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Perinatal BPA exposure at low doses impairs oral tolerance and immunization to ovalbumin in offspring rats at adulthood (Abstract 1)

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Aims: Bisphenol A (BPA) used in food packaging impacts gut epithelial barrier after perinatal exposure. Because antigen sampling by gut epithelium drives mucosal immune response, our aim was to address the consequences of perinatal BPA exposure at low doses on oral tolerance and immunization at adulthood. **Methods:** Dams were treated *per os* from gestation day 15 to pup weaning with BPA [0.5, 5 or 50µg/kg/d] or vehicle (corn oil). Female offsprings (day 45) were used to assess para- and transcellular jejunal permeability by Ussing chambers, and immune response to ovalbumin (OVA) after either oral tolerance, immunization or oral challenge. **Results:** Perinatal BPA exposure decreased jejunal paracellular permeability by 2-fold at 0.5 and 50µg/kg/d, and by 3-fold at all doses for transcellular permeability ($p < 0.05$). BPA exposure at 5 and 50µg/kg/d increased anti-OVA IgG titers after an oral tolerance protocol ($116 \pm 62 \times 10^3$ and $86 \pm 29 \times 10^3$ respectively vs $7.2 \pm 2.2 \times 10^3$ in controls; $p < 0.04$). Anti-OVA IgG titers were only increased at 5µg/kg/d after OVA immunization. Enhanced humoral response in rats exposed to 5µg/kg/d was associated with higher IFN γ secretion by spleen in OVA-sensitized (2-fold) and MLN of OVA-tolerized (20-fold) rats ($p < 0.05$). Finally, oral OVA challenge in BPA group increased MPO activity (316 ± 34 vs 184 ± 22 U/g protein in controls; $p < 0.05$), IFN γ concentration (2-fold, $p < 0.05$), and decreased TGF β concentration (3-fold, $p < 0.05$) in the colon, indicating inflammation. **Conclusion:** Perinatal exposure to low doses of BPA decreased jejunal paracellular and transcellular permeability, and impaired oral tolerance and immunization to dietary antigens at adulthood. BPA treatment during perinatal period affects intestinal homeostasis in a nonlinear dose-response relationship. These results suggest that perinatal period is a critical window for BPA exposure that may trigger food intolerance in later life.