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ADMINISTRATION OF ZOLMITRIPTAN ATTENUATES METHAMPHETAMINE PREFERENCE IN ADOLESCENT MALE AND FEMALE RATS

Background: Activation of serotonin (5-HT)1B receptors modulates the expression, but not the acquisition, of methamphetamine (METH) preference in adult male mice. In the present study, we investigated whether activation of 5-HT1B receptors affects the acquisition of METH preference in adolescent rats. Specifically, using the Conditioned Place Preference (CPP) paradigm, a validated animal model of drug reward, we examined whether administration of Zolmitriptan, a 5-HT1B receptor agonist, before METH affects the development of METH-induced CPP in male and female adolescent rats.

Methods: Male and female adolescent rats (postnatal day [PD] 28) underwent a 10-day CPP procedure. Specifically, on days 1 and 10, rats were tested for their preconditioning and postconditioning place preferences, respectively, during 20-min sessions. On days 2-9, rats were conditioned for 30-min with saline or METH on alternating days. During METH conditioning days, rats were randomly assigned to receive an injection of Zolmitriptan (0 or 10 mg/kg) 15 min before the administration of saline or METH (0.125, 0.25, 0.5, 1.0 mg/kg).

Results: Male rats exhibited METH-induced CPP when they were conditioned with either 0.25 or 0.5 mg/kg of METH. Administration of Zolmitriptan (10 mg/kg) prior to METH resulted in a decreased preference for the METH-paired compartment when rats were conditioned with the 0.25 mg/kg METH dose, but not when rats were conditioned with the 0.5 mg/kg METH dose, which continued to show METH-induced CPP. In females, rats displayed METH-induced CPP after administration of any of the doses of METH used (i.e., 0.125, 0.25, 0.5, or 1.0 mg/kg). In contrast, female rats administered Zolmitriptan prior to METH did not exhibit METH-induced CPP, with the exception of the rats that received the 0.5 mg/kg METH dose.

Conclusion: The present findings demonstrate that activation 5-HT1B receptors with Zolmitriptan reduces the acquisition of METH-induced CPP in male and female adolescent rats, suggesting that age, sex, and species may be important factors in demonstrating a role of 5-HT1B receptors in modulating METH reward, as prior work in adult male mice did not demonstrate a role of 5-HT1B receptors in the acquisition of METH preference. When considered together, these findings further validate targeting the 5-HT1B receptor in the treatment of psychostimulant addiction.