

DEVELOPMENTAL EXPOSURE TO ENVIRONMENTAL CONTAMINANTS, POLYCHLORINATED BIPHENYLS, IMPACT VOIDING PARAMETERS IN YOUNG ADULT MICE

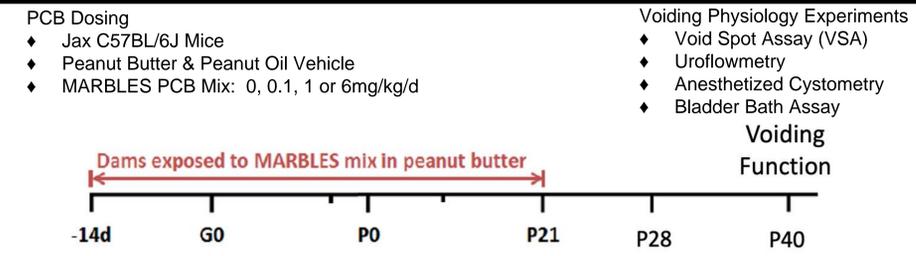
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Background

- Development is an especially critical window during which environmental contaminants can induce lasting effects on the offspring, yet the role of these chemicals in shaping urinary function is not completely understood.
- Polychlorinated biphenyls (PCBs) are ubiquitous environmental contaminants with known impacts on the central nervous system and are implicated as risk factors for autism – a condition which often has comorbid lower urinary tract symptoms (LUTS). Yet impacts of PCBs on other systems such as the lower urinary tract are understudied.

Hypothesis: Exposure to PCBs at human relevant concentrations during development, leads to voiding abnormalities once mice reach adulthood.

Methods



PCBs increase the frequency of animals producing higher urine spot counts

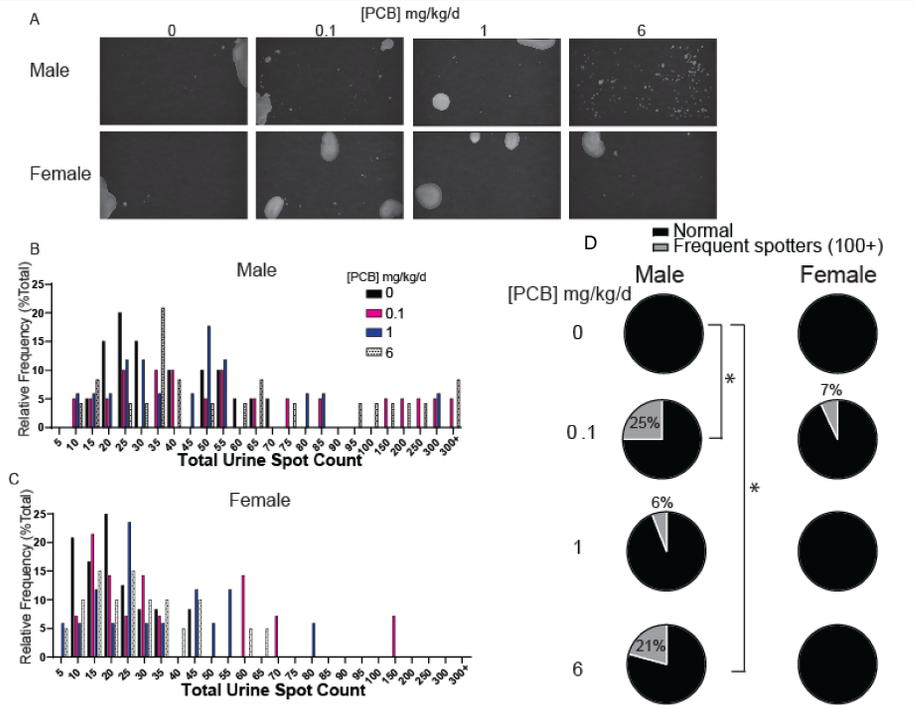


Fig. 1. VSA testing conducted on young adult male and female mice aged P40-P50. (A) Images of VSA. Parameters examined following the 4 hour VSA include (B-C) relative frequency (in % total), and (D) frequent spotter percentage defined as 100+ urine spots. Results are mean ± SEM n=17-24 males, n=14-24 females. * indicates significant difference from vehicle control. P < 0.05 were considered significant. A bar and * indicate significant differences as determined by Fisher's exact test.

PCBs increase the number of small urine spots

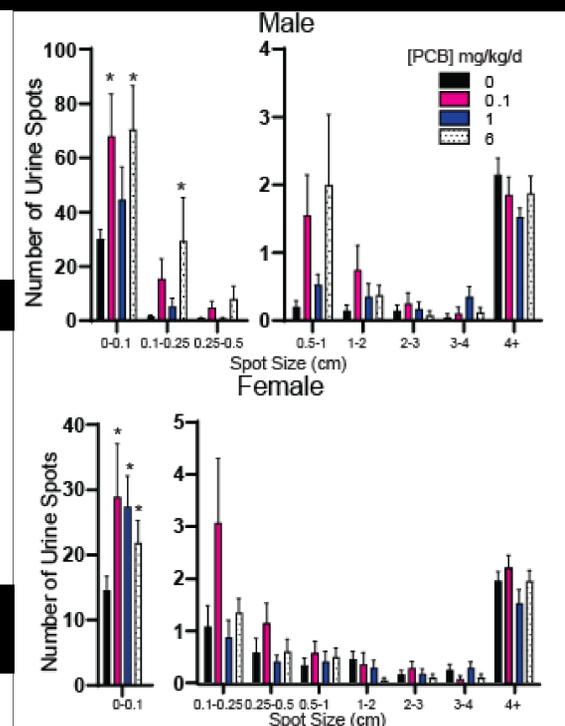


Fig. 2. VSA testing conducted on young adult male and female mice aged P40-P50. Urine spot size distribution. Results are mean ± SEM n=17-24 males, n=14-24 females. * indicates significant difference from vehicle control. P < 0.05 were considered significant. * indicates significant differences as determined by Two-way ANOVA followed by Dunnett's multiple comparisons test.

PCBs decrease intervoid interval in females but increase max void pressure in males

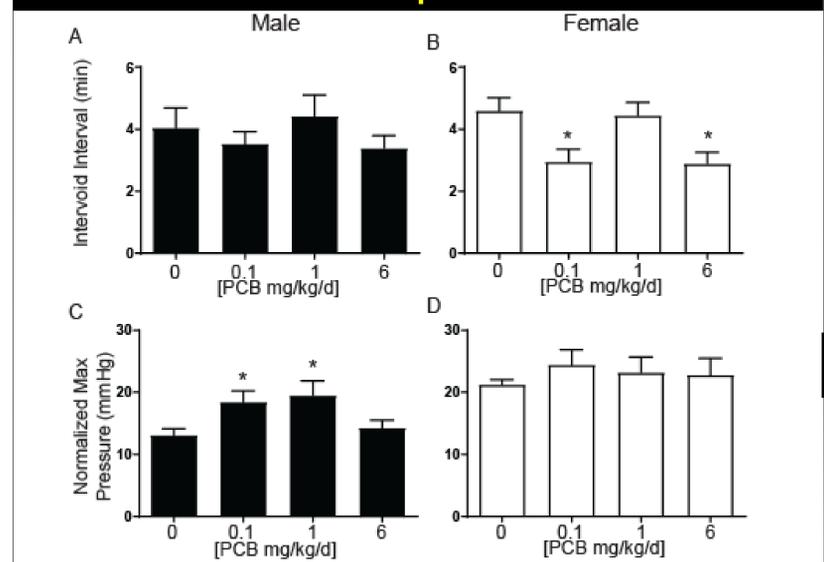


Fig. 3. Cystometry conducted on young adult male and female mice aged P49. (A-B) intervoid interval, (C-D) normalized max pressure (maximum subtracted from baseline pressure). Results are mean ± SEM n=6-10 males, n=8-14 females. * indicates significant difference from vehicle control. P < 0.05 were considered significant as determined by Welch's ANOVA, one-way ANOVA followed by Dunnett's multiple comparisons test or one-way ANOVA followed by Dunnett's multiple comparisons test on log transformed data.

PCBs increase drop-like voids in male mice at the lowest concentration

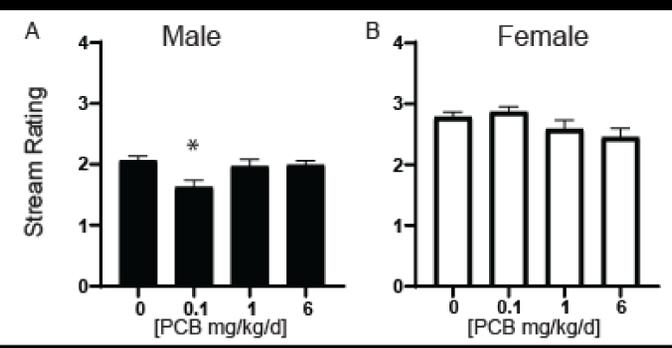


Fig. 4. Uroflowmetry conducted on young adult male and female mice aged P45. Urine stream rating was assessed. Results are mean ± SEM n=15-24 males, n=13-21 females. * indicates significant difference from vehicle control. P < 0.05 were considered significant as determined by Kruskal-Wallis test followed by Dunn's multiple comparisons test.

PCBs increase sensitivity to contractile stimuli in a sex & dose-dependent manner

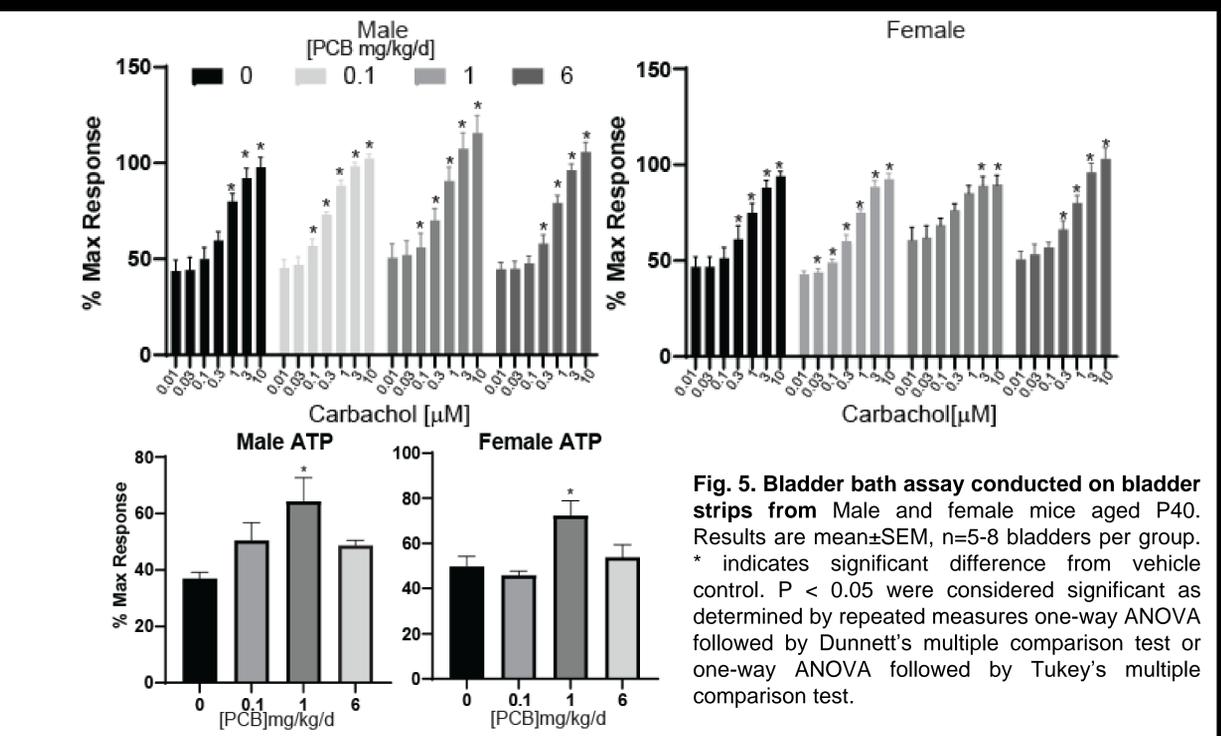


Fig. 5. Bladder bath assay conducted on bladder strips from Male and female mice aged P40. Results are mean±SEM, n=5-8 bladders per group. * indicates significant difference from vehicle control. P < 0.05 were considered significant as determined by repeated measures one-way ANOVA followed by Dunnett's multiple comparison test or one-way ANOVA followed by Tukey's multiple comparison test.

Conclusions

- Effects of developmental PCB exposure on voiding in young adult offspring were sex- and dose-dependent. Overall PCBs in:
 - Males: Increase small urine spots, drop-like pattern, and voiding pressure. Increase sensitivity to cholinergic or purinergic stimulation.
 - Females: Increase small urine spots and decrease void interval. Increase or decrease sensitivity to cholinergic stimulation. Increase sensitivity to purinergic stimulation.
- PCBs do not exhibit a classic dose response. This is consistent with PCB effects in other tissues, but underlying mechanisms are not understood. Changes in response to cholinergic or purinergic signaling within the bladder could contribute and is an area of future study.