Impact of plastic contaminants on central pattern generator neural circuits in the spinal locomotor circuit of neonatal mice

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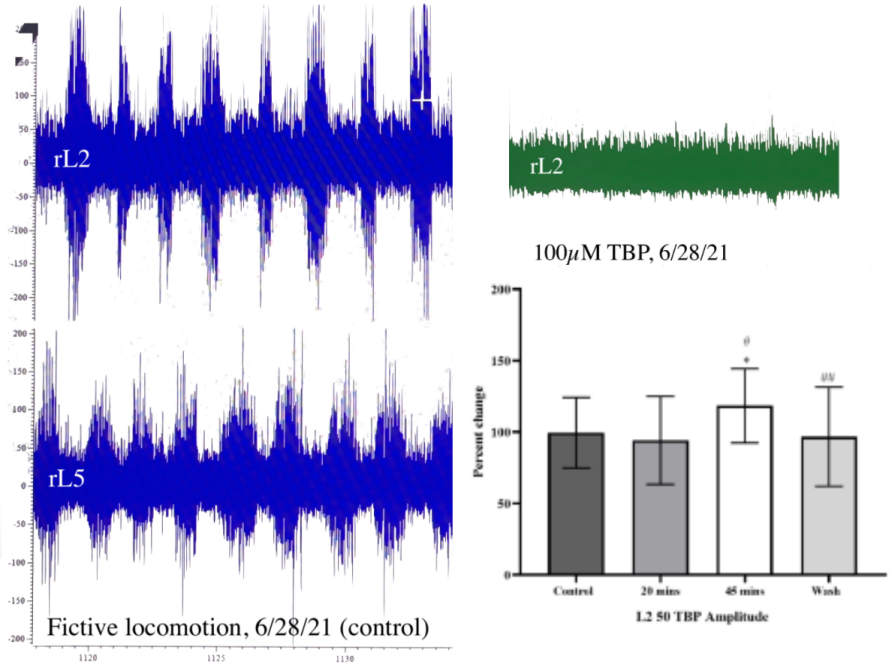
Background and objectives: Over 65% of the world's plastic pollution contains di-n-butyl phthalate (DBP) and tributyl phosphate (TBP), plasticizers that can pass through the blood-brain barrier and contaminate the brain and central nervous system. Previous studies have focused on the effect of BPA and DEHP (other common plasticizers) on invertebrate model organisms. Our study aims to elucidate the effects of plasticizers on a neonatal mouse model and to understand the molecular mechanisms that TBP and DBP have on locomotor behavior. **Methods**: Fictive locomotion was induced in a neonatal mouse spinal cord with 5-HT and NMDA, and then TBP was introduced at varying concentrations (10µM, 50 µM, 100 µM). Parameters of burst amplitude, burst duration, and cycle period of rhythmic firing were comparatively analyzed over time and over varied concentrations. **Results:** The L2 flexor ventral root data at 10µM and 50 µM of TBP consistently showed increased burst amplitude, burst duration (reduction in firing organization), and cycle period. Recordings from L2 and L5 ventral roots showed 100µM TBP is highly disruptive yet reversible. **Conclusions:** The results suggest that TBP causes an increase in network level inhibition, implying effects at the motor-neuron, interneuron, and central pattern generator levels. The reversible increased burst duration and cycle period suggest TBP causes a neurotransmitter-based disruption to the cellular mechanism of action. Future experimentation will examine the effects of DBP on fictive locomotion individually and with TBP. To determine the effects of oxidative stress and 5-HT and DA neurotransmitter imbalance, antioxidants, 5-HT3 antagonists, and D2 agonists with TBP and/or DBP will further specify the mechanism of action behind plastic induced locomotor disruption.



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References: Holahan, M, et al, Preadolescent Phthalate (DEHP) Exposure Is Associated With Elevated Locomotor Activity and Reward-Related Behavior and a Reduced Number of Tyrosine Hydroxylase Positive Neurons in Post-Adolescent Male and Female Rats, *Toxicological Sciences*, Volume 165, Issue 2, October 2018, Pages 512–530, https://doi.org/10.1093/toxsci/kfy171

Rama-Krishnan Poopal, et al. Biochemical and behavior effects induced by diheptyl phthalate (DHpP) and Diisodecyl phthalate (DIDP) exposed to zebrafish, Chemosphere, Volume 252, 2020, 126498, ISSN 0045-6535, https://doi.org/10.1016/j.chemosphere.2020.126498.