Neurobiology of Parent/Infant Attachment

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Silver Hill Hospital Grand Rounds
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Gustav Klimt, Mother and Child

Disclosures

In compliance with the ACCME Standards for Commercial Support of CME, as the speaker I do not have any relevant financial relationships to disclose in relation to this presentation.

Millie Rincón-Cortés, PhD · University of Texas at Dallas

Educational Objectives

As a result of participating in this activity, you should be able to:

1. **Describe how adversity exposure disrupts maternal caregiving**
2. **Explain how adversity exposure influences reward-related brain activity**
3. **Evaluate the usefulness of rodent models for studying the etiology of depressive disorders**

Lab Research Interests

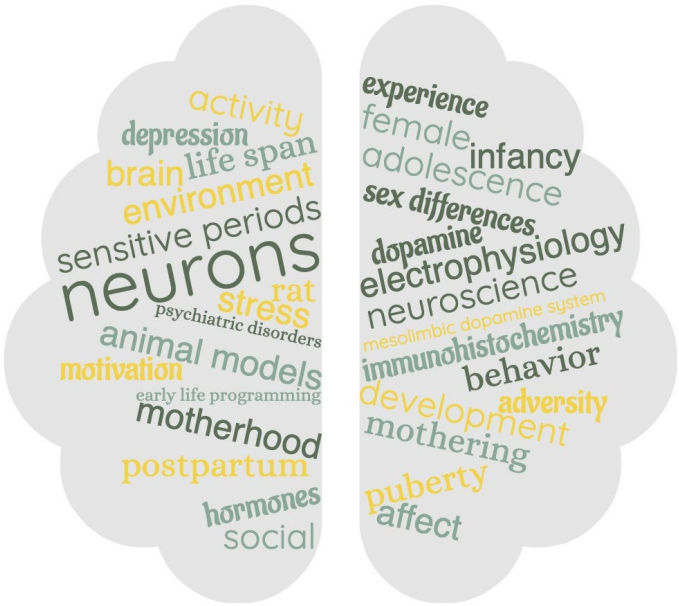
M- Motherhood
A- Adversity
D- Development
R- Reward
E- Environment/Experience

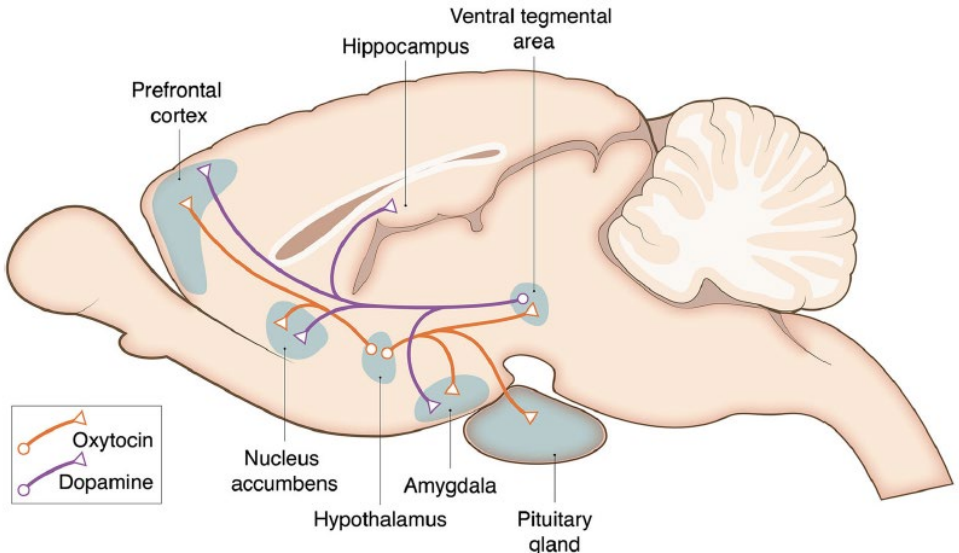


Experience-Dependent Plasticity of the Mesolimbic Reward System

- How do distinct types of experiences induce adaptations within the brain's reward circuitry (i.e., mesolimbic dopamine system)?

- How are these effects modulated by factors such as sex and developmental stage?





The mother-infant bond is among the strongest social attachments formed by most mammals

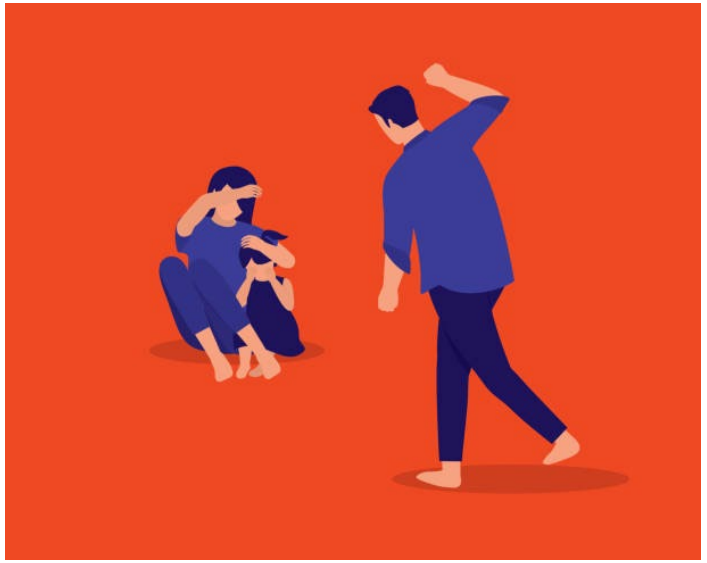




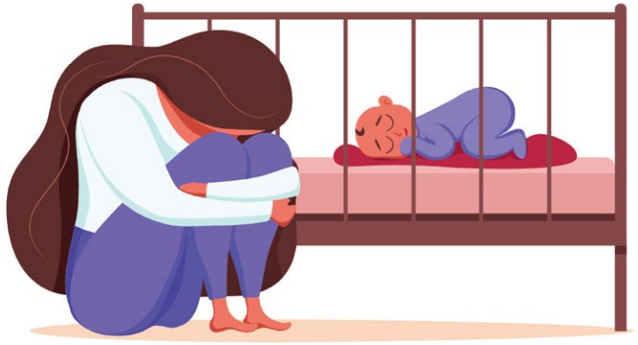












Adverse environments disrupt the mother-infant bond

- Low resource environments/poverty
- Housing instability
- Family violence
- Maternal mental health conditions

Maternal adversity can compromise behavioral and brain function in both mother and child

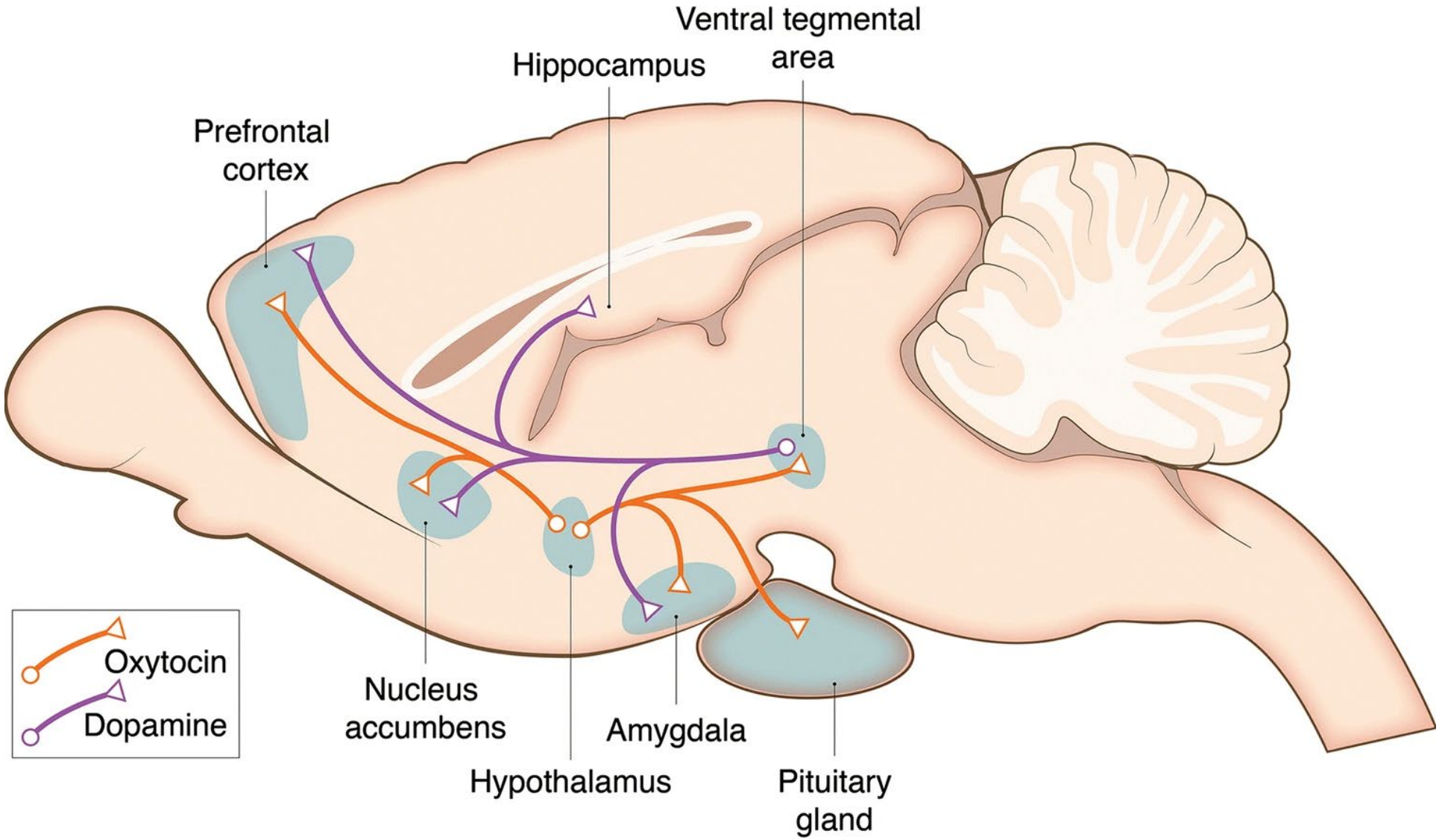
Postpartum adversity is a translational risk factor for postpartum depression (PPD)



PPD symptoms

- **Low mood, excessive sadness**
- **Loss of interest or pleasure (anhedonia)**
- **Detachment from baby**
- Feelings of worthlessness or guilt
- Loss of energy or fatigue
- Changes in weight or appetite
- Changes in sleep patterns (insomnia or hypersomnia)
- Impaired concentration or indecisiveness
- Suicidal ideation or attempt and recurrent thoughts of death





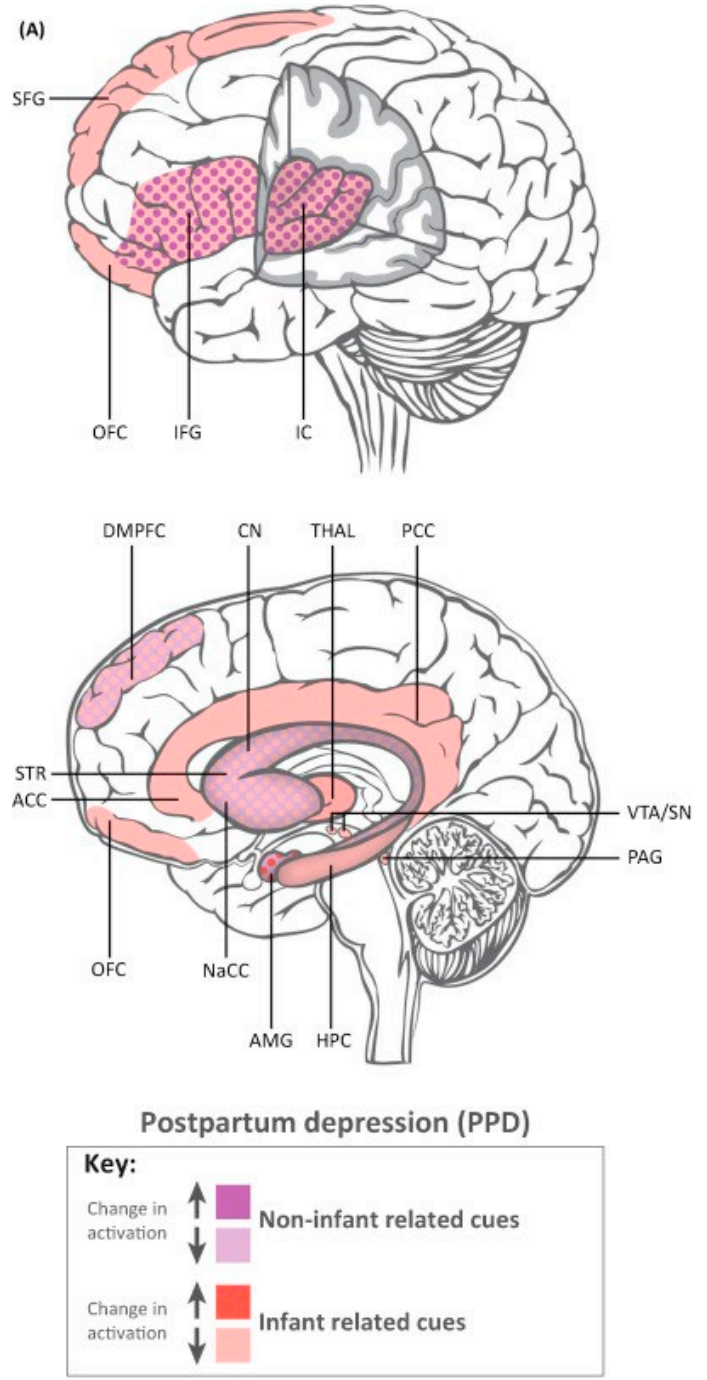
Post and Leuner, 2019

The maternal reward system is dysfunctional in PPD

Human neuroimaging studies indicate deficient mesolimbic DA brain activity in mothers with PPD

- Brain areas highlighted have key roles in neural networks associated with:
  - stress regulation (ACC, HPC, AMY)
  - reward/motivation (STR, VTA, NAc)
  - sensory processing (PAG, THAL)
  - executive functioning (PFC regions)

- **Brain activation (fMRI signal) within the maternal reward system is reduced in mothers with PPD**
  - VTA
  - NAc



Pawluski, Lonstein and Fleming, 2017



How does postpartum adversity influence maternal behavior and motivation in the rat dam?

Are there effects on mesolimbic dopamine function?

Modeling Environmental Adversity in Maternal Rodents





Social

Physical

Permanent pup removal: Rincón-Cortés and Grace 2021
Pawluski et al. 2009 and Demarchi et al. 2023



Control: 1800mL bedding +nestlet



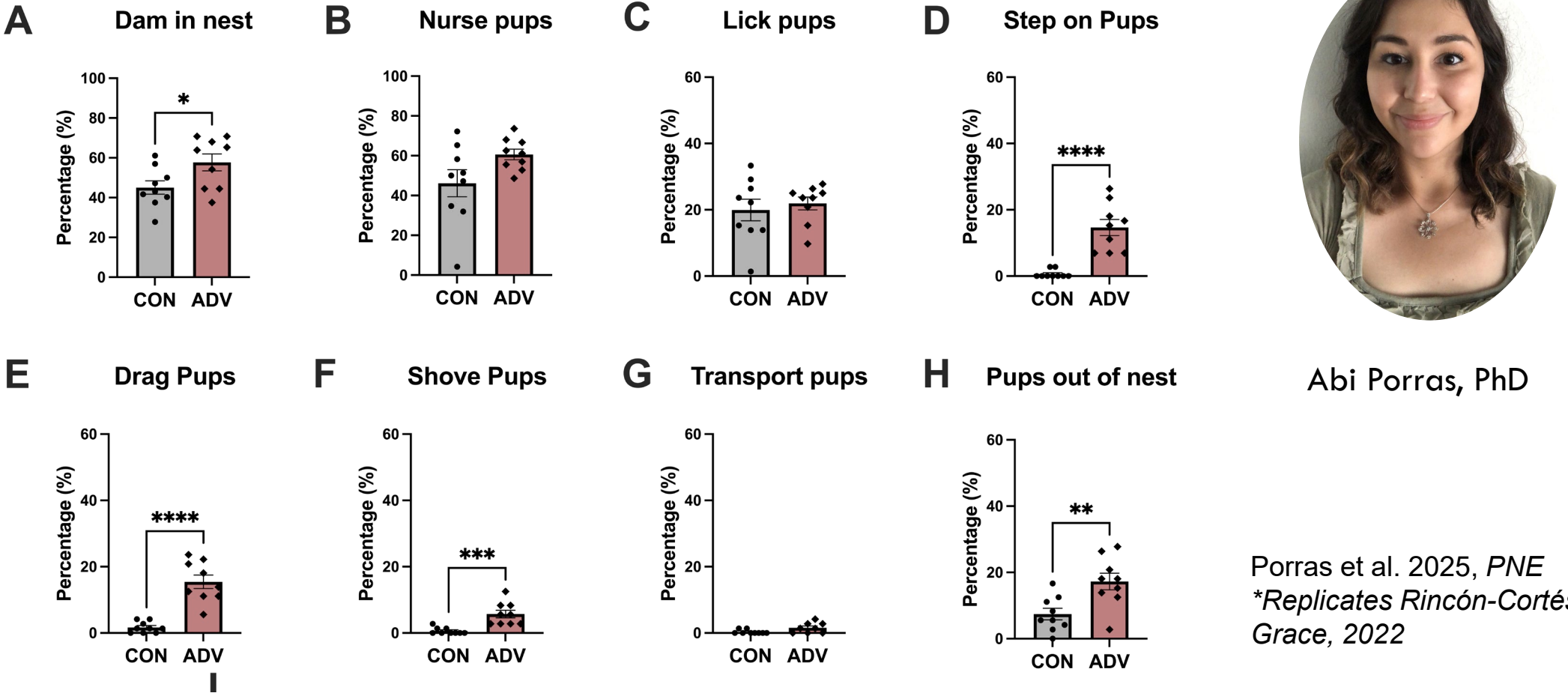
Scarcity-adversity: 500mL bedding

Modeling postpartum adversity in rodents through resource scarcity from postpartum days (PD) 2-9

Gilles et al.1996; Avishai-Eliner et al. 2001; Ivy et al. 2008; Raineki, et al 2010, 2012; Rincón-Cortés and Sullivan 2016; Yan, Rincón-Cortés, et al 2017; Perry et al. 2019; Raineki, Opendak, et al 2019; Eck et al. 2020; Rincón-Cortés and Grace, 2022; Lauraine et al. 2024; Nguyen et al. 2025; Porras et al. 2025; Salazar et al. 2025; Lauraine and Rincón-Cortés, 2026; Jackson et al. 2026; Nguyen et al. 2026

Scarcity-adversity dams exhibit increased adverse pup-directed maternal behaviors

Overall (PD 2-7)



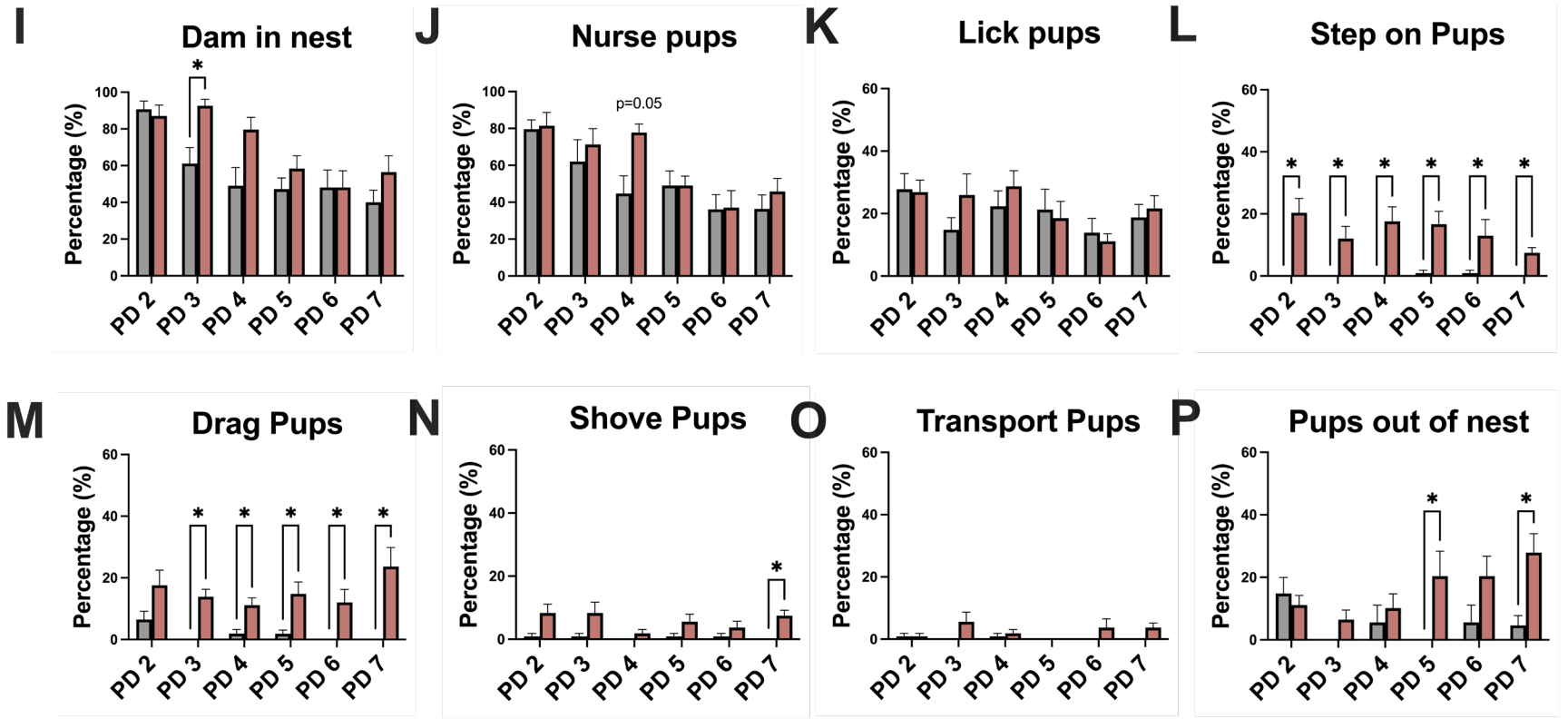
Abi Porras, PhD

Porras et al. 2025, *PNE*
**Replicates Rincón-Cortés and Grace, 2022*

ADV dams had higher % of stepping, dragging, shoving pups, nest-building and scattered litter.

Dams exposed to scarcity-adversity exhibit increased adverse pup-directed maternal behaviors

By Day (PD 2-7)



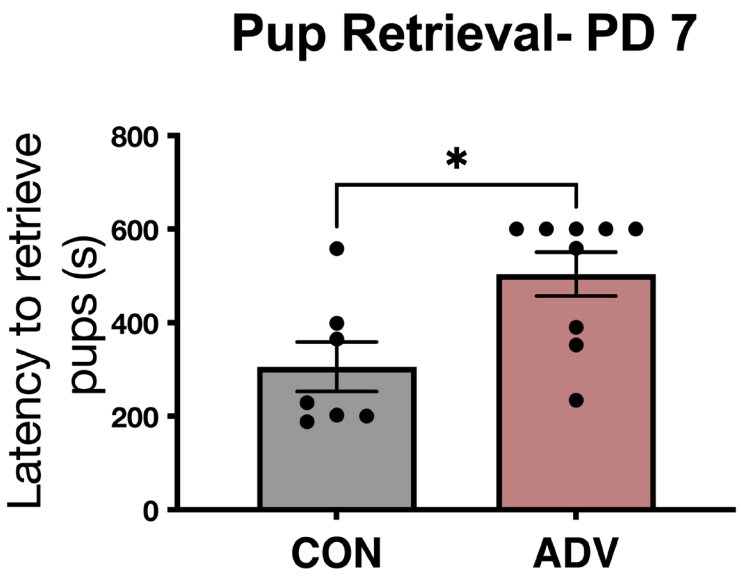


Abi Porras, PhD

Porras et al. 2025, *PNE*

Pup stepping and dragging are the most robust behaviors in ADV dams

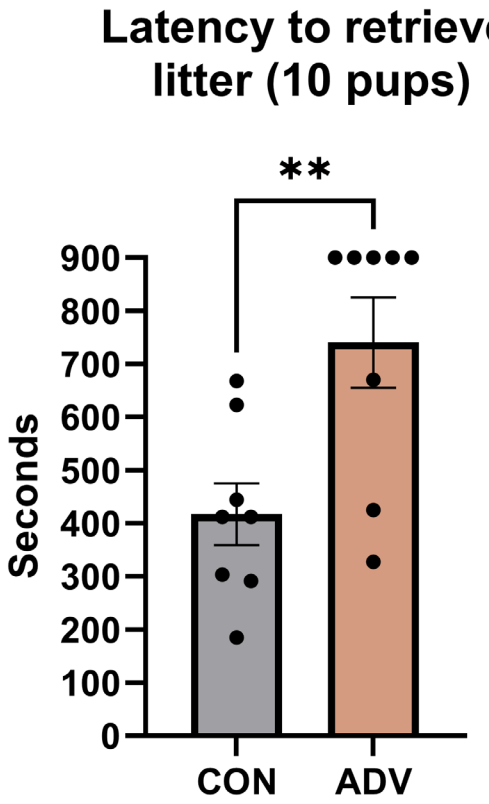
Scarcity-adversity dams display impaired pup retrieval at PD 7 and increased FST immobility at PD 9

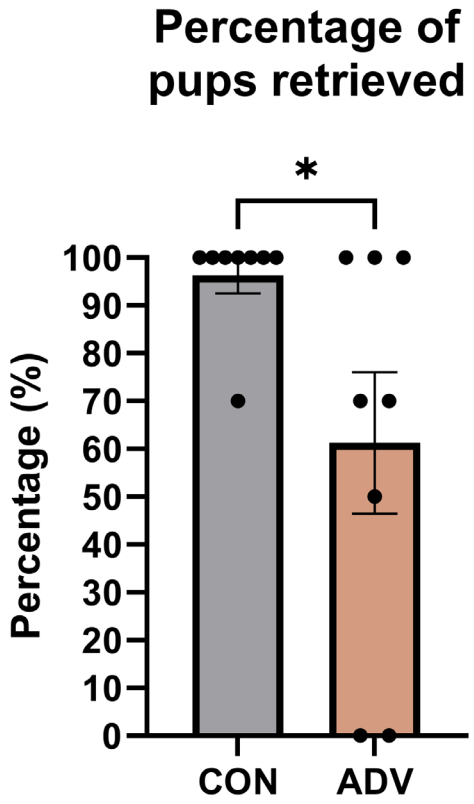


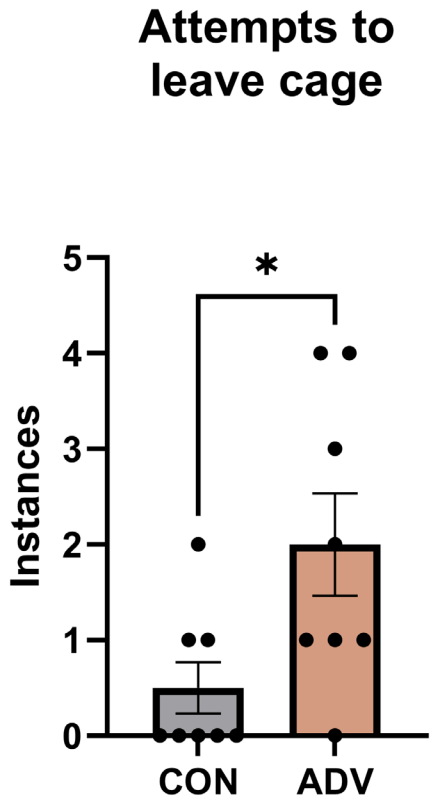


Adapted from Rincón-Cortés and Grace NPP, 2022

Scarcity-adversity dams have longer latencies to retrieve pups, retrieve fewer pups, and engage in escape behavior more often on PD 5







Jackson et al in prep

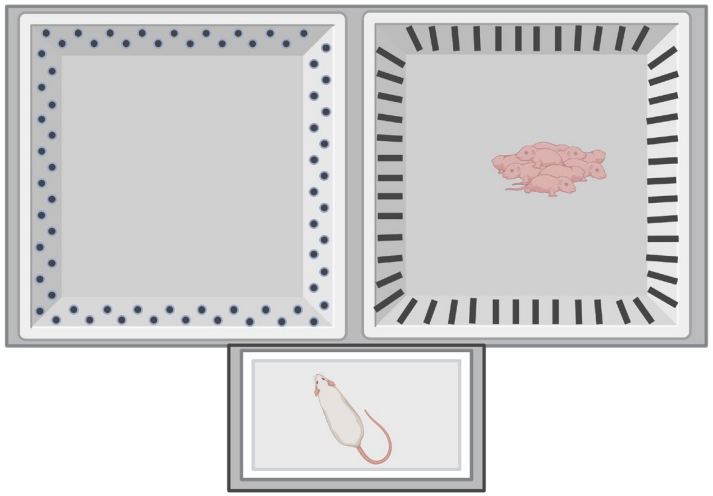


Skylar Mendez

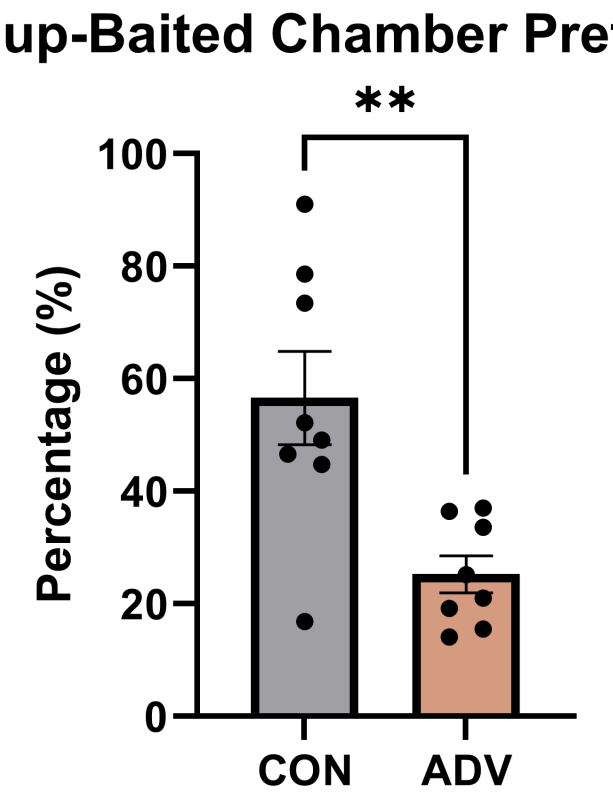


Jeffy Jackson

Scarcity-adversity dams exhibit impaired pup-induced conditioned place preference on PD 6



PD 3-6





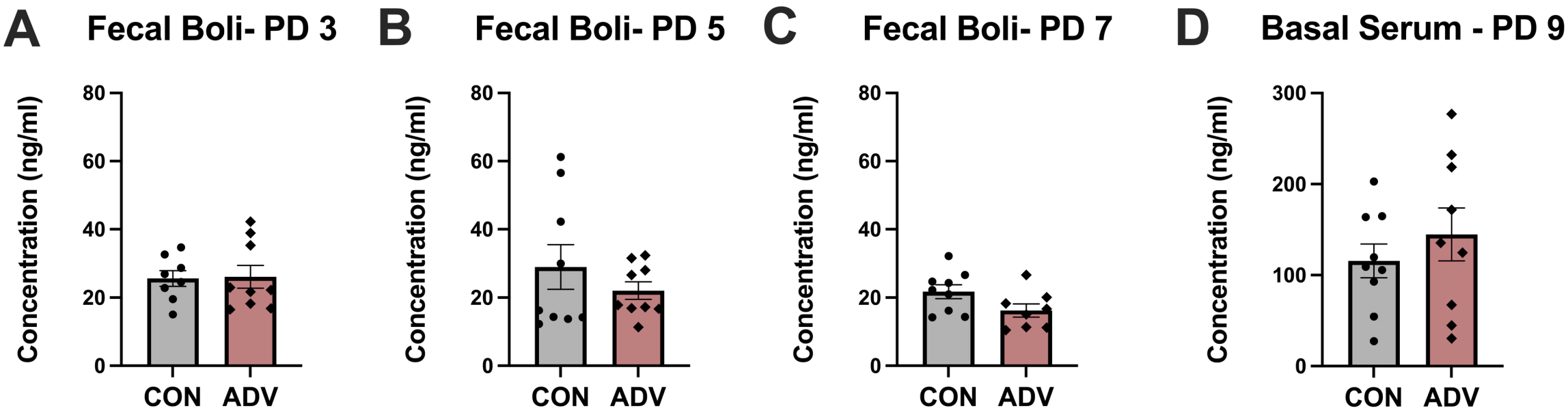
Skylar Mendez



Christine Nguyen

Unpublished data, Rincón-Cortés lab

Scarcity-adversity dams exhibit adverse caregiving and maternal motivation deficits in the absence of basal corticosterone elevation



Porras et al. 2025, *PNE*

Measuring VTA DA neuron activity using *in vivo* electrophysiology

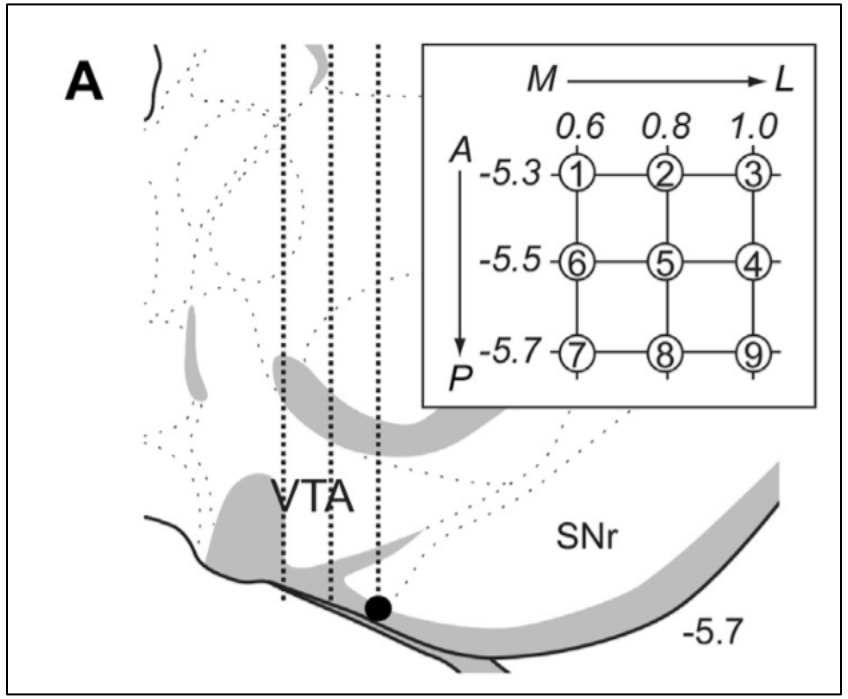
Recording Characteristics

- Anesthetized rats
- Single-unit, Extracellular
- Glass electrodes
- Dopamine neurons identified using well-established criteria (Ungless and Grace, 2012)

Parameters Measured

- Population Activity (i.e. “cells/track”)
- Firing Rate
- Burst Firing

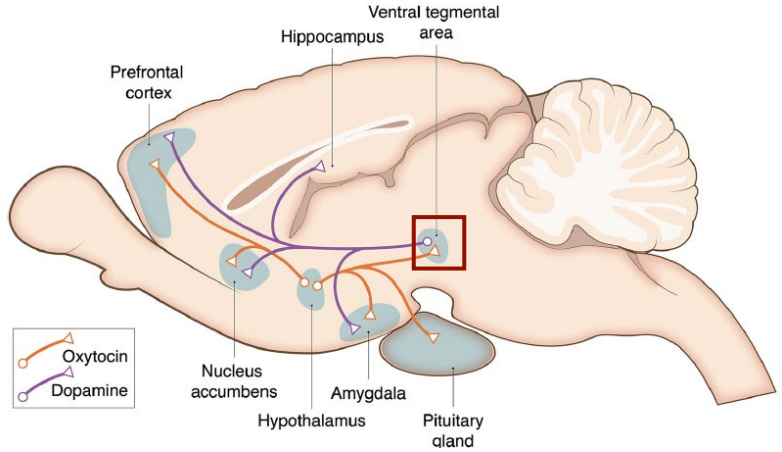
Quantifying Population Activity



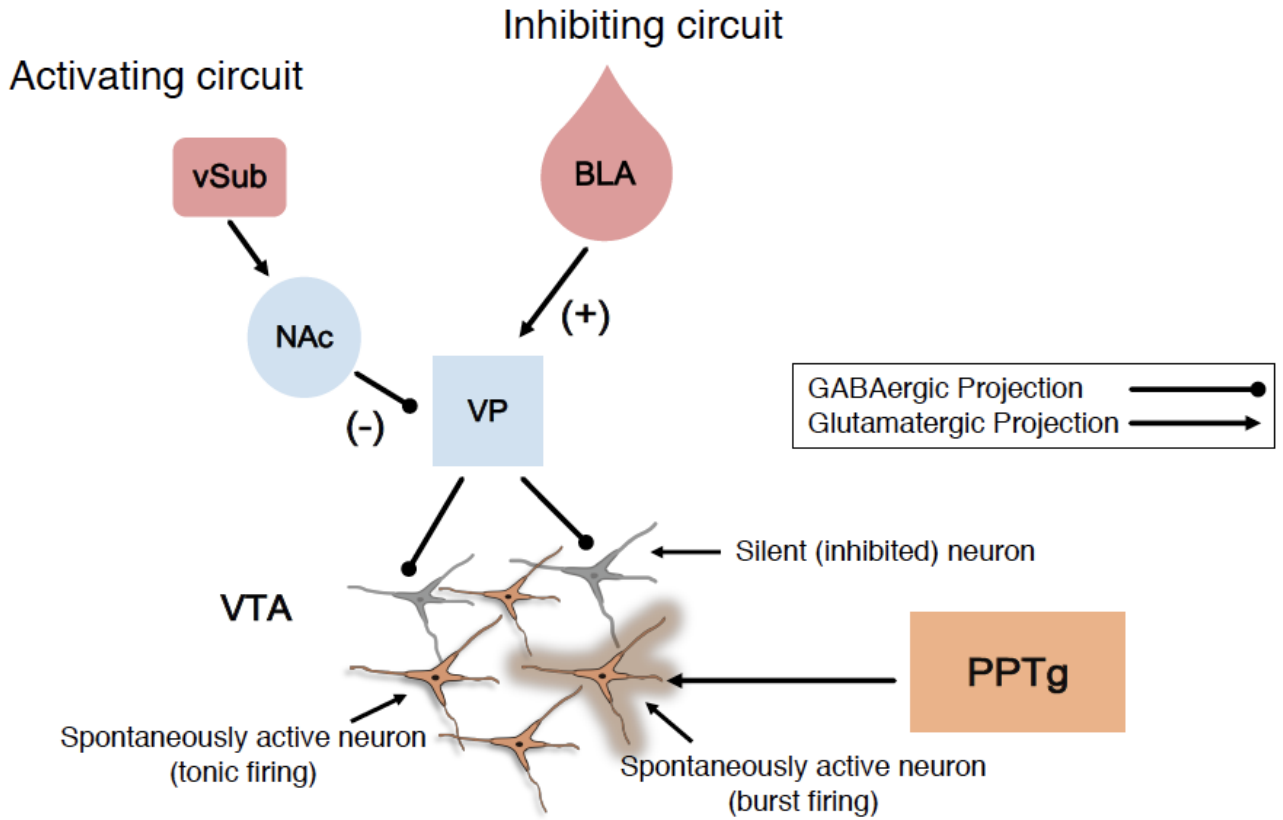
Chang and Grace, 2012

VTA population activity

= the # of spontaneously active DA neurons

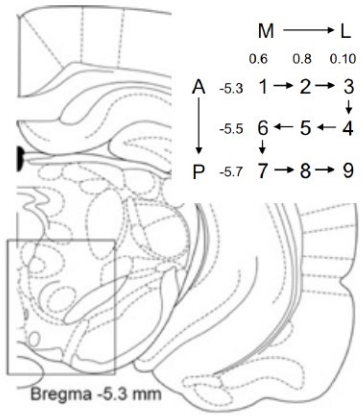


- In rats, about half of DA neurons are spontaneously active
- VTA population activity is regulated by 2 opposing circuits
- DA neurons must be spontaneously active to burst fire, which leads to DA release
- Population activity sets the baseline tone of DA system responsivity

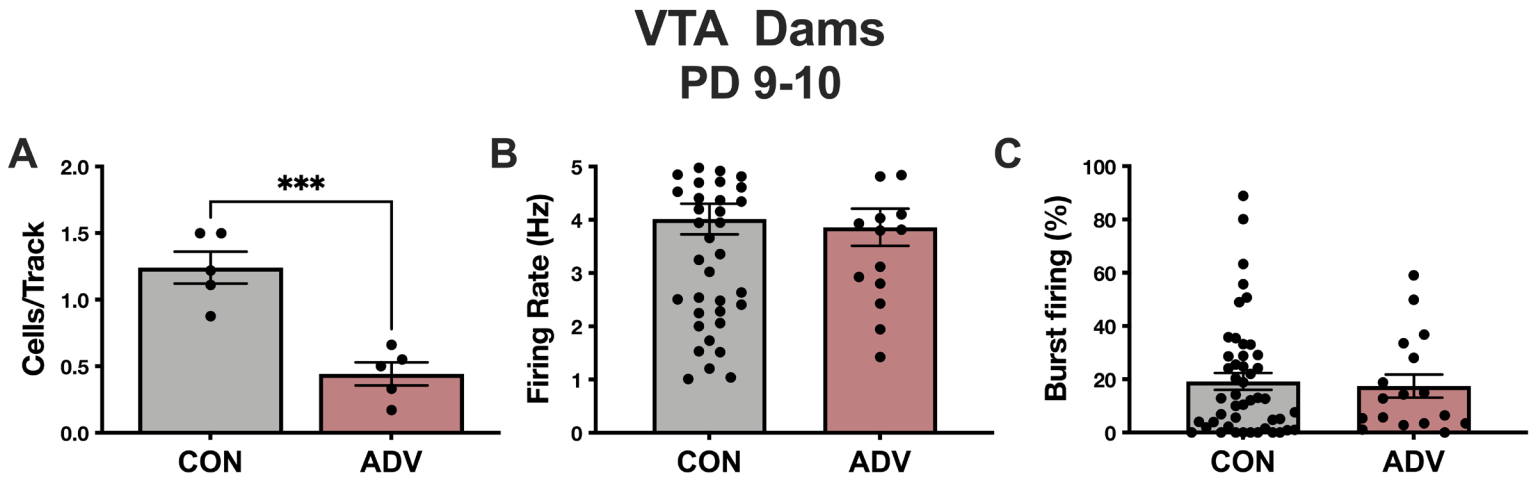


Rincón-Cortés and Grace, 2020

ADV-exposed dams exhibit transient downregulation of VTA DA neuron population activity







Selective effect on population activity

Adapted from Rincón-Cortés and Grace *NPP*, 2022

Fiber photometry: From anesthetized recordings to awake, behaving dams

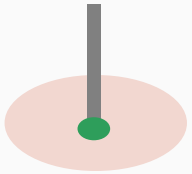
A fluorescent sensor makes VTA DA neurons **glow when active**, so we can watch them during caregiving



1

Express the sensor

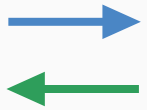
Cre-dependent GCaMP7f in TH-Cre rats labels only DA neurons



2

Implant an optic fiber

A thin fiber sits just above the VTA



3

Record fluorescence

Light excites GCaMP; more Ca^{2+} = more activity = more glow



4

Align to behavior

Signal (zΔF/F) is time-locked to caregiving events

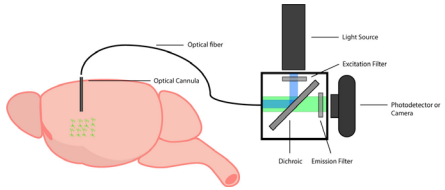
SO FAR: ANESTHETIZED SINGLE-UNIT

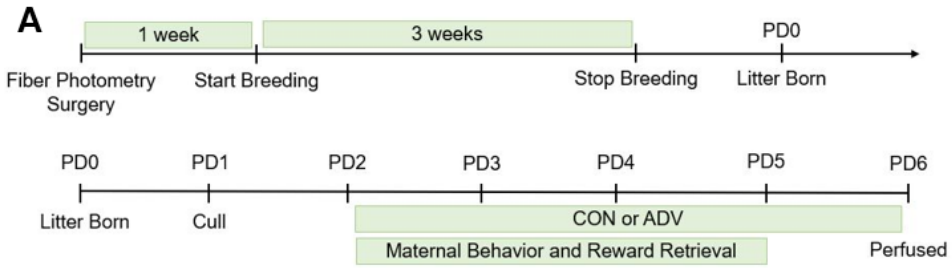
- Individual DA neurons
- Baseline state: how many cells are active
- No behavior during recording

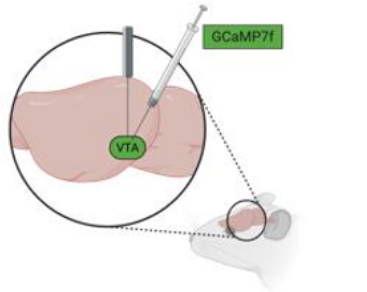
NEXT: AWAKE FIBER PHOTOMETRY

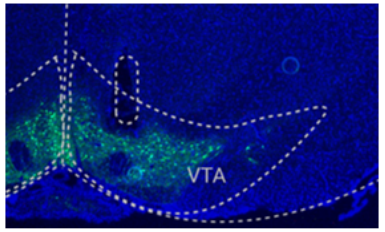
- Population activity of VTA DA neurons
- Moment-to-moment, during caregiving with pups
- Same dam recorded daily, PD 2–5

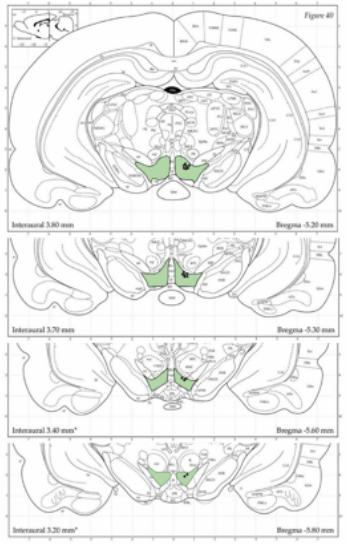
What are VTA DA neurons doing during adaptive and maladaptive maternal behaviors?

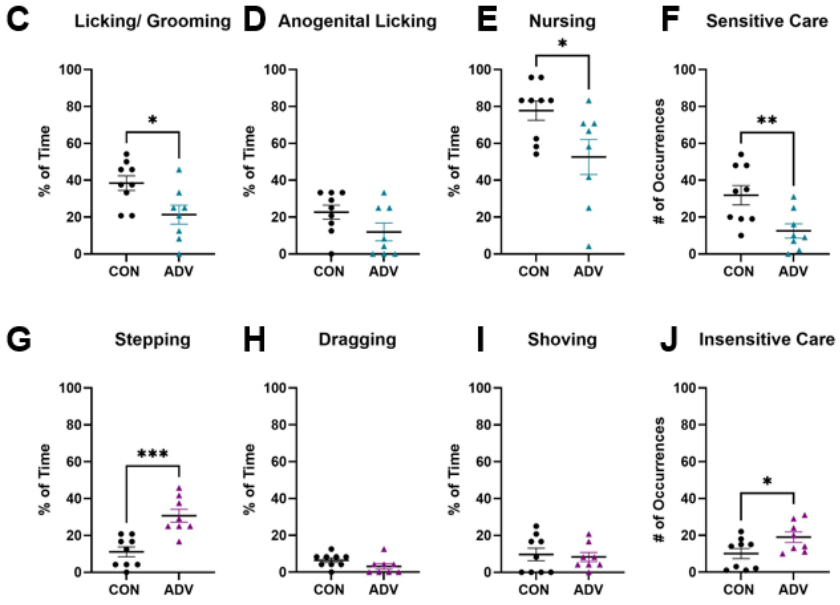


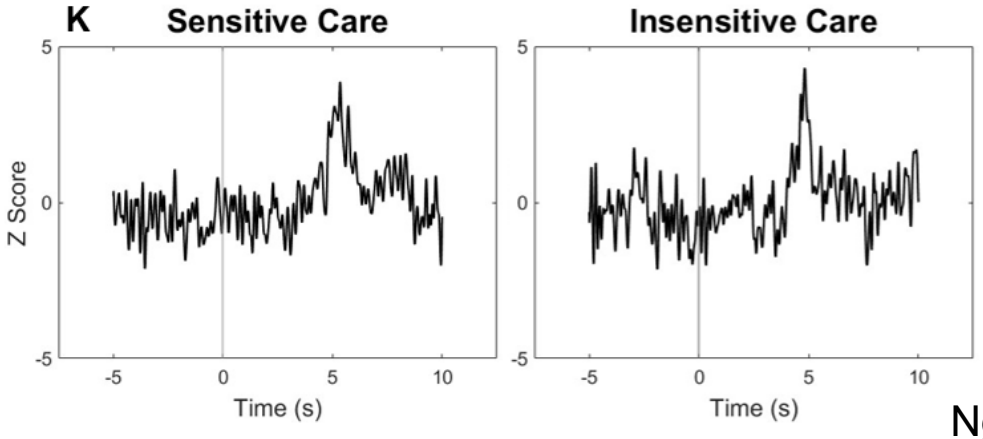










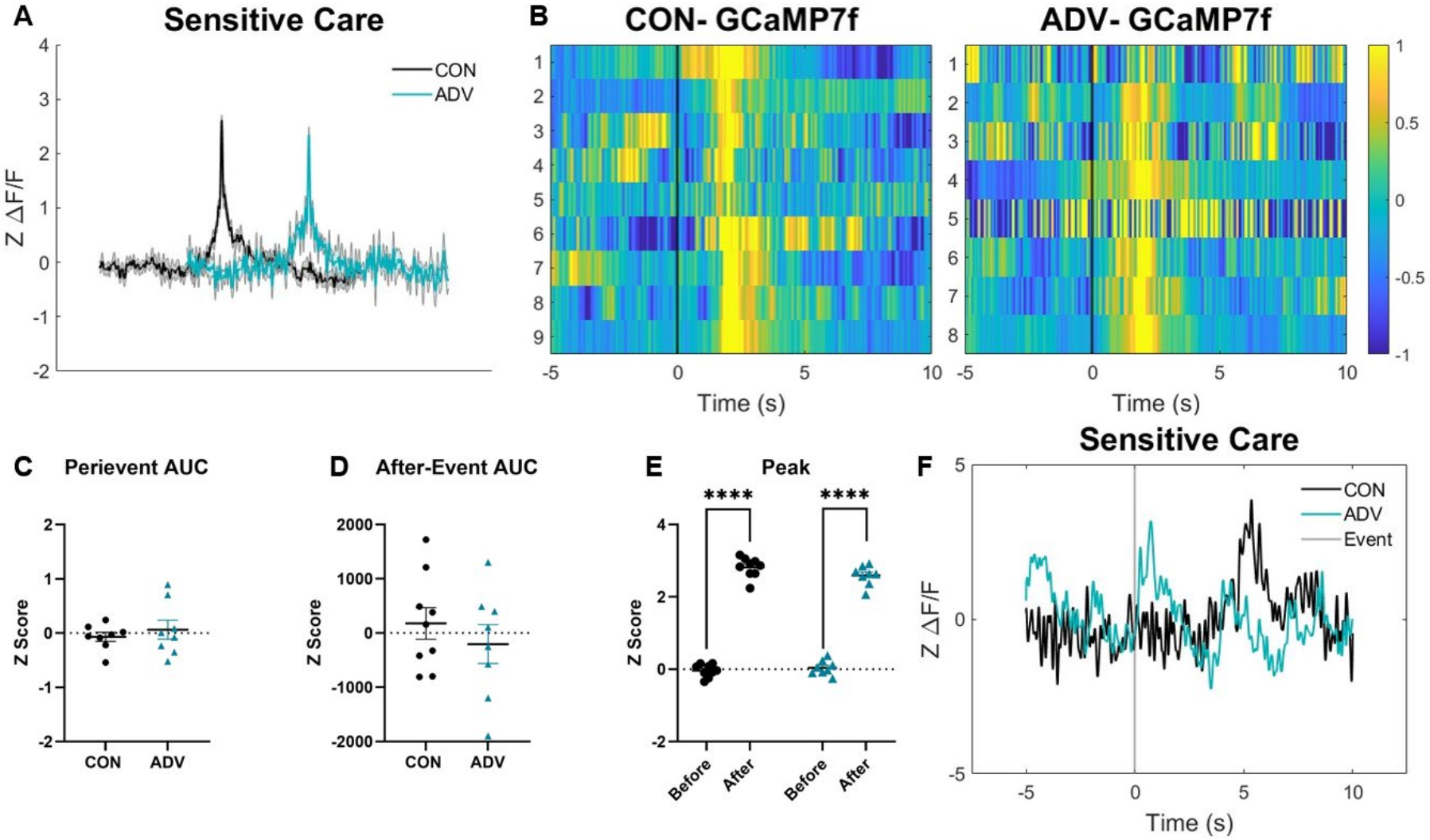




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Nguyen et al. 2026, *JNeurosci*

Scarcity-adversity dams do NOT show differences during sensitive caregiving

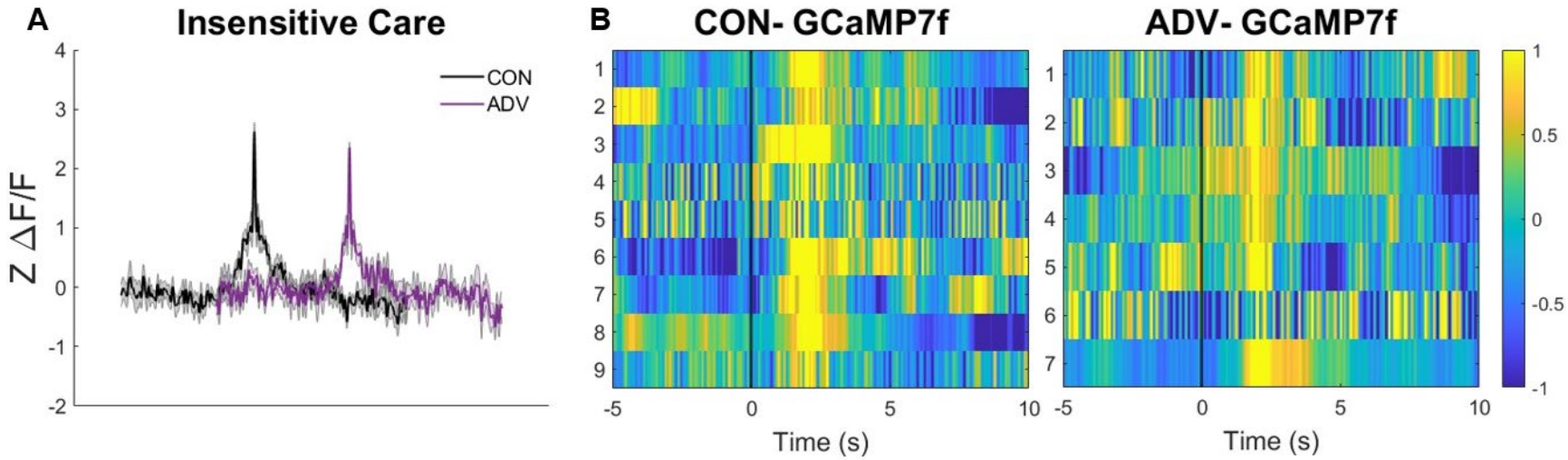




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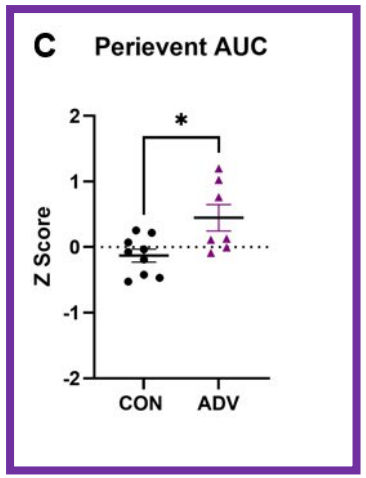
Nguyen et al. 2026, *JNeurosci*

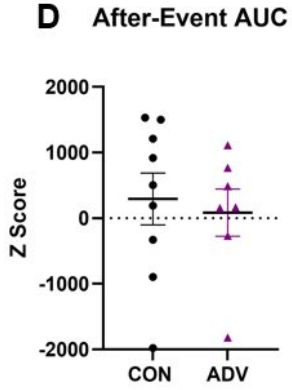
Scarcity-adversity dams show elevated peri-event AUC around insensitive pup-directed behaviors

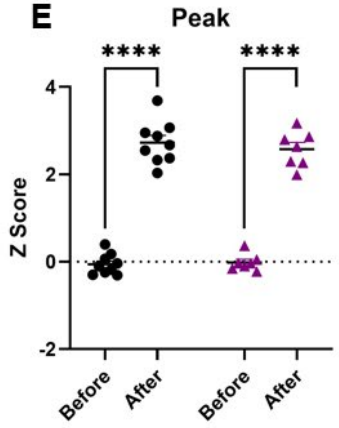


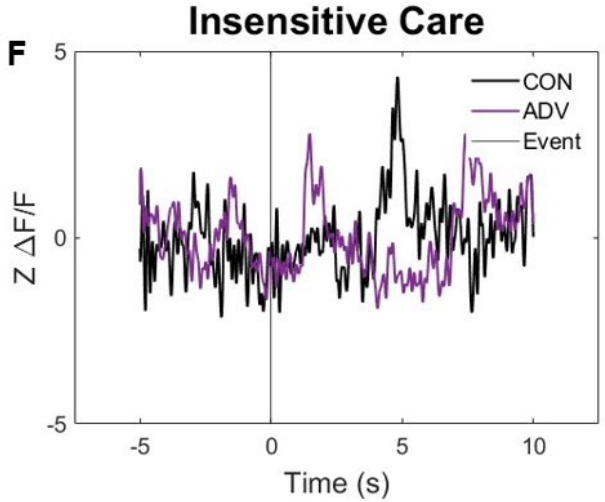


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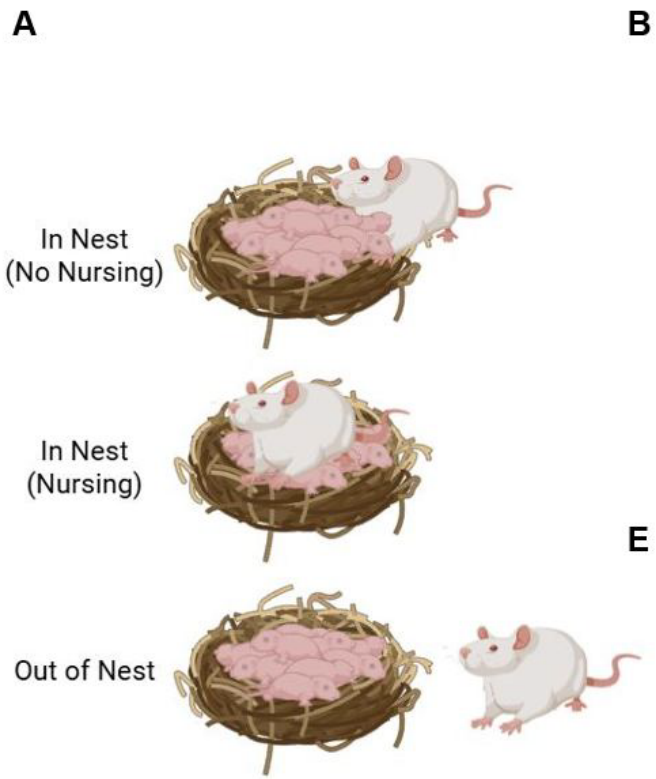


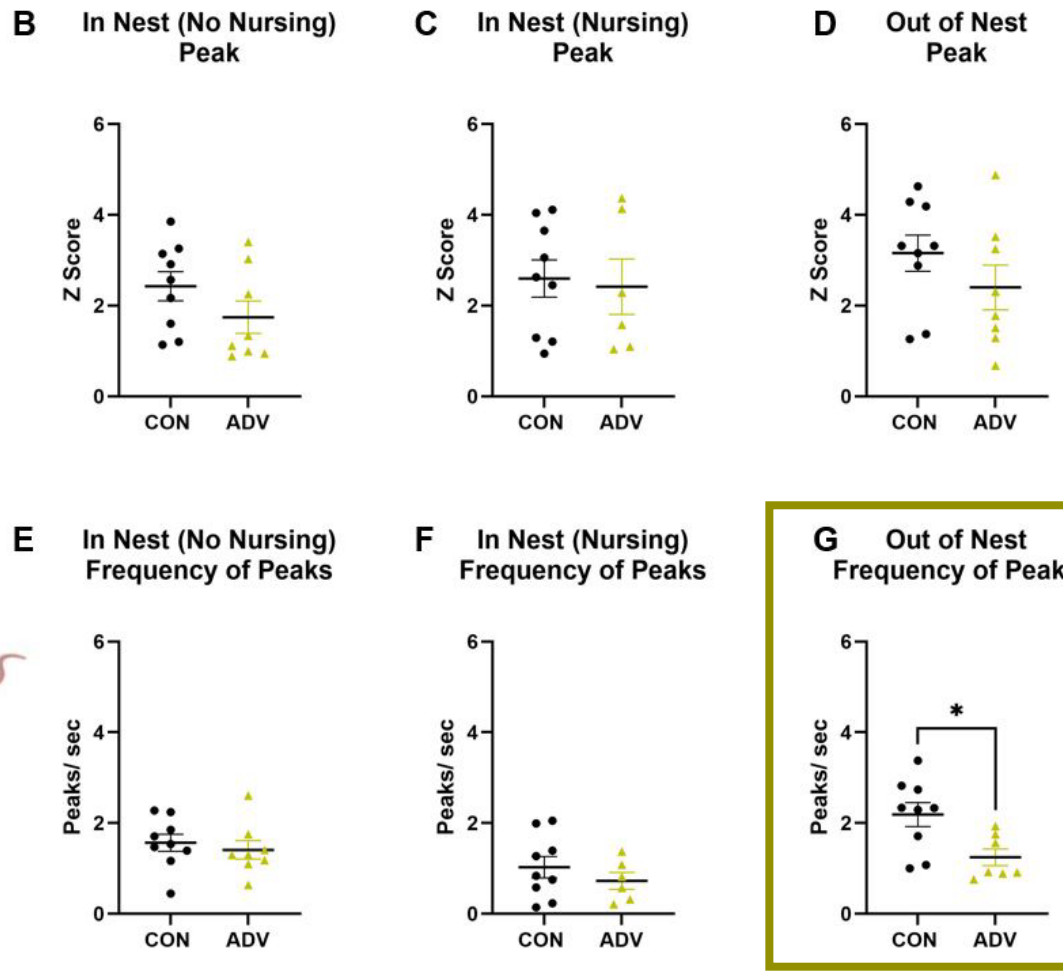


ADV prolongs VTA DA responses around insensitive care

Nguyen et al. 2026, *JNeurosci*

Scarcity-adversity dams show reduced frequency of peaks while away from pups



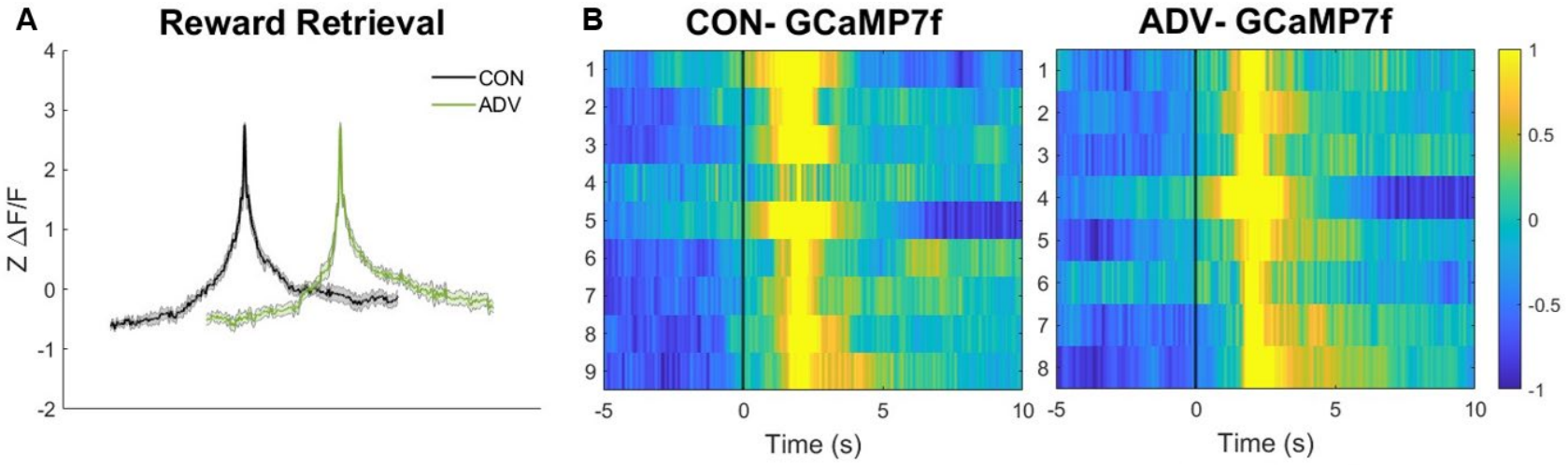




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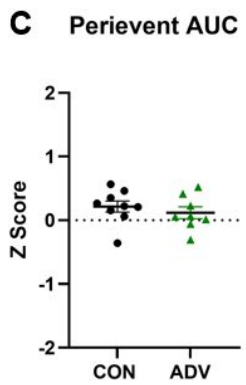
Nguyen et al. 2026, *JNeurosci*

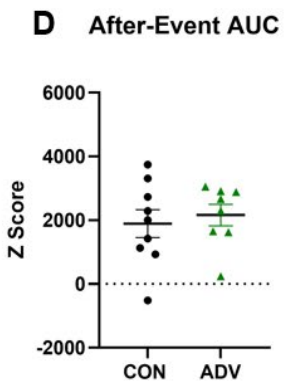
ADV dams do NOT show differences in response to food reward retrieval

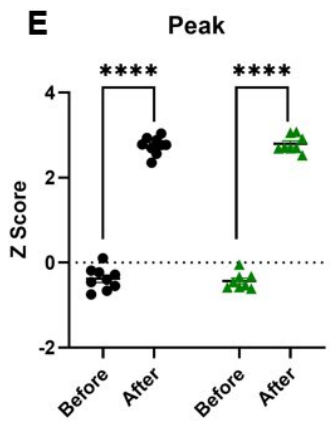


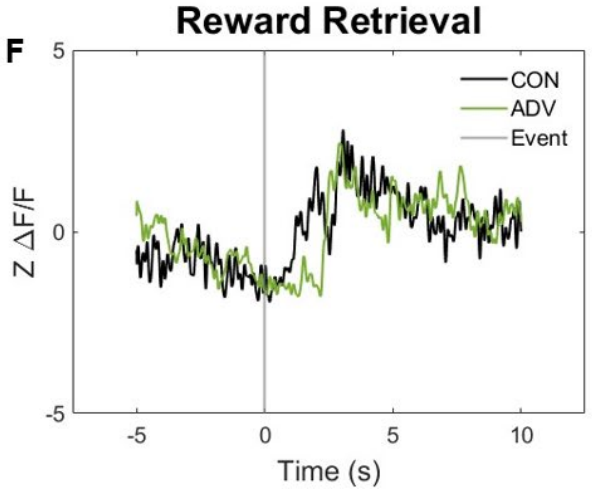


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Summary Part I

- Postpartum scarcity-adversity exposure increases adverse caregiving
- Postpartum scarcity-adversity impairs maternal motivation
  - Pup retrieval
  - Pup-induced CPP
- No change in basal CORT levels
- Single-unit recordings →VTA DA population activity is transiently reduced
- Photometry → VTA DA neuron activity is:
  - Unchanged during sensitive care
  - Elevated around insensitive caregiving
  - Reduced during pup separation
  - Unchanged during food reward

Part II: Offspring Effects

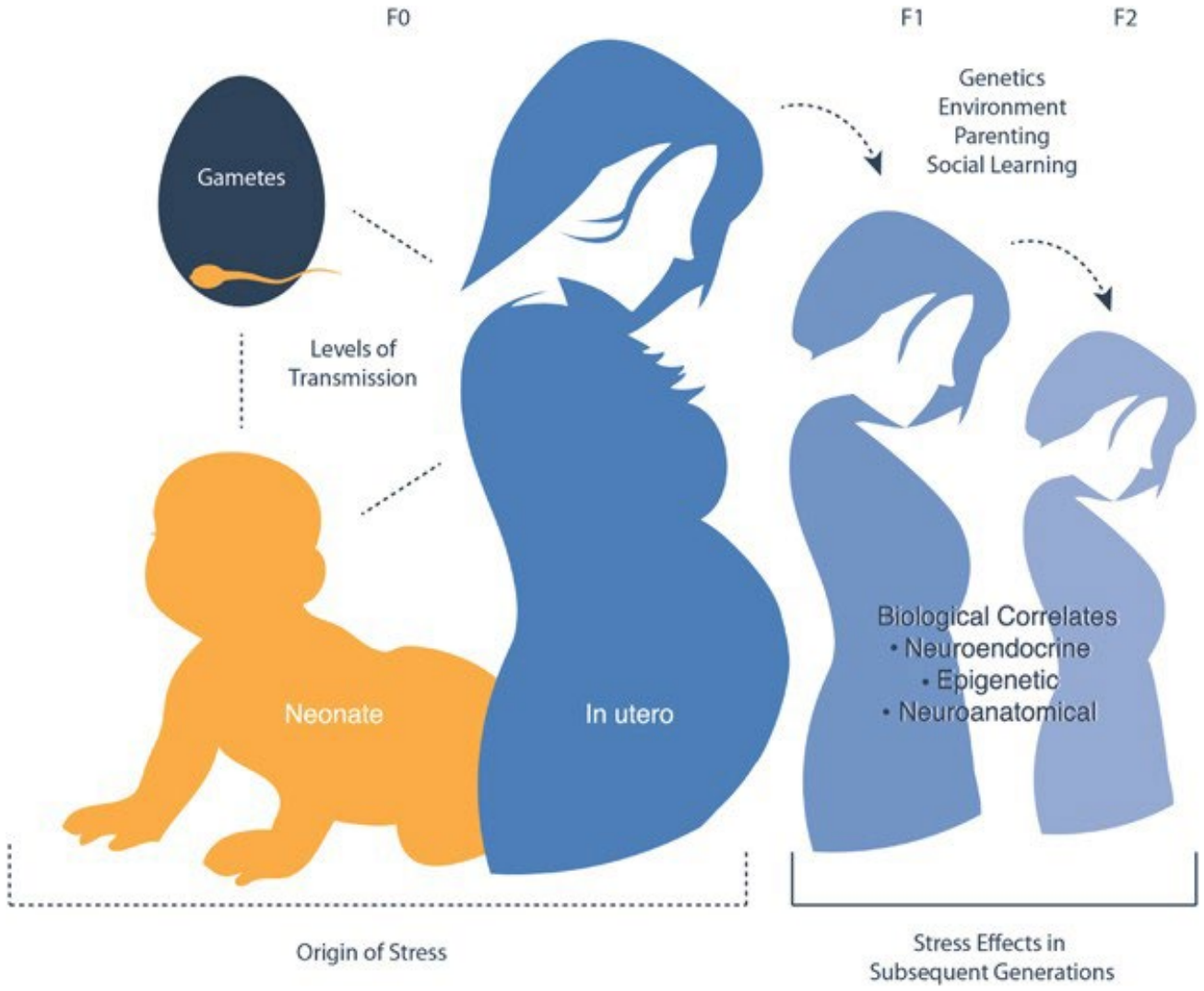


Inter- and trans-generational transmission of adversity

Parental stress/adversity can be transmitted:

- Gametes
- Gestational uterine environment
- **Early postnatal care**

Some studies suggest that parenting behaviors can also be transmitted.

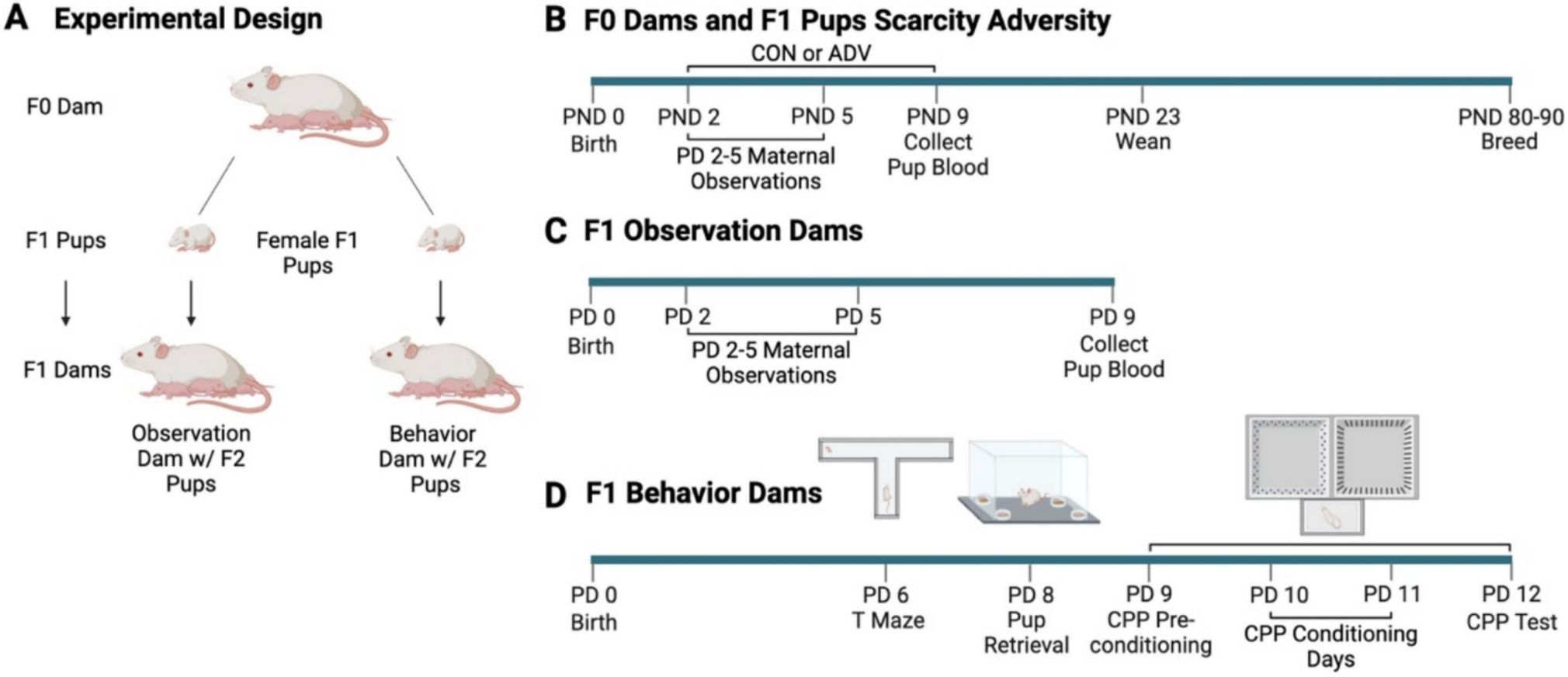


Bowers and Yehuda 2016

Can adverse caregiving be “inherited”?



Assessing the impact of early life scarcity-adversity on later life maternal behaviors



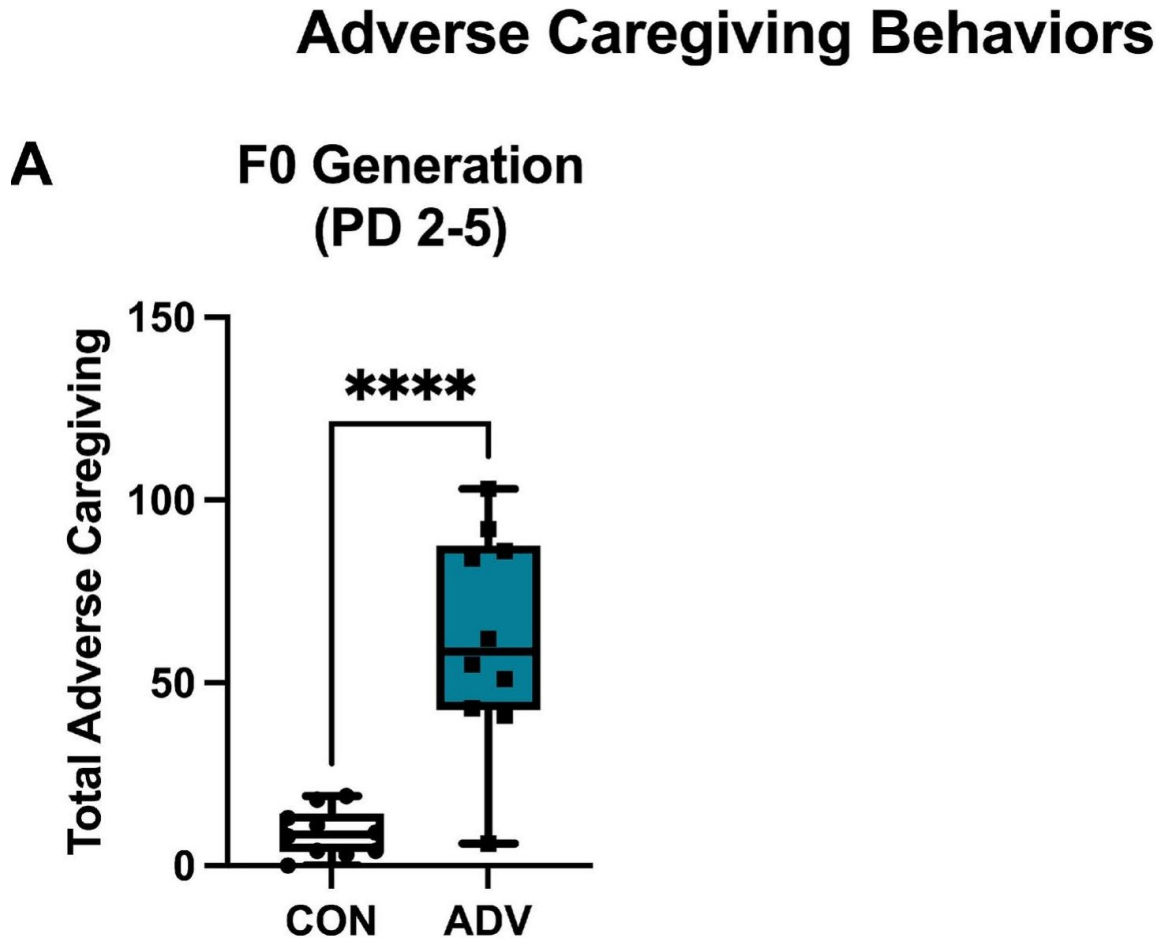


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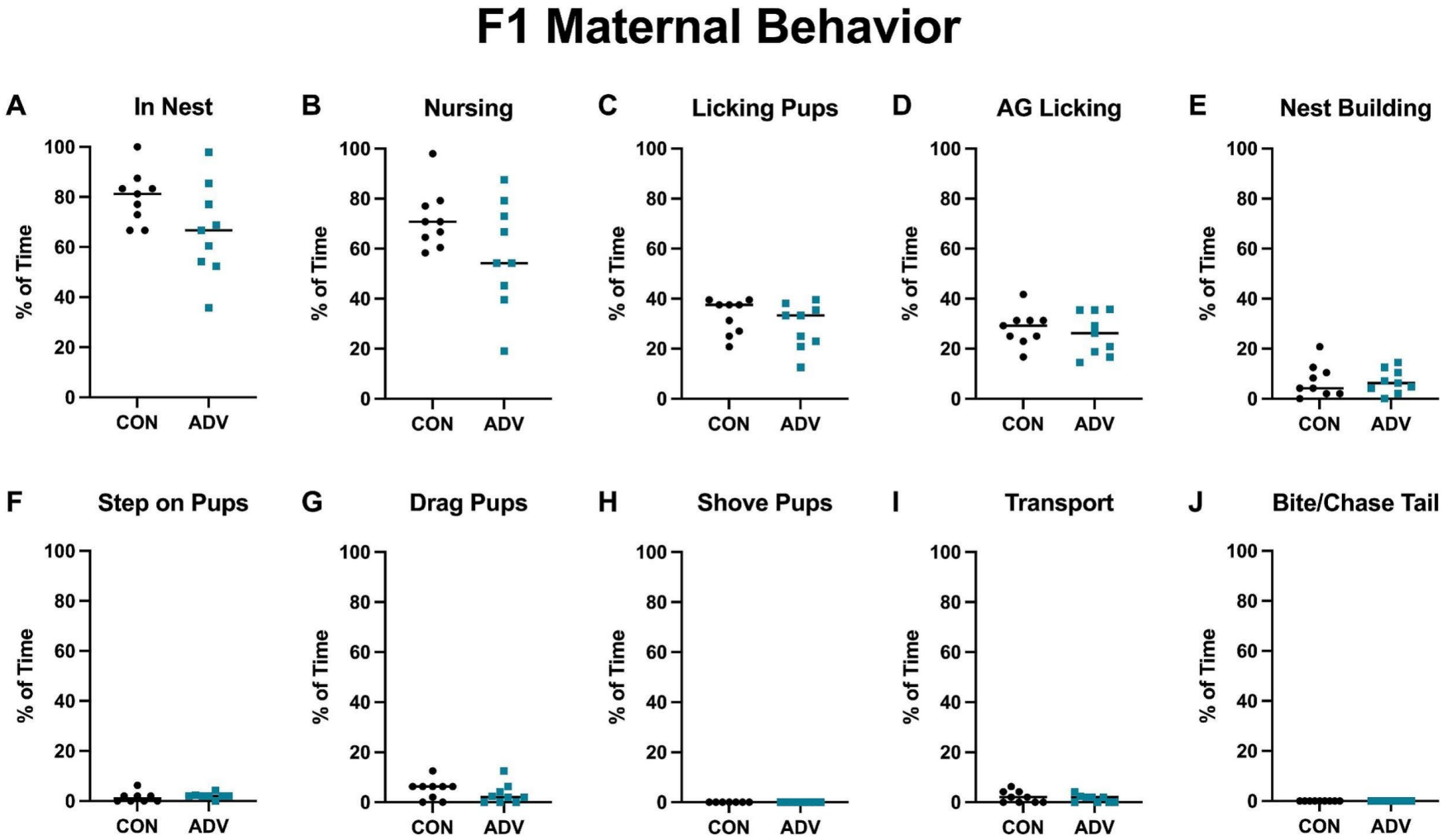
Melissa Salazar

Scarcity-adversity increases adverse caregiving in the rat dam (F0) but not in the female offspring receiving adverse caregiving during early life (F1)



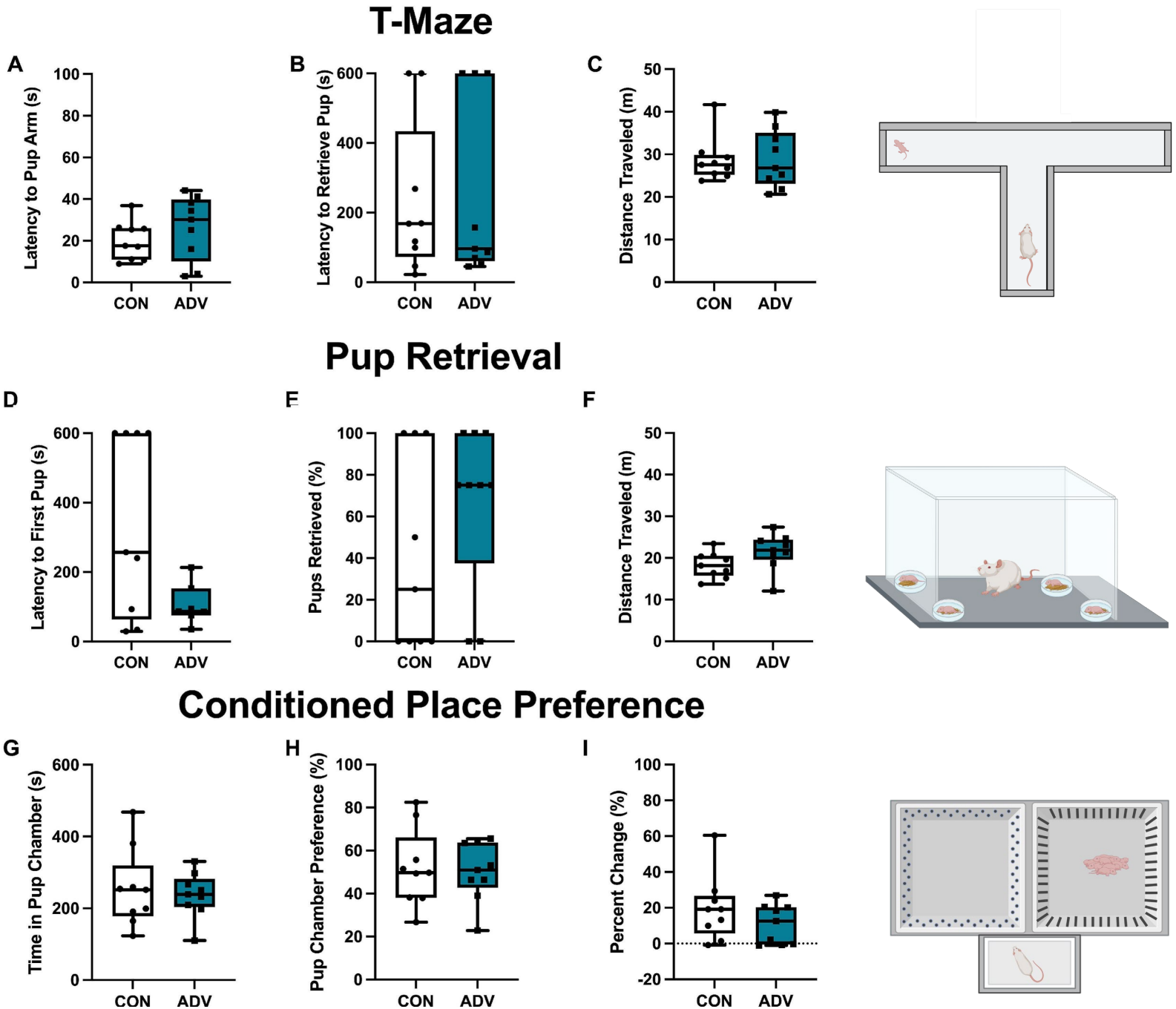
Nguyen et al. 2025, *Hormones and Behavior*

No impact of early life scarcity-adversity on later life maternal behavior



Nguyen et al. 2025, *Hormones and Behavior*

No impact of early life scarcity-adversity on later life maternal motivation



Nguyen et al. 2025, *Hormones and Behavior*

Impact of early life scarcity-adversity on later life reward-related behavioral and brain function



Early life resource scarcity disrupts reward-related brain and behavioral processes

Anhedonia Following Early-Life Adversity Involves Aberrant Interaction of Reward and Anxiety Circuits and Is Reversed by Partial Silencing of Amygdala Corticotropin-Releasing Hormone Gene

Jessica L. Bolton, Jenny Molet, Limor Regev, Yuncai Chen, Neggy Rismanchi, Elizabeth Haddad, Derek Z. Yang, Andre Obenaus, and Tallie Z. Baram

Enduring disruption of reward and stress circuit activities by early-life adversity in male rats

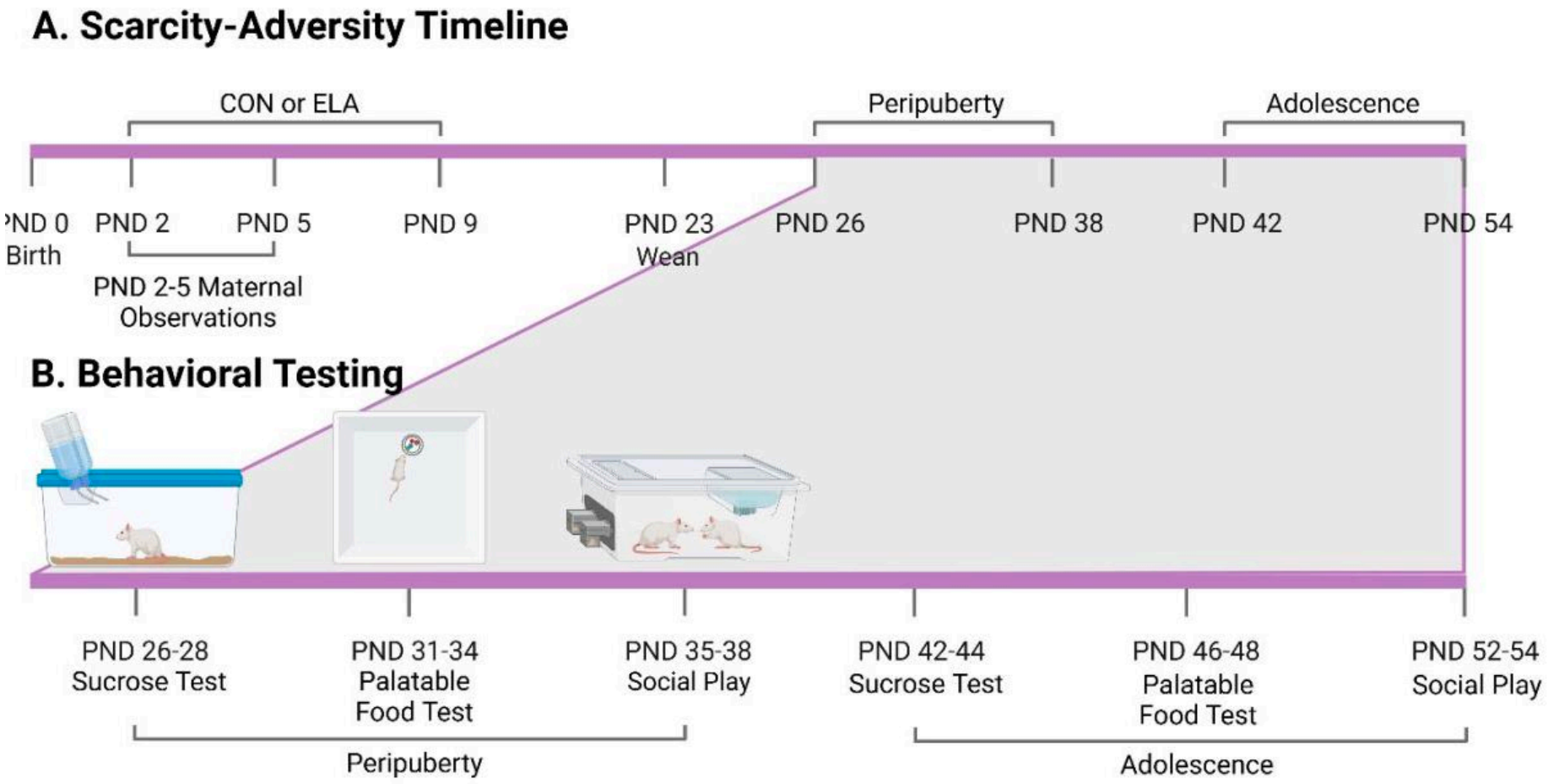
Sophia C. Levis[1,2]✉, Matthew T. Birnie[1,3], Jessica L. Bolton[1,3,4], Christina R. Perrone[2], Johanna S. Montesinos[2], Tallie Z. Baram[1,3] and Stephen V. Mahler[2]

- *When do effects emerge?*
- *Sex differences?*

Early resource scarcity alters motivation for natural rewards in a sex- and reinforcer-dependent manner

Alexia V. Williams[1] · James Flowers[1] · Kennedy S. Coates[1] · Atiba Ingram[1] · Alexandra T. Hehn[1] · Molly Dupuis[1] · Mathieu E. Wimmer[1] · Marco Venniro[2] · Debra A. Bangasser[1,3]

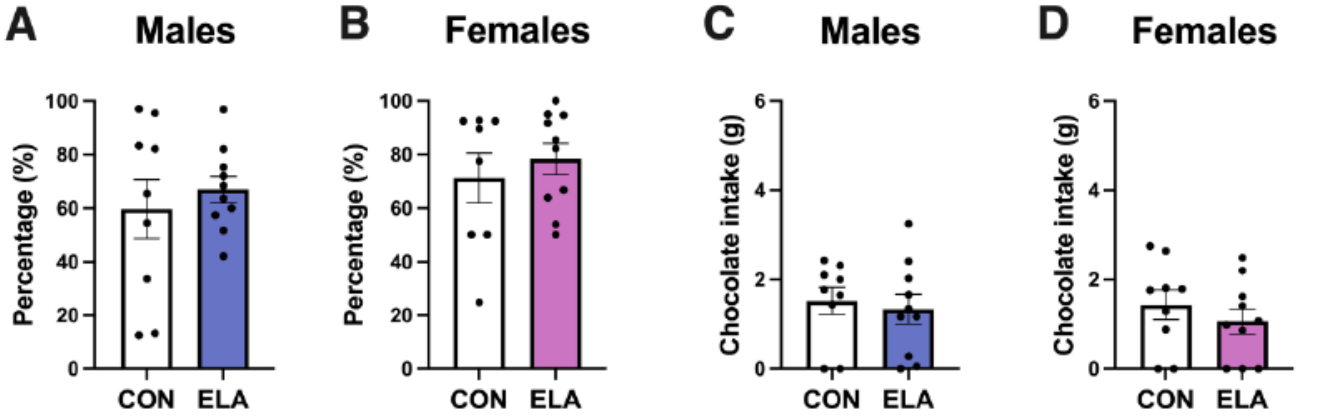
Measuring the development of behavioral responses to natural rewards following ELA



Salazar et al. 2025

No impact of ELA during peripuberty



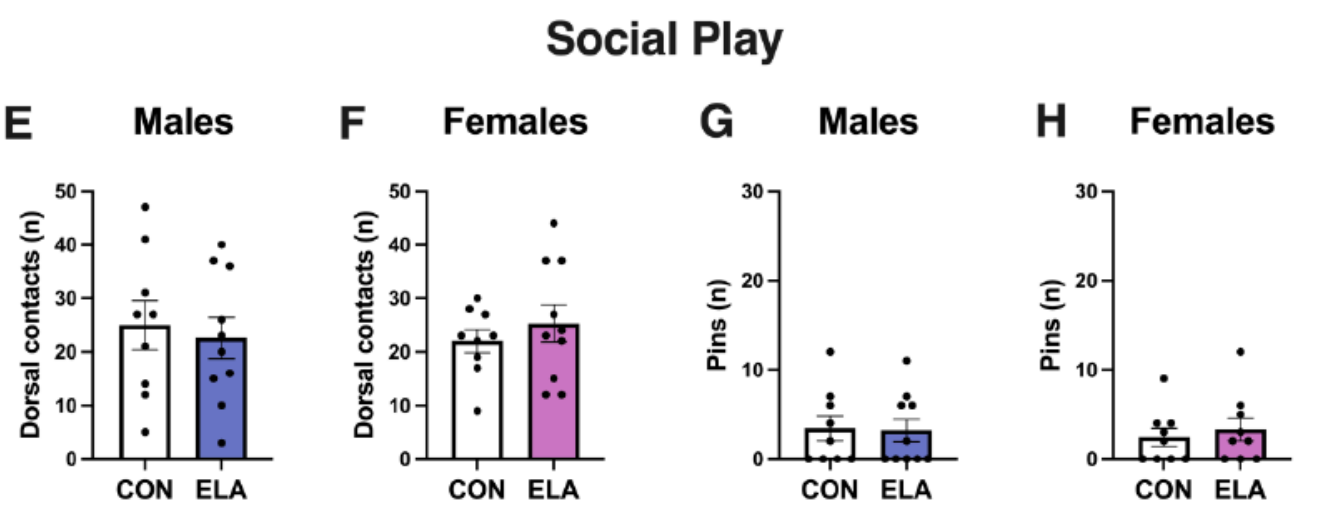






Melissa Salazar





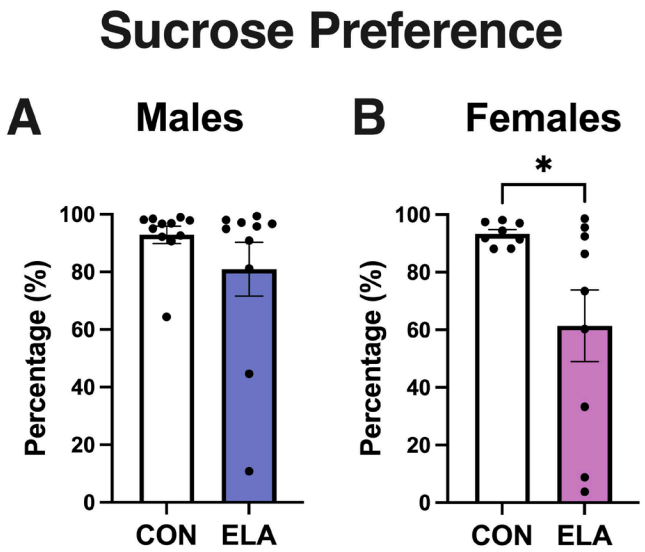


Christine Nguyen

Salazar et al. 2025, *Frontiers in Behav Neurosci*

ELA exerts sex-specific effects during adolescence







Melissa Salazar

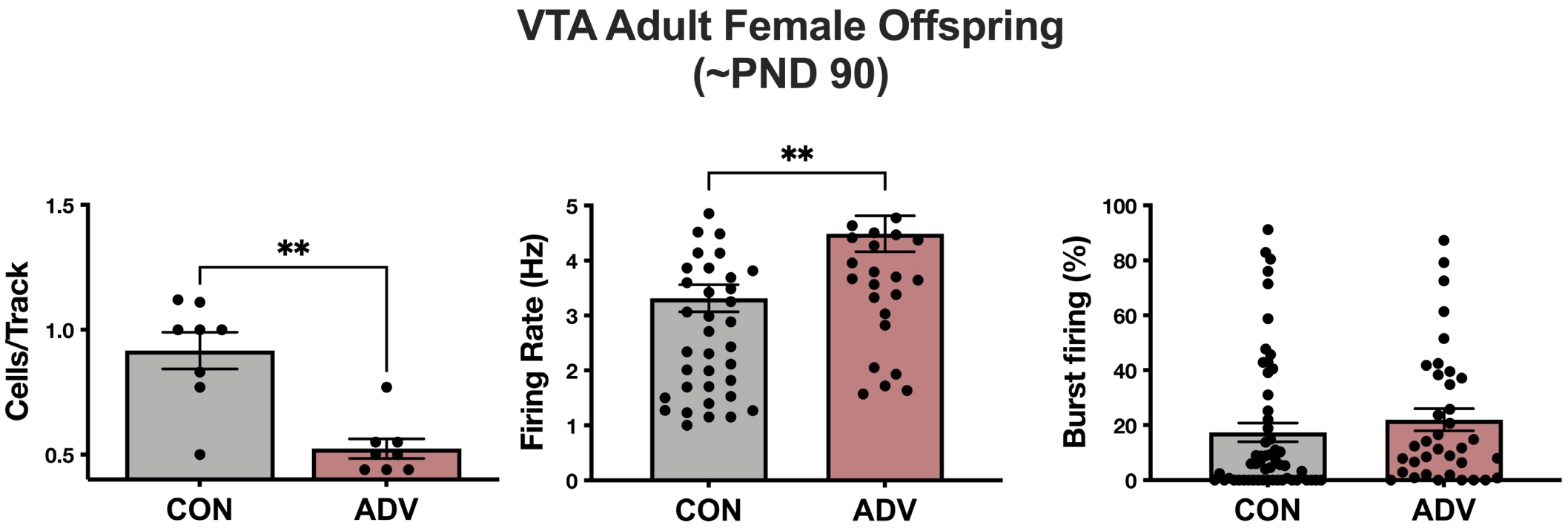


Christine Nguyen

Salazar et al. 2025, *Frontiers in Behav Neurosci*

What is the long-term impact of early life scarcity-adversity

(PND 2-9 rearing with an ADV dam) on VTA function?

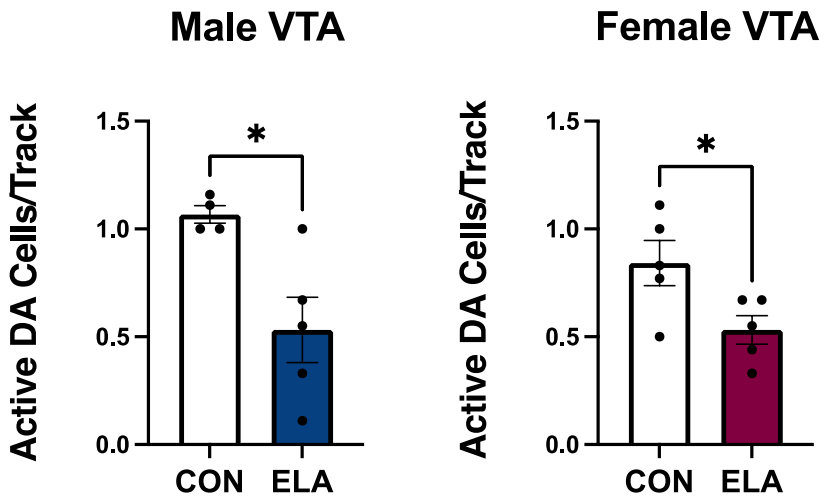


Adult female rats exposed to early life scarcity-adversity exhibit a long-lasting attenuation in VTA population activity

Adapted from Rincón-Cortés and Grace, 2022 *NPP*

ELA reduces adult VTA DA activity

- ELA reduces VTA population activity in both males and females
- *When do these effects emerge?*
- *What is the functional relevance of this long-lasting DA attenuation? Links to behavior?*



Unpublished data, Rincón-Cortés lab

Summary Part II

- No impact of ELA on later life maternal behavior in female rats
- Effects of ELA on reward responsivity emerge during adolescence
- ELA exerts sex-dependent effects during adolescence
  - **Reduced sucrose preference** in females but not males
  - **Reduced social play** in males but not females
- ELA-induced deficits in reward responsivity may be linked to blunted dopaminergic system function
  - Emergence of downregulated DA system function is unknown
  - Functional links to behavior unknown

OBJECTIVE 3

Evaluating Rodent Models

Evaluating resource scarcity as a model for **adversity-related depressive disorders** such as PPD

FACE VALIDITY

Resembles the disorder?

- Impaired, insensitive caregiving
- Reduced maternal motivation (retrieval, pup CPP)
- Anhedonia-like reduced reward responsivity in offspring

CONSTRUCT VALIDITY

Similar cause and biology?

- Low-resource environment mirrors a known PPD risk factor
- Blunted mesolimbic DA, paralleling reduced VTA/NAc fMRI responses in PPD

WHAT RODENTS ADD

What can't we do in humans?

- Causal, timed manipulation of adversity
- Cell- and circuit-level recording in mother and offspring
- Intergenerational designs in months, not decades

LIMITATIONS

Subjective symptoms
Low mood, guilt and suicidality cannot be measured in rodents

Species differences
Litter-based care and a compressed developmental timeline

Predictive validity
Response to PPD treatments not yet tested in this model

TAKE-HOME MESSAGE

The Big Picture

Maternal adversity converges on the **mesolimbic DA system,** in mothers and in their offspring

MOTHER (F0)

Adversity blunts maternal motivation

- More adverse caregiving, slower pup retrieval
- Blunted pup reward learning (CPP)
- ↓ VTA DA population activity, but only during/shortly after adversity, without a basal CORT rise

OFFSPRING (F1)

Reward deficits emerge in adolescence

- Sex-specific: ↓ sucrose preference in females, ↓ social play in males
- Long-lasting ↓ VTA DA activity in adulthood

NEXT GENERATION

Adverse caregiving is not inherited

- F1 females show normal maternal behavior and motivation
- The cycle of adverse care can be broken

TOWARD INTERVENTIONS

Therapeutic target
Mesolimbic DA function in PPD-related motivational deficits

Window of opportunity
Adolescence, when ELA effects on reward first emerge

Sex matters
Sex-specific vulnerability should guide treatment

Rincón-Cortés Lab

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- Christine Nguyen, BS
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- Sasha Oak
- Paolaenid Rodney-Hernández, BS
- Riya Thomas
- Erin Lauraine, BS
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- Jasmine Peters

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- Melissa Salazar, BS
- Jeffy Jackson, BS
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Questions??? Contact me!

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National Institutes of Health

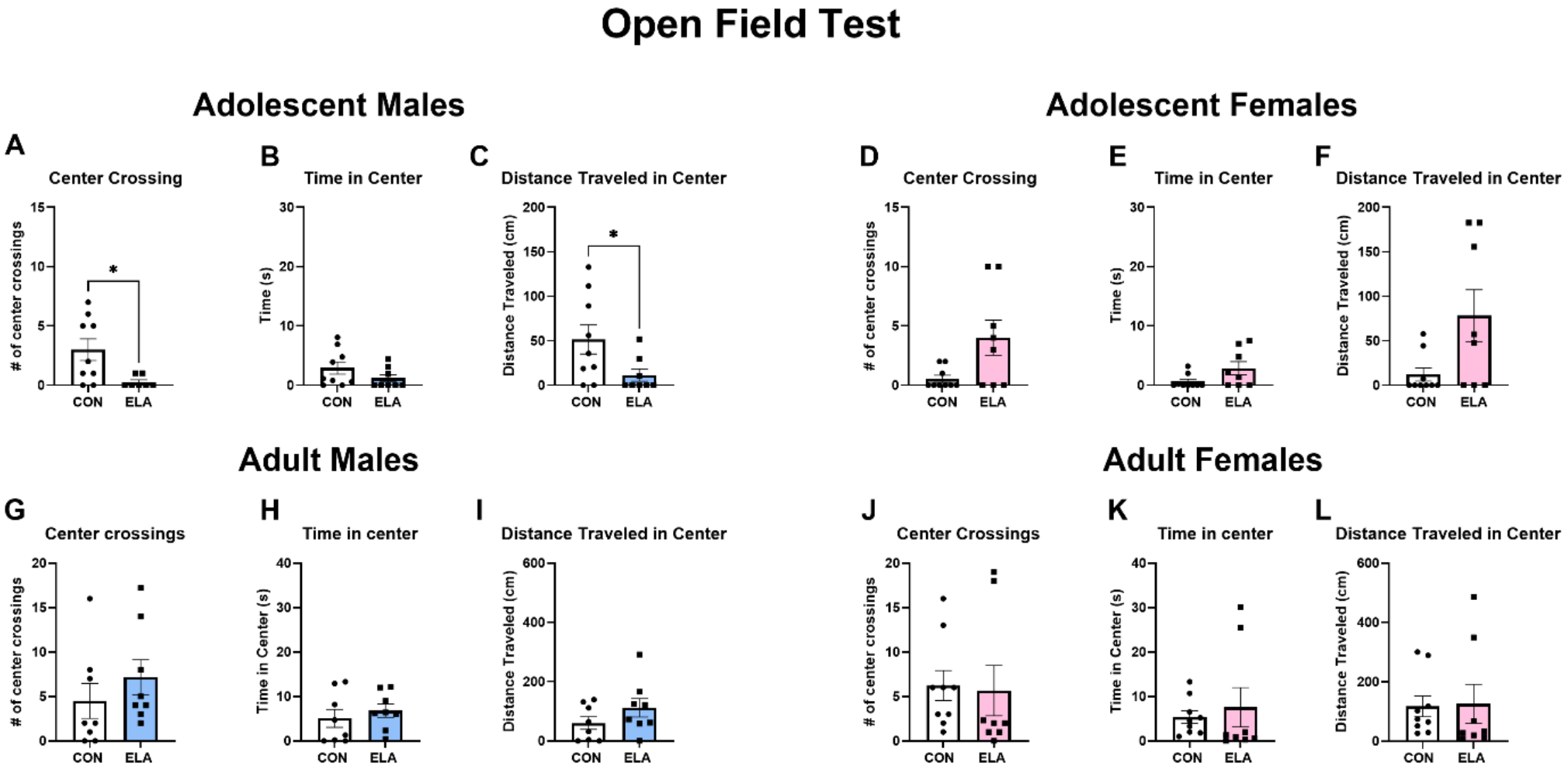
K01-MH128800
R03-HD110673

Acknowledgments

https://labs.utdallas.edu/madrelab/

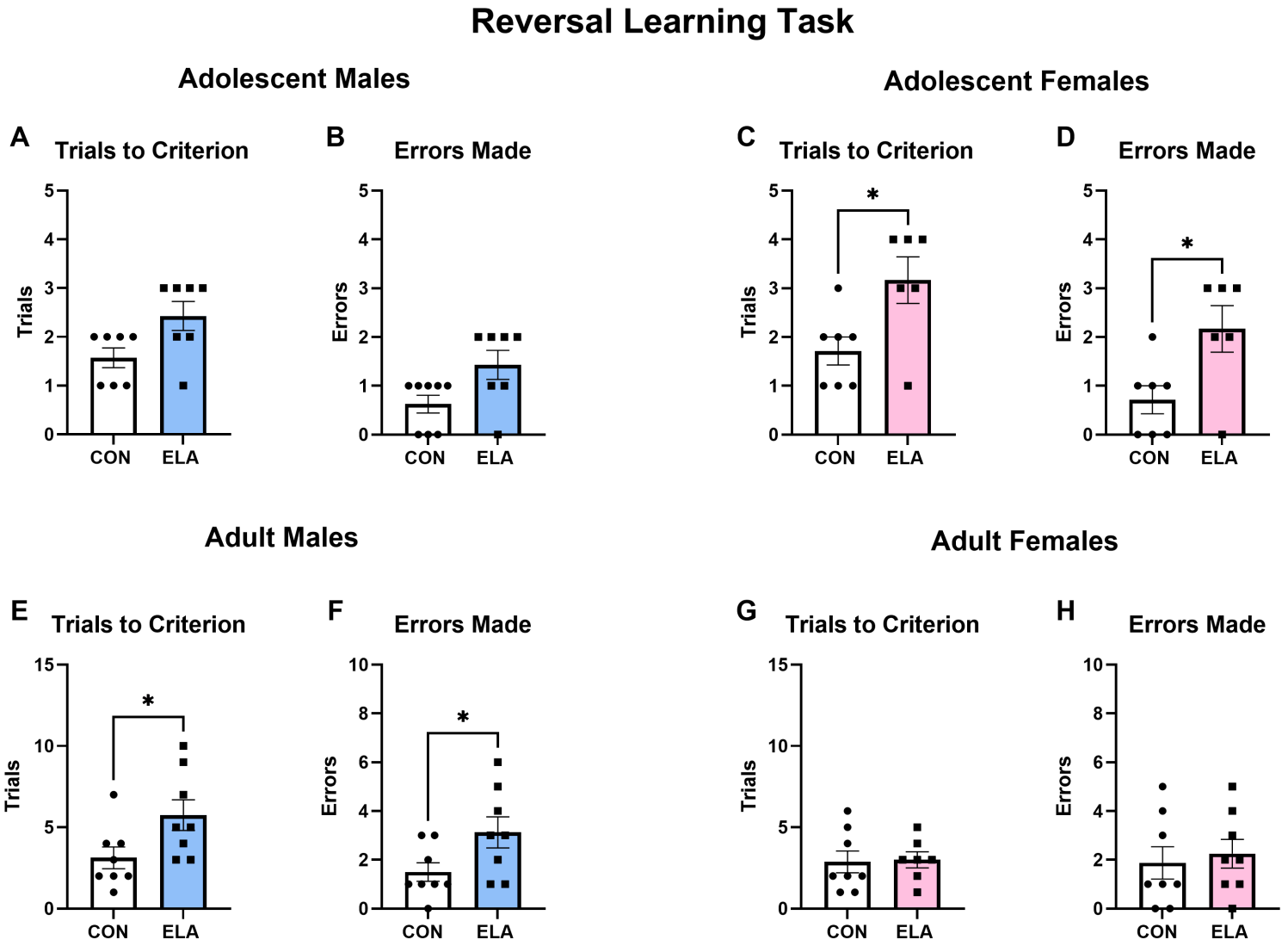
Additional Slides

Sex-specific effects of early life scarcity-adversity on adolescent anxiety-like behavior



Jackson, Kroener and Rincón-Cortés, in prep

Sex- and age-specific effects of early life scarcity-adversity on reversal learning



Jackson, Kroener and Rincón-Cortés, in prep