

Breakout Session 6: Track A

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

Dr. Cole Vonder Haar

Assistant Professor, Ohio State University



THE OHIO STATE
UNIVERSITY

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

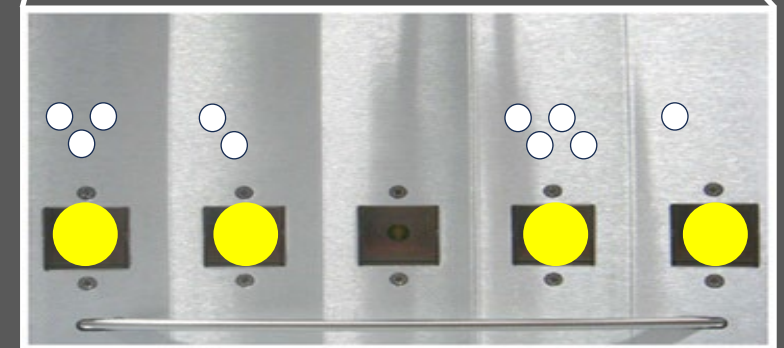
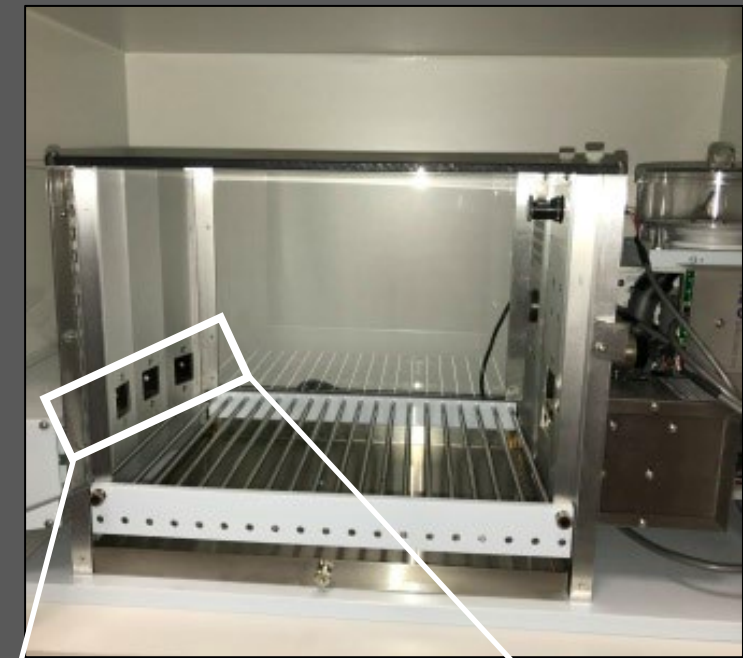
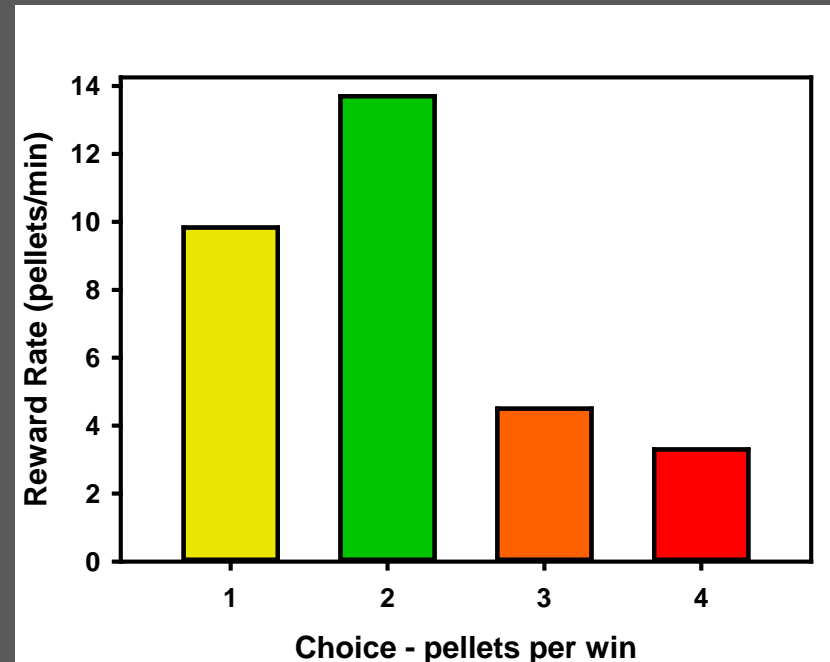
Department of Neuroscience

03/28/2024

Disclosures: Consultant, Turner Scientific

Background

- Decision-making under uncertainty/risk
- Rat model of decision-making
 - Inspiration from human Iowa Gambling Task¹
 - “Rodent Gambling Task”²



¹Bechara et al, 1994

²Zeeb 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^{1,2,3}
- Rat model replicates these findings^{4,5,6,7}

¹Levine et al., 2005

²Sigurdardottir et al., 2010

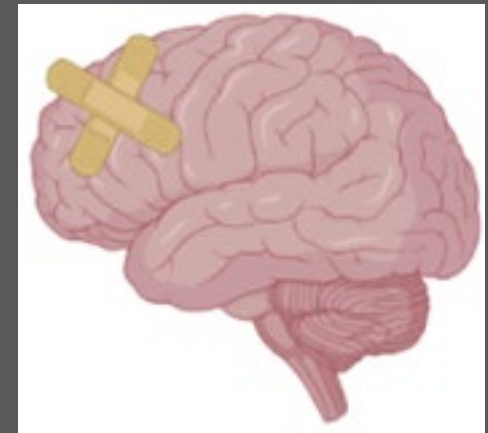
³Cotrena et al., 2014

⁴Shaver et al., 2019

⁵Ozga-Hess et al., 2020

⁶Frankot et al., 2022

⁷Vonder Haar et al., 2022



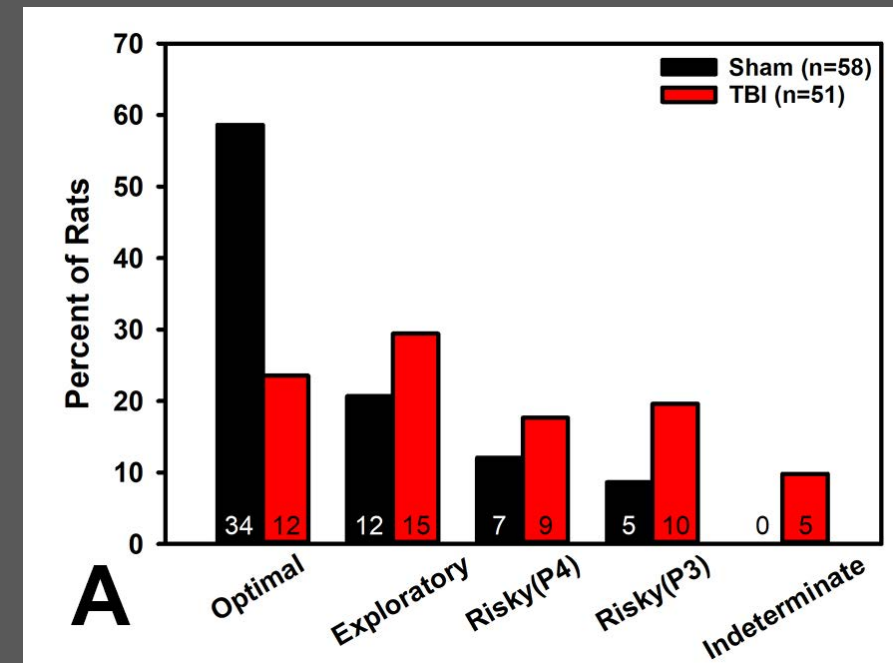
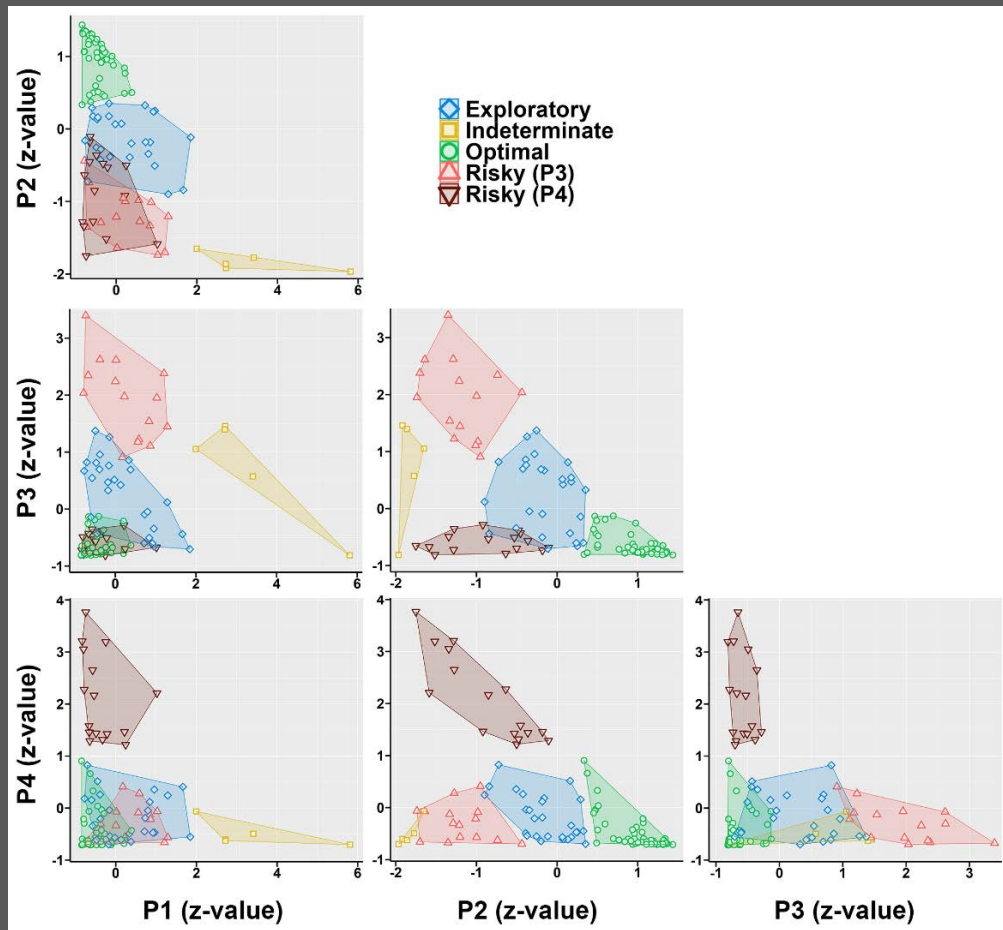
The Dataset

- 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
Totals			396 (58)	243	153

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

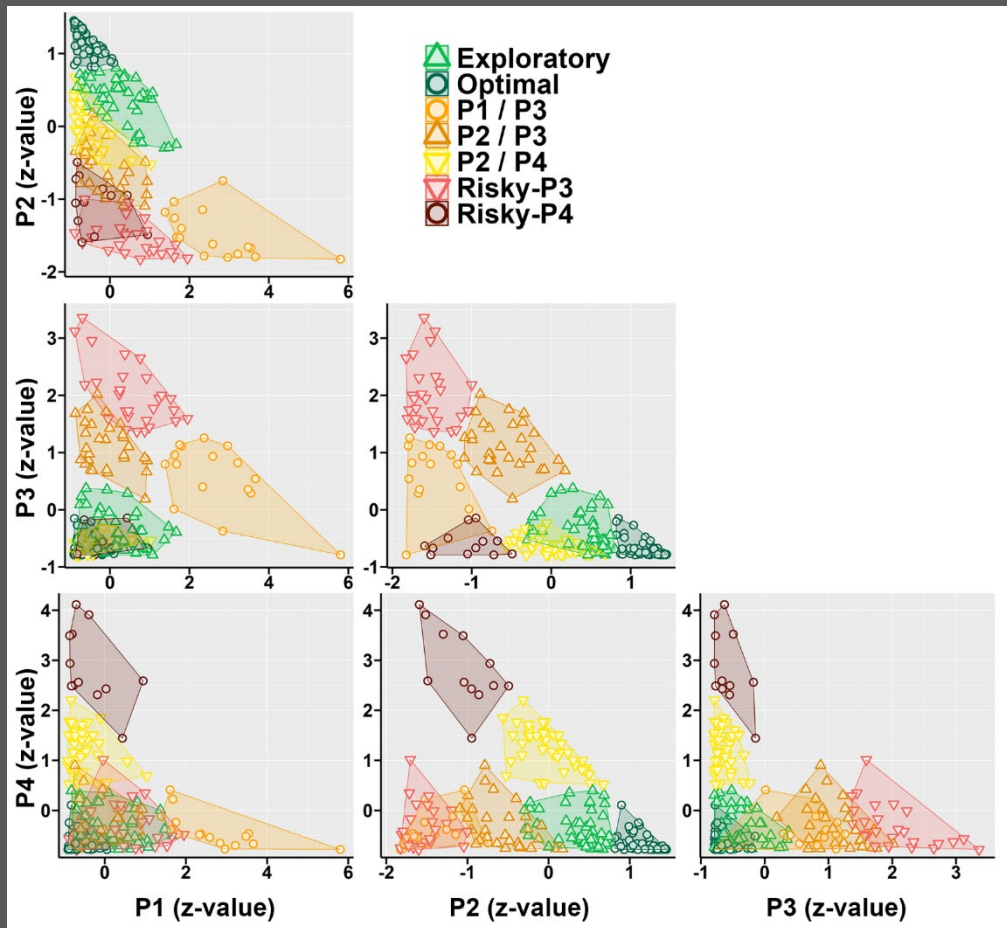


Vonder Haar et al., 2022, *Front. Behav. Neurosci*

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

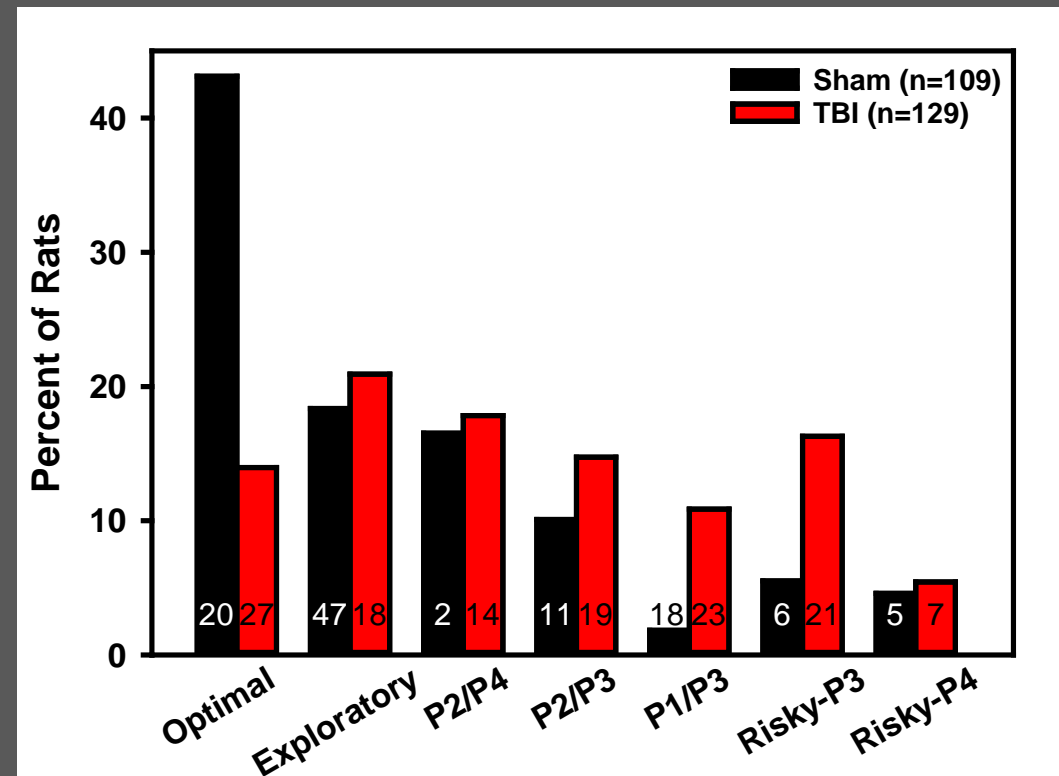
<https://github.com/VonderHaarLab/>

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

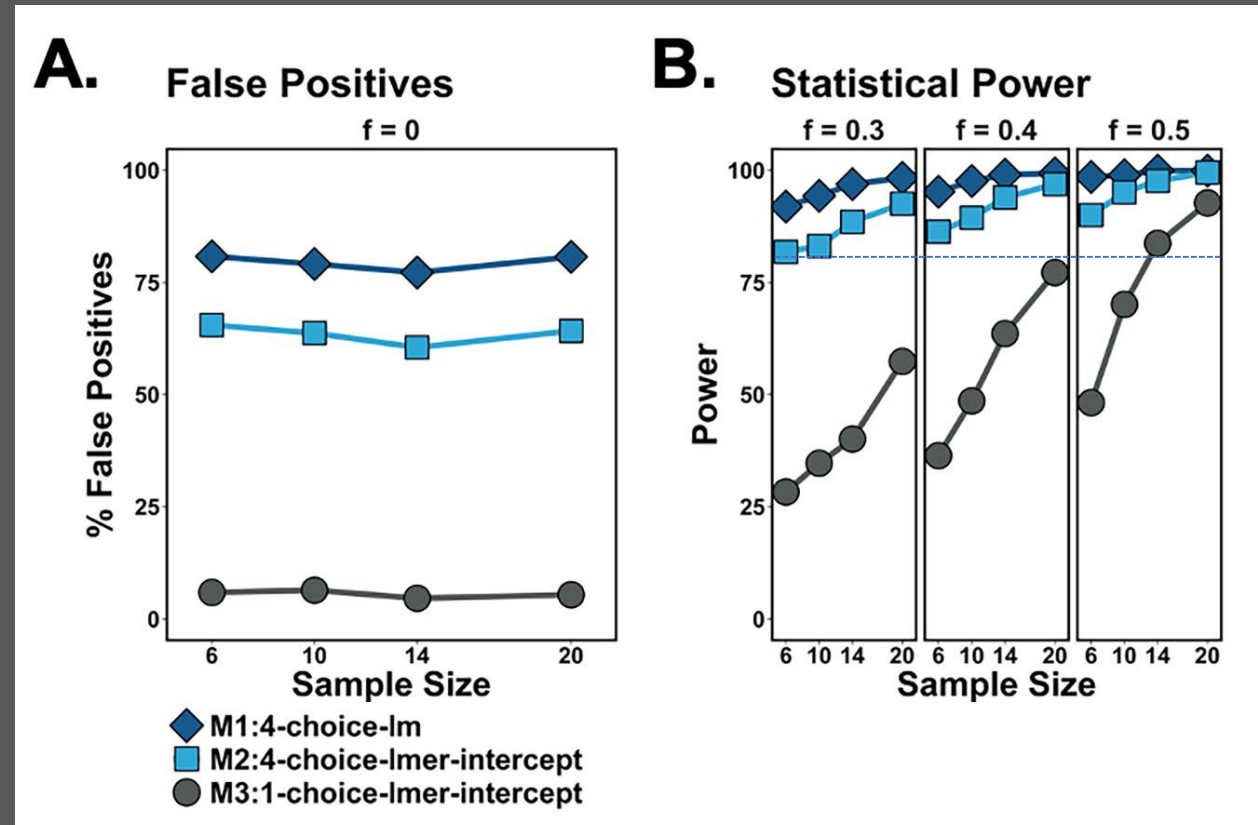
Applications: Statistical Methodology

- 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



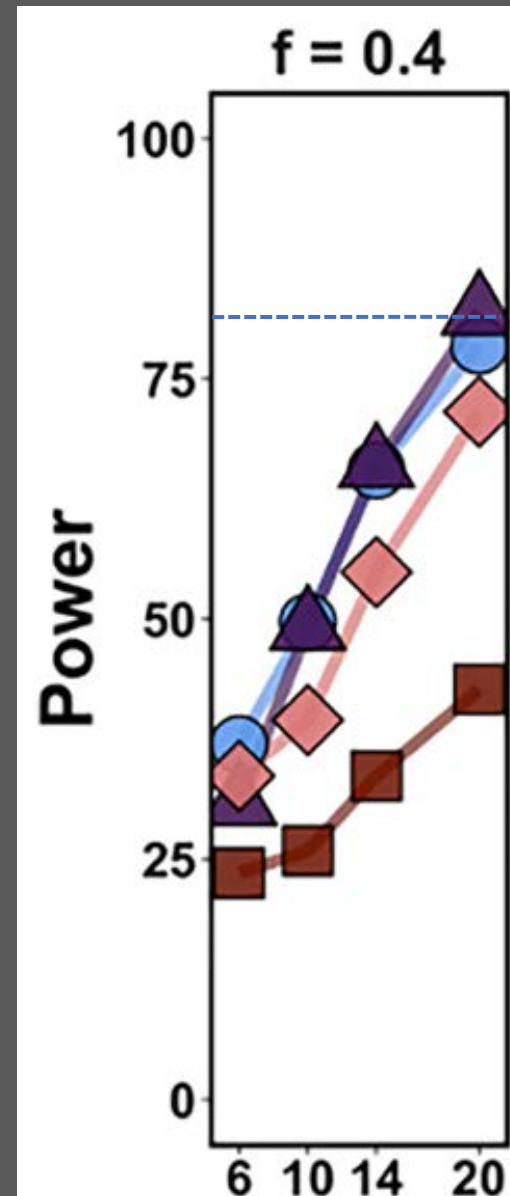
Analyses of Interdependent Data

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



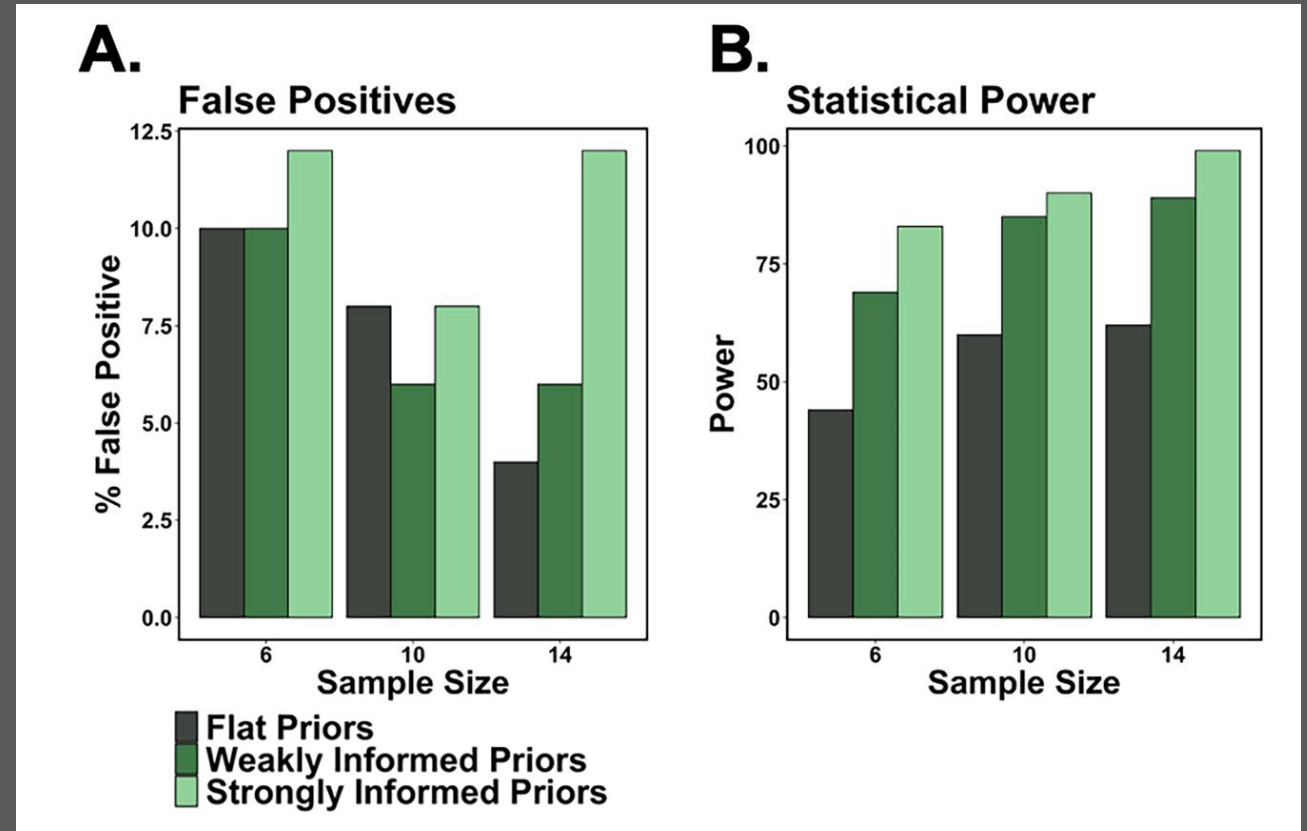
Analyses of Interdependent Data

- 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)
Jon Godbout (OSU)
Katy Lenz (OSU)
Michael Bailey (NWCH)
Phil Popovich (OSU)
Kristina Kigerl (OSU)
Yael Vodovotz (OSU)
_Rich Bruno (OSU)
Leah Pyter (OSU)
Erica Glasper (OSU)
Mike E Young (KSU)
Amy Wagner (PITT)
Adam Ferguson (UCSF)
Dhakshin Ramanathan (UCSD)

Funding

NINDS R01-NS110905-05S1
DOD HT9425-23-1-0538
DOD HT9425-23-1-1003
NIMH R01-MH085739
International Center for Responsible Gaming
OSU Chronic Brain Injury Program
OSU Neuroscience Research Institute