Developmental exposure to the environmental toxicant, polychlorinated biphenyls, leads to increases in mouse bladder volume and nerve density

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Background: Environmental contaminants are risk factors for several disorders, yet their ability to contribute to lower urinary tract (LUT) function is understudied. Polychlorinated biphenyls (PCBs) are a group of chemicals for which developmental exposures have been linked to elevated autism risk. Children with autism often suffer from higher incidence of LUT symptoms, yet whether there is a connection between PCBs and bladder function in this population, or in typically developing individuals, is a current gap in fully understanding the etiology of LUT dysfunction. As a first step in addressing this gap, we test the hypothesis that developmental exposure to PCBs in mice, results in alterations to the bladder which could contribute to urinary function.

Methods: An environmentally relevant mixture of PCBs was used to mimic the top congeners and their proportions found in serum of mothers at risk of having a child with a neurodevelopmental disorder. Wild type mouse dams were dosed daily with either 0, 0.1, 1 or 6 mg/kg/d PCB, two weeks prior to mating, through gestation and lactation. Resultant offspring were weaned at 3 weeks of age, and bladders collected for morphometric and immunohistochemical analysis at 4 and 7 weeks of age.

Results: Effects of PCBs on bladder morphology were sex- and dose-dependent. Males more greatly affected than females. In developmentally exposed male mice there was a significant increase in bladder volume in the 6mg/kg PCB versus control group in 4 week old mice, which persisted to at least 7 weeks of age. In 4 week old mice there were no changes in bladder mass, muscle or epithelial thickness. However, βIII-tubulin, a marker of total nerve fiber density, was increased in bladder suburothelium of male mice of the 6mg/kg PCB versus control group. Expression of calcitonin gene related protein (CGRP), a marker of sensory nerve fibers, was also increased in the highest compared to lowest PCB dose groups. These measures are underway in 7 week old animals.

Conclusions: Developmental PCB exposure can alter bladder morphology in mice weeks after the final PCB exposure. While we did not observe evidence of obstruction, we did observe PCB-induced increases in bladder innervation, especially within the suburothelium. The functional consequences of PCB-induced increases in suburothelial nerve density on sensation, bladder contractility and ultimately voiding function are areas of future study. Supported by NIH awards R00ES029537 and T32ES007015.