7-2024

EFFECTS OF DIAZEPAM, D-AMPHETAMINE, AND MORPHINE ON RATS' CHOICES BETWEEN FOOD ALONE AND FOOD WITH DELAYED SHOCK

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By

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THESIS

Submitted to
Northern Michigan University
In partial fulfillment of the requirements
For the degree of

MASTER OF SCIENCE

College of Graduate Studies and Research

July 2024

SIGNATURE APPROVAL FORM

Thesis Title:

This thesis by Mackenzie Susan Baranski is recommended for approval by the student's Thesis Committee and Department Head in the Department of Psychological Science and by the Dean of Graduate Studies and Research.

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ABSTRACT

EFFECTS OF DIAZEPAM, D-AMPHETAMINE, AND MORPHINE ON RATS' CHOICES BETWEEN FOOD ALONE AND FOOD WITH DELAYED SHOCK

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Repeated choices that result in immediate reinforcing consequences followed by delayed aversive consequences are commonly associated with failures in "self-control". The present study evaluated acute effects of diazepam, *d*-amphetamine, and morphine on rats' choices using a variable-delay procedure that arranged choices involving conflicting-valence consequences. Rats pressed response levers to choose between a single-valence consequence (1 food pellet) and a conflicting-valence consequence (3 food pellets followed by a delayed shock). In each condition, the delay to shock varied systematically in a fixed sequence across blocks of trials of a session. After choice was stable, rats were exposed to acute administration of diazepam, *d*-amphetamine, and morphine. Effects of the drugs were shown by changes in patterns of choice of the single-valence consequence across the delays in each session, area under the curve, and response latencies. In sessions in baseline, following vehicle administration, and sessions conducted on the day before drug administrations, single-valence consequence choice was generally highest in blocks with short delays to shock and lowest in blocks with long delays, showing that effects of shock were an inverse function of the delay to shock. Following administration of diazepam, effects of shock on choice generally decreased, but this effect depended on the diazepam dose. Following administration of *d*-amphetamine, effects of shock on choice generally increased, but this effect depended on the *d*-amphetamine dose. Administration of morphine generally had no systematic effect on choice. This study sheds light on the general effects of commonly prescribed drug classes on choice in the conflicting-consequences paradigm.

ACKNOWLEDGMENTS

I would like to thank Drs. Cory and Forrest Toegel for their instruction and guidance in experimental design, data analysis, and most importantly scientific writing. I have learned a great deal from them and cannot thank them enough for their mentorship. I am grateful to my other thesis committee members, Dr. Adam Prus and Dr. Sally Huskinson for their helpful comments and suggestions on this document and their time. I would also like to thank my fiancé Lukas Denner, for all of his love and support, as I would not have been able to complete this milestone without him. I would like to thank my mom, Susan Baranski, for her lifetime of guidance and unyielding support to my academic and professional endeavors. Additionally, I would like to thank my fellow graduate students in the Department of Psychological Science, specifically Carson Yahrmarkt, Haillie McDonough, Logan Zupko, Haylee Snyder, and Lexi Dalton for their support and encouragement throughout this process. I would also like to thank all the amazing members of the Toegel Lab for their help caring for the animals and conducting sessions. I would also like to thank Northern Michigan University's Excellence in Education Program for the grant that helped fund this experiment.

This thesis follows format prescribed by the *Publication manual of The American Psychological Association* and the Department of Psychological Science.

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INTRODUCTION

In everyday life, individuals are faced with choosing among an array of options that produce various combinations of reinforcing and aversive consequences in the long- and short-term. For example, a hungry individual may choose to eat spicy foods that taste good immediately (reinforcing consequence) but also produce heartburn hours after consumption (aversive consequence). Alternatively, they could have chosen to eat food that was not as spicy and therefore does not result in later aversive consequences. Despite the aversive heartburn that follows the consumption of spicy food, many individuals habitually consume spicy food and suffer the delayed aversive consequences on a regular basis.

Repeated choices that produce immediate reinforcing consequences followed by delayed aversive consequences are commonly associated with problematic behavior, such as smoking, overeating, drug use, gambling, and sexual risk-taking (Estle et al., 2023). For example, repeatedly choosing to smoke cigarettes (which produce immediate reinforcers) can result in harmful consequences to one's health that become problematic over time. Although an ample amount of research has documented the long-term problems that these choice patterns can produce (de Groot et al., 2018), many individuals regularly choose to produce immediate reinforcers regardless of the delayed aversive consequences that accompany them.

The Delay-of-Gratification Paradigm

The problematic behavioral patterns described above have often been categorized as impulsive. The *Diagnostic and Statistical Manual of Mental Disorders* (American Psychiatric Association (APA), 2013, p.61) defines impulsivity as hasty actions that (a) occur in the moment

without forethought, (b) have high potential for harm to the individual, and (c) may reflect a desire for immediate rewards or an inability to delay gratification. In laboratory studies of choice involving delay of gratification, generally, choice of a small and more immediate reinforcer is characterized as impulsive, whereas choice of a large but delayed reinforcer is characterized as self-controlled. Procedures that study impulsive and self-controlled choice by arranging choice between small immediate and large delayed reinforcers fall into the delay-of-gratification paradigm (also referred to as "delay discounting" or "temporal discounting" procedures). These procedures have been studied widely in arrangements using humans and a variety of other animals (Madden & Johnson, 2010). To date, a wide variety of maladaptive behaviors have been correlated with human impulsive decision making in the delay-of-gratification models, including alcohol misuse (e.g., MacKillop et al., 2011), illicit substance abuse (e.g., heroin, Kirby et al.,1999; opioids, Kirby & Petry, 2004; stimulants, Monterosso et al., 2007), smoking (e.g., Audrain-McGovern et al., 2009, Bickel et al., 1999), risky sexual behavior (e.g., Johnson & Bruner, 2012), fast-food consumption (e.g., Garza et al., 2016), texting while driving (Hayashi et al., 2016), pathological gambling (e.g., Dixon et al., 2003), needle sharing (Odum et al., 2000), and poor medication adherence (e.g., Epstein et al., 2021, Lebeau et al., 2016).

The study of delay-of-gratification started with a series of experiments conducted by Mischel et al. in the 1960s and 1970s. In Mischel and Ebbesen's (1970) study, children (3 years 6 months to 5 years 8 months) were presented with a choice: They could consume an immediate but mildly desirable snack option (pretzels), or they could wait for the experimenter to come back to the room after 15 minutes and receive a more desirable snack option (cookies). Approximately two-thirds of the children demonstrated successful delay-of-gratification by choosing to wait for the large delayed option (cookies). Multiple follow-up studies have

longitudinally tracked and assessed the behavioral patterns and other psychological traits shown over time by the same participants in Mischel and Ebbesen (1970) and similar studies conducted by this research group. For example, Mischel et al. (1988) assessed personality ratings of the preschool children who participated in their experiments 10 years later. The results showed that the children who delayed gratification were rated higher by their parents compared to children who did not on several measures, such as “resisting temptation”, “being attentive”, and “having a better ability to deal with stress and obstacles”. Shoda et al. (1990) also followed up with the original participants of the initial studies and found that the children who successfully delayed gratification had overall higher scores on the SAT. Overall, this early descriptive research made an initial case for the potential importance of studying choice patterns of large delayed reinforcers compared to small, more immediate reinforcers.

Review articles have highlighted the substantial amount of research on the delay-of-gratification paradigm has been conducted using animal models (e.g., de Wit & Mitchell, 2010). Ainslie (1974) was one of the first researchers to evaluate this paradigm using pigeons. Sessions took place in operant chambers with one response key and a feeder. Sessions were arranged into 50 trials, each lasting 19 s. At the start of a trial, the key was lit green for 7.5 s or until a pigeon pecked the key. If a pigeon did not peck the green key, the key was turned off for 4.5 s and then lit red for 3 s. If a pigeon did not peck the red key during the 3 s that it was lit, a large reinforcer (4 s access to food) was provided. If a pigeon pecked the red key during that 3 s (an impulsive choice), the key was turned off and a small reinforcer (2 s of food) was provided immediately. Following the small reinforcer, the key remained off for the remainder of the 19-s trial. If, however, the green key was pecked, the key was turned off until 15 s had elapsed from the start of the trial. Then access to food was provided for 4 s (a large reinforcer). Pecking the green key

allowed the pigeon to engage in self-control: The pigeon's peck on the green key prevented the production of the small reinforcer and assured the delivery of the large reinforcer.

As in Mischel and Ebbesen's (1970) study, pigeons could choose a large, delayed outcome over a small, immediate outcome. Unlike in Mischel and Ebbesen's (1970) study, few of the pigeons engaged in self-control (2 out of the 10 pigeons) and most of the pigeons reliably pecked the red key instead of waiting (8 out of the 10 pigeons), resulting in the immediate access to the small reinforcer (Ainslie, 1974). This study showed that the delay-of-gratification paradigm of self-control could be studied in non-human animals and that most pigeons acted "impulsively" under this specific experimental arrangement. However, the bounds under which individuals would make self-controlled or impulsive choices was relatively unexplored.

Parametric Evaluations of Delay-of-Gratification

In 1987, James Mazur progressed this research area by pioneering a procedure that permitted a parametric analysis of how the delay until the receipt of a large reinforcer changes an individual's patterns of choices between a large delayed reinforcer and a small immediate reinforcer. This study used an *adjusting-delay* procedure, in which the delay to the large reinforcer is adjusted based on each subject's previous choices.

Pigeons completed experimental sessions in operant chambers with a feeder and three response keys. Sessions lasted for 64 trials, grouped into 16 blocks of 4 trials each. At the start of a session, the middle response key was lit. A peck on this key darkened the middle key and lit the left and right response keys. A peck on one of the keys produced a small reinforcer (2 s access to food). A peck on the other key produced a large reinforcer (6 s access to food) that was accessible only after a programmed delay. In the first two trials of a block, only one of the keys was available at a time. A peck on the lit key produced the consequence normally associated

with that key (i.e., a small immediate or large delayed reinforcer). These *sample* trials ensured that pigeons had recent exposure to the consequences of pecking each key. The last two trials of a block were *choice* trials, in which both keys were lit and pigeons could choose which consequence to produce by pecking one of the lit keys. Pecking a key produced the consequence normally associated with that key (i.e., a small immediate or large delayed reinforcer).

The delay to the large reinforcer was adjusted across blocks based on the distribution of choices during the choice trials in the previous block. If a pigeon chose the large delayed reinforcer in both choice trials, then the delay to the large reinforcer was raised by 1 s for the next block of trials. If a pigeon chose the small immediate reinforcer in both choice trials, then the delay to the large reinforcer was reduced by 1 s for the next block of trials. If a pigeon chose each consequence once, then the delay was unchanged. Sessions took place daily until the pigeon reliably chose both options equally often for a minimum of 12 sessions. This pattern of choice indicated indifference between the consequences, suggesting that the two consequences were equivalent in value. When choice was reliably indifferent over a minimum of 12 sessions, it was considered stable. After choice was considered stable in a condition, the delay to the small reinforcer was changed systematically across conditions (0 s, 1 s, 2 s, 6 s, 10 s, 12 s, 14 s, and 20 s) and choice was allowed to stabilize again. This allowed Mazur to identify the specific delay at which the large and small reinforcers, each delivered at different delays, had equal value (i.e., indifference points). Mazur found that stable delays to the large reinforcer at indifference points were longest when the small reinforcer was delayed by longer amounts of time – indicating that pigeons were sensitive to the relative temporal placement of the small and large reinforcers. For the first time, researchers were able to investigate not just whether individuals would make an

impulsive choice, but how varying a parameter (in this case, delay) of the small and large reinforcer changed individual subjects' choices systematically.

To allow the prediction of how the value of a large reinforcer changes across untested delays, Mazur developed a mathematical model of delay discounting, which is shown below:

$$V = A / (1 + kD)$$

In this equation, V represents the predicted value of the large reinforcer at a given delay, A represents the amount of the large reinforcer, and D represents the delay to the large reinforcer. The parameter *k* is the rate at which the large reinforcer value decreases per unit of delay. This model has been used in numerous studies and is generally considered to fit delay discounting data well (McKerchar et al., 2009).

Evenden and Ryan (1996) continued the study of delay-of-gratification by implementing a variation on Mazur's (1987) procedure that allowed them to study choice following acute drug administration more easily by incorporating several delays of reinforcement into one session. Their arrangement was similar to Mazur's (1987) procedure, except that (a) they used rats instead of pigeons and (b) the delay to the large reinforcer was varied across blocks of each session independent of the individual's choices during choice trials. Their procedure, hereafter called the *variable-delay* procedure, arranged each session into 5 blocks of 12 trials (60 trials in total). In each trial, male rats could press a lever that produced 1 pellet delivered immediately or a lever that produced 3 or 5 pellets delivered after a predetermined delay. As in Mazur's adjusting-delay procedure, the first two trials of a block were sample trials that exposed rats to the consequences of pressing each lever. Then the rats were exposed to 10 choice trials in which they could choose between the consequences arranged on the two levers. The delay to the large reinforcer was varied systematically across blocks (Block 1: 0 s, Block 2: 10 s, Block 3: 20 s,

Block 4: 40 s, and Block 5: 60 s). Effects of delay on "self-controlled" choice was measured by evaluating the percentage of choice trials in which rats chose the large reinforcer in each of the 5 blocks arranged in a session. An average for large reinforcer choice was then calculated across rats for each delay in each block.

In general, results from Evenden and Ryan (1996) approximated results from Mazur (1987). Preferences for the large reinforcer were highest when the relative delay to the large reinforcer was shortest and decreased as a function of the delay to the large reinforcer in a pattern that resembled a hyperbola. Because the set of delays can all be evaluated within one session, this procedure was well-suited for evaluating effects of drugs on rats' choices.

In addition to contributing a new method to study self-controlled choice (i.e., the variable-delay procedure), Evenden and Ryan (1996) also evaluated effects of acute administration of various drugs classes, including antidepressants (imipramine, citalopram), stimulants (*d*-amphetamine), serotonin antagonists (metergoline), anticonvulsants (carbamazepine), benzodiazepines (diazepam), and antipsychotics (haloperidol). Sessions were conducted 5 days per week. In some of those sessions (2 per week), rats were injected with saline prior to the session. This allowed an evaluation of choice in the absence of drug effects. In some sessions (2 per week), rats were injected with one of several doses of the tested drugs to evaluate both the drugs' overall effects on choice as well as how raising or reducing doses of the drugs affected choice. Though many experiments had since implemented the adjusting-delay procedure used by Mazur (1987), the introduction of the variable-delay procedure allowed researchers to evaluate acute drug effects while studying delay of gratification parametrically.

Effects of Drugs on Delay of Gratification

The incorporation of drugs into delay-of-gratification research has added a new element to our understanding of choice. To date, several studies have evaluated effects drugs on choice in the delay-of-gratification paradigm (e.g., de Wit & Mitchell, 2010). Importantly, researchers have found systematic differences in drug effects on choice between drug classes, and both similar and different effects among drugs within the same class. Because treatments for diagnoses that are characterized by impulsive choices (e.g., Attention-Deficit/Hyperactivity Disorder, ADHD) often involve the prescription of medication, studying dose-dependent effects of commonly prescribed drugs on choice is a worthwhile endeavor.

Patterns of impulsive choice are one of the symptoms observed among people diagnosed with ADHD (APA, 2013, p.60). Patients with these disorders are commonly prescribed stimulants, such as *d*-amphetamine, to assist in producing treatment goals (e.g., reducing or increasing attention). Thus, stimulants have been a target drug of study for delay-of-gratification research. For example, Evenden and Ryan (1996) administered varying doses of *d*-amphetamine to male rats and found that *d*-amphetamine reduced "self-controlled" choice of the large delayed reinforcer, but only when a relatively high dose (1.0 mg/kg base form) was administered. The low dose tested (0.3 mg/kg base form) did not affect choice systematically.

Slezak and Anderson (2009) replicated the general procedure used in Evenden and Ryan (1996) with an expanded range of doses (0.1, 0.3, 1.0, 1.7, and 3.0 mg/kg salt form). As with Evenden and Ryan (1996), a variable-delay procedure was used in which male rats chose between a small reinforcer (1 food pellet) and a large reinforcer (3 food pellets) delivered after an ascending or descending variable delay (0, 5, 10, 20, 40 s or 40, 20, 10, 5, 0 s) by pressing response levers. As in Evenden and Ryan (1996), results from Slezak and Anderson (2009)

showed that *d*-amphetamine decreased "self-controlled" choice of the large delayed reinforcer, and that effects of *d*-amphetamine increased as a function of the dose.

Although the research discussed above showed that *d*-amphetamine decreased choice of the large delayed reinforcer, several studies have found the opposite effects under some conditions. Cardinal et al. (2000) acutely and chronically administered a range of doses (0.3, 1.0, and 1.6mg/kg salt form) of *d*-amphetamine to male Lister hooded rats in a variable-delay procedure. Rats were either assigned to a no-signal group or a signal group where a stimulus light was illuminated during the delay. For rats in the no-signal group, *d*-amphetamine administration decreased "self-controlled" choice of the large delayed reinforcer as in some prior research (e.g., Evenden & Ryan, 1996). For rats in the signal group, *d*-amphetamine administration increased choice of the large delayed reinforcer. These results suggest that effects of *d*-amphetamine on choice can depend on signals and, when large delayed reinforcers are signaled, *d*-amphetamine can increase "self-controlled" choice.

Perry et al. (2008) acutely administered a range of *d*-amphetamine doses (0.5, 1.0, 2.0mg/kg base form) to rats using an adjusting-delay procedure. Male Sprague-Dawley rats in this study were raised in either an enriched condition with other rats and environmental stimuli (e.g., rat toys) or an isolated condition without other rats or added stimulation. When *d*-amphetamine was administered, there was an increase in "self-controlled" choice of the large delayed reinforcer for rats raised in isolated environments. For rats raised in enriched environments, there was a decrease in "self-controlled" choice following *d*-amphetamine administration. Together, these studies suggest that *d*-amphetamine has mixed effects on choice in the delay-of-gratification paradigm and can depend on other aspects of the experimental arrangement including the use of signals and the degree of exposure to an enriched environment.

Benzodiazepines have been well studied in the delay-of-gratification paradigm (e.g., Cardinal et al., 2000; Evenden & Ryan, 1996; Huskinson & Anderson, 2012). These drugs are known to produce anxiolytic effects and have often been prescribed to treat anxiety and insomnia (Nowell et al., 1997). Diazepam is a benzodiazepine that has been widely studied in delay discounting research (e.g., Evenden & Ryan, 1996; Huskinson & Anderson, 2012). For example, Evenden and Ryan (1996) administered varying doses of diazepam (0.3mg/kg and 1.0mg/kg base form) while studying choice using the variable-delay procedure and found that diazepam increased "self-controlled" choice of the large reinforcer, but that all tested doses had similar effects on choice across delays (0, 10, 20, 40, 60 s). Huskinson & Anderson (2012) acutely administered higher doses of diazepam (1.0mg/kg, 3.0mg/kg, 10.0mg/kg salt form) to both Lewis and Fischer 344 rats in a variable-delay procedure and found that diazepam increased "self-controlled" choice of the large delayed reinforcer for Fischer 344 rats across delays which varied based on percent large reinforcer choice (either 0, 2, 4, 8, and 16 s, or 0, 10, 20, 40, and 60 s). Diazepam also increased choice of the large delayed reinforcer for individual Lewis rats at varying doses but did not have an overall systematic effect on Lewis rats.

Opioids are another classification of drug that have been studied acutely using variable-delay procedures. Opioids are commonly prescribed to individuals for pain after undergoing serious or extensive surgeries. Problematically, many opioids that are effective pain relievers also have high abuse liability (Clark & Schumacher, 2017). Opioids also result in many overdoses, illustrated by the more than 68,000 deaths in the US in 2020 that were a result of opioid overdose (Mattson et al., 2021). Pitts and McKinney (2005) studied effects of the opioid morphine on self-controlled choice using the variable-delay procedure. In their study, male rats pressed response levers to choose between a small reinforcer (one 3-s presentation of sucrose

water) and a large reinforcer (four 3-s presentations of sucrose water separated by 0.5 s) delivered after a variable delay. The administered doses of morphine (1.0mg/kg, 3.0mg/kg, 5.6mg/kg salt form) produced slight but nonsignificant shifts toward the smaller and more immediate choice, but no dose-dependent effects were observed. Pattij et al. (2009) used a variable-delay procedure in which male rats could choose between a small reinforcer (1 food pellet) or a large reinforcer (4 pellets) delivered after a variable delay 0, 5, 10, 20, and 40 s) by nose poking at one of two locations. The tested doses of morphine (0.3mg/kg, 1.0mg/kg, 3.0mg/kg, 6.0mg/kg base form) in Pattij et al.'s study generally decreased "self-controlled" choice of the large reinforcer but did not have dose-dependent effects on choice. Together these studies reflect that opioids increase choice of the small and more immediate reinforcers, but the effects of tested opioids on choice have normally been small.

The Conflicting-Valence Paradigm

The studies discussed so far have all dealt with the delay-of-gratification paradigm in which individuals choose between two reinforcing events. However, many problematic situations related to self-controlled choice involve a single choice that produces a reinforcing event and a delayed, aversive event. In these situations, a single response produces consequences of conflicting valence – one reinforcing (sometimes referred to as "positive") and one aversive (sometimes referred to as "negative"). This paradigm is called the *conflicting-valence* paradigm (see also "dual-valence" paradigm; Toegel, 2018). The conflicting-valence paradigm has received increased attention in recent years (e.g., Dumas, 2014; Rodriguez et al., 2018; Toegel, 2018).

As with the delay-of-gratification paradigm, researchers have evaluated the conflicting-valence paradigm using both adjusting-delay and variable-delay procedures. Toegel (2018) used

an adjusting-delay procedure in which male rats could choose a conflicting-valence consequence (2 food pellets immediately followed by a delayed shock [0.8 mA, 200 ms]) or a single-valence consequence (2 food pellets after an adjusting delay) by pressing one of two response levers. Across conditions, the delay between the immediate food and the shock programmed in the conflicting-valence consequence was changed systematically (delays to shock evaluated: 1, 2, 4, 8, 16, 32, 64 s). Within conditions, the delay to food in the single-valence consequence was adjusted based on rats' choices in each block of trials. As in Mazur (1987), sessions lasted for 64 trials, grouped into 16 blocks of 4 trials each. The first two trials of a block were sample trials that ensured that rats had recent exposure to the consequences of pressing each lever. Then, rats were exposed to two choice trials in which both levers were extended, and the rat could choose which consequence (single- or conflicting-valence) to produce.

The delay to the single-valence consequence was adjusted across blocks based on the distribution of choices during each block. If a rat chose the single-valence consequence in both choice trials, then the delay to food in the single-valence consequence was raised by 2 s for the next block of trials. If a rat chose the conflicting-valence consequence in both choice trials, then the delay to the food in the single-valence consequence was reduced by 2 s for the next block of trials. If a rat chose each consequence once, then the delay was unchanged. This procedure remained in place until rats were consistently indifferent between the single- and conflicting-valence consequences across several sessions, indicating that the two consequences (delayed food and immediate food with delayed shock) were equivalent in value for that condition. The degree to which choice of the single-valence consequence persisted at longer delays showed the effectiveness of delayed shock in each condition. The results of this study showed that delayed

shock had its greatest effect on “self-controlled” choice of the single-valence consequence when the delay to the shock was short, and that the effects of shock decreased as the delay increased.

In a similar study, Dumas (2014) used an adjusting-delay procedure in which male rats could press response levers to choose either a single-valence consequence (1 food pellet immediately and no shock) or a conflicting-valence consequence (2 or 3 food pellets immediately followed by a shock delivered after an adjusting delay). Across conditions, the intensity (mA) or duration (ms) of the delayed shock was changed systematically (intensities evaluated: 0.2, 0.4, 0.6, 0.8, 1.0 mA; durations evaluated: 100, 200, 400 ms). Sessions lasted for 64 trials, grouped into 16 blocks of 4 trials each. The first two trials of a block were sample trials that ensured that rats had recent exposure to the consequences of pressing each lever. Then rats were exposed to two choice trials in which both levers were extended, and the rat could choose which consequence (single- or conflicting-valence) to produce.

The delay between the large reinforcer and the shock in the conflicting-valence consequence was adjusted across blocks of trials within and across sessions based on the distribution of choices during choice trials in each block. If a rat chose the conflicting-valence consequence in both choice trials, then the delay to shock was reduced by 2 s for the next block of trials. If a rat chose the single-valence consequence in both choice trials, then the delay to shock in the conflicting-valence consequence was raised by 2 s for the next block of trials. If a rat chose each consequence once, then the delay was unchanged. Shock intensity and duration remained constant within each condition but were manipulated across the different conditions. After indifference points were identified with a specific shock intensity and duration, a different combination was tested. This allowed an assessment of how changes to the intensity and duration of shock alters the effects of the immediate reinforcing consequence (2 or 3 food pellets). Results

showed that shock devalued the large food reinforcer as a direct function of the intensity and duration of the shock. That is, the longer (in ms) and more intense (in mA) the shock, the more that "self-controlled" choice of the single-valence consequence persisted – until, eventually, the shock was delayed to the point that the large reinforcer plus delayed shock was equivalent in value to the small reinforcer.

Rodriguez et al. (2018) were the first to evaluate this conflicting-valence paradigm using the variable-delay procedure developed by Evenden and Ryan (1996). In their study, male rats chose between 1 food pellet delivered immediately or 4 food pellets delivered immediately and a shock delivered after a variable delay by pressing the response levers. Sessions were arranged in 5 blocks of 8 trials. The initial shock value was set at 0.5 mA for 1 s, but was adjusted based on the proportion of preference for the conflicting-valence consequence. Across blocks, the delay between the large reinforcer and shock was changed in either an increasing (0, 5, 10, 20, 40 s) or decreasing (40, 20, 10, 5, 0 s) order independent of the rats' choices. The first two trials of each block were sample trials that ensured that rats had recent exposure to the consequences of pressing each lever. Then, rats were exposed to six choice trials in which both levers were extended, and the rat could choose which consequence (single- or conflicting-valence) to produce.

Patterns of "self-controlled" choice were evaluated by comparing the percentage of choices of the single-valence consequence (i.e., the small reinforcer) across blocks of each session. Consistent with Toegel (2018), results showed that "self-controlled" choice of the single-valence consequence was highest in the stable situation with the shortest delay in shock and decreased as a function of the delay to the shock. The findings from this procedure have

been replicated in recent research (Gonzalez & Orduna, 2022; Liley et al., 2019; Liley et al. 2022) and the protocols have been described in a recent technical article (Orsini & Simon, 2021).

The Present Study

The present study builds upon the scientific literature on "self-controlled" decision-making by evaluating choice after the administration of drugs with the conflicting-valence paradigm research. As in the Rodriguez et al. (2018) study, the present study evaluated effects of delayed shock on choice in a variable-delay procedure with rats. Rats were exposed to choices between 1 food pellet immediately (single-valence consequence) or 3 food pellets delivered immediately followed by a shock that occurred after a predetermined delay (conflicting-valence consequence). The delay to the shock varied systematically in a fixed order within each session, independent of the rats' responding. We then evaluated the dose-dependent effects of diazepam, *d*-amphetamine, and morphine on "self-controlled" choice in the conflicting-valence paradigm. The present study builds on this area of research by evaluating effects of these commonly prescribed drug classes on choice involving conflicting-valence consequences.

METHOD

Subjects

Ten experimentally naive, male Sprague-Dawley rats were maintained at 85 percent (± 2%) of their free-feeding body weights by food pellets (BioServ 45-mg grain pellets) delivered during experimental sessions and supplemental feedings of standard lab chow in the home cage 30 minutes to an hour after the sessions had ended. Two rats were used as pilot rats to test safe and behaviorally effective doses for each drug. The remaining eight rats were used in the main experiment and are included in the main data below. Target weights were adjusted periodically according to growth charts provided by the supplier. The rats were housed in pairs in a temperature-controlled room with a 12:12 hr light/dark cycle. Water was freely available in the home cages. The treatment of the rats, in and out of the experimental sessions, complied with a protocol approved by the Northern Michigan University Animal Care and Use Committee.

Apparatus

Sessions were conducted in four operant-conditioning chambers (Med Associates Inc., St. Albans, VT) enclosed in ventilated, sound-attenuating cabinets. The interior of each chamber is 27.9 cm long, 20.5 cm high, and 20.9 cm deep. The ceiling and sidewalls are constructed of clear acrylic, and the end walls of stainless steel. The floor consists of 18 stainless-steel rods .47 cm in diameter, spaced approximately 1.57 cm apart. On the front wall are two retractable levers. Each lever is 4.5 cm wide, 0.2 cm thick, and protrudes 2.0 cm into the chamber when inserted. The inside edges of the levers are spaced 8.0 cm apart (6.45 cm from the middle of the wall). The

tops of the levers are positioned 7.4 cm from the floor. White cue lights (No. 1820 bulb) are located approximately 5.5 cm above each lever but was not used in the present experiment. An audio speaker is mounted on the back wall outside of the chamber. Food pellets are delivered into a feeder centered on the front wall. Aversive stimulation consisted of scrambled foot shock controlled by a constant-current shock generator (Med Associates ENV-414S). General illumination was provided by a house light (No. 1820 bulb) located on the back wall. White noise (80 dB) masked extraneous sounds. Experimental events were controlled and recorded with computers running programs written in Visual Studio. Computers were connected to the chambers via digital interfaces (Measurement Computing, model PCI-PDIS08).

Drug Preparations

Three drugs were evaluated in the present study at low, medium, and high doses: Diazepam (0.25mg/kg, 0.50mg/kg, and 1.00mg/kg salt form), *d*-amphetamine (0.25mg/kg, 0.50mg/kg, and 1.00mg/kg salt form), and morphine (2.50mg/kg, 5.00mg/kg, and 10.00mg/kg salt form). Drugs were purchased from Sigma-Aldrich (St. Louis, Missouri, USA). Diazepam sulfate was dissolved in 0.9 percent saline solution plus 15 percent concentration of Tween 80 prior to administration. *d*-Amphetamine sulfate and morphine sulfate were dissolved in 0.9 percent saline solution prior to administration. Each drug dose was delivered at a concentration of 1.0 mg/mL and at a volume of 1.0 mL/kg. For each drug, each dose was administered twice per rat. The order of administered doses was randomized for each rat. At least 1 week separated the administration of different drugs.

Preliminary Training

Because the rats were experimentally naive, each rat received preliminary training to establish food pellet deliveries as reinforcers, responding on both levers, and a preference for the

large food reinforcer (3 food pellets) over the small food reinforcer (1 pellet). Each pellet delivery was accompanied by a 1000 Hz tone lasting 1 s. When multiple pellets (e.g., 3) were delivered, the tone lasted an equivalent number of seconds as the number of pellets delivered (e.g., three pellets was accompanied by a 3-s tone). If pellet delivery was contingent upon a lever press (all conditions after feeder training), the levers were retracted for the duration of the sound.

Feeder Training

The purpose of feeder training was to establish the delivery of food pellets as reinforcers. Both levers were retracted throughout feeder training. At the start of the session, the houselight was lit, the white noise was turned on, and 3 pellets were delivered into the feeder. After the rat consumed the 3 pellets, individual pellets were delivered manually in progressively increasing intervals, starting at 15 s between deliveries. Feeder training was complete when: (a) the time between each of the last 5 pellet deliveries averaged at least 60 s, (b) the rat's head is at least 3 in away from the feeder when the pellets are delivered, and (c) the rat consumed each of the last 5 pellets within 3 s of delivery.

Lever-Press Training

When a rat completed feeder training, lever-press training began during the following session. On the first day of lever-press training, the left lever was extended, and each press produced a food pellet (a fixed-ratio 1 schedule, FR 1). This session was considered complete when 80 pellets were delivered from pressing the lever. On the second day, the right lever was extended, and each press produced a food pellet (a fixed-ratio 1 schedule, FR 1). This session was considered complete when 80 pellets were delivered from pressing the lever. On the third day, alternating levers were presented every 10 presses, and each press produced a food pellet (a fixed-ratio 1 schedule, FR 1). This session was complete when 80 pellets were delivered from

pressing the alternating levers. Lever-press training was considered complete when a rat completed a full session on each lever and one session with the alternating levers with reliable responding.

General Procedure

Sessions were conducted six days per week (Sunday-Friday) at approximately the same time each day. After the rat was placed in the operant chamber, a 5-minute delay preceded the start of the session to allow the rat to recover from any effects of handling. During this delay, all chamber lights and sound were off, and the levers were retracted. At the start of each session, the houselight was lit and the white noise was turned on. The houselight remained lit throughout the entire session. Sessions ended after the rat completed six blocks of seven trials or 90 minutes elapsed, whichever came first.

Each session consisted of a series of six blocks of trials. Across trials, rats were presented with a choice between two consequences that were arranged following a single lever press on one of two levers: a conflicting-valence lever and a single-valence lever. Each trial was programmed to last for 90 s but did not end within 15 s of a food or shock delivery. This ensured that the delivery of a consequence did not coincide with the start of the next trial. A trial-yoking procedure prevented differences in trial durations and overall reinforcement rates that could arise from delayed events on the conflicting-valence lever. If a trial in which the conflicting-valence lever was pressed exceeded the 90-s programmed duration, subsequent trials were programmed to last an equivalent duration until the occurrence of the next trial in which the conflicting-valence lever was pressed. If, after the yoking procedure started, a trial in which the conflicting-valence lever was completed within the programmed 90-s duration, subsequent trials reverted to the programmed 90-s duration.

Sample Trials

The first two trials of each block were sample trials. These sample trials ensured that each rat had recent exposure to the consequence associated with each lever before being presented with a choice between the two levers. In a sample trial, only one lever was inserted into the chamber. A single press on that lever retracted the lever and produced the consequence(s) associated with that lever (consequences vary by evaluation type, described below). Then, the time remaining in the trial elapsed and the next trial would start. The next trial was a sample trial on the other lever. Again, a single press retracted the lever, produced the consequence associated with that lever, and lasted until the remaining trial time elapsed. The first sample trial of every session was always a sample choice for the consequence available following a press on the conflicting-valence lever (the lever that produced the conflicting-valence consequence). This allowed the yoking procedure to start immediately in the session, if necessary. The single-valence lever was always available in the second sample trial. In the following blocks of trials in the session, the order of sample trials was determined randomly.

Choice Trials

After completing the two sample trials, rats were exposed to five choice trials. During choice trials, both levers were inserted into the chamber and rats could press one of the levers to produce the consequence associated with the lever. After a single response on a lever, both levers were retracted, and the consequence associated with the pressed lever was delivered. After the remaining trial time elapsed, the next choice trial would start. When a rat completed the five choice trials arranged in a block, the next block began. Sessions lasted until six blocks had been completed.

Food-Magnitude Evaluation

The purpose of the food-magnitude evaluation was to ensure that rats were sensitive to the different magnitude food reinforcers that were programmed on the two levers during the experiment proper. As described above, sessions in this evaluation were divided into six blocks of seven trials each, starting with two sample trials and ending with five choice trials. In the food-magnitude evaluation, a press on one lever (left or right) produced a large reinforcer (3 food pellets) immediately. A press on the other lever produced a small reinforcer (1 food pellet) immediately.

The food-magnitude evaluation lasted for a minimum of three sessions and until a rat chose the lever associated with the large reinforcer on at least 24 of 30 (80%) choice trials for three consecutive sessions. When choice met the 80 percent criteria for three sessions, the number of food pellets that constituted the large reinforcer was recorded for the rat and was used as the large reinforcer throughout the remainder of the experiment. The large and small reinforcers were then associated with the opposite levers and the evaluation was repeated to ensure that differences in choice resulted from the difference in reinforcer magnitude and not lever bias. All rats in this experiment reliably preferred 3 pellets to 1 pellet when both options were available immediately, and this preference was retained when the levers were switched. After the number of pellets that constituted a large reinforcer was determined for each rat, this evaluation was repeated once per week on Sundays to ensure that rats were still sensitive to the difference in pellet amounts produced by the different levers independent of the effects of delayed shock (described below).

Shock-Magnitude Evaluation

The shock-magnitude evaluation was designed to ensure that the rats were sensitive to the shock that followed the large food reinforcer as a part of the conflicting-valence consequence, but not so sensitive that choice of the conflicting-valence consequence was eliminated. In this evaluation, rats chose between a small reinforcer (1 food pellet) delivered immediately and a large reinforcer (3 food pellets) delivered immediately and followed by a delayed shock. As described above, sessions in this evaluation were divided into six blocks of seven trials each, starting with two sample trials and ending with five choice trials. A press on one lever (left or right) produced a small reinforcer (1 food pellet) delivered immediately. A press on the other lever produced a large reinforcer (3 food pellets) immediately and a shock delivered after a variable delay (2 to 64 s) that was manipulated across blocks in each session. Delays were presented in a descending order across the blocks of each session in the following order: 64 s, 32 s, 16 s, 8 s, 4 s, and 2 s during Blocks 1-6, respectively.

For all rats, the evaluation began with a 200-ms shock of 0.5 mA. Because the shock's effects changed after consistent exposure to the consequences (i.e., habituation or sensitization), shock intensity (mA) and duration (ms) were adjusted using the procedure below. The shock-magnitude evaluation was complete when the following criteria were met: At least 10 completed sessions at the shock intensity and duration, the percent choice of the single-valence consequence in the 2-s block for the last three sessions was within 20 percent of the percent-choice of the single-valence consequence in the 2-s block for the previous 3 sessions, and at least 6 sessions at this shock intensity and duration were done and percent choice of the single-valence consequence was 60 percent or greater in the 2-s block. When the criteria were met, the shock parameters (mA and ms) were recorded for each rat and used for the remainder of the evaluation

(except for on Sundays when the food-magnitude evaluations occurred). When the shock evaluation was complete, results from the final six sessions were used as the baseline.

Adjustments to Shock Intensity (mA) and Duration (ms)

If, after two consecutive sessions, a rat's choices were either insensitive to the effects of delayed shock (i.e., habituation, measured as choice of the food plus shock lever is 40 percent or more during the block with the 2 s delay) or too sensitive to the effects of delayed shock (i.e., sensitization, measured as reliably choosing not to press a lever and ending sessions due to reaching the maximum time limit) then an adjustment was made to the magnitude (intensity [mA] or duration [ms]) of the delayed shock. First, the intensity of the shock was adjusted by 0.1 mA (raised if choice was insensitive, reduced if choice was too sensitive). If this was sufficient to bring choice under control of delayed shock (i.e., choice of the conflicting-valence consequence during the choice trials was less than 40 percent in the block with the 2-s delay and rats reliably finish sessions), then the sessions would proceed with using this adjusted mA level. If the adjusted shock magnitude was insufficient in affecting choice in the desired direction during the next two sessions, then another 0.1 mA adjustment would occur in the same direction (raised or reduced).

If the adjustment affected choice more than anticipated under the new intensity (i.e., choice became too sensitive or insensitive to shock), then the previous intensity was reinstated for two sessions. If the reinstatement of the previous shock intensity was sufficient to bring choice under control of delayed shock (i.e., choice of the conflicting-valence consequence during choice trials was less than 40 percent in the block with the 2-s delay and rats reliably finished sessions), then the sessions proceeded using this adjusted mA level. If, under the reinstated shock intensity, choice was similar to the previous exposure to that intensity (i.e., either insensitive or

too sensitive), then the new intensity was reinstated with an adjustment to the duration (± 100 ms) of the shock. If a rat reached a level of 1.0 mA, 200 ms and this shock magnitude was insufficient in affecting choice in the desired direction during the next two sessions, the shock intensity was reset to 0.5 mA and the shock duration was raised by 100 ms.

If, under the new intensity of shock, choice was too sensitive to shock, the duration was reduced by 100 ms. If under the new intensity of shock, choice was insensitive to shock, then the duration was raised by 100 ms. If this was sufficient to decrease choice of the small reinforcer, then the sessions proceeded with using this intensity and duration. If not, the same titration of intensity and duration would continue.

After at least 10 sessions took place and the shock-magnitude evaluation criteria were met for six consecutive sessions, the shock-magnitude evaluation was considered complete and results from the final six sessions were used as a measurement of choice of the two consequences at baseline. This procedure, hereafter referred to as the *variable-delay evaluation* was repeated using the shock parameters identified during the shock-magnitude evaluation to study the effects of drug administration on choice of the conflicting-valence consequence.

Drug Administration

Effects of diazepam, *d*-amphetamine, and morphine were evaluated across multiple doses to identify dose-dependent effects of drugs on behavior. Prior to the experiment, doses used in prior research were tested and adjusted in an ascending order on two pilot subjects (MB5 and MB6) to determine three doses per drug (low, moderate, and high) that were safe and behaviorally effective. All drugs were administered intra-peritoneally (i.p.) at a set amount of time before the start of the session. Diazepam was administered 10 min prior to the beginning of the session. *d*-Amphetamine was administered 10 min before the beginning of the session.

Morphine was administered 15 min prior to the beginning of the session. Sessions lasted a maximum of 90 min (minimum of 63 min) so that the drugs could produce behaviorally active effects for the duration of the session.

Drug effects were evaluated using a regular schedule that permitted an evaluation of (a) continued preference for the large reinforcer over the small reinforcer, (b) effects of delayed shock on choice in the absence of drug administration, and (c) acute effects of various doses of drugs on choice of the conflicting-valence consequence (a large food reinforcer immediately plus a delayed shock). Table 2 shows the normal schedule of sessions and events that took place each week.

Food-magnitude evaluation sessions (described above) took place weekly on Sundays to ensure that rats were still sensitive to the difference in magnitudes arranged by large and small food reinforcers that were programmed on the two levers during the experiment. To qualify for variable-delay evaluation sessions (described above) rats first had to pass the food-magnitude evaluation by choosing the large reinforcer on at least 80 percent of choice trials over the course of the session.

Variable-delay evaluation sessions took place five days per week (Monday-Friday). Sessions that occurred on Mondays, Wednesdays, and Thursdays occurred without any drug/saline administrations. Sessions on Mondays and Thursdays were used in the "no-administration" analyses described below. To qualify for a drug administration on the following Tuesday or Friday, rats must have passed the no-administration session by completing the session and choosing the single-valence consequence on at least 60 percent of choice trials during the 2-s delay-to-shock block. Drugs or saline injections (saline only) were administered before sessions on Tuesdays and Fridays. No sessions were conducted on Saturdays.

Data Analysis

The percent choice of the single-valence consequence was the primary dependent measure in this study. Delay discounting functions were plotted on graphs as the percent choice of the single-valence consequence across the varying delays to shock. When drugs were administered, the delay discounting functions were plotted on individual graphs for each drug and dose of the drug. Effects of drugs were evaluated by comparing percent choice of the single-valence consequence across delays to shock programmed as part of the conflicting-valence consequence in each session in baseline sessions, sessions with saline administration, and sessions with low, medium, and high doses of each drug. Drugs that decreased effects of the delayed shock on choice were identified when choice of the single-valence consequence decreased compared to baseline, saline, and no-administration sessions. Drugs that increased effects of delayed shock on choice were identified when choice of the single-valence consequence increased relative to baseline, saline, and no-administration sessions.

Area under the curve (AUC) was calculated with the formula provided by Myerson et al. (2001) by drawing vertical lines down to the x-axis from each delay value to form trapezoids. These trapezoid areas were then summed together and divided by the total area of the graph. The AUC measurements provide complimentary quantitative analyses that assist with visual inspection of the choice patterns.

Statistical Analysis

One-way repeated measures ANOVAs with Dunnet's multiple comparison tests were conducted to compare AUC measures collected during sessions that followed vehicle (saline) administration and with those obtained during baseline sessions, no-administration sessions, and sessions that followed each of the three doses of each of the tested drugs (diazepam, *d*-

amphetamine, and morphine). Any *p*-values less than .05 ($p < .05$) were considered to be statistically significant. To allow the inclusion of baseline measures of AUC in the statistical analysis, the most recent two sessions of the six stable sessions were used. This was because saline and the other drug sessions were only comprised of two sessions, and therefore only two sessions could be used in the statistical analysis to represent baseline. Means and standard deviations were calculated for latency data.

RESULTS

Pilot Rats

Before the experiment proper, two rats (MB5 and MB6) were exposed to the experimental conditions with an ascending order of doses at each drug. These rats we ran to determine doses that produced behavioral effects (either on choice or motor activity). Results from these rats parallel those described below but will not be discussed in depth in this document. See Appendix A, B, and C for graphical and table representations.

Baseline Effects of Delay on Choice of the Single-Valence Consequence

The left-most columns of Figures 1, 3, and 5 show effects of delayed shock on choice between the single-valence consequence and the conflicting-valence consequence as a function of the delay to shock in the conflicting-valence consequence during the six stable baseline sessions. This column is repeated in each of the figures to promote ease of comparisons between the patterns of choices made during the stable baseline sessions, no-administration sessions conducted on days immediately preceding drug administration sessions, and drug administration sessions. The patterns of choices of the single-valence consequence in drug administration sessions are represented by white symbols and no-administration sessions are represented by black symbols. Except for in the left-most column, data points represent the mean percent choice of the single-valence consequence at each delay to shock programmed as part of the conflicting-valence consequence, averaged across the two no-administration (black) sessions conducted immediately preceding each dose or in the two sessions conducted after saline/drug administration (white). Error bars extend one standard deviation above and below the mean.

For all rats, delayed shock generally exerted its largest effects on choice in blocks with relatively short delays between the large food reinforcer and the delayed shock (2-s delay for 6 rats, 4-s for MB8, and 16-s for MB3). This is illustrated by the high percentage of choice trials in which rats chose the single-valence consequence when the delay to shock programmed on the conflicting-valence consequence was short. The effects of shock were generally weakest when delayed by 64 s, and the effects increased as the delay was reduced within each session. This was the general pattern in 7 of 8 cases. For one rat, MB2, choice of the single-valence consequence followed the same general pattern as with the other rats, except in the block with the delay of 64 s, which produced the second highest choice of the single-valence consequence. Overall, effects of shock on choice of the single-valence consequence were generally an inverse function of the delay programmed in the block.

Drug Effects

In the following sections, the effects of the three drugs and their three doses will be discussed. Each drug section begins with a discussion of the patterns of choice obtained during the sessions following saline administration and comparisons to patterns obtained during the six stable baseline sessions and no-administration sessions conducted on the day before drug administrations. Then, patterns obtained in sessions following administration of saline will be compared to patterns obtained in sessions following the three doses of each drug. Each of these sections will discuss the patterns of choice across delays to shock, areas under the curves (AUCs), and latencies to press each lever during the sample trials arranged across delays to shock.

Effects of Diazepam

Saline. Figure 1 shows the effects of delayed shock on patterns of choice of the single-valence consequence across the six stable baseline sessions (leftmost column), the two saline sessions and the accompanying no-administration sessions (second column) and the two sessions that followed low, medium, and high doses of diazepam alongside the accompanying no-administration sessions (columns 3, 4, and 5). Overall, patterns of choice of the single-valence consequence following saline administration generally resembled patterns obtained during the six stable baseline sessions and the no-administration sessions conducted on the day before saline and drug administrations. The percentage of choices of the single-valence consequence was generally highest in blocks with relatively short delays (e.g., 2 s, 4 s, 8 s, 16 s) between the large food reinforcer and the delayed shock and decreased as a function of longer delays (e.g., 32 s and 64 s), although this pattern was not always observed (e.g., MB3 and MB10).

Figure 2 shows another measure of the patterns of choices obtained in Figure 1, as the area under the curve (AUC). The top panels in Figure 2 show average AUC for the group of rats and results from a one-way repeated-measures ANOVA that compares the group means during baseline and during no-administration and drug-administration sessions across doses of diazepam. The bottom panels show mean AUCs from individual rats across the six stable sessions of baseline and the two drug-administration and no-administration sessions for saline and the low, medium, and high doses of diazepam.

Results from AUC comparisons paralleled comparisons of choice patterns. For the group of rats, comparisons of the mean AUCs across the baseline sessions relative to those obtained after saline administration were not statistically significant (p = .8566) according to the repeated-measures ANOVA with multiple comparisons. Neither was the comparison between AUCs after

saline administration compared to the no-administration session conducted the day before saline administration (p = .9919) and the days before low (p = .9992), medium (p = .9984), and high (p = .8916) doses of diazepam. For seven of the rats (MB1, MB3, MB8, MB9, MB10, MB11, and MB12), mean AUCs during sessions following saline administration were within one standard deviation of the baseline AUC. Together these results suggest that choice of the single-valence consequence were similar in sessions that followed saline administration and in baseline and no-administration sessions.

Main Effects of Diazepam Administration. Diazepam decreased choice of the single-valence consequence as a function of the diazepam dose administered when compared to vehicle (saline). This finding is illustrated by the choice patterns in Figure 1 and shown clearly by the AUC results shown in Figure 2. As shown in the top-right panel of Figure 2, the repeated-measures ANOVA conducted on the group AUC results show a main effect of diazepam relative to saline ($F_{[4, 75],}$ = 11.02, p < .001) and no significant main effect of saline compared to no-administration sessions ($F_{[4, 75]}$ = 0.33, p = .8566). Multiple comparisons were conducted to compare AUCs after saline administration to those obtained in sessions after low (0.25mg/kg), medium (0.50mg/kg), and high (1.00mg/kg) doses of diazepam using Dunnett's multiple comparisons test. Results from these comparisons are described below, alongside descriptions of choice patterns and latencies to produce single-valence and conflicting-valence consequences during sample trials.

Low Dose (0.25mg/kg). Generally, diazepam decreased choice of the single-valence consequence as a function of the diazepam dose administered; however, effects of the low dose of diazepam on choice was not significant. This effect is illustrated by the patterns in Figure 1. In sessions following 0.25mg/kg of diazepam administration, the pattern of choice of the single-

valence consequence was shifted downward slightly relative to the pattern obtained in saline sessions (5 of 8 rats; MB1, MB2, MB3, MB10, and MB12) and no-administration sessions (5 of 8 rats; MB1, MB2, MB9, MB10, and MB12), but the differences in the curves were small.

These findings can be viewed more clearly by comparing the AUC measures shown in Figure 2. Although a significant main effect was found for diazepam administration, results for the AUC at the 0.25mg/kg dose were similar to saline and the differences were not significant according to Dunnett's multiple comparisons test (p = .1775). When compared to saline, individual AUCs obtained in the sessions following 0.25mg/kg dose of diazepam were decreased in five cases (MB1, MB2, MB3, MB11, and MB12), very similar in two cases (MB8 and MB10) and increased in one case (MB9). For all eight rats, the AUC obtained during the 0.25mg/kg diazepam administration sessions was decreased relative to the no-administration sessions and the same pattern was found for four of the eight rats (MB1, MB2, MB11, and MB12) compared to the AUC obtained in the stable baseline sessions.

Medium Dose (0.50mg/kg). The medium (0.50mg/kg) dose of diazepam decreased choice of the single-valence consequence. This effect is illustrated by choice patterns in the third column of Figure 1. When 0.50mg/kg of diazepam was administered, choice patterns of the single-valence consequence shifted downward relative to the pattern obtained in saline sessions for seven rats (MB1, MB2, MB3, MB8, MB10, MB11, and MB12), compared to the stable baseline sessions for seven rats (MB1, MB2, MB3, MB8, MB10, MB11, and MB12), and compared to no-administration sessions for every rat.

As shown in Figure 2, group results for the AUC in sessions that followed 0.50mg/kg administration were significantly lower than those that followed saline administration dose according to Dunnett's multiple comparisons test (p = .0006). Mean AUC during 0.50mg/kg

diazepam administration sessions was decreased relative to saline for seven rats (MB1, MB2, MB3, MB8, MB10, MB11, and MB12) and very similar for one rat (MB9), decreased relative to baseline for the same seven rats, and decreased relative to no-administrative sessions for every rat.

High Dose (1.00mg/kg). Administration of the high dose (1.00mg/kg) of diazepam shifted the function downward and decreased choice of the single-valence consequence as a function of delay to shock. This effect is shown in Figure 1 by the downward shift in the pattern of choice of the single-valence consequence across shock under 1.00mg/kg diazepam administration (rightmost column) relative to the pattern produced after saline administration for all eight rats. When 1.00mg/kg of diazepam was administered, choice patterns of the single-valence consequence shifted downward relative to the pattern obtained in saline sessions for all eight rats, compared to the stable baseline sessions for all eight rats, and compared to no-administration sessions for all eight rats.

As shown in Figure 2, group results for the AUC in sessions that followed 1.00mg/kg administration were significantly lower than those that followed saline administration dose according to Dunnett's multiple comparisons test ($p < .0001$). Mean AUC during 1.00mg/kg diazepam administration sessions was decreased relative to saline for all eight rats, decreased relative to baseline for all rats, and decreased relative to no-administrative sessions for all rats.

Sample Trial Latencies. Tables 4 and 5 show the mean latency to respond, in s, during sample trials for both the single-valence (Table 4) and conflicting-valence (Table 5) consequences during the six stable baseline sessions, saline sessions, and sessions with the three doses of diazepam. Diazepam did not reliably increase or decrease mean latencies to produce either consequence in a systematic way across delays within rats or across rats. Across rats and

doses of diazepam, the mean latency to produce the single-valence consequence was generally short (*M* = 2.68 s, SD = 16.42 s; range: 0.36-220.57 s). Across rats, the mean latency to produce the single-valence consequence was generally short across blocks in low dose (*M* = 0.97 s, SD = 0.51, range: 0.36-3.40 s), medium dose (*M* = 7.32 s, SD = 33.37, range: 0.41-220.57 s), and high dose (*M* = 24.38 s, SD = 14.20, range: 0.38-99.12 s) of diazepam. When compared to mean latencies for baseline (*M* = 0.83, SD = 0.33) and saline (*M* = 0.82, SD = 0.38) across blocks, diazepam did not reliably produce any systematic changes in latency. As shown above, the latency to produce the single-valence consequence during sample trials was not affected systematically by dose of diazepam. The mean latencies for the three doses do appear to increase systematically, but this is due to a few latencies at the medium and high doses that did not follow a systematic trend. The mean latency to produce the conflicting-valence consequence was longer than single-valence latencies (*M* = 35.88 s, SD = 70.83 s; range: 0.25-390.31 s).

Across rats, the mean latency to produce the conflicting-valence consequence was generally longer than the mean single-valence latencies across blocks in low dose (*M* = 39.57 s, SD = 76.58, range: 0.30-333.84 s), medium dose (*M* = 33.19 s, SD = 72.20, range: 0.52-390.31 s), and high dose (*M* = 45.29 s, SD = 73.26, range: 0.43-233.18 s) of diazepam, although not systematic across all rats. However, some rats showed increasing trends in mean latency, specifically in the 2-s block. For example, for MB8 and MB11, as the dose of diazepam increased, conflicting-valence consequence mean latencies in the 2-s block increased as well. Their mean latencies also increased in comparison to those measured in baseline and saline sessions. Overall, mean latencies to produce the conflicting-consequence tended to be longer than latencies to produce the single-valence consequence, and diazepam appeared to produce

dose-dependent increases in conflicting-valence consequences latencies for some rats (MB8 and MB11), but effects of delay and drug dose on latencies were usually not systematic.

Effects of d-Amphetamine

Saline. Figure 3 shows the effects of delayed shock on patterns of choice of the single-valence consequence across the six stable baseline sessions (leftmost column), the two saline sessions and the accompanying no-administration sessions (second column) and the two sessions that followed low, medium, and high doses of *d*-amphetamine alongside the accompanying no-administration sessions (columns 3, 4, and 5). Overall, patterns of choice of the single-valence consequence following saline administration generally resembled patterns obtained during the six stable baseline sessions and the no-administration sessions conducted on the day before saline and drug administrations. For all rats, the percentage choice of the single-valence consequence was generally highest blocks with relatively short delays to shock (e.g., 2 s, 4 s, 8 s, 16 s) decreased as a function of longer delays (e.g., 32 s and 64 s).

The top panels in Figure 4 show average AUC for the group of rats and results from a one-way repeated-measures ANOVA that compares the group means during baseline and during no-administration and drug-administration sessions across doses of *d*-amphetamine. The bottom panels show mean AUCs from individual rats across the six stable sessions of baseline and the two drug-administration and no-administration sessions for saline and the low, medium, and high doses of *d*-amphetamine. Results from AUC comparisons paralleled comparisons of choice patterns. For the group of rats, comparisons of the mean AUCs across the baseline sessions relative to those obtained after saline administration was not statistically significant ($p = .8383$) according to the repeated-measures ANOVA with multiple comparisons. Neither was the comparison between AUCs after saline administration compared to the no-administration session

conducted the day before saline administration (p = .9331) and the days before low (p = .9288), medium (p = .9883), and high (p = .9883) doses of *d*-amphetamine. For five of the rats (MB1, MB3, MB8, MB11, and MB12), mean AUCs during saline sessions were within one standard deviation of the baseline AUC. Together these results suggest that choice of the single-valence consequence were similar in saline sessions and in baseline and no-administration sessions.

Main Effects of *d*-Amphetamine Administration. Administration of *d*-amphetamine increased choice of the single-valence consequence as a function of the dose administered when compared to vehicle (saline). This finding is illustrated by the choice patterns in Figure 3 and shown clearly by the AUC results shown in Figure 4. As shown in the top-right panel of Figure 4, the repeated-measures ANOVA conducted on the group AUC results show a main effect of *d*-amphetamine relative to saline ($F_{[4, 74]}$ = 6.22, p = .0002) and no significant main effect of saline compared to no-administration sessions ($F_{[4, 75]}$ = 0.36, p = .8383). Multiple comparisons were conducted to compare AUCs after Saline administration to those obtained in sessions after low (0.25mg/kg), medium (0.50mg/kg), and high (1.00mg/kg) doses of *d*-amphetamine using Dunnett's multiple comparisons test. Results from these comparisons are described below, alongside descriptions of choice patterns and latencies to produce single-valence and conflicting-valence consequences during sample trials.

Low Dose (0.25mg/kg). Effects of the low dose are illustrated in the third column of Figure 3. When 0.25mg/kg of *d*-amphetamine was administered, it shifted the pattern of choice of the single-valence consequence upward compared to the pattern obtained in saline sessions for two rats (MB1 and MB9), compared to baseline sessions for 3 rats (MB1, MB9, and MB11), and compared to no-administration sessions for one rat (MB1). These findings can be viewed more clearly by comparing the AUC measures shown in Figure 4. Although a significant main effect

was found for *d*-amphetamine administration, results for the AUC at the 0.25mg/kg dose were similar to saline and the differences were not significant according to Dunnett's multiple comparisons test (p = .9894). When compared to saline, individual AUCs obtained in the sessions following 0.25mg/kg dose of *d*-amphetamine were increased in five cases (MB1, MB8, MB9, MB11, and MB12). Mean AUC obtained during the 0.25mg/kg *d*-amphetamine administration sessions was increased (slightly in the case of MB2) compared to the six stable baseline sessions for seven rats (MB1, MB2, MB8, MB9, MB10, MB11, and MB12) and compared to no-administration sessions for three rats (MB1, MB11, and MB12).

Medium Dose (0.50mg/kg). The medium (0.50mg/kg) dose of *d*-amphetamine increased choice of the single-valence consequence. This effect is illustrated by choice patterns in the fourth column of Figure 3. When 0.50mg/kg of *d*-amphetamine was administered, choice patterns of the single-valence consequence shifted upward relative to the pattern obtained in saline sessions for all eight rats, compared to the stable baseline sessions for all rats, and compared to no-administration sessions for all rats.

As shown in Figure 4, group results for the AUC in sessions that followed 0.50mg/kg administration were significantly higher than those that followed saline administration dose according to Dunnett's multiple comparisons test (p = .0319). Mean AUC during 0.50mg/kg *d*-amphetamine administration sessions was increased compared to saline for every rat, compared to baseline for every rat, and no-administrative sessions for seven rats (all except MB11).

High Dose (1.00mg/kg). Administration of the high dose (1.00mg/kg) of *d*-amphetamine shifted the function upward and increased choice of the single-valence consequence as a function of delay to shock. This effect is shown in Figure 3 by the upward shift in the pattern of choice of the single-valence consequence across shock delays under 1.00mg/kg *d*-amphetamine

administration (rightmost column) relative to the pattern produced after saline administration for all eight rats. When 1.00mg/kg of *d*-amphetamine was administered, choice patterns of the single-valence consequence also shifted upward relative to the pattern obtained in stable baseline sessions for all eight rats and compared to no-administration sessions for all eight rats. It is worth noting here that effects of shock under the 1.00mg/kg administration were so aversive for one rat (MB8) that the rat did not complete either variable-delay evaluation session at that dose. Because the latency data (described below) do not suggest motor impairment for this rat at this dose, the current interpretation is that the 1.00mg/kg dose increased effects of the delayed shock that is part of the conflicting-valence consequence.

As shown in Figure 4, group results for the AUC in sessions that followed 1.00mg/kg administration of *d*-amphetamine were significantly higher than those that followed saline administration dose according to Dunnett's multiple comparisons test ($p = .0273$). Excluding results for the rat that did not complete either session at the 1.00mg/kg dose (MB8), mean AUC during 1.00mg/kg *d*-amphetamine administration sessions was increased relative to saline for all seven rats, increased relative to baseline for seven rats, and increased relative to no-administration sessions for all seven rats.

Sample Trial Latencies. Tables 6 and 7 show the mean latency to respond, in s, during sample trials for both the single-valence (Table 6) and conflicting-valence (Table 7) consequences during the six stable baseline sessions, saline sessions, and sessions with the three doses of *d*-amphetamine. Administration of *d*-amphetamine did not reliably increase or decrease latencies to produce either consequence in a systematic way across delays within rats or across rats. Across rats and doses, the mean latency to produce the single-valence consequence was generally short in every block ($M = 0.84$ s, SD = 0.40 s; range: 0.37-4.58 s). Across rats the mean

latency to produce the single-valence consequence was generally short across blocks in low dose (*M* = 0.83 s, SD = 0.35, range: 0.40-2.32 s), medium dose (*M* = 0.76 s, SD = 0.23, range: 0.38-1.23 s), and high dose (*M* = 0.81 s, SD = 0.32, range: 0.39-1.83 s) of *d*-amphetamine. When compared to single-valence consequence mean latencies for baseline and saline, *d*-amphetamine did not produce systematic increases in mean single-valence latencies. Also, the latency to produce the single-valence consequence during sample trials was not affected systematically by dose of *d*-amphetamine.

The mean latency to produce the conflicting-valence consequence in sample trials tended to be longer than the mean single-valence latencies (*M* = 36.45 s, SD = 95.18 s; range: 0.27-548.47 s). Across rats the mean latency to produce the conflicting-valence consequence was generally longer than the single-valence consequence mean latency in low dose (*M* = 43.66 s, SD = 111.08, range: 0.29-486.50 s), medium dose (*M* = 68.91 s, SD = 126.81, range: 0.27-548.47 s), and high dose (*M* = 38.36 s, SD = 99.68, range: 0.45-525.73 s) of *d*-amphetamine, although not systematic across all rats.

Although some rats had increased mean latencies in baseline and saline sessions, many high mean-latencies occurred in the *d*-amphetamine dose sessions. This supports the idea that higher doses of *d*-amphetamine increased sensitivity to shock, therefore resulting in longer latencies for the consequence producing the shock. Some mean latencies for the sample conflicting-valence consequence were so high that they resulted in the long inter-trial intervals due to the yoking procedure, resulting in incomplete sessions (e.g., MB8). Overall, variation in mean latencies to produce the conflicting-valence consequence were not systematic across all rats, but some rats experienced high mean latencies due to an increased sensitization to shock as a result of *d*-amphetamine doses.

Effects of Morphine

Saline. Figure 5 shows the effects of delayed shock on patterns of choice of the single-valence consequence across the six stable baseline sessions (leftmost column), the two saline sessions and the accompanying no-administration sessions (second column) and the two sessions that followed low, medium, and high doses of morphine alongside the accompanying no-administration sessions (columns 3, 4, and 5). Overall, patterns of choice of the single-valence consequence following saline administration generally resembled patterns obtained during the six stable baseline sessions and the no-administration sessions conducted on the day before saline and drug administrations. For most rats (all but MB11), the percentage choice of the single-valence consequence was generally highest in blocks with relatively short delays to shock (e.g., 2 s, 4 s, 8 s, 16 s) and decreased as a function of longer delays (e.g., 32 s and 64 s).

The top panels in Figure 6 show average AUC for the group of rats and results from a one-way repeated-measures ANOVA that compares the group means during baseline and during no-administration and drug-administration sessions across doses of morphine. The bottom panels show mean AUCs from individual rats across the six stable sessions of baseline and the two drug-administration and no-administration sessions for saline and the low, medium, and high doses of morphine. Results from AUC comparisons paralleled comparisons of choice patterns. For the group of rats, comparisons of the mean AUCs across the baseline sessions relative to those obtained after saline administration was not statistically significant ($p = .9949$) according to the repeated-measures ANOVA with multiple comparisons. Neither was the comparison between AUCs after saline administration compared to the no-administration session conducted the day before saline administration ($p = .9998$) and the days before low ($p = .9987$), medium ($p = .9968$), and high ($p = .9998$) doses of morphine. For six of the rats (MB3, MB8, MB9, MB10,

MB11, and MB12), mean AUCs during sessions following saline administration were within one standard deviation of the baseline AUC. Together these results suggest that choice of the single-valence consequence were similar in sessions that followed saline administration and in baseline and no-administration sessions.

Main Effects of Morphine Administration. Administration of morphine did not affect choice of the single-valence consequence systematically as a function of the dose administered when compared to vehicle (saline). This finding is illustrated by the choice patterns in Figure 5 and shown clearly by the AUC results shown in Figure 6. As shown in the top-right panel of Figure 6, the repeated-measures ANOVA conducted on the group AUC results show that there is no main effect of morphine relative to saline ($F_{[4, 70],} = 0.38$, $p = .8192$) and no significant main effect of saline compared to no-administration sessions ($F_{[4, 75]} = 0.05$, $p = .9949$). Multiple comparisons were conducted to compare AUCs after saline administration to those obtained in sessions after low (2.50mg/kg), medium (5.00mg/kg), and high (10.00mg/kg) doses of morphine using Dunnett's multiple comparisons test. Results from these comparisons are described below, alongside descriptions of choice patterns and latencies to produce single-valence and conflicting-valence consequences during sample trials.

Low Dose (2.50mg/kg). Effects of the low dose of morphine (2.50mg/kg) are illustrated in the third column of Figure 5. When 2.50mg/kg of morphine was administered, it did not affect the pattern of choice of the single-valence consequence systematically compared to the pattern obtained in saline, baseline, or no-administration sessions for any rat.

These findings can be viewed more clearly by comparing the AUC measures shown in Figure 6. Results for the AUC at the 2.50mg/kg dose were similar to saline, and the differences were not significant according to Dunnett's multiple comparisons test ($p = .9729$). When

compared to saline, individual AUCs obtained in the sessions following low dose of morphine were similar for six rats (MB1, MB2, MB8, MB9, MB10, and MB11) and slightly lower for two rats (MB3 and MB12). Mean AUCs obtained during the low morphine administration sessions were unsystematic when compared to baseline and no-administration sessions.

Medium Dose (5.00mg/kg). When 5.00mg/kg of morphine was administered, it did not shift the pattern of choice systematically upward or downward relative to the pattern obtained in saline sessions, stable baseline sessions, and no-administration sessions. These unsystematic findings are also shown by AUC measures in Figure 6. Results for the AUC at the 5.00mg/kg dose were similar to AUCs produced in saline sessions, and the differences were not significant according to Dunnett's multiple comparisons test (p = .9429). When compared to AUCs from saline, baseline, and no-administration sessions, individual AUCs obtained in the sessions following medium dose of morphine were similar and differences were unsystematic for all rats who reliably completed sessions following the medium dose (all except MB3). One rat (MB3) did not complete either session that followed administration of 5.00mg/kg morphine. In combination with latency data below, these failures to complete sessions were attributed to motor impairment rather than a change in sensitivity to delayed aversive stimulation (described below).

High Dose (10.00mg/kg). As with administration of low and medium doses of morphine, administration of the high (10.00mg/kg) dose of morphine did not shift the pattern of choice systematically upward or downward relative to the pattern obtained in saline sessions, stable baseline sessions, or no-administration sessions. These unsystematic findings are also shown by the AUC measures in Figure 6. AUCs in sessions following 10.00mg/kg morphine administration were similar to those produced in saline sessions, and the differences were not significant according to Dunnett's multiple comparisons test (p = .8940). When compared to

AUCs from saline, baseline, and no-administration sessions, individual AUCs obtained in the sessions following medium dose of morphine were similar and differences were unsystematic for all rats who reliably completed sessions following the medium dose (all except MB3, MB8, and MB12). Three rats (MB3, MB8, and MB12) did not complete either session that followed administration of 10.00mg/kg morphine.

Sample Trial Latencies. Tables 8 and 9 show the mean latency to respond, in s, during sample trials for both the single-valence (Table 8) and conflicting-valence (Table 9) consequences during the six stable baseline sessions, saline sessions, and sessions with the three doses of morphine. Across rats and doses, the latency to produce the single-valence consequence during sample trials was generally short (*M* = 3.66 s, SD = 18.16 s; range: 0.33-197.38 s). Across all rats, the mean latency to produce the single-valence consequence was generally short across blocks in low dose (*M* = 0.95 s, SD = 1.25, range: 0.34-9.38 s), medium dose (*M* = 0.85 s, SD = 0.62, range: 0.33-4.71 s), and high dose (*M* = 14.23 s, SD = 37.66, range: 0.41-197.38 s) of morphine. As shown above, the mean latency to produce the single-valence consequence was not affected systematically by morphine dose. When compared to mean latencies for baseline and saline, morphine dose did not systematically affect the single-valence consequence mean latencies.

The mean latency to produce the conflicting-valence consequence in sample trials was longer than the mean latency for the single valence consequence (*M* = 27.96 s, SD = 65.66 s; range: 0.17-479.58 s). Across rats, the mean latency to produce the conflicting-valence consequence was generally longer across blocks in low dose (*M* = 24.82 s, SD = 79.29, range: 0.43-479.58 s), medium dose (*M* = 39.15 s, SD = 74.13, range: 0.25-283.09 s), and high dose (*M* = 39.06 s, SD = 73.43, range: 0.17-270.16 s) of morphine, but did not follow any systematic

trends. Although some rats had high mean latencies in baseline (e.g., MB2 in 2-s block, MB9 in 64-s block) and saline (e.g., MB1 in 2- and 16-s block, MB3 in 2-s block, MB8 in 32-s block, MB11 in 64-s block) sessions, 22 high mean-latency data (60 s or longer) occurred in sessions following morphine administration. These high latencies in morphine sessions did not appear to occur reliably across all blocks of a session. Some mean latencies for the sample conflicting-valence consequence were so high that they resulted in the long inter-trial intervals due to the yoking procedure, resulting in incomplete sessions (ex. MB3, MB12). Although not systematic within rats, mean latencies to produce the conflicting-valence consequence were often longer than the single-valence consequence. This leads to speculation that morphine could be exerting an effect on the conflicting-valence consequence despite the fact that it did not reliably affect choice between the single- and conflicting-valence consequences.

DISCUSSION

Choices involving conflicting-valence consequences occur frequently in daily life. These choice situations can be problematic for people who habitually produce conflicting reinforcing and delayed aversive consequences because their behavior is under the control of the reinforcing portion of the conflicting consequence and is not sufficiently controlled by the delayed aversive portion of the consequence. By studying manipulations that affect choice in conflicting-valence consequences experiments (e.g. delay to the event, drug administration), research can shed light on important decision-making situations and eventually inform the treatment of problematic choice patterns.

The present experiment evaluated the effects of drug administration on choice patterns in a conflicting-valence consequence model. Rats were presented with choices between a single-valence consequence (1 food pellet immediately) or a conflicting-valence consequence (3 food pellets immediately followed by a delay to shock). Effects of delayed shock were evaluated across blocks in which the delay to shock was decreased systematically. Effects of three different drug compounds on choice between single- and conflicting-valence consequences were each evaluated separately and across different doses using a variable-delay procedure. Choice of the single-valence consequence decreased as a function of the delay to shock programmed in the aversive portion of the conflicting-valence consequence. Shock exerted the strongest effect on choice when the delay to it was short (shown by high percentage choice of the single-valence consequence) and systematically weaker effects as the delay to the shock was raised (shown by a

gradual shift from the producing the single-valence consequence to producing the conflicting-valence consequence). Results from the study replicate prior research on choice involving conflicting-valence consequences, parallel prior research on drug effects on choice involving delayed gratification and extend our understanding of factors that influence choice of consequences that are reinforcing in the short-term and aversive in the long term in daily life.

Prior Research Involving Conflicting-Valence Consequences

The findings from the present study highlight how delayed shock affects choice of a large immediate reinforcer. These results are in line with research by Dumas (2014), Rodriguez et al. (2018), and Toegel (2018). Dumas used a version of Mazur's (1987) adjusting-delay procedure to evaluate choice between a small amount of food immediately (single-valence consequence) and a larger amount of food followed by a delayed shock (conflicting-valence consequence). The intensity of the shock or duration of the shock was manipulated across conditions. This procedure allowed them to identify the delay to shock at which the conflicting-valence consequence was equivalent in value to the single-valence consequence for each rat in each condition. Similar to the present results, the effectiveness of delayed shock in devaluing the large reinforcer changed as a function of the intensity and duration of the shock. For all rats, delayed shock generally exerted its largest effects on choice in blocks with relatively short delays between the large food reinforcer and the delayed shock. Generally, choice of the single-valence consequence changed systematically as an inverse function of the delay to shock when the delay to shock was manipulated within each session.

The present results also align with Rodriguez et al. (2018) in that the effects that delayed shock has on choice are weakened as the delay to shock is raised systematically. Rodriguez et al. evaluated choice using a version of Evenden and Ryan's (1996) variable-delay procedure. In

Rodriguez et al.'s study, rats were presented with a choice between a small amount of immediate food (single-valence consequence) and a larger amount of immediate food followed by a delayed shock (conflicting-valence consequence) and the delay to shock was manipulated systematically in a fixed sequence across blocks of each session. This procedure allowed them to assess the changing preferences between the single-valence consequence and the conflicting-valence consequence across the set of delays in each session. Rats generally chose the single-valence consequence in blocks in which the delay to shock was short. As the delay to shock was manipulated, choice of the single-valence consequence generally changed as an inverse function of the delay to shock.

The present results noted above are also in line with research by Toegel (2018). Toegel used an adjusting-delay procedure to evaluate choice patterns between delayed food (single-valence consequence) and immediate food followed by a delayed shock (conflicting-valence consequence). The delay to shock was manipulated across conditions. This procedure allowed the identification of the delay to food at which the conflicting-valence consequence was equivalent in value to the single-valence consequence for each rat as the delay to shock was manipulated across conditions. Overall, shock devalued the immediate food as an inverse function of the delay to shock. When the delay to shock was short, it was most effective at reducing the value of immediate food. Similar to the present experiment, as the delay to shock was raised, its effects on choice weakened systematically. Taken together, the present results and all of the previous studies have shown similar results in the effects of conflicting consequences on choice patterns.

Prior Research Involving Drug Administration

Prior research has studied the effects of diazepam, *d*-amphetamine, and morphine in delay-of-gratification studies (Evenden and Ryan, 1996; Huskinson and Anderson, 2012; Slezak and Anderson, 2009; Pitts and McKinney, 2005; Pattij et al., 2009). In many of these studies, the procedure presents subjects with a choice between a small immediate reinforcer and a large but delayed reinforcer. The present study evaluated effects of these commonly studied drugs using an arrangement that provided rats with choices between a small immediate food reinforcer (single-valence consequence) and a large immediate food reinforcer and a delayed shock (conflicting-valence consequence).

Diazepam. Diazepam reliably decreased effects of shock on choice across rats across the three doses. Both the medium and high dose of diazepam produced significant decreases in choice of the single-valence consequence relative to stable sessions, no-administration sessions, and saline sessions, however the effects of the low dose of diazepam on choice were not significant and followed a similar pattern to saline administration. Overall, choice of the single-valence consequence decreased as the delay to shock increased, and larger decreases in choice of the single-valence consequence occurred as a function of the delay to shock in sessions with medium and high doses of diazepam.

In delay-of-gratification studies, benzodiazepines increased the choice of the large delayed reinforcer (often multiple delayed food pellets) relative to the small immediate reinforcer (often a single food pellet; Evenden and Ryan, 1996; Huskinson and Anderson, 2012). In the present study, diazepam increased choice of the conflicting-valence consequence (3 immediate food pellets followed by a delayed shock) relative to the single-valence consequence (a single food pellet). Due to the anxiolytic effects of benzodiazepines, this result can be interpreted as

diazepam reducing the aversiveness of the delayed shock, resulting in more choice of the "impulsive" conflicting-valence consequence.

***d*-Amphetamine.** *d*-Amphetamine generally increased effects of delayed shock on choice across rats. The medium and high dose of *d*-amphetamine produced significant increases in choice of the single-valence consequence relative to stable sessions, no-administration sessions, and saline sessions. However, differences between choice patterns in sessions with the low dose of *d*-amphetamine and sessions with saline were not significant or consistent across rats. Overall, choice of the single-valence consequence decreased as the delay to shock increased, and smaller decreases in choice of the single-valence consequence occurred as a function of the delay to shock in sessions with medium and high doses of diazepam.

In some research (Evenden and Ryan, 1996; Slezak and Anderson, 2009), researchers have found that the administration of *d*-amphetamine decreased choice of the large delayed reinforcer as a function of delay compared to choice of the large reinforcer following vehicle administration or no injection. That is, as the delay to the large reinforcer increases, choice of the immediate but small reinforcer increases. In other research (Cardinal et al., 2000), stimulants administered increased choice of the large delayed reinforcer when delays were signaled and decreased choice of the large delayed reinforcer when delays were not signaled. Pitts and McKinney (2005) noted a decrease in choice of the small immediate reinforcer in their variable-delay procedure study when the stimulant methylphenidate was administered.

One major difference between these past studies and the present study is the addition of a delayed aversive consequence, in this case shock, which was delivered as a part of the conflicting-valence consequence. It is possible that the effects of *d*-amphetamine found in the present study resulted from increased sensitivity to shock. In prior research in which *d*-

amphetamine was administered in a punishment procedure (Hendry and Van Toller, 1964; Miczek, 1973), *d*-amphetamine increased rats' sensitivity to the punishing effects of shock – which was shown when shocks of the same magnitude and duration were more effective in suppressing behavior maintained by food in sessions in which *d*-amphetamine had been administered to the rat.

In the present experiment, *d*-amphetamine's effects may have heightened the rat's sensitivity to shock, therefore resulting in a decrease in choice of the conflicting-valence consequence and a corresponding increase in choice of the single-valence consequence, the small immediate reinforcer. The latency data for the sample conflicting-valence consequence trials support this possibility. Although some rats had increased mean latencies in baseline and saline sessions, many high mean-latencies occurred in the *d*-amphetamine dose sessions. Some mean latencies for the sample conflicting-valence consequence were so high that they resulted in the yoking procedure causing long inter-trial intervals that resulted in incomplete sessions (e.g., MB8).

Another explanation for the decrease in choice of the conflicting-valence consequence is the anorectic effect of *d*-amphetamine, as noted by other studies (Vickers et al., 2017; Heal and Smith, 2022). Because both an increased sensitivity to shock and decreased appetite could result in rats choosing large food with delayed shock less frequently, it could be difficult to disentangle these effects. Further research is needed as it is important to fully understand the effects of stimulants such as *d*-amphetamine that are commonly prescribed for disorders that are associated with "impulsive" behaviors.

Morphine. Morphine did not reliably increase or decrease the effects of shock across rats relative to stable sessions, no-administration sessions, and saline sessions. The percentage choice

of the single-valence consequence decreased as a function of the delay to shock in the conflicting-valence consequence, but patterns of choice were not affected systematically by any of the tested doses of morphine.

In prior delay-of-gratification research, the effects of opioids such as morphine on choice patterns have produced increased choice of the small and more immediate reinforcers, but the effects of tested opioids on choice have normally been small. When Pitts and McKinney (2005) administered morphine in a variable delay procedure, relative to the patterns found across delays under no administration and vehicle administration, the administered doses of morphine produced slight but nonsignificant shifts toward the smaller and more immediate choice, and no dose-dependent effects were observed. Pattij et al (2009) administered morphine in a variable-delay procedure and found that morphine shifted choice toward the small reinforcer generally but did not produce dose-dependent effects on choice. In the current study, morphine did not systematically increase or decrease choice of the single-valence consequence as a function of the morphine dose administered.

Some past studies (e.g., Grilly et al., 1980) have hypothesized that the analgesic effects of morphine disrupt the rats' ability to detect the shock, and therefore are more likely to choose the option involving shock due to an increased tolerance of aversive consequences. The findings from the present study are not in line with this hypothesis. Unlike Grilly et al.'s (1980) prediction, choice of the conflicting-valence consequence did not increase in sessions that followed opioid administration, nor was there a reduction in response latency to produce the conflicting-valence consequence during sample trials. Based on the present findings, choice that produces conflicting consequences does not appear to be affected systematically by the acute administration of morphine; however, it is unclear whether this finding holds under conditions of

chronic administration, which more accurately parallels conditions experienced by individuals with opioid use disorder (Shearer et al., 2020). Given the heightened use of illicit opioids documented in the United States in recent years (Mattson et al., 2021), the study of choice involving conflicting-valence consequences may be a crucial area to study to further our understanding of choice among marginalized or high-risk groups like people living with substance use disorders.

The results of the present study highlight the need for further research of drug administration in conflicting-valence consequence procedures. Despite a long history of drug administration in delay-of-gratification models, research involving drug administration and choice of conflicting consequences is relatively new and unexplored. Further studies using the conflicting-consequences model can expand our understanding of effects of various drug classes and whether the results parallel findings obtained in delay-of-gratification models. For the drug classes that have mixed results in the literature, future research involving multiple drugs of the same class could provide insight into possible differences between specific drugs, if any. For example, future research involving *d*-amphetamine and conflicting consequences should work to address the possible sensitivity-inducing and anorectic for the effects of *d*-amphetamine on aversive consequences.

Another possibly important area of future study is to understand effects of chronic drug administration on choice situations involving conflicting-valence consequences. It is important to understand this difference in comparison to illicit drug administration where doses might not always necessarily be determined or acutely administered. Future studies of similar drugs could benefit from using a chronic administration approach.

CONCLUSION

The present research could provide valuable insights into unanticipated or unstudied effects of common compounds that are routinely prescribed in daily life. Medical professionals in the United States commonly prescribe stimulants such as *d*-amphetamine to individuals with ADHD, benzodiazepines such as diazepam to individuals with anxiety-related disorders, and opioids to people suffering from painful ailments. These drugs could have unanticipated effects on susceptibility to conflicting-valence consequences that are reinforcing in the short-term and harmful in the long-term. From this lens, results from the present study suggest that benzodiazepines may serve to lessen control of choice by delayed aversive events, and that stimulants may serve to heighten control by delayed aversive events.

In conclusion, the present study used a variable-delay procedure to assess drug effects on choice patterns in a conflicting-valence paradigm. Results from the present study replicate and extend prior work on choice involving conflicting-valence consequences. As with previous findings, effects exerted on choice by delayed shock were an inverse function of the delay programmed between the reinforcing and aversive consequences. Choice patterns across delays to shock following the administration of compounds researched commonly in delay-discounting procedures (i.e., diazepam, *d*-amphetamine, and morphine) produced patterns that paralleled findings from research in delay discounting. Generally, the benzodiazepine (diazepam) had a dose-dependent effect of decreasing control of choice by the delayed shock; the stimulant (*d*-amphetamine) had a dose-dependent effect of increasing control of choice by the delayed shock;

and the opioid (morphine) had no systematic effect on choice. By administering the three selected drug classes, the present study provides comparisons to previous drug-administration research involving “impulsive” and “self-controlled” choice as well as insights into the effects of commonly prescribed drug classes. The findings from the current study may have implications for further research in both the basic and applied fields and highlights the need for more research to better understand the effects of drug administration on choice involving both reinforcing and aversive consequences.

REFERENCES

Ainslie, G. W. (1974). Impulse control in pigeons. *Journal of the Experimental Analysis of Behavior*, *21*(3), 485–489. https://doi.org/10.1901/jeab.1974.21-485

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). https://doi.org/10.1176/appi.books.9780890425787

Audrain-McGovern, J., Rodriguez, D., Epstein, L. H., Cuevas, J., Rodgers, K., & Wileyto, E. P. (2009). Does delay discounting play an etiological role in smoking or is it a consequence of smoking? *Drug and Alcohol Dependence*, *103*(3), 99-106. https://doi.org/10.1016/j.drugalcdep.2008.12.019

Bickel, W. K., Odum, A. L., & Madden, G. J. (1999). Impulsivity and cigarette smoking: delay discounting in current, never, and ex-smokers. *Psychopharmacology*, *146*(4), 447-454. https://doi.org/10.1007/PL00005490

Cardinal, R. N., Robbins, T. W., & Everitt, B. J. (2000). The effects of *d*-amphetamine, chlordiazepoxide, alpha-flupenthixol and behavioural manipulations on choice of signalled and unsignalled delayed reinforcement in rats. *Psychopharmacology*, *152*(4), 362–375. https://doi.org/10.1007/s002130000536

Clark, D. J., & Schumacher, M. A. (2017). America's opioid epidemic: Supply and demand considerations. *Anesthesia and Analgesia*, *125*(5), 1667–1674. https://doi.org/10.1213/ANE.0000000000002388

de Groot, P. M., Wu, C. C., Carter, B. W., & Munden, R. F. (2018). The epidemiology of lung cancer. *Translational Lung Cancer Research*, *7*(3), 220–233. https://doi.org/10.21037/tlcr.2018.05.06

de Wit, H., & Mitchell, S. H. (2010). Drug effects on delay discounting. In Impulsivity: The behavioral and neurological science of discounting (pp. 213–241). *American Psychological Association*. https://doi.org/10.1037/12069-008

Dixon, M. R., Marley, J., & Jacobs, E. A. (2003). Delay discounting by pathological gamblers. *Journal of Applied Behavior Analysis*, *36*(4), 449-458 https://doi.org/10.1901/jaba.2003.36-449

Dumas, A. D. (2014). *Choice between reinforcers with and without delayed shock* [Master's thesis, West Virginia University]. https://doi.org/10.33915/etd.5515

Epstein, L. H., Paluch, R. A., Stein, J. S., Quattrin, T., Mastrandrea, L. D., Bree, K. A., ... & Bickel, W. K. (2021). Delay discounting, glycemic regulation and health behaviors in adults with prediabetes. *Behavioral Medicine*, *47*(3), 194-204 https://doi.org/10.1080/08964289.2020.1712581

Estle, S. J., Green, L., Myerson, J., & Yeh, Y. H. (2023). Discounting of outcomes in which immediate gains are followed by delayed losses. *Journal of the Experimental Analysis of Behavior*, *119*(1), 36–48. https://doi.org/10.1002/jeab.813

Evenden, J. L., & Ryan, C. N. (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. https://doi.org/10.1007/s002130050121

Garza, K. B., Ding, M., Owensby, J. K., & Zizza, C. A. (2016). Impulsivity and fast-food consumption: a cross-sectional study among working adults. *Journal of the Academy of Nutrition and Dietetics*, *116*(1), 61-68. https://doi.org/10.1016/j.jand.2015.05.003

González-Barriga, F., & Orduña, V. (2022). Spontaneously hypertensive rats show higher impulsive action, but equal impulsive choice with both positive and aversive consequences. *Behavioural Brain Research*, *427*, 113858. https://doi.org/10.1016/j.bbr.2022.113858

Grilly, D.M., Genovese, R.F., & Nowak, M.J. (1980). Effects of morphine, *d*-amphetamine, and pentobarbital on shock and light discrimination performance in rats. *Psychopharmacology*, *70*, 213-217. https://doi.org/10.1007/BF00435317

Hayashi, Y., Miller, K., Foreman, A. M., & Wirth, O. (2016). A behavioral economic analysis of texting while driving: Delay discounting processes. *Accident Analysis & Prevention*, *97*, 132-140. https://doi.org/10.1016/j.aap.2016.08.028

Heal, D.J., & Smith, S.L. (2021). Prospects for new drugs to treat binge-eating disorder: Insights from psychopathology and neuropharmacology. *Journal of Psychopharmacology*, *36*(6), 680-703. https://doi.org/10.1177/02698811211032475

Hendry, D.P. & Van-Toller, C. (1964). Fixed-ratio punishment with continuous reinforcement. *Journal of the Experimental Analysis of Behavior*, *7(*4), 292-300. https://doi.org/10.1901%2Fjeab.1964.7-293

Huskinson, S. L., & Anderson, K. G. (2012). Effects of acute and chronic administration of diazepam on delay discounting in Lewis and Fischer 344 rats. *Behavioural Pharmacology*, *23*(4), 315–330. https://doi.org/10.1097/FBP.0b013e3283564da4

Johnson, M. W., & Bruner, N. R. (2012). The sexual discounting task: HIV risk behavior and the discounting of delayed sexual rewards in cocaine dependence. *Drug and Alcohol Dependence*, *123*(1-3), 15-21. https://doi.org/10.1016/j.drugalcdep.2011.09.032

Kirby, K.N. & Petry, N.M. (2004). Heroin and cocaine abusers have higher discount rates for delayed rewards than alcoholics or non-drug-using controls. *Addiction, 99*, 461–471. https://doi.org/10.1111/j.1360-0443.2003.00669.x

Kirby, K. N., Petry, N. M., & Bickel, W. K. (1999). Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *Journal of Experimental Psychology: General*, *128*(1), 78. https://doi.org/10.1037/0096-3445.128.1.78

Lebeau, G., Consoli, S. M., Le Bouc, R., Sola-Gazagnes, A., Hartemann, A., Simon, D., ... & Lemogne, C. (2016). Delay discounting of gains and losses, glycemic control and therapeutic adherence in type 2 diabetes. *Behavioural Processes*, *132*, 42-48. https://doi.org/10.1016/j.beproc.2016.09.006

Liley, A. E., Gabriel, D. B. K., Sable, H. J., & Simon, N. W. (2019). Sex differences and effects of predictive cues on delayed punishment discounting. *ENeuro*, *6*(4), ENEURO.0225-19.2019. https://doi.org/10.1523/ENEURO.0225-19.2019

Liley, A. E., Gabriel, D. B. K., & Simon, N. W. (2022). Lateral orbitofrontal cortex and basolateral amygdala regulate sensitivity to delayed punishment during decision-making. *ENeuro*, *9*(5), ENEURO.0170-22.2022. https://doi.org/10.1523/ENEURO.0170-22.2022

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*, *216*, 305–321. https://doi.org/10.1007/s00213-011-2229-0

Madden, G., & Johnson, P. (2010). A delay-discounting primer. *Impulsivity: The Behavioral and Neurological Science of Discounting*, 1–39. https://doi.org/10.1037/12069-001

Mattson CL, Tanz LJ, Quinn K, Kariisa M, Patel P, Davis NL. (2021) Trends and geographic patterns in drug and synthetic opioid overdose deaths — United States, 2013–2019. *Morbidity and Mortality Weekly Report 70*(6), 202-207. http://dx.doi.org/10.15585/mmwr.mm7006a4

Mazur, J. E. (1987). An adjusting procedure for studying delayed reinforcement. In M. L. Commons, J. E. Mazur, J. A. Nevin, & H. Rachlin (Eds.), *The effect of delay and of intervening events on reinforcement value* (pp. 55–73). Lawrence Erlbaum Associates, Inc.

McKerchar, T. L., Green, L., Myerson, J., Pickford, T. S., Hill, J. C., & Stout, S. C. (2009). A comparison of four models of delay discounting in humans. *Behavioural Processes*, *81*(2), 256–259. https://doi.org/10.1016/j.beproc.2008.12.017

Miczek, K.A. (1973) Effects of scopolamine, amphetamine, and chlordiazepoxide on punishment. *Psychopharmacology, 28*(4), 373-389. https://doi.org/10.1007/bf00422757

Mischel, W., & Ebbesen, E. B. (1970). Attention in delay of gratification. *Journal of Personality and Social Psychology*, *16*(2), 329–337. https://doi.org/10.1037/h0029815

Mischel, W., Shoda, Y., & Peake, P. K. (1988). The nature of adolescent competencies predicted by preschool delay of gratification. *Journal of Personality and Social Psychology*, *54*(4), 687–696. https://doi.org/10.1037//0022-3514.54.4.687

Monterosso, J. R., Ainslie, G., Xu, J., Cordova, X., Domier, C. P., & London, E. D. (2007). Frontoparietal cortical activity of methamphetamine-dependent and comparison subjects performing a delay discounting task. *Human Brain Mapping*, *28*(5), 383-393. https://doi.org/10.1002/hbm.20281

Myerson, J., Green, L., & Warusawitharana, M. (2001). Area under the curve as a measure of discounting. *Journal of the Experimental Analysis of Behavior*, *76*(2), 235–243. https://doi.org/10.1901/jeab.2001.76-235

Nowell, P. D., Mazumdar, S., Buysse, D. J., Dew, M. A., Reynolds, C. F., & Kupfer, D. J. (1997). Benzodiazepines and zolpidem for chronic insomnia: A meta-analysis of treatment efficacy. *Journal of the American Medical Association*, *278*(24), 2170–2177.

Odum, A. L., Madden, G. J., Badger, G. J., & Bickel, W. K. (2000). Needle sharing in opioid dependent outpatients: Psychological processes underlying risk. *Drug and Alcohol Dependence*, *60*(3), 259-266. https://doi.org/10.1016/S0376-8716(00)00111-3

Orsini, C. A., & Simon, N. W. (2020). Reward/punishment-based decision making in rodents. *Current Protocols in Neuroscience*, *93*(1), e100. https://doi.org/10.1002/cpns.100

Pattij, T., Schetters, D., Janssen, M. C. W., Wiskerke, J., & Schoffelmeer, A. N. M. (2009). Acute effects of morphine on distinct forms of impulsive behavior in rats. *Psychopharmacology*, *205*(3), 489–502. https://doi.org/10.1007/s00213-009-1558-8

Perry, J.L., Stairs, D.J., & Bardo, M.T. (2008) Impulsive choice and environmental enrichment: Effects of *d*-amphetamine and methylphenidate. *Brain Behavioral Research*, *193*(1), 48-54. https://doi.org/10.1016%2Fj.bbr.2008.04.019

Pitts, R. C., & McKinney, A. P. (2005). Effects of methylphenidate and morphine on delay-discount functions obtained within sessions. *Journal of the Experimental Analysis of Behavior*, *83*(3), 297–314. https://doi.org/10.1901/jeab.2005.47-04

Rodríguez, W., Bouzas, A., & Orduña, V. (2018). Temporal discounting of aversive consequences in rats. *Learning & Behavior*, *46*(1), 38–48. https://doi.org/10.3758/s13420-017-0279-9

Shoda, Y., Mischel, W., & Peake, P. K. (1990). Predicting adolescent cognitive and self-regulatory competencies from preschool delay of gratification: Identifying diagnostic

conditions. *Developmental Psychology*, *26*, 978–986. https://doi.org/10.1037/0012-1649.26.6.978

Shearer, R.D., Howell, B.A., Bart, G., & Winkelman, T.N.A. (2020). Substance use patterns and health profiles among US adults who use opioids, methamphetamine, or both, 2015-2018. *Drug and Alcohol Dependence*, *214*, 108162. https://doi.org/10.1016/j.drugalcdep.2020.108162

Slezak, J. M., & Anderson, K. G. (2009). Effects of variable training, signaled and unsignaled delays, and *d*-amphetamine on delay-discounting functions. *Behavioural Pharmacology*, *20*(5–6), 424–436. https://doi.org/10.1097/FBP.0b013e3283305ef9

Toegel, F. J. (2018). *Effects of Delay and Signals on Choice between Delayed Food Alone and Immediate Food with Delayed Shock* [Doctoral Dissertation, West Virginia University]. https://doi.org/10.33915/etd.3748

Vickers, S.P., Goddard, S., Brammer, R.J., Hutson, P.H., & Heal, D.J. (2017). Investigation of impulsivity in binge-eating rats in a delay-discounting task and its prevention by the *d*-amphetamine prodrug, lisdexamfetamine. *Journal of Psychopharmacology*, *31*(6), 784–797. https://doi.org/10.1177/0269881117691672

Tables

Table 1

Dose Range, Pretreatment Time, and Administration Route

Compound	Doses	Time(min)	Administration
Diazepam	0.25mg/kg, 0.50mg/kg, 1.00mg/kg	10 min	i.p.
d-Amphetamine	0.25mg/kg, 0.50mg/kg, 1.00mg/kg	10 min	i.p.
Morphine	2.50mg/kg, 5.00mg/kg, 10.00mg/kg	15 min	i.p.

Note. This table displays the range of doses, pretreatment time, and administration route for each compound.

Table 2

Weekly Session Schedule

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
0	Drug (1-4)	0	0	Drug (1-4)		5

Note. This table displays the weekly schedule of lab sessions. #0 corresponds to variable-delay evaluation sessions with shock but no drug administration. #1-4 corresponds to the days where one of the 4 compounds was administered (1. Saline, 2. Diazepam, 3. *d*-Amphetamine, and 4. Morphine) along with variable-delay evaluation sessions with shock. #5 corresponds to food-magnitude evaluation sessions, which do not include drug administration or shock.

Table 3

Stable Shock levels and order of drug doses per rat

Rat	Stable Shock Level	Diazepam				*d*-Amphetamine				Morphine			
MB1	0.7 mA 400 ms	H	S	L	M	L	M	H	S	S	L	M	H
MB2	0.6 mA 600 ms	S	L	M	H	S	L	M	H	M	H	S	L
MB3	0.9 mA 400 ms	L	M	H	S	H	S	L	M	H	S	L	M
MB8	0.9 mA 500 ms	L	M	H	S	M	H	S	L	S	L	M	H
MB9	0.9 mA 400 ms	M	H	S	L	S	L	M	H	S	L	M	H
MB10	0.9 mA 400 ms	S	L	M	H	M	H	S	L	H	S	L	M
MB11	1.0 mA 400 ms	S	L	M	H	S	L	M	H	H	S	L	M
MB12	0.7 mA 400 ms	M	H	S	L	M	H	S	L	L	M	H	S

Note. This table displays the stable shock levels in terms of intensity (mA) and duration (ms) for each rat and the order of doses per drug for each rat. Letters refer to saline (S) administration, and the low (L), medium (M), and high (H) doses of each drug, respectively.

Table 4

Mean Latencies to Produce Single-Valence Consequences across Sample Trials by Delay (s) to Shock and Diazepam Dose for Each Rat.

Mean Latencies (s) to Produce Single-Valence Consequence												
Rat	64 s		32 s		16 s		8 s		4 s		2 s	
MB1												
BSL	1.72	(1.5)	0.68	(0.2)	0.85	(0.3)	0.74	(0.2)	0.90	(0.4)	0.90	(0.2)
Saline	1.23	(0.6)	0.79	(0.2)	1.01	(0.2)	0.83	(0.1)	0.95	(0.1)	1.18	(0.5)
0.25	1.19	(0.3)	0.80	(0.1)	1.08	(0.4)	0.63	(0.1)	0.99	(0.3)	0.77	(0.1)
0.50	2.20	(0.2)	0.48	(0.0)	0.61	(0.2)	0.63	(0.1)	0.86	(0.1)	1.59	(0.2)
1.00	99.12	(52.7)	1.10	(0.3)	0.91	(0.5)	0.74	(0.1)	1.39	(0.8)	1.48	(0.6)
MB2												
BSL	0.81	(0.3)	0.74	(0.4)	0.85	(0.3)	0.70	(0.2)	0.75	(0.1)	0.77	(0.3)
Saline	0.75	(0.3)	0.75	(0.1)	0.59	(0.3)	0.65	(0.1)	0.48	(0.1)	0.59	(0.3)
0.25	0.62	(0.0)	0.91	(0.6)	0.91	(0.6)	0.95	(0.1)	0.59	(0.1)	0.45	(0.0)
0.50	1.00	(0.5)	0.74	(0.1)	1.23	(0.0)	0.93	(0.3)	0.51	(0.1)	0.65	(0.2)
1.00	0.96	(0.6)	0.79	(0.1)	1.19	(0.5)	0.84	(0.1)	0.97	(0.3)	0.93	(0.0)
MB3												
BSL	0.60	(0.2)	0.59	(0.1)	0.73	(0.3)	0.84	(0.4)	0.56	(0.3)	0.55	(0.2)
Saline	0.56	(0.2)	0.45	(0.1)	0.80	(0.2)	0.66	(0.0)	0.59	(0.0)	0.47	(0.2)
0.25	0.44	(0.0)	0.66	(0.3)	0.41	(0.0)	0.59	(0.1)	0.74	(0.2)	0.59	(0.1)
0.50	220.6	(217.8)	0.63	(0.0)	0.45	(0.1)	0.41	(0.1)	0.66	(0.2)	0.87	(0.4)
1.00	1.14	(0.3)	0.68	(0.1)	0.49	(0.1)	0.56	(0.1)	0.47	(0.0)	0.65	(0.3)
MB8												
BSL	0.87	(0.3)	0.59	(0.0)	0.73	(0.3)	0.60	(0.1)	0.77	(0.3)	0.87	(0.4)
Saline	1.07	(0.5)	0.59	(0.1)	0.62	(0.1)	0.63	(0.2)	0.55	(0.2)	0.95	(0.0)
0.25	1.42	(0.3)	0.66	(0.1)	0.69	(0.0)	1.55	(0.7)	0.95	(0.2)	0.97	(0.3)
0.50	1.18	(0.5)	0.78	(0.0)	1.08	(0.4)	1.36	(0.9)	1.10	(0.1)	0.90	(0.3)
1.00	1.39	(0.3)	0.99	(0.1)	1.08	(0.4)	0.68	(0.2)	0.96	(0.3)	1.08	(0.1)
MB9												
BSL	1.63	(0.2)	1.34	(0.9)	1.61	(1.4)	1.39	(0.3)	1.01	(0.3)	1.61	(1.0)
Saline	1.77	(0.7)	0.81	(0.2)	0.95	(0.2)	0.81	(0.3)	0.65	(0.1)	0.66	(0.0)
0.25	1.64	(0.2)	3.40	(2.9)	1.85	(1.2)	1.68	(0.9)	1.41	(0.6)	1.19	(0.3)
0.50	85.39	(83.6)	1.04	(0.6)	0.64	(0.1)	0.56	(0.1)	0.59	(0.2)	0.72	(0.2)
1.00	6.88	(5.7)	0.98	(0.1)	0.94	(0.3)	1.04	(0.2)	0.95	(0.1)	0.84	(0.1)
MB10												
BSL	0.48	(0.2)	0.56	(0.2)	0.39	(0.1)	0.43	(0.0)	0.48	(0.2)	0.39	(0.0)
Saline	2.68	(0.9)	0.41	(0.0)	0.51	(0.0)	0.52	(0.1)	0.52	(0.1)	0.46	(0.0)
0.25	0.45	(0.1)	0.47	(0.0)	0.72	(0.3)	0.36	(0.0)	0.47	(0.1)	0.45	(0.1)
0.50	1.31	(0.6)	0.48	(0.0)	0.60	(0.1)	0.66	(0.2)	0.66	(0.3)	0.60	(0.0)
1.00	0.53	(0.2)	0.42	(0.0)	0.39	(0.1)	0.41	(0.0)	0.52	(0.2)	0.38	(0.1)
MB11												
BSL	1.33	(0.4)	0.89	(0.3)	0.80	(0.1)	0.83	(0.3)	1.02	(0.4)	1.04	(0.5)
Saline	1.16	(0.3)	1.23	(0.2)	0.81	(0.0)	0.92	(0.2)	1.12	(0.5)	0.73	(0.1)
0.25	1.29	(0.2)	0.92	(0.2)	1.10	(0.2)	0.93	(0.2)	0.96	(0.2)	1.02	(0.1)
0.50	1.31	(0.4)	1.02	(0.4)	0.79	(0.2)	0.75	(0.3)	0.57	(0.1)	1.58	(0.6)

1.00	1.92	(1.2)	2.59	(1.8)	1.06	(0.4)	1.04	(0.2)	1.04	(0.3)	18.51	(17.6)
MB12												
BSL	0.94	(0.4)	0.56	(0.2)	0.60	(0.2)	0.71	(0.3)	0.68	(0.2)	0.64	(0.2)
Saline	0.73	(0.2)	0.70	(0.1)	0.63	(0.1)	0.74	(0.2)	1.06	(0.6)	0.83	(0.2)
0.25	0.96	(0.1)	1.15	(0.5)	1.13	(0.6)	1.36	(0.2)	1.00	(0.5)	1.20	(0.2)
0.50	1.62	(0.5)	4.66	(3.2)	0.92	(0.1)	1.70	(1.0)	0.79	(0.2)	1.01	(0.1)
1.00	0.92	(0.1)	0.95	(0.1)	0.51	(0.0)	1.01	(0.3)	0.79	(0.0)	0.89	(0.1)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three diazepam doses. Numbers above 100 are expressed to one decimal place.

Table 5

Mean Latencies to Produce Conflicting-Valence Consequences across Sample Trials by Delay (s) to Shock and Diazepam Dose for Each Rat.

Mean Latencies (s) to Produce Conflicting-Valence Consequence												
Rat	64 s		32 s		16 s		8 s		4 s		2 s	
MB1												
BSL	0.87	(0.2)	1.55	(1.4)	0.91	(0.2)	0.84	(0.3)	45.31	(70.1)	13.93	(29.5)
Saline	168.9	(168.2)	0.86	(0.1)	0.68	(0.1)	201.2	(199.7)	15.06	(13.9)	78.91	(78.4)
0.25	0.73	(0.1)	0.63	(0.1)	0.79	(0.3)	1.06	(0.3)	0.61	(0.1)	0.66	(0.0)
0.50	1.75	(0.8)	0.75	(0.0)	1.17	(0.3)	0.66	(0.1)	0.87	(0.1)	55.53	(54.9)
1.00	3.86	(1.7)	0.91	(0.0)	1.16	(0.4)	1.08	(0.2)	1.59	(0.4)	0.85	(0.1)
MB2												
BSL	1.27	(0.7)	1.12	(0.6)	0.85	(0.4)	0.76	(0.4)	0.68	(0.3)	102.7	(228.1)
Saline	0.25	(0.0)	1.12	(0.0)	0.73	(0.1)	0.82	(0.0)	308.1	(307.1)	0.75	(0.1)
0.25	0.99	(0.4)	0.73	(0.0)	1.11	(0.3)	1.66	(1.1)	0.94	(0.0)	0.54	(0.2)
0.50	2.05	(0.6)	1.57	(0.7)	0.52	(0.3)	0.59	(0.1)	0.93	(0.1)	0.63	(0.0)
1.00	1.72	(1.2)	1.31	(0.0)	0.72	(0.0)	1.06	(0.4)	0.66	(0.1)	0.86	(0.3)
MB3												
BSL	61.88	(95.9)	0.97	(0.5)	0.63	(0.1)	0.79	(0.2)	0.74	(0.2)	15.33	(25.8)
Saline	75.92	(75.2)	0.62	(0.2)	2.54	(2.0)	83.00	(82.4)	175.9	(171.1)	0.85	(0.0)
0.25	1.10	(0.3)	1.05	(0.1)	57.90	(57.1)	32.64	(31.3)	333.8	(118.7)	1.14	(0.4)
0.50	90.48	(66.6)	0.75	(0.1)	0.75	(0.1)	1.17	(0.1)	1.15	(0.0)	1.23	(0.5)
1.00	3.28	(1.8)	1.13	(0.4)	0.90	(0.4)	0.88	(0.0)	77.81	(75.8)	0.61	(0.1)
MB8												
BSL	0.57	(0.1)	1.16	(0.4)	2.46	(3.1)	1.41	(0.9)	6.15	(10.8)	12.37	(20.2)
Saline	1.26	(0.0)	193.5	(191.4)	219.0	(217.8)	153.2	(153.2)	302.6	(300.2)	0.94	(0.0)
0.25	1.62	(1.0)	15.04	(12.7)	147.5	(145.2)	191.6	(114.3)	110.8	(43.6)	52.71	(50.8)
0.50	2.05	(1.4)	58.58	(56.2)	147.3	(145.4)	157.4	(148.5)	219.5	(65.1)	113.8	(111.8)
1.00	124.9	(122.9)	228.8	(123.4)	84.64	(82.8)	3.88	(1.5)	135.6	(134.2)	152.2	(150.3)
MB9												
BSL	88.93	(60.9)	0.77	(0.1)	0.80	(0.1)	0.84	(0.2)	4.39	(7.4)	8.61	(16.7)
Saline	94.67	(77.3)	2.74	(2.2)	0.91	(0.1)	1.27	(0.0)	19.63	(18.5)	82.41	(80.6)
0.25	150.9	(147.8)	0.93	(0.1)	151.5	(150.7)	308.1	(82.8)	5.81	(5.3)	83.07	(74.4)
0.50	18.42	(17.2)	2.55	(1.0)	11.11	(10.2)	1.55	(0.7)	2.41	(0.8)	4.46	(3.0)
1.00	180.5	(178.2)	0.88	(0.2)	1.00	(0.2)	1.30	(0.1)	102.6	(101.9)	1.13	(0.2)
MB10												
BSL	0.39	(0.1)	0.66	(0.3)	0.91	(0.4)	2.40	(2.4)	0.81	(0.2)	0.71	(0.4)
Saline	1.03	(0.2)	11.65	(8.1)	14.99	(6.3)	15.90	(13.7)	54.73	(51.5)	36.19	(28.7)
0.25	0.30	(0.0)	1.61	(0.3)	1.62	(0.7)	1.18	(0.1)	2.30	(0.9)	2.41	(0.6)
0.50	390.3	(390.0)	1.90	(1.5)	0.86	(0.5)	0.60	(0.2)	1.41	(1.0)	0.77	(0.1)
1.00	0.43	(0.2)	0.45	(0.1)	0.45	(0.2)	2.02	(1.7)	1.48	(0.7)	0.79	(0.1)

MB11												
BSL	0.80	(0.3)	1.17	(0.5)	2.68	(3.8)	0.66	(0.2)	1.09	(0.9)	4.09	(6.5)
Saline	1.10	(0.2)	7.52	(6.9)	0.68	(0.1)	0.69	(0.0)	0.92	(0.2)	1.89	(1.1)
0.25	0.69	(0.2)	1.52	(0.4)	1.29	(0.2)	1.02	(0.0)	0.96	(0.2)	12.12	(11.5)
0.50	1.29	(0.6)	0.97	(0.4)	0.86	(0.0)	1.10	(0.4)	0.94	(0.0)	102.1	(99.4)
1.00	2.93	(1.1)	1.55	(0.7)	2.09	(1.4)	1.51	(0.6)	1.08	(0.3)	131.8	(40.5)
MB12												
BSL	1.04	(0.5)	1.23	(0.3)	1.10	(0.4)	9.06	(17.0)	1.37	(0.9)	0.83	(0.3)
Saline	0.85	(0.1)	1.98	(1.1)	191.0	(190.2)	0.51	(0.2)	1.15	(0.4)	2.48	(0.5)
0.25	111.4	(110.5)	20.11	(19.4)	79.78	(79.3)	1.45	(0.9)	0.75	(0.3)	0.84	(0.3)
0.50	0.63	(0.1)	2.97	(0.5)	1.65	(0.0)	69.75	(67.2)	0.82	(0.0)	112.3	(111.2)
1.00	3.53	(2.5)	131.1	(30.6)	233.2	(37.7)	188.2	(11.5)	217.4	(15.8)	136.2	(112.6)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three diazepam doses. Numbers above 100 are expressed to one decimal place.

Table 6

Mean Latencies to Produce Single-Valence Consequences across Sample Trials by Delay (s) to Shock and d-Amphetamine Dose for Each Rat.

	Mean Latencies (s) to Produce Single-Valence Consequence					
Rat	64 s	32 s	16 s	8 s	4 s	2 s
MB1						
BSL	1.72 (1.5)	0.68 (0.2)	0.85 (0.3)	0.74 (0.2)	0.90 (0.4)	0.90 (0.2)
Saline	1.04 (0.2)	0.82 (0.1)	1.13 (0.3)	0.94 (0.1)	0.98 (0.2)	0.75 (0.2)
0.25	2.32 (0.3)	0.77 (0.1)	1.22 (0.3)	0.95 (0.2)	0.88 (0.3)	1.02 (0.3)
0.50	0.76 (0.1)	0.92 (0.6)	0.55 (0.2)	0.84 (0.4)	1.01 (0.1)	0.95 (0.0)
1.00	1.83 (1.0)	0.59 (0.1)	0.98 (0.2)	1.16 (0.0)	1.37 (0.7)	1.26 (0.9)
MB2						
BSL	0.81 (0.3)	0.74 (0.4)	0.85 (0.3)	0.70 (0.2)	0.75 (0.1)	0.77 (0.3)
Saline	0.53 (0.1)	1.14 (0.3)	0.95 (0.1)	0.93 (0.2)	0.77 (0.2)	0.89 (0.2)
0.25	0.77 (0.3)	0.59 (0.3)	0.92 (0.2)	0.67 (0.2)	0.72 (0.1)	0.95 (0.4)
0.50	0.42 (0.0)	0.48 (0.1)	1.17 (0.1)	0.92 (0.1)	0.96 (0.0)	1.09 (0.5)
1.00	0.77 (0.4)	1.34 (0.2)	0.82 (0.1)	0.77 (0.0)	1.04 (0.2)	0.73 (0.1)
MB3						
BSL	0.60 (0.2)	0.59 (0.1)	0.73 (0.3)	0.84 (0.4)	0.56 (0.3)	0.55 (0.2)
Saline	0.67 (0.2)	0.62 (0.2)	0.69 (0.1)	0.87 (0.3)	0.83 (0.0)	1.23 (0.7)
0.25	0.44 (0.1)	0.60 (0.0)	0.84 (0.4)	0.64 (0.1)	0.52 (0.0)	0.41 (0.0)
0.50	0.69 (0.2)	0.57 (0.1)	0.42 (0.1)	0.70 (0.1)	0.85 (0.2)	0.48 (0.0)
1.00	0.41 (0.0)	0.74 (0.2)	0.75 (0.1)	0.56 (0.1)	0.45 (0.1)	0.68 (0.1)
MB8						
BSL	0.87 (0.3)	0.59 (0.0)	0.73 (0.3)	0.60 (0.1)	0.77 (0.3)	0.87 (0.4)
Saline	0.73 (0.1)	1.00 (0.2)	0.63 (0.1)	0.65 (0.0)	0.83 (0.0)	1.56 (0.4)
0.25	1.02 (0.3)	0.76 (0.2)	0.79 (0.3)	0.66 (0.1)	0.78 (0.0)	1.56 (0.2)
0.50	0.98 (0.3)	0.84 (0.2)	0.77 (0.1)	0.77 (0.0)	0.89 (0.3)	1.06 (0.3)
1.00	0.63 (0.2)	0.65 (0.0)	0.78* (---)	0.61* (---)	0.53* (---)	--- (---)
MB9						
BSL	1.63 (0.2)	1.34 (0.9)	1.61 (1.4)	1.39 (0.3)	1.01 (0.3)	1.61 (1.0)
Saline	1.30 (0.4)	1.62 (0.9)	1.38 (0.5)	0.90 (0.1)	0.70 (0.1)	0.71 (0.0)
0.25	1.30 (0.4)	1.62 (0.9)	1.38 (0.5)	0.90 (0.1)	0.70 (0.1)	0.71 (0.0)
0.50	1.23 (0.4)	0.64 (0.1)	0.66 (0.3)	0.63 (0.2)	0.62 (0.0)	0.70 (0.0)
1.00	0.81 (0.1)	0.97 (0.0)	0.74 (0.0)	0.56 (0.1)	0.61 (0.1)	0.90 (0.2)
MB10						
BSL	0.48 (0.2)	0.56 (0.2)	0.39 (0.1)	0.43 (0.0)	0.48 (0.2)	0.39 (0.0)
Saline	0.45 (0.1)	0.73 (0.3)	0.52 (0.0)	0.51 (0.1)	0.41 (0.0)	0.37 (0.0)
0.25	0.43 (0.0)	0.53 (0.1)	0.40 (0.1)	0.65 (0.2)	0.41 (0.1)	0.43 (0.0)
0.50	0.45 (0.0)	0.48 (0.1)	0.57 (0.1)	0.39 (0.0)	0.38 (0.0)	0.43 (0.0)
1.00	0.42 (0.0)	0.45 (0.0)	0.46 (0.1)	0.56 (0.0)	0.41 (0.0)	0.39 (0.0)

MB11						
BSL	1.33 (0.4)	0.89 (0.3)	0.80 (0.1)	0.83 (0.3)	1.02 (0.4)	1.04 (0.5)
Saline	0.86 (0.1)	0.67 (0.0)	0.57 (0.1)	0.65 (0.1)	1.13 (0.2)	0.66 (0.1)
0.25	1.02 (0.2)	0.70 (0.2)	0.68 (0.0)	0.73 (0.2)	1.08 (0.7)	0.66 (0.2)
0.50	0.81 (0.1)	0.45 (0.1)	0.63 (0.1)	0.82 (0.1)	0.73 (0.0)	0.95 (0.2)
1.00	0.72 (0.0)	0.63 (0.3)	0.93 (0.3)	0.55 (0.1)	0.59 (0.0)	0.85 (0.2)
MB12						
BSL	0.94 (0.4)	0.56 (0.2)	0.60 (0.2)	0.71 (0.3)	0.68 (0.2)	0.64 (0.2)
Saline	0.91 (0.1)	1.27 (0.1)	0.74 (0.0)	0.95 (0.3)	0.84 (0.1)	0.90 (0.3)
0.25	0.84 (0.0)	0.73 (0.1)	0.69 (0.1)	0.72 (0.1)	0.96 (0.2)	0.98 (0.1)
0.50	0.92 (0.1)	0.91 (0.3)	0.93 (0.2)	0.99 (0.3)	0.66 (0.0)	1.20 (0.4)
1.00	1.18 (0.1)	1.20 (0.2)	1.34 (0.6)	1.30 (0.2)	1.20 (0.1)	0.85 (0.1)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three *d*-amphetamine doses. An asterisk represents mean latencies from only one session, due to an incomplete session. Dashes (---) indicate incomplete data at the specific delay and dose because of incomplete session(s). Numbers above 100 are expressed to one decimal place.

Table 7

Mean Latencies to Produce Conflicting-Valence Consequences across Sample Trials by Delay (s) to Shock and d-Amphetamine Dose for Each Rat.

	Mean Latencies (s) to Produce Conflicting-Valence Consequence					
Rat	64 s	32 s	16 s	8 s	4 s	2 s
MB1						
BSL	0.87 (0.2)	1.55 (1.4)	0.91 (0.2)	0.84 (0.3)	45.31 (70.1)	13.93 (29.5)
Saline	1.03 (0.5)	1.46 (0.1)	1.41 (0.2)	1.41 (0.6)	118.8 (117.7)	0.88 (0.3)
0.25	0.89 (0.1)	1.69 (0.3)	1.12 (0.1)	1.02 (0.1)	28.70 (26.9)	439.4 (218.7)
0.50	199.7 (199.0)	1.36 (0.1)	0.64 (0.1)	1.16 (0.2)	1.52 (0.2)	338.2 (0.0)
1.00	198.7 (197.8)	0.87 (0.2)	1.86 (1.3)	29.37 (28.7)	0.72 (0.1)	1.15 (0.7)
MB2						
BSL	1.27 (0.7)	1.12 (0.6)	0.85 (0.4)	0.76 (0.4)	0.68 (0.3)	102.7 (228.1)
Saline	1.10 (0.6)	1.02 (0.3)	0.44 (0.2)	0.70 (0.1)	0.53 (0.0)	0.27 (0.0)
0.25	0.61 (0.1)	0.29 (0.1)	0.45 (0.3)	0.54 (0.1)	0.52 (0.1)	2.63 (2.1)
0.50	0.56 (0.0)	0.59 (0.1)	0.70 (0.2)	0.48 (0.1)	0.52 (0.0)	0.53 (0.0)
1.00	1.38 (0.6)	0.57 (0.1)	0.45 (0.1)	0.52 (0.1)	0.59 (0.0)	0.52 (0.0)
MB3						
BSL	61.88 (95.9)	0.97 (0.5)	0.63 (0.1)	0.79 (0.2)	0.74 (0.2)	15.33 (25.8)
Saline	66.59 (65.8)	1.51 (0.8)	1.48 (0.6)	79.92 (79.5)	0.89 (0.0)	0.59 (0.1)
0.25	0.47 (0.1)	2.59 (1.7)	0.92 (0.3)	0.54 (0.1)	0.87 (0.2)	0.48 (0.1)
0.50	0.77 (0.1)	0.75 (0.0)	168.5 (167.6)	3.82 (3.0)	3.42 (0.3)	372.0 (371.3)
1.00	213.4 (32.8)	0.73 (0.1)	1.59 (0.6)	0.59 (0.0)	12.09 (11.4)	1.99 (1.3)
MB8						
BSL	0.57 (0.1)	1.16 (0.4)	2.46 (3.1)	1.41 (0.9)	6.15 (10.8)	12.37 (20.2)
Saline	412.2 (279.8)	2.22 (0.1)	0.74 (0.1)	1.38 (0.9)	1.35 (0.5)	1.57 (1.1)
0.25	143.4 (142.4)	85.06 (84.2)	486.5 (398.6)	2.34 (0.4)	3.12 (0.7)	109.5 (102.7)
0.50	1.48 (0.3)	11.34 (4.7)	352.7 (351.3)	24.03 (23.0)	241.0 (185.3)	112.0 (108.7)
1.00	132.3 (130.6)	525.7 (524.3)	0.50* (---)	2.14* (---)	687.0* (---)	--- (---)
MB9						
BSL	88.93 (60.9)	0.77 (0.1)	0.80 (0.1)	0.84 (0.2)	4.39 (7.4)	8.61 (16.7)
Saline	164.7 (135.8)	0.70 (0.0)	1.03 (0.1)	0.99 (0.1)	1.17 (0.4)	18.41 (16.7)
0.25	426.3 (184.8)	0.75 (0.0)	0.83 (0.1)	2.66 (1.4)	0.91 (0.1)	3.83 (2.3)
0.50	548.5 (356.7)	0.77 (0.2)	1.02 (0.1)	0.82 (0.0)	104.4 (103.4)	1.07 (0.1)
1.00	318.6 (18.5)	3.19 (1.6)	21.37 (3.1)	4.16 (0.5)	10.82 (3.0)	0.95 (0.2)
MB10						
BSL	0.39 (0.1)	0.66 (0.3)	0.91 (0.4)	2.40 (2.4)	0.81 (0.2)	0.71 (0.4)
Saline	0.41 (0.1)	0.47 (0.1)	0.73 (0.2)	1.64 (0.7)	2.23 (0.4)	2.57 (0.8)
0.25	0.30 (0.0)	0.57 (0.1)	2.31 (0.6)	1.03 (0.4)	1.87 (0.4)	2.68 (0.6)
0.50	0.27 (0.0)	1.47 (0.2)	0.95 (0.4)	2.21 (0.1)	4.48 (3.0)	1.85 (0.3)
1.00	0.64 (0.1)	1.79 (0.9)	0.93 (0.4)	1.91 (1.2)	1.07 (0.4)	2.89 (0.5)

MB11												
BSL	0.80	(0.3)	1.17	(0.5)	2.68	(3.8)	0.66	(0.2)	1.09	(0.9)	4.09	(6.5)
Saline	1.01	(0.5)	1.39	(0.2)	128.1	(127.4)	0.65	(0.0)	30.84	(30.2)	31.95	(30.3)
0.25	0.77	(0.2)	104.8	(104.1)	0.59	(0.4)	26.86	(26.1)	91.91	(90.0)	0.70	(0.0)
0.50	1.02	(0.0)	1.78	(0.4)	100.1	(99.0)	0.78	(0.2)	1.20	(0.3)	0.62	(0.0)
1.00	1.13	(0.1)	0.73	(0.1)	1.26	(0.0)	1.54	(1.0)	1.09	(0.2)	19.62	(18.8)
MB12												
BSL	1.04	(0.5)	1.23	(0.3)	1.10	(0.4)	9.06	(17.0)	1.37	(0.9)	0.83	(0.3)
Saline	1.16	(0.5)	2.13	(0.2)	1.73	(0.1)	1.64	(0.7)	2.03	(0.2)	2.40	(0.2)
0.25	0.84	(0.3)	1.62	(0.2)	1.02	(0.5)	1.05	(0.4)	1.23	(0.3)	106.7	(105.4)
0.50	227.7	(4.2)	1.09	(0.6)	1.03	(0.5)	256.8	(135.5)	1.67	(0.2)	208.4	(0.9)
1.00	1.04	(0.5)	1.45	(0.4)	1.93	(0.4)	10.20	(9.5)	138.3	(103.4)	16.41	(7.9)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three *d*-amphetamine doses. An asterisk represents mean latencies from only one session, due to an incomplete session. Dashes (---) indicate incomplete data at the specific delay and dose because of incomplete session(s). Numbers above 100 are expressed to one decimal place.

Table 8

Mean Latencies to Produce Single-Valence Consequences across Sample Trials by Delay (s) to Shock and Morphine Dose for Each Rat.

	Mean Latencies (s) to Produce Single-Valence Consequence					
Rat	64 s	32 s	16 s	8 s	4 s	2 s
MB1						
BSL	1.72 (1.5)	0.68 (0.2)	0.85 (0.3)	0.74 (0.2)	0.90 (0.4)	0.90 (0.2)
Saline	0.98 (0.1)	1.36 (0.1)	0.77 (0.2)	0.86 (0.5)	0.70 (0.3)	1.03 (0.3)
2.50	0.98 (0.0)	1.34 (0.1)	0.62 (0.1)	1.01 (0.1)	0.88 (0.1)	1.14 (0.5)
5.00	1.20 (0.4)	0.87 (0.2)	0.70 (0.1)	1.12 (0.4)	0.57 (0.2)	0.91 (0.1)
10.00	1.92 (1.2)	0.54 (0.0)	0.68 (0.1)	1.31 (0.0)	0.72 (0.0)	0.69* (---)
MB2						
BSL	0.81 (0.3)	0.74 (0.4)	0.85 (0.3)	0.70 (0.2)	0.75 (0.1)	0.77 (0.3)
Saline	0.38 (0.0)	0.86 (0.1)	0.73 (0.1)	0.63 (0.0)	0.64 (0.1)	0.70 (0.1)
2.50	0.45 (0.0)	0.45 (0.1)	0.63 (0.3)	0.68 (0.3)	0.81 (0.1)	0.73 (0.2)
5.00	0.81 (0.4)	0.77 (0.1)	0.72 (0.1)	0.88 (0.3)	1.07 (0.4)	0.58 (0.0)
10.00	1.49 (1.1)	3.80 (2.3)	1.02 (0.2)	0.81 (0.1)	1.13 (0.4)	0.83 (0.1)
MB3						
BSL	0.60 (0.2)	0.59 (0.1)	0.73 (0.3)	0.84 (0.4)	0.56 (0.3)	0.55 (0.2)
Saline	0.45 (0.0)	0.66 (0.0)	0.63 (0.1)	0.66 (0.0)	0.63 (0.0)	0.43 (0.1)
2.50	0.47 (0.1)	0.64 (0.0)	0.91 (0.1)	0.65 (0.0)	0.98 (0.5)	0.48 (0.1)
5.00	0.95 (0.5)	0.63 (0.1)	0.66 (0.1)	0.57 (0.1)	0.63* (---)	0.34* (---)
10.00	2.16 (0.6)	1.13 (0.7)	73.20 (72.0)	1.08* (---)	1.78* (---)	123.9* (---)
MB8						
BSL	0.87 (0.3)	0.59 (0.0)	0.73 (0.3)	0.60 (0.1)	0.77 (0.3)	0.87 (0.4)
Saline	0.95 (0.4)	0.48 (0.0)	0.44 (0.1)	0.69 (0.1)	0.58 (0.1)	0.71 (0.1)
2.50	0.78 (0.3)	1.38 (0.1)	0.63 (0.0)	0.66 (0.1)	0.60 (0.2)	0.87 (0.2)
5.00	0.93 (0.4)	0.88 (0.4)	0.51 (0.2)	0.76 (0.0)	0.49 (0.1)	0.72 (0.1)
10.00	0.66 (0.1)	0.49 (0.0)	0.71 (0.1)	0.70 (0.1)	0.84 (0.3)	0.91* (---)
MB9						
BSL	1.63 (0.2)	1.34 (0.9)	1.61 (1.4)	1.39 (0.3)	1.01 (0.3)	1.61 (1.0)
Saline	0.74 (0.2)	0.80 (0.2)	0.73 (0.0)	0.88 (0.2)	1.01 (0.3)	1.61 (1.0)
2.50	9.38 (8.6)	1.11 (0.5)	0.67 (0.3)	0.79 (0.1)	0.70 (0.0)	0.70 (0.1)
5.00	4.71 (1.3)	0.89 (0.0)	0.99 (0.2)	0.65 (0.0)	0.94 (0.2)	1.11 (0.2)
10.00	84.74 (84.2)	14.24 (13.3)	5.71 (4.9)	1.02 (0.4)	1.09 (0.4)	0.77 (0.1)
MB10						
BSL	0.48 (0.1)	0.56 (0.2)	0.39 (0.1)	0.43 (0.0)	0.48 (0.2)	0.39 (0.0)
Saline	0.37 (0.0)	0.37 (0.0)	0.34 (0.0)	0.41 (0.0)	0.34 (0.0)	0.63 (0.2)
2.50	0.44 (0.0)	0.34 (0.0)	0.45 (0.1)	0.48 (0.1)	0.94 (0.2)	0.55 (0.2)
5.00	0.33 (0.0)	0.41 (0.1)	0.62 (0.2)	0.63 (0.3)	0.45 (0.0)	0.40 (0.0)
10.00	1.72 (0.8)	0.47 (0.2)	0.41 (0.0)	0.50 (0.2)	1.05 (0.7)	110.5 (109.5)

MB11										
BSL	1.33	(0.4)	0.89	(0.3)	0.80	(0.1)	0.83	(0.3)	1.02	(0.4)	1.04	(0.5)
Saline	0.58	(0.1)	0.63	(0.1)	0.45	(0.2)	0.74	(0.3)	0.81	(0.4)	0.55	(0.1)
2.50	0.71	(0.0)	0.77	(0.2)	0.80	(0.4)	0.55	(0.2)	0.70	(0.2)	0.73	(0.0)
5.00	1.17	(0.0)	0.55	(0.1)	0.64	(0.2)	0.88	(0.0)	0.58	(0.1)	0.37	(0.0)
10.00	1.15	(0.8)	0.74	(0.0)	197.4	(196.6)	2.05	(0.0)	47.36	(43.2)	14.70	(14.2)
MB12										
BSL	0.94	(0.4)	0.56	(0.2)	0.60	(0.2)	0.71	(0.3)	0.68	(0.2)	0.64	(0.2)
Saline	1.14	(0.2)	1.39	(0.3)	1.06	(0.1)	1.07	(0.2)	1.28	(0.1)	1.27	(0.5)
2.50	0.89	(0.3)	1.30	(0.1)	0.90	(0.1)	1.09	(0.0)	0.77	(0.2)	1.09	(0.3)
5.00	0.95	(0.5)	0.92	(0.2)	1.12	(0.1)	1.24	(0.2)	0.62	(0.2)	0.76	(0.2)
10.00	1.21	(0.1)	0.76	(0.3)	0.70	(0.1)	0.90	(0.4)	1.11*	(---)	1.06*	(---)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three morphine doses. An asterisk represents mean latencies from only one session, due to an incomplete session. Dashes (---) indicate incomplete data at the specific delay and dose because of incomplete session(s). Numbers above 100 are expressed to one decimal place.

Table 9

Mean Latencies to Produce Conflicting-Valence Consequences across Sample Trials by Delay (s) to Shock and Morphine Dose for Each Rat.

	Mean Latencies (s) to Produce Conflicting-Valence Consequence											
Rat	64 s		32 s		16 s		8 s		4 s		2 s	
MB1												
BSL	0.87	(0.2)	1.55	(1.4)	0.91	(0.2)	0.84	(0.3)	45.31	(70.1)	13.93	(29.5)
Saline	0.81	(0.0)	1.09	(0.0)	150.2	(148.5)	0.98	(0.2)	11.71	(11.0)	244.4	(239.9)
2.50	1.51	(0.9)	1.43	(0.4)	26.18	(24.1)	2.89	(1.6)	0.94	(0.0)	92.73	(91.2)
5.00	0.70	(0.0)	2.30	(0.2)	1.41	(0.1)	243.6	(241.2)	21.14	(20.0)	48.48	(46.8)
10.00	0.79	(0.1)	3.60	(2.5)	1.68	(0.3)	222.4	(221.8)	199.7	(198.5)	0.91	(0.1)
MB2												
BSL	1.27	(0.7)	1.12	(0.6)	0.85	(0.4)	0.76	(0.4)	0.68	(0.3)	102.7	(228.1)
Saline	0.98	(0.5)	0.82	(0.4)	0.47	(0.3)	0.68	(0.0)	0.66	(0.1)	0.90	(0.2)
2.50	0.50	(0.0)	0.43	(0.0)	0.99	(0.4)	0.69	(0.0)	0.44	(0.1)	0.81	(0.4)
5.00	1.48	(1.0)	0.95	(0.3)	0.35	(0.0)	0.52	(0.0)	0.63	(0.2)	1.02	(0.5)
10.00	1.25	(0.4)	1.77	(0.6)	0.63	(0.2)	1.38	(0.3)	0.75	(0.1)	0.89	(0.3)
MB3												
BSL	61.88	(95.9)	0.97	(0.5)	0.63	(0.1)	0.79	(0.2)	0.74	(0.2)	15.33	(25.8)
Saline	0.60	(0.2)	0.53	(0.0)	0.83	(0.3)	64.18	(63.4)	0.64	(0.1)	70.52	(69.7)
2.50	0.81	(0.3)	0.88	(0.4)	0.88	(0.6)	0.73	(0.2)	0.49	(0.0)	58.80	(58.3)
5.00	0.37	(0.0)	35.49	(35.0)	186.2	(185.7)	64.12	(63.5)	0.30	(0.3)	140.2*	(---)
10.00	99.22	(98.3)	6.34	(5.8)	11.24	(6.2)	1.20*	(---)	67.28*	(---)	10.06*	(---)
MB8												
BSL	0.57	(0.1)	1.16	(0.4)	2.46	(3.1)	1.41	(0.9)	6.15	(10.8)	12.37	(20.2)
Saline	58.56	(57.3)	109.6	(108.4)	2.31	(0.3)	0.41	(0.2)	14.41	(2.8)	0.50	(0.2)
2.50	0.63	(0.2)	1.07	(0.3)	6.87	(6.1)	5.10	(4.9)	1.02	(0.2)	479.6	(14.9)
5.00	58.34	(57.5)	109.7	(108.3)	1.67	(0.9)	0.25	(0.0)	9.01	(8.2)	247.6	(246.9)
10.00	160.7	(159.7)	1.34	(0.5)	199.7	(199.4)	1.87	(0.3)	5.47	(4.3)	0.17	(0.2)
MB9												
BSL	88.93	(60.9)	0.77	(0.1)	0.80	(0.1)	0.84	(0.2)	4.39	(7.4)	8.61	(16.7)
Saline	222.8	(30.9)	79.32	(73.1)	1.02	(0.5)	0.72	(0.1)	22.45	(20.8)	11.94	(11.2)
2.50	219.8	(19.9)	25.88	(24.9)	16.21	(15.1)	4.71	(3.5)	8.28	(7.0)	13.96	(12.7)
5.00	283.0	(60.7)	1.32	(0.6)	0.83	(0.4)	13.59	(12.7)	5.43	(2.0)	2.09	(1.3)
10.00	49.24	(43.7)	6.88	(5.7)	2.41	(1.5)	0.93	(0.3)	2.23	(1.4)	2.02	(0.9)
MB10												
BSL	0.39	(0.0)	0.66	(0.3)	0.91	(0.4)	2.40	(2.4)	0.81	(0.2)	0.71	(0.4)
Saline	0.70	(0.3)	0.84	(0.1)	1.51	(0.2)	0.75	(0.3)	1.33	(0.3)	2.05	(0.6)
2.50	0.47	(0.1)	1.57	(0.3)	0.84	(0.2)	1.48	(0.5)	1.24	(0.3)	1.01	(0.3)
5.00	0.73	(0.1)	0.98	(0.3)	1.27	(0.2)	2.20	(1.4)	2.11	(0.5)	1.95	(0.1)
10.00	0.73	(0.1)	0.98	(0.3)	3.51	(0.1)	2.04	(1.9)	4.02	(0.2)	2.87	(0.7)

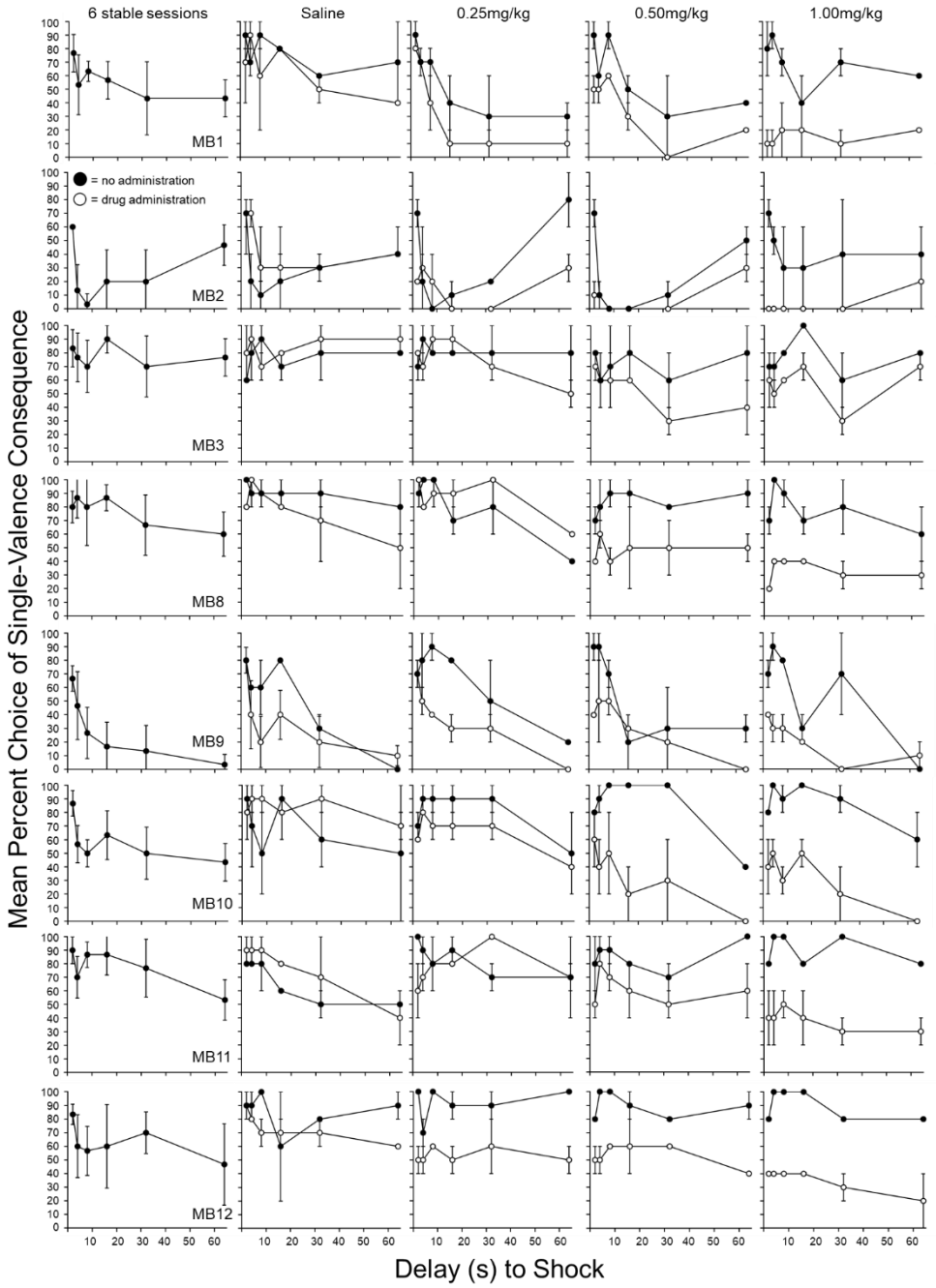
MB11												
BSL	0.80	(0.3)	1.17	(0.5)	2.68	(3.8)	0.66	(0.2)	1.09	(0.8)	4.09	(6.5)
Saline	164.4	(160.1)	2.11	(0.9)	66.42	(64.8)	31.56	(30.9)	0.95	(0.2)	0.55	(0.4)
2.50	197.5	(195.7)	0.61	(0.0)	2.00	(1.3)	0.93	(0.2)	0.72	(0.3)	0.57	(0.2)
5.00	1.42	(0.6)	109.0	(108.2)	0.67	(0.0)	19.05	(18.6)	1.89	(0.1)	41.07	(40.3)
10.00	116.8	(113.0)	1.26	(0.9)	68.42	(67.9)	2.56	(2.1)	0.26	(0.1)	1.53	(0.1)
MB12												
BSL	1.04	(0.5)	1.23	(0.3)	1.10	(0.4)	9.06	(16.9)	1.37	(0.9)	0.83	(0.3)
Saline	1.02	(0.5)	0.39	(0.0)	0.65	(0.2)	1.14	(0.3)	1.70	(1.3)	0.66	(0.4)
2.50	0.88	(0.1)	1.48	(0.9)	1.55	(0.2)	1.01	(0.2)	1.25	(0.9)	1.13	(0.1)
5.00	210.7	(209.5)	1.38	(0.8)	0.68	(0.2)	0.88	(0.6)	0.69	(0.3)	0.59	(0.3)
10.00	1.04	(0.4)	1.70	(0.1)	270.1	(268.5)	0.84*	(---)	247.4*	(---)	84.63*	(---)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three morphine doses. An asterisk represents mean latencies from only one session, due to an incomplete session. Dashes (---) indicate incomplete data at the specific delay and dose because of incomplete session(s). Numbers above 100 are expressed to one decimal place.

Figures

Figure 1

Patterns of Choice of the Single-Valence Consequence as a Function of the Delay to Shock in the Conflicting-Valence Consequence, arranged by Dose of Diazepam.

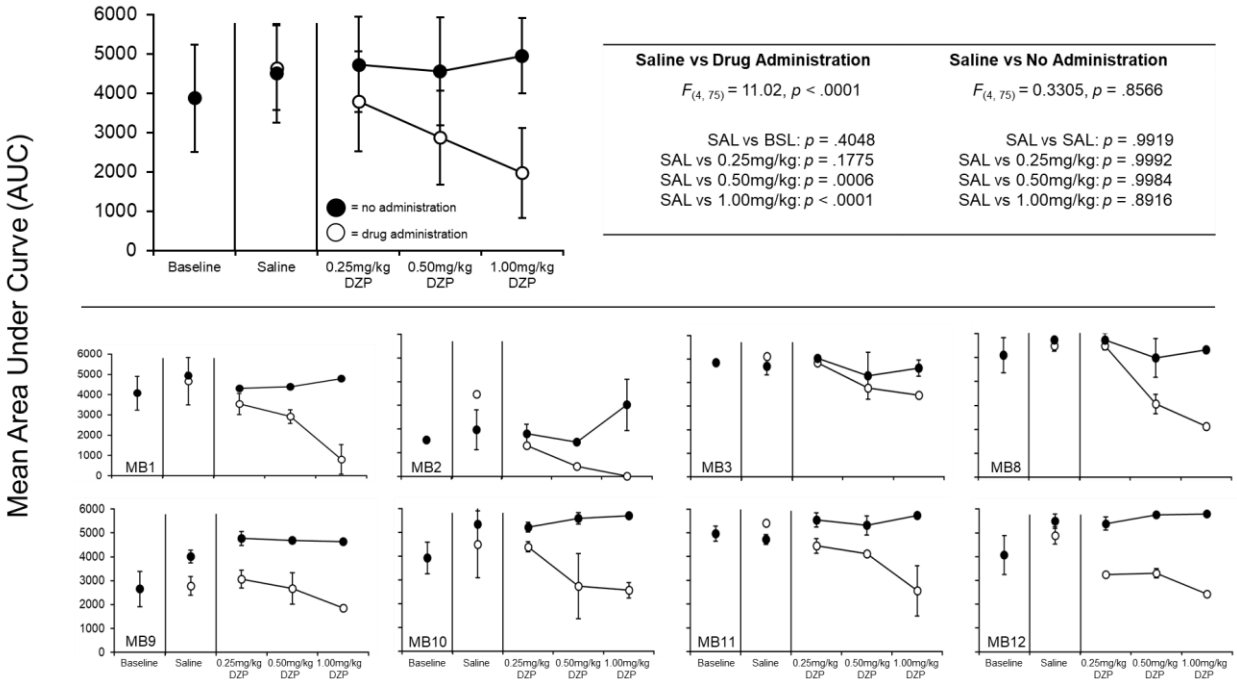


Note. Mean percent choice of the single-valence consequence as a function of the delay to shock in the conflicting-valence consequence. The leftmost column shows results from six stable baseline sessions for each rat, and the remaining columns show results from the two sessions

conducted after saline or diazepam administration (0.25, 0.50, or 1.00mg/kg; white symbols) or no-administration sessions (black symbols).

Figure 2

Mean Area Under Curve by Dose of Diazepam.

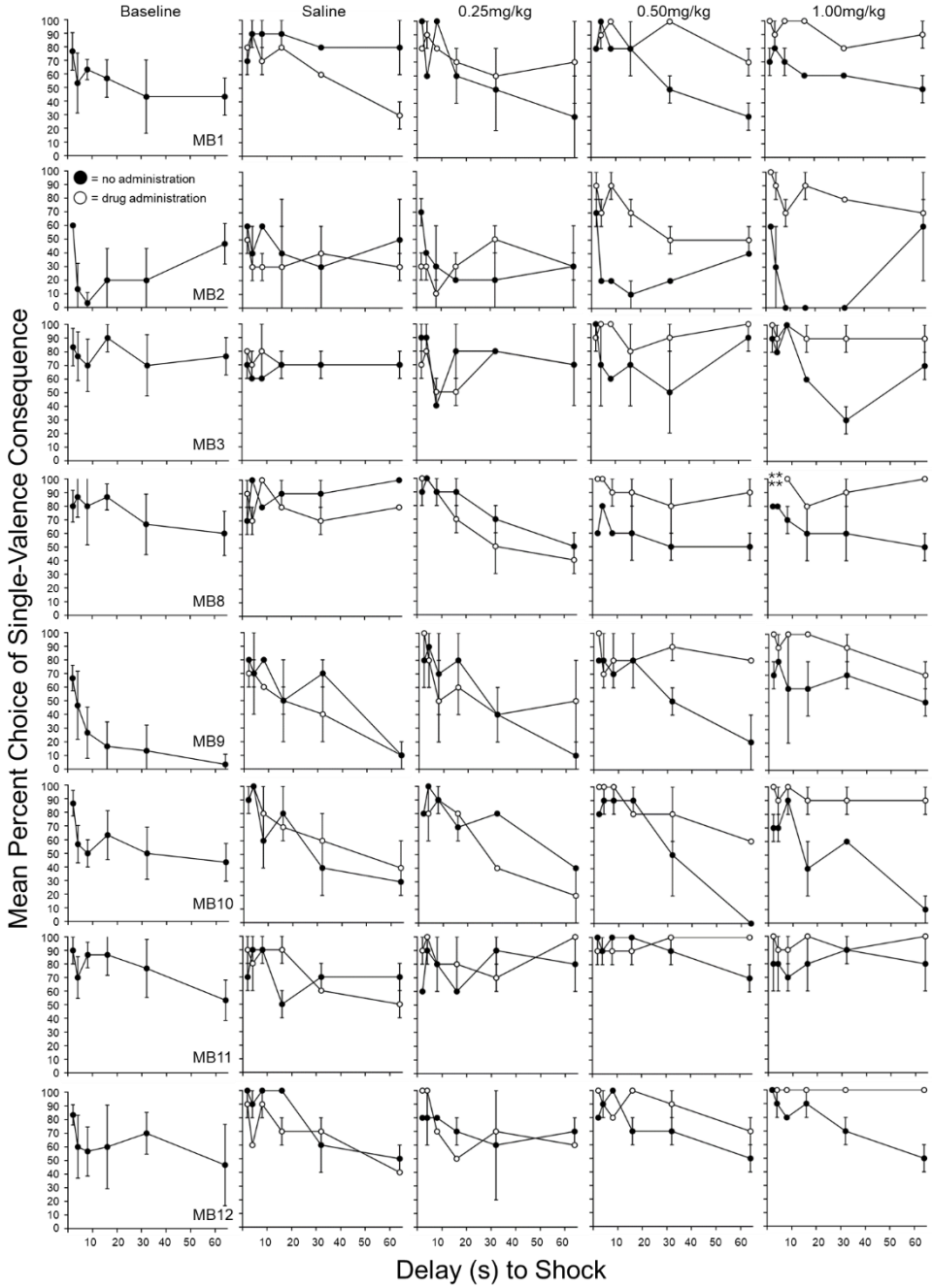


Saline vs Drug Administration	Saline vs No Administration
$F_{(4, 75)} = 11.02$, $p < .0001$	$F_{(4, 75)} = 0.3305$, $p = .8566$
SAL vs BSL: $p = .4048$	SAL vs SAL: $p = .9919$
SAL vs 0.25mg/kg: $p = .1775$	SAL vs 0.25mg/kg: $p = .9992$
SAL vs 0.50mg/kg: $p = .0006$	SAL vs 0.50mg/kg: $p = .9984$
SAL vs 1.00mg/kg: $p < .0001$	SAL vs 1.00mg/kg: $p = .8916$

Note. Mean area under the curve (AUC) across the six stable baseline sessions, the two sessions following administration of saline, and three doses of diazepam (0.25mg/kg, 0.50mg/kg, 1.00mg/kg), and the two no-administration sessions that preceded each administration. Error bars extend one standard deviation above and below each mean and were allowed to extend beyond the y-axis in one case (MB10, saline, 6160) to keep the y-axis used in the figures consistent. The table shows the results of the ANOVA that compares saline to drug administrations (left) and saline to days before drug administration (right).

Figure 3

Patterns of Choice of the Single-Valence Consequence as a Function of the Delay to Shock in the Conflicting-Valence Consequence, arranged by Dose of d-Amphetamine.

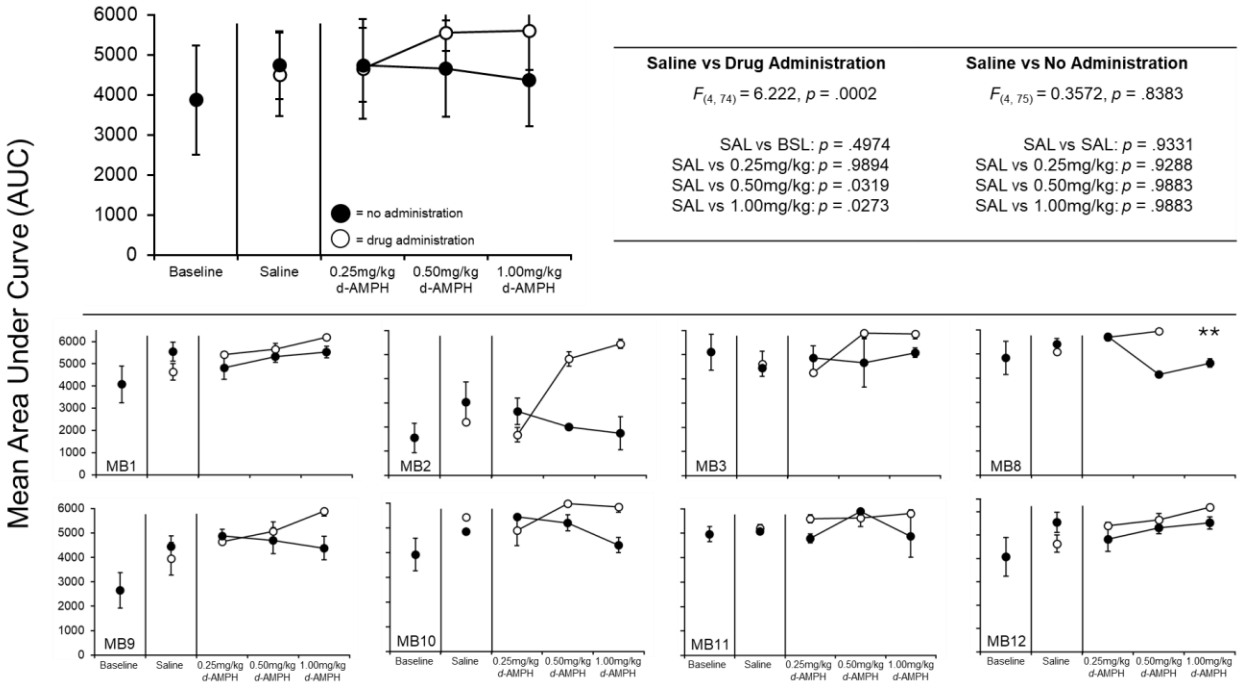


Note. Mean percent choice of the single-valence consequence as a function of the delay to shock in the conflicting-valence consequence. The leftmost column shows results from six stable baseline sessions for each rat, and the remaining columns show results from the two sessions

conducted after saline or *d*-amphetamine administration (0.25, 0.50, or 1.00mg/kg; white symbols) or no-administration sessions (black symbols). Asterisks indicate data are not available from one (*) or two (**) *d*-amphetamine sessions at a specific delay and dose.

Figure 4

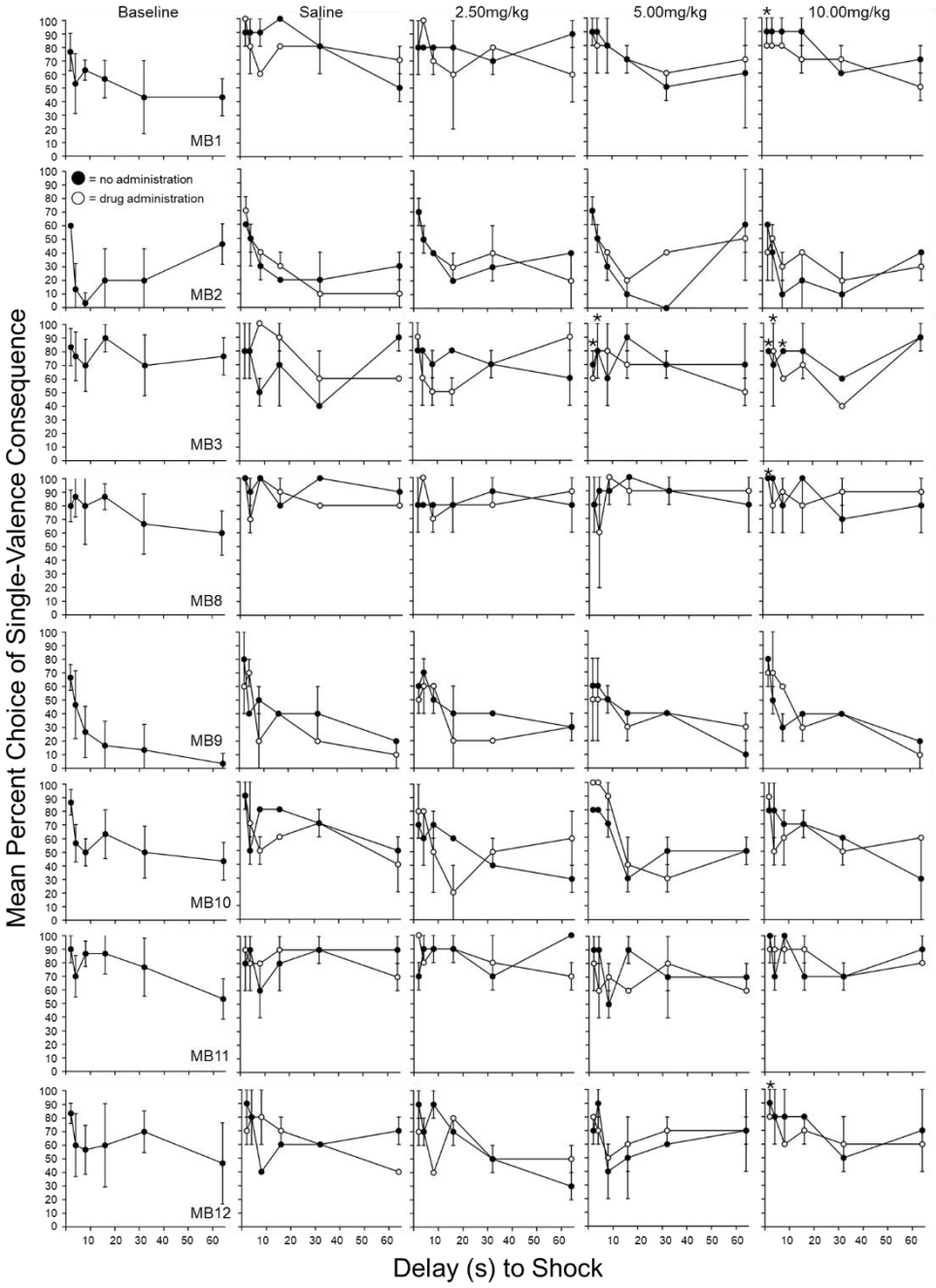
Mean Area Under Curve by Dose of d-Amphetamine.



Note. Mean area under the curve (AUC) across the six stable baseline sessions, the two sessions following administration of saline, and three doses of *d*-amphetamine (0.25mg/kg, 0.50mg/kg, 1.00mg/kg), and the two no-administration sessions that preceded each administration. Error bars extend one standard deviation above and below each mean. Asterisks indicate that one (*) or two (**) sessions were not completed for a rat at a drug dose. AUCs from incomplete sessions were omitted from statistical comparisons.

Figure 5

Patterns of Choice of the Single-Valence Consequence as a Function of the Delay to Shock in the Conflicting-Valence Consequence, arranged by Dose of Morphine.

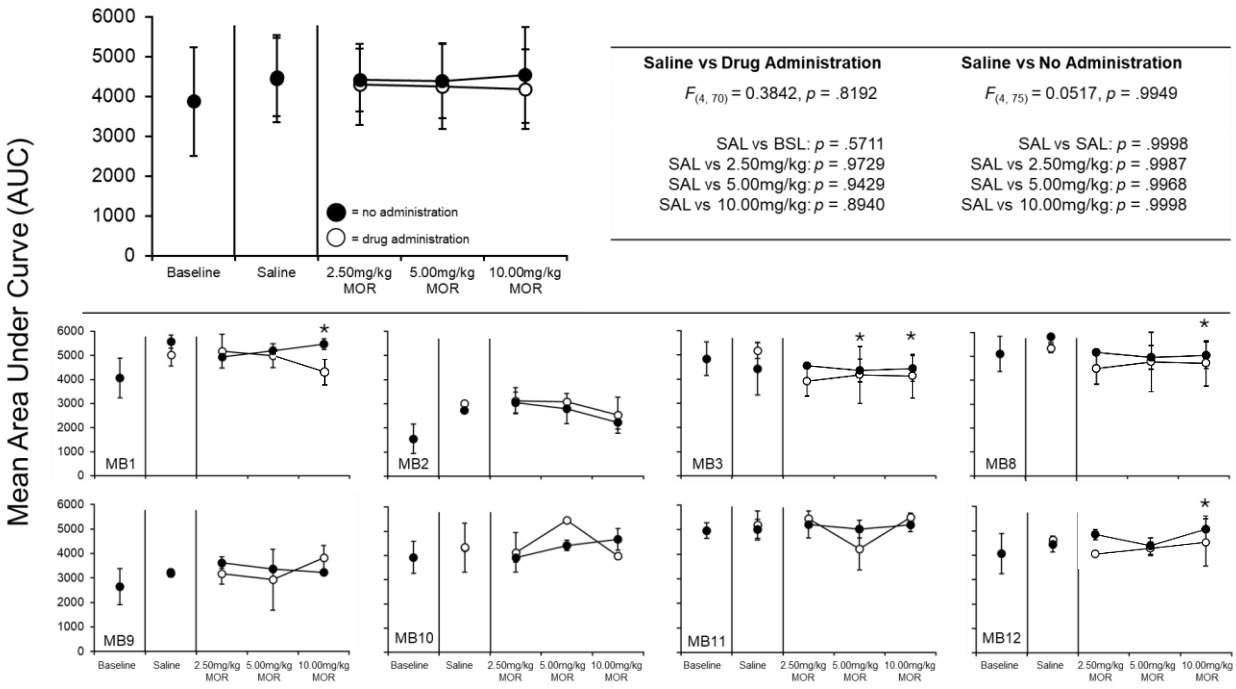


Note. Mean percent choice of the single-valence consequence as a function of the delay to shock in the conflicting-valence consequence. The leftmost column shows results from six stable baseline sessions for each rat, and the remaining columns show results from the two sessions

conducted after saline or morphine administration (2.50, 5.00, or 10.00mg/kg; white symbols) or no-administration sessions (black symbols). Asterisks indicate data are not available from one (*) or two (**) morphine sessions at a specific delay and dose.

Figure 6

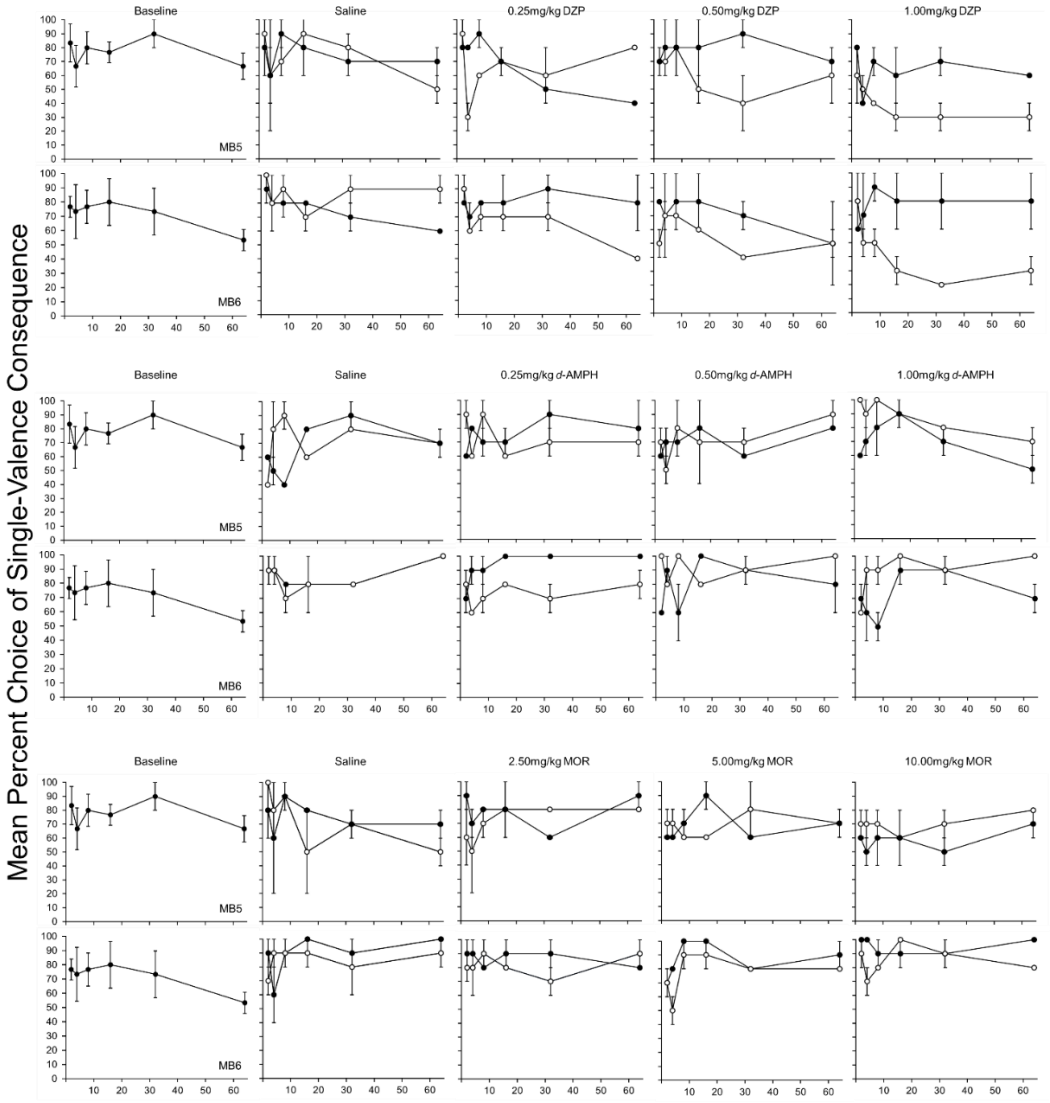
Mean Area Under Curve by Dose of Morphine.



Note. Mean area under the curve (AUC) across the six stable baseline sessions, the two sessions following administration of saline, and three doses of morphine (2.50mg/kg, 5.00mg/kg, 10.00mg/kg), and the two no-administration sessions that preceded each administration. Error bars extend one standard deviation above and below each mean. Asterisks indicate that one (*) or two (**) sessions were not completed for a rat at a drug dose. AUCs from incomplete sessions were omitted from statistical comparisons.

APPENDIX A

CHOICE PATTERNS AS A FUNCTION OF THE DELAY TO SHOCK IN THE CONFLICTING-VALENCE CONSEQUENCE, ARRANGED BY DOSE OF DIAZEPAM, D-AMPHETAMINE, AND MORPHINE



Note. Mean percent choice of the single-valence consequence as a function of the delay to shock in the conflicting-valence consequence. The leftmost column shows results from six stable baseline sessions for each rat, and the remaining columns show results from the two sessions conducted after saline or drug administration (white symbols) or no-administration sessions (black symbols). 2.00mg/kg of *d*-amphetamine was also administered but was not further considered for the study and therefore not included in this figure. 1.25mg/kg of morphine was also administered but was not further considered for the study and therefore not included in this figure.

APPENDIX B

MEAN LATENCIES ACROSS VARYING DIAZEPAM, D-AMPHETAMINE, AND MORPHINE DOSES ON SAMPLE SINGLE-VALENCE CONSEQUENCE

	Sample Single-Valence Consequence Latency (s)											
Rat	64		32		16		8		4		2	
Diazepam												
MB5												
BSL	0.66	(0.27)	0.92	(0.44)	0.63	(0.18)	0.63	(0.23)	0.66	(0.20)	0.59	(0.14)
Saline	0.45	(0.02)	0.81	(0.20)	0.55	(0.02)	0.61	(0.08)	0.42	(0.06)	0.56	(0.04)
0.25	0.55	(0.01)	0.62	(0.10)	0.58	(0.25)	0.58	(0.28)	0.89	(0.53)	0.44	(0.06)
0.50	0.56	(0.05)	1.17	(0.28)	0.46	(0.18)	0.75	(0.30)	0.77	(0.03)	0.62	(0.10)
1.00	0.66	(0.06)	0.70	(0.06)	0.48	(0.04)	0.52	(0.09)	0.51	(0.20)	0.58	(0.14)
MB6												
BSL	1.03	(0.29)	0.85	(0.21)	0.83	(0.27)	0.86	(0.15)	0.80	(0.15)	1.00	(0.15)
Saline	1.30	(0.27)	0.97	(0.06)	0.72	(0.08)	0.50	(0.02)	0.83	(0.19)	0.72	(0.19)
0.25	1.09	(0.09)	0.86	(0.25)	0.70	(0.02)	0.67	(0.02)	0.64	(0.08)	1.21	(0.30)
0.50	1.43	(0.43)	0.92	(0.23)	0.83	(0.06)	0.95	(0.36)	0.88	(0.14)	0.69	(0.05)
1.00	1.41	(0.34)	1.40	(0.43)	1.09	(0.07)	1.14	(0.50)	0.91	(0.20)	0.99	(0.27)
d-Amphetamine												
MB5												
BSL	0.66	(0.27)	0.92	(0.44)	0.63	(0.18)	0.63	(0.23)	0.66	(0.20)	0.59	(0.14)
Saline	0.53	(0.17)	0.52	(0.09)	0.59	(0.02)	0.46	(0.15)	0.84	(0.12)	0.77	(0.07)
0.25	0.60	(0.02)	1.12	(0.08)	0.61	(0.03)	0.77	(0.03)	0.69	(0.04)	0.79	(0.06)
0.50	0.43	(0.04)	0.76	(0.35)	0.74	(0.24)	0.48	(0.10)	0.69	(0.09)	0.60	(0.18)
1.00	0.51	(0.05)	0.75	(0.36)	0.88	(0.37)	0.73	(0.03)	0.97	(0.27)	0.76	(0.12)
MB6												
BSL	1.03	(0.29)	0.85	(0.21)	0.83	(0.27)	0.86	(0.15)	0.80	(0.15)	1.00	(0.15)

Saline	1.81	(0.53)	0.61	(0.11)	0.74	(0.07)	0.77	(0.02)	0.67	(0.14)	0.85	(0.18)
0.25	1.14	(0.11)	0.83	(0.02)	0.69	(0.06)	1.03	(0.14)	0.49	(0.01)	0.58	(0.08)
0.50	1.14	(0.08)	0.70	(0.03)	0.87	(0.23)	0.88	(0.16)	3.02	(2.49)	2.98	(0.64)
1.00	1.66	(0.10)	0.99	(0.07)	0.94	(0.27)	2.33	(0.38)	0.87	(0.06)	0.85	(0.15)
Morphine												
MB5												
BSL	0.66	(0.27)	0.92	(0.44)	0.63	(0.18)	0.63	(0.23)	0.66	(0.20)	0.59	(0.14)
Saline	0.65	(0.09)	0.74	(0.02)	0.62	(0.01)	0.81	(0.06)	0.81	(0.20)	0.70	(0.40)
2.50	0.82	(0.21)	0.33	(0.02)	0.51	(0.15)	0.58	(0.20)	0.55	(0.10)	0.70	(0.30)
5.00	0.73	(0.02)	1.16	(0.44)	0.47	(0.05)	0.98	(0.58)	2.18	(1.76)	0.55	(0.28)
10.00	0.79	(0.10)	147.01	(145.46)	1.22	(0.64)	0.79	(0.45)	100.84	(100.09)	1.29	(0.51)
MB6												
BSL	1.03	(0.29)	0.85	(0.21)	0.83	(0.27)	0.86	(0.15)	0.80	(0.15)	1.00	(0.15)
Saline	1.45	(0.16)	0.70	(0.09)	0.70	(0.02)	0.96	(0.06)	0.84	(0.17)	0.70	(0.03)
2.50	0.99	(0.01)	0.86	(0.44)	1.13	(0.50)	1.00	(0.27)	1.59	(1.12)	0.59	(0.02)
5.00	1.31	(0.11)	0.84	(0.01)	1.03	(0.13)	0.69	(0.01)	1.11	(0.20)	0.56	(0.13)
10.00	1.20	(0.22)	1.09	(0.26)	32.57	(26.87)	0.76	(0.04)	156.19	(68.55)	138.83	(49.23)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three doses each for diazepam, *d*-amphetamine, and morphine.

APPENDIX C

MEAN LATENCIES ACROSS VARYING DIAZEPAM, D-AMPHETAMINE, AND MORPHINE DOSES ON SAMPLE CONFLICTING-VALENCE CONSEQUENCE

	Sample Conflicting-Valence Consequence Latency (s)											
Rat	64		32		16		8		4		2	
Diazepam												
MB5												
BSL	0.48	(0.14)	1.64	(0.55)	1.38	(0.46)	1.11	(0.36)	0.85	(0.21)	31.52	(29.04)
Saline	0.77	(0.24)	1.49	(0.12)	1.84	(0.20)	1.53	(0.63)	0.96	(0.35)	94.29	(93.26)
0.25	0.86	(0.00)	0.97	(0.42)	1.13	(0.36)	0.76	(0.32)	0.84	(0.08)	0.76	(0.07)
0.50	0.63	(0.27)	1.02	(0.39)	1.27	(0.28)	1.90	(0.01)	0.84	(0.11)	1.24	(0.54)
1.00	1.16	(0.34)	1.10	(0.07)	1.35	(0.84)	0.74	(0.09)	0.94	(0.25)	12.66	(12.00)
MB6												
BSL	28.31	(21.32)	5.33	(4.30)	1.64	(0.94)	12.22	(25.32)	4.71	(4.66)	0.79	(0.41)
Saline	3.20	(2.38)	2.13	(1.45)	0.86	(0.11)	22.13	(19.45)	27.16	(25.91)	33.90	(31.24)
0.25	1.17	(0.02)	0.81	(0.16)	3.53	(3.05)	1.46	(0.81)	0.60	(0.15)	4.65	(4.27)
0.50	1.75	(0.19)	2.15	(1.04)	67.76	(66.01)	1.00	(0.42)	19.38	(18.77)	0.71	(0.02)
1.00	3.70	(0.06)	0.58	(0.08)	0.92	(0.28)	1.93	(0.38)	1.60	(0.31)	1.16	(0.05)
d-Amphetamine												
MB5												
BSL	0.48	(0.14)	1.64	(0.55)	1.38	(0.46)	1.11	(0.36)	0.85	(0.21)	31.52	(29.04)
Saline	0.54	(0.10)	1.25	(0.02)	1.03	(0.42)	1.32	(0.51)	0.90	(0.29)	0.79	(0.01)
0.25	0.72	(0.07)	1.62	(0.48)	2.17	(1.27)	0.78	(0.23)	0.58	(0.20)	1.41	(0.33)
0.50	0.69	(0.05)	2.37	(0.60)	39.07	(36.74)	1.20	(0.49)	0.66	(0.27)	1.06	(0.60)
1.00	0.50	(0.02)	46.64	(45.78)	50.05	(48.50)	34.60	(34.05)	0.73	(0.01)	0.52	(0.20)
MB6												
BSL	28.31	(21.32)	5.33	(4.30)	1.64	(0.94)	12.22	(25.32)	4.71	(4.66)	0.79	(0.41)

Saline	1.62	(0.15)	1.95	(0.78)	0.52	(0.02)	7.41	(6.53)	3.38	(2.04)	1.44	(0.44)
0.25	0.90	(0.07)	1.11	(0.08)	2.59	(0.52)	2.48	(0.06)	0.98	(0.02)	1.42	(0.11)
0.50	32.45	(30.20)	0.94	(0.61)	2.42	(0.72)	58.32	(057.74)	2.91	(1.24)	39.02	(38.59)
1.00	1.78	(0.52)	2.95	(0.30)	3.47	(2.11)	42.65	(41.27)	1.64	(0.22)	1.14	(0.55)
Morphine												
MB5												
BSL	0.48	(0.14)	1.64	(0.55)	1.38	(0.46)	1.11	(0.36)	0.85	(0.21)	31.52	(29.04)
Saline	0.81	(0.06)	1.03	(0.03)	1.13	(0.12)	1.13	(0.16)	9.83	(7.74)	0.99	(0.15)
2.50	0.82	(0.21)	0.33	(0.02)	0.51	(0.15)	0.58	(0.20)	0.55	(0.10)	0.70	(0.30)
5.00	0.73	(0.02)	1.16	(0.44)	0.47	(0.05)	0.98	(0.58)	2.18	(1.76)	0.55	(0.28)
10.00	0.79	(0.10)	147.01	(145.46)	1.22	(0.64)	0.79	(0.45)	100.84	(100.09)	1.29	(0.51)
MB6												
BSL	28.31	(21.32)	5.33	(4.30)	1.64	(0.94)	12.22	(25.32)	4.71	(4.66)	0.79	(0.41)
Saline	1.98	(0.81)	1.88	(0.29)	1.36	(0.11)	1.52	(0.68)	0.96	(0.40)	2.55	(1.68)
2.50	2.09	(0.81)	1.66	(1.14)	1.25	(0.11)	2.58	(1.63)	0.88	(0.09)	1.15	(0.68)
5.00	3.24	(1.98)	1.60	(0.26)	0.90	(0.54)	1.22	(0.09)	1.50	(0.88)	1.16	(0.05)
10.00	79.80	(28.04)	1.11	(0.09)	0.88	(0.19)	0.96	(0.34)	0.81	(0.09)	1.49	(0.90)

Note. Mean latencies and standard deviations on the sample single-valence consequence across baseline, saline, and the three doses each of diazepam, *d*-amphetamine, and morphine.

APPENDIX D

IACUC APPROVAL FORM

Application to Use Vertebrate Animals in Research, Testing or Instruction

NORTHERN MICHIGAN UNIVERSITY

Project Title (If using external funds, enter the title used on the grant application): Evaluating Drug Effects on Self-Controlled Choice in Rats

Shaded area for IACUC use only.

Application Number: 439 Modification
Date Application Received: 7/14/2023
☒Approved ☐ Denied on July 24, 2023

General Instructions
Please check the IACUC website to ensure you are using the current version of the form. All parts of this form *must be submitted electronically* to the Institutional Animal Care and Use Committee (email: IACUC@nmu.edu) and the relevant Department Head or other departmental designee. Review of this application will commence upon receiving the electronic application, but the project may not begin until all required approval signatures are obtained via Right Signature. Please contact the IACUC chair (email: IACUCChr@nmu.edu) if you have any questions.

Review Dates:
Designated Member Review of applications (appropriate for USDA Use Categories B and C) will be completed within two weeks after receipt of the electronic application.

Full Committee Review of applications will take place on the last Friday of every month. Applications for Full Committee Review must be electronically received by the first Friday of the month. Full Committee Review is required for applications that fall under USDA Use Categories D and E. Applications that fall under USDA Use Categories B and C will receive Full Committee Review if requested by an IACUC member. Detailed procedures on the IACUC review processes are located at the IACUC website.

I. Principal Investigator (Must be a faculty member or Department Head): Cory Toegel

Co- Investigator: Forrest Toegel, Adam Prus, Mackenzie Baranski

Department: Psychological Science

Phone number: 906-227-2982

II. Funding Sources/Course Information and Dates

If the proposed work is for a course, please include the number of the course and title of the course
N/A

Funding Sources (External & Internal, if applicable) Internal
Additional Funding Pending (click on the correct box)? ☐Yes ☒No

Project/Course Start Date: March 9, 2023
End Date (three year maximum): March 8, 2026

This application is (check one) ☐New ☒ Modification of an application currently approved by the Institutional Animal Care and Use Committee (a **new** protocol must be submitted after three years)