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# Effects of Estrogen and Bisphenol-A Exposure During Adolescent Development: A Behavioral Analysis

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# Effects of Estrogen and Bisphenol-A Exposure During Adolescent Development: A Behavioral Analysis



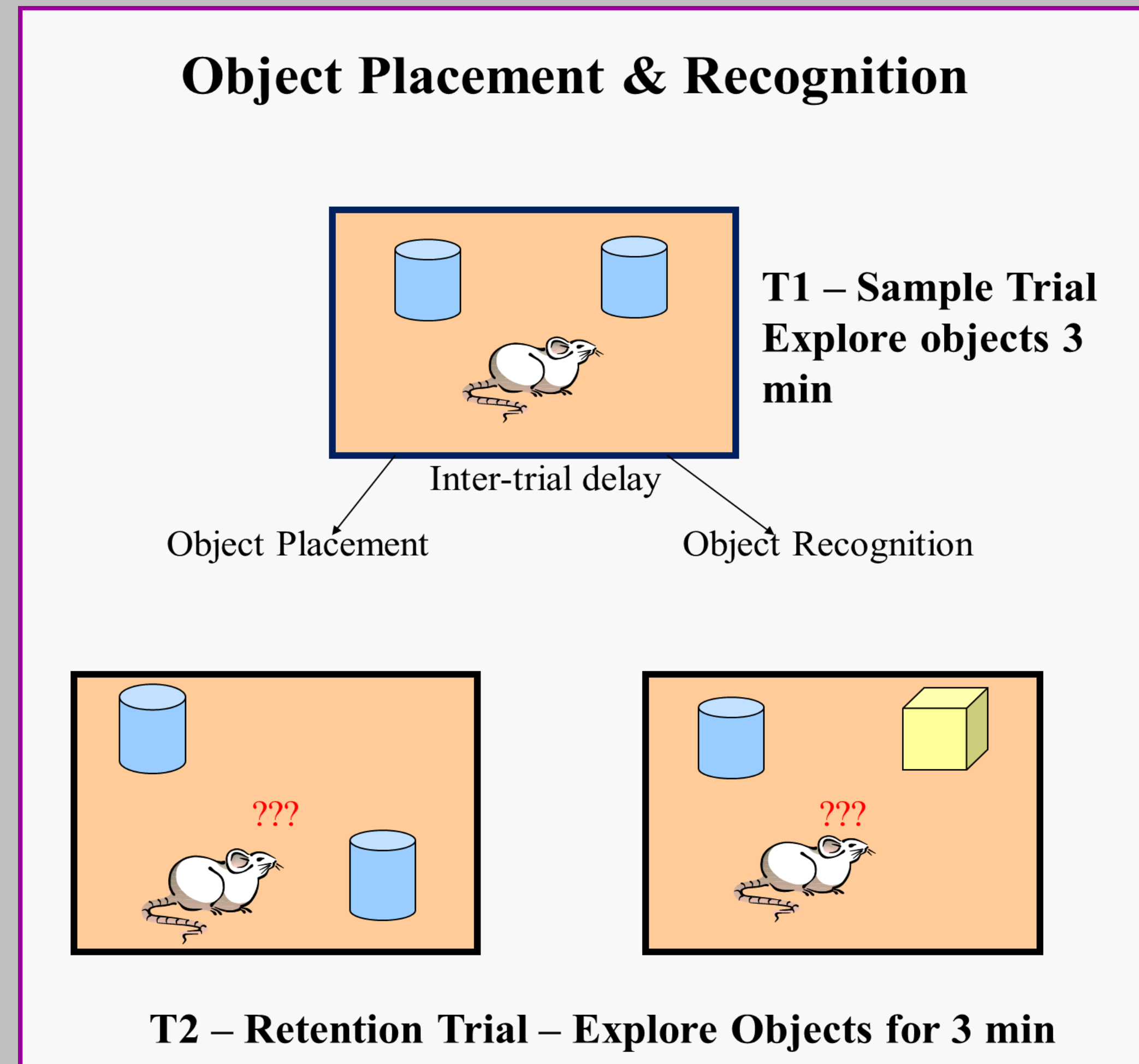
Kelly Brown, Jennifer Hagedorn, & Melissa Yacubich (Mentor: R.E. Bowman)

## 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).

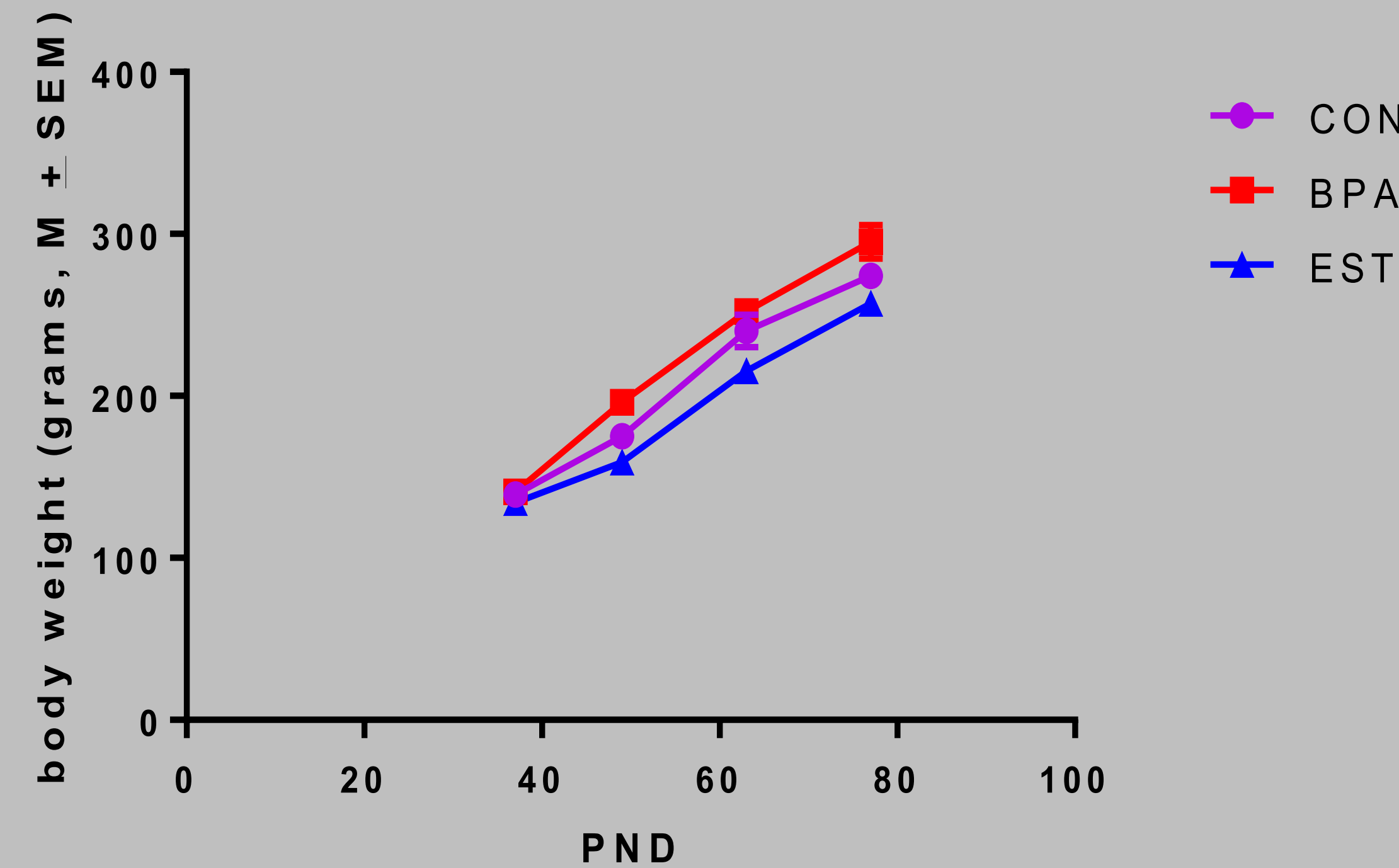
Most research investigating the effects of BPA in animal models has focused on exposure during early prenatal and neonatal periods which results in behavioral, structural and physiological alterations; however, adolescence is another important development period that is characterized by profound hormonal changes. Our laboratory has been investigating BPA exposure during the juvenile period of development (Diaz-Weinstein, et al., 2012; Bowman, et al., 2014; Bowman, et al., 2015) and have found that anxiety, cognition, and neuronal morphology are all altered.

Our previous studies have all been conducted in gonadally intact male and female adolescent rats; this leads to the difficult interpretation of the extent to which observed effects may be due to the BPA exposure versus natural fluctuations in gonadal hormones. Additionally, Estrogen (E) is known to be neuroprotective, enhance memory, and increase dendritic spine density. However, while Estrogen (E) has been widely studied in adults and aging rats, estrogen replacement studies in juvenile rats has only recently begun to be investigated. Thus, this experiment examined the effects of adolescent BPA exposure in juvenile rats under controlled hormone conditions, i.e., ovariectomized (OVX) females receiving estrogen (E) replacement or placebo.

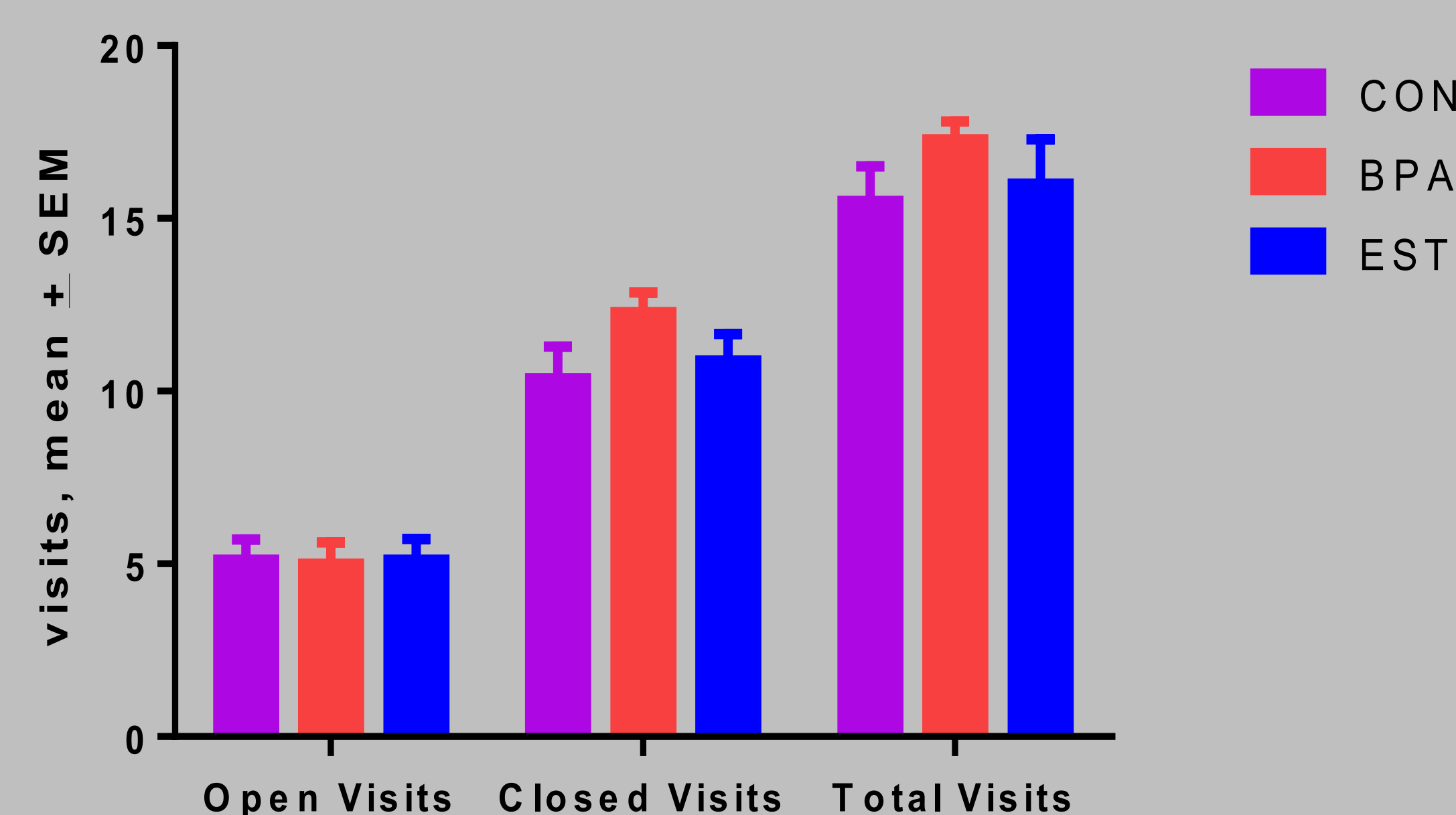


## RESULTS:

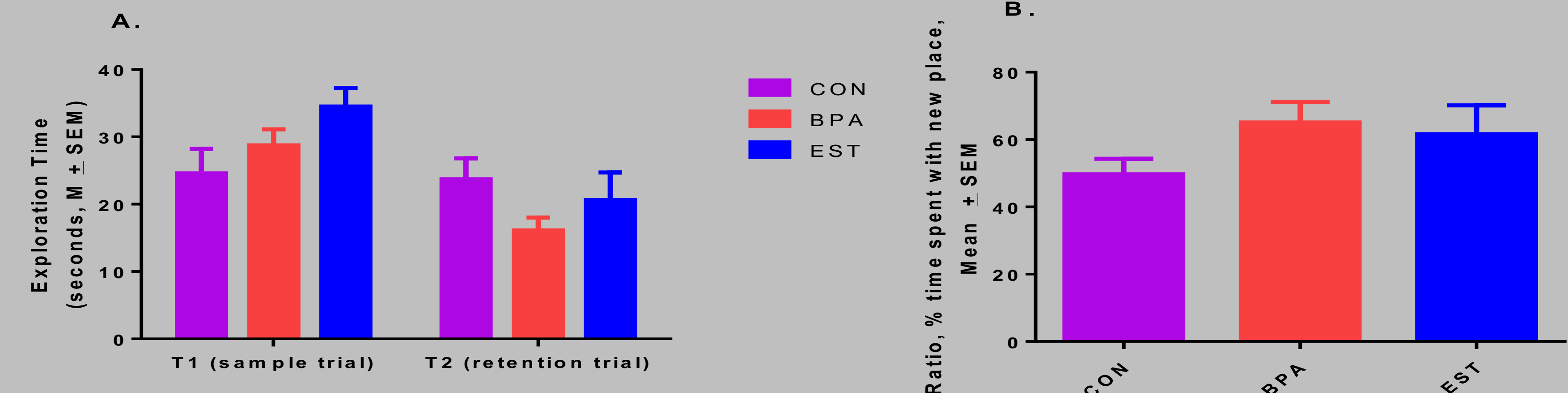
### Effects of BPA & EST on Weight Gain



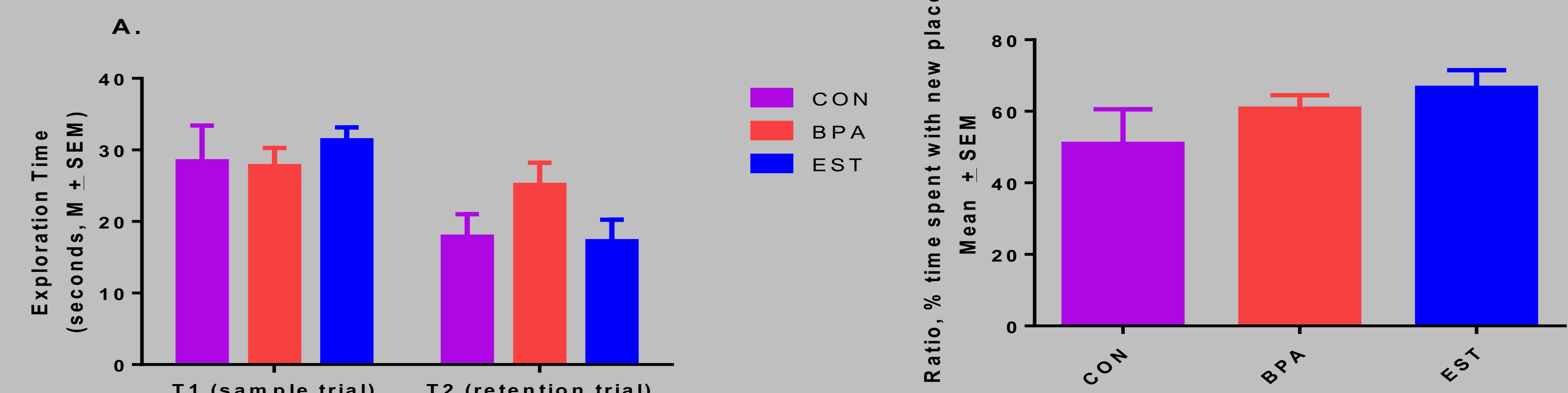
### Elevated Plus Maze



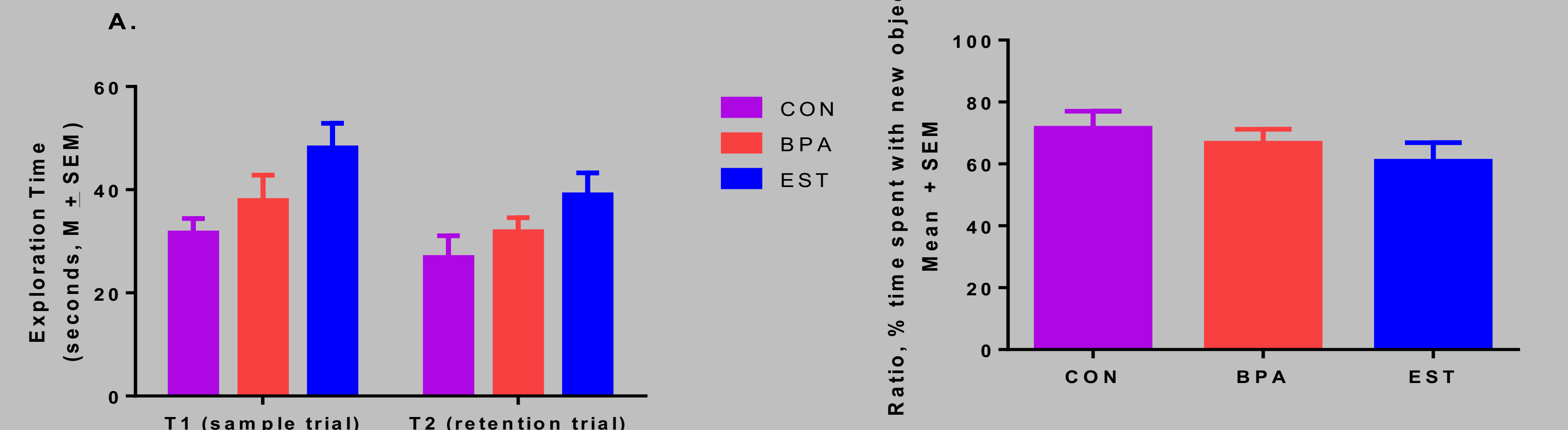
### Object Placement: 1 hr inter-trial delay



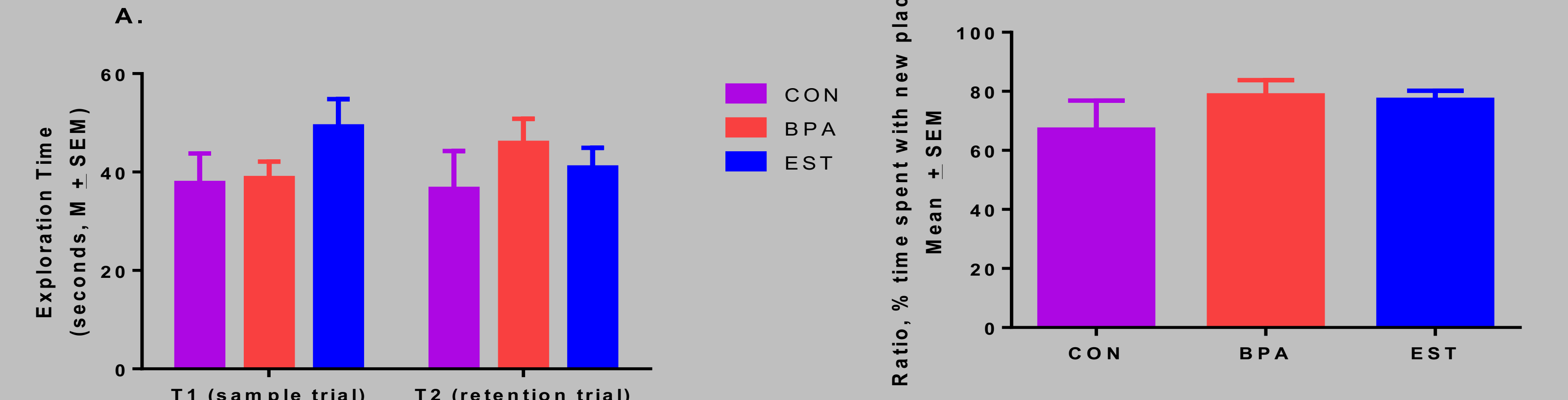
### Object Placement: 2 hr inter-trial delay



### Object Recognition: 1 hr inter-trial delay



### Object Recognition: 2 hr inter-trial delay



## CONCLUSIONS & FUTURE DIRECTIONS:

- As mentioned previously, studies investigating BPA exposure have only recently begun to be administered in adolescence. Previous studies conducted in our laboratory have shown that BPA exposure in juvenile periods of development causes alterations in anxiety, cognition, and neuronal morphology. Because of these previous findings, we were surprised that no individual behavioral group differences arose in the current study.
- A possible explanation for these outcomes could be that the abundance of neuronal growth and development that occurs during adolescence could have masked any effects the BPA or Estrogen would have had on cognitive development.
- Another important consideration is that this novel data in the OVX model and could suggest that the effects of BPA and E exposure during adolescent development is dependent on endogenous gonadal hormones.
- While there were no significant behavioral effects, adolescent BPA and E exposure significantly altered weight gain. This provides physiological evidence of the treatment effects.
- For future work, our laboratory plans to re-rerun this student in the fall to confirm the lack of behavioral effects.
- Additionally, future studies will directly examine adolescent exposure to BPA alone compared to BPA + E to provide more insight on the interaction between the two.

## METHODS:

### Subjects

- Female (n=24) Sprague Dawley rats were used in the present study. Females were ovariectomized at postnatal (PND) 21 and arrived in our laboratory on PND 25. Subjects double housed in standard cages and were randomly assigned to a control (vehicle control), BPA (40 µg/kg bodyweight), or E group (40 µg/kg bodyweight) group.
- All animals received subcutaneous injections PND 38-49. Subjects were weighted regularly.
- Behavioral testing began in adulthood (PND 77 - 90).

### Elevated Plus Maze

- Anxiety was measured during a 5 min trial. The number of visits to the open and closed arms was recorded.

### Object Placement and Recognition Tests

- Spatial memory was tested using the object placement and non-spatial working memory was tested using the object recognition test.
- Subjects received a 10 min acclimation trial and were tested for memory with inter-trial delays of 1 and 2 hrs. Time spent with the old versus new location/object is recorded.

