DEVELOPMENTAL EXPOSURE TO MDMA INDUCES EARLY HYPERACTIVITY AND MOTOR DYSFUNCTION IN ZEBRAFISH (*DANIO RERIO*)

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INTRODUCTION: 3,4-Methylenedioxymethamphetamine (MDMA) is a synthetic psychoactive substance mainly used in recreational settings, acting as a potent releaser of serotonin, norepinephrine, and dopamine. However, at abusive concentrations, MDMA can induce significant neurotoxic effects, including neurobehavioral alterations, suggesting possible dysfunctions in the developing nervous system. In this context, the zebrafish stands out as an effective experimental vertebrate model for assessing developmental and behavioral changes, contributing to applied research in neurotoxicology. OBJECTIVE: Evaluate whether exposure to MDMA during development induces neurotoxicity in the embryonic-larval stage of zebrafish. MATERIALS AND METHODS: Embryos at the blastula stage, previously selected, were exposed to different concentrations of MDMA (1.0, 2.5, and 5.0 µg/mL), with a non-exposed control group maintained. The tail coiling assay was performed at 26 hpf to assess potential neurotoxic effects during embryonic development within the tested concentration range. To analyze neuromotor impairments, the larval photomotor response assay was conducted at 144 hpf using ZebraBox software to quantify locomotor activity in response to alternating light stimuli. RESULTS AND CONCLUSION: MDMA showed significant effects in the tail coiling test at the concentration of 1.0 µg/mL, indicating early neurotoxicity, impaired coordination of motor development, and neural hyperexcitation. MDMA induced concentration and light cycle-dependent behavioral changes. An increase in burst duration was observed at 2.5 µg/mL in light cycles and a decrease at 5.0 µg/mL in dark cycles. The inter-burst interval increased at 1.0 µg/mL and decreased at 5.0 µg/mL in dark cycles. Freezing behavior duration was reduced at 1.0 µg/mL in both light and dark cycles. Additionally, swimming distance and larval speed increased at 2.5 µg/mL in light cycles and decreased at 5.0 µg/mL in dark cycles. Thus, these findings demonstrate that MDMA induces significant neurotoxic effects, impairing neurobehavioral development and motor coordination, contributing to the understanding of risks associated with the use of psychoactive substances such as MDMA.

Keywords: zebrafish; psychoactive; neurotoxicity; developmental toxicity.