Effects of Plasticizer Dibutyl Phthalate (DBP) and Neuroprotectant Curcumin on Mammalian Locomotor Activity

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Pollution is one of the most significant environmental stressors, posing a substantial public health threat. Among its many sources, plastic waste is one of the major contributors to pollution, especially as its production continues to increase exponentially. Plastics are often enriched with plasticizers, which are chemical compounds used to enhance specific characteristics, such as softness and ductility. They can easily leach into food products, the environment, and human tissues. Dibutyl phthalate (DBP), one of the most commonly used plasticizers, can induce the production of reactive oxygen species, causing oxidative stress and cell death. DBP exposure leads to memory and learning impairment, inflammation, and damage to the central nervous system[2]. Curcumin, the active component in turmeric, has been shown to have antioxidant, anti-inflammatory, and anti-apoptotic effects by neutralizing reactive oxygen species, making it a promising candidate for mitigating the effects of plasticizers[3]. While previous studies have examined the effect of DBP on behavior and organ systems, our project focuses on the impact of DBP on locomotion and central pattern generators (CPG), neuronal networks that control rhythmic activity.

To investigate the impact of DBP on locomotion and the CPG, we dissected and isolated the spinal cord of neonatal mice aged 0 to 5 days via ventral laminectomy[4]. Fictive locomotor activity was induced by perfusing the cord with 6 μM NMDA and 9 μM 5-HT. Once a stable rhythm was established, we recorded activity from the L2 and L5 ventral roots for 20 minutes, corresponding to flexor and extensor muscle activity, respectively, and used these recordings as our control. DBP was then added to the perfusion at concentrations of 10, 25, or 50 μM, and recordings were obtained for 60 minutes. Lastly, we performed a wash with 6 μM NMDA and 9 μM 5-HT for 90 minutes to check if the impact of DBP is reversible. We analyzed burst amplitude, which shows motor neuron recruitment, burst duration, which shows the intrinsic excitability of the CPG, and cycle period, which shows the speed controlled by the CPG. We hypothesized that DBP would decrease locomotor activity by decreasing burst amplitude and increasing burst duration and cycle period.

Our preliminary findings show a decrease in amplitude following the application of DBP, suggesting lower neuronal recruitment. This reflects the hypothesis that DBP has an inhibitory effect, potentially driven by mitochondrial damage and oxidative stress, diminishing the energy available to neurons and their ability to fire. Interestingly, we observed decreases in burst duration and cycle period, which suggest higher excitability of the CPG and motor neurons. This enhanced excitability could be attributed to an early toxic excitatory effect of DBP that we expect to diminish with prolonged exposure. Across all three parameters of burst amplitude, burst duration, and cycle period, the effects of DBP appeared to be dose-dependent and have limited reversibility. Additionally, our preliminary data suggested that DBP has a more enhanced impact on the L5 root, which controls extensor muscle activity. This imbalance shows that the activity of the CPG is flexor-dominated, as its location in the upper lumbar region drives the initial timing of the neuronal activity. The preliminary experiments we conducted with curcumin suggested that the concentrations of curcumin we used (5 to 100 μM) are too high, as the neuronal rhythm of both ventral roots worsened and became more unstable. Additional experiments are needed to confirm the dose-dependent trend across the three parameters and identify a concentration of curcumin that mitigates DBP toxicity.

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