased over time between FLEHS I and II (Table S1).

3. Results

3.1. Participant characteristics

Participant characteristics differed slightly across the two study populations (Table 1). Mothers were a median of 30 years of age at delivery and reported a median BMI of 22 kg/m² prior to their pregnancy. The majority were nulliparous, highly educated, and did not smoke during pregnancy. More than 95% children were full-term. The distributions of BMI measurements by child age are presented in Table S3. Registered BMI data of more than half of study population were available during the first three years, followed by less BMI data collected at the start of the school period (4–6 years of age), and then more data available at the later period (6–8 years of age). POP levels decreased over time between FLEHS I and II (Table S1). In the pooled datasets, p,p′-DDE (102.8 ng/g lipid) exhibited the highest median level among OCs, while the median level of PFOA (1500 ng/L) was much lower than PFOS (2700 ng/L). Pearson correlations ranged from moderate to high within OCs (0.24–0.89) and between PFAS (0.60), while confounding, we also performed multi-pollutant analyses using elastic net (ENET) (Zou and Hastie, 2005) in the R package glmnet (Friedman et al., 2010), a variable selection technique that more effectively tackles multicollinearity than single-pollutant models (Agier et al., 2016; Govarts et al., 2020; Lentes et al., 2018). We conducted ENET modelling separately for OCs and PFAS across 100 imputed datasets. The optimal degree of penalization, within each imputed dataset was determined by minimization of 10-fold cross-validation error. To address the variability arising from imputation and instability inherent to penalization models, we took the mean of ENET effect estimates fitted on 100 imputed datasets for those exposures selected (β ≠ 0) in more than half of the 100 models (Cadiou and Slama, 2021; Lentes et al., 2019). Subsequently, we conducted stability selection (Meinshausen and Bühlmann, 2010) to control false selection rate using routines from R package stabel (Shah and Samworth, 2013) that were modified to allow subsampling from different imputed datasets.

For the analysis of childhood growth, we used the R packages lmnet (Bates et al., 2015) and splines (Friedman et al., 2010) to fit linear mixed models with fixed effects of s[age] with child-specific random intercepts and random coefficients for s[age] (Elhakeem et al., 2021; Mendez et al., 2011). We then calculated sex-specific BMI z-scores at birth and 2 years, respectively, according to internal standardization. Subsequently, the change in BMI z-scores was defined as infant growth. Second, the BMI trajectory was characterized as childhood growth based on repeated measurements of BMI from birth up to 8 years, prior to possible growth acceleration due to early puberty (Papadopoulou et al., 2021).
the correlations between OCs and PFAS (0.08–0.31) were relatively low (Fig. S3).

3.2. Prenatal POP exposures and infant growth

In the analysis of infant growth, PCB-153 showed a positive association in the single-pollutant model, with an increase of 0.11 (95% CI: 0.07, 0.15) in BMI z-score change per IQR of PCB-153 (33.6 ng/g lipid) (Table 2). This association was consistent in the multi-pollutant approach that PCB-153 was selected in 99 of the 100 OCs-specific ENET models (Table 2). p,p′-DDE was selected in 84 out of the 100 penalized ENET models with a decrease of 0.05 in BMI z-score change per IQR of exposure (123.5 ng/g lipid); however, the effect estimate for p,p′-DDE was imprecise in the single-pollutant model (Table 2).

In this study of mother-child pairs from Flanders, Belgium, the relationship between prenatal exposure to POPs and childhood growth in the intervals of 0–2 years and of 0–8 years was examined. We found indications that PCB-153 was associated with increased infant growth in the first 2 years and that p,p′-DDE was associated with decreased infant growth, although these associations were imprecise and unstable.

### Table 1

Study population characteristics of mother-child pairs in FLEHS cohorts, Flanders, Belgium.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Maternal education</td>
<td></td>
<td></td>
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<tr>
<td>Low</td>
<td>129 (11)</td>
<td>5 (5)</td>
<td>22 (9)</td>
<td>151 (11)</td>
<td>27 (8)</td>
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<tr>
<td>Median</td>
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<td>24 (24)</td>
<td>73 (30)</td>
<td>513 (36)</td>
<td>97 (28)</td>
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<tr>
<td>High</td>
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<td>69 (70)</td>
<td>149 (60)</td>
<td>708 (50)</td>
<td>218 (63)</td>
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<td>5 (1)</td>
<td>46 (3)</td>
<td>4 (1)</td>
</tr>
<tr>
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<td></td>
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<tr>
<td>0</td>
<td>717 (61)</td>
<td>56 (57)</td>
<td>106 (40)</td>
<td>817 (58)</td>
<td>156 (45)</td>
</tr>
<tr>
<td>1</td>
<td>312 (27)</td>
<td>29 (29)</td>
<td>80 (32)</td>
<td>392 (28)</td>
<td>109 (32)</td>
</tr>
<tr>
<td>≥ 2</td>
<td>142 (12)</td>
<td>14 (14)</td>
<td>66 (27)</td>
<td>208 (15)</td>
<td>80 (23)</td>
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<tr>
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<td>0 (0)</td>
<td>1 (0)</td>
<td>1 (0)</td>
<td>1 (0)</td>
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<tr>
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<td></td>
<td></td>
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<tr>
<td>Non-smoking</td>
<td>966 (82)</td>
<td>94 (95)</td>
<td>212 (86)</td>
<td>1178 (83)</td>
<td>306 (88)</td>
</tr>
<tr>
<td>Smoking</td>
<td>185 (16)</td>
<td>4 (4)</td>
<td>29 (12)</td>
<td>214 (15)</td>
<td>33 (10)</td>
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<tr>
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<td>1 (1)</td>
<td>6 (2)</td>
<td>26 (2)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Infant’s sex</td>
<td></td>
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<td></td>
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<tr>
<td>Boy</td>
<td>559 (48)</td>
<td>47 (47)</td>
<td>120 (49)</td>
<td>679 (48)</td>
<td>167 (48)</td>
</tr>
<tr>
<td>Girl</td>
<td>612 (52)</td>
<td>52 (53)</td>
<td>127 (51)</td>
<td>739 (52)</td>
<td>179 (52)</td>
</tr>
<tr>
<td>Pre-pregnancy BMI (kg/m²)</td>
<td>22.4 (20.3–25.1)</td>
<td>22.0 (20.3–24.7)</td>
<td>22.3 (20.4–24.8)</td>
<td>22.3 (20.3–25.0)</td>
<td>22.2 (20.4–24.8)</td>
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<tr>
<td>Missing, N (%)</td>
<td>47 (4)</td>
<td>1 (1)</td>
<td>2 (1)</td>
<td>49 (3)</td>
<td>3 (1)</td>
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<tr>
<td>Maternal age at delivery (years)</td>
<td>30.0 (27.0–32.0)</td>
<td>30.5 (28.0–33.0)</td>
<td>30.0 (28.0–33.0)</td>
<td>30.0 (29.0–33.0)</td>
<td>30.0 (28.0–33.0)</td>
</tr>
<tr>
<td>Missing, N (%)</td>
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<td>1 (1)</td>
<td>0 (0)</td>
<td>20 (1)</td>
<td>1 (0)</td>
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<tr>
<td>Gestational age</td>
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<tr>
<td>Preterm</td>
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<td>2 (2)</td>
<td>5 (2)</td>
<td>43 (3)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Full-term</td>
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<td>96 (97)</td>
<td>237 (96)</td>
<td>1358 (96)</td>
<td>333 (88)</td>
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<td>Missing</td>
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<td>1 (1)</td>
<td>5 (2)</td>
<td>17 (1)</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Lipid (g/L)</td>
<td>2.0 (1.6–2.5)</td>
<td>–</td>
<td>2.0 (1.7–2.3)</td>
<td>2.0 (1.7–2.4)</td>
<td>–</td>
</tr>
<tr>
<td>Missing, N (%)</td>
<td>60 (5)</td>
<td>–</td>
<td>3 (1)</td>
<td>63 (4)</td>
<td>–</td>
</tr>
<tr>
<td>Birth weight</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2500 g</td>
<td>21 (2)</td>
<td>0 (0)</td>
<td>5 (2)</td>
<td>26 (2)</td>
<td>5 (1)</td>
</tr>
<tr>
<td>≥2500 g</td>
<td>1143 (98)</td>
<td>99 (100)</td>
<td>242 (98)</td>
<td>1385 (98)</td>
<td>341 (99)</td>
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<tr>
<td>Missing, N (%)</td>
<td>7 (1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>7 (0)</td>
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</tbody>
</table>

Abbreviations: OC, organochlorines; PFAS, poly- and perfluoroalkyl substances; p,p′-DDE, dichlorodiphenyl dichloroethylene; PCB-138, -153, –180, polychlorinated biphenyls 138, 153, 180; HCB, hexachlorobenzene; PFOA, perfluorooctanoic acid; PFOS, perfluorooctane sulfonic acid; BMI, body mass index; P, percentile.

Note: a Percentages may not add up to 100 due to rounding. b The subgroup of FLEHS I where PFAS data was available.

3.3. Prenatal POP exposures and childhood growth trajectories

In the analysis of childhood growth trajectories, we did not observe any clear differences in growth by exposure levels, as reflected by the non-significant interaction terms between exposures and child age, and the largely overlapping 95% confidence interval (CI) bands for the mean BMI as function of child age at P10 and P90 of exposure levels (Fig. 1). No effect modification by child sex was observed (p-values for three-way interactions ranged from 0.28 to 0.84).

3.4. Sensitivity analysis

The analyses of infant growth limited to children with 3 or more BMI measurements were consistent with the main analyses based on the full sample size, albeit with slight difference in the magnitude of effect estimates (Table S5, Fig. S5). Findings from cohort-stratified models were in line with the pooled analysis (data not shown). The results after excluding preterm children were consistent with the main analyses (data not shown). The results of complete case analysis were mostly in line with those using multiple imputed data (Tables S4 and S6; Figs. S6 and S7).

4. Discussion

In this study of mother-child pairs from Flanders, Belgium, the relationship between prenatal exposure to POPs and childhood growth in the intervals of 0–2 years and of 0–8 years was examined. We found indications that PCB-153 was associated with increased infant growth in the first 2 years and that p,p′-DDE was associated with decreased infant growth, although these associations were imprecise and unstable.
associated with higher concentrations of PCBs (congeners 118, 138, 153, 180) in cord blood (Verhulst et al., 2009). The observed larger perturbations of childhood growth trajectories up to 8 years of age.

Findings do not support that prenatal POP exposures led to persistent perturbations of childhood growth trajectories up to 8 years of age.

4.1. Prenatal POP exposures and infant growth

Our observation that exposure to PCB-153 may contribute to increased infant growth is consistent with one study also using data from FLEHS I cohort but with smaller sample size, which has reported increased BMI-score through 3 years of age in Flemish children was of 1039 children at 6 months (Yang et al., 2021). However, in some other studies (Izatt et al., 2015; Mendez et al., 2011; Valvi et al., 2014) which have either pooled data from several cohorts across different stages (i.e., infant growth from birth to age 2 and childhood growth trajectories from birth to age 8). The sample size of the study was enhanced by pooling data from two cohorts and imputing missing values. In addition, the prospective longitudinal study design with long-term follow-up and detailed information on confounders are also advantages of our study. Health risk assessment of chemical exposures was improved by accounting for multiple pollutants simultaneously. Moreover, the consistency of our sensitivity analysis results also enhanced the overall robustness of our findings.

There are also some limitations of the present study. First, information on breastfeeding that contributes to exposure in early life was not studies that reported positive or negative associations had lower concentrations. The disparity in findings across studies may be explained by possible non-monotonic dose-response relationship between EDCs and adverse health effects (Vandenberg et al., 2012), and the differences in the exposure levels. Two studies have reported inverse associations between prenatal PFAS and anthropometric measurements in the first 2 years of infancy, one from 1010 Danish mother-child pairs and the other from 334 U.S. pairs (Andersen et al., 2010; Shoaff et al., 2018), however, these associations were not found to be significant in our study.

Overall, different POP levels, growth stages and growth outcome definitions made the interpretations and conclusions among previous studies on infant growth rather mixed and difficult to compare. In addition, most studies mentioned above only assessed single-pollutant models, which could suffer from some degree of co-exposure confounding bias from other chemical exposures (Cohen and Jefferies, 2019). Therefore, additional studies with different exposure and outcome windows and multi-pollutant approaches are needed to validate our results and more comprehensively assess the research question.

Although the mechanisms underlying POP exposures and obesity are not entirely clear, p,p'-DDE has been suggested to disrupt fatty acid compositions in rats (Rodríguez-Alcalá et al., 2015) and have effects on regulators of adipogenesis in mice and human cells (Cano-Sancho et al., 2017). PCBs have been found to interfere with thyroid hormones (Dirinck et al., 2011; Koppe et al., 2006) and glucose metabolism (Lee et al., 2007; Wu et al., 2017).

4.2. Prenatal POP exposures and childhood growth trajectories

We did not observe differences in BMI trajectories associated with prenatal POP levels and therefore the present study did not provide evidence on the persistence of effects of early-life POP exposures. Despite having BMI measurements over 8 years, the distribution of measurements was unbalanced as data was collected through different resources during three time periods, and this may have hampered the statistical power to detect perturbations caused by POP exposures. To our knowledge, no previous study has reported the influence of OCs on long-term childhood growth trajectories and additional studies are needed to verify our results. In a recent study of 345 U.S. mother-child pairs (Braun et al., 2021), prenatal PFOS was associated with alterations in BMI trajectories over the first 12 years of life, which differs from our results; this may be due to relatively lower levels of PFOS in our study population. In concordance with our study, prenatal PFOS was not found to affect BMI trajectory throughout childhood (Braun et al., 2021), although the median concentration of PFOS in that study is five times higher than ours. We did not evaluate multi-pollutant models for growth trajectories because our data did not provide enough statistical power to perform these models, coupled with the fact that no association was observed in the single-pollutant models.

4.3. Strengths and limitations

There are several strengths of the present study worth highlighting. One of the major strengths is the repeated anthropometric measurements of children over a long period, allowing us to explore the relationships between prenatal exposure to POPs and childhood growth at different stages (i.e., infant growth from birth to age 2 and childhood growth trajectories from birth to age 8). The sample size of the study was enhanced by pooling data from two cohorts and imputing missing values. In addition, the prospective longitudinal study design with long-term follow-up and detailed information on confounders are also advantages of our study. Health risk assessment of chemical exposures was improved by accounting for multiple pollutants simultaneously. Moreover, the consistency of our sensitivity analysis results also enhanced the overall robustness of our findings.

There are also some limitations of the present study. First, information on breastfeeding that contributes to exposure in early life was not
available, thus we could not evaluate other sensitive time windows of exposure. However, in practice prenatal and postnatal exposures to OCS are highly correlated even with differences in breastfeeding duration, limiting the power to disentangle sensitive exposure windows related to breastfeeding duration (Lenters et al., 2019; Verner et al., 2015); as for PFAS, they are less carried in breast milk as they are not lipophilic; so we are confident that these cord blood levels of POPs provide a robust measure of pre- and (early) postnatal exposure to POPs. Second, BMI measurements were not assessed at fixed timepoints, but rather at irregular intervals, so that we had to conduct comprehensive models to estimate BMI at birth and age 2 for the infant growth analysis. Lastly, residual confounding bias may exist due to uncontrolled unmeasured confounders, although we expect this to be minimal as we did account for a wide range of covariates that have been shown to be important.

5. Conclusion

This study provides some support for effect of prenatal PCB-153 on elevated infant growth. Prenatal p,p'-DDE may be associated with reduced infant growth. No persistent effects of prenatal POP exposures across childhood were observed. Larger prospective studies with repeated measures and advanced multi-pollutant approaches are warranted to validate these results and inform policy recommendations.

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Author contributions statement

AC: Conceptualization, Data curation, Formal analysis, Methodology, Interpretation of results, Writing - original draft, Writing - review & editing. LP: Methodology, Interpretation of results, Supervision, Writing - review & editing. EG: Data curation, Writing - review & editing. JL: Conceptualization, Funding acquisition, Supervision, Writing - review & editing. RV: Conceptualization, Funding acquisition, Intergration of results, Supervision, Writing - review & editing. VL: Conceptualization, Interpretation of results, Supervision, Writing - review & editing. SR: Conceptualization, Interpretation of results, Supervision, Writing - review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data that has been used is confidential.

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