ESKETAMINE PREVENTS MORPHINE-CONDITIONED PLACE PREFERENCE IN FEMALE OFFSPRING OF OPIOID-ADDICTED MOTHERS

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INTRODUCTION: Opioid use disorder is a chronic and recurrent condition that represents a major public health concern. Tolerance, dependence (addiction), withdrawal syndrome, and relapse are frequently triggered upon the discontinuation of opioid use. Maternal-fetal exposure to opioids can result in impaired fetal development and withdrawal-related symptoms in the newborn. Preventing relapse remains the greatest challenge in achieving long-term success in detoxification, as current pharmacological strategies demonstrate efficacy primarily during the remission phase and show limited effectiveness in the later stages of recovery. From an innovative perspective, Esketamine (ESK), the S-enantiomer of ketamine, has demonstrated beneficial effects on the central nervous system (CNS). It is currently used to manage impulsive-compulsive behaviors, as well as emotional and physical symptoms in treatment-resistant depression, including cases associated with suicide risk—conditions closely linked to substance dependence. Thus, ESK emerges as a promising therapeutic alternative for addiction treatment, particularly due to its influence on neurotransmitter networks and its neuromodulatory effects on hedonic pathways—mechanisms often difficult to reverse. **OBJECTIVE:** This study aimed to evaluate the therapeutic potential of ESK on behavioral parameters associated with morphine (MORPH) preference in rats (Ethics Comittee Approval: CEUA-UFSM: 2935220824). **MATERIALS AND METHODS:** Adolescent female rats-offspring of MORPH-addicted mothers exposed during the perinatal period to progressively increasing doses of MORPH (4.0 to 10.5 mg/kg, s.c., twice daily for 42 days), were treated with ESK (20 mg/kg, i.p.), administered either acutely (A-ESK: every 5 days) or subchronically (SC-ESK: daily) for a total of 10 days. Following ESK treatment, the animals were subjected to the conditioned place preference (CPP) paradigm with MORPH (4.0 mg/kg, i.p.) for 4 consecutive days. Twenty-four hours after the last MORPH administration, craving-related behavior was evaluated (MORPH-CPP). **RESULTS:** The findings showed that both acute and subchronic ESK treatments effectively prevented MORPH-CPP, as evidenced by a significant reduction in drug-seeking behavior. **CONCLUSION:** These results highlight the therapeutic potential of ESK in the treatment of opioid dependence, a condition for which existing pharmacological approaches remain predominantly symptomatic, and support its emergence as a promising candidate for future clinical investigations targeting substance use disorders.

Keywords: Opioid use disorder; Perinatal exposure; Drug-seeking behavior.

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