



**ANNOUNCEMENT OF FINAL ORAL EXAMINATION
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY**

CANDIDATE: Elizabeth Riley

DEPARTMENT OR PROGRAM: Neuroscience

TITLE OF DISSERTATION: "Effects of Cocaine on Visual Processing in Zebrafish"

DATE, TIME, AND PLACE: Tuesday, July 21, 2015 at 2:00p.m.
Boston University School of Medicine
72 E. Concord Street (Room L 1008)
Boston, MA 02118

EXAMINING COMMITTEE

FIRST READER: Dr. Irina Zhdanova

SECOND READER: Dr. Tarik Haydar

THIRD READER: Dr. Donald O'Malley

**CHAIRMAN OF THE
EXAMINING COMMITTEE:** Dr. Jennifer Luebke Email: jluebke@bu.edu

**ADDITIONAL
COMMITTEE MEMBERS:** Dr. Hui Feng

Members of the committee are asked to confirm attendance by replying directly to the Chairman of the Examining Committee.

ALL MEMBERS OF THE SCHOOL OF MEDICINE FACULTY ARE INVITED TO ATTEND.

EFFECTS OF COCAINE ON VISUAL PROCESSING IN ZEBRAFISH

ELIZABETH RILEY

Boston University School of Medicine, 2015

Major Professor: Irina Zhdanova, M.D., Ph.D., Professor of Anatomy and
Neurobiology

ABSTRACT

Psychostimulants are known to alter visual function acutely and on withdrawal, and can cause attention deficit following prenatal exposure. However, psychostimulants can also improve visual attention in patients with attention deficit. The mechanisms involved in these contrasting effects remain largely unknown.

To determine the role of specific brain regions and the dopamine system in the impact of cocaine exposure on visual processing, we employed two-photon microscopy and a transgenic larval zebrafish expressing the calcium indicator GCaMP-HS. We documented neuronal responses to contrasting visual stimuli, red light (LF) and dark (DF) flashes.

We found that in the optic tectum neuropil (TOn), both stimuli elicited similar responses, though after repeated stimulus presentation, habituation developed to DF only. The dorsal telencephalon (dTe) responded and habituated to LF only. Acute cocaine (0.5 μ M) reduced neuronal responses to LF in both brain regions and prevented habituation of dTe neurons to LF, but did not modify responses or habituation to DF.

Prenatal cocaine exposure (PCE) did not modify baseline responses, but it prevented the acute effects of cocaine on LF responses in both regions and habituation in dTe, with no impact on DF responses. PCE also significantly reduced D1 dopamine receptor expression in TOn and cerebellum, but not dTe or the eye.

Fish lacking the dopamine transporter (DATKO) retained normal D1 expression throughout the brain, baseline responses to LF in both TOn and dTe, and response reduction following cocaine in TOn. However, they demonstrated abnormal swimming behavior, and neither their swimming behavior nor dTe responses to LF were modified by cocaine.

We discovered that in zebrafish, a diurnal vertebrate, responses to light not only require the primary visual processing center TO (superior colliculus in mammals), but also higher level processing by dTe. Responses to light but not darkness are modified by cocaine, unless the fish lack DAT or were exposed to PCE. Together, our results demonstrate specific effects of cocaine on visual processing mediated by the dopamine system, and provide a novel animal model for further investigation of these phenomena and development of new therapeutic approaches.