The Prenatal Bisphenol A Exposure Effects on Neural Signalling Activity in Male Rat's Hippocampus and its Neurobehavioral Outcomes

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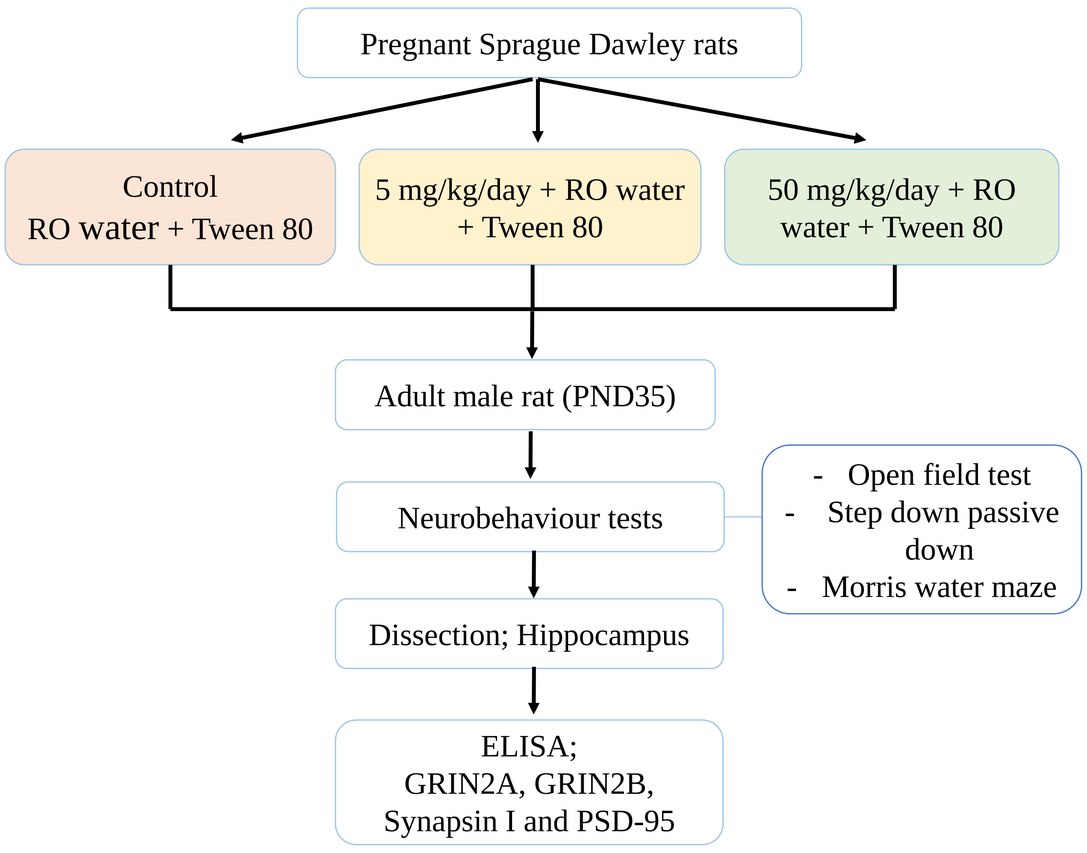
INTRODUCTION

BPA is an organic compound used to produce polycarbonate plastic and epoxy resins which mainly can be found in plastic bottles, coating of cans, toys items, dental materials and others[1]. Risk assessment studies showed BPA compounds can leached into food stuff and environment. During pregnancy, the maternal BPA exposure may affect the foetus development via placenta-mediated interactions[2]. The pleiotropic actions of BPA may induce the developmental disorder of the brain and nervous system of the foetus by acting as steroid receptor agonists or antagonists which then interfere the normal hormonal regulation and proper function of neuroendocrine systems[3]. In terms of memory and learning function, the biochemical action of BPA may disrupt the expression level of NMDAR subunits and synaptic plasticity marker in hippocampus leading to inhibition of neuron cell signalling function. The prenatal BPA exposure may induce learning and memory deficits when reaching adulthood as any disruption to this critical period will be genetically inherited throughout life[4].

OBJECTIVE

To determine effects of prenatal BPA exposure on the level of N-Methyl-D-Aspartate receptor (NMDAR) subunits (GRIN2A and GRIN2B) with synaptic plasticity markers (Synapsin I and PSD-95) in the neural signalling pathway and its neurobehavioral outcomes.

METHODS



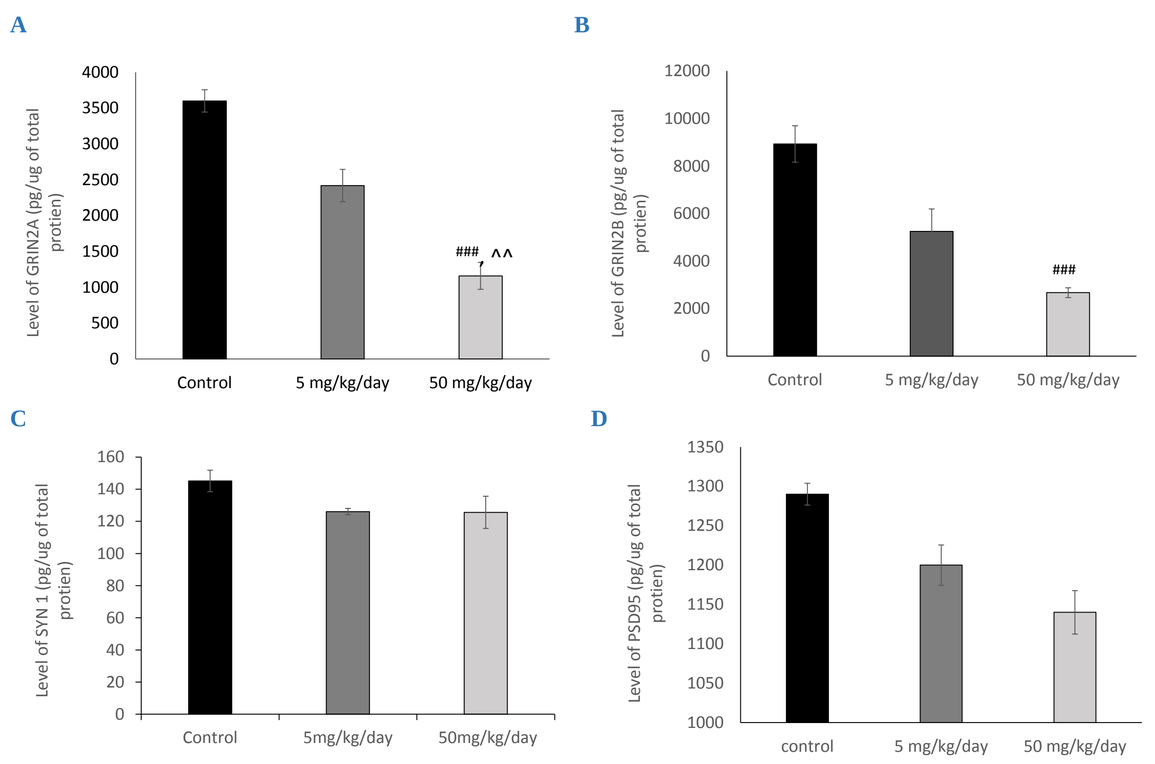
CONCLUSION

- The prenatal BPA exposure downregulated the level of NMDAR subunits (GRIN2A and GRIN2B) and synaptic plasticity markers (SYN I and PSD-95) in adult male rat hippocampus.
- The disruption of NMDAR subunits and synaptic plasticity marker in the hippocampus induced the impairment in learning and memory function of rats.
- The findings are assumed to be related with modulation of estrogen-related receptors (ERRs) pathway by BPA which contribute to inhibition of neural signalling pathway in adult male rat hippocampus.

References:
1. Ribeiro, E., Ladeira, C., & Viegas, S. (2017). Occupational Exposure to Bisphenol A (BPA): A Reality That Still Needs to Be Unveiled. *Toxics*, *5*(3). https://doi.org/10.3390/toxics5030022
2. Acconcia, F., Pallottini, V., & Marino, M. (2015). Molecular Mechanisms of Action of BPA. *Dose-Response*, *13*(4), 155932581561058. https://doi.org/10.1177/1559325815610582
3. Wolstenholme, J. T., Rissman, E. F., & Connelly, J. J. (2011). The role of Bisphenol A in shaping the brain, epigenome and behavior. *Hormones and Behavior*, *59*(3), 296–305. https://doi.org/10.1016/j.yhbeh.2010.10.001
4. Rolfo, A., Nuzzo, A. M., De Amicis, R., Moretti, L., Bertoli, S., & Leone, A. (2020). Fetal–Maternal Exposure to Endocrine Disruptors: Correlation with Diet Intake and Pregnancy Outcomes. *Nutrients*, *12*(6), 1744. https://doi.org/10.3390/nu12061744

RESULTS

ELISA;



NEUROBEHAVIOURAL TESTS;

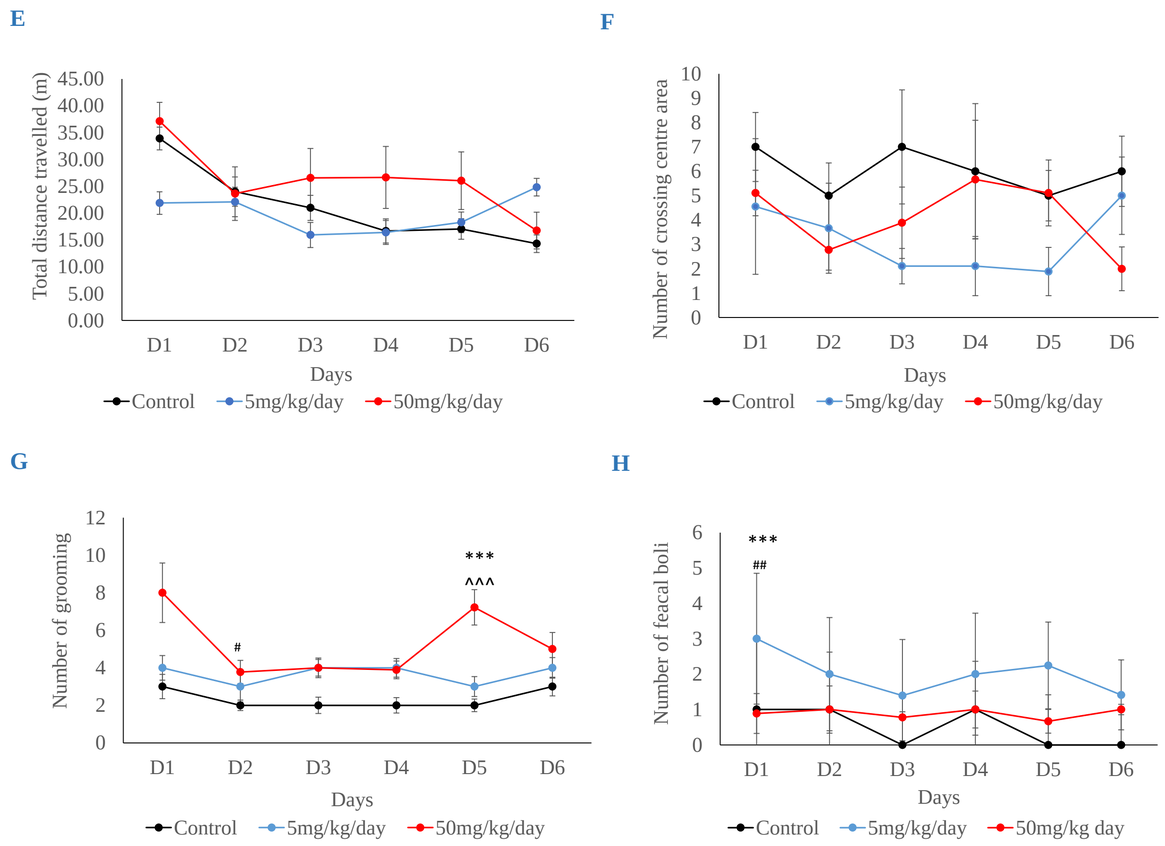


Figure 1: Effects of prenatal BPA exposure on proteins expression in adult male rat hippocampus by ELISA and its neurobehavioral test at adult stage. ELISA; n=4 (mean ± SEM); (A) GRIN2A (B) GRIN2B (C) SYN I, (D) PSD-95 by one way ANOVA with post Hoc Bonferroni analysis. Neurobehavioral test; n=9 (mean ± SEM); (E) Total distance travel (F) Number of crossing centre area (G) Number of grooming (H) Number of feacal boli (I) Step down passive avoidance test (J) Morris water maze by two way ANOVA with post Hoc Bonferroni analysis. *p<0.05 control vs 5mg/kg/day, #p<0.05 control vs 50mg/kg/day, ##p<0.01 control vs 50mg/kg/day, ***p<0.001 control vs 5mg/kg/day, ###p<0.001 control vs 50mg/kg/day, ^^p<0.01 5mg/kg/day vs 50mg/kg/day, ^^^p<0.001 5mg/kg/day vs 50mg/kg/day.