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### **Behavioral and neurochemical long-term consequences of intranasal chlorpyrifos formulation administration in mice**

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Environmental pollution negatively affects cognitive performance and accelerates its decline associated with age. Inhalation or intranasal (IN) administration of xenobiotics constitutes a feasible route for substance delivery to the brain. Recently, we described that CF-1 mice exposed to a commercial formulation of chlorpyrifos (fCPF) exhibited recognition memory and anxiety impairments, together with disturbances in both, the redox balance and cholinergic and glutamatergic enzymes activities. In the present work, we studied the long-term consequences of IN fCPF administration (10 mg/kg, every other day, for 15 to 30 days) in mice. After a 4 to 8 months fCPF-free washout period, fur appearance improved, and the number of body injuries decreased in fCPF treated mice. Scores in recognition memory and anxiety levels were similar between the control and fCPF-treated group. Notably, spatial learning and memory were improved in fCPF treated group. Neurochemical markers of oxidative stress and the activities of enzymes belonging to the cholinergic and glutamatergic pathways showed significant differences from the control group even after 8 months. Neurochemical disturbances in IN fCPF-treated mice were also modeled using the human neuroblastoma cell line SH-SY5Y treated with fCPF and CPF. The obtained results suggest that previous exposure to fCPF induces long-term modifications in the brain biochemistry that could be responsible for the phenotypic and behavioral observations.

**Keywords:** chlorpyrifos; intranasal administration; memory; anxiety; oxidative stress; glutamatergic and cholinergic system