

## **Breakout Session 6: Track A**

# **Behavioral Phenotyping of Risky Decision-Making After TBI in a Rat Model Enables Evaluation of Statistical Methodology**

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WEXNER MEDICAL CENTER

# Behavioral phenotyping of risky decision-making after TBI in a rat model enables evaluation of statistical methodology

**Cole Vonder Haar**

Injury and Recovery Laboratory

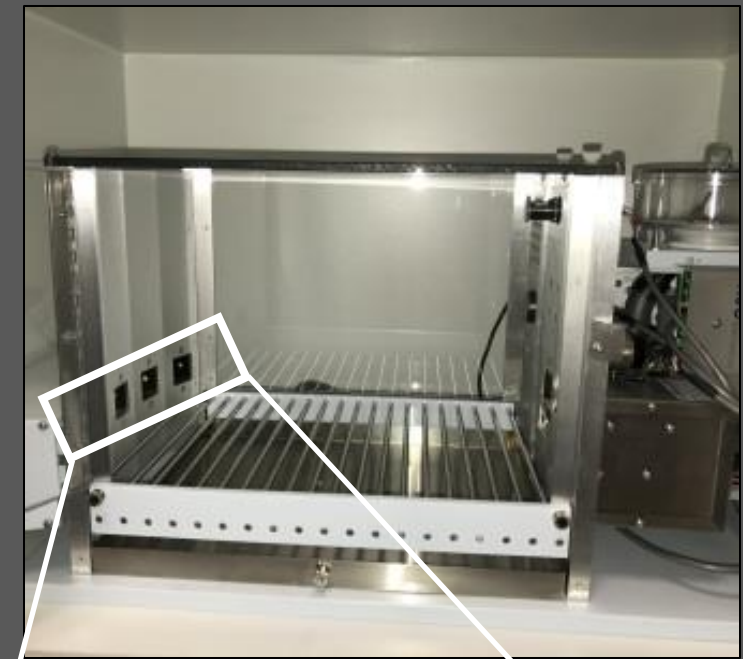
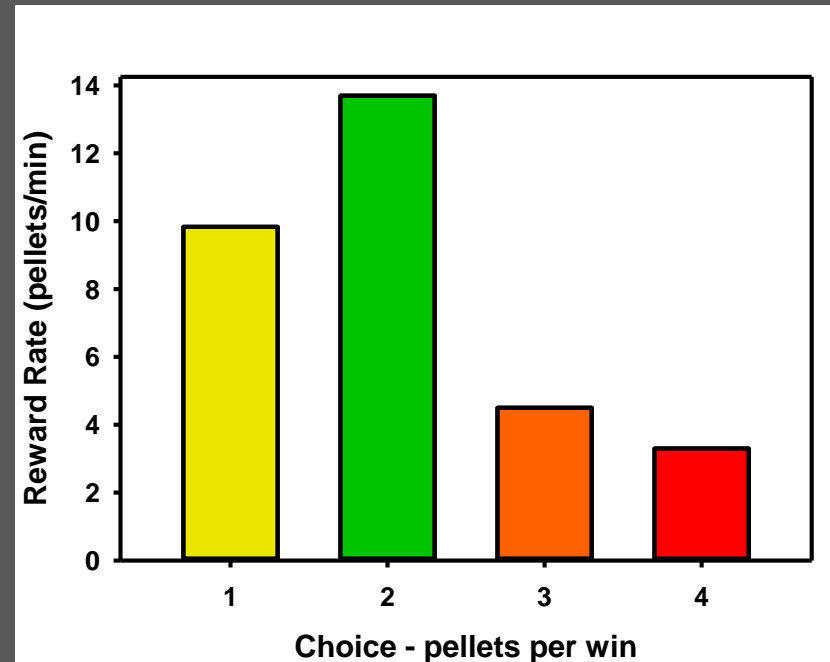
Department of Neuroscience

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Disclosures: Consultant, Turner Scientific

# Background

- Decision-making under uncertainty/risk
- Rat model of decision-making
  - Inspiration from human Iowa Gambling Task<sup>1</sup>
  - “Rodent Gambling Task”<sup>2</sup>



<sup>1</sup>Bechara et al, 1994

<sup>2</sup>Zeeb et al., 2009

# Background

- TBI affects >2.8 million people each year in the US
  - Approximately 0.85% of the population
- Impaired decision-making in patients after TBI<sup>1,2,3</sup>
- Rat model replicates these findings<sup>4,5,6,7</sup>

<sup>1</sup>Levine et al., 2005

<sup>2</sup>Sigurdardottir et al., 2010

<sup>3</sup>Cotrena et al., 2014

<sup>4</sup>Shaver et al., 2019

<sup>5</sup>Ozga-Hess et al., 2020

<sup>6</sup>Frankot et al., 2022

<sup>7</sup>Vonder Haar et al., 2022



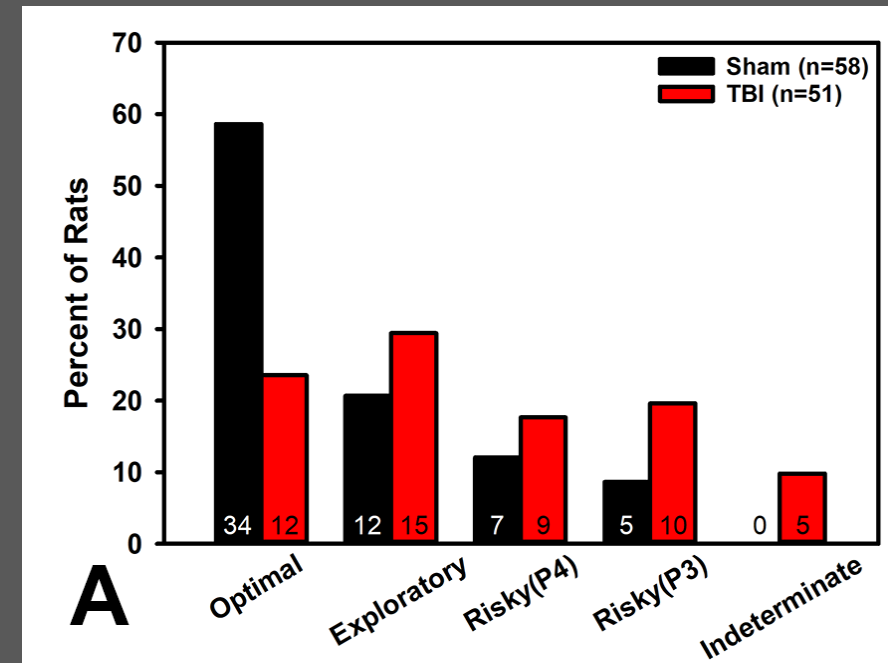
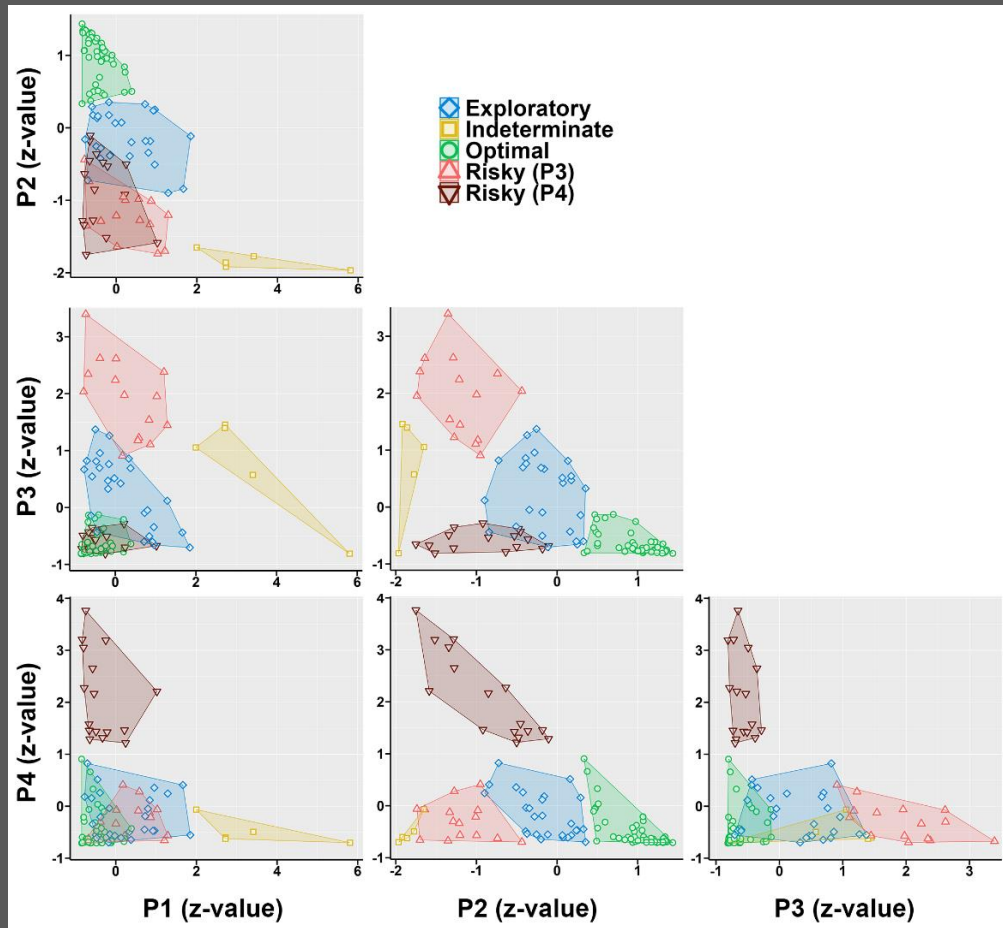
# The Dataset

- Compilation of TBI studies on the RGT
- Overall stats
  - 396 rats
  - 25,170 sessions (~62/rat)
  - 2,356,661 lines of data (~5,805/rat)
- Aggregated/processed data
  - 24,957 session-level summaries of choice
  - 20,425 sessions with no/control manipulations (“pure”)

Study ID	Reference	Training (Pre/Post-Injury)	Total (f)	TBI + Sham	Intervention
CCI-A	Shaver, 2019	Both	44 (0)	44	0
CCI-E	Ozga-Hess, 2020	Post	25 (0)	25	0
HFD-A	Frankot, 2023	Pre	36 (0)	18	18
CCI-D	Vonder Haar, in prep	Post	46 (0)	22	24
CCI-Q	Vonder Haar, in prep	Pre	48 (0)	20	28
CCI-R	Wampler, in prep	Pre	34 (34)	34	0
CCI-S	Wampler, in prep	Pre	21 (0)	21	0
CCI-T	Bressler, in prep	Post	24 (0)	24	0
CCI-U	McCloskey, in prep	Post	47 (24)	0	47
MCB-A	Martens, in prep	Pre	47 (0)	23	24
MCB-C	Speas, in prep	Pre	24 (0)	12	12
<b>Totals</b>			<b>396 (58)</b>	<b>243</b>	<b>153</b>

# Rat Decision-Making Profiles

- K-means clustering on stable data
  - N=109 initial rats
- Not all rats are optimizers
- TBI rats very unlikely to be “optimal” category

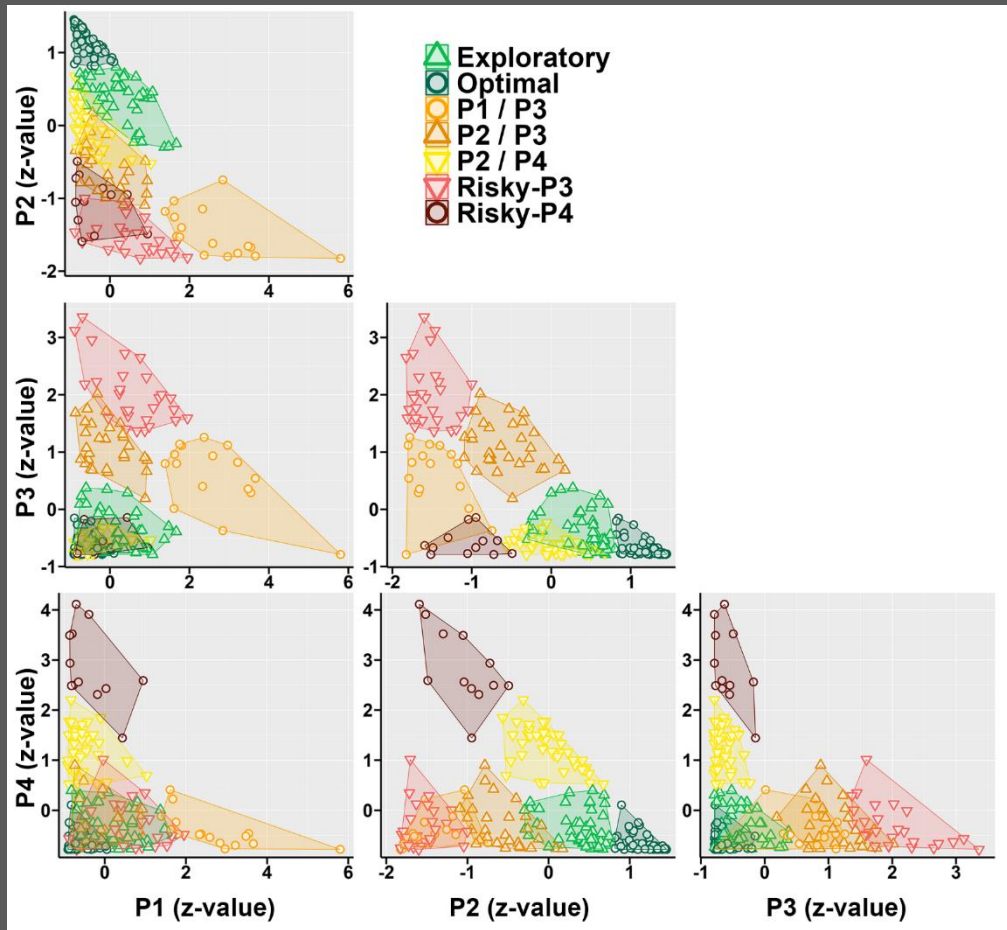


Vonder Haar et al., 2022, *Front. Behav. Neurosci*

<https://odc-tbi.org/data/703>

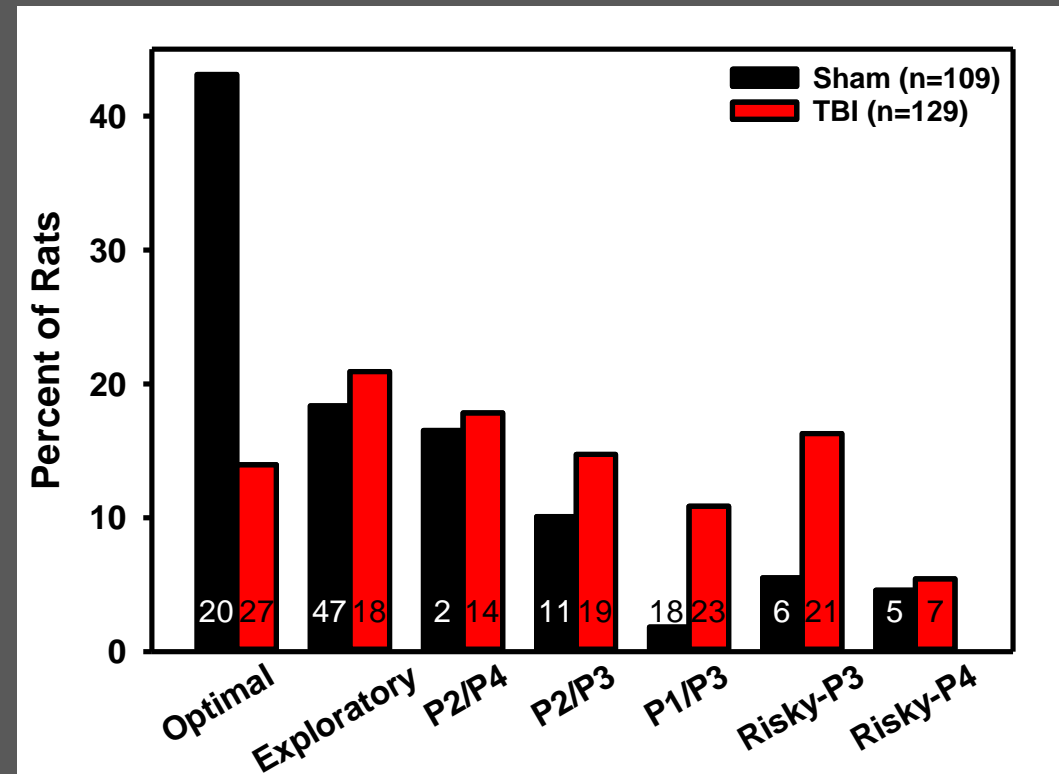
<https://github.com/VonderHaarLab/>

# Rat Decision-Making Profiles



Unpublished data

- Unpublished data from larger set
  - 7 phenotypes



# Questions Arising from these Data

- What are the biological factors are linked to given phenotypes?
- What gives rise to these stable decision phenotypes?
- Biological data still in process
  - Gut microbiome
  - Brain pathology (IHC)
- Analyses of behavioral phenotype development in process



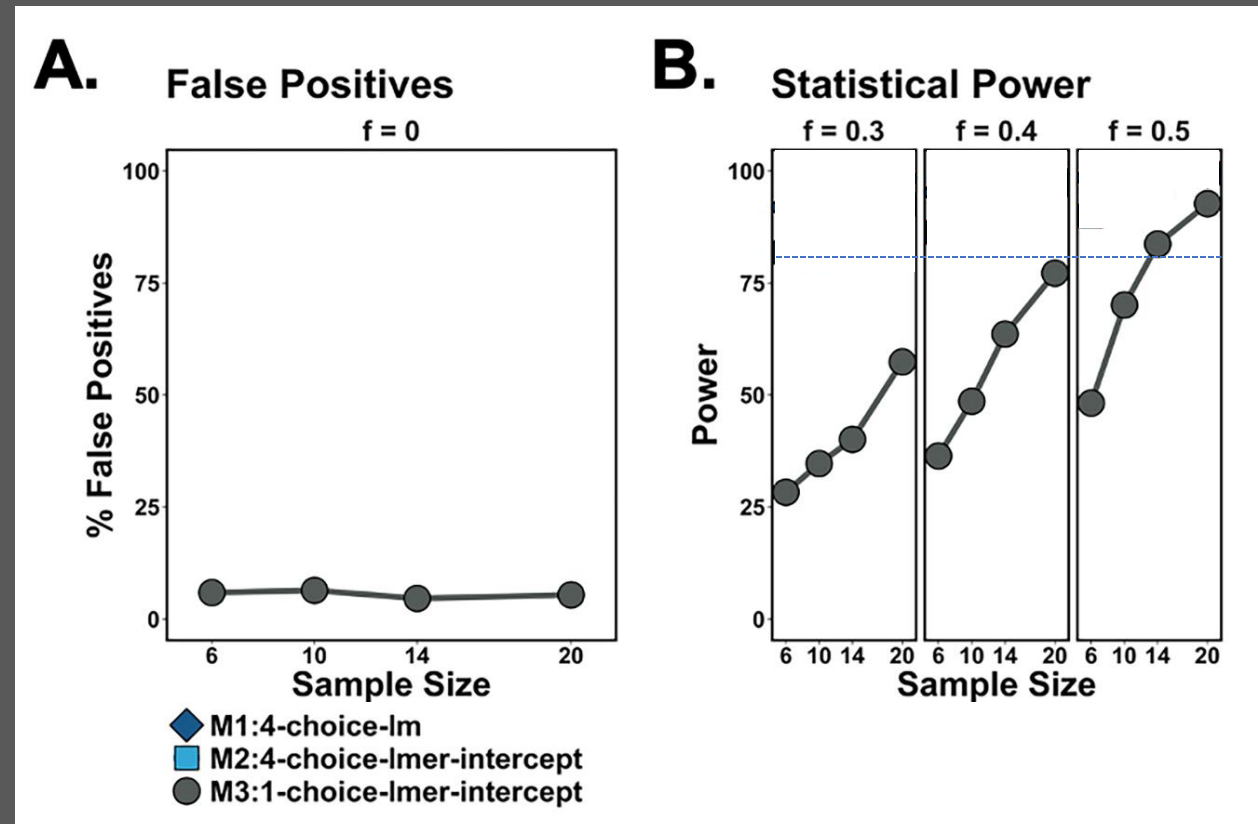
# Applications: Statistical Methodology

- Compositional data
  - Statistical problems due to dependency
  - Choice of one option excludes other options
- Simulated rat TBI data
  - Based on observed phenotypes
  - Monte Carlo studies
    - 4 effect sizes, 4 sample sizes
    - 16,000 datasets



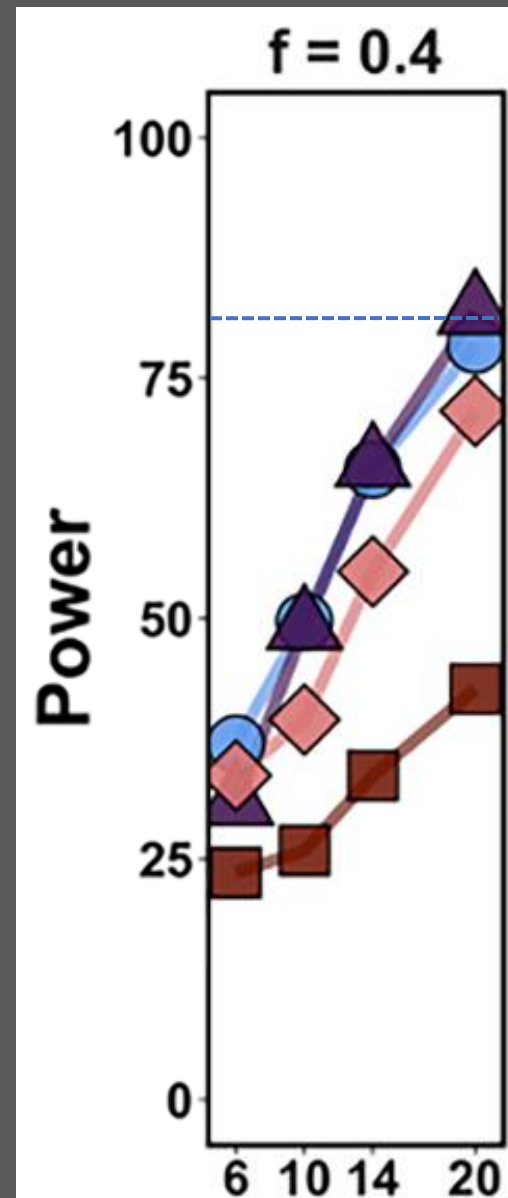
# Analyses of Interdependent Data

- Linear models (e.g., ANOVA)
  - Not accounting for dependency in any way
  - Anticipated 18.6% family-wise FP rate for 4 comparisons



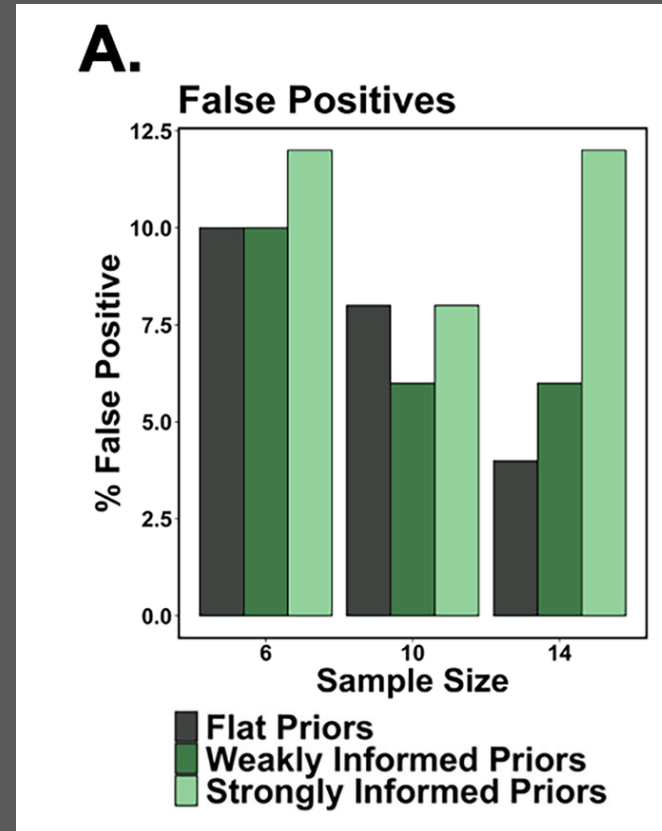
# Analyses of Interdependent Data

- Models accounting for dependency
  - Rescued FP
  - Low power



# Analyses of Interdependent Data

- Bayesian method accounting for dependency
- Low, but not 5% FP
- Large gains in power



# Conclusions

- Large rat decision-making dataset
- Enables phenotyping of decision profiles
  - Can be used to drive biological questions
- Enables simulation-based evaluations of statistical methodology

# Lab Team

## Current

Cole Vonder Haar, Ph.D. (PI)  
Kris Martens, Ph.D. (co-I)  
Travis Smith, Ph.D. (co-I)  
Erskine Chu, Ph.D. (Postdoc)  
Savana Burke (Master's student)  
Katie Koontz (Postbac student)  
Jenna McCloskey, B.S. (Tech)  
Berkin Bilkin, B.S. (Tech)  
Fikir Arega (Ugrad)  
Mia Eleid (Ugrad)  
Alex Gentry (Ugrad)  
Sathvik Jami (Ugrad)  
Max McLeod (Ugrad)  
Lizza O'Connell (Ugrad)

## Recent

**Peyton Mueller, Ph.D.** (Postdoc)  
**Michelle Frankot, Ph.D.** (Postdoc/Ph.D.)  
Kristen Pechacek, Ph.D.  
Sarah Wampler, M.S.  
Noah Bressler (Tech)  
Anna Gaughan (Ugrad)  
Carissa Gratzol (Ugrad)  
Iman Sattar (Ugrad)  
Garrett Sommer (Ugrad)  
Reagan Speas (Ugrad)



## Collaborators

Olga Kokiko-Cochran (OSU)    Rich Bruno (OSU)  
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Katy Lenz (OSU)           Erica Glasper (OSU)  
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Phil Popovich (OSU)       Amy Wagner (PITT)  
Kristina Kigerl (OSU)      **Adam Ferguson (UCSF)**  
Yael Vodovotz (OSU)      Dhakshin Ramanathan (UCSD)

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