

## Prenatal Paraben Exposure Impacts Infant Overweight Development and in vitro Adipogenesis

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**Abstract :** The worldwide production of endocrine disrupting compounds (EDC) has risen dramatically over the last decades, as so has the prevalence for obesity. Many EDCs are believed to contribute to this obesity epidemic, by enhancing adipogenesis or disrupting relevant metabolism. This effect is most tremendous in the early prenatal period when priming effects find a highly vulnerable time window. Therefore, we investigate the impact of parabens on childhood overweight development and adipogenesis in general. Parabens are ester of 4-hydroxy-benzoic acid and part of many cosmetic products or food packing. Therefore, ubiquitous exposure can be found in the westernized world, with exposure already starting during the sensitive prenatal period. We assessed maternal cosmetic product consumption, prenatal paraben exposure and infant BMI z-scores in the prospective German LINA cohort. In detail, maternal urinary concentrations (34 weeks of gestation) of methyl paraben (MeP), ethyl paraben (EtP), n-propyl paraben (PrP) and n-butyl paraben (BuP) were quantified using UPLC-MS/MS. Body weight and height of their children was assessed during annual clinical visits. Further, we investigated the direct influence of those parabens on adipogenesis in-vitro using a human mesenchymal stem cell (MSC) differentiation assay to mimic a prenatal exposure scenario. MSC were exposed to 0.1 – 50  $\mu$ M paraben during the entire differentiation period. Differentiation outcome was monitored by impedance spectrometry, real-time PCR and triglyceride staining. We found that maternal cosmetic product consumption was highly correlated with urinary paraben concentrations at pregnancy. Further, prenatal paraben exposure was linked to higher BMI Z-scores in children. Our in-vitro analysis revealed that especially the long chained paraben BuP stimulates adipogenesis by increasing the expression of adipocyte specific genes (PPAR $\gamma$ , ADIPOQ, LPL, etc.) and triglyceride storage. Moreover, we found that adiponectin secretion is increased whereas leptin secretion is reduced under BuP exposure in-vitro. Further mechanistic analysis for receptor binding and activation of PPAR $\gamma$  and other key players in adipogenesis are currently in process. We conclude that maternal cosmetic product consumption is linked to prenatal paraben exposure of children and contributes to the development of infant overweight development by triggering key pathways of adipogenesis.

**Keywords :** adipogenesis, endocrine disruptors, paraben, prenatal exposure

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