MITOCHONDRIAL AND DOPAMINERGIC IMPAIRMENTS INDUCED BY METAL MIXTURES IN *C. ELEGANS*

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INTRODUCTION: Heavy metals, including methylmercury (MeHg) and manganese (Mn), are widely distributed in the Earth's crust and are associated with neurotoxicity, affecting dopaminergic function. While both metals are known to share common toxicity pathways, such as mitochondrial dysfunction and dopaminergic neurodegeneration, limited research has explored the combined effects of MeHg and Mn exposure. **OBJECTIVE:** Using *Caenorhabditis elegans,* (*C elegans*), we assessed the effects of acute co-exposure to MeHg and Mn on dopaminergic neuron integrity, neurobehaviors related and mitochondrial function. **MATERIALS AND METHODS:** L1 worms of wild type strain (N2) were exposed to metals individually and in combination for 1 hour, and toxicological parameters were assessed 48h after exposure. Concentrations of Mn (30mM) and MeHg (20 uM) were chosen for the assays. For dopaminergic neurons assessment the strain BY200 (*dat-1*p::GFP) was used. High-resolution respirometry was conducted using mitochondrial-enriched fraction. **RESULTS:** Morphological disruptions in dopaminergic neurons were observed in the co-exposure group, together with impaired locomotion, reduced basal slowing response (BSR), and increased swimming-induced paralysis (SWIP). Mitochondrial dysfunction was also evident, with Mn-induced impairment of mitochondrial respiration, while co-exposure led to compensatory increases in several mitochondrial activities, including OXPHOS CI and citrate synthase activity. **CONCLUSION:** The differential sensitivity of these endpoints to the metal combination underscores the importance of evaluating co-exposure scenarios to capture a more comprehensive view of the potential neurotoxic risks associated with environmental contaminants upon real-life exposure scenarios. These findings reinforce the need to assess combined exposures, particularly in environments with complex contamination profiles, as neurotoxic risks may exceed those from individual toxicants.

Keywords: co-exposure; neurotoxicity; mitochondrial dysfunction