



Delay, probability and effort discounting in rats: implications for psychopathology

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Disclosures/Conflict of Interest

➤ None

Session Objectives

- Describe the relationship between delay discounting (DD) and psychopathology
- Describe similarities and differences between delay discounting and discounting due to other types of cost (probability and effort)
- Describe ways in which these other type of discounting may be related to psychopathology

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More DD associated with diagnosis of various psychopathologies

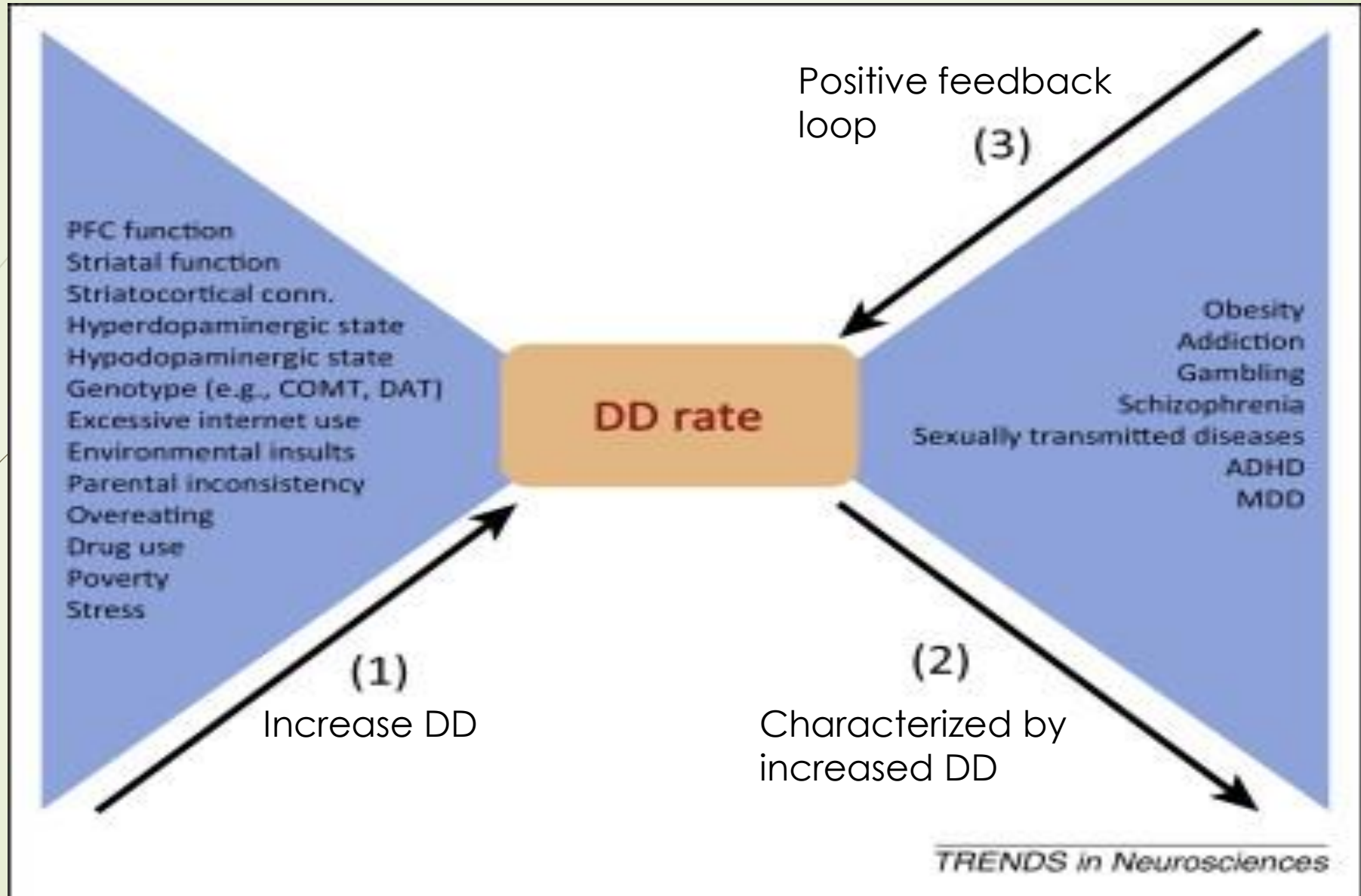
- ADHD
- Conduct disorder
- Borderline personality disorder
- Schizophrenia
- Obsessive compulsive disorder
- Bipolar disorder
- Parkinson's disease
- Depression: mixed
- Substance use – most examined...

Type	Positive (criterion > control)	Negative (criterion = control)	Positive (%)
All ($k=64$)	48	16	75
Alcohol ($k=17$)	11	6	65
Tobacco ($k=19$)	15	4	79
Stimulant ($k=6$)	6	0	100
Marijuana ($k=1$)	0	1	0
Opiate ($k=3$)	3	0	100
Pathological gambling ($k=7$)	4	3	57
Mixed ($k=11$)	9	2	82

Mackillop et al. (2011) Delayed reward discounting and addictive behavior: A meta-analysis. *Psychopharmacology*, 216(3), 305-321.

How is an individual's level of DD related to problem behaviors?

- Hypothesis 1: pre-existing difference?
- Hypothesis 2: consequence associated with developing the condition?
- Hypothesis 3: recidivism/treatment efficacy indicator?



Volkow & Baler (2015) NOW vs LATER brain circuits: implications for obesity and addiction. *Trends in Neurosciences*, 38 (6), 345-352.

Selecting animal procedures to
examine these relationships

Comparing the Adjusting Amount and the Independent Block procedures

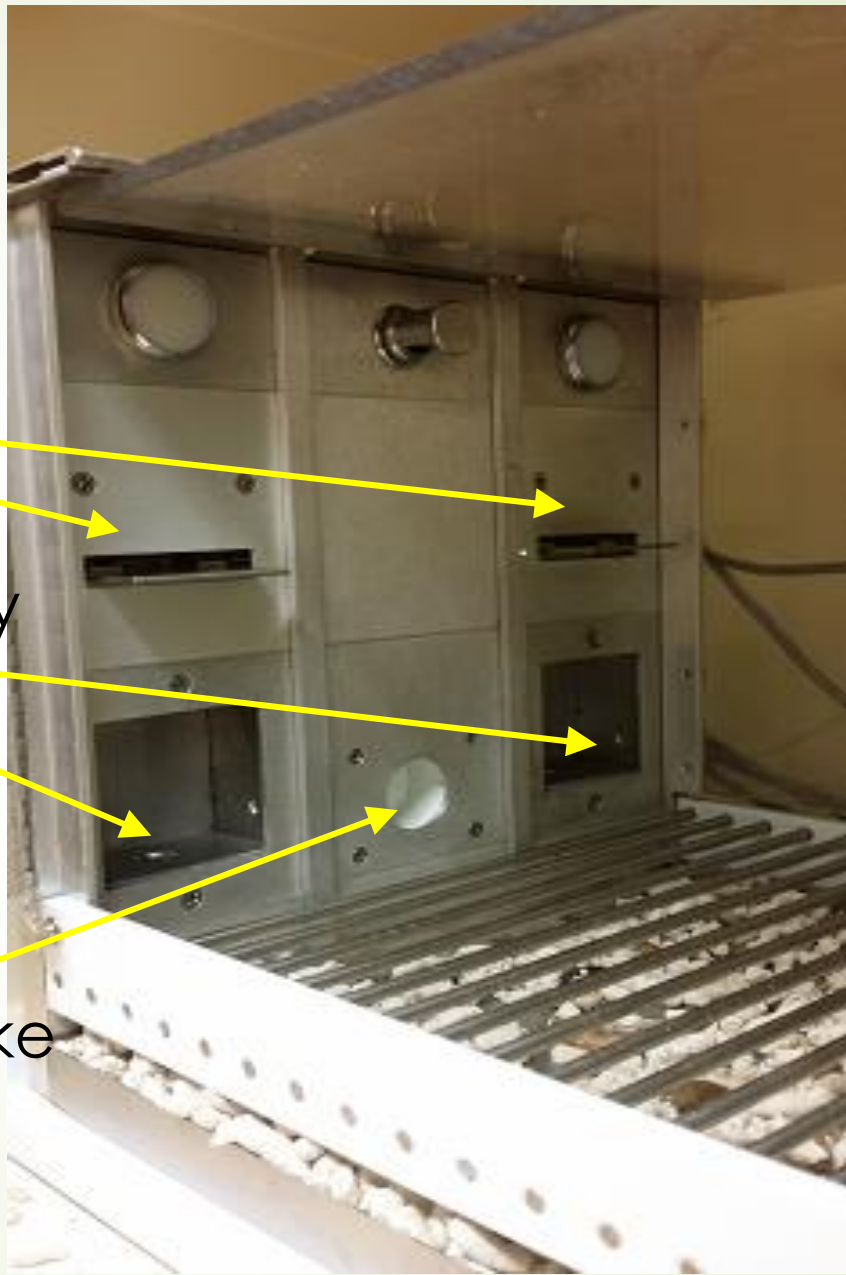
- ▶ 48 male and female rats
- ▶ ABA design: Independent Block – Adjusting Amount – Independent Block
- ▶ Recommend - also check out:
 - ▶ Craig et al. (2014). Do the adjusting-delay and increasing-delay tasks measure the same construct: delay discounting? *Behavioural Pharmacology*, 25(4), 306-315.
 - ▶ Green et al. (2007). Do adjusting-amount and adjusting-delay procedures produce equivalent estimates of subjective value in pigeons? *Journal of the Experimental Analysis of Behavior*, 87(3), 337-347.

Equipment

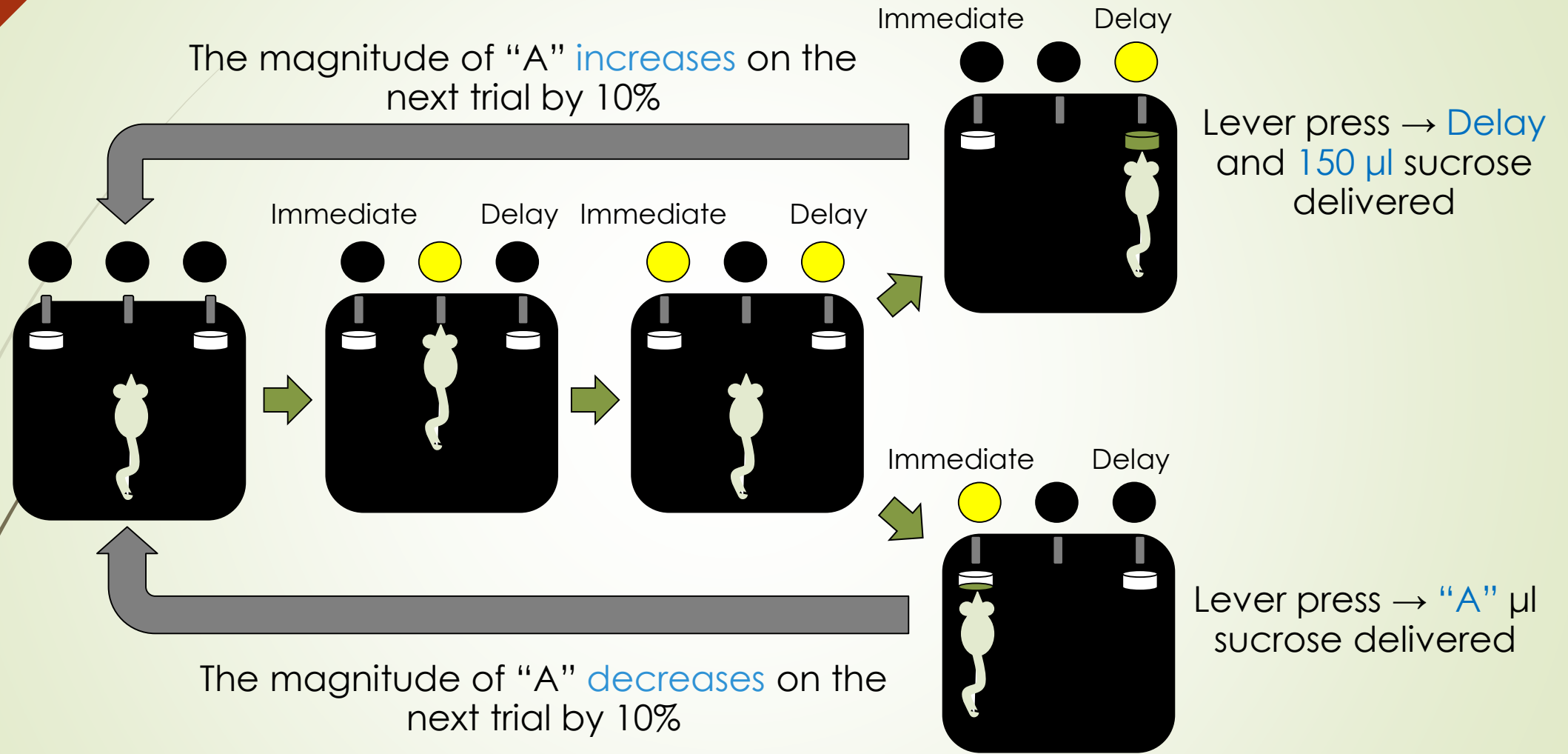
lever

sucrose delivery well

center nosepoke

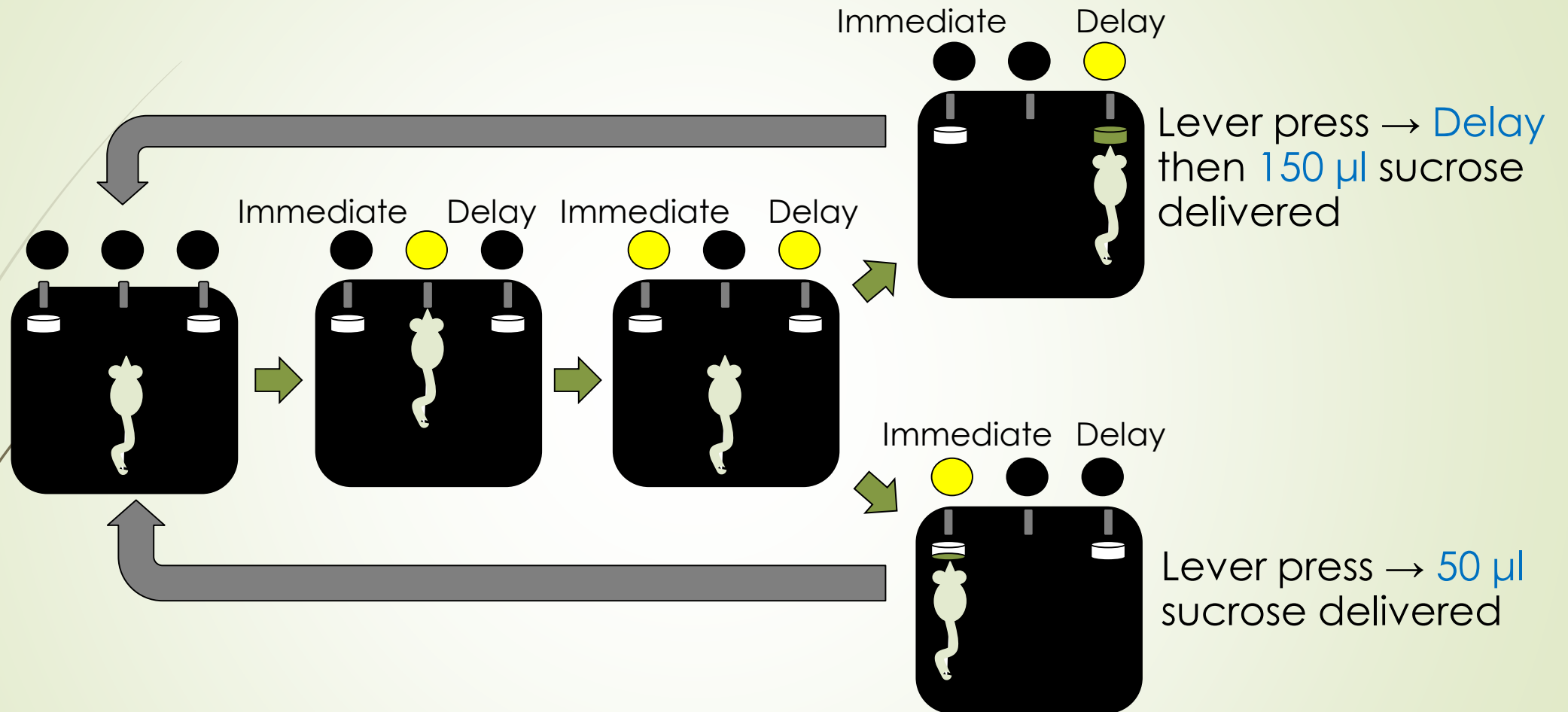


Adjusting amount procedure schematic



Richards et al. (1997). Determination of discount functions in rats with an adjusting-amount procedure. *Journal of the Experimental Analysis of Behavior*, 67(3), 353-366.

Independent block procedure - 1

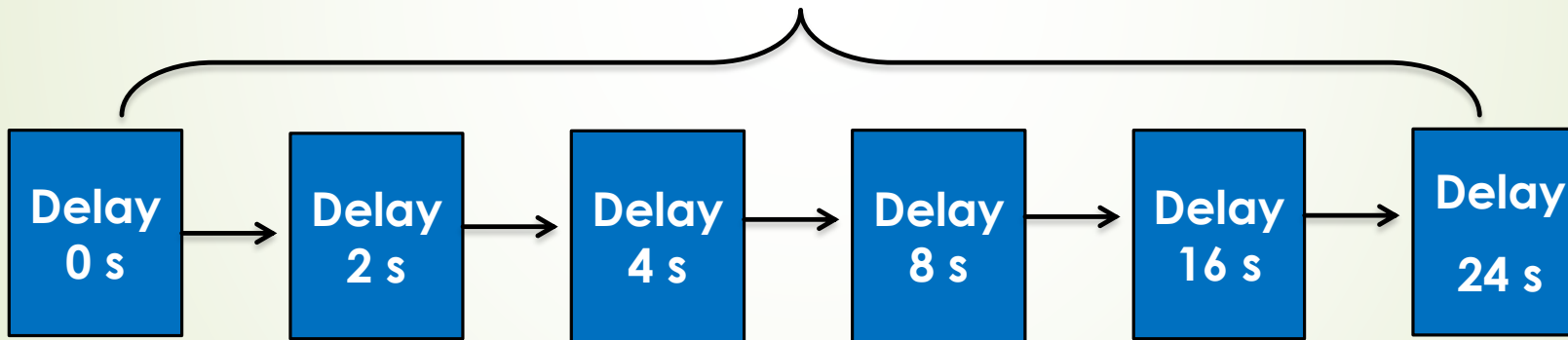


Delay side = right for all subjects

Evenden & Ryan (1996). The pharmacology of impulsive behaviour in rats: The effects of drugs on response choice with varying delays of reinforcement. *Psychopharmacology*, 128(2), 161-170.

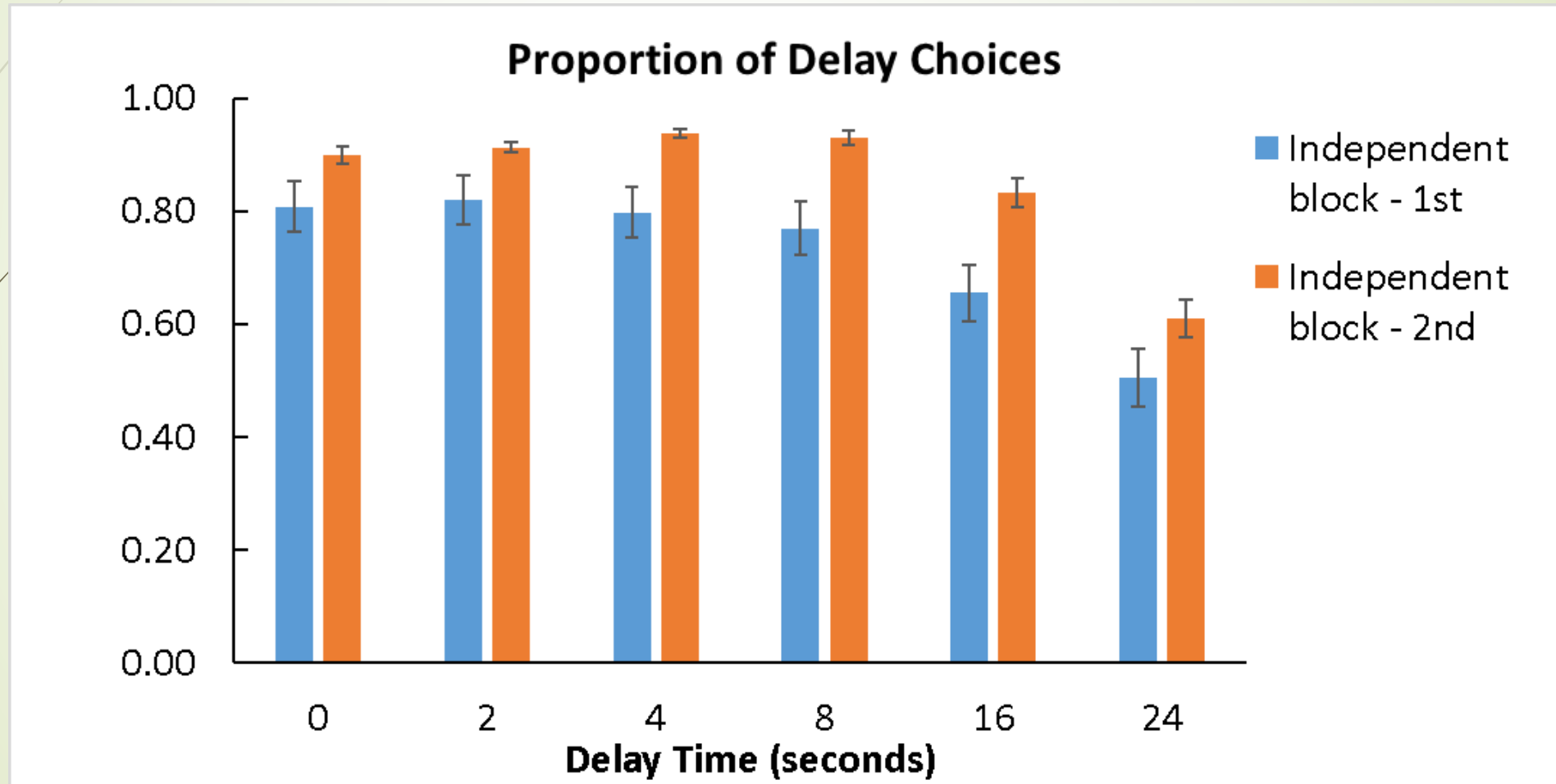
Independent blocks procedure - 2

**6 Blocks of 12 free choices (+ 4 forced choices)
delay increases SYSTEMATICALLY over blocks**

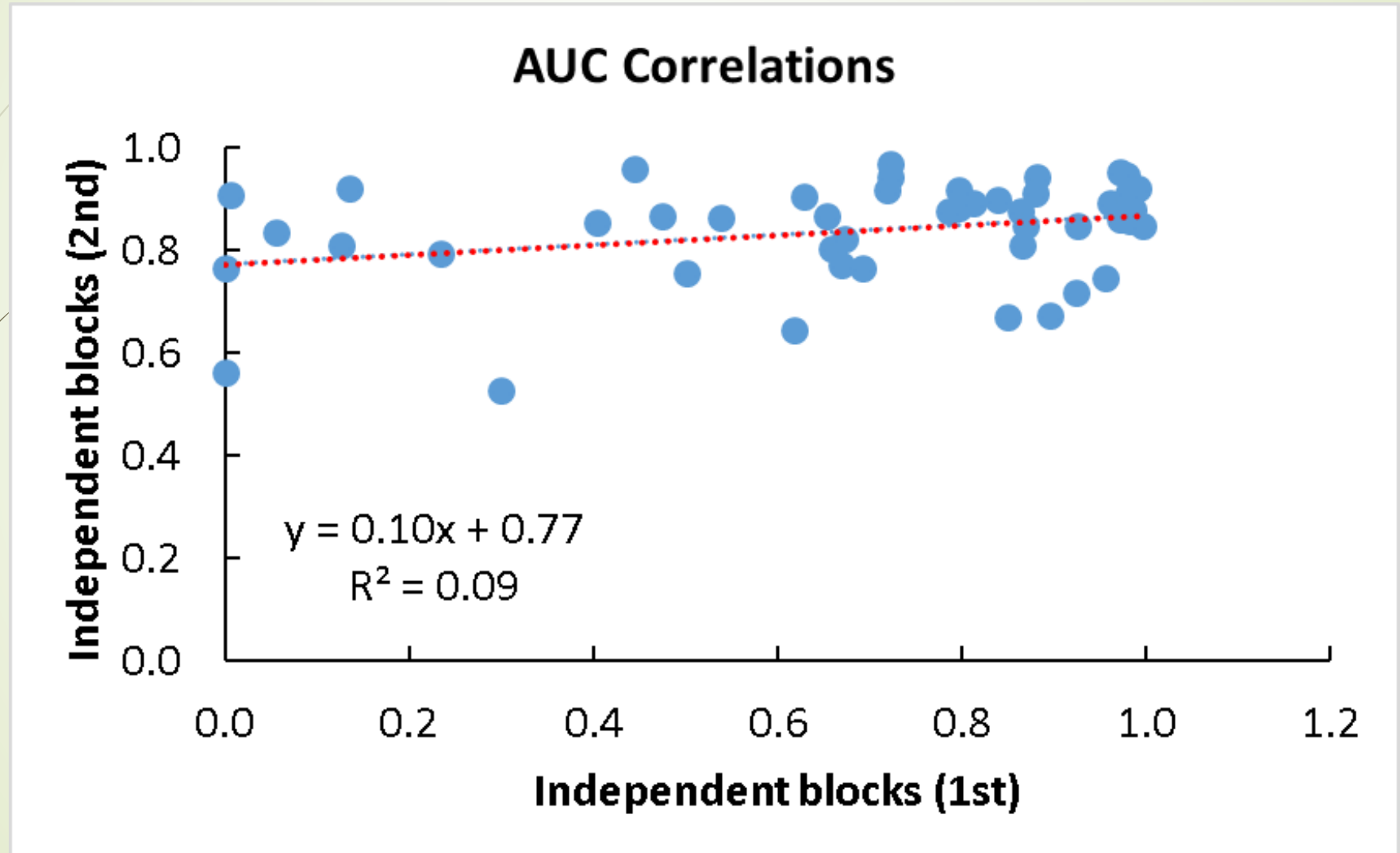


Independent block	Adjusting amount
Multiple delays/session	One delay/session
Fixed size immediate reward	Variable size immediate reward
Fixed size delayed reward	Fixed size delayed reward
DV = Percent choice	DV = Immediate reward size at indifference

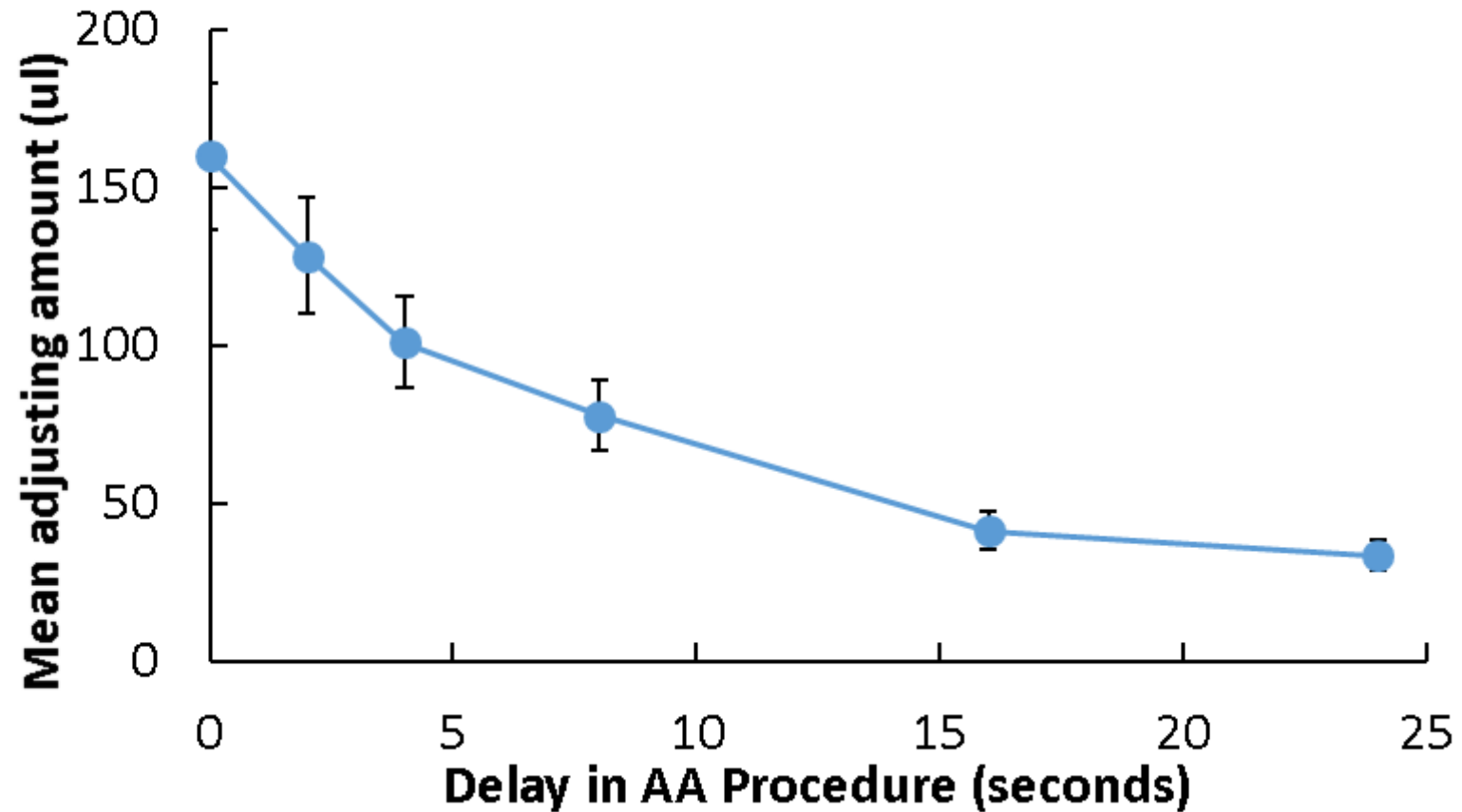
Significant increase in choice of LL between Independent Block periods of ABA design



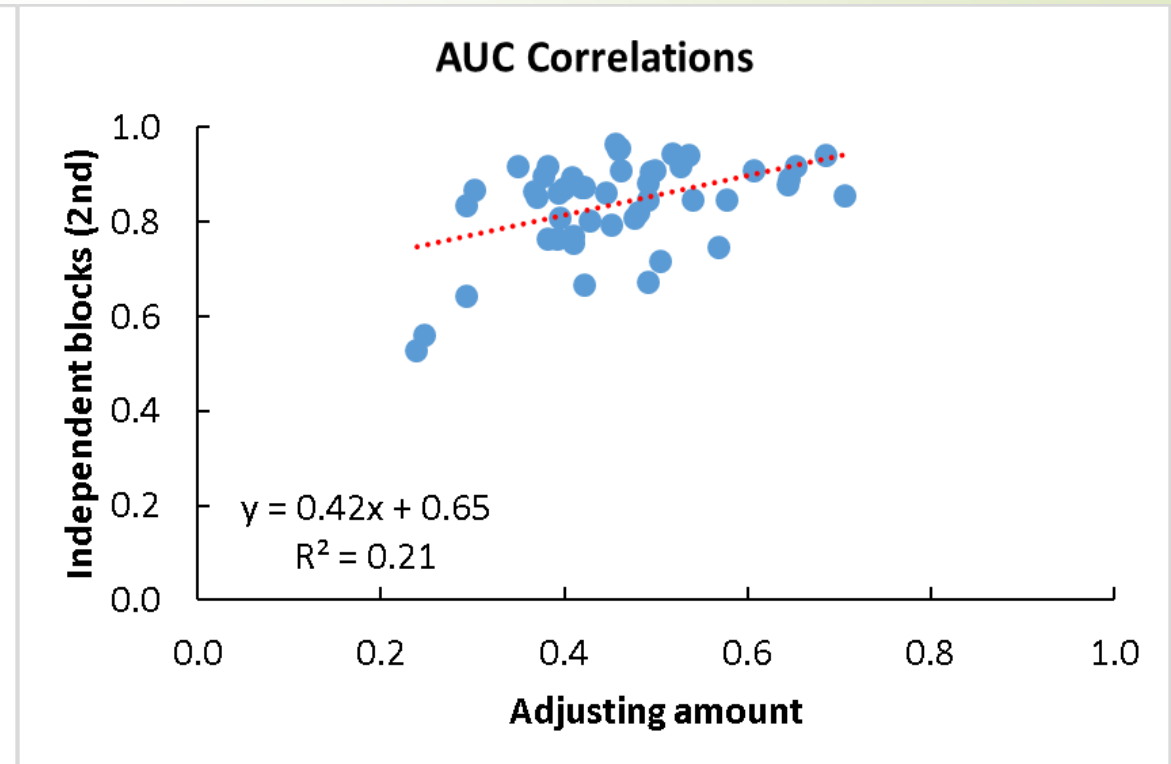
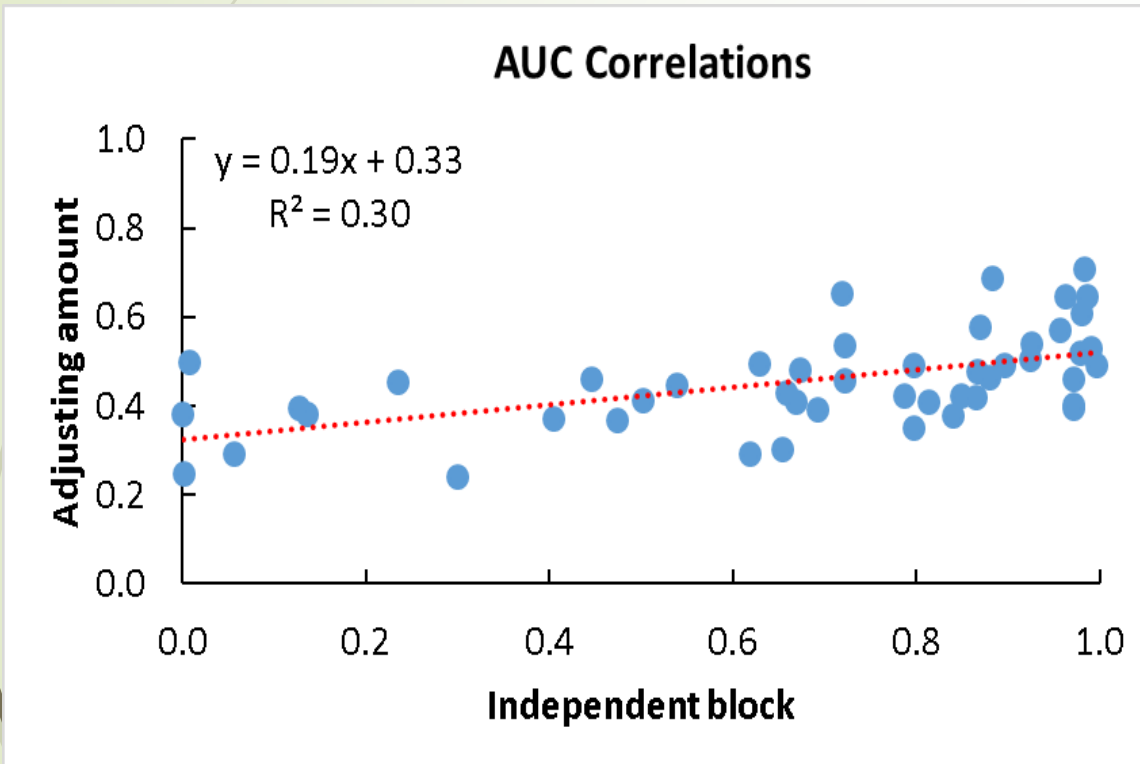
Areas Under the Curve (AUCs) are not correlated due to increased LL choice



Rats discounted systematically in the adjusting amount procedure



Limited positive correlations between DD assessed using each procedure

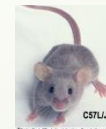
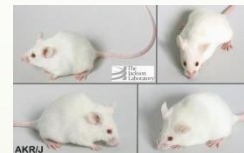
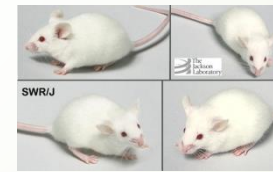
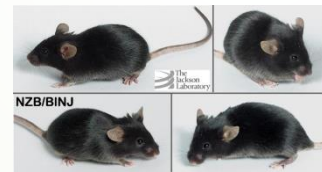
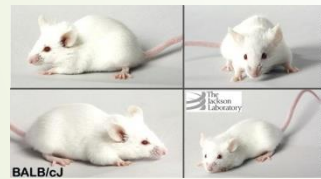
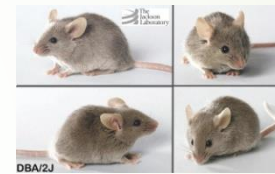
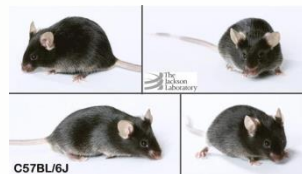


Results summary and conclusions

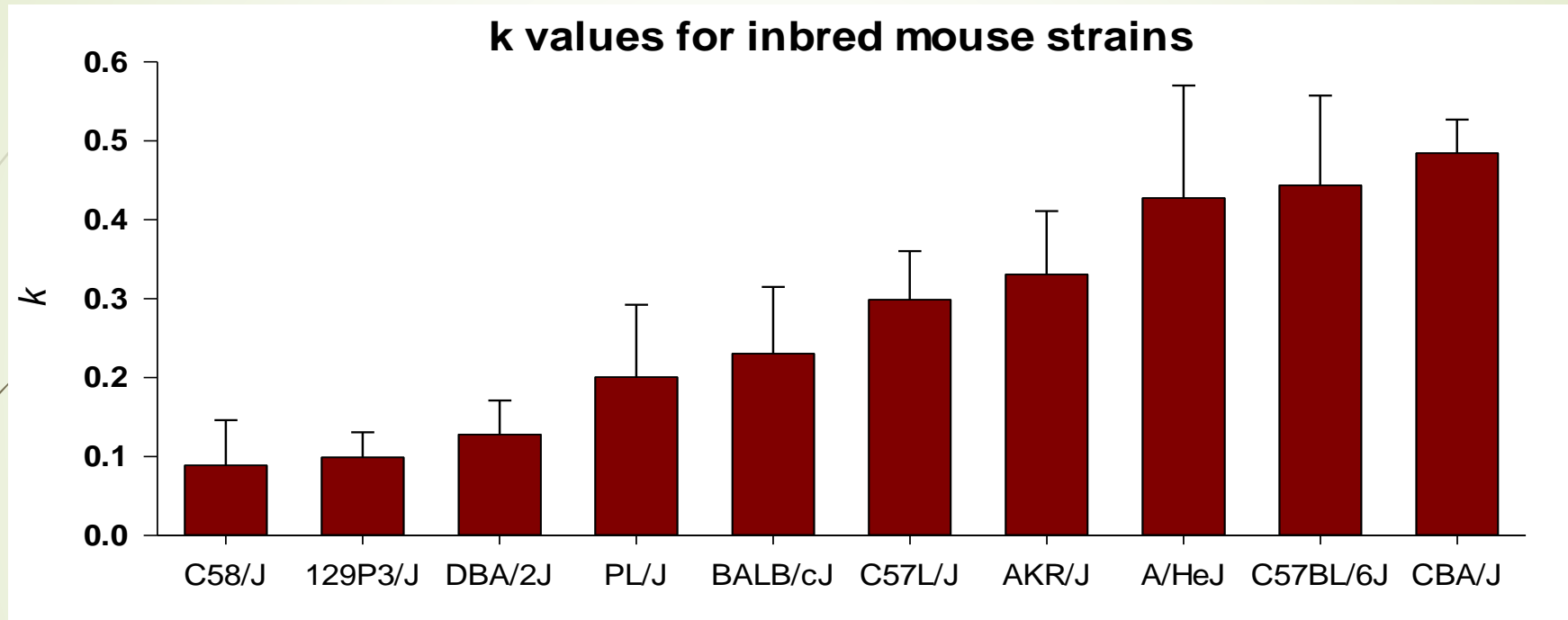
- Typical discount functions obtained in all 3 conditions
- Reduced LL choices in 2nd Independent Block condition relative to 1st
- Positive correlation between AUCs for Independent Block and Adjusting Amount procedures
- Implications for research...
 - Which procedure to use?
 - Will results generalize?

Using DD procedures in mice to assess the DD-alcohol dependence relationship

- 15 inbred mouse strains:
A/HeJ, AKR/J, BALB/cJ, C3H/HeJ, C57BL/6J, C57L/J,
C58/J, CBA/J, DBA/1J, DBA/2J, NZB/B1NJ, PL/J, SJL/J,
SWR/J, 129P3/J



Strain differences in mice indicate a heritable component for DD ($h^2 = 0.32$)



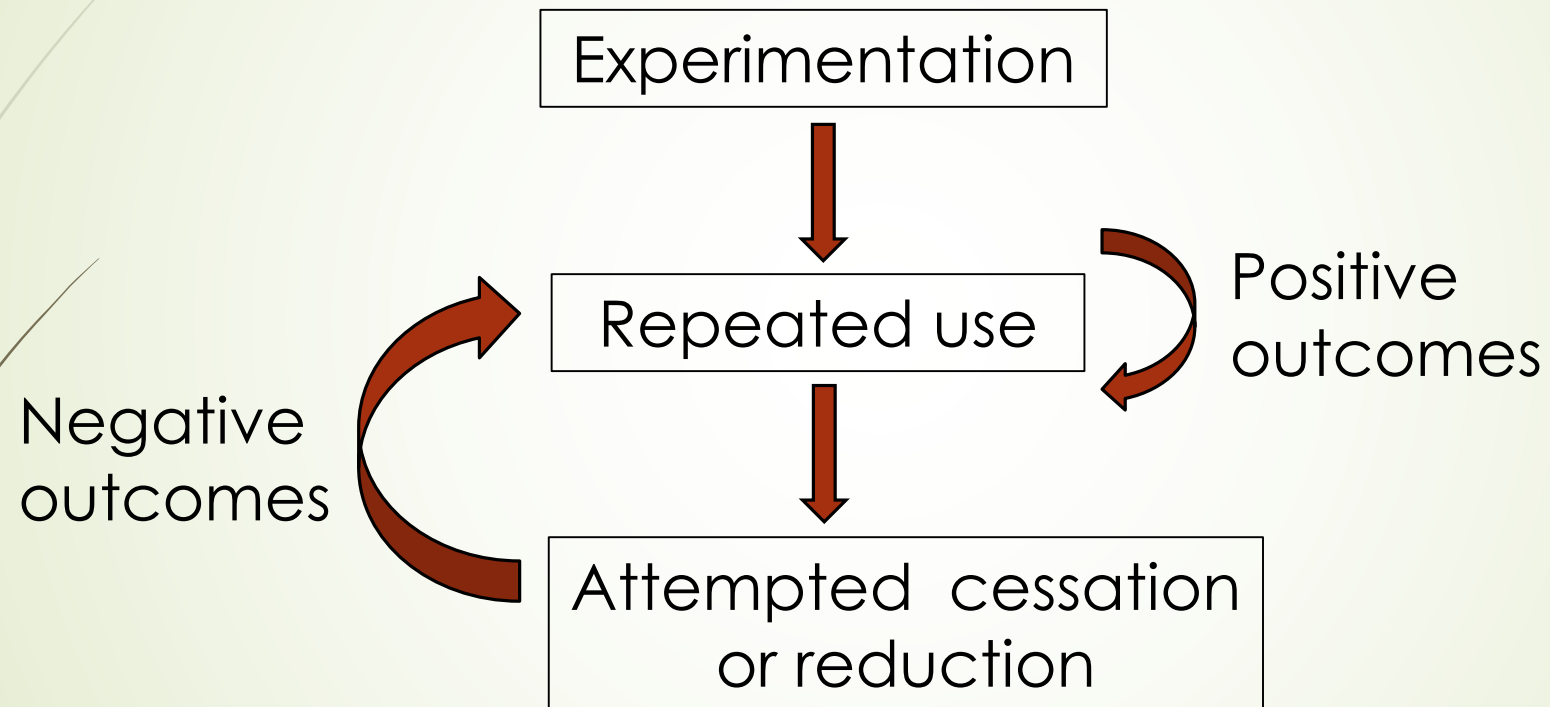
Similar h^2 values results reported by:

Isles et al (2004) - 4 strains of mice

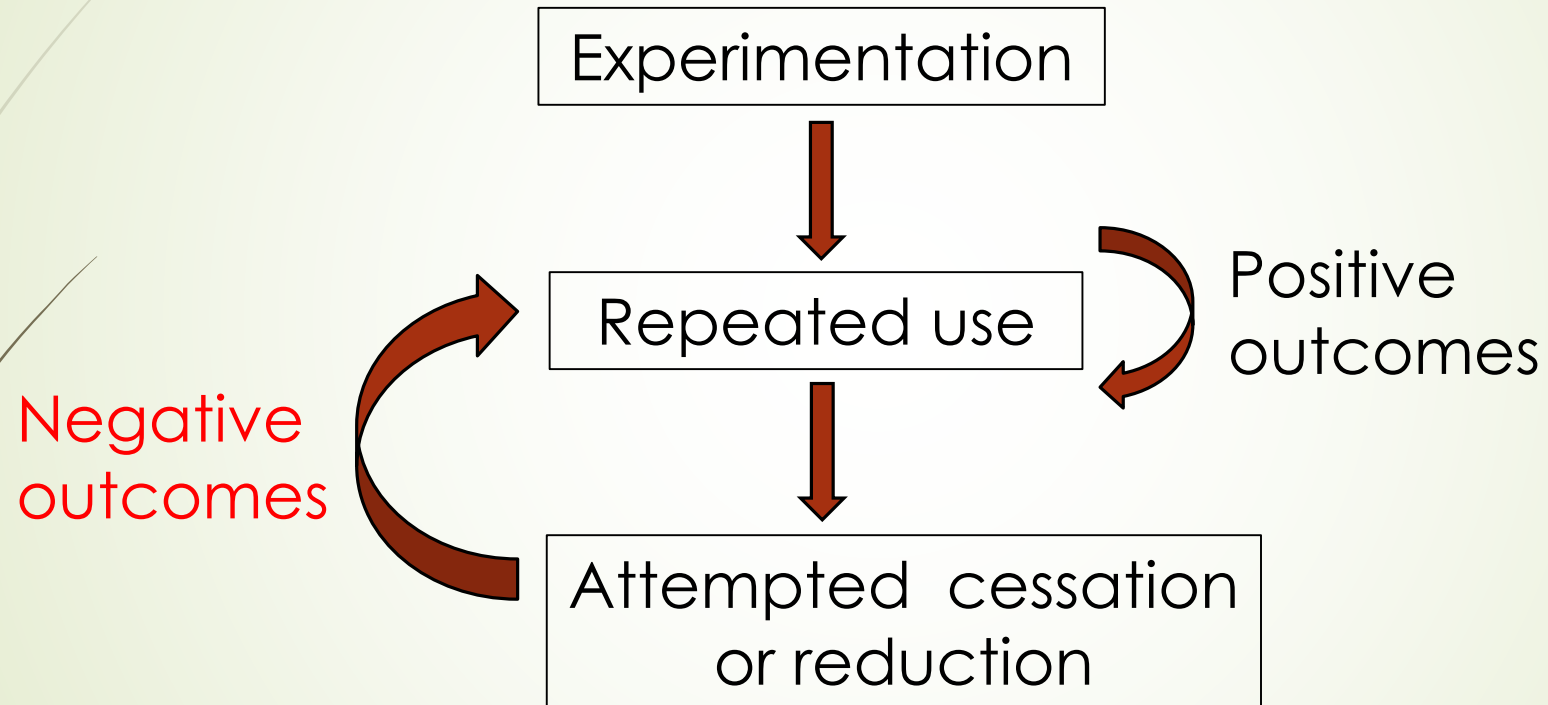
Wilhelm & Mitchell (2009) - 6 strains of rat

Anokhin et al. (2010; 2015) – twins

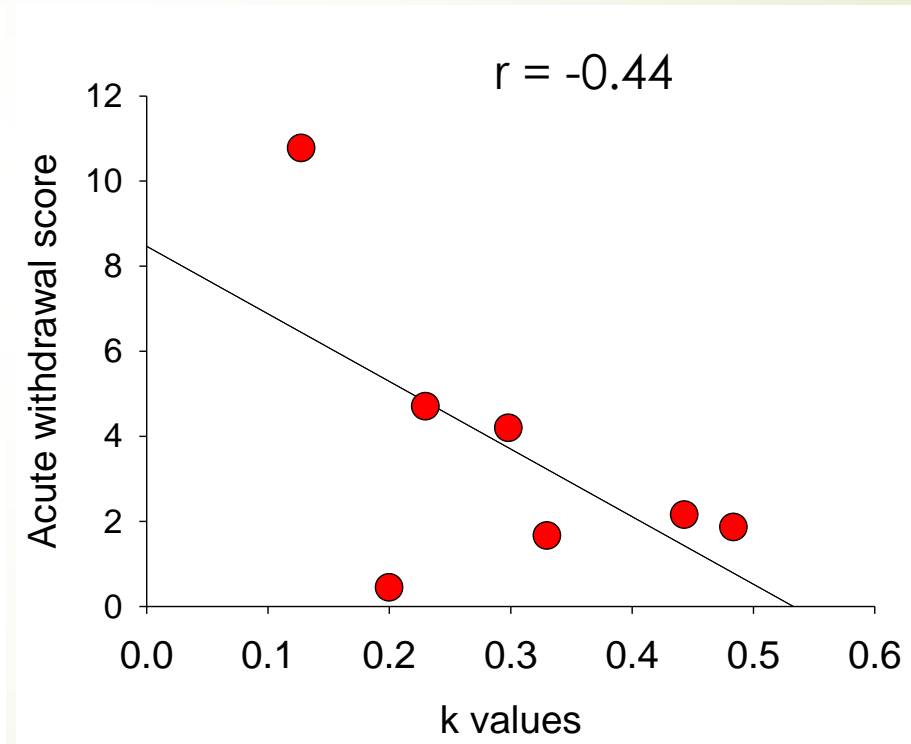
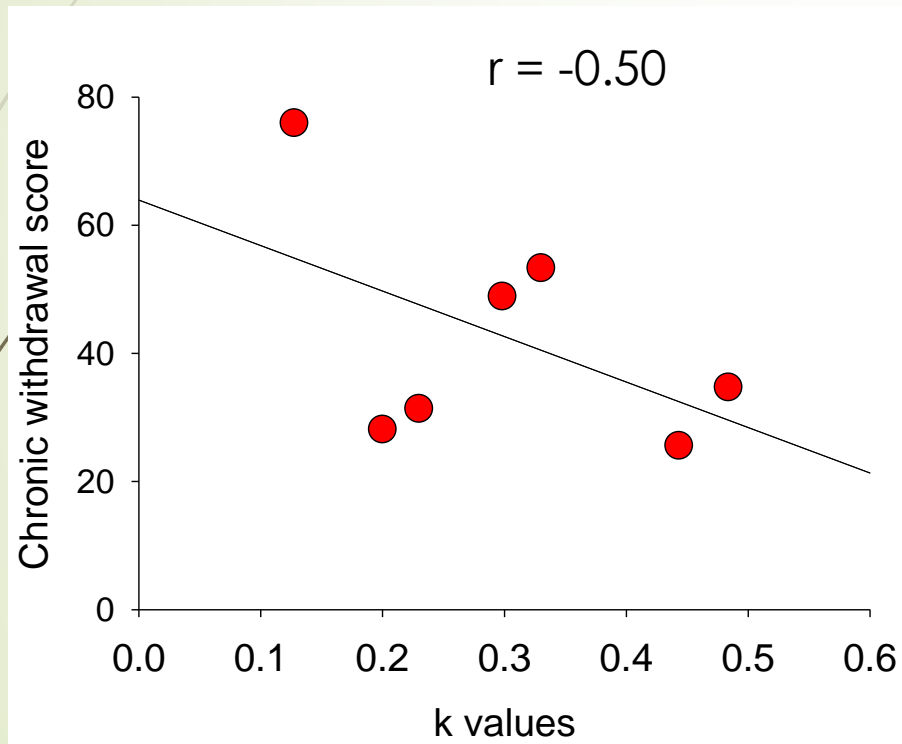
How might genotype influence alcohol use?



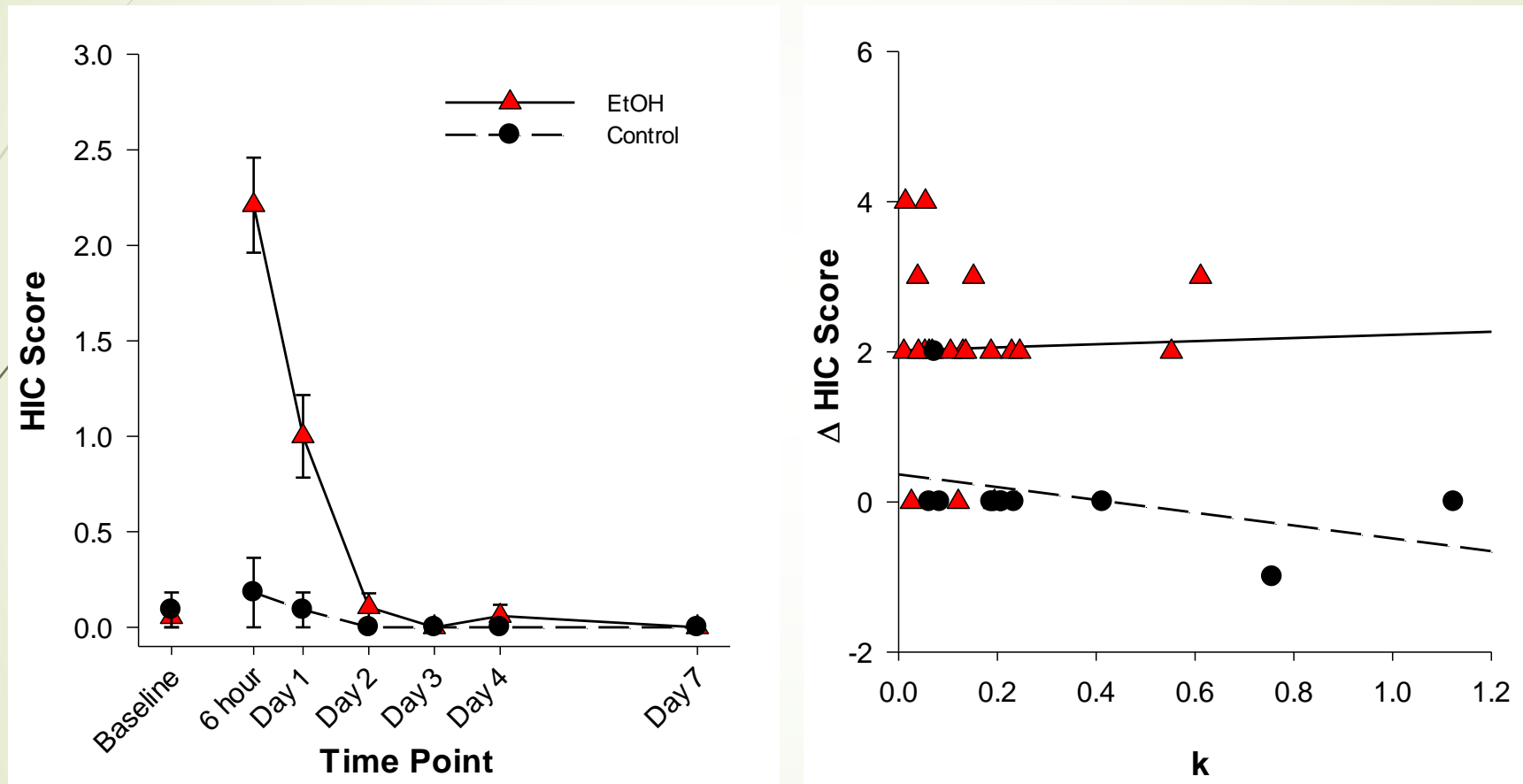
How might genotype influence alcohol use?



Low negative correlation between DD and ethanol-related traits (negative outcomes) obtained for inbred strains of mice

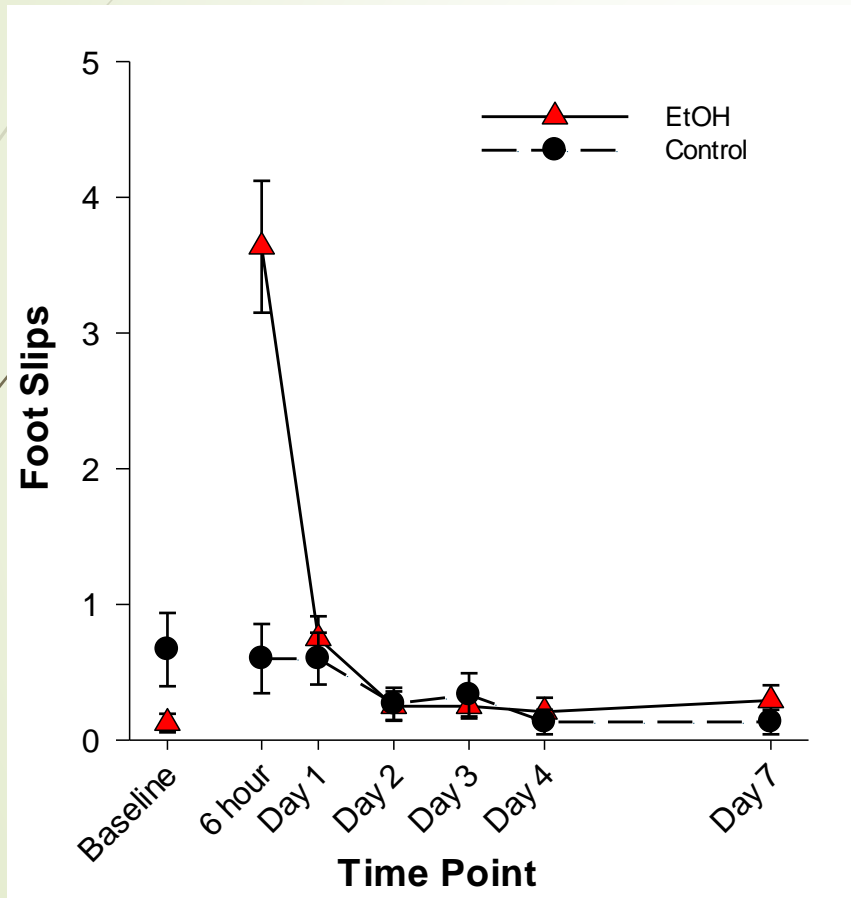


DD was unrelated to withdrawal (HIC score) in genetically heterogeneous (WSC) mice

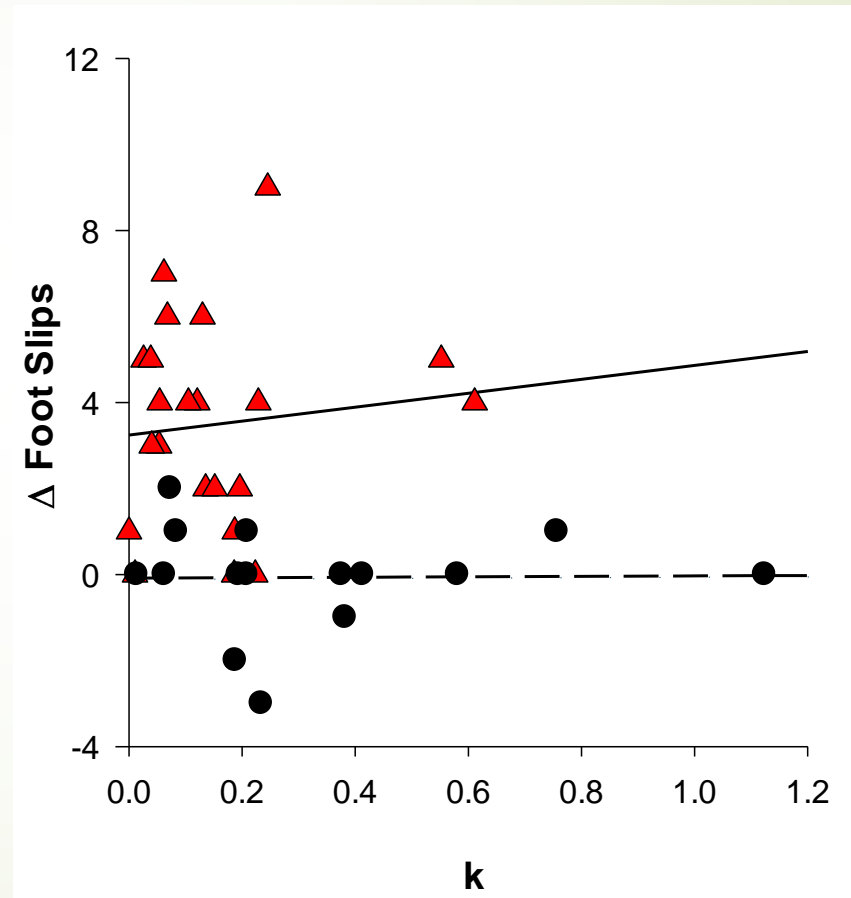


(EtOH: n = 19; Control: n = 11)

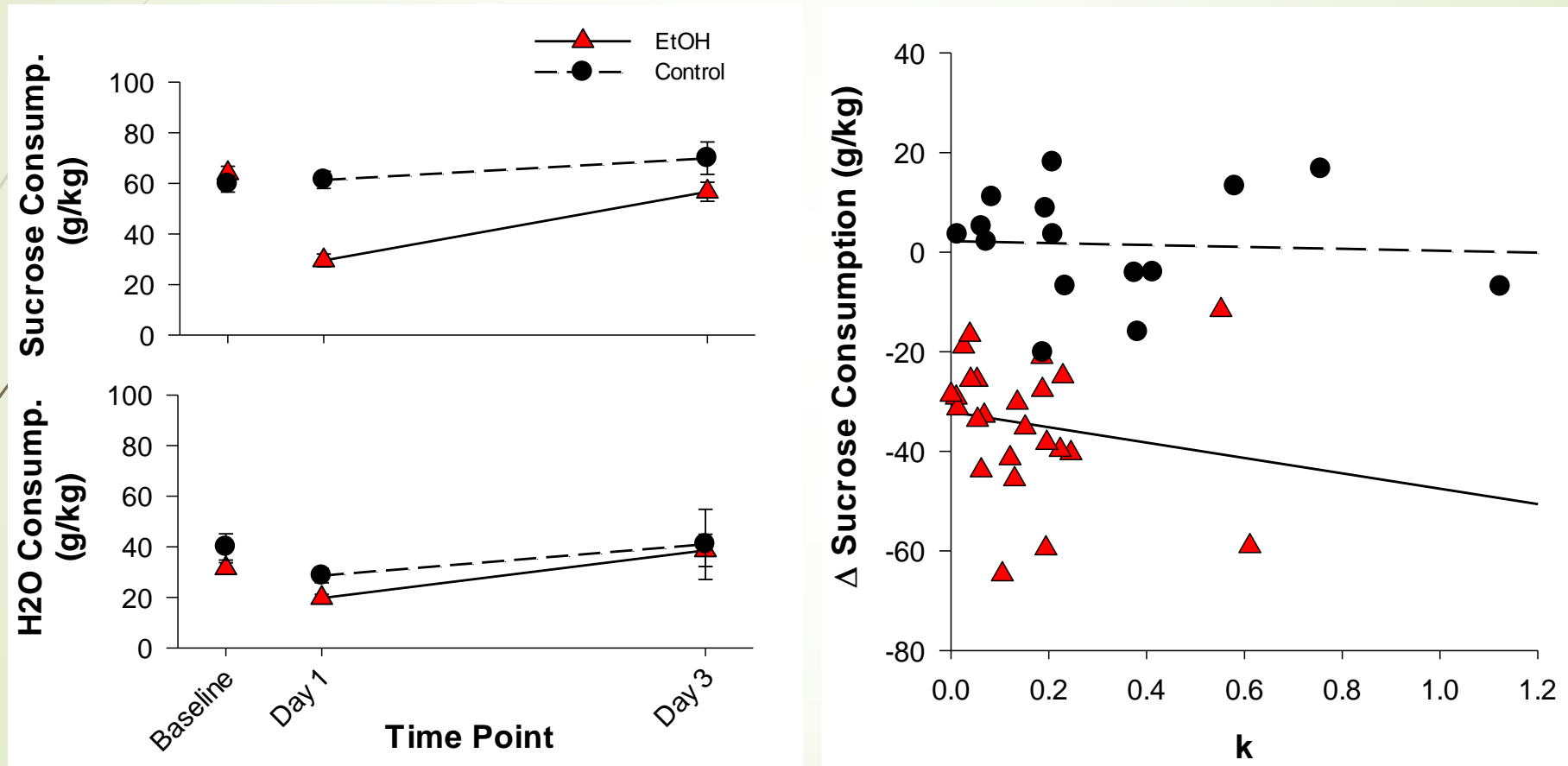
DD was unrelated to motor symptoms during withdrawal in genetically heterogeneous (WSC) mice



(EtOH: n = 24; Control: n = 15)

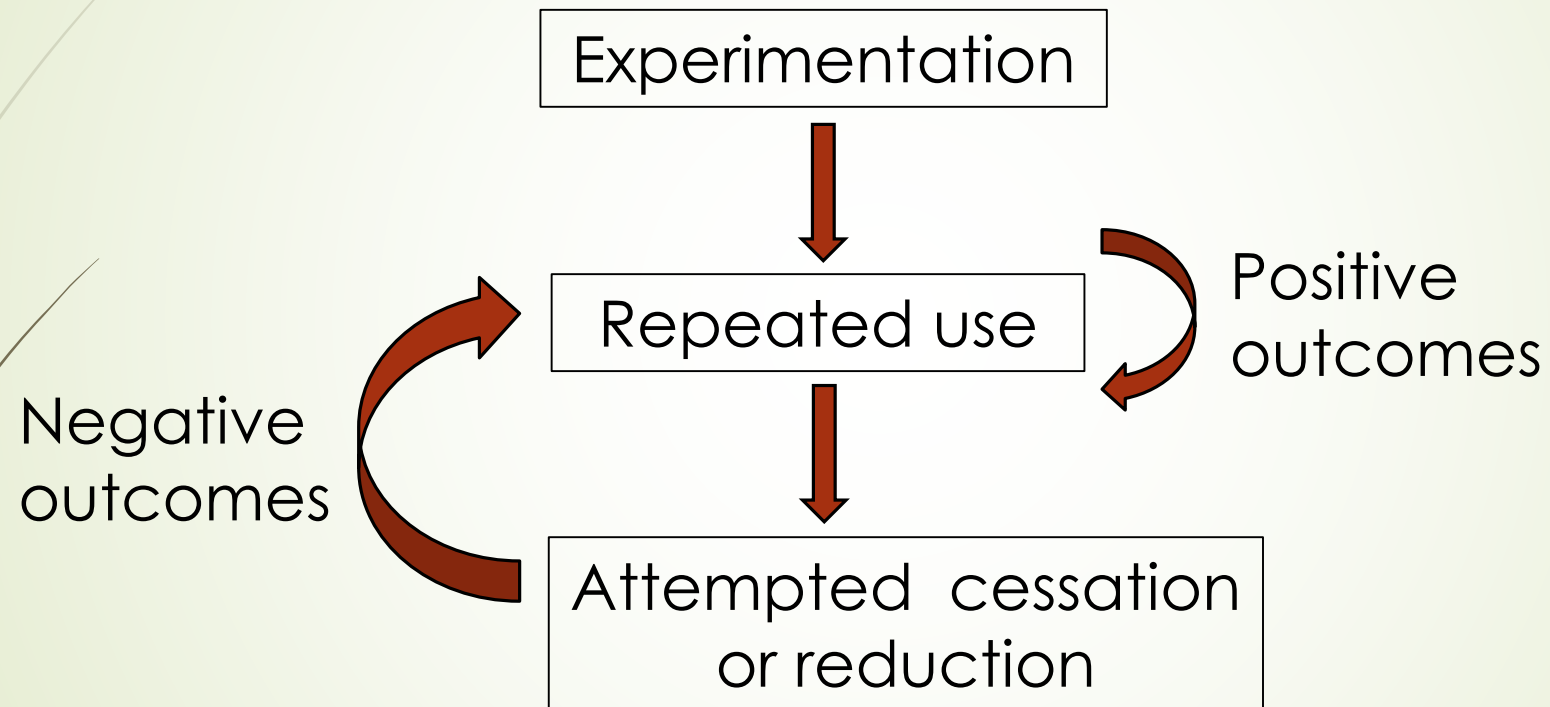


Delay discounting was unrelated to motivation (sucrose consumption) during withdrawal in genetically heterogeneous (WSC) mice

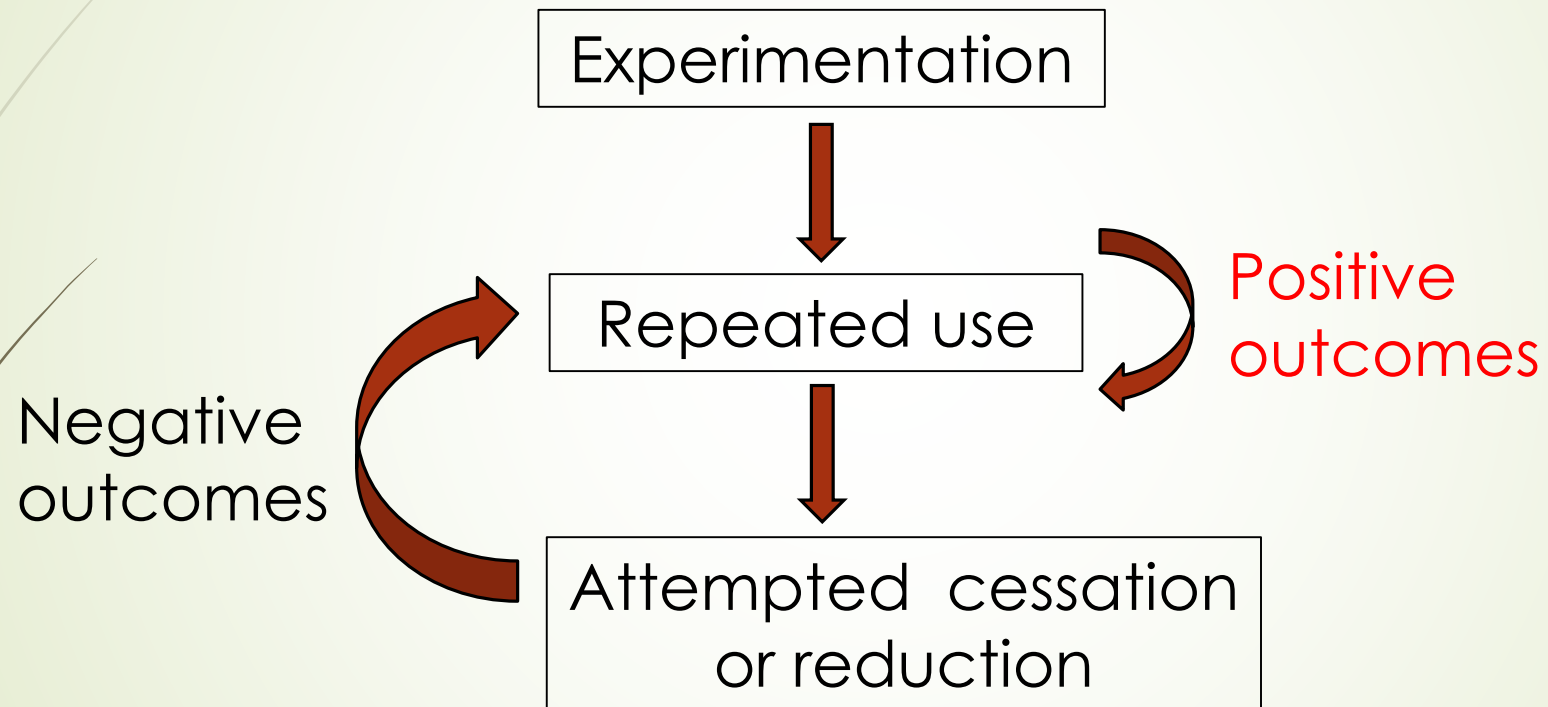


(EtOH: $n = 24$; Control: $n = 15$)

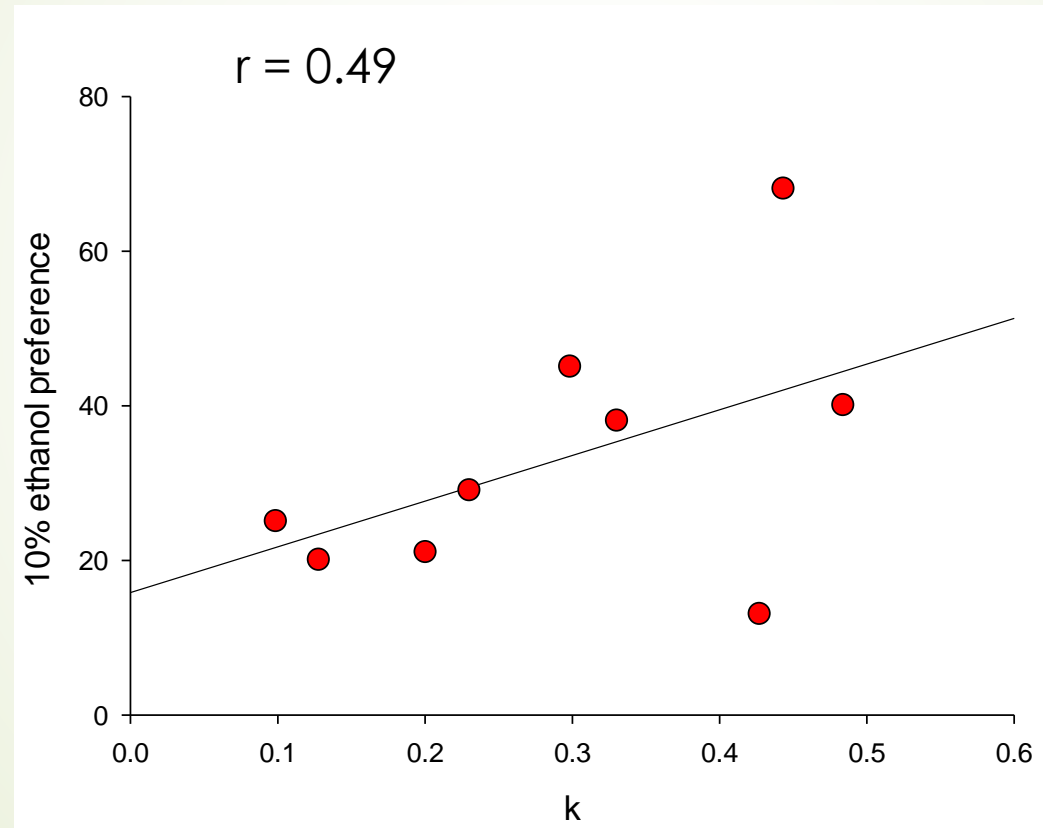
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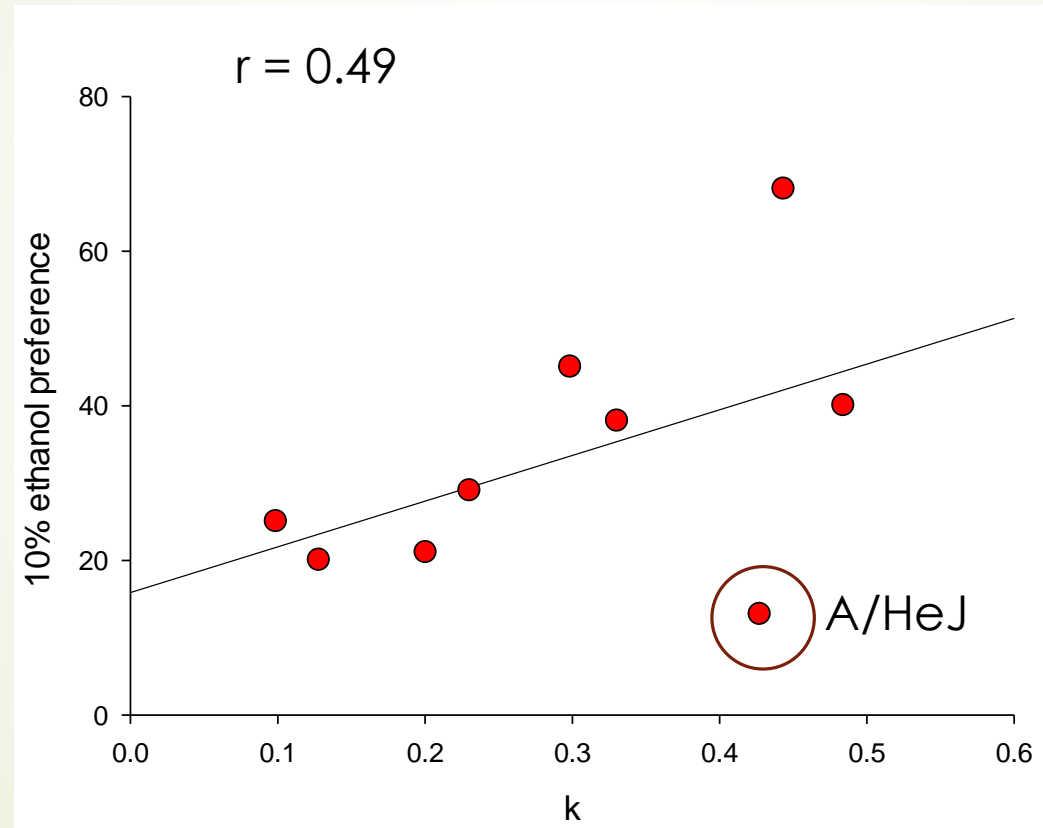
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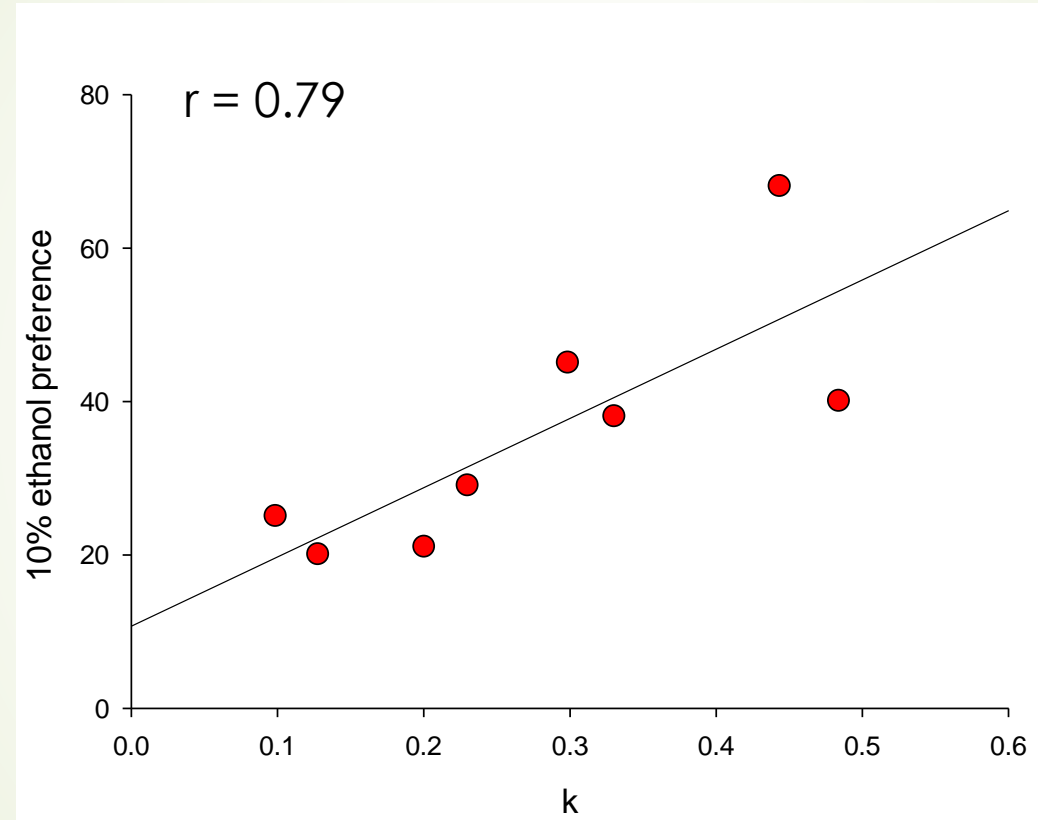
DD is not associated with higher ethanol preference



DD is not associated with higher ethanol preference



DD is associated with higher ethanol preference in A/HeJ outlier removed



A/HeJ were cryo-preserved by JAX right after this study
– when revived they suffered from several eye abnormalities
and can't be ordered

Results summary and conclusions

- DD is heritable, indicating a genetic component
- DD does not seem to be related to withdrawal signs in terms of genes (inbred strains) or nongenetically-driven processes
- DD may be related to alcohol consumption but more work needs to be done on characteristics of the positive outcomes driving this
- Implications for research...
 - Behavioral approaches can be used to identify shared genetic contributions to substance use

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Relationship between DD and probability and effort discounting

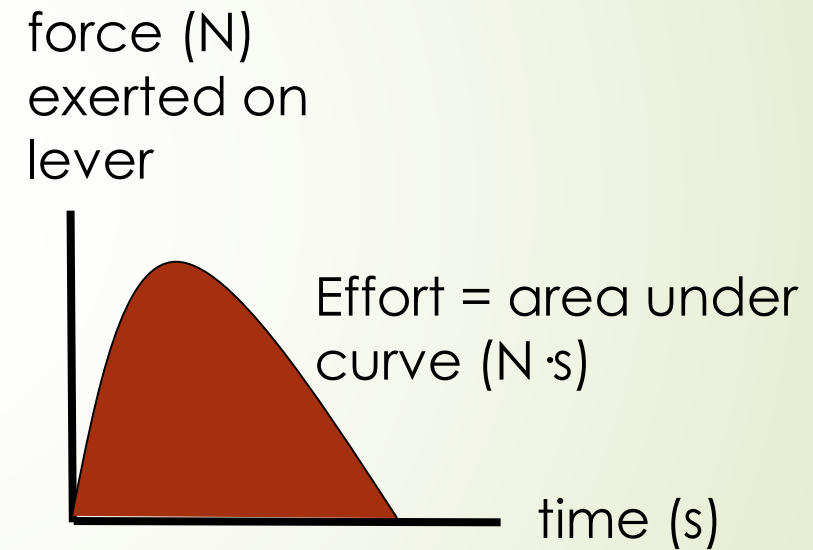
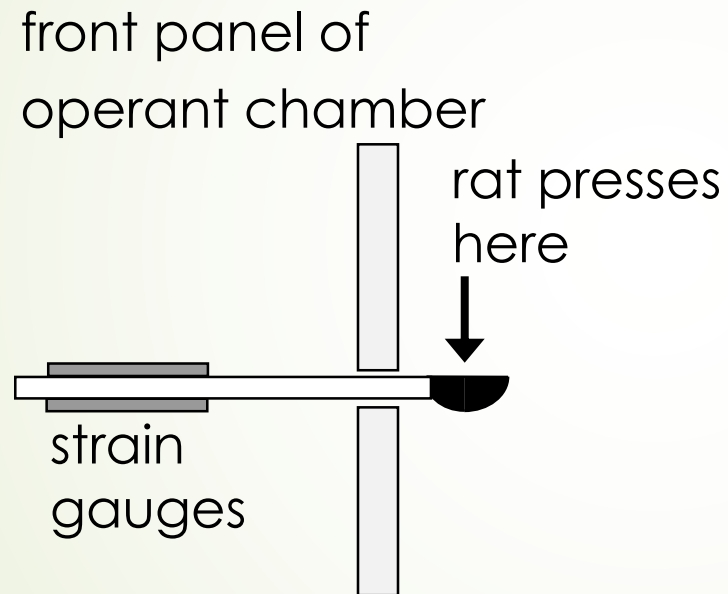
Study details -1

- 27 male rats
- Costs were the wait time or **delay** before the reinforcer was delivered, the **probability** that the reinforcer was delivered, or the **effort** required to obtain it.
- All rats rotated through tasks using each cost variant.

Study details -2

- ▶ “Low” cost: reward delivery delay = 0 s, reward delivery with $p = 1$, press with minimum effort = 0.01 Ns (1 g-force for 1 second)

Manipulating and measuring effort within responses



Study details -3

► “Low” cost: reward delivery delay = 0 s, reward delivery with $p = 1$, press with minimum effort = 0.01 Ns (1 g-force for 1 second)

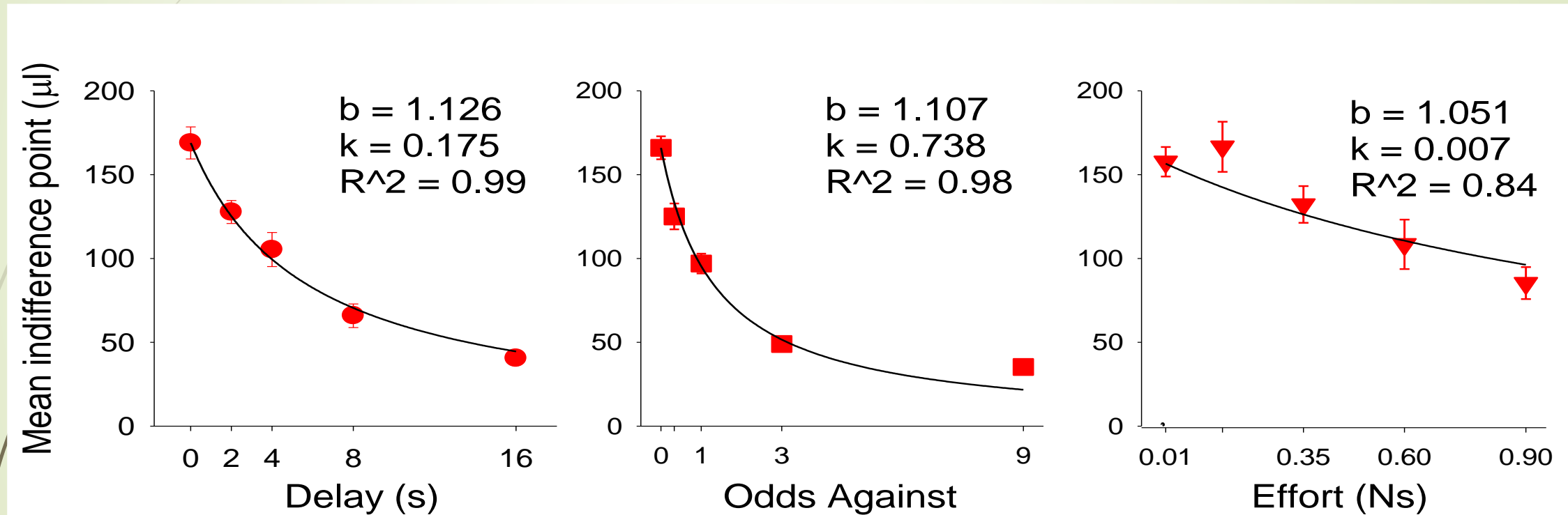
► “High” cost (varied between sessions):

Delay: delivery delay = 0, 2, 4, 8, 16 s, minimum press effort = 0.01 Ns, reward delivered with $p = 1$

Probability: reward delivered with $p = 1, 0.9, 0.75, 0.5, 0.25$, reward delivery delay = 0 s, minimum press effort = 0.01 Ns

Effort: minimum press effort = 0.01, 0.15, 0.30, 0.60, 0.90 Ns, reward delivery delay = 0 s, reward delivery with $p = 1$

Typical hyperbolic discounting curves were obtained



Discounting indices were not well correlated

Tasks	<i>k</i>		AUC	
	Rho	p	Rho	p
Delay - Probability	0.26	0.20	0.53	<0.01
Delay - Effort	0.25	0.20	0.07	0.73
Probability - Effort	0.50	<0.01	0.19	0.35

Results summary and conclusions

- Discounting functions can be created for probability and effort, that resemble hyperbolic DD functions.
- Correlations between each is low: Individuals that discount delayed rewards may not discount probabilistically delivered rewards or effort-requiring rewards similarly.
- Implications for research...
 - Relationship to psychopathology cannot be assumed.
 - Some shared mechanisms but not identical.

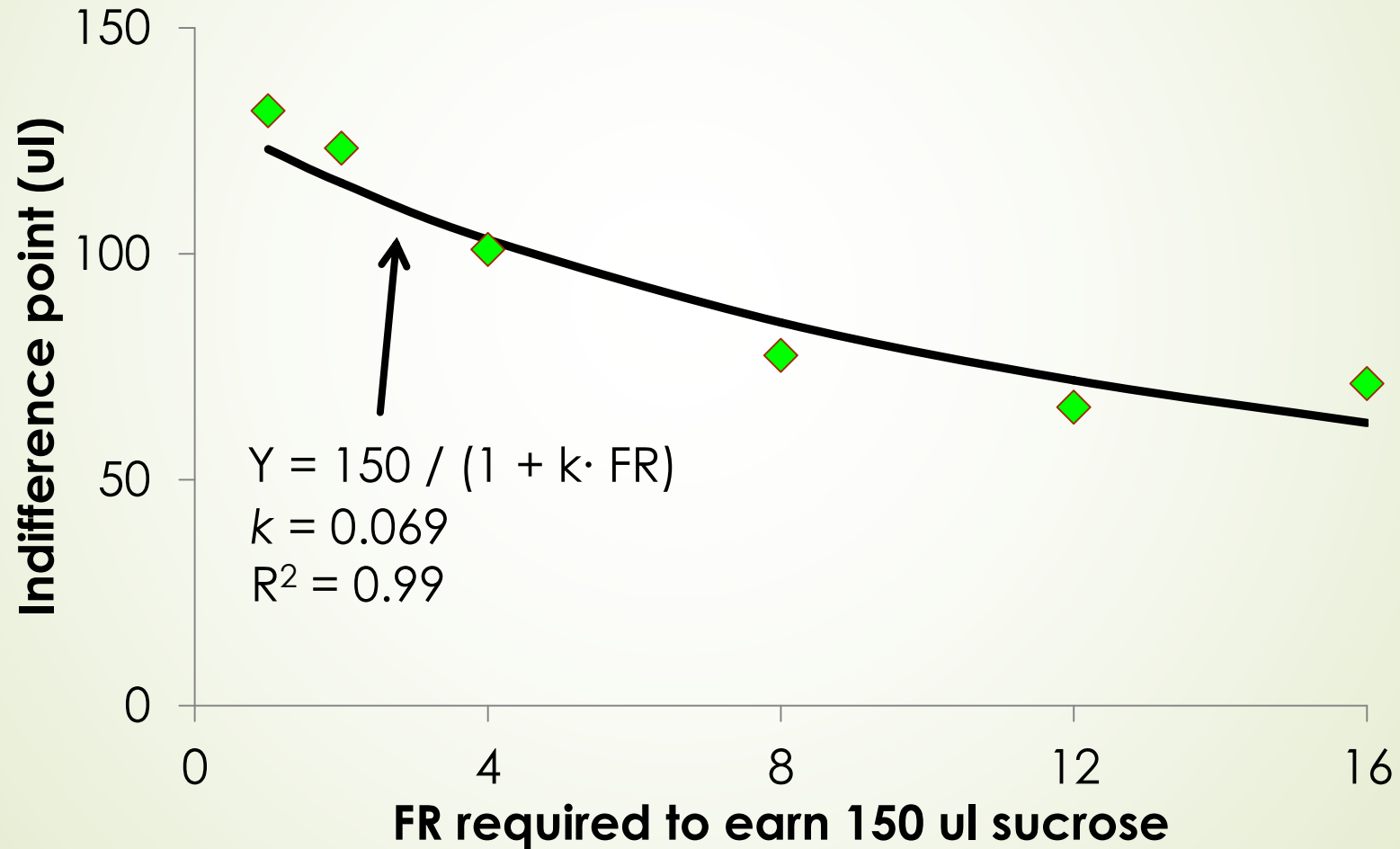
Effort can be manipulated in numerous ways

- ▶ Force required to register that a lever press occurred
e.g., Hunter & Davison, 1982
- ▶ Climbing ramps/walls with different gradients or heights,
pulling weighted trays, etc.
e.g., McCulloch, 1934; Thompson, 1944; Tsai 1932
- ▶ FR schedules of different values
e.g., Herrnstein, 1958; Herrnstein & Loveland, 1975; MacDonall, 1988

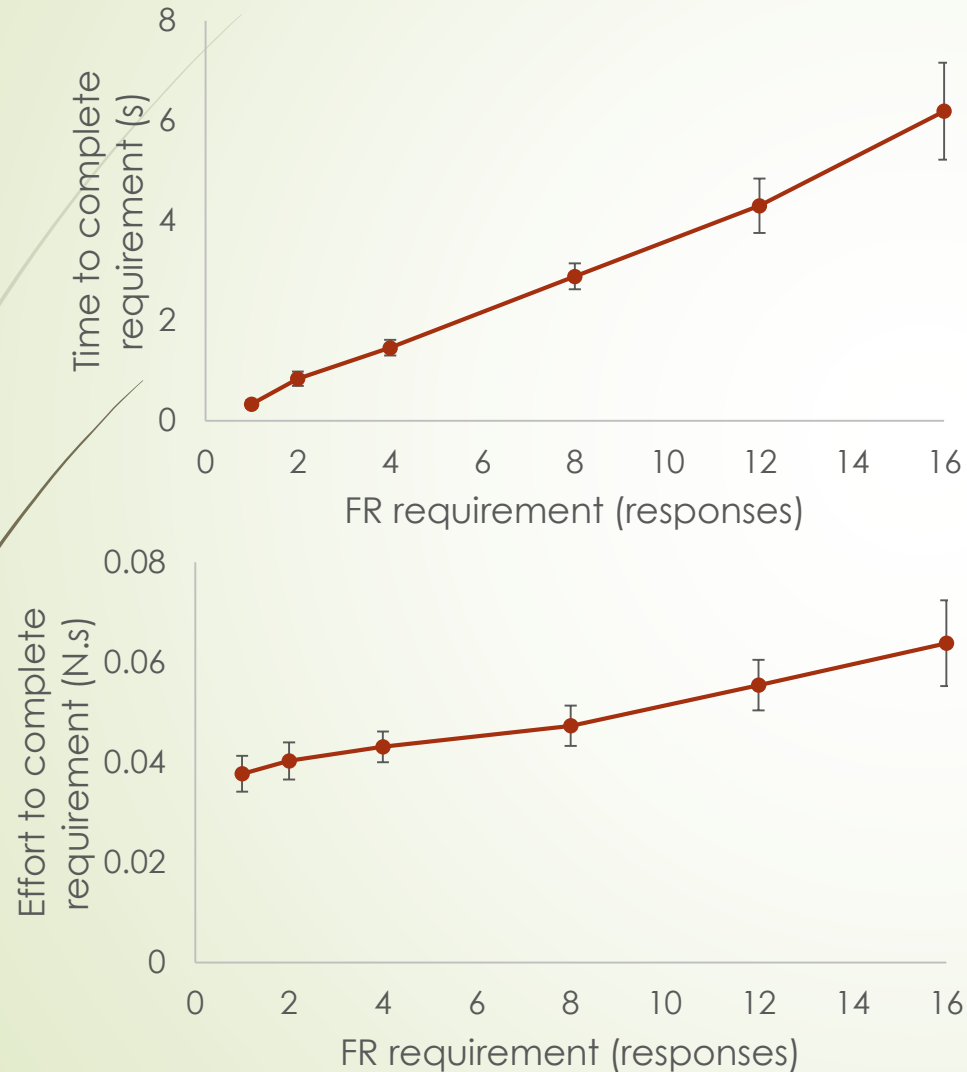
Effort discounting (effort is FR requirement)

46

N = 7 male Long Evans rats



Relationship between different costs measures

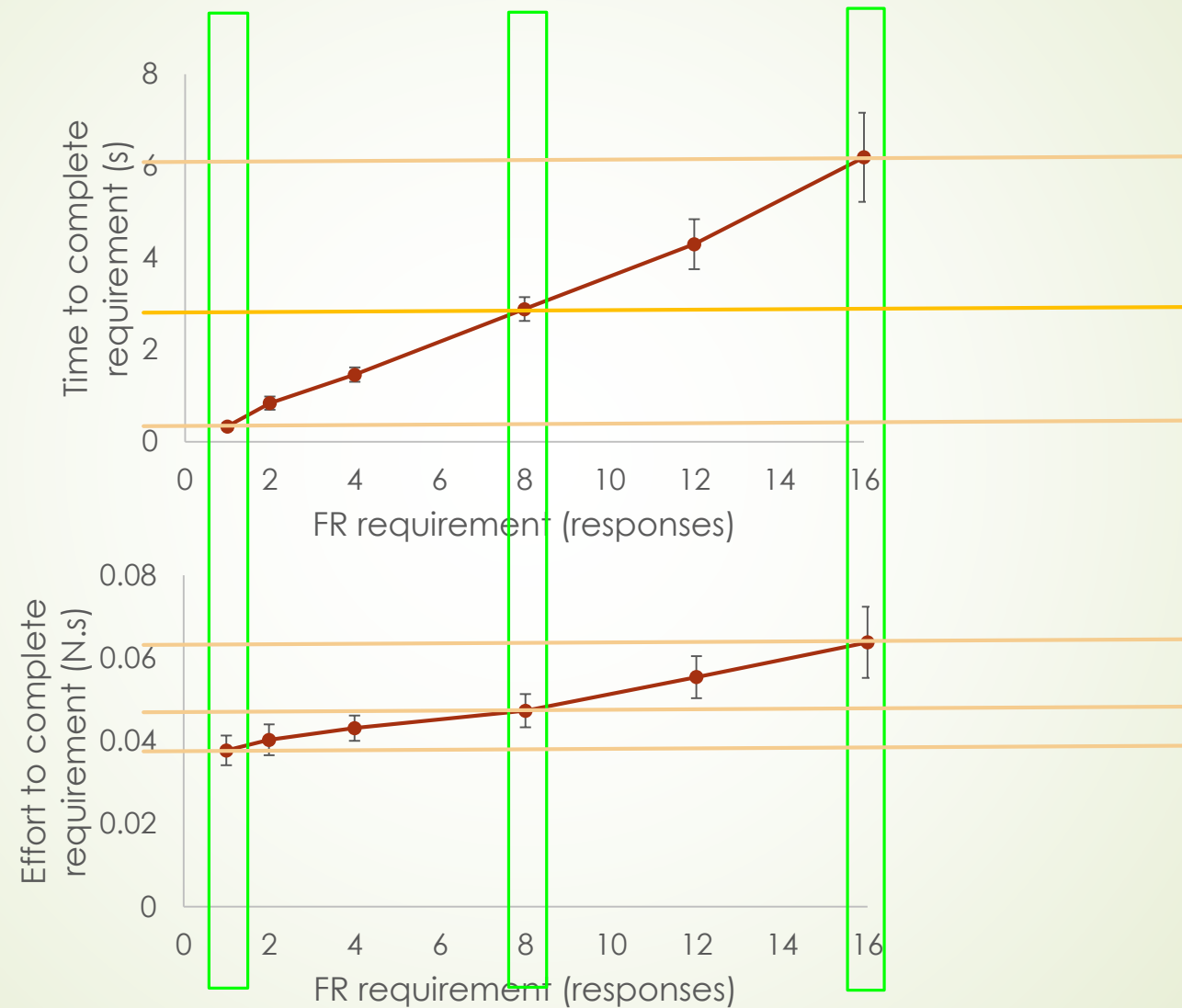


Time costs for all FR-values are significantly different

Effort costs for FR-values are not different between all values e.g., FR1 is not different from FR2 or FR4.

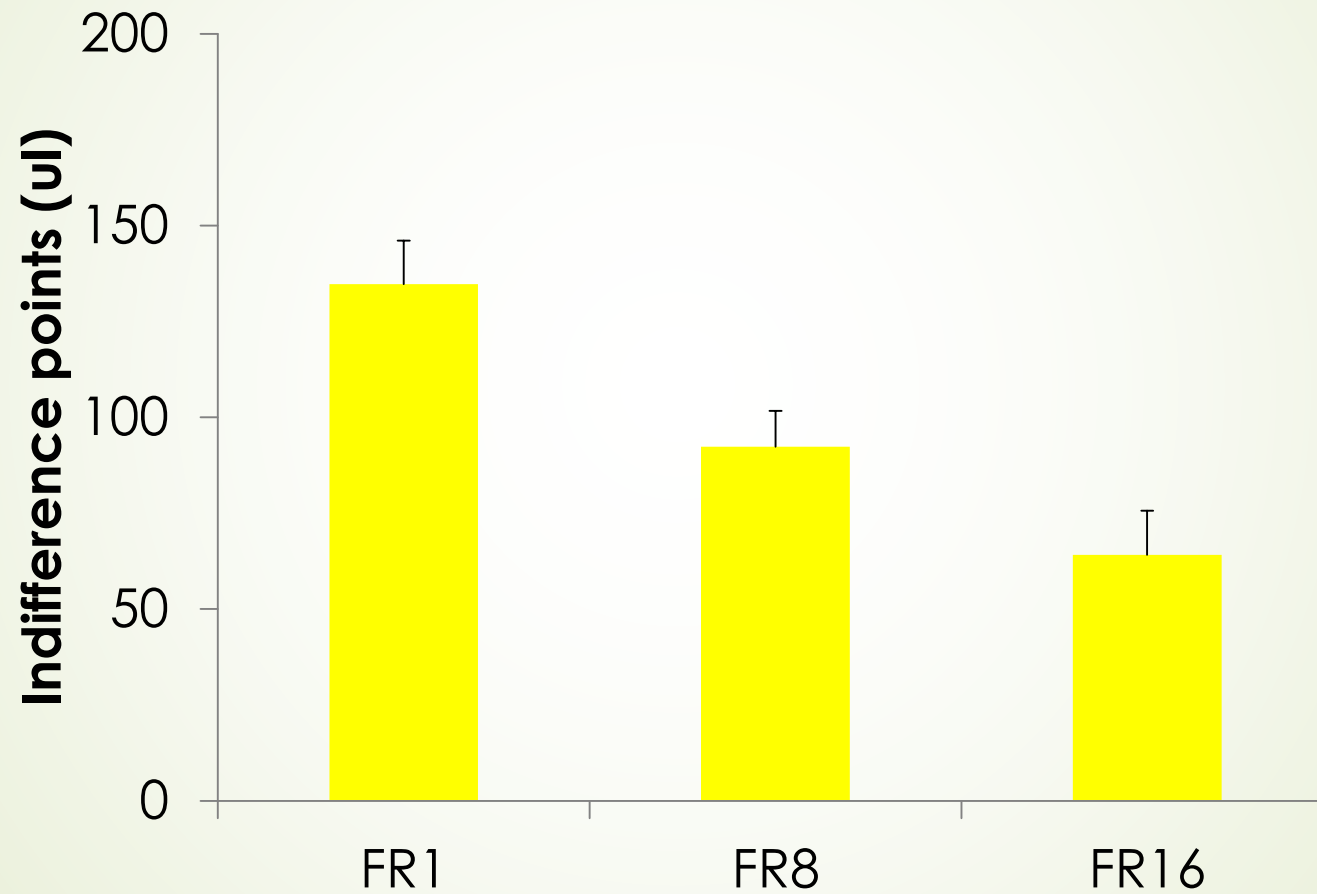
Creating yoked delay and effort schedules

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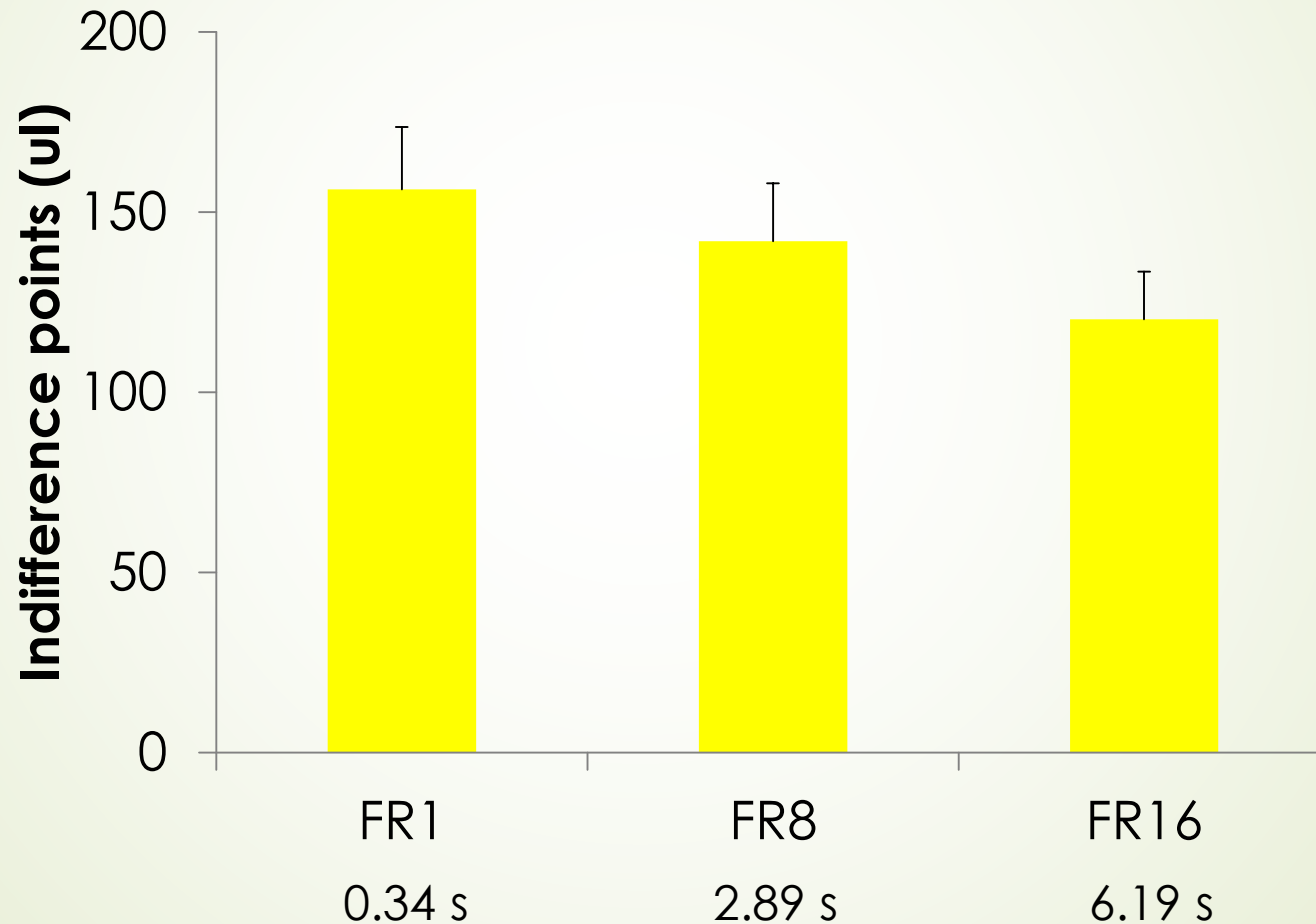


Adjusting amount discounting (N= 6)

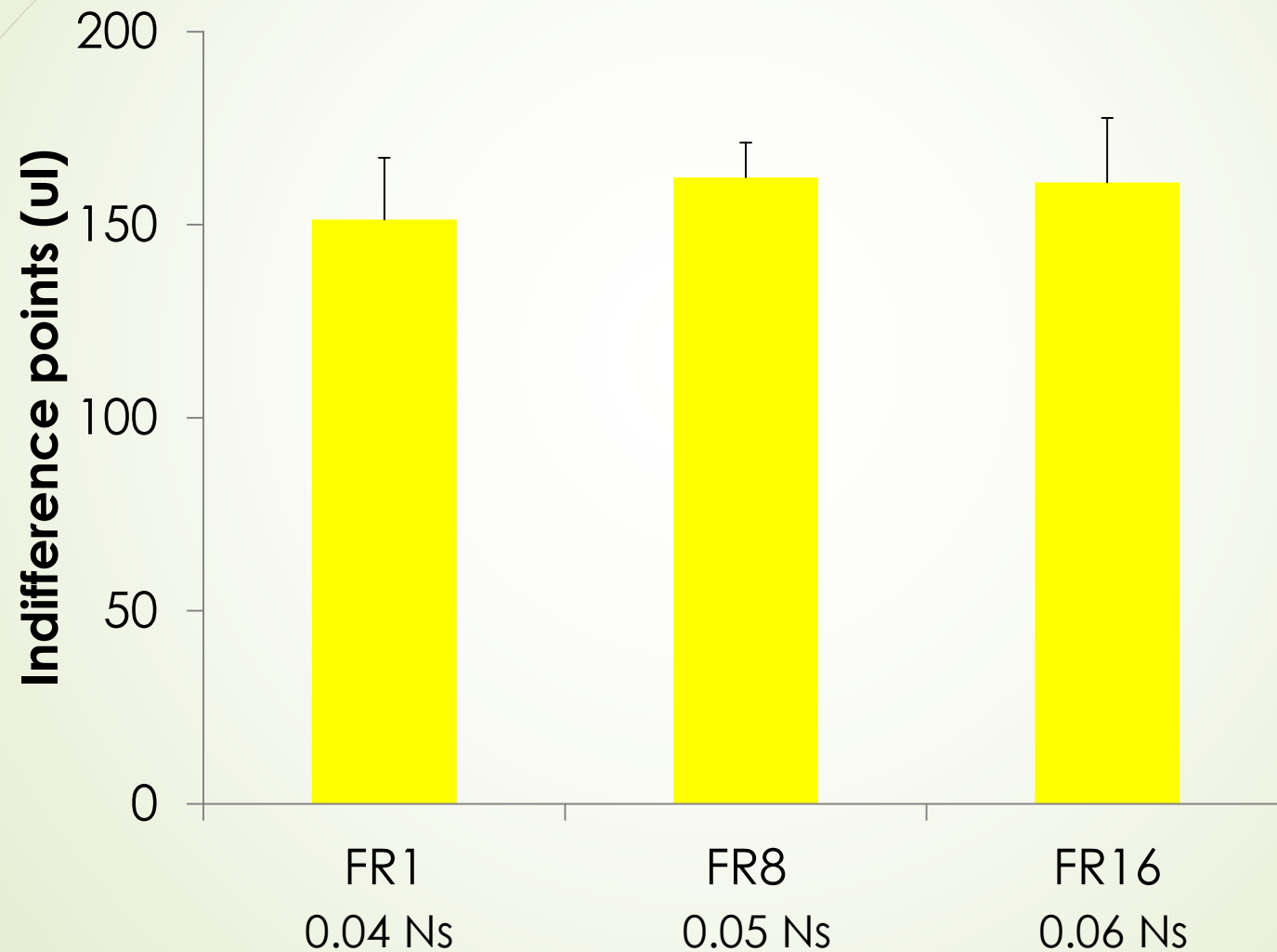
49



Yoked time to complete FR schedule discounting



Yoked effort to complete FR schedule

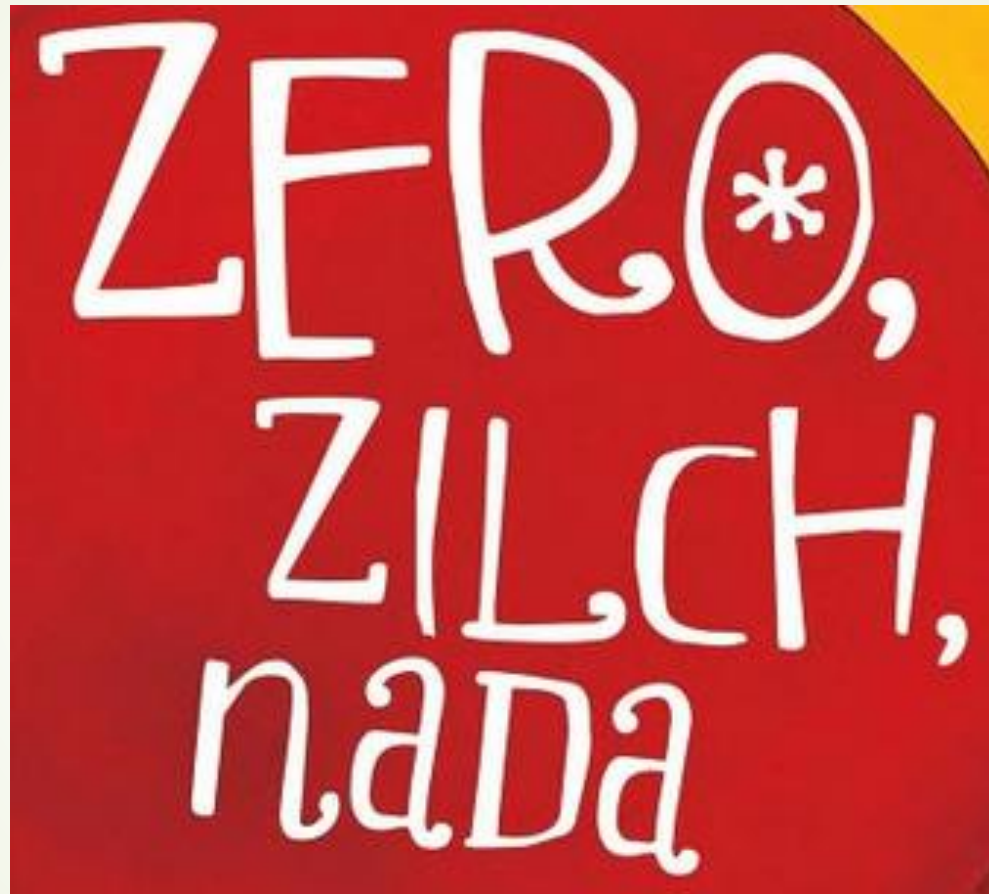


Results summary and conclusions

- Discounting functions can be created using FR schedules that resemble hyperbolic DD functions.
- Yoked time condition led to less extreme discounting and yoked effort led to no discounting, implying FR-effort discounting is due to an interaction of time and effort.
- Implications for research...
 - Effort manipulated using ratio schedules is NOT the same as effort manipulated using response force over time.

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A red rectangular graphic with a yellow corner in the top right. The text is written in white, stylized, hand-drawn letters. The first line is 'ZERO,' with an asterisk inside the zero. The second line is 'ZILCH,'. The third line is 'naDa' in a lowercase, cursive-like font.

ZERO,
ZILCH,
naDa

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Acknowledgements

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PARC
Portland Alcohol Research Center





OHSU

Thank You