

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

ISRAEL GARCIA CARACHURE

Master's Program in Experimental Psychology

APPROVED:

---

Sergio D. Iñiguez, Ph.D., Chair

---

Laura E. O'Dell, Ph.D.

---

Luis M. Carcoba, M.D., Ph.D.

---

Bruce S. Cushing, Ph.D.

---

Stephen L. Crites, Jr., Ph.D.  
Dean of the Graduate School

Copyright ©

by

Israel Garcia Carachure

2020

PREVIEW

## **Dedication**

To those who were influential in my education.

PREVIEW

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

by

ISRAEL GARCIA CARACHURE

THESIS

Presented to the Faculty of the Graduate School of  
The University of Texas at El Paso  
in Partial Fulfillment  
of the Requirements  
for the Degree of

MASTER OF ARTS

Department of Psychology  
THE UNIVERSITY OF TEXAS AT EL PASO

August 2020

ProQuest Number:28090385

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent on the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 28090385

Published by ProQuest LLC (2020). Copyright of the Dissertation is held by the Author.

All Rights Reserved.

This work is protected against unauthorized copying under Title 17, United States Code  
Microform Edition © ProQuest LLC.

ProQuest LLC  
789 East Eisenhower Parkway  
P.O. Box 1346  
Ann Arbor, MI 48106 - 1346

## Acknowledgements

I would like to pay my special regards to my adviser, Dr. Sergio D. Iñiguez, for his persistent guidance, support, and rigorous scientific training. Thank you for being a positive role model, not only for myself, but also for all underrepresented students. In addition, I would like to recognize my committee members, Drs. Laura E. O'Dell, Bruce S. Cushing, and Luis M. Carcoba for their invaluable insight and feedback on this study. In addition, I want to thank Samuel A. Castillo, Joshua Preciado-Piña, Anapaula Themann, Minerva Rodriguez, and Omar Lira for their technical assistance throughout this project. A special shout-out to Francisco Flores-Ramirez for being a prominent colleague and comrade during our memorable time at UTEP. Furthermore, I wish to express my deepest gratitude to my parents, MariaCristina Carachure and Rafael Garcia, along with my relatives, Nalleli, James, Rafael, Kelly, Jairo, Isaac, and Katherine, for their sacrifices contributing to my education, and for their continuous devotion, support, and motivation. My special thanks goes to my beloved friend, Arantxa K. Martinez, for her valuable input, words of encouragement, and patience during my academic training. Lastly, I would like to thank the LSAMP (Louis Stokes Alliance for Minority Participation) *Bridge to Doctorate* program for financially supporting me throughout this study.

## 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.



## Table of Contents

Acknowledgements.....	v
Abstract.....	vi
Table of Contents.....	vii
List of Tables.....	ix
List of Figures.....	x
Chapter 1: Introduction.....	1
Chapter 2: Methods & Materials.....	4
2.1 Animals.....	4
2.2 Drugs.....	4
2.3 Experimental Design.....	4
2.4 Conditioned Place Preference.....	5
2.5 Sucrose Preference.....	7
2.6 Statistics.....	8
Chapter 3: Results.....	9
3.1 Adolescent KET exposure does not influence cocaine preference in adult mice.....	9
3.2 Adolescent KET exposure does not alter sucrose preference in adult mice.....	9
3.3 Adult KET pre-exposure does not alter cocaine preference in later life.....	10
3.4 Adult KET pre-exposure does not alter sucrose preference in later life.....	10
3.5 Acute and long-term effects of adolescent or adult KET exposure on body weight.....	11
Chapter 4: Discussion.....	12
4.1 Summary.....	12
4.2 Enduring Effects of KET Pre-exposure in female mice.....	12

4.3 Sex-specific Effects of KET Pre-exposure.....	15
4.4 Acute and Long-Term Effects of KET on Body Weight.....	16
4.5 Limitations.....	17
4.6 Conclusion.....	18
References.....	19
Vita.....	34

PREVIEW