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

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Pollution is one of many environmental stressors and is a significant public health threat. Plastic in particular poses the biggest issue, especially as its production increases exponentially, reaching 360 million metric tons in 2024. Oftentimes, plasticizers are added to single-use plastics to improve qualities such as flexibility and softness. Dibutyl Phthalate (DBP) is one of the most commonly used plasticizers, and because it is artificially added, it can leach into food products and human tissue. DBP has been shown to cause oxidative stress by inducing the release of free radicals and reactive oxygen species (ROS), leading to inflammation, impairment of memory, and damage at the level of the central nervous system. Curcumin, which is the active component in turmeric, has been shown to have antioxidant, anti-inflammatory, and anti-apoptotic effects by neutralizing ROS, which makes it seem like a promising potential intervention for plasticizers. Central pattern generators (CPG) are the neuronal networks responsible for rhythmic activities like locomotion and heartbeat. Studies have focused on the effect of DBP on larger organ systems and behavior, but not on neuronal networks like CPG or locomotion. We focused on testing the effect of DBP on the spinal ventral roots that control flexor and extensor muscle activity in hindlimb walking.

The experiment used the in-vitro mouse model using mice 0-5 days old. Using drugs such as serotonin and NMDA, we induced fictive locomotor activity (bursting) in the spinal cords of these mice, which was captured using electrodes connected to the L2 and L5 ventral roots of the spinal cord. Once the rhythm had stabilized, DBP was added to the perfusion in varying concentrations for 45-60 minutes, then washed using solution without DBP for 60-90 minutes, to determine reversibility. Using Spike2, we collected several parameters, including the amplitude, duration, and cycle period of the bursts and how these changed when DBP was added.

Our findings show a decrease in amplitude following DBP exposure, suggesting lower neuronal recruitment. This reflects an inhibitory effect of DBP, potentially driven by mitochondrial damage and oxidative stress, which diminishes the energy available to neurons and hinders their ability to fire. In contrast, the observed decreases in cycle period and burst duration show higher excitability of the CPG and the motor neurons, as they fire more frequently. This enhanced excitability might reflect early toxic excitatory effects of DBP, though it is expected to diminish with prolonged exposure. Additionally, the activity of the CPG is flexor-dominated because of its location in the upper lumbar region of the cord. Since the flexor roots drive the initial timing of activity, the relatively delayed role of L5 (primarily extensor) roots may account for their heightened sensitivity to DBP's effects.

During preliminary experiments with curcumin, the neuronal rhythm of both ventral roots appeared to worsen in response to the application of curcumin. This suggests that the concentration of curcumin tested might be too high and induce a neurotoxic effect. In the future, it is needed to further test the effect of curcumin and determine a concentration of curcumin that does not destabilize the neuronal rhythm. Additionally, further tests with only DBP are needed to confirm the dose-dependent trend across the three parameters tested.

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