

# Methamphetamine effects on adolescent brain development in both sexes

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## Introduction

- Females in both humans and rat models often exhibit faster rates of addiction than males<sup>1</sup>
- Vulnerability to drug addiction in adolescents (ADOLs) may lead to higher relapse rates<sup>2</sup> and faster rates of addiction<sup>3</sup>
- The brain is developing in adolescence, including the prefrontal cortex (PFC) and the nucleus accumbens (NAc), which are regions involved in self-control and reward systems, respectively<sup>4</sup>
- Our lab previously found that adult rats of both sexes exposed to amphetamine during ADOL had reduced expression of dopamine D<sub>1</sub> receptors (D<sub>1</sub>R) in the medial PFC but no change in the NAc<sup>5</sup>

## Purpose

- Determine how age and sex influence methamphetamine's (METH) effects on the brain and behavior

## Hypothesis

- Females will take more methamphetamine than males
- No significant difference in NAc D<sub>1</sub>R expression, but reduced PFC D<sub>1</sub>R levels in both males and females

## Methods



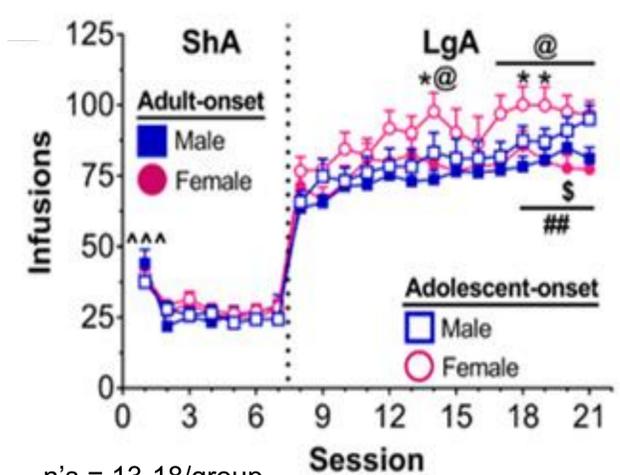
- Rats' activity is measured by an operant cage where a computer records nosepoke responses
- Habituation period-rats in cage for 1 day to allow them to become familiarized with surroundings with no reinforcer given

Subjects: Male and female Sprague Dawley rats

Table 1: Rat's self-administered 0.1 mg/kg METH attached through a metal tether in a nose-poke operant chamber

	Reinforcer	Short access (ShA) 2hrs/day	Long access (LgA) 6hrs/day	Tissue collection
ADOL male	METH	P40-47	P48-61	P82
Adult male	METH	P90-97	P98-111	P132
ADOL female	METH	P40-47	P48-61	P82
Adult female	METH	P90-97	P98-111	P132

## Behavioral Analysis



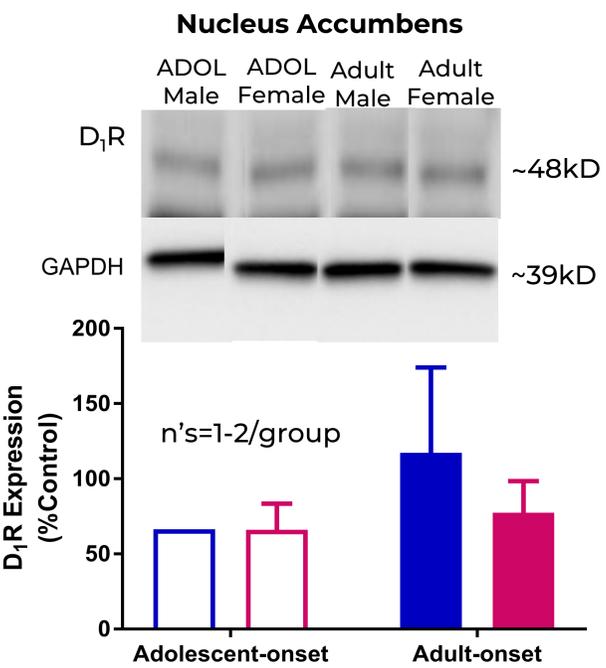
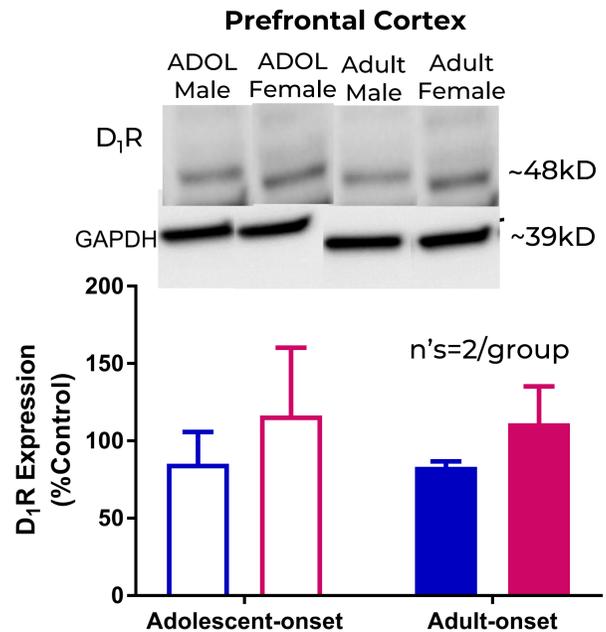
n's = 13-18/group  
 \**p* < .05 vs. first LgA session for females  
 ##*p* < .01 vs. first LgA session for males  
 @*p* < .05 vs. first LgA session for adolescent-onset  
 \$*p* < .05 vs. first LgA session for adult-onset  
 ^^*p* < .001 vs. each ShA session  
 \*\*\**p* < .001 vs. each LgA session

### Results:

- Adolescents display increased METH intake compared to adult counterparts
- Females show increased METH intake compared to males
- Adolescent females escalated their METH intake the quickest compared to all other groups

## Protein Analyses

- by means of western blot



### Results:

- Males may exhibit lower levels of D<sub>1</sub>R expression in the PFC
- Adult-onset male METH rats may be different from the other groups (i.e. brain is less resistant to drug-induced plasticity)

## Discussion

- Changes in the amount of expression of D<sub>1</sub>R in the :
  - PFC suggests there are more sex related changes than age
  - NAc suggests there are more age related changes than sex
- Question:** Are ADOLs compared to adults more sensitive to drug-induced changes in neural function and behavior? Males to females?
  - Based on our current results, it appears that both age and sex influence D<sub>1</sub>R expression following METH, but their effects may depend on brain region.

## Future Work

- Study was limited to only expression of protein receptors rather than testing for function of the receptors
- Future work will include testing for function by use of electrophysiology with similar methods

## References

- Lynch, W.J., 2006
- Poudel & Gaudam, 2017
- Chen et al., 2009
- Casey et al., 2008
- Kang et al., 2016
- Image source: Fluofarma

## Acknowledgments

Financial support was provided by the National Science Foundation under grant #NSF REU 1559908/1559929, as part of the Phenotypic Plasticity Research Experience for Community College Students, through the University of Illinois at Urbana-Champaign Institute for Genomic Biology and Parkland College. <http://precs.igb.illinois.edu/>

Special thanks to Dr. Shuo Kang, Dr. Nathan Schroeder, Dr. C. Britt Carlson, and technical and support staff at the Institute for Genomic Biology.

