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Effects of Estrogen and Bisphenol-A Exposure During Adolescent Development: A Golgi Study

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Introduction

Bisphenol-A (BPA), a common environmental endocrine disruptor, modulates estrogenic, androgenic, and antiandrogenic effects throughout the lifespan. BPA is produced in large quantities globally in the manufacturing of polycarbonate plastics, the resin lining of cans, and is found in other products such as dental sealants and receipt paper. Potential health hazards exist because alterations in temperature and pH can cause leaching of BPA from plastics (for review, vom Saal & Hughes, 2005) and detectable levels of BPA have been reported in saliva, urine, blood, breast milk, and the placenta of humans and animals (Biedermann et al., 2010; Geens et al., 2011; Rubin, 2011).

Most research investigating the effects of BPA in animal models has focused on exposure during early prenatal and neonatal periods which results in behavioral, structural and physiological alterations; however, adolescence is another important development period that is characterized by profound hormonal changes. Furthermore, while oral administration of BPA is the main pathway of exposure, parenteral (e.g., injections) avoids first-pass metabolism in the liver and may more closely mimic the everyday exposure experienced by humans.

Our laboratory has recently shown that adolescent exposure to low-dose BPA increases anxiety and impairs memory (Diaz Weinstin, et al., 2013) when tested during adolescence. The current study was designed to determine whether adolescent low-dose BPA exposure alters spine density immediately and if its effects would carry through to adulthood.

Method

Eighteen female Sprague Dawley rats ovariectomized at 21 days of age.

At age 6 weeks, the rats were randomly assigned to either

•Control: saline

•Bisphenol-A exposed: Each rat received a daily subcutaneous injection, 40 µg/kg bodyweight, at the nape of the neck for one week. The BPA was initially dissolved in ethanol for stock solutions and diluted with saline for the injection.

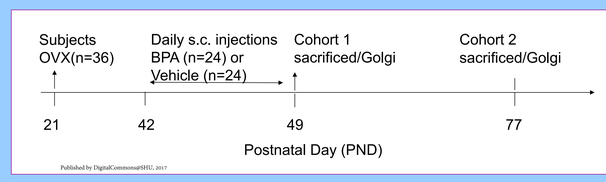
•Estrogen: Each rat received a daily subcutaneous injection, 50 µg/kg bodyweight, at the nape of the neck for one week.

•Rats were sacrificed at day 49 and day 79 and processed for Golgi Impregnation.

•Brains were sliced using a cryostat and mounted to slides.

•Spine density on apical and basal dendrites of CA1 hippocampal region (CA1) pyramidal cells and granule cells were counted.

•Analysis: Two way ANOVA test used for post-hoc analysis



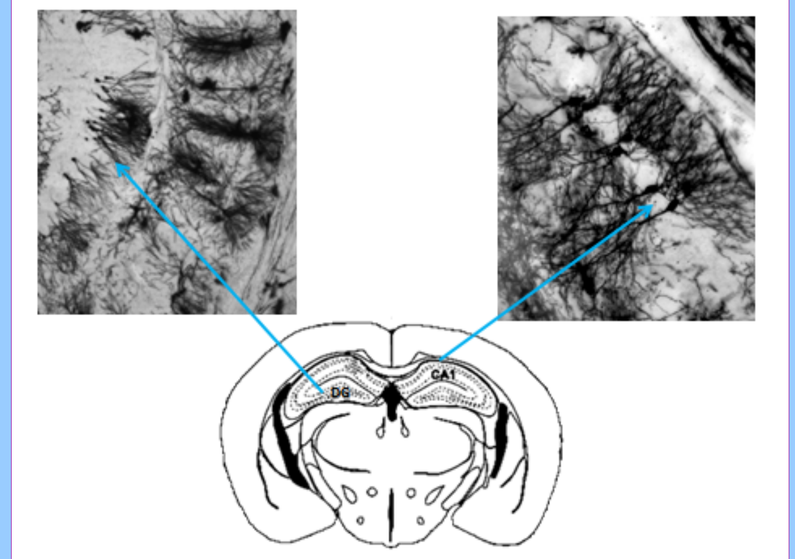


Figure 1: Bottom: coronal section through the rat hippocampus showing location of the dentate gyrus (DG) and CA1 regions. Golgi impregnated granule cells (upper left) and CA1 pyramidal cells (upper right). 10x

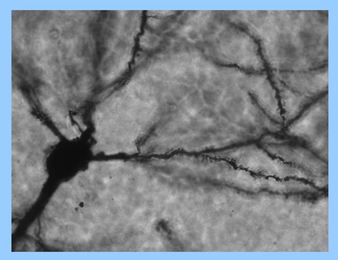


Figure 2: Pyramidal cell

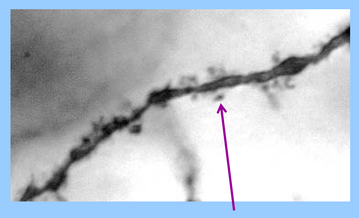
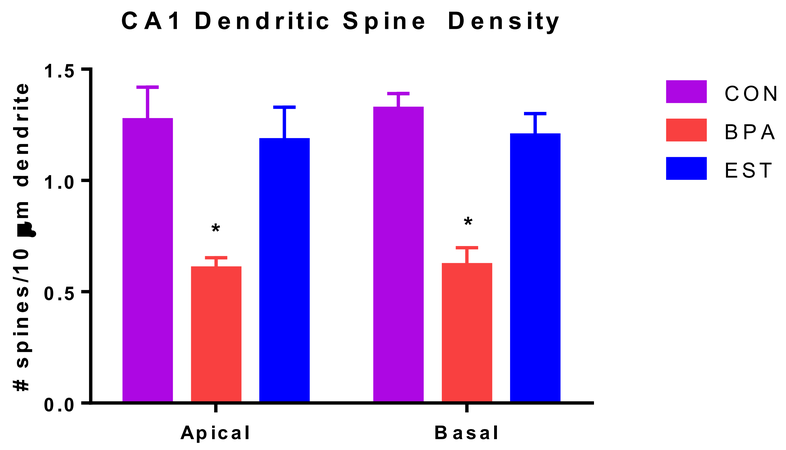


Figure 3: Section of dendrite with spines (100x under oil)

Results

CA1 Pyramidal Cells



CA1 Granule Cells and Prefrontal Cortex

- Cells are in the process of being observed and analyzed.

Discussion & Conclusion

- Short-term, low dose BPA exposure during the critical period of adolescent development markedly decreased spine density in both basal and apical dendrites in pyramidal neurons CA1 when assessed at 49d .
- Dendritic spine counts for granule cells at 49 and 77 and CA1 at 77 days are in progress.
- The CA1 data indicate that BPA effects at 49 days are greater than those seen previously in adults.
- These results suggest that age is a critical factor in BPA induced plasticity during adolescence.

Future Studies

- BPA exposure in combination with Estrogen to observe the possible estrogen protection mechanism against the harmful effects of BPA.
- Observe the effects of BPA in other anatomical locations of the brain: Hypothalamus, Prefrontal Cortex, Amygdala, CA3.