KETAMINE PRE-EXPOSURE DOES NOT INFLUENCE LATER-LIFE RESPONSES TO REWARD-RELATED STIMULI IN FEMALE C57BL/6 MICE

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Dedication

To those who were influential in my education.

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by

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Abstract

Preclinical work indicates that exposure to traditional antidepressant medications, in adolescent and adult female subjects, alters reward-related behavior later in life. In recent years, the anesthetic ketamine (KET), now used as a fast-acting antidepressant, has shown promising therapeutic efficacy for the management of depression. However, the potential long-term behavioral consequences of KET exposure across development have not been thoroughly assessed. Thus, to address this issue, we examined if KET exposure, during adolescence or early adulthood, results in enduring alterations in responsivity to the rewarding properties of sucrose and cocaine later in life. Specifically, female C57BL/6 mice were randomly assigned to receive repeated intraperitoneal injections of KET (0 [vehicle; VEH] or 20 mg/kg) for 15 consecutive days during the adolescent (postnatal day [PD] 35-49), or early adult (PD70-84) stage of development. Twenty-one days after KET or VEH exposure, female mice (PD70+ or PD105+, respectively) were assessed on their reactivity to a sucrose solution (1%) adopting a two-bottle choice procedure, or cocaine (0, 5, or 10 mg/kg) using the conditioned place preference test, two well-established measures of reward-seeking behavior. We found that 21-days post KET exposure, female mice spent significantly higher time in the cocaine-paired chamber ($p<0.05$). However, KET pre-exposure, either during adolescence (PD35-49) or early adulthood (PD70-84), did not influence the preference magnitude for sucrose or cocaine 21-days later (PD70+ and PD105+, respectively). Collectively, our data suggest that exposure to KET does not induce long-term changes to reward-related stimuli, in female C57BL/6 mice.

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