DEVELOPMENTAL POLYCHLORINATED BIPHENYL (PCB) EXPOSURE CONTRIBUTES TO BLADDER DYSFUNCTION IN MICE

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Background: Lower urinary tract symptoms (LUTS) are a marked comorbidity in individuals with neurodevelopmental disorders (NDDs). Yet underlying factors contributing to LUTS risk in individuals with and without NDDs, is not completely understood. Early life environmental exposures to polychlorinated biphenyls (PCBs), have been implicated in NDD risk, however, their effects on peripheral targets like bladder are unknown. With the link of early life PCB exposure and NDD risk, it is worth considering whether LUT comorbidities are related to PCB exposure. As an initial step in addressing this question, we test the hypothesis that developmental PCB exposure contributes to bladder dysfunction in young adult wild type mice.

Methods: C57Bl/6J mouse dams were dosed with a PCB mix which mimic those found in serum of women at risk of having a child with a NDD. Dams were dosed daily via the diet at 0, 0.1, 1 or 6mg/kg PCB two weeks prior to mating, through gestation and lactation. Voiding function was assessed in offspring 6-8 weeks of age using void spot assay (VSA, n=17-24), uroflowmetry (n=14-24), and anesthetized cystometry (n=7-10) to provide assessment of voiding function in awake and anesthetized mice. Bladder bath assays (n=3-5) were used to examine bladder contractility in *ex vivo* bladder preparations.

Results: Developmental PCB exposure significantly alters urine spot size distribution during VSA testing. Compared to control, PCBs increase the number of small diameter (0-0.1cm) urine spots in the 0.1 and 6mg/kg PCB groups in males, and all dose groups in females. Uroflowmetry testing reveals that in male mice only, PCBs decrease void stream strength rating in the 0.1mg/kg PCB dose group versus control, indicative of a more drop like void pattern. In mice undergoing anesthetized cystometry, PCBs have a significant overall dose effect, decreasing intervoid interval in the 0.1 mg/kg/d and 6 mg/kg/d PCB groups compared to control. Ongoing preliminary studies from bladder bath assays suggest that PCBs may alter sensitivity to contractile stimuli.

Conclusions:These results support the hypothesis that developmental PCB exposures can contribute to voiding function in mice. Overall PCB effects on voiding function correspond to increased small diameter urine spots, drop like voids and shorter time intervals between voids. Further studies into mechanisms associated with these sex and dose-dependent effects for PCB exposure are warranted. Supported by NIH awards [R00ES029537, T32ES007015, and U54DK104310].