

# Interventions aimed at changing impulsive choice in rats: Effects of immediate and relatively long delay to reward training

Adam E. Fox\*, Emma J. Visser, Alycia M. Nicholson

St. Lawrence University, United States



## ARTICLE INFO

### Keywords:

Delay-exposure training  
Impulsive choice  
Delay discounting  
Timing  
Intervention  
Rat

## ABSTRACT

A relatively strong preference for smaller-sooner rewards (SSR) over larger-later rewards (LLR) is associated with a host of maladaptive behavioral patterns. As such, the clinical implications for increasing preference for LLR are profound. There is a growing body of literature that suggests extended exposure to delayed reward may increase preference for LLR in rats. However, questions remain about the underlying mechanism driving this effect and the extent to which extended exposure to immediate rewards may decrease LLR choice. In Experiment 1, we tested effects of a differential-reinforcement-of-low-rates schedule (DRL) to increase LLR choice using a pretest/posttest design with Wistar rats as subjects. We compared this group to a group of rats exposed to a differential-reinforcement-of-high-rates schedule (DRH). The DRH intervention has never been employed in this research context, but explicitly programs an immediate response-reinforcement requirement. In Experiment 2, we tested effects of an intervention with a delay longer than those used in the delay discounting pretest and posttest. No previous research has tested effects of an intervention delay this long, relative to the delay discounting task. We compared this group to a group exposed to a delay that was part of the delay discounting pretest and posttest and to a group exposed to a traditional no-delay, fixed-ratio (FR) 2 control intervention. In both experiments, we found that exposure to delayed rewards in the intervention phase significantly increased LLR choice relative to pretest performance. These findings replicate and extend a growing body of literature showing that delay exposure increases preference for LLR. We also found significant decreases in LLR choice from pretest to posttest in the DRH and no-delay intervention groups in Experiments 1 and 2, respectively. This is the first report of such an effect and has implications for understanding and interpreting effects of delay exposure training in past and future research. Our results also suggested no relationship between improved temporal tracking of reward and increases in LLR choice as a result of delay exposure training.

## 1. Delay exposure training

Broadly speaking in terms of health and behavior, a consistent, strong preference for smaller-sooner rewards (SSR) over larger-later rewards (LLR), when the LLR is optimal over time, is not good. This operationalization of impulsivity is known as steep delay discounting, and it is a pattern of behavior that may underlie a host of other maladaptive behaviors such as substance abuse (Anker et al., 2009; Heil et al., 2006; MacKillop et al., 2011; MacKillop et al., 2015; Madden et al., 1997; Stein and Madden, 2013; Yi et al., 2010), pathological gambling (Alessi and Petry, 2003; Dixon et al., 2003; Petry and Casarella, 1999; Petry, 2001), obesity (Amlung et al., 2016; Rasmussen et al., 2010; Weller et al., 2008), and risky sexual behavior (Chesson et al., 2006; Lawyer et al., 2010). It is also associated with psychological disorders such as attention-deficit/hyperactivity disorder (ADHD)

(Barkley et al., 2001; Binder et al., 2000; Demurie et al., 2012; Scheres et al., 2006; Wilson et al., 2011) and schizophrenia (Heerey et al., 2007). This relationship has led researchers to consider steep discounting as a trans-disease process that may serve as a behavioral marker for addiction and other maladaptive behavior patterns (Bickel and Mueller, 2009; Bickel et al., 2012). Indeed, there is evidence in rats that steep discounting predicts cocaine and alcohol self-administration (Perry et al., 2005, 2008; Poulos et al., 1995).

The aforementioned research highlights the importance of better understanding and mitigating strong preferences for SSR in humans. Given the trans-disease nature of steep discounting, reducing it may in turn reduce the probability that a person will engage in a range of other maladaptive behaviors. In other words, increasing the subjective value of LLR may have far reaching clinical implications, and, while the rate at which an organism discounts LLR tends to be stable over time, even

\* Corresponding author.

E-mail address: [afox@stlawu.edu](mailto:afox@stlawu.edu) (A.E. Fox).

<https://doi.org/10.1016/j.beproc.2018.11.009>

Received 20 June 2018; Received in revised form 12 November 2018; Accepted 19 November 2018

Available online 20 November 2018

0376-6357/ © 2018 Elsevier B.V. All rights reserved.

trait-like in nature (Odum, 2011), research has shown that it is malleable in humans and non-humans.

In humans, preference for LLR has increased as a result of working-memory training (Bickel et al., 2011), episodic future thinking (Daniel et al., 2013; Peters and Büchel, 2010), money-management training (Black and Rosen, 2011), and framing manipulations (DeHart and Odum, 2015; Read et al., 2005). In non-humans, working-memory training has not resulted in increased LLR choice (Renda et al., 2015), but long-term training involving exposure to delayed rewards (sometimes called delay-exposure training) has been shown to consistently increase LLR choice (Bailey et al., 2018; Renda and Madden, 2016; Smith et al., 2015; Stein et al., 2013, 2015). In particular, response-initiated fixed-interval (RIFI) training appears to produce the most robust effects (Bailey et al., 2018). See a recent review of experimental manipulations of delay discounting from Rung and Madden (2018) for an expanded discussion of the range of manipulations previously tested.

In order to translate the effects of delay exposure training in rats to humans, we must understand the behavioral mechanism underlying the effect, which at this point remains mostly unclear. One possible mechanism by which exposure to delayed rewards may increase preference for LLR is by changing timing processes (i.e. changes in subjective time perception). Some previous research supports this hypothesis (Marshall et al., 2014; Smith et al., 2015). Other recent research, however, has found no relationship between improvements in interval timing and exposure to delayed rewards (Eckard and Kyonka, 2018; Rung et al., 2018). Other possible mechanisms may also be responsible for the shift in choice behavior. For example, exposure to delayed rewards may decrease aversion to delay and avoidance of LLR in favor of SSR. Individual differences in impulsive choice behavior in rats suggests that some rats are more likely to avoid delayed rewards (Galtres et al., 2012; Kirkpatrick et al., 2015), and that extended, forced exposure to delayed rewards increases choice for LLR most for rats that were more impulsive in a pretest (Smith et al., 2015). Some other underlying mechanism may also be at work, such as changes in reinforcement sensitivity (e.g., Pitts, 2014) or extending the organism's temporal horizon (e.g., Lin and Epstein, 2014; Snider et al., 2016).

Furthermore, if exposure to delayed rewards increases LLR choice, then it seems plausible that the opposite is also true. That is, that long-term exposure to immediate rewards may decrease LLR choice. This, too, remains unclear. Renda et al. (2018) reported that in a posttest, rats exposed to training involving immediate rewards were no different from rats that experienced no training (a maturation/handle control). However, while the maturation/handle control rats became slightly less impulsive in the posttest, the rats that experienced the immediate-reward training did not; and since choice was near exclusive for the SSR at the intermediate and long delays for all groups in the pretest, any potential increases in choice for the SSR may have been masked by a floor effect. Thus, more research is needed to understand the possible effects of extended immediate-reward exposure on posttest impulsive choice behavior.

In the two experiments presented below, our primary objective was twofold. First, we assessed if exposure to immediate rewards during an intervention phase impacted posttest LLR choice in a delay discounting task. We did this by employing two different types of immediate-reward control groups in a pretest-posttest design: a differential-reinforcement-of-high-rate (DRH) schedule in Experiment 1 and a fixed-ratio (FR) 2 schedule in Experiment 2. The latter FR 2 control group is typically used (Bailey et al., 2018; Renda and Madden, 2016; Renda et al., 2018; Rung et al., 2018). Second, we assessed whether extended, forced exposure to delayed rewards increased LLR choice. We did this by employing a differential-reinforcement-of-low-rates (DRL) schedule in Experiment 1 and Response-Initiated Fixed-Interval (RIFI) schedules in Experiment 2. In Experiment 2 we also assessed if exposure to a relatively long FI during the intervention phase, with a delay longer than those experienced during the pretest or posttest, impacted posttest choice for the LLR option. It is currently unknown if exposure to delays

longer than those used in the discounting assessments also increase LLR choice. We compared this group to the FR 2 immediate-reward group and to a group that experienced more typical FI delay-exposure training with a delay that was part of the pretest and posttest. We also took measures of timing accuracy and precision immediately following the posttest in Experiment 2 to assess any differences between our intervention groups.

## 2. Experiment 1

There are three possible scenarios by which rats exposed to delayed rewards are less impulsive than rats in an immediate-reward control group in a post-intervention delay discounting task. First, choice for these rats may shift toward the LLR option, while choice for the immediate-reward control group rats remains constant. Second, choice for the immediate-reward rats may shift toward the SSR option, while choice for the delayed-reward rats remains constant. There are no current reports of such a scenario, however, in past research, floor effects may have masked potential increases in SSR preference, as discussed above (Renda et al., 2018; Rung et al., 2018). Finally, it is possible that choice for the delayed-reward rats shifts toward the LLR option, while choice for the immediate-reward rats shifts toward the SSR option. Again, the former, but not the latter, has been demonstrated previously.

Our goal in Experiment 1 was to test if exposure to a DRL schedule increased preference for LLR choice. To do so, we exposed rats to a delay discounting pretest and matched them to experimental groups based on pretest area under the curve (AUC) (Myerson et al., 2001). One group was then exposed to a DRL schedule and the other to a DRH schedule for 60 days. The DRH intervention allowed for a control group in which experience with immediate reinforcement is explicitly programmed, whereas in previous research there may be long latencies between the first and second response in the FR 2 schedule that are reinforced. In other words, the DRH group is an immediate-reward control group in which inter-response latencies are required to be short for reinforcement to occur. Nonetheless, we predicted that LLR choice for the DRL rats would increase in the posttest (Smith et al., 2015), and that we would observe no change in LLR choice for the DRH rats.

### 2.1. Method

#### 2.1.1. Subjects

Subjects were 16 naïve male Wistar rats obtained from Charles River Laboratories. All rats were approximately eight weeks old at the start of the experiment and were maintained at 85% +/- 15 g of their free-feeding weight as calculated based on growth curve data obtained from the supplier. The rats were pair-housed in translucent polycarbonate with dimensions of 46 (l) x 25 (w) x 21 (h) cm. Bedding included beta chips or alpha dry/corn cob mix. Water was continuously available in the home cages as was some form of enrichment, including plastic chew toys, cardboard tubes, and paper towel. The temperature in the vivarium was approximately 70 +/- 2 ° Fahrenheit. There was a 12/12 h light and dark cycle, and the lights turned on at approximately 8:00 a.m. Testing occurred during the light cycle.

#### 2.1.2. Apparatus

The experiment was conducted using four standard operant chambers with retractable levers obtained from MED Associates (St. Albans, VT, USA) and controlled using Med-PC IV® software, a PC, and a Med-PC interface located in an adjacent room using. The interior of each chamber measured approximately 12 in wide, 8.25 in high, and 9.5 in deep and was in a sound attenuating cubicle. The front, back, and ceiling of the chambers were made of Plexiglas. The floor was made of thin metal bars running from the front to the back of the chamber positioned approximately 0.5 in apart. The right and left sides of the chambers were aluminum. The left side panel contained a house light in

the top center of the wall and a tone generator in the top right that produced approximately 3000 Hz tones at approximately 75 dB. The right side panel contained two retractable levers, each approximately 2.5 in from the floor, 1 in from the wall, and 2 in apart. Directly between and below the levers was a food hopper opening that measured 2 in by 2 in and was 1 in from the floor. A pellet dispenser delivered 45-mg dustless precision purified-diet food pellets (BioServ, NJ, USA). A 1-in diameter lamp was located approximately 1.5 in above each lever. Lever presses were recorded when a force of approximately 0.2 N was applied to the lever. Ventilation fans mounted on the top of the right panel of the sound attenuating cubicles provided white noise.

### 2.1.3. Procedure

All rats were first manually shaped to press levers for food reinforcement. This was followed by two days of fixed-ratio (FR) 1 training with 30 trials on each lever, randomly selected without replacement in blocks of 10 trials (five left, five right) for 60 total trials. The schedule on each lever was then changed to a FI 2 s and 5 s schedule for one day each.

The delay discounting pretest immediately followed lever training. The task was based on a discounting procedure used by Green and Estle (2003), which has shown strong test-retest reliability and evidence for superior discrimination of delays compared to other similar tasks (Peterson et al., 2015). In the task, the SS option was always a signaled response-initiated fixed-interval (Signaled-RIFI) (see Fox and Kyonka, 2016) 5-s schedule that resulted in one food pellet and the LL option was a Signaled-RIFI schedule with delays of 10, 25, and 40 s (presented in an ascending order across conditions) that resulted in two food pellets. Location (left or right lever) of the LL option was counter-balanced across rats. For both options, a single lever press resulted in the illumination of the light above the lever, retraction of the alternate lever, and the start of the FI. A single press after the FI elapsed resulted in reinforcer deliver. During choice trials, both levers were available at the start of a trial and during forced-choice trials only one lever was available. Sessions lasted for seven blocks of 10 choice trials, one SS trial, and one LL trial, randomly selected without replacement, for 84 total trials or 1.5 h, whichever occurred first. Sessions only timed out for four sessions across three rats, always when the LL option was 40 s. Each LL condition lasted a minimum of five sessions and until there were no visual trends in the proportion of LL choice across three consecutive sessions. The intertrial interval (ITI) was 30 s during which time all lights were extinguished and levers retracted. The fixed 30-s ITI resulted in the LL option providing higher momentary rates of reinforcement at the 10- and 25-s delays, and rates equal to the SS option at the 40-s delay—assuming constant latencies to initiate the FIs. Fixed ITIs were used because they more closely resemble natural contingencies where the time between choices is not titrated based on the previous choice (Odum, 2011; Peterson et al., 2015) and because they have been used in previous similar research (Bailey et al., 2018; Peterson et al., 2015).

Immediately following the pretest, area under the curve (AUC) was calculated for each rat based on choice during the pretest. AUC was calculated using the following equation:  $((D_{25} - D_{10}) * ((LLChoice_{10} + LLChoice_{25}) / 2)) + ((D_{40} - D_{25}) * ((LLChoice_{25} + LLChoice_{40}) / 2))$ , where  $D$  represents the normalized LL delay and  $LLChoice$  represents the proportion of LL choices at each of the LL Delays. We normalized the LL delays so that by using this equation AUC could range from 0 (exclusive preference for the SS option) to 1.0 (exclusive preference for the LL option). All rats were then rank ordered based on their individual AUC values, matched, and randomly assigned to either the DRL ( $N = 8$ ) or the DRH ( $N = 8$ ) intervention group.

The DRL schedule requirement was an inter-response time (IRT) of at least  $X$  s, where  $X$  started at 17.5 s and was increased 1 s each day to a terminal 30-s criteria. The DRH schedule requirement was an IRT of less than  $X$  s, where  $X$  started at 17.5 s and was decreased 1 s each day to a

terminal 5-s criteria. For both schedules, IRTs that failed to meet the requirement reset the timer. For example, at DRL 30 s, at least 30 s had to elapse between responses for reinforcement delivery. If this requirement was not met, another 30 s had to elapse before the subsequent response could meet the schedule requirement for reinforcement delivery.

Sessions lasted until 100 reinforcers were delivered or 1.5 h elapsed, whichever occurred first. During the intervention phase, the reinforcer was always one pellet and the active lever on each trial was randomly selected without replacement from a list of five left-lever trials and five right-lever trials. The intervention phase lasted for 60 days, with the final 46 days at the terminal schedule values.

The delay discounting posttest immediately followed the intervention phase and was exactly the same as the pretest, except that the initial condition (5-s SS versus 10-s LL) lasted a minimum of 10 sessions. This was done because choice behavior of several rats was slow to adjust to the transition to the posttest choice task and we wanted to ensure we obtained stable behavior for all rats.

## 2.2. Data analysis

We analyzed the raw choice proportion data using a generalized multilevel logistic regression (GMLR) approach using the open-access software *R* (Team, 2013). Proportion data were weighted using the “weights” function. We used the *lme4* package for model fitting and the *lsmeans* package for post-hoc comparisons (Tukey corrected). GMLR is the recommended data analysis approach for these types of data (Young, 2018). This approach reduces chances of Type I error by fitting parameters at both the group (fixed effects) and individual (random effects) level (Boisgontier and Cheval, 2016). GMLR takes advantage of the power provided by including all choices in the model, which increases precision relative to traditional approaches, like analysis of variance (ANOVA), which use single-point means. For similar recent approaches see Bailey et al. (2018) and Renda et al. (2018).

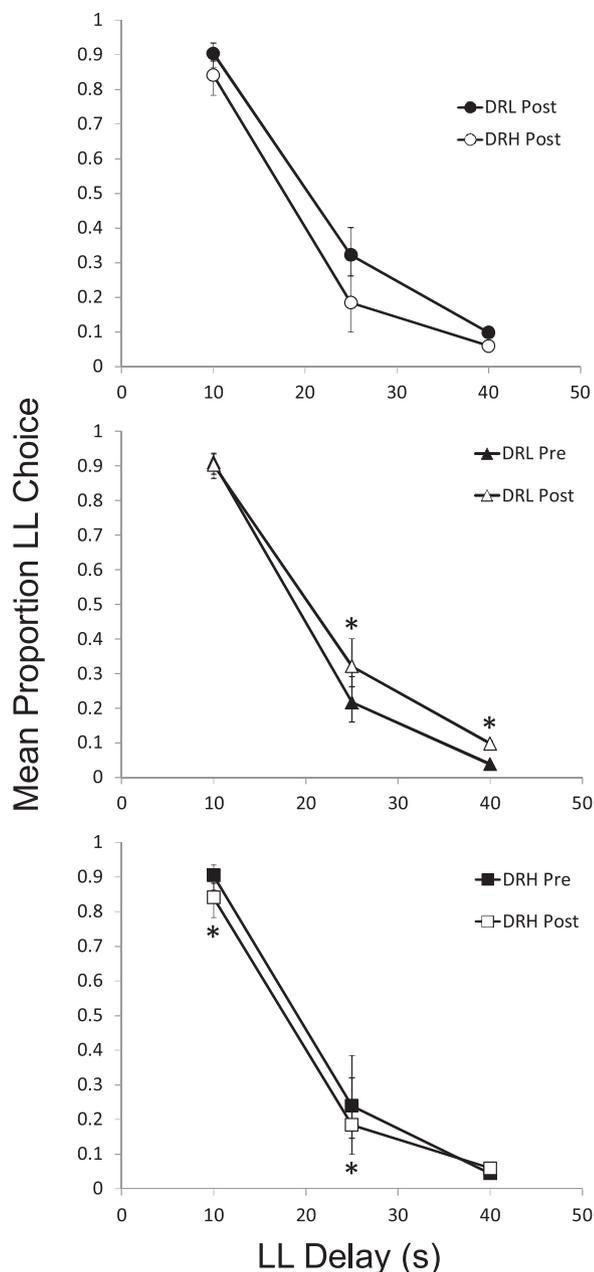
In our approach to modeling, categorical variables were effect coded. These variables included Test (pre and post) and Group (DRL and DRH). The delay parameter was adjusted to be LL/SS ratio in each condition (Young, 2018) and was a continuous variable in the model. In all, the model included 20,125 total choice observations across all rats in both groups, pretest and posttest. This included choice data for the last three sessions in each condition during the pretest and posttest for each rat.

Our approach to model fitting was to start with a model that included the full factorial of fixed effects. We did so because we anticipated an interaction based on previous research. We started with a parsimonious random-effects structure and added complexity to find the best fitting model using Akaike Information Criterion (AIC) and the *anova* function in *R* to compare models (Bates et al., 2015). The best fitting model included the full factorial of fixed effects (Group\*Test\*LL/SS Ratio), and LL/SS Ratio and Subject as random effects. The model included a random intercept as well. We used the standard  $p < .05$  criterion for significance.

## 2.3. Results and discussion

The matching procedure successfully equated impulsive choice in the two groups prior to the intervention phase. The best fitting GMLR model indicated no significant differences between groups during the pretest at any of the LL delays.

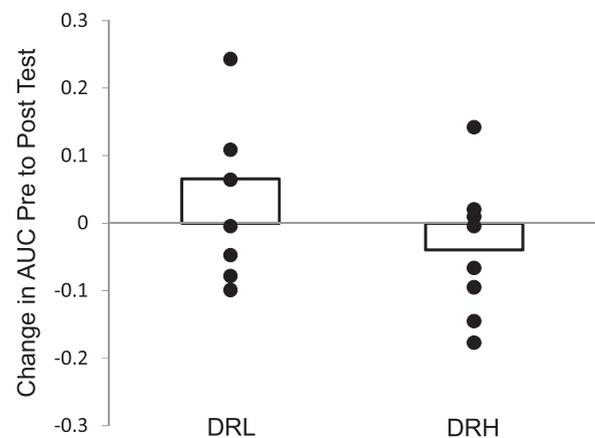
An independent-samples *t* test revealed significantly higher response rates in the DRH group ( $M = 26.64$ ,  $SD = 4.24$ ) than the DRL group ( $M = 2.26$ ,  $SD = 0.45$ ),  $t(14) = 16.18$ ,  $p < .001$ ,  $d = 8.64$ , during the last five sessions of the intervention phase. The intervention schedules successfully manipulated response rates and inter-food intervals in the two groups. The rats in the DRL and DRH groups were experiencing relatively long and short delays between responses and



**Fig. 1.** Mean proportion of LL choice for the DRL and DRH groups during the posttest (top panel), and mean proportion of LL choice during the pretests and posttests for the DRL group (middle panel) and DRH group (bottom panel) in Experiment 1. Error bars show error from best fitting GMLR model (see Section 2.2). \* = statistically significant difference ( $p < .05$ ).

reinforcers, respectively.

Fig. 1 shows the mean proportion of LL choice for rats in the DRL and DRH groups during the posttest in the top panel. The middle and bottom panels of Fig. 1 show comparisons of pretest and posttest choice for the DRL and DRH groups, respectively. All graphs show error bars from best fitting GMLR model (see Section 2.2. Data Analysis). The best fitting model revealed that DRH ( $z = 12.94$ ,  $p < .001$ ) and DRL ( $z = 13.41$ ,  $p < .001$ ) group assignment, Test ( $z = -6.76$ ,  $p < .001$ ), and the LL/SS Ratio ( $z = -13.13$ ,  $p < .001$ ) were significant predictors of choice. The model also revealed significant Group  $\times$  Test ( $z = -2.09$ ,  $p = .04$ ), Test  $\times$  LL/SS Ratio ( $z = 8.13$ ,  $p < .001$ ), and Group  $\times$  Test  $\times$  LL/SS Ratio ( $z = -2.12$ ,  $p = .03$ ) interactions. To further analyze the significant interaction between all three independent variables, we conducted post-hoc comparisons between groups during the posttest at



**Fig. 2.** Change in area under the curve (AUC) from pretest to posttest for rats in the DRL and DRH groups in Experiment 1. Data points show individual rats and bars show group means.

each LL delay, and between the pretest and posttest within each group at each LL Delay (see Section 2.2. Data Analysis for details). These comparisons revealed that while the DRL group was less impulsive than the DRH group during the posttest at all three LL delays, these differences were not statistically significant; however, the DRL group was significantly less impulsive during the posttest at the 25-s ( $z = 8.34$ ,  $p < .001$ ) and 40-s ( $z = 6.85$ ,  $p < .001$ ) LL delays (middle panel, Fig. 1), and the DRH group was significantly more impulsive during the posttest at the 10-s ( $z = -5.80$ ,  $p < .001$ ) and 25-s ( $z = -5.01$ ,  $p < .001$ ) LL delays (bottom panel, Fig. 1), compared to pretest choice.

To compare the results of the GMLR model to more traditional forms of analysis, we also compared the change in AUC from pretest to posttest between the two groups. Fig. 2 shows that AUC for rats in the DRL group mostly remained constant or increased in the posttest, while AUC for rats in the DRH group mostly remained constant or decreased. An independent-samples  $t$  test revealed no significant difference between groups, and one-sample  $t$  tests revealed neither group differed significantly from zero (no change). These data are generally consistent with the results of the GMLR analysis, however, no statistically significant differences were observed, likely because AUC data are a result of aggregating 20,125 choices, some repeated measures, down to 16 data points without repeated measures, greatly reducing power.

Finally, we assessed timing during the LL forced-choice trials during the post-test from stable sessions for all rats. Although these were not formal examinations of timing behavior, one measure of timing in a Signaled-RIFI schedule is the median response during the FI (Peterson et al., 2015). Later median responses are typically considered indicative of better timing precision and tracking of delay. Fig. 3 shows median response times for each group during the pretest and posttest. All of the data points essentially overlap, and non-parametric comparisons (Wilcoxon Signed Rank Test for within group comparisons and Mann-Whitney U Tests for between group comparisons), revealed nothing systematic. The only significant differences were rats in the DRL group had significantly later median response times in LL 40-s forced-choice trials during the pretest than the DRH group; and rats in the DRH group had significantly sooner median response times in LL 10-s forced-choice trials during the posttest than the pretest. Furthermore, the relative change in the median response time from pretest to posttest across all conditions was not associated with the change in AUC from pretest to posttest. Fig. 4 shows this relationship. In fact, there is a non-significant negative correlation: As relative median response times increased from pretest to posttest (i.e. timing improved), AUC decreased from pretest to posttest,  $r(16) = -.23$ ,  $p = .398$ . This is the opposite of the expected relationship if improved timing precision is driving decreases in impulsive choice as a result of delay exposure training.

In summary, we found that training on a DRL 30-s schedule resulted

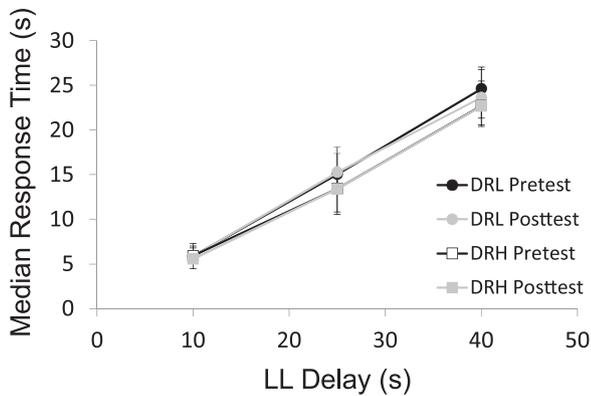


Fig. 3. Median response times during LL forced-choice trials at each of the LL delays during the pretest and posttest for the DRL and DRH groups in Experiment 1. Error bars show range.

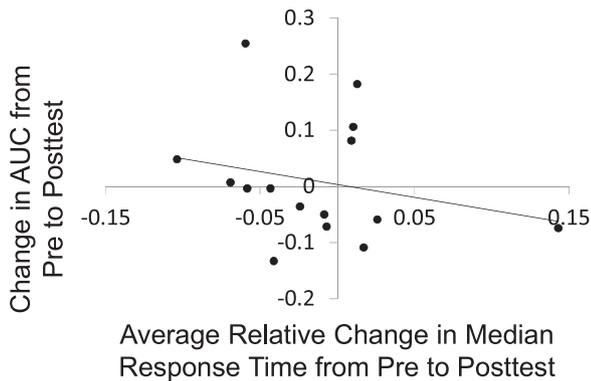


Fig. 4. Change in area under the curve (AUC) from pretest to posttest as a function of average relative change from pretest to posttest in median response time during LL forced choice trials in Experiment 1. Data are pooled across groups and each data point represents an individual rat.

in significant within-subject reductions in impulsive choice at the intermediate and long LL delays. This finding is generally consistent with several recent reports of delay exposure reducing impulsive choice in rats (Bailey et al., 2018; Marshall et al., 2014; Renda et al., 2018; Rung et al., 2018; Stein et al., 2013, 2015), and one report of a DRL schedule intervention reducing impulsivity (Smith et al., 2015). Although some within-groups pretest to posttest differences were significant, we did not observe between-group differences during the posttest. Nevertheless, the direction of the effect was consistent with previous research: the DRL group was less impulsive than the DRH group across all three LL delays. This is the first report, however, of immediate reward exposure training increasing impulsive choice. Renda et al. (2018) recently reported that immediate-reward training did not increase impulsive choice, but may have mitigated decreases in impulsive choice related to maturation. However, this observation was cautious because of a “preponderance of impulsive choice at baseline” (Renda et al., 2018 p. 10)—i.e. a floor effect. Here we show that immediate-reward training in the form of a DRH schedule increased impulsive choice at the 10- and 25-s LL delays. We did not observe an increase at the 40-s LL delay, possibly due to a floor effect as well.

We also found that relative changes in timing precision were unrelated to changes in AUC from pretest to posttest. This finding is inconsistent with the notion that improved timing precision is the mechanism responsible for decreases in impulsive choice as a result of exposure to delayed reward. It is consistent with a report of DRL schedules only transiently degrading timing precision (Eckard and Kyonka, 2018), and reports that timing precision is unrelated to changes in impulsive choice as a result of exposure to delayed rewards

(Rung et al., 2018). Though, our findings should be interpreted with caution as they are based on a fairly rudimentary measure of timing (Experiment 2 was designed to address this and is described below).

These findings are important for how delay exposure training research is to be evaluated—especially as researchers search for the underlying behavioral mechanisms by which delay exposure reduces impulsive choice. First, experiments that do not employ a pretest, which is many (e.g., Bailey et al., 2018; Renda and Madden, 2016; Stein et al., 2013, 2015), should be interpreted cautiously (but c.f., Smith et al., 2015; Stuebing et al., 2018; Renda et al., 2018). In this research, between-group differences during the posttest may be due to increases in impulsive choice in the immediate-reward group, decreases in impulsive choice in the delayed-reward group, or some combination. Our findings in Experiment 1 suggest it may be a combination, and we sought to explore this further in Experiment 2.

The Experiment 1 results are also important because we show these effects of immediate and delayed-reward exposure after just 60 days of intervention training. This is relatively short compared to previous research where the intervention phase can last more than 100 days (e.g., Renda et al., 2018; Rung et al., 2018).

Despite being statistically significant, the increases and decreases in LLR choice from the pretest to the posttest for the DRH and DRL groups, respectively, were quite modest. These differences were only observable by employing the powerful GMLR framework. It is not clear if they are clinically relevant, especially considering no clear differences at the aggregate level (changes in AUC; Fig. 2). A longer intervention phase may have resulted in larger changes in impulsive choice from pretest to posttest and significant between group differences in the posttest. We also used a relatively small number of rats (16; eight per group) compared to similar work which has employed considerably more. For example, recently Bailey et al. (2018) used 24 to 36 rats per group, Renda et al. (2018) 17 per group, and Rung et al. (2018) 12 per group. Employing more animals would increase power and perhaps the between group differences we observed in the posttest would have been statistically significant. This is likely given the relative size of our group difference was similar or larger to those recently reported (e.g., Bailey et al., 2018).

There is substantial, growing evidence that exposure to delayed rewards decreases impulsive choice; however, the underlying mechanism driving the effect remains largely unknown. Timing data from Experiment 1 suggest that improvements in timing precision may not underlie the effect, but Experiment 2 was designed to explore this further. Experiment 2 was also designed to further test the notion that exposure to immediate rewards significantly decreases LLR choice and test effects of exposure to relatively long delays during the intervention phase.

### 3. Experiment 2

One possible mechanism by which time-based interventions increase choice for LLR is by changes in timing processes (i.e. subjective time perception). To this end, research has shown that improved timing precision is associated with decreases in impulsive choice (Marshall et al., 2014; Peterson and Kirkpatrick, 2016; Smith et al., 2015). However, reductions in impulsive choice often result in decreased sensitivity to increases in LL delay (e.g., Bailey et al., 2018)—in other words, apparent reduced sensitivity to time. Consistent with Experiment 1 results, recent reports also show no relation between changes in timing and decreases in impulsive choice as a result of exposure to delayed rewards (Rung et al., 2018), and that training on a DRL schedule decreases timing precision in a peak procedure, even when the DRL schedule value is the same as the FI duration used in the peak procedure (Eckard and Kyonka, 2018). Furthermore, the disruption in timing reported by Eckard and Kyonka was transient—only observed for several sessions—and as such cannot be responsible for any changes in impulsive choice as a result of delay exposure, which are robust at

retests conducted months later (Peterson et al., 2015; Renda and Madden, 2016).

There are other possible mechanisms by which delayed-reward exposure might increase LLR choice. One is reductions in delay aversion and delay avoidance. In other words, the LL delay becomes less aversive as experience with relatively long delays to reward increases. Under this assumption, it is also possible that prolonged experience with immediate rewards increases aversion to delay. Both of these hypotheses are consistent with our results from Experiment 1.

One prediction of the delay aversion reduction hypothesis is that if delay exposure training alone, and not learning about the specific time intervals involved in the choice task, drives reductions in impulsive choice, then it shouldn't matter so much what the actual delay is that is used during intervention training. For example, we used a 30-s DRL schedule in Experiment 1, but this hypothesis predicts that using delays outside those used in the choice task (e.g., 60 or 80 s) should be just as effective, possibly more. The fact that in previous research different delays and schedules have been used during training also supports this possibility. However, no research has yet compared effects of delay exposure training using delays within and outside the delays used in the choice task.

Experiment 2 was designed to further assess these predictions. We did so by using three groups of rats in a pretest/posttest design similar to that used in Experiment 1. After the pretest, one group was exposed to a no-delay intervention, one group was exposed to a 30-s intervention, and one group was exposed to a 60-s intervention. We assessed timing of the 30-s LL delay using a peak procedure implemented immediately after the posttest. We employed the no-delay group as a standard control group in Experiment 2 in order to see if we could replicate decreases in LLR choice that we observed for the DRH group in Experiment 1. We also used shorter LL delays for the intermediate and long LL delay conditions in an attempt to avoid floor effects.

### 3.1. Method

#### 3.1.1. Subjects

Subjects were 24 naïve male Wistar rats approximately eight weeks of age at the start of the experiment. Rats were obtained from Charles River Laboratories at approximately four weeks of age. Food restriction and housing were the same as in Experiment 1.

#### 3.1.2. Apparatus

Same as Experiment 1.

#### 3.1.3. Procedure

All rats were first shaped to press levers for food reinforcement. This was followed by two to four days of FR 1 training with 30 trials on each lever, randomly selected without replacement in blocks of 10 trials (five right, five left) for 60 total trials. The delay discounting pretest followed immediately and was the same as that described in Experiment 1, except the LL delay was 10, 20, and 30 s (presented in an ascending order across conditions). We reduced the intermediate and long LL delays in order to avoid floor effects caused by exclusive preference for the SS option. Sessions lasted for five blocks of 10 choice trials, one SS trial, and one LL trial, randomly selected without replacement, for 60 total trials or 1 h, whichever occurred first. Sessions only timed out for 32 total sessions across 10 rats, always when the LL option was 30 s, except for one rat in the 60-s intervention group in which sessions timed out nine times during the pretest across all three LL conditions. Typically, when sessions timed out only a few trials went uncompleted. Each LL condition lasted a minimum of six sessions and until there were no visual trends in the proportion of LL choice across three to five consecutive sessions. Location of the LL option was counterbalanced across rats. The ITI was 30 s, making the LL option optimal in all conditions in terms of momentary rate of reinforcement.

Immediately following the pretest, area under the curve (AUC) was

calculated for each rat based on choice during the pretest. AUC was calculated using the same method as that described in Experiment 1. All rats were then rank ordered based on their individual AUC values, matched, and randomly assigned to the 30-s ( $N = 8$ ), 60-s ( $N = 8$ ), or no-delay ( $N = 8$ ) intervention group.

During the intervention phase, rats in the 30-s and 60-s groups experienced a Signaled-RIFI schedule with an interval duration corresponding to group assignment. Rats in the no-delay group experienced a FR 2 schedule, but the light above the lever was still illuminated upon the first response in the ratio. The reinforcer was either one or two pellets, randomly selected without replacement from a list of five one-pellet trials and five two-pellet trials, and the active lever on each trial was randomly selected without replacement from a list of five left-lever trials and five right-lever trials.

Sessions for the 60-s group always lasted 2 h. In order to control for cumulative obtained reinforcement during the intervention phase, we yoked the average number of completed trials for the 60-s group to the maximum number of possible trials the 30-s and no-delay groups could complete each day. Sessions for the 30-s and no-delay groups could also timeout after 1.5 h, but this rarely occurred. In all, the yoking procedure was successful and rats in the 60-s ( $M = 31.49$ ,  $SD = 6.03$ ), 30-s ( $M = 31.58$ ,  $SD = 1.04$ ), and no-delay ( $M = 32.12$ ,  $SD = 0.09$ ) groups completed approximately the same number of trials each day on average. The 30-s and no-delay groups had averages that slightly exceeded the 60-s group because we set the max as the yoked total plus 5 trials at the start of the intervention phase to account for rats that may not finish the maximum number of trials. When it became clear that the five-trial buffer wasn't necessary, we removed it. It lasted six sessions. The intervention phase lasted until rats in each group completed an average of 1000 trials. This took 32 sessions.

The delay discounting posttest immediately followed the intervention phase and was exactly the same as the pretest, except that the initial condition (5-s SS versus 10-s LL) lasted a minimum of 10 sessions. This was done because choice behavior of several rats was slow to adjust to the transition to the posttest choice task and we wanted to ensure stable behavior for all rats.

After the posttest, all rats experienced three sessions of a peak procedure. The active lever during this phase was the lever assigned as the LL lever for each rat. Reinforcers were always two pellets. During a food trial, the lever was inserted and the first press initiated a 30-s FI. On food trials, the first response after 30 s produced reinforcement (two pellets). Therefore, food trials were the same as LL forced-choice trials when the LL delay was 30 s in the discounting procedure. Peak trials started the same, but lasted 90 s from the response that initiated the FI, and never resulted in food delivery. At the end of the 90 s, the lever was retracted, light extinguished, and the ITI commenced. The ITI remained 30 s. Trials occurred in blocks of five trials with four food trials and one peak trial per block, randomly selected without replacement from a list. Sessions lasted for 1 h.

### 3.2. Data analysis

#### 3.2.1. Choice

We analyzed the raw choice proportion data using the same GMLR approach as that described in Experiment 1. Group (30 s, 60 s, no delay) and Test (pre and post) were coded as categorical variables and the LL/SS Ratio was continuous. The categorical variables were effect coded. The best fitting model included the full factorial of fixed effects (Group\*Test\*LL/SS Ratio), and LL/SS Ratio and Subject as random effects. The model included a random intercept as well. We used the same method of model fitting as described in Experiment 1 and again used the standard  $p < .05$  criterion for significance. Data from the last three sessions in each condition during the pretest and posttest for each rat were used in the analysis.

### 3.2.2. Peak procedure

Only peak trials were used in the analysis and all peak trials from all three sessions were used for each rat. To quantify response-rate gradients, the following Gaussian function was fitted to the data up to time  $2t$ , where  $t$  was the scheduled interval duration, for each rat to maximize variance accounted for (VAC) using a nonlinear optimization algorithm (Microsoft Excel Solver):

$$y(t) = me^{-(t-a)^2/2p^2} \tag{1}$$

where  $m$  is the height of the peak (maximum rate),  $a$  is the time of the peak (peak location; timing accuracy), and  $p$  is the standard deviation (width of the peak; timing precision). The model provided a good fit to the response-gradient data with a mean VAC of .78 ( $SD = .16$ ) across rats. One rat from the 60-s group was omitted from the analysis because the model provided a poor fit ( $VAC = .01$ ). This rat's response gradient data are included in the mean response gradients shown below.

### 3.3. Results and discussion

The matching procedure successfully equated impulsive choice in the three groups prior to the intervention phase. The best fitting GMLR model indicated no significant differences between groups during the pretest.

The top panel in Fig. 5 shows the mean proportion of LL choice for each group in the posttest. The second, third, and fourth panels of Fig. 5 show comparisons of pretest and posttest choice for the 30-s, 60-s, and no-delay groups, respectively. All graphs show error bars from the best fitting GMLR model. The best fitting model revealed that 30-s ( $z = 13.10, p < .001$ ), 60-s ( $z = 13.31, p < .001$ ), and no-delay ( $z = 11.11, p < .001$ ) group assignment, Test ( $z = 6.67, p < .001$ ), and the LL/SS Ratio ( $z = -14.16, p < .001$ ) were significant predictors of choice. The model also revealed several significant interactions, including a Group  $\times$  Test  $\times$  LL/SS Ratio interaction ( $z = -8.33, p < .001$ ). To further analyze the significant interaction between all three independent variables, we conducted post-hoc comparisons between groups during the posttest at each LL delay, and between the pretest and posttest within each group at each LL delay. These comparisons revealed that the no-delay group was more impulsive than the 30-s ( $z = 2.26, p = .04$ ) and 60-s ( $z = 2.60, p = .03$ ) groups during the posttest in the 10-s LL condition. While the no-delay group was also more impulsive than the other two groups at the 20- and 30-s LL delays, these differences were not statistically significant.

Within-group comparisons revealed the 30-s group was significantly less impulsive during the posttest at the 10-s ( $z = 2.13, p = .033$ ) and 30-s ( $z = 6.26, p < .001$ ) LL delays; shown in the second panel of Fig. 5. The 60-s group was significantly less impulsive during the posttest at just the 30-s ( $z = 11.97, p < .001$ ) LL delay; shown in the third panel of Fig. 5. Finally, the no-delay group was significantly more impulsive during the posttest at the 10-s ( $z = -3.52, p < .001$ ), 20-s ( $z = -10.09, p < .001$ ), and 30-s ( $z = -6.90, p < .001$ ) LL delays; shown in the bottom panel of Fig. 5. For a closer inspection of how choice changed at the individual rat level, Fig. 6 shows the change in the proportion of LL choice from pretest to posttest for each rat in each condition (means shown as bars). These data are consistent with the results from the GMLR model: the majority of rats in the no-delay group were more impulsive during the posttest at all three LL delays. There was a clear decrease in impulsive choice at the 30-s LL delay for the 30-s and 60-s groups, but there was little change across rats at the 10- and 20-s LL delays.

To compare the results of the GMLR modeling to more traditional forms of analysis, we compared the change in AUC from pretest to posttest between the three groups. Fig. 7 shows the mean (bars) and individual (data points) changes in AUC from pretest to posttest for each group. A one-way ANOVA, revealed a significant effect of group,  $F(2,23) = 6.58, p = .006, \eta_p^2 = 0.28$ . Post-hoc, Tukey corrected

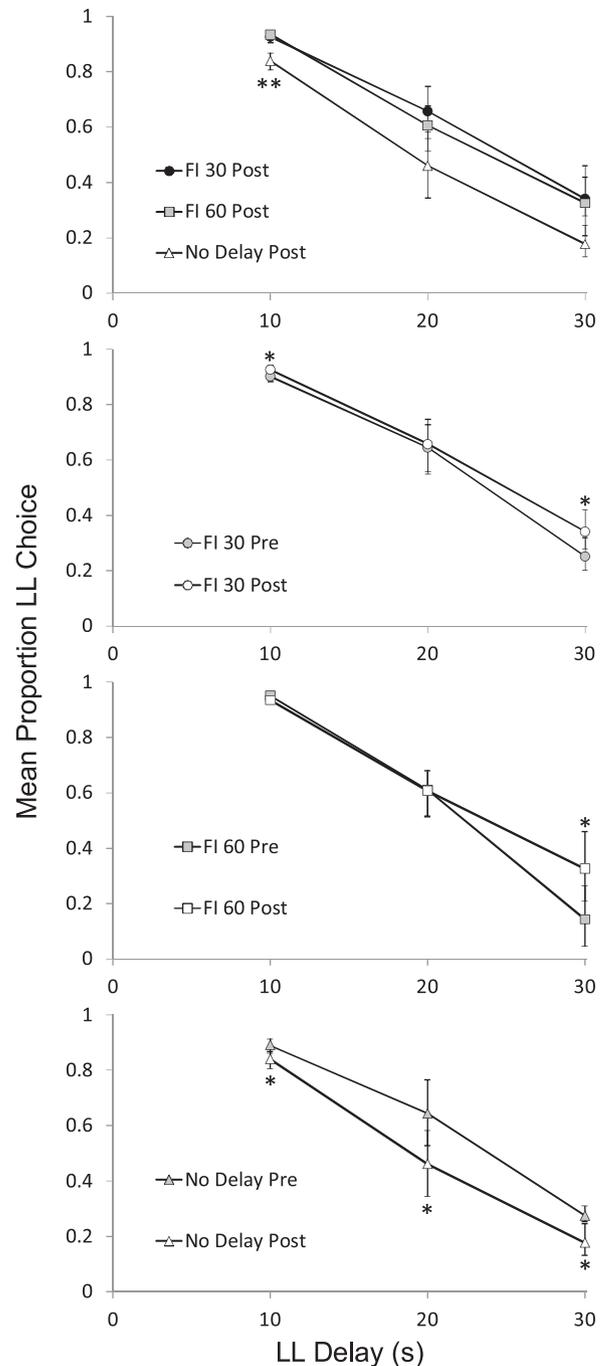


Fig. 5. Mean proportion of LL choice for the 30-s, 60-s, and no-delay groups during the posttest (top panel), and during the pretests and posttests for the 30-s (second panel), 60-s (third panel), and no-delay (bottom panel) groups in Experiment 2. Error bars show error from best fitting GMLR model (see Section 2.2). \* = statistically significant difference ( $p < .05$ ). \*\* = No-delay group statistically significantly different from both 30-s and 60-s groups ( $p < .05$ ).

comparisons revealed significant differences between the no-delay group and the 30-s ( $p = .015$ ) and 60-s ( $p = .012$ ) groups. This effect appears driven largely by the fact that, based on AUC, all the no-delay rats became more impulsive in the posttest, but most of the rats in the 30-s and 60-s groups became less impulsive or did not change much from the pretest.

Finally, we assessed timing of the 30-s LL delay in a peak procedure immediately following the posttest. Fig. 8 shows mean response rate gradients with the best fitting Gaussian model (Eq. (1)) for each group. The peak curves are somewhat flatter than in traditional peak

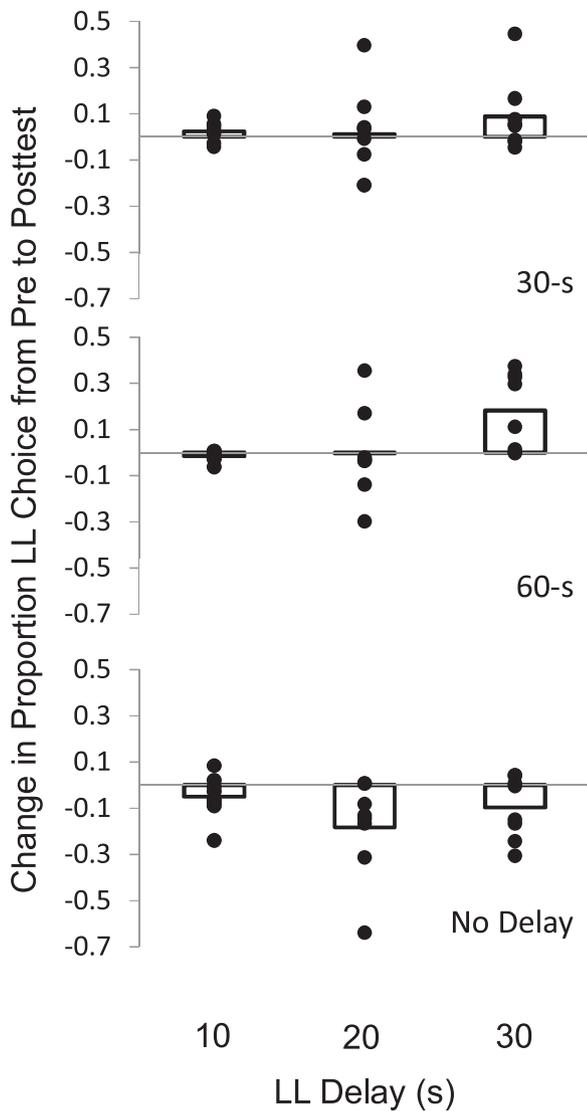


Fig. 6. Change in the proportion of LL choice from pretest to posttest for rats in the 30-s (top panel), 60-s (middle panel), and no-delay (bottom panel) groups in Experiment 2. Each data point represents an individual rat and the bars represent the group mean.

procedures, likely due to a combination of little exposure to peak trials and the response-initiated schedules (Fox and Kyonka, 2013, 2014, 2015, 2016). Nevertheless, the 30-s group was the most accurate (*accuracy parameter* = 37.67) and precise (*precision parameter* = 26.81), followed by the 60-s group (*accuracy parameter* = 42.89, *precision parameter* = 38.50), and the no-delay group (*accuracy parameter* = 42.62, *precision parameter* = 40.17). The rate of responding at the peak time was also highest for the 30-s group (90.91 responses/min), followed by the 60-s group (84.19 responses/min) and the no-delay group (69.44 responses/min). That the 30-s group showed the most accurate and precise timing of the 30-s interval should not be surprising, considering the extensive training on that interval duration those rats experienced during the intervention phase.

The most pertinent question for the timing analysis, however, is whether or not timing precision predicted posttest impulsive choice and/or the change in impulsive choice from pretest to posttest. Fig. 9 shows the correlation between the pretest to posttest change in AUC and timing precision in the peak procedure (top panel),  $r(21) = -.32$ ,  $p = .162$ , and posttest AUC and timing precision in the peak procedure (bottom panel),  $r(21) = .12$ ,  $p = .614$ , pooled across groups. Three rats were omitted, one because the Gaussian model did not fit the data well

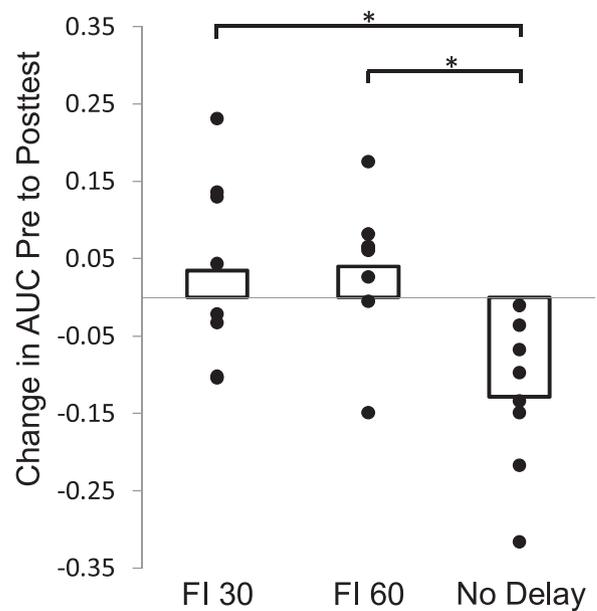


Fig. 7. Change in area under the curve (AUC) from pretest to posttest for rats in the 30-s, 60-s, and no-delay groups in Experiment 2. Data points show individual rats and bars show group means. \* = statistically significant difference ( $p < .05$ ).

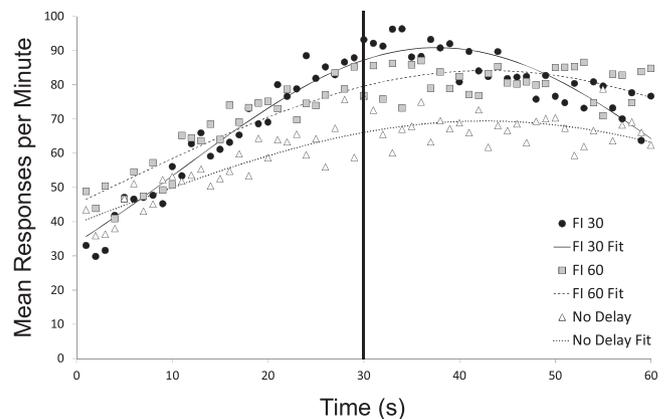
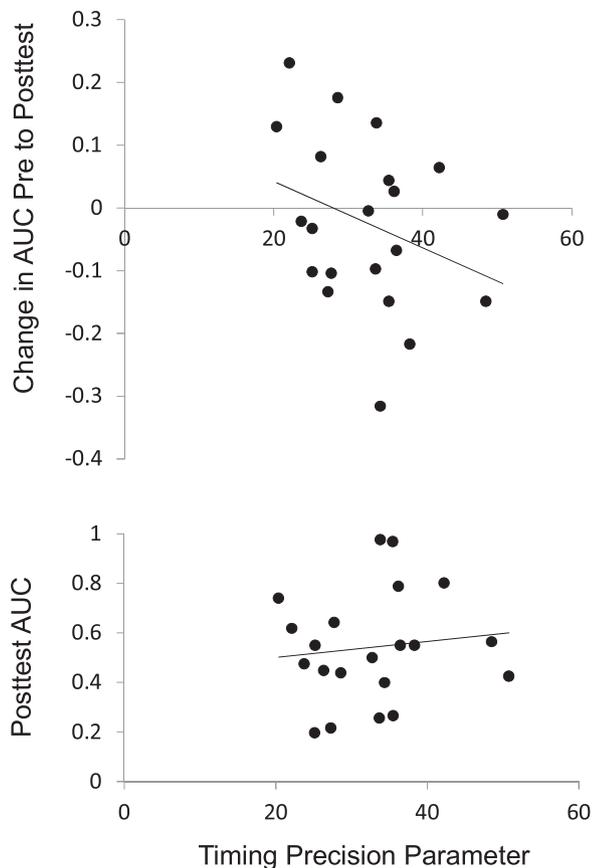


Fig. 8. Mean peak response gradients, with the best fitting Gaussian function overlaid, for the 30-s, 60-s, and no-delay groups during the peak procedure in Experiment 2. Horizontal solid line represents time of food availability on food trials (30 s).

(see Section 3.2. Data Analysis), and two more because their precision parameter values from the best fitting model were outliers and were greatly skewing the correlations. The correlations within groups were consistent with the overall relationships shown in Fig. 9. We also tested timing precision as a predictor of LL choice in the best fitting GMLR model described above. Timing precision was not a significant predictor of LL choice ( $z = 1.17$ ,  $p = .242$ ). In sum, while rats in the 30-s group timed the 30-s LL delay with greater precision and accuracy than rats in the 60-s and no-delay groups, across rats timing precision was not predictive of changes in LL choice from pretest to posttest (top graph, Fig. 9) or posttest LL choice (bottom graph, Fig. 9).

In Experiment 2, we found that exposure to delayed rewards resulted in increased choice for the LLR option. For the most part, this effect was observed at only the longest LL delay (30 s). Compared to previous research, we used a briefer intervention period and controlled for cumulative reinforcers earned during the intervention phase. This finding adds to a growing body of literature showing exposure to delayed rewards decreases impulsive choice in rats (Bailey et al., 2018;



**Fig. 9.** The top panel shows the change in area under the curve (AUC) from pretest to posttest as a function of the timing precision parameter estimate from the best fitting Gaussian model fit to peak response gradients for each rat across all three groups. The bottom panel shows posttest AUC as a function of the timing precision parameter estimate from the best fitting Gaussian model fit to peak response gradients for each rat across all three groups. Lines represent best fitting linear regression function. Neither relationship was statistically significant.

Marshall et al., 2014; Renda et al., 2018; Rung et al., 2018; Stein et al., 2013, 2015). We also found that extended exposure to immediate rewards increased impulsive choice, which we observed across all of the LL delays in the no-delay group. This replicates a similar effect observed in Experiment 1, where we found exposure to a DRH schedule increased impulsive choice in the posttest at the short and intermediate LL delays.

In addition, although previous work has suggested that increases in timing precision may underlie the effect of reduced impulsive choice as a result of exposure to delayed rewards, we are at least the second (Rung et al., 2018) to show that timing precision was not predictive of posttest impulsive choice or changes in impulsive choice from pretest to posttest.

We are the first to report an increase in LLR choice using an intervention duration greater than those used in the delay discounting assessment (60-s group). That the results for the 60-s group were similar to those observed for the 30-s group suggests that 1) the mechanism driving the posttest reduction in impulsive choice may not be timing intervals/delays more precisely (also supported by results from the peak procedure), and 2) that relatively longer delays may not result in relatively greater decreases in impulsive choice—though that is based on limited data and warrants further investigation.

#### 4. General discussion

Taken together, the results of Experiments 1 and 2 replicate and extend previous research showing reductions in impulsive choice as

result of exposure to delayed rewards (Bailey et al., 2018; Marshall et al., 2014; Renda et al., 2018; Rung et al., 2018; Stein et al., 2013, 2015). The effect appears robust across intervention schedule type (e.g., FI, variable interval (VI), DRL), schedule value (intervals both within and outside the range used in the delay discounting assessment), intervention duration, rat strain (e.g., Wistar, Long Evans, Sprague Dawley), and discounting assessment method (e.g., both within- and across-session manipulations of the LL delay, manipulations of the SS delay, and manipulations of reward magnitude). Furthermore, the effect is sustained during retests months after exposure training (Bailey et al., 2018; Renda and Madden, 2016). We also found that extended exposure to immediate rewards, both a DRH in Experiment 1 and FR 2 in Experiment 2, may increase impulsive choice. This finding is important because often experiments like the ones presented here do not include a pretest (e.g., Bailey et al., 2018, but c.f. Renda et al., 2018; Rung et al., 2018; Smith et al., 2015; Stuebing et al., 2018), which means that observed effects may be the result of reduced impulsivity in the delayed-reward group and/or increased impulsivity in the immediate-reward group. Findings from Experiment 1 and 2 suggest a combination is possible. Within-subject analyses may help elucidate effects of delay-exposure training and will be an important part of future research.

Furthermore, the timing analyses from Experiments 1 and 2 indicate that improved timing precision may not underlie the reduction in impulsive choice observed in the posttest. Previous work has suggested such a mechanism (Galtress et al., 2012; Kirkpatrick et al., 2015; Marshall et al., 2014; Peterson et al., 2015), but we are at least the second (Rung et al., 2018) to show no relationship between timing precision and changes in impulsive choice. This is further supported by work showing DRL schedules transiently disrupt, not improve timing precision (Eckard and Kyonka, 2018). Instead, especially given the results of the 60-s group in Experiment 2, our findings may support the hypothesis that a reduction in aversion to delayed rewards underlies the reduction in impulsive choice. Moreover, extended exposure to immediate rewards may bias rats away from LL options—i.e. perhaps increase aversion to delayed reward and increase avoidance of delay—as suggested by the results of our DRH group in Experiment 1 and no-delay group in Experiment 2. Although our findings are consistent with such a hypothesis, we have no clear empirical evidence to support it presently and cannot exclude other possible mechanisms.

Although the results of Experiments 1 and 2 increase our understanding of how and why exposure to delayed and immediate rewards modify impulsive choice behavior, much remains a mystery. For example, it is unclear if the effects would generalize to different settings, tasks, reinforcers, etc.—though the effect is robust at retest, in particular for FI interventions (Bailey et al., 2018). It is not clear how much training is necessary to affect impulsive choice, though our findings suggest relatively short exposure (approximately 1000 trials in Experiment 2) may be enough. The effect was recently reported in female rats (Stuebing et al., 2018), but it isn't clear if it would hold for inbred rat strains, genetic KO strains, etc. Also, it is unclear if signaled delays must be used during intervention training as they were presently and in previous work (e.g., Rung et al., 2018; Stuebing et al., 2018), or if unsignaled delays or briefly signaled delays would have the same effect—this may be particularly relevant for translation to applied settings where delays to reinforcement may or may not be explicitly signaled.

Future research may also employ different types of control groups, for example, a maturation/handle control group (Renda et al., 2018), given that we observed increases in impulsive choice as a result of immediate-reward training. The increase in SSR choice for the DRH (Experiment 1) and FR 2 (Experiment 2) groups helped drive differences between groups in the posttests and similar effects may be partially responsible for between-group differences previously reported. Using a maturation/handle control group in future research may lessen the robustness of effects of delay exposure training on LLR choice.

Finally, and perhaps most importantly, it is not clear if the effect

would generalize to humans or how the training would be implemented for human subjects. The translation to human subjects is a considerable roadblock to delay exposure training having real clinical implications. It is difficult to imagine how one might test effects of such repeated and extended exposure to delayed rewards (thousands of trials over weeks to months) in humans. This seems especially difficult considering the procedural differences when testing delay discounting in humans and non-humans (Vanderveldt et al., 2016). Humans are typically asked hypothetical questions between monetary amounts delivered at delays of days to years, whereas non-humans are exposed to contingencies, experience real outcomes, food is the reinforcer, and the delays are in the seconds to minutes range. One possible initial path forward might be to test the intervention in children using an intervention that can be integrated into their day-to-day schedule. DRL schedules may provide a systematic means by which reinforcers can be appropriately spaced in time without extinguishing appropriate behavior in a natural setting. A simplified discounting assessment may also be advantageous—perhaps a “marshmallow test” type of assessment (Mischel et al., 1972) is a good place to start because it can be quickly and easily implemented on a regular basis in a natural setting.

The implications of such work are far reaching. The vast majority of chronic health conditions in humans are a result of choosing SSR over LLR—e.g., sitting instead of moving (exercise), eating cake instead of kale, choosing soda over water, etc. In addition, there is a clear and strong relationship between steep discounting and substance abuse, obesity, risky sexual behavior, and other maladaptive behavior patterns (Bickel and Mueller, 2009; Bickel et al., 2012). Increasing preference for LLR in at risk populations and for society more generally, could improve health at scale, reducing healthcare costs and improving quality of life. The results of Experiments 1 and 2 are a small, important step forward, but much work remains.

## Acknowledgements

The authors thank the Dr. Robert J Feiguine P’18 Endowment and Daniel F. ‘65 and Ann H. Sullivan Endowment for Student Faculty Research supporting the St. Lawrence Summer Research Fellows Program (to AMN & EJV). Portions of these data were presented at the Eastern Psychological Association’s annual conference in 2018. Experiment 1 was conducted in partial fulfillment of the requirements of a St. Lawrence University Summer Research Fellowship awarded to AMN. Experiment 2 was conducted as part of senior thesis research conducted by AMN and EJV. Experiment 2 also served as partial fulfillment of the requirements to graduate with honors in psychology for AMN. The authors thank Paige Currie, Colin Hart, Julie Joyce, Cole Poulin, and Abigail Schreder for assistance conducting the experiments. The authors declare no competing interests. Please address correspondence to AEF at afox@stlawu.edu.

## References

- Alessi, S.M., Petry, N.M., 2003. Pathological gambling severity is associated with impulsivity in a delay discounting procedure. *Behav. Proc.* 64, 345–354. [https://doi.org/10.1016/S0376-6357\(03\)00150-5](https://doi.org/10.1016/S0376-6357(03)00150-5).
- Amlung, M., Petker, T., Jackson, J., Balodis, I., MacKillop, J., 2016. Steep discounting of delayed monetary and food rewards in obesity: a meta-analysis. *Psychol. Med. (Paris)* 46, 2423–2434. <https://doi.org/10.1017/S0033291716000866>.
- Anker, J.J., Perry, J.L., Gliddon, L.A., Carroll, M.E., 2009. Impulsivity predicts the escalation of cocaine self-administration in rats. *Pharmacol. Biochem. Behav.* 93, 343–348. <https://doi.org/10.1016/j.pbb.2009.05.013>.
- Bailey, C., Peterson, J.R., Schnegelsiepen, A., Stuebing, S.L., Kirkpatrick, K., 2018. Durability and generalizability of time-based intervention effects on impulsive choice in rats. *Behav. Proc.* <https://doi.org/10.1016/j.beproc.2018.03.003>.
- Barkley, R.A., Edwards, G., Laneri, M., Fletcher, K., Metevia, L., 2001. Executive functioning, temporal discounting, and sense of time in adolescents with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD). *J. Abnorm. Child Psychol.* 29, 541–556. [10.1023/1012233310098](https://doi.org/10.1023/1012233310098).
- Bates, D., Kiegl, R., Vasisith, S., Baayen, H., 2015. Parsimonious Mixed Models. Retrieved from. <https://arxiv.org/abs/1506.04967>.
- Bickel, W.K., Jarmolowicz, D.P., Mueller, E.T., Koffarnus, M.N., Gatchalian, K.M., 2012.

- Excessive discounting of delayed reinforcers as a trans-disease process contributing to addiction and other disease-related vulnerabilities: emerging evidence. *Pharmacol. Ther.* 134, 287–297. <https://doi.org/10.1016/j.pharmthera.2012.02.004>.
- Bickel, W.K., Mueller, E.T., 2009. Toward the study of trans-disease processes: a novel approach with special reference to the study of co-morbidity. *J. Dual Diag.* 5, 131–138. <https://doi.org/10.1080/15504260902869147>.
- Bickel, W.K., Yi, R., Landes, R.D., Hill, P.F., Baxter, C., 2011. Remember the future: working memory training decreases delay discounting among stimulant addicts. *Biol. Psychiatry* 69, 260–265. <https://doi.org/10.1016/j.biopsych.2010.08.017>.
- Binder, L.M., Dixon, M.R., Ghezzi, P.M., 2000. A procedure to teach self-control to children with attention deficit hyperactivity disorder. *J. Appl. Behav. Anal.* 33, 233–237. <https://doi.org/10.1901/jaba.2000.33-233>.
- Black, A.C., Rosen, M.I., 2011. A money management-based substance use treatment increases valuation of future rewards. *Addict. Behav.* 36, 125–128. <https://doi.org/10.1016/j.addbeh.2010.08.014>.
- Boisgontier, M.P., Cheval, B., 2016. The anova to mixed model transition. *Neuro. Biobehav. Rev.* 68, 1004–1005. <https://doi.org/10.1016/j.neubiorev.2016.05.034>.
- Chesson, H.W., Leichliter, J.S., Zimet, G.D., Rosenthal, S.L., Bernstein, D.I., Fife, K.H., 2006. Discount rates and risky sexual behaviors among teenagers and young adults. *J. Risk Uncertain.* 32, 217–230. <https://doi.org/10.1007/s11166-006-9520-1>.
- Daniel, T.O., Stanton, C.M., Epstein, L.H., 2013. The future is now: Reducing impulsivity and energy intake using episodic future thinking. *Psychol. Sci.* 24, 2339–2342. <https://doi.org/10.1177/0956797613488780>.
- DeHart, W.B., Odum, A.L., 2015. The effects of the framing of time on delay discounting. *J. Exp. Anal. Behav.* 103, 10–21. <https://doi.org/10.1002/jeab.125>.
- Demurie, E., Roeyers, H., Baeyens, D., Sonuga-Barke, E., 2012. Temporal discounting of monetary rewards in children and adolescents with ADHD and autism spectrum disorders. *Dev. Sci.* 15, 791–800. <https://doi.org/10.1111/j.1467-7687.2012.01178.x>.
- Dixon, M.R., Marley, J., Jacobs, E.A., 2003. Delay discounting by pathological gamblers. *J. Appl. Behav. Anal.* 36, 449–458. <https://doi.org/10.1901/jaba.2003.36-449>.
- Eckard, M.L., Kyonka, E.G., 2018. Differential reinforcement of low rates differentially decreased timing precision. *Behav. Proc.* 151, 111–118. <https://doi.org/10.1016/j.beproc.2018.02.022>.
- Fox, A.E., Kyonka, E.G., 2013. Pigeon responding in fixed-interval and response-initiated fixed-interval schedules. *J. Exp. Anal. Behav.* 100, 187–197. <https://doi.org/10.1002/jeab.38>.
- Fox, A.E., Kyonka, E.G., 2014. Choice and timing in pigeons under differing levels of food deprivation. *Behav. Proc.* 106, 82–90. <https://doi.org/10.1016/j.beproc.2014.04.018>.
- Fox, A.E., Kyonka, E.G., 2015. Timing in response-initiated fixed intervals. *J. Exp. Anal. Behav.* 103, 375–392. <https://doi.org/10.1002/jeab.120>.
- Fox, A.E., Kyonka, E.G., 2016. Effects of signaling on temporal control of behavior in response-initiated fixed intervals. *J. Exp. Anal. Behav.* 106, 210–224. <https://doi.org/10.1002/jeab.226>.
- Galtres, T., Garcia, A., Kirkpatrick, K., 2012. Individual differences in impulsive choice and timing in rats. *J. Exp. Anal. Behav.* 98, 65–87. <https://doi.org/10.1901/jeab.2012.98-65>.
- Green, L., Estle, S.J., 2003. Preference reversals with food and water reinforcers in rats. *J. Exp. Anal. Behav.* 79, 233–242. <https://doi.org/10.1901/jeab.2003.79-233>.
- Heerey, E.A., Robinson, B.M., McMahon, R.P., Gold, J.M., 2007. Delay discounting in schizophrenia. *Cog. Neuropsychem.* 12, 213–221. <https://doi.org/10.1080/13546800601005900>.
- Heil, S.H., Johnson, M.W., Higgins, S.T., Bickel, W.K., 2006. Delay discounting in currently using and currently abstinent cocaine-dependent outpatients and non-drug-using matched controls. *Addict. Behav.* 31, 1290–1294. <https://doi.org/10.1016/j.addbeh.2005.09.005>.
- Kirkpatrick, K., Marshall, A.T., Smith, A.P., 2015. Mechanisms of individual differences in impulsive and risky choice in rats. *Comp. Cog. Behav. Rev.* 10, 45. <https://doi.org/10.3819/ccbr.2015.100003>.
- Lawyer, S.R., Williams, S.A., Prihodova, T., Rollins, J.D., Lester, A.C., 2010. Probability and delay discounting of hypothetical sexual outcomes. *Behav. Proc.* 84, 687–692. <https://doi.org/10.1016/j.beproc.2010.04.002>.
- Lin, H., Epstein, L.H., 2014. Living in the moment: Effects of time perspective and emotional valence of episodic thinking on delay discounting. *Behav. Neurosci.* 128, 12.
- MacKillop, J., Amlung, M.T., Few, L.R., Ray, L.A., Sweet, L.H., Munafo, M.R., 2011. Delayed reward discounting and addictive behavior: a meta-analysis. *Psychopharmacology (Berl.)* 216, 305–321. <https://doi.org/10.1007/s00213-011-2229-0>.
- MacKillop, J., Gray, J.C., Amlung, M., 2015. Delay Discounting and Addictive Behavior: Review of the Literature and Identification of Emerging Priorities. *Addictions*. Routledge, pp. 25–56.
- Madden, G.J., Petry, N.M., Badger, G.J., Bickel, W.K., 1997. Impulsive and self-control choices in opioid-dependent patients and non-drug-using control patients: drug and monetary rewards. *Exp. Clin. Psychopharmacol.* 5, 256. <https://doi.org/10.1037/1064-1297.5.3.256>.
- Marshall, A.T., Smith, A.P., Kirkpatrick, K., 2014. Mechanisms of impulsive choice: I. Individual differences in interval timing and reward processing. *J. Exp. Anal. Behav.* 102, 86–101. <https://doi.org/10.1002/jeab.88>.
- Mischel, W., Ebbsen, E.B., Raskoff Zeiss, A., 1972. Cognitive and attentional mechanisms in delay of gratification. *J. Pers. Soc. Psychol.* 21, 204. <https://doi.org/10.1037/h0032198>.
- Myerson, J., Green, L., Warusawitharana, M., 2001. Area under the curve as a measure of discounting. *J. Exp. Anal. Behav.* 76, 235–243. <https://doi.org/10.1901/jeab.2001.76-235>.

- Odum, A.L., 2011. Delay discounting: I'm a k, you're a k. *J. Exp. Anal. Behav.* 96, 427–439. <https://doi.org/10.1901/jeab.2011.96.423>.
- Perry, J.L., Larson, E.B., German, J.P., Madden, G.J., Carroll, M.E., 2005. Impulsivity (delay discounting) as a predictor of acquisition of IV cocaine self-administration in female rats. *Psychopharmacology (Berl.)* 178, 193–201. <https://doi.org/10.1007/s00213-004-1994-4>.
- Perry, J.L., Nelson, S.E., Carroll, M.E., 2008. Impulsive choice as a predictor of acquisition of IV cocaine self-administration and reinstatement of cocaine-seeking behavior in male and female rats. *Exp. Clin. Psychopharmacol.* 16, 165. <https://doi.org/10.1037/1064-1297.16.2.165>.
- Peters, J., Büchel, C., 2010. Episodic future thinking reduces reward delay discounting through an enhancement of prefrontal-medioprefrontal interactions. *Neuron* 66, 138–148. <https://doi.org/10.1016/j.neuron.2010.03.026>.
- Peterson, J.R., Hill, C.C., Kirkpatrick, K., 2015. Measurement of impulsive choice in rats: Same- and alternate-form test-retest reliability and temporal tracking. *J. Exp. Anal. Behav.* 103, 166–179. <https://doi.org/10.1002/jeab.124>.
- Peterson, J.R., Kirkpatrick, K., 2016. The effects of a time-based intervention on experienced middle-aged rats. *Behav. Proc.* 133, 44–51. <https://doi.org/10.1016/j.beproc.2016.11.002>.
- Petry, N.M., 2001. Pathological gamblers, with and without substance abuse disorders, discount delayed rewards at high rates. *J. Abnorm. Psychol.* 110, 482. <https://doi.org/10.1037/0021-843X.110.3.482>.
- Petry, N.M., Casarella, T., 1999. Excessive discounting of delayed rewards in substance abusers with gambling problems. *Drug Alcohol Depend.* 56, 25–32. [https://doi.org/10.1016/S0376-8716\(99\)00010-1](https://doi.org/10.1016/S0376-8716(99)00010-1).
- Pitts, R.C., 2014. Reconsidering the concept of behavioral mechanisms of drug action. *J. Exp. Anal. Behav.* 101, 422–441.
- Poulos, C.X., Le, A.D., Parker, J.L., 1995. Impulsivity predicts individual susceptibility to high levels of alcohol self-administration. *Behav. Pharmacol.* 6, 810–814. <https://doi.org/10.1097/00008877-199512000-00006>.
- Rasmussen, E.B., Lawyer, S.R., Reilly, W., 2010. Percent body fat is related to delay and probability discounting for food in humans. *Behav. Proc.* 83, 23–30. <https://doi.org/10.1016/j.beproc.2009.09.001>.
- Read, D., Frederick, S., Orsel, B., Rahman, J., 2005. Four score and seven years from now: the date/delay effect in temporal discounting. *Manag. Sci.* 51, 1326–1335. <https://doi.org/10.1287/mnsc.1050.0412>.
- Renda, C.R., Madden, G.J., 2016. Impulsive choice and pre-exposure to delays: III. Four-month test-retest outcomes in male wistar rats. *Behav. Proc.* 126, 108–112. <https://doi.org/10.1016/j.beproc.2016.03.014>.
- Renda, C.R., Rung, J.M., Hinnenkamp, J.E., Lenzini, S.N., Madden, G.J., 2018. Impulsive choice and pre-exposure to delays: IV. effects of delay-and immediacy-exposure training relative to maturational changes in impulsivity. *J. Exp. Anal. Behav.* <https://doi.org/10.1002/jeab.432>.
- Renda, C.R., Stein, J.S., Madden, G.J., 2015. Working-memory training: effects on delay discounting in male long evans rats. *J. Exp. Anal. Behav.* 103, 50–61. <https://doi.org/10.1002/jeab.115>.
- Rung, J.M., Buhusi, C.V., Madden, G.J., 2018. Reducing impulsive choice: V. The role of timing in delay-exposure training. *Behav. Proc.* <https://doi.org/10.1016/j.beproc.2018.04.018>.
- Rung, J.M., Madden, G.J., 2018. Experimental reductions of delay discounting and impulsive choice: A systematic review and meta-analysis. *J. Exp. Psychol. Gen.* 147, 1349.
- Scheres, A., Dijkstra, M., Ainslie, E., Balkan, J., Reynolds, B., Sonuga-Barke, E., et al., 2006. Temporal and probabilistic discounting of rewards in children and adolescents: effects of age and ADHD symptoms. *Neuropsychologia* 44, 2092–2103. <https://doi.org/10.1016/j.neuropsychologia.2005.10.012>.
- Smith, A.P., Marshall, A.T., Kirkpatrick, K., 2015. Mechanisms of impulsive choice: II. Time-based interventions to improve self-control. *Behav. Proc.* 112, 29–42. <https://doi.org/10.1016/j.beproc.2014.10.010>.
- Snider, S.E., LaConte, S.M., Bickel, W.K., 2016. Episodic future thinking: expansion of the temporal window in individuals with alcohol dependence. *Alcohol. Clin. Exp. Res.* 40, 1558–1566. <https://doi.org/10.1111/acer.13112>.
- Stein, J.S., Johnson, P.S., Renda, C.R., Smits, R.R., Liston, K.J., Shaham, T.A., et al., 2013. Early and prolonged exposure to reward delay: effects on impulsive choice and alcohol self-administration in male rats. *Exp. Clin. Psychopharmacol.* 21, 172. <https://doi.org/10.1037/a0031245>.
- Stein, J.S., Madden, G.J., 2013. Delay discounting and drug abuse: empirical, conceptual, and methodological considerations. *The Wiley-blackwell Handbook of Addiction Psychopharmacology*. Wiley Online Library, pp. 165–208.
- Stein, J.S., Renda, C.R., Hinnenkamp, J.E., Madden, G.J., 2015. Impulsive choice, alcohol consumption, and pre-exposure to delayed rewards: II. Potential mechanisms. *J. Exp. Anal. Behav.* 103, 33–49. <https://doi.org/10.1002/jeab.116>.
- Stuebing, S.L., Marshall, A.T., Triplett, A., Kirkpatrick, K., 2018. Females in the forefront: time-based intervention effects on impulsive choice and interval timing in female rats. *Anim. Cog.* 21, 759–772.
- Team, R.C., 2013. R: a Language and Environment for Statistical Computing.
- Vanderveldt, A., Oliveira, L., Green, L., 2016. Delay discounting: pigeon, rat, human—does it matter? *J. Exp. Psychol. Anim. Learn. Cog.* 42, 141. <https://doi.org/10.1037/xan0000097>.
- Weller, R.E., Cook III, E.W., Avsar, K.B., Cox, J.E., 2008. Obese women show greater delay discounting than healthy-weight women. *Appetite* 51, 563–569. <https://doi.org/10.1016/j.appet.2008.04.010>.
- Wilson, V.B., Mitchell, S.H., Musser, E.D., Schmitt, C.F., Nigg, J.T., 2011. Delay discounting of reward in ADHD: application in young children. *J. Child Psychol. Psychiatry* 52, 256–264. <https://doi.org/10.1111/j.1469-7610.2010.02347.x>.
- Yi, R., Mitchell, S.H., Bickel, W.K., 2010. Delay discounting and substance abuse-dependence. *Impulsivity: the Behavioral and Neurological Science of Discounting*. pp. 191–211.
- Young, M.E., 2018. Discounting: a practical guide to multilevel analysis of choice data. *J. Exp. Anal. Behav.* 109, 293–312. <https://doi.org/10.1002/jeab.316>.