



Improving choice and timing processes through time-based interventions

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Every day decisions: 35,000



\$20-30 per day



1-2 drinks per day



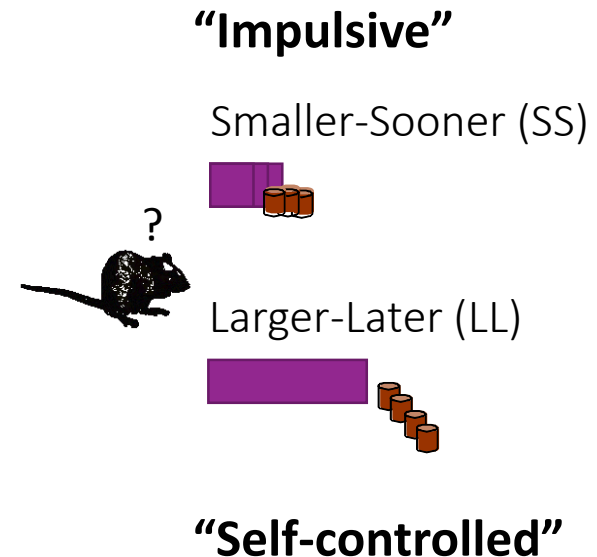
15-20 bites per day





Choice: Measurement

- Offer rats choices between smaller-sooner (SS) and larger-later (LL) rewards (based on Green & Estle, 2003)
 - SS lever = 1 pellet in 10 s
 - LL lever = 2 pellets in 30 s
 - ITI = 60 s
- Can manipulate delay to and/or magnitude of reward
- Choices of SS indicate impulsive choice in all cases as they earn fewer rewards





Temporal discounting functions and choice

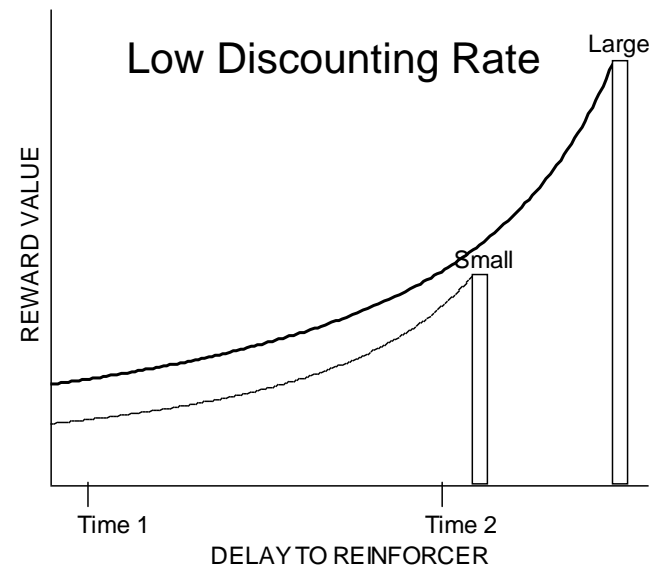
Hyperbolic Discounting: $V = A / (1 + kD)$

V = Subjective Value

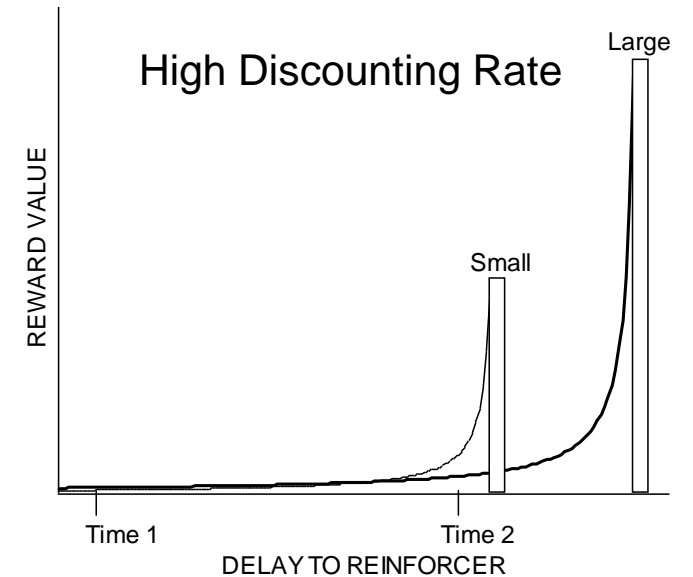
A = Amount

D = Delay

k = discounting rate



Prefers LL



Prefers SS



Individual differences in delay discounting

- Delay discounting appears to be a stable trait variable
 - Test-retest correlations for humans in the .6-.7 range over periods from 1 week to 1 year; comparable to other trait variables (e.g., Jimura et al., 2011; Johnson, Bickel, & Baker, 2007; Kirby, 2009; Matusiewicz et al., 2013; Ohmura et al., 2006)
 - Test-retest correlations in the .6-.7 range for rats over periods of 1 to 5 months (Peterson, Hill, & Kirkpatrick, 2015)
- Individual differences in delay discounting are related to:
 - Substance abuse (e.g., Bickel & Marsch, 2001; Carroll et al., 2009; deWit, 2008)
 - Pathological gambling (e.g., Alessi & Petry, 2003; MacKillop et al., 2011; Reynolds et al., 2006)
 - Obesity (e.g., Davis et al., 2010)
 - ADHD (e. g., Barkley et al., 2001; Solanto et al., 2001; Sonuga-Barke, 2002)
- Delay discounting is a trans-disease process (e.g., Bickel & Mueller, 2009)



Origins of Individual Differences: Timing Processes

- Adolescents with ADHD:
 - Exhibit poorer temporal discrimination abilities (Barkley et al. 2001; Smith et al. 2002)
 - Display steeper impulsive choice functions than controls (e.g., Barkley et al. 2001; Scheres et al. 2010; Wilson et al. 2011)
- More impulsive humans:
 - Overestimate interval durations (Baumann & Odum, 2012)
 - Demonstrate poorer temporal discrimination abilities (Van den Broek, Bradshaw, & Szabadi, 1987)
- More impulsive rats:
 - Demonstrate poorer temporal discrimination abilities and weaker delay tolerance (Marshall et al., 2014; McClure et al., 2014)



Altering individual differences: Time-based interventions

- Exposure to delays reduces impulsive choice in rats (Madden et al. 2011, Stein, Johnson, et al. 2013, Stein et al. 2015) **and humans** (Eisenberger and Adornetto 1986)
- Gradually increasing the delay to the LL reward maintained preference for the LL outcome in:
 - Adults with development disabilities (Dixon et al. 1998)
 - Children with ADHD (Binder, Dixon, and Ghezzi 2000; Neef, Bicard, and Endo 2001)
 - Adults with moderate to severe intellectual disabilities (Dixon, Rehfeldt, and Randich 2003)

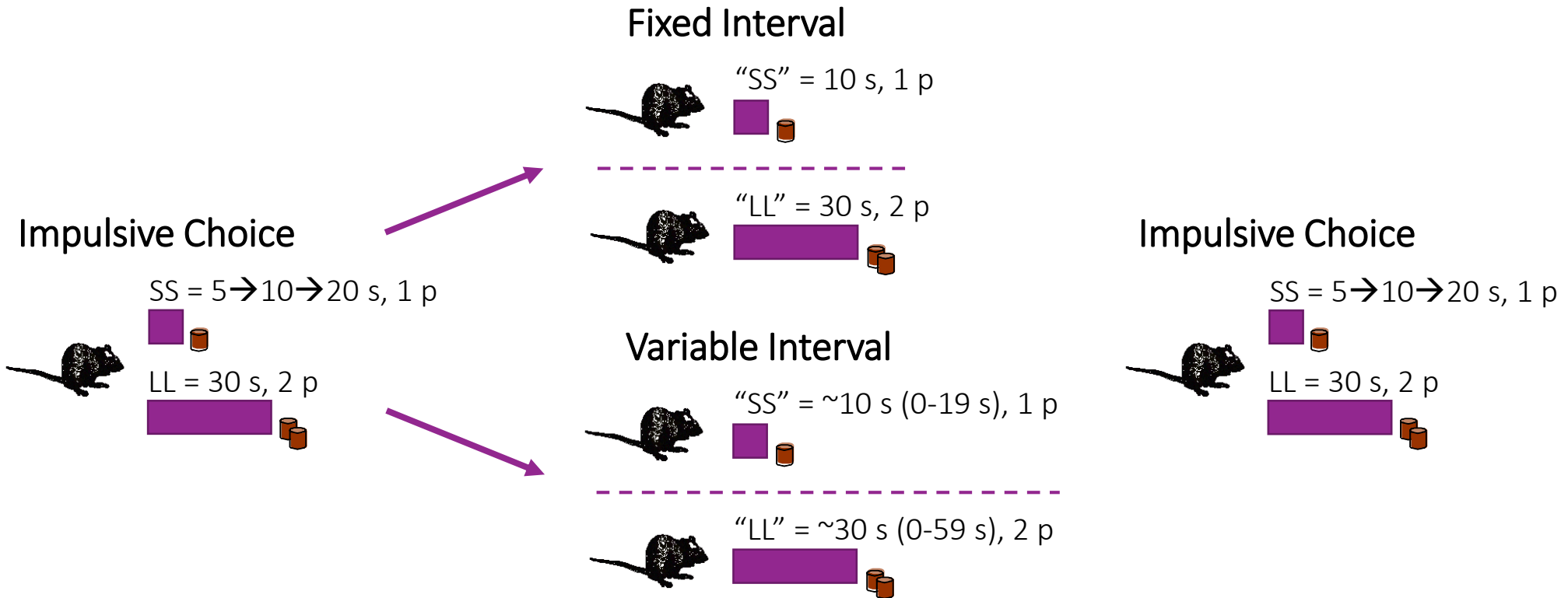
Time-based interventions: Questions

Is mere delay exposure is sufficient?

Or, does the nature of the delay exposure matter?



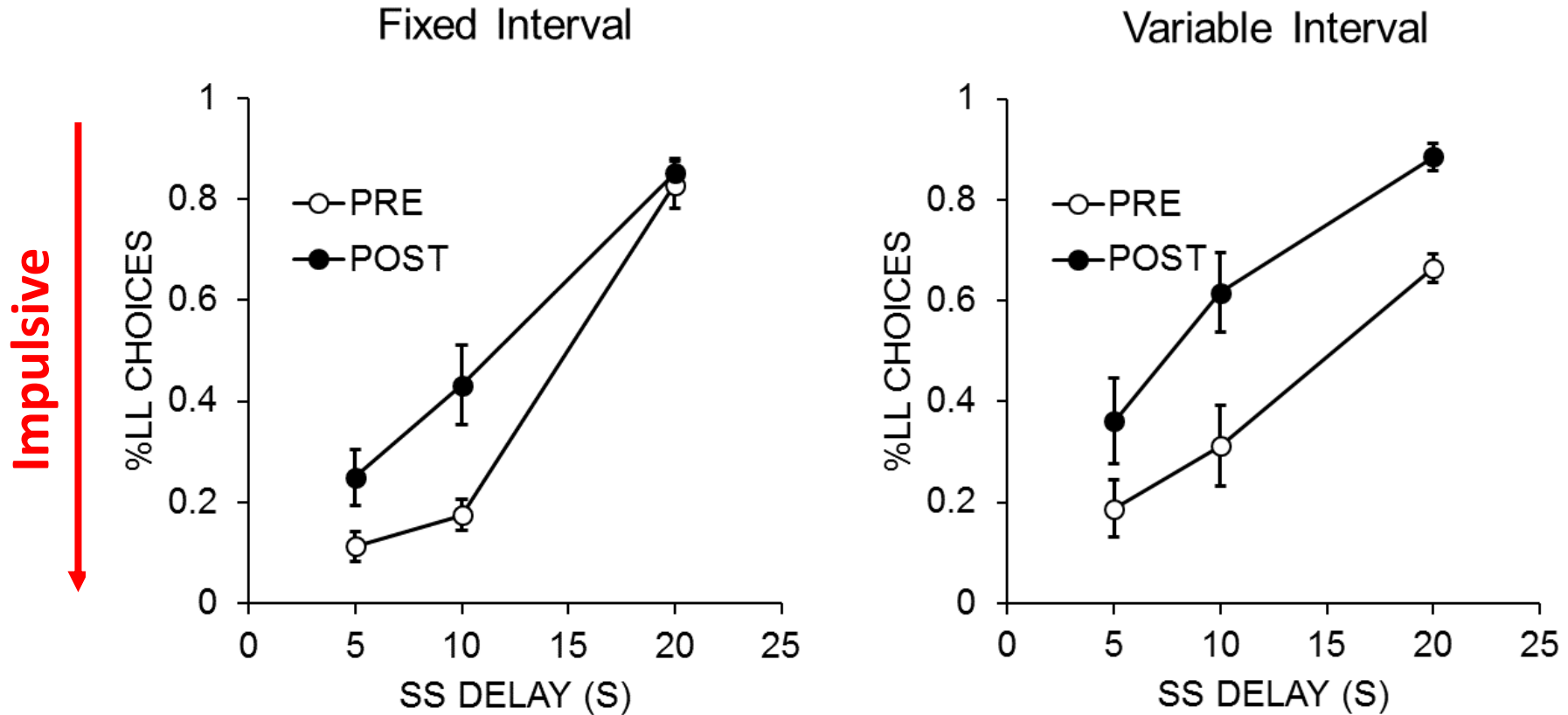
Time-based intervention: Interval schedules



Smith, Marshall, & Kirkpatrick (2015)



FI and VI Interventions: Choice



Both FI and VI interventions significantly increased LL choices

Smith, Marshall, & Kirkpatrick (2015)



Interlude: ANOVA to Mixed Model Transition

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Discussion

The anova to mixed model transition

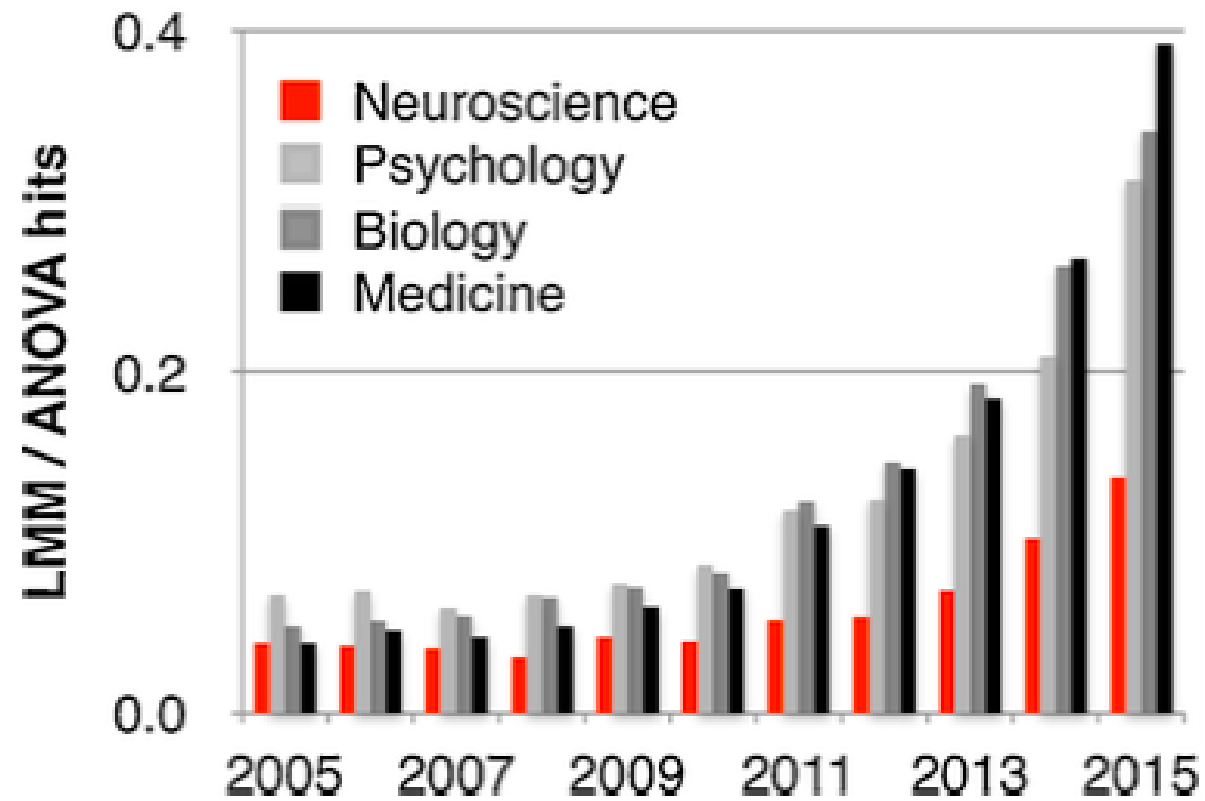
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ANOVA to Mixed Model Transition





Mixed Effects Regression Models vs. ANOVA

- ANOVA treats delay or magnitude as categorical
- As a work-around, researchers fit a continuous equation (e.g., hyperbolic) to collapsed data and then analyze k-values with t-tests or ANOVA
 - However, the statistical analysis does not have any information regarding the precision of the estimates provided by the curve fitting analysis
- Mixed effects models are repeated measures regression models, so continuous variables can be readily included in the models
- Our choice dependent measures are logistic
 - Choice data are binary (SS vs. LL)
- Can use all choices
- Adding random effects (fits to individuals) can increase power to detect fixed (group-level) effects
 - Outliers are pulled towards the group fits (shrinkage), and they carry less weight in the group estimates
 - Uses population-level estimates to reduce Type I error (important for replication crisis)



Why use all of the choices?

- Confidence and likelihood
- Increased power



OR



Choice of Cake = 2 times
Choice of Fruit = 1 time

Choice of Cake = 20 times
Choice of Fruit = 10 times

Choice of Cake = 200 times
Choice of Fruit = 100 times

All = .67



Mixed Effects Regression Models vs. ANOVA

- Can deal with non-systematic data **without participant removal!!!**



Mixed-Effects Models and Non-Systematic Data

- 106 Participants
- Completed Kirby questionnaire
 - 27 different amount-delay combination
- Analyzed choice functions using mixed effects model
- Individual choices ($SS = 0$; $LL = 1$) were entered into the model
- The predictor variable was Log k-value
 - Tested the slope and intercept of the choice function
 - The intercept was centered on the median k-value

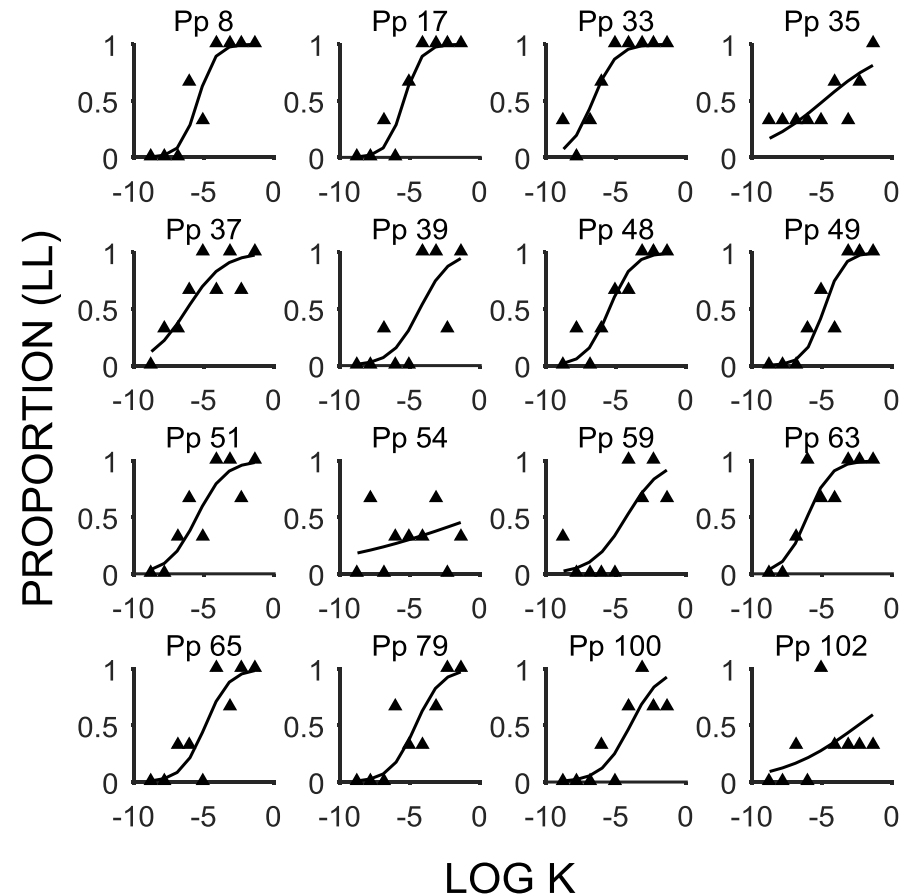


Mixed-Effects Models and Non-Systematic Data

- Identified participants based on Johnson and Bickel (2008)
- Systematic functions
- Non-systematic Type 1 – functions with one or more changes in direction
- Non-systematic Type 2 – functions with minimal change between the lowest and highest k-value



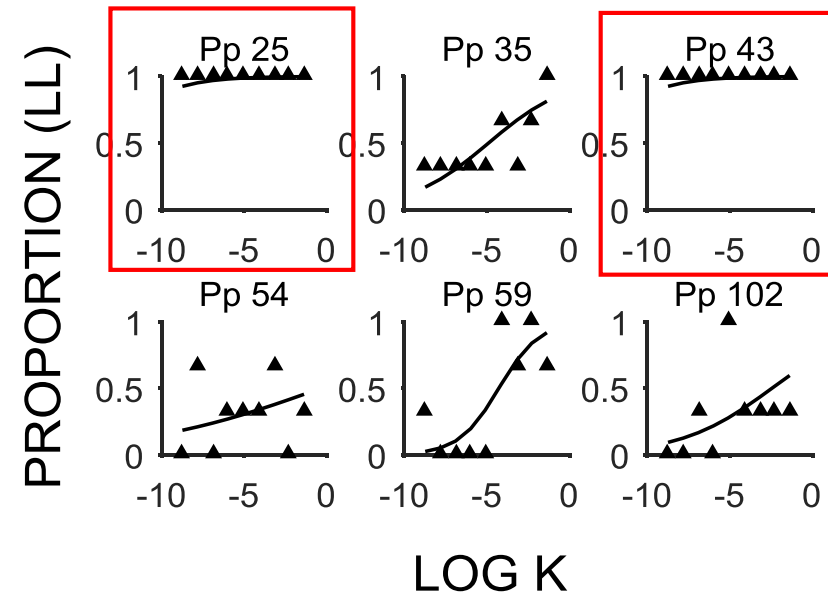
Non-systematic Type 1



Kirkpatrick et al.. (in press)



Non-systematic Type 2



Shrinkage

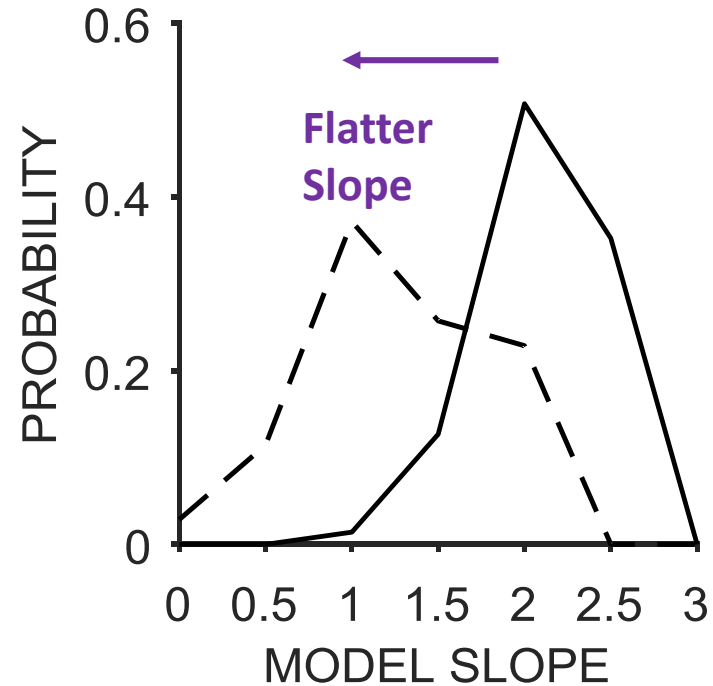
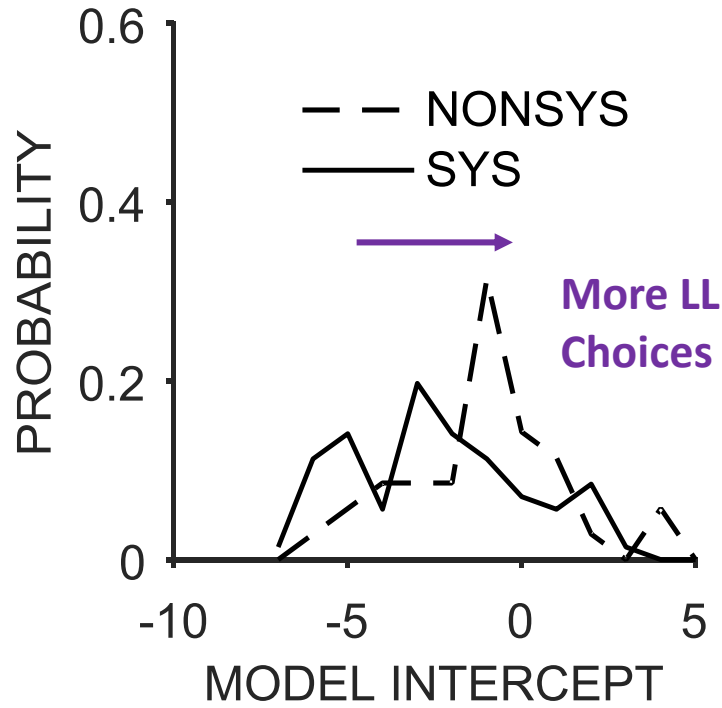
Kirkpatrick et al.. (in press)



Systematic vs. Non-systematic functions

The non-systematic participants made more LL choices at the intercept

The non-systematic participants had a flatter slope (i.e., less sensitive to k-value)





ANOVA vs. Mixed Effects Models

- One more thing...
- They resolve the conflict between pressures:
 - The need to conduct group-level statistics
 - Focus on individuals
- Mixed models focus on both the individual and the group in an integrated framework



Time-based interventions: Questions

- How long do the interventions last? (longevity)
- Do the interventions only promote delay processes within the choice procedure? (generalizability)
 - Or does the intervention affect choice overall?

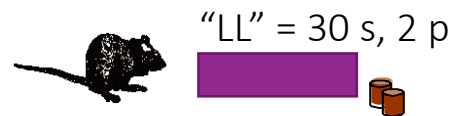


Longevity of Intervention Effects

Fixed Interval

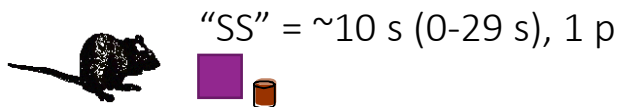


"SS" = 10 s, 1 p

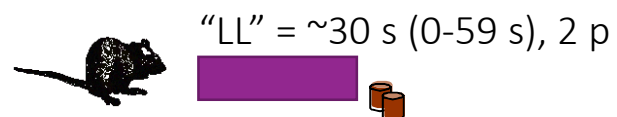


"LL" = 30 s, 2 p

Variable Interval

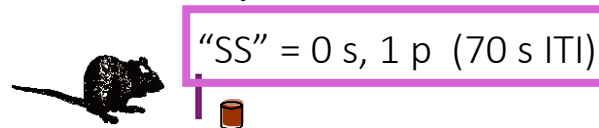


"SS" = ~10 s (0-29 s), 1 p

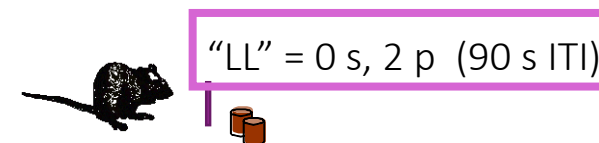


"LL" = ~30 s (0-59 s), 2 p

No Delay

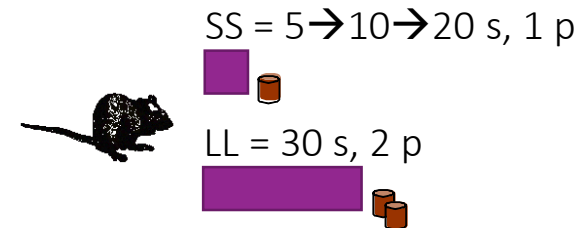


"SS" = 0 s, 1 p (70 s ITI)



"LL" = 0 s, 2 p (90 s ITI)

Impulsive Choice: 0 months



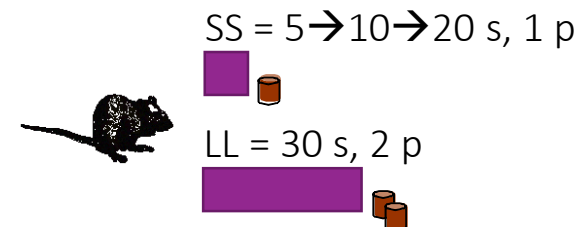
SS = 5 → 10 → 20 s, 1 p

LL = 30 s, 2 p

9 months



Impulsive Choice: 9 months



SS = 5 → 10 → 20 s, 1 p

LL = 30 s, 2 p

Bailey et al. (in press)



Mixed Effects Regression Models vs. ANOVA

- Mixed effects regression models can also be used to parse out different mechanisms of the interventions within the choice task



Delay Processing: Analysis Methods

- Test the slope
 - Sensitivity to SS delay
 - Should map most closely onto delay discounting
- Test the intercept at 0 s
 - Preference for immediacy
- Test the intercept at 30 s
 - Preference for larger magnitude

SS Delay Task

SS = 5 → 10 → 20 s, 1 p



LL = 30 s, 2 p

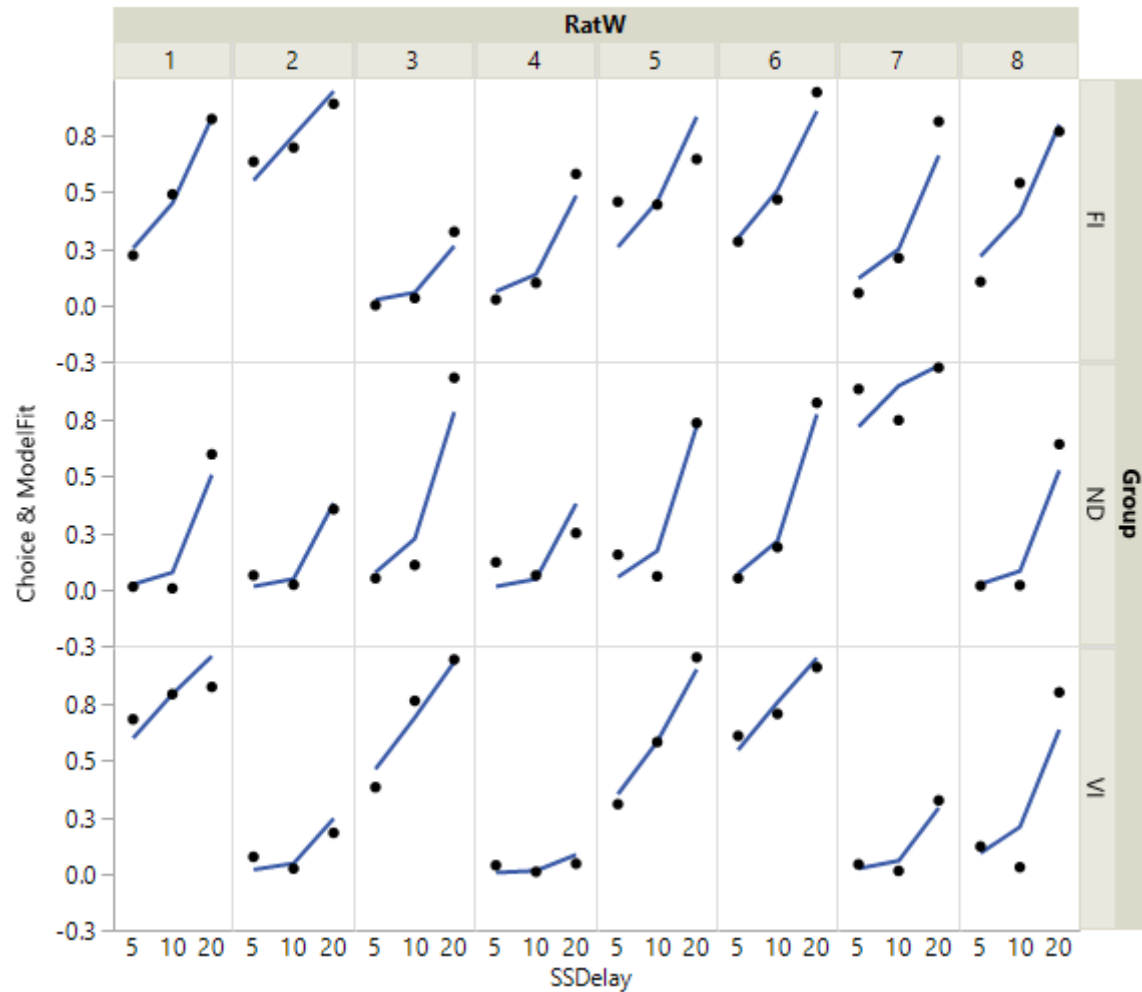


You can also compute k-values!

Wileyto et al. (2004); Young (2017)

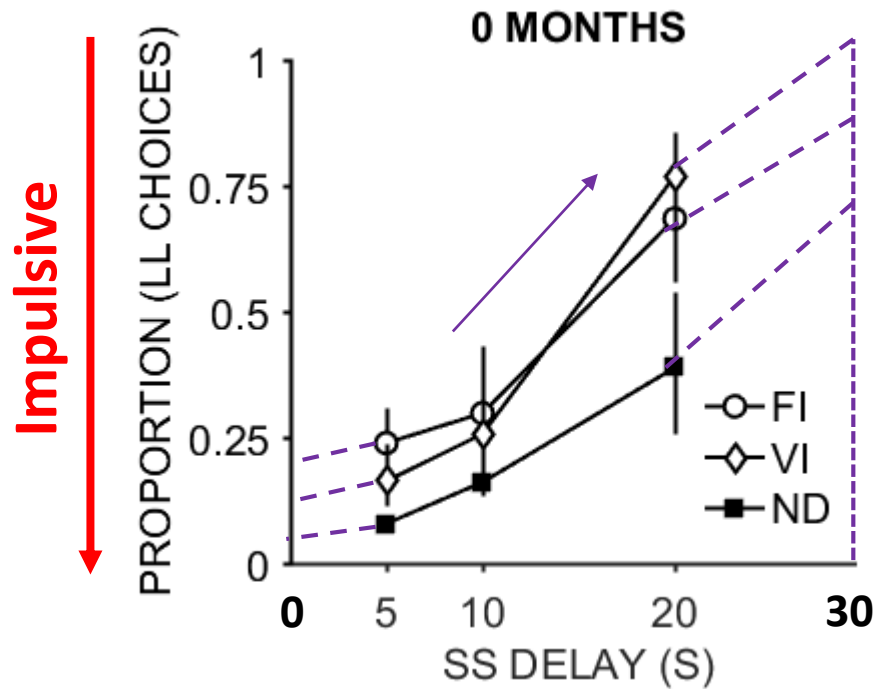


Mixed Effects Model Fits to Individual Rats: 0 Months





Longevity of Intervention Effects

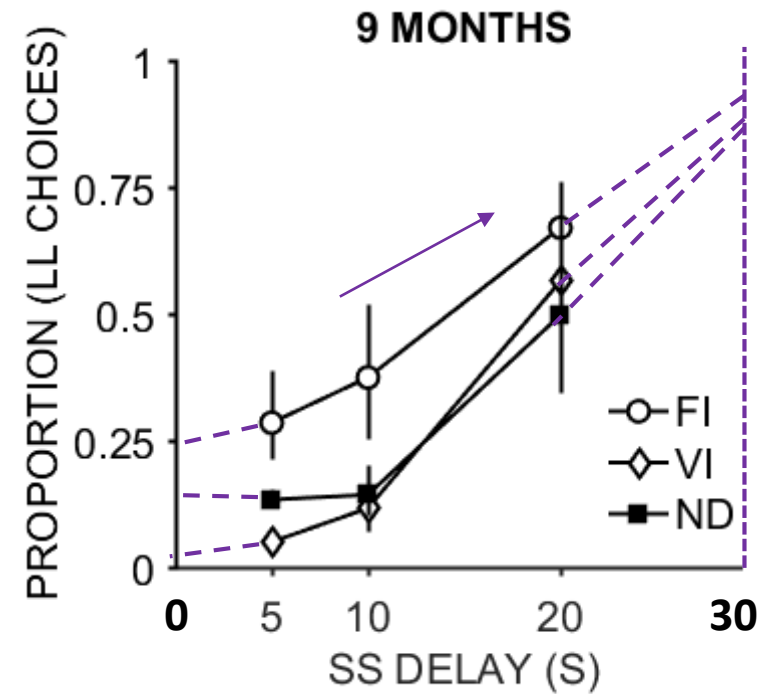
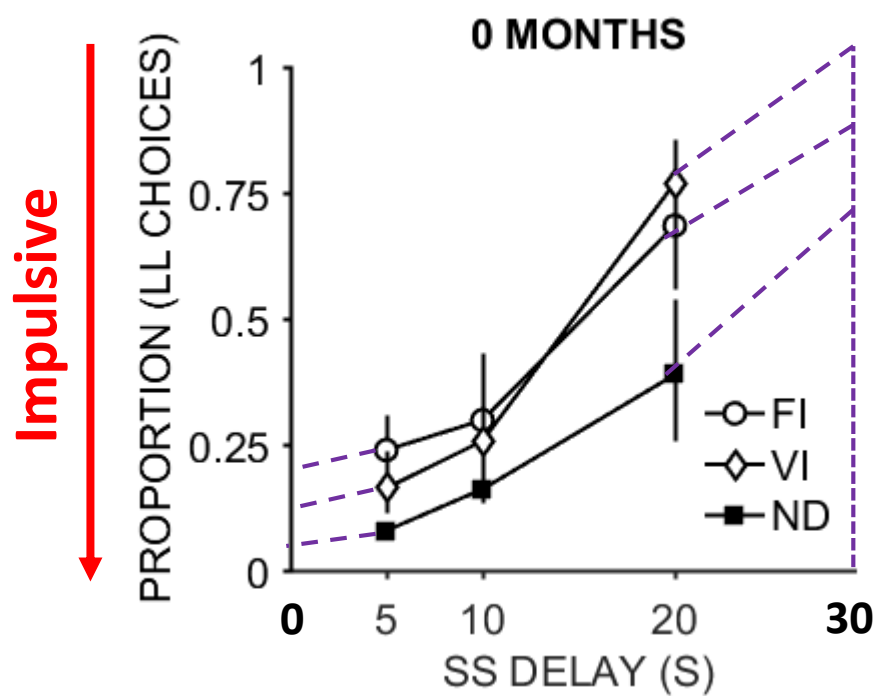


Both FI and VI reduced preference for immediacy
VI increased preference for the larger magnitude
FI decreased sensitivity to SS delay

Bailey et al. (in press)



Longevity of Intervention Effects

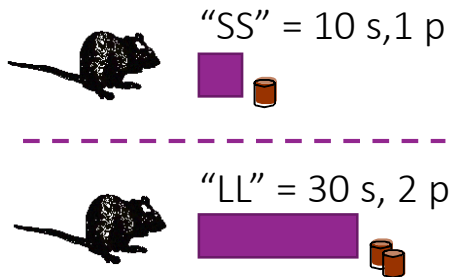


No significant group differences at either intercept
FI group showed reduced sensitivity to SS delay
VI group no longer showed any intervention effect

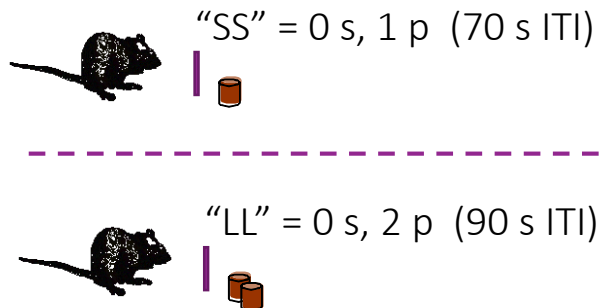


Generalizability of Intervention Effects

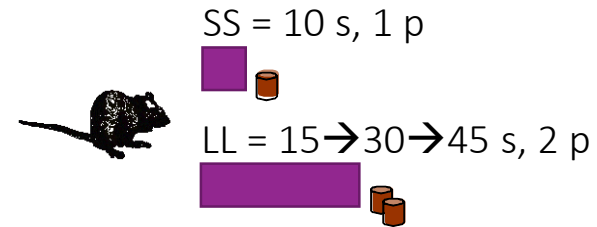
Fixed Interval



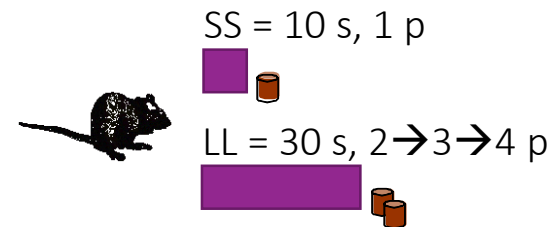
No Delay



LL Delay Task



LL Magnitude Task



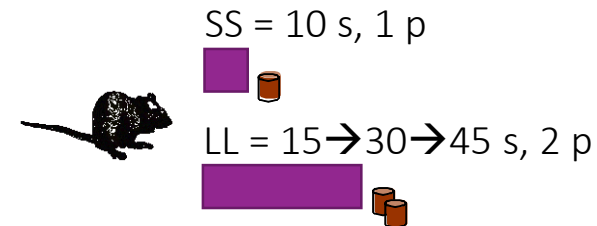
Bailey et al. (in press)



Analysis Methods: LL Delay Task

- Test the slope
 - Sensitivity to LL delay
 - Should map onto delay discounting rate
- Test the intercept at 10 s
 - Preference for the larger magnitude

LL Delay Task

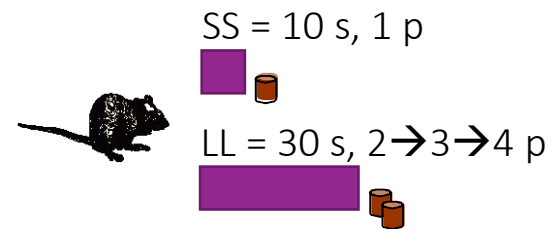




Analysis Methods: LL Magnitude

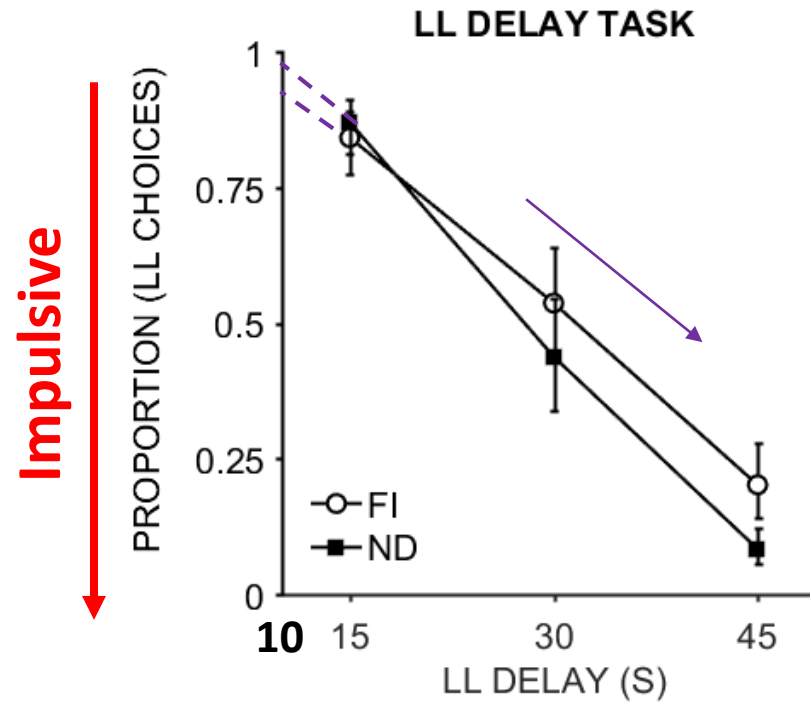
- Test the slope
 - Sensitivity to LL magnitude
 - Should map onto delay discounting rate
- Test the intercept at 1 p
 - Preference for the shorter delay

LL Magnitude Task





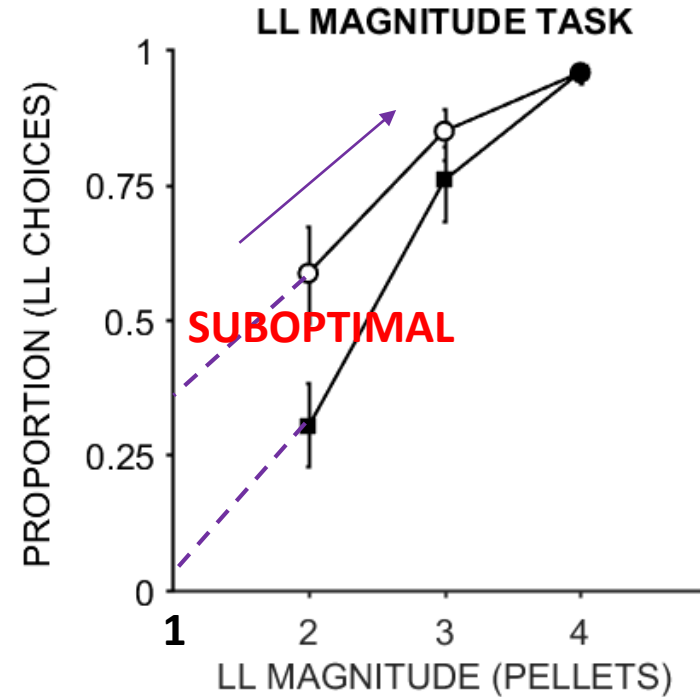
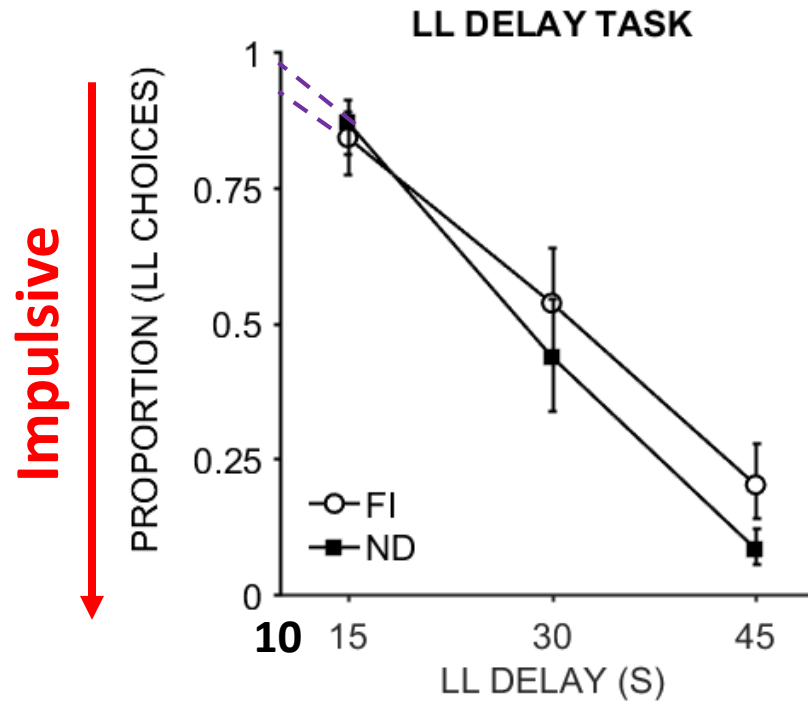
Generalizability of intervention effects



No group differences in magnitude preference
FI group showed reduced sensitivity to LL delay



Generalizability of intervention effects



FI group showed reduced preference for the shorter delay
FI group showed reduced sensitivity to LL magnitude

Bailey et al. (in press)



Interim summary: FI Intervention

- Reduced preferences for immediacy in SS delay task and reduced preferences for shorter delays in LL magnitude task
 - This suggests that the FI intervention may increase the preference for longer delays, even when those preferences are suboptimal
- Reduced sensitivity to delay in SS and LL delay tasks and reduced sensitivity to magnitude in LL magnitude task
 - This suggests that the FI intervention may decrease the delay discounting rate
- Persisted for at least 9 months



Interim summary: VI Intervention

- Reduced preferences for immediacy in SS delay task
 - This suggests that the VI intervention may increase the preference for longer delays
- Reduced sensitivity to delay in SS delay task
 - This suggests that the VI intervention may decrease the delay discounting rate
- Did not persist when tested after a 9-month delay – suggests that training with specific delays is more effective
 - We have not tested intermediate delays

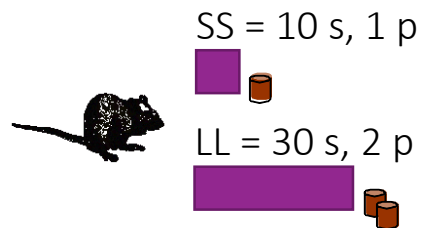


Inhibition and Self-control

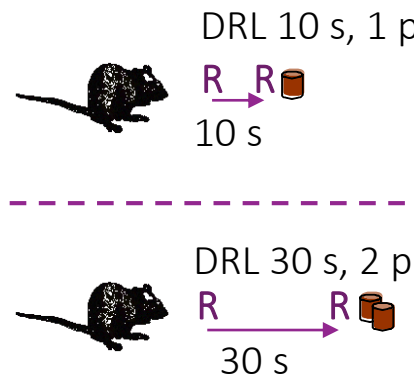


Inhibitory time-based intervention

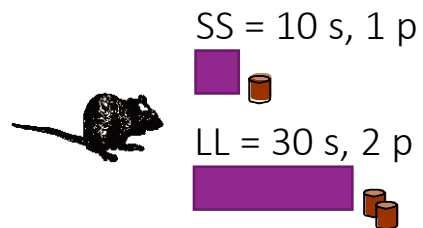
Impulsive Choice



DRL Intervention



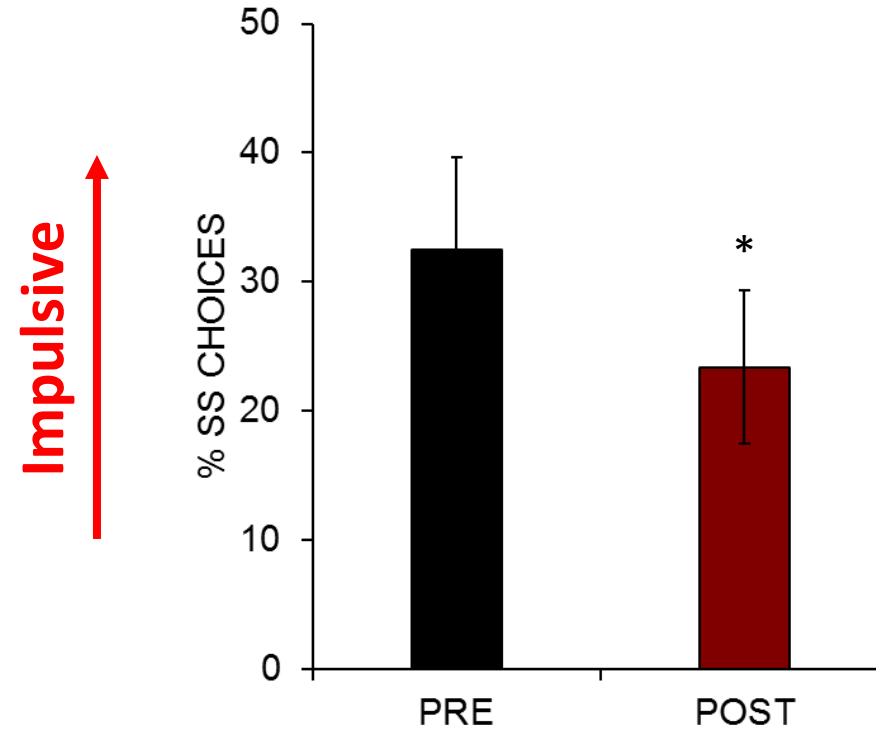
Impulsive Choice



Smith, Marshall, & Kirkpatrick (2015)



Intervention effects on choice



The intervention significantly decreased impulsive choices

Time-based interventions: Questions

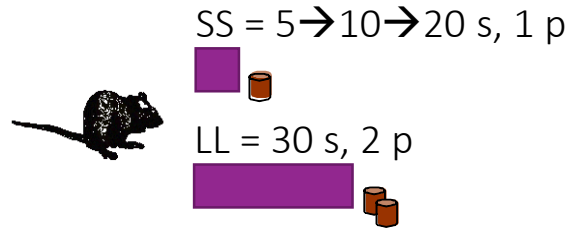
Are the interventions merely inducing self-control (or perhaps delay tolerance)?

Or, are there effects on timing processes?



Time-based intervention: Interval schedules

Impulsive Choice

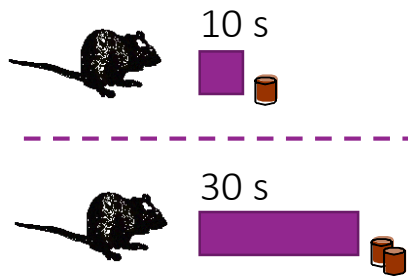


Peak trials

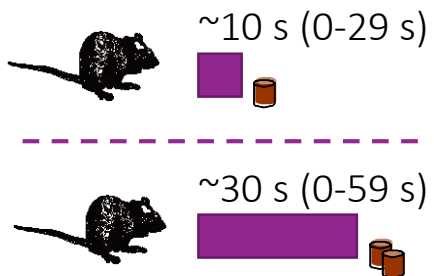
SS = 90 s, 0 p

LL = 90 s, 0 p

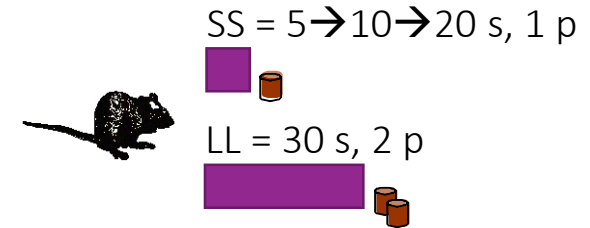
Fixed Interval



Variable Interval



Impulsive Choice



Peak trials

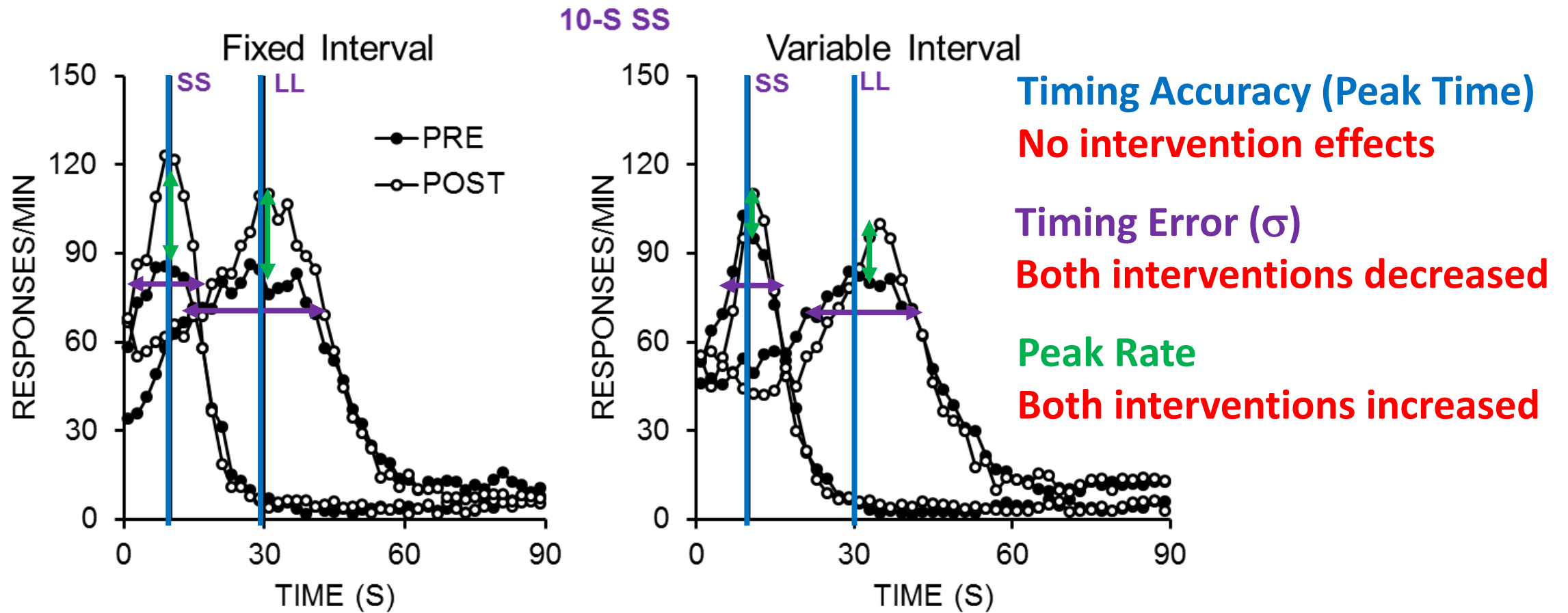
SS = 90 s, 0 p

LL = 90 s, 0 p

Smith, Marshall, & Kirkpatrick (2015)



FI and VI Interventions: Timing





Inhibitory time-based intervention

Impulsive Choice



SS = 5 → 10 → 20 s, 1 p



LL = 30 s, 2 p



Peak trials

SS = 90 s, 0 p



LL = 90 s, 0 p



DRL Intervention



DRL 10 s



10 s

DRL 30 s



30 s

Impulsive Choice



SS = 5 → 10 → 20 s, 1 p



LL = 30 s, 2 p



Peak trials

SS = 90 s, 0 p



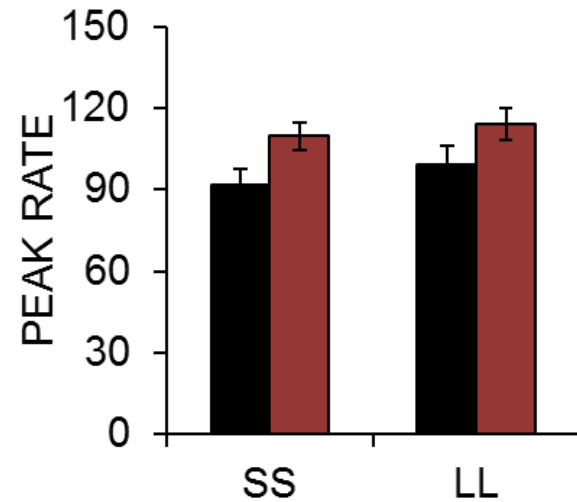
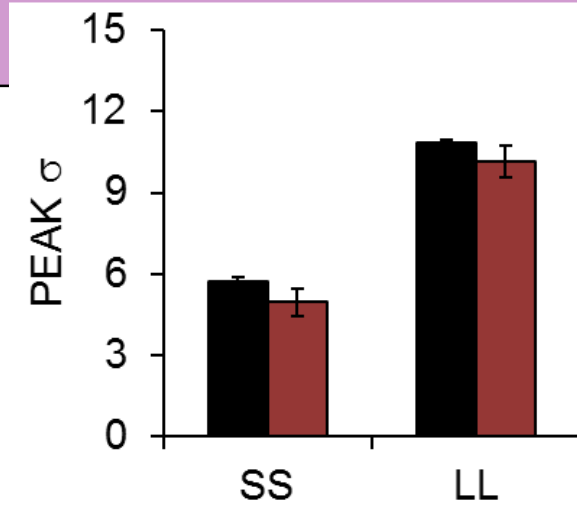
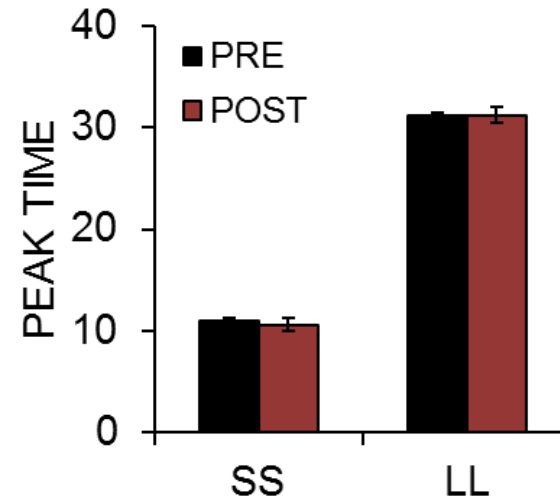
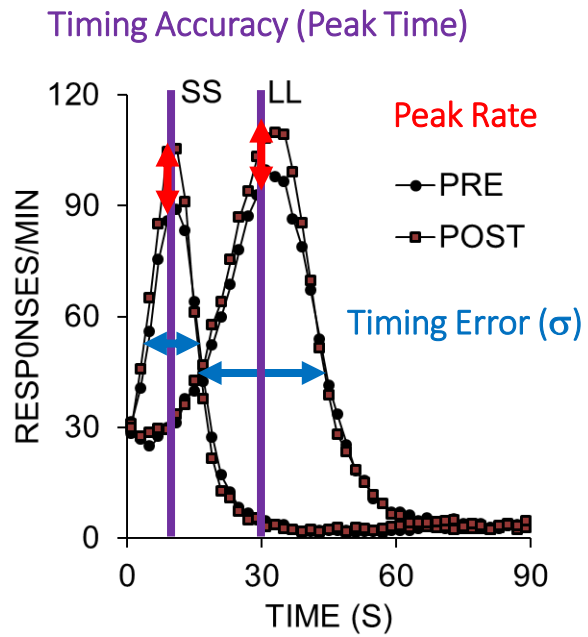
LL = 90 s, 0 p



Smith, Marshall, & Kirkpatrick (2015)



DRL intervention: Timing



Smith, Marshall, & Kirkpatrick (2015)

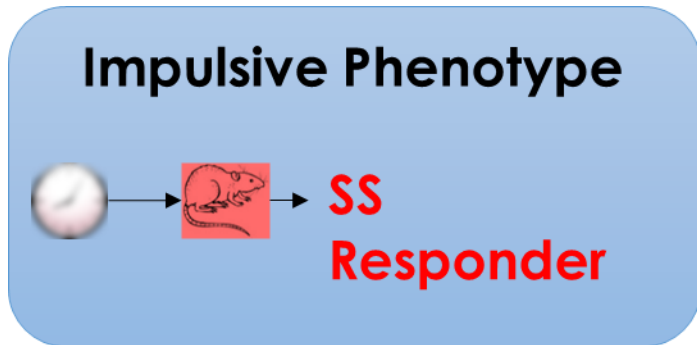


Time-based interventions: Summary

- FI, VI, and DRL interventions improved timing precision while also improving self-control
 - Peaks were had smaller standard deviations (narrower) and higher peak rates
- Combined with the individual differences patterns, these results suggest that poor (noisy) timing may be an important target for intervention work
 - Rats (and people) utilize timing processes when performing on FI, VI, and DRL schedules, and timing appears to improve as a result
 - FI may better target poor timing due to extensive practice with timing specific intervals, which may explain the longevity of effects



Overall summary



Reduced discounting rate
Reduced preference for immediacy/short delays

Impulsive



SS Responders



Self-controlled



LL Responders

Time-based intervention

Pathways to disease/disorder development



Time-based interventions: Extensions

- We have also demonstrated intervention effects on impulsive choice using fixed and variable interval schedules with:
 - ADHD/drug abuse model – Lewis rats (Smith et al., 2015)
 - Middle aged male rats (Peterson & Kirkpatrick, 2016)
 - Female rats –KansABA poster by Schnegelsiepen et al.



Time-based interventions: Future Directions

- Identify and target specific mechanisms within the timing system
- Develop human translational applications – KansABA poster by Duran et al.
- Implement interventions to alter pathways to disease



Acknowledgments



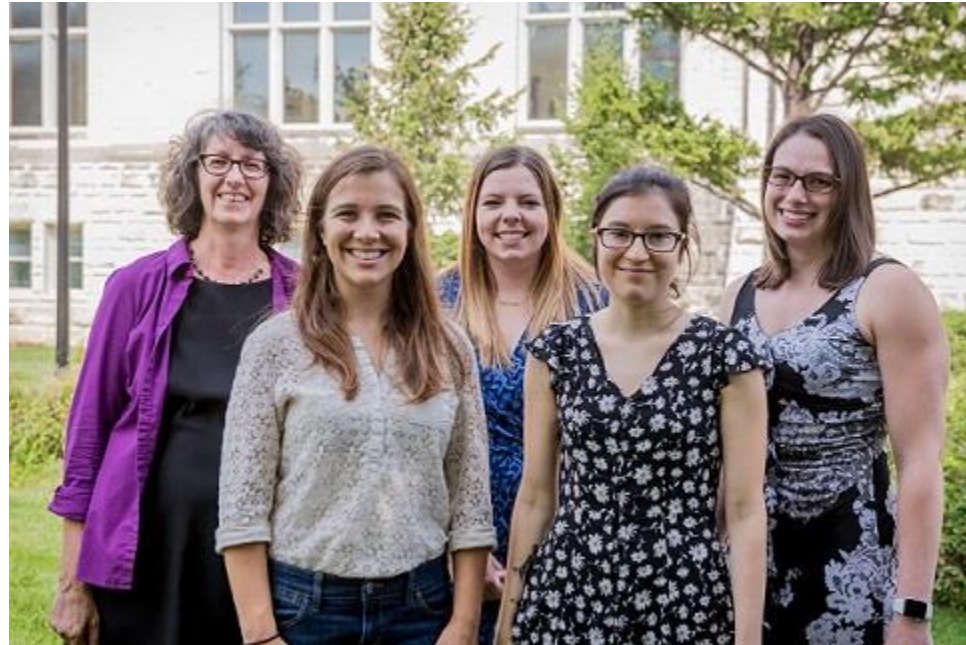
Andrew
Marshall



Jen
Peterson



Aaron
Smith



Cassi
Friday (Binkley)

Catherine
Steele (Hill)

Sarah
Stuebing

Carrie
Bailey



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