Characterizing the Effects of Di(2-ethylhexyl)phthalate (DEHP) and Curcumin on the Mammalian Spinal Central Pattern Generator Circuit

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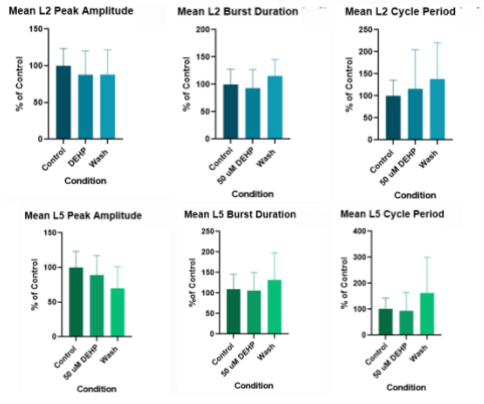
This project explores the effects of plasticizer DEHP and antioxidant curcumin on mammalian locomotion. Plasticizers, such as DEHP, are chemicals added to plastics that result in the accumulation of reactive oxygen species (ROS) within the body, physiological dysfunction, and locomotor deficits (Li et al., 2016). Application of antioxidants, which reduce the activity and production of ROS, have been shown to ameliorate the locomotor effects associated with DEHP exposure on the behavioural level (Tseng et al., 2013). No research exists exploring the neuroprotective capabilities of curcumin or analyzing effects on the level of neuronal circuits in the mammalian locomotor network. Mammalian locomotion is driven by the lumbar spinal central pattern generator (CPG), which produces the rhythmic motor neuron activity required for walking (Whelan, 2000). This circuit can be activated in the isolated neonatal mouse spinal cord via drug application to produce locomotor-like activity, which is an effective model to explore the effects of DEHP and curcumin on mammalian locomotion (Acevedo et al., 2016).

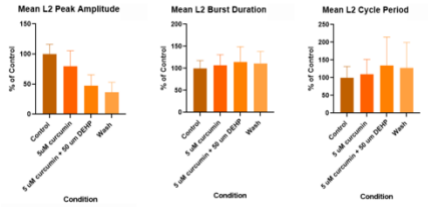
Locomotor-like activity was induced in the isolated spinal cords of neonatal mice (0-6 days) using serotonin and NMDA. To characterize the effects of the plasticizer, I perfused the spinal cords in 50 uM DEHP followed by a wash. To determine the neuroprotective capabilities of curcumin, I preincubated activated spinal cords in 5 uM curcumin, then perfused these cords in a solution of 50 uM DEHP and 5 uM curcumin before performing another wash. Electrophysiological activity was recorded from the L2 and L5 flexor and extensor ventral roots using glass suction electrodes and the peak burst amplitude, burst duration, and cycle period of the locomotor-like activity was compared across all drug conditions.

I observed that application of 50 uM DEHP induced no significant changes in the locomotor activity produced by the L2 and L5 ventral roots but a trend of decreasing activity throughout the experiments. Interestingly, 5 uM curcumin preincubation seemed to reduce the activity of the network and exacerbated the negative effects of DEHP application. This suggests that 50 uM of DEHP is too dilute a concentration to induce significant locomotor deficits whereas 5 uM of curcumin is too high of a concentration to produce neuroprotective effects, and informed my future use of 100 uM DEHP and 1 uM curcumin.

50 uM DEHP Results:



5 uM Curcumin Results:



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