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Effects of Oxycodone and Methylphenidate on Self-Control with Aversive Outcomes

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ABSTRACT

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In the context of choice, one is said to show self-control under numerous conditions in which consideration is given to the delayed outcomes of each option. This can be difficult: both reinforcing and aversive outcomes become less effective as they are increasingly delayed. Several socially significant issues arise from a failure of delayed, aversive outcomes to impact choice, especially when immediate, reinforcing outcomes are available. Identifying the conditions under which choice is sensitive to delayed outcomes is critical to shifting choices toward alternatives in which contact with delayed, aversive outcomes is minimized. Two experiments were conducted with the aim of charactering how preference for an outcome that includes immediate reinforcement and a delayed, aversive outcome changes as a function of the delay to the aversive outcome. In Experiment 1 a discrete-trial choice procedure was used. Rats chose, by pressing one of two levers, between two outcomes: a small reinforcer alone and a large reinforcer plus a delayed shock. The delay to shock was lowered each session and changes in choice were measured. Rats preferred the lever that produced the large reinforcer plus shock when the delay to shock was long; however, preference switched to the small reinforcer alone as the delay to shock was lowered each session. Acute effects of oxycodone and methylphenidate were assessed on this behavioral baseline. Oxycodone's effects on choice depended on the dose: low doses produced a slight, and inconsistent, increase in choice of the large reinforcer plus shock and high doses produced a slight increase in choice the small reinforcer. Methylphenidate typically increased choice of the small reinforcer. In Experiment 2 a concurrent-chains procedure was used. Rats chose between two outcomes, both of which included a reinforcer and a delayed shock. Each outcome differed, however, in the relative delay to shock: one delay was short and the other was long. The relative delays to shock arranged as an outcome for pressing each lever was changed either within or across sessions. Choice was not sensitive to changes in the relative delays to shock: rats chose the levers that produced the short and long delays to shock equally. Neither oxycodone nor methylphenidate produced dose-related changes in sensitivity to delayed shock at a dose, or doses, that did produce general disruption of behavior. Difficulties of studying drug effects on self-control with aversive events are discussed.

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Effects of Oxycodone and Methylphenidate on Self-Control with Aversive Outcomes

The study of choice represents an interesting and complex area of psychology. Humans have the opportunity to engage in numerous responses at any point; even a rat in a relatively barren operant-conditioning chamber can choose between sniffing, grooming, or lever pressing. Behavior analysts have studied choice by measuring how the allocation of behavior changes as a function of different outcomes (Mazur, 2013; Pierce & Cheney, 2008, p. 193). In simple choice situations, in which outcomes only vary along one dimension, this is a relatively easy task. When choosing between outcomes that are reinforcing, humans (and nonhuman animals, hereafter "animals") generally prefer outcomes that are larger, sooner, and certain (rather than smaller, later, or uncertain). The inverse is generally true for punishment; punishers that are smaller, later, and less certain are generally preferred (see Hineline & Rosales-Ruiz, 2013; *cf.* Badia et al., 1973). Such simple comparisons, although important, bear little resemblance to the choices that underlie a number of socially significant issues. Rather, choices that involve a tradeoff between multiple dimensions of the outcomes (e.g., amount, delay, or probability) make for a more interesting, and complex, analysis. One area in which this approach has been applied is the study of *self-control*.

Although self-control has been operationalized several different ways, it most often involves a tradeoff between amounts of, and delays to, reinforcement (Ainslie, 1974; Logue, 1988, Monterosso & Ainslie, 1999; Rachlin, 1974). For example, a child who chooses a smaller, sooner reinforcer (e.g., pretzels now) rather than a larger, later reinforcer (e.g., cookies later) may be said to have made an *impulsive choice* (Mischel & Ebbesen, 1970). Conversely, a child able to delay gratification and wait for the larger, later reinforcer may be said to show *self-*

control. Choice for the larger, later reinforcer maximizes reinforcement but requires the child to wait for its receipt.

The smaller, sooner versus larger, later model of self-control has proven to be invaluable for characterizing how choice changes as a function of the delay to reinforcement in studies with both humans (e.g., Rachlin et al., 1991; see Reynolds, 2006 for a review) and animals (e.g., Mazur, 1987). Across species, the findings have been relatively consistent: the efficacy of a stimulus as a reinforcer declines as a function of its delay, a relation described as *delay discounting* (Madden & Johnson, 2010). This relation is well described by a hyperbolic equation (Mazur, 1987):

$$V = A/(1 + kD), \quad (1)$$

in which V (value) represents the reinforcing efficacy of an outcome, *A* represents the absolute amount of reinforcement, and *D* represents the delay to reinforcement. The parameter *k* reflects the steepness of the function and has been used as a quantitative description of sensitivity to delay (Madden & Johnson, 2010; Odum, 2011). Figure 1 displays two hypothetical discounting functions that relate the value of an outcome to its delay. Both functions decrease as a function of delay; however, the dashed function, labeled "Impulsive," declines more rapidly in value as delay increases. Alternatively, the solid function, labeled "Self-Control," shows a slower decline in value as a function of delay. The terms "self-control" and "impulsive" provide relative descriptions of sensitivity to reinforcement delay, and although there is no *k* cutoff for impulsivity, research with humans has shown that higher *k* values (obtained by asking participants to make a series of choices between hypothetical, monetary outcomes; e.g., Rachlin et al., 1991) are associated with behavior typically considered more impulsive, such as illicit substance use (Coffey et al., 2003; Madden et al., 1997; Kirby & Petry, 2004), cigarette smoking

(Bickel et al., 1999; Johnson et al., 2007; Reynolds et al., 2007), and binge eating (Manwarring et al., 2011).

The present experiments were designed to expand the study of delay discounting. I will begin by describing some procedures commonly used to study self-control with animals. Next, some gaps in the literature will be identified. Of particular interest is that common conceptualizations of self-control, and procedures used to study it, fail to incorporate aversive outcomes. Third, drug effects on self-control will be briefly reviewed, with an emphasis on the behavioral effects of the prescription drugs oxycodone (a narcotic prescribed for pain relief) and methylphenidate (a stimulant prescribed for attention-deficit/hyperactivity disorder). Finally, the procedures and results of two experiments that were conducted will be reported and discussed.

Procedures for Studying Self-Control

Procedures to study self-control share several common elements. First, a subject (typically a rat or pigeon) is placed in a chamber with two concurrently available response options (e.g., levers or keys) that can be operated to produce different outcomes. For example, a rat may press the left lever to produce one food pellet and press the right lever to produce four food pellets. Second, the subject chooses between the outcomes associated with each alternative by satisfying some schedule. The most commonly used schedule is a fixed ratio (FR) 1, in which a single response is required. Another commonly used schedule, the variable-interval (VI) schedule, produces the outcome contingent on the first response after a variable period of time. Third, each session incorporates two types of trials. In *forced-choice trials*, only one response option is available at a time to ensure exposure to the arranged outcomes. In *free-choice trials*, both response options are concurrently available, and the subject can freely respond on either. Fourth, the time between the start of each trial is held constant by an adjusting intertrial interval:

after delivery of a reinforcer on one trial, a period in which subsequent choices cannot be made must elapse before the next trial begins. If the time between trials is not held constant, repeated choice of the smaller, sooner reinforcer could result in a greater reinforcement rate than would be available for the larger, later reinforcer, because of its delay. Thus, the intertrial interval ensures that choice of the larger, later reinforcer maximizes reinforcement over the course of the session.

Adjusting-Delay Procedure

An adjusting-delay procedure for studying self-control was developed by Mazur (1987). Pigeons chose between a relatively small reinforcer (e.g., 2-s access to grain) after some fixed delay and a relatively large reinforcer (e.g., 6-s access to grain) after a delay that was adjusted based on the pigeons' choices. Across blocks of trials, repeated choice of the large reinforcer raised its delay, whereas repeated choice of the small reinforcer lowered the delay to the large reinforcer. The delay to the large reinforcer was titrated across blocks of trials in this manner until an indifference point was found, in which both options were chosen an approximately equal number of times. Indifference points provide a measure of the value of delayed reinforcers relative to (more) immediate alternatives. Mazur plotted the indifference points from a series of conditions, in which the fixed delay to the small reinforcer was manipulated. The resulting function was well described by Equation 1.Generating a discounting function with the adjusting-delay procedure can require a considerable number of sessions.

Within-Session Escalating Delay Procedure

A more efficient procedure for studying delay discounting was developed by Evenden and Ryan (1996). Choice is measured between outcomes that change within each session; this approach is marked by its efficiency because Equation 1 can be fit to the data collected in a single session, rather than across conditions. Evenden and Ryan arranged for rats to choose (FR

1) between a smaller, sooner reinforcer (one food pellet delivered immediately) and a larger, later reinforcer (five food pellets after a delay). The delay to the large reinforcer was raised across blocks of trials within each session (0, 10, 20, 40, and 60 s). Each block consisted of two forced-choice trials, one for each outcome, and eight to 12 free-choice trials in which the rat could respond on either lever. The primary dependent measure was the percentage of free-choice trials in which the large reinforcer was chosen each block. Across blocks, choice of the large reinforcer systematically decreased as its delay was raised. This within-session procedure has become the procedure of choice for studying effects of numerous manipulations on delay discounting, including drugs (e.g., Anderson & Woolverton, 2005; Cardinal et al., 2000; Eppolito et al., 2013; Pitts & McKinney, 2005) and behavioral interventions (e.g., delay-exposure training; Fox et al., 2019; Renda et al., 2020; Smith et al., 2015).

Concurrent-Chains Procedures

Although the concurrent-chains procedure was originally developed to study delayed reinforcement (Autor, 1969; see also, Chung & Herrnstein, 1964), it has since been used to study choice as a function of various dimensions of reinforcement, including frequency, delay, magnitude, and probability in isolation (Fantino, 1969; Grace et al., 2003; Herrnstein, 1964; Ito & Asaki, 1982; Orduña et al. 2013; Rodewald et al., 2010; Yates et al., 2020) or in combination (Kyonka & Grace, 2008; Orduña, 2015; Pitts & Febbo, 2004). The subject must complete a chain of responses to receive the reinforcer. In the initial link of the chain, or choice link, the subject can respond freely across two alternatives; the first response after a VI schedule elapses grants entry into the terminal link corresponding with the chosen alternative. In the terminal link, or outcomes link, the subject must respond to satisfy another schedule, after which the primary reinforcer is delivered.

The advantage of requiring multiple responses in the initial link is that changes in choice can be scaled more precisely (de Villiers, 1977; Herrnstein, 1961; Perone, 1991). Because a relatively large sample of behavior is collected in a VI schedule, more subtle, but systematic, changes in response allocation can be detected across parametric manipulation of the independent variable (e.g., reinforcement delay). Conversely, when an FR 1 is used, the scaling of choice depends on the number of trials per block (i.e., if there are 10 blocks, a 10% change in percent choice is accounted for by a single response). The primary dependent measure on concurrent-chains procedures is the ratio of responses in the initial link, calculated as the number of initial link responses on the left lever divided by the number of responses on the right lever. Indeed, initial-link response ratios have been shown to closely correspond to the reinforcement ratios in the terminal links, a relation initially described as the matching law by Herrnstein (1961; see also Baum & Rachlin, 1969; Davison & McCarthy, 1988; Staddon, 1968; Grace, 1994; McDowell, 1988). Equation 2 shows the simplest version of the matching law (or *strict matching*):

$$B_1/B_2 = R_1/R_2. \quad (2)$$

Here the ratio of two different responses (B_1/B_2) is directly proportional to the ratio of reinforcement (R_1/R_2) available as consequences for those responses. The matching law has been observed across multiple species and dimensions of reinforcement; however, the fit of the matching relation to the data of individual subjects can be improved by adding two parameters to account for regular deviations from strict matching. The generalized form of the matching law (see Baum, 1974) is often expressed as a linear function:

$$\text{Log}(B_1/B_2) = a\text{Log}(R_1/R_2) + \text{Log}b, \quad (3)$$

in which B_1/B_2 and R_1/R_2 are the ratios of behavior and reinforcement in each alternative. The parameter *a* is the slope of the line and is generally understood as a measure of *sensitivity* to differences in the reinforcing value of the terminal links. The parameter *b* is the y-intercept, and measures bias for an alternative (e.g., a rat may have a bias for the left lever, even when the left and right levers produce the same outcome).

Only a few studies have used concurrent-chains procedures to study self-control. For example, Pitts and Febbo (2004) arranged a concurrent-chains procedure in which choice in the initial link granted access to one of two, mutually exclusive terminal links, which differed in terms of the amount and delay of reinforcement. In one terminal link, a small reinforcer (2-s access to food) was always delayed by 2 s. In the other terminal link, a large reinforcer (4-s access to food) was delivered after a 2, 10, 20, 30, or 40 s; the delay to the large reinforcer was raised across blocks, within a session. Thus, pigeons chose between smaller, soon and larger, later outcomes. Within each session, the ratio of responses for each alternative (large/small) in the initial link decreased as the delay to the large reinforcer was raised. Changes in response ratios for all five pigeons were well described by a version of Eq. 3, in which the reciprocal ratio of delays, or immediacy ratio ($^{1/Delay}/_{1/Delay}$), substituted for the reinforcement term (R_1/R_2). Despite the utility of applying the matching framework to the study of self-control, very few researchers have taken this approach (Oliveira et al., 2014; Orduña, 2015).

Self-Control Involving Aversive Outcomes

The procedures described above have proven useful for studying choice between smaller, sooner and larger, later reinforcers; however, other conceptualizations of self-control are worth considering. Notably, when Skinner (1953) referred to self-control, it was in the context of a choice that resulted in two outcomes: short-term reinforcement and delayed aversive

outcomes[1](1953, pp. 230-231). For example, consumption of alcohol may leave one feeling euphoric, confident, or relaxed in the short-term, but hungover or ill the following day. Skinner suggested that, in such a case, self-control occurred when responses were made to mitigate contact with the aversive outcomes, such as declining offers to go out drinking, committing to being the designated driver (and abstaining from the consumption of alcohol), or only bringing enough money to purchase one drink.

Other researchers have considered that self-control with aversive outcomes can be treated as the inverse of self-control with reinforcement (e.g., Logue, 1988, Monterosso & Ainslie, 1999). For example, Rachlin (1974) suggested that self-control can be shown by selecting a smaller, sooner aversive outcome rather than a larger, later one. In his example, if someone has a toothache, visiting the dentist may result in a relatively immediate, aversive experience (e.g., the cost and pain of getting a filling), and ignoring the toothache may result in a delayed, but much more aversive experience (e.g., the cost and pain of getting a root canal; loss of the tooth). An individual shows self-control by choosing the option that minimizes overall contact with aversive outcomes. Showing the kinds of self-control described by Skinner (1953) and Rachlin both require that delayed, aversive outcomes affect choice. In practice, this is difficult, because aversive outcomes (much like reinforcers) become less effective (i.e., discount) as they are increasingly delayed (Mischel et al. 1969). Thus, identifying conditions under which choice is, and is not, sensitivity to delayed aversive outcomes is critical for addressing issues related to

[1] Aversive outcomes are defined as stimuli that can function as punishers. However, when sufficiently delayed, these outcomes may no longer function as punishing stimuli. For ease of exposition, stimuli that have been shown to function aversively when presented immediately (e.g., electric shock) will be referred to as aversive outcomes.

self-control; however, self-control with aversive events has failed to generate much experimental research.

The neglect of this area of research is surprising; many socially significant issues are characterized by insensitivity to delayed aversive outcomes. For example, several of the diagnostic criteria for Opioid Use Disorder relate to continued opioid use (a short-term reinforcer) despite concomitant aversive outcomes (e.g., loss of employment, failure at school, interpersonal problems; American Psychological Association, 2013, p. 541). Excessive consumption of unhealthy foods can be tempting despite the potential for weight gain or risk of heart disease. Common among these examples is that the delayed aversive outcomes of choices do not function as effective punishers (i.e., they do not decrease the behavior that produce them). Furthering our understanding of the conditions under which delayed aversive outcomes do and do not function as punishers is fundamental to addressing failures of self-control in the world of human affairs; however, relatively little research has focused on how aversive outcomes are affected by delay, either in general (Banks & Vogel-Sprott, 1966; Baron, 1965; Camp et al. 1967; Kamin, 1959; Myer & Ricci, 1968; Trenholme & Baron, 1975) or in the context of self-control (Deluty, 1978; Deluty et al., 1983).

The dearth of studies on self-control involving aversive outcomes may reflect the general underrepresentation of punishment in the literature (see Lerman & Vorndran, 2002). Or perhaps researchers are dissuaded from studying aversive outcomes because doing so requires consideration of both reinforcement and punishment variables. Indeed, a schedule of punishment must be conjoined with a schedule of reinforcement for its effects to be measured. However, doing so requires rigid control of several variables related to the delivery of both the punishing and reinforcing stimuli (see Estes, 1944; Hineline & Rosales-Ruiz, 2013). Some of these

variables are related to the delivery of the punisher, such as its delay (Baron, 1965; Camp et al., 1967; Kamin, 1959; Renner, 1966), intensity (Azrin, 1960), and schedule (Deluty, 1976). The efficacy of a punisher also depends on the conditions of reinforcement. All else being equal, a punisher may be less effective when the behavior is maintained by a relatively rich schedule of reinforcement (Toegel et al., 2022, Exp. 5; see Hineline & Rosales-Ruiz, 2013, p. 489) or may be more effective when reinforcement is available for an alternative, unpunished response (Bouzas, 1978; Herman & Azrin, 1964; Holz, 1968).

A further complication to studying aversive outcomes is that the similarities and differences between reinforcement and punishment as behavioral processes are still not well understood. The two processes have opposing effects: reinforcement *strengthens* behavior and punishment *weakens* it. Some have suggested that there is an asymmetry in the size of the relative effects and that punishing outcomes affect behavior disproportionally more than reinforcing ones (Kahneman & Tversky, 1979). Indeed, in studies that have arranged for reinforcement and punishment along the same dimension (e.g., point gain vs point loss with human participants), the punishing effect of point loss was greater than the reinforcing effect of an equivalent magnitude of point gain (Kuroda et al., 2018; Rasmussen & Newland, 2008; *cf.* Farley & Fantino, 1978). Arranging for direct comparisons of the relative effects of reinforcement and punishment is much more difficult in the animal lab, but the challenges inherent to studying punishment do not justify its neglect. Punishment is commonplace, and a comprehensive account of behavior will require the inclusion of punishment in laboratory models of choice.

Self-Control as Conflicting Choice

The *conflicting choice* examples of self-control described by Skinner (1953) represent one approach to integrate the study of aversive outcomes into the choice literature. Still, this approach has only been taken in a handful of studies (e.g., Epstein, 1984, Experiment 3). Woolverton et al. (2012) arranged for rhesus monkeys to choose between outcomes that resulted in small infusions of cocaine alone (a reinforcer) or cocaine plus delayed histamine (a punisher) by pressing one of two concurrently available levers. In Phase 1, a response on one lever produced an immediate cocaine infusion (delivered over a 10-s period) whereas a response on a second lever produced the same dose of cocaine and either saline or histamine (1 s after the end of the cocaine infusion). Each session consisted of four forced-choice trials and 20 free-choice trials. Across sessions, the dose of histamine was manipulated. In Phase 2, responding on both levers produced cocaine and histamine infusions and the delay to histamine infusion for one of the levers was manipulated across conditions (1, 10, 30, 60, 180, 360, 720 s). Overall, histamine was shown to punish responding for cocaine. In Phase 1, percent choice of the cocaine-only option increased as a function of histamine dose for all rhesus monkeys. Similarly, in Phase 2, choice of the option that resulted in delayed histamine increased from less than 30% when the delay was short (1 to 30 s) to nearly 100% when the delay was relatively long (360 to 720 s). The effect of delay to histamine on choice was reasonably well described by a hyperbolic function (Eq. 1). Overall, choice was shown to be sensitive to changes in both punisher intensity (dose of histamine) and delay.

In two unpublished studies in our lab, an adjusting-delay procedure (similar to that described by Mazur, 1987) was used to study conflicting choice. Each session was divided into blocks of four trials: two forced-choice trials and two free-choice trials. Dumas (2014) arranged

for rats to choose between one food pellet, a *single-valence* outcome, and two pellets plus a delayed shock, a *dual-valence* outcome. Across blocks of trials, the delay to shock was adjusted based on choice in the free-choice trials until an indifference point was found. The indifference point in each condition can be interpreted as the delay to shock that devalued two pellets to be equal in value to one pellet. Dumas manipulated the intensity (0.05 to 0.8 mA) and duration (100 to 200 ms) of shock and found that indifference points tended to increase as the intensity and duration of shock increased. When shock intensity was low (< 0.4 mA), the corresponding indifference point was short (e.g., less than 5 s), but as shock intensity was raised, indifference points also increased: it took a longer delay to shock to devalue the two pellets to be equal in value to one pellet.

In a subsequent study, Toegel (2018) arranged for rats to choose between one food pellet plus a delayed shock and one pellet alone, delivered after a delay. In this study it was the delay to the lone pellet that was adjusted across blocks of trials. Across conditions, Toegel manipulated the fixed delay to shock. When the delay to shock was short, the indifference point for delayed food was relatively long; on average, shock delivered 2 s after food was approximately equal to food alone delayed by 30 s. As the delay to shock was raised, the indifference points for delayed food decreased in a manner consistent with that described by Eq. 1 (i.e., hyperbolic discounting); shock devalued food to a lesser extent as its delay was increased. The studies by Dumas (2014) and Toegel (2018) highlight two variations of the adjusting-delay procedure that can be used to study conflicting choice, identify some of the parameter values that may affect choice, and establish some common results between the conflicting choice and delay of reinforcement literatures.

A within-session procedure similar to that described by Evenden and Ryan (1996) was used by Rodruguez et al. (2018) to study conflicting choice. Rats chose between two concurrently available levers to produce either a single food pellet (single valence) or four food pellets plus a delayed shock (dual valence). Each session was divided into five blocks and each block consisted of eight trials: two forced-choice trials and six free-choice trials. The delay to shock did not change within a block but rather was manipulated across blocks in either an ascending (0, 5, 10, 20, 40 s) or descending (40, 20, 10, 5, 0 s) sequence. Rodriguez et al. (2018) found that the percentage of trials in which the food plus shock lever was chosen increased as the delay to shock increased. Changes in choice were well described by Eq. 1 with no systematic effect of the order of delay presentation. These findings were replicated by Liley et al. (2019), although some procedural differences should be noted. First, Liley et al. used an ascending sequence of delays to shock (0, 4, 8, 12, 16 s) and included a no-shock block in which rats chose between one and four pellets as the final block of each session. Second, effects of adding a signal during the delay to shock were assessed. The cue light above the lever associated with food plus shock was turned on for the duration of the delay until shock. Adding this signal tended to decrease choice of the lever associated with food plus shock across all delay conditions: the signal increased the efficacy of shock.

Drug Effects on Self-Control

The experimental analysis of self-control has perhaps garnered the most attention in the context of drug effects. Indeed, many of the experimental models of self-control described above were either designed as a preparation for studying drug effects (e.g., Evenden & Ryan, 1996) or have subsequently been used to study drug effects on choice (see de Wit & Mitchell, 2010; Perry & Carroll, 2008; Reynolds, 2006; Yi et al., 2010 for reviews). Understanding effects of drugs on

self-control is important for at least two reasons. First, measures of self-control have been shown to be negatively associated with substance abuse (e.g., Carroll et al., 2010; Perry & Carroll, 2008; Yi et al., 2010). Drug users typically make more impulsive choices compared to non-drug users in studies of discounting with hypothetical monetary outcomes (see Carroll et al., 2010; Yi et al., 2010). It remains unclear, however, whether drugs make individuals more impulsive or if impulsive individuals are more likely to use drugs (Beardsley et al., 2014; Weafer et al., 2014). Second, measures of delay discounting have been shown to be affected by drugs, at least in the delayed reinforcement framework. Characterizing acute effects of drugs on self-control may be helpful for uncovering some of the behavioral mechanisms by which drugs affect choice and can help inform interventions related to substance use.

Effects of Opioids on Self-control

Effects of opioids (a drug class that includes heroin, morphine, and oxycodone) on self-control are of particular interest. Use of the synthetic opioid oxycodone starting in the early 1990's has precipitated the declaration of a public health crisis in the United States (National Institute on Drug Abuse, 2021). This crisis has disproportionally affected rural communities in Appalachia (e.g., West Virginia, eastern Kentucky, and southwestern Virginia; Van Zee, 2009). Although it has become clear that prescription opioids are highly addictive, behavioral effects of oxycodone are still not well understood. The few available studies suggest that opioid use is associated with decreased self-control. For example, Madden et al. (1997) found that heroin-dependent individuals discounted hypothetical money more steeply compared to matched, non-drug dependent controls (see also, Giordano et al., 2002; Kirby et al., 1999).

Most studies of self-control with animals have examined effects of morphine. Pitts and McKinney (2005) arranged for rats to choose between a smaller, sooner and larger, later

reinforcer on a within-session procedure. Morphine tended to decrease self-control (i.e., increase choice of the smaller, sooner reinforcer). These general findings have been replicated across studies that have used morphine (Epolito et al., 2013; Harvey-Lewis et al., 2012; Kieres et al., 2004; Pattij et al., 2009), although some exceptions have been reported (e.g., Maguire et al., 2016).

The experimental literature on oxycodone's effects on self-control is relatively sparse (e.g., Zacny & de wit, 2009). In a recent study by Hunt et al. (2020), rats responded on a concurrent-chains procedure in which the terminal links produced different amounts of reinforcement. Of interest was how sensitive the rat's responding in the initial link was to changes in reinforcement amount in the terminal link. The levers associated with the large and small reinforcers alternated every five sessions. Oxycodone decreased sensitivity to reinforcement amount: response ratios tended to shift toward indifference as the dose was raised. Although these findings only account for one of the relevant variables involved in self-control, reinforcement amount, they suggest one behavioral mechanism by which opioids might affect choice: by decreasing the impact of reinforcer magnitude on choice.

Effects of Stimulants on Self-Control

Effects of stimulants (a drug class that includes *d*-amphetamine, methamphetamine, methylphenidate, and cocaine) on self-control have been studied extensively by researchers; however, effects of these drugs on self-control vary greatly across studies. *d*-Amphetamine and methylphenidate, are two stimulants that are commonly prescribed for their therapeutic effects (e.g., decrease the impulsive symptoms of attention-deficit hyperactivity disorder; Bradley, 1937; Kendall et al., 2008). In animal models of self-control, effects of these drugs are generally consistent with the therapeutic effect: they increase choice of the larger, later reinforcer (i.e.,

increase self-control; Pitts & McKinney, 2005; Slezak et al., 2014; van Gaalen et al., 2006; Wade et al., 2000; Winstanley et al., 2003). However, the opposite effect has also been reported (a decrease in self-control; Evenden & Ryan, 1996) and in some studies, effects of these stimulants depends on procedural variables (Tanno et al., 2014; Krebs et al., 2016; see de Wit & Mitchell, 2010 for a review). These inconsistencies in the literature warrant additional research. Converging evidence across procedures that isolate different variables related to self-control may help disentangle these discrepancies.

The conflicting choice model of self-control shows promise as a preparation for studying drug effects. Procedures like those described by Rodriguez et al. (2018) and Liley et al. (2019) share many features with commonly used drug baselines (e.g., Evenden & Ryan, 1996), but I am not aware of any published studies that have studied drug effects within the conflicting-choice model. Studying drug effects on self-control with aversive outcomes is of interest for at least three reasons. First, prescription drugs (e.g., OxyContin®, Adderall®) may have behaviorally active effects that could be detrimental but are overlooked because of the therapeutic benefits (e.g., pain reduction, increased attention). In the case of opioid use, decreases in self-control, in addition to high abuse potential (van Zee, 2009), could contribute to potentially harmful behavior such as the misuse of prescription opioids (e.g., oxycodone; Vowles et al., 2015) or the use of illicit alternatives (e.g., fentanyl, heroin; Carlson et al., 2016) because the aversive outcomes associated with these responses do not sufficiently impact choice. Second, drugs can function as tools for uncovering similarities (or differences) across behavioral processes (i.e., reinforcement and punishment; Branch, 2006). Differential drug effects on behavior maintained by delayed reinforcement or punished by delayed aversive outcomes may reflect fundamental differences in the ways each process governs behavior. Third, it is of interest to identify some of the behavioral

mechanisms by which drugs affect behavior (Pitts, 2014). For example, oxycodone may decrease self-control choice by decreasing the effectiveness of delayed aversive outcomes. The conflicting-choice procedures described above show promise as a means of teasing apart different sources of control (quantitatively), so that the relevant variables that affect choice can be identified, particularly sensitivity to delayed aversive outcomes. This approach can then inform the development of targeted behavioral interventions for deficits of self-control (e.g., drug abuse).

Statement of the Problem

Choices made outside the laboratory are complex and often result in multiple outcomes that can differ across multiple dimensions (e.g., amount, delay, and valence [i.e., positive or negative]). For example, many socially significant shortcomings of self-control involve a failure of delayed, aversive outcomes to control behavior in lieu of immediate, reinforcing outcomes. The goal of the experiments described below was to isolate some of these variables using two different types of choice procedures. In both procedures, rats responded to produce both reinforcing – food – and aversive – shock – outcomes. Of primary interest was quantifying how choice changed as a function of the delay to shock arranged as an aversive outcome on one of the response options. In Experiment 1, rats responded under the conflicting-choice procedure (similar to that described by Liley et al., 2019; Rodriguez et al., 2018). In Experiment 2, an exploratory approach was taken to develop a novel concurrent-chains procedure for studying sensitivity of choice to delayed shock. Once responding on each procedure was considered stable, effects of methylphenidate and oxycodone were determined.

Experiment 1

In Experiment 1, a discrete-trial choice procedure (similar to the one described by Liley et al., 2019; Rodriguez et al., 2018) was used to assess several delays to shock within each session. This procedure served as a behavioral baseline to assess effects of two different drugs: oxycodone and methylphenidate. In the delay-discounting literature, morphine has been shown to decrease choice of larger, later reinforcers (e.g., Pitts & McKinney, 2005); however, effects of oxycodone in the conflicting-choice arrangement have not been assessed. If oxycodone decreases the efficacy of delayed aversive outcomes, then it could be predicted that oxycodone will increase choice of the dual-valence outcome. This shift in choice would show a decrease in self-control (as described by Skinner, 1953) because it increases contact with the delayed aversive outcomes. Methylphenidate was selected because it was predicted to have the opposite effect. In the delay-discounting literature, methylphenidate typically increases choice of larger, later reinforcers (e.g., Pitts & McKinney, 2005; Slezak et al., 2014; van Gaalen et al., 2006; Wade et al., 2000; Winstanley et al., 2003). One account for this finding is that methylphenidate increases the efficacy of delayed outcomes, thus larger, later reinforcers maintain their values despite the delay. If methylphenidate increased the efficacy of delayed shock in the conflicting-choice arrangement, then it could be predicted to decrease choice of the dual-valence outcome (i.e., increase self-control because contact with the aversive outcome is minimized).

Method

Subjects

Six experimentally naïve, male Sprague Dawley rats were maintained at 80% (± 2%) of their free-feeding weights, with periodic adjustments made on the basis of a growth curve for Sprague-Dawley rats. Rat chow supplemented food reinforcers obtained during the experimental

sessions; chow was provided 30-60 min after a session and at a comparable time on days without a session. The rats were approximately 60 days old upon arrival and were pair housed in a temperature-controlled room with a reverse 12:12 light/dark cycle. Water was always available in the home cage. Treatment of the rats, within and outside of experimental sessions, was in compliance with the guidelines set by the West Virginia University Animal Care and Use Committee.

Apparatus

Six standard operant-conditioning chambers were used (Med Associates Inc.). Each was housed in a sound-attenuating cubicle. The interior of each chamber was 31.5 cm wide, 25 cm deep, and 25 cm high. The front wall of each chamber was equipped with two retractable levers (5 cm wide, 6 cm from the grid floor). Above each lever was a 3-cm cue light and centered between the levers was an 8 x 8 cm aperture in which grain-based food pellets (45 mg, BioServ) were dispensed. Centered on the back wall, 1.5 cm below the ceiling, was a 28-volt houselight that was turned on during sessions. The grid floor was attached to a shock generator (ENV-414) that could provide a scrambled electric current across the bars of the grid. Each chamber was equipped with a speaker that could play white noise and tones of different frequencies.

Procedure

Preliminary Training

Before the experiment proper, preliminary training was conducted to establish delivery of pellets as reinforcers and strengthen responding on both levers. The houselight and white noise were turned on at the outset of each session and remained on for the duration, except during pellet delivery. During preliminary training and all subsequent conditions, the delivery of a pellet was accompanied by a 1-s 500-Hz tone. When the reinforcer consisted of multiple pellets, they

were delivered 0.1-s apart and the tone lasted 1 s per pellet. At the outset of the initial training session, three pellets were delivered, after which pellets were delivered at increasing variable intervals until the deliveries were at least 60 s apart, on average (i.e., a variable time 60-s schedule was used). This procedure continued until the rat reliably consumed a pellet within a few seconds of delivery. Next, lever-press training sessions began. One lever was extended into the chamber and responses were reinforced on a fixed-ratio (FR) 1 schedule (i.e., each response produced a pellet). After 10 pellet deliveries, the lever was retracted, and the opposite lever was extended into the chamber until another 10 pellets were delivered. The FR 1 schedule alternated between the levers after every 10 pellet deliveries until a total 100 pellets were delivered or 1 hr elapsed, whichever came first.

General Procedure and Preliminary Conditions

Sessions were normally conducted seven days per week at about the same time of day. To reduce effects of handling during the trip from vivarium to lab, a 5-min blackout, in which all lights remained off and the levers were retracted, preceded each session. Each session consisted of six blocks of eight trials: two forced-choice trials and six free-choice trials. At the outset of each trial, the houselight was turned on and either one lever (forced-choice trials) or both levers (free-choice trials) were extended into the chamber. The cue light above each lever was turned on whenever the lever was extended. A single response immediately produced the outcome(s) associated with the chosen lever; either a small reinforcer (one food pellet) or a large reinforcer (two to three food pellets). The intertrial interval began immediately after the reinforcement cycle. If a response was not made within 15 s of the start of the trial, an omission was recorded and the intertrial interval began. During the intertrial interval the lever(s) were retracted, house and cue lights turned off, and white noise remained on. The duration of the intertrial interval was

adjusted to hold the duration of each trial constant at 80 s. Thus, each session lasted 64 min (6 blocks x 8 trials x 80 s = 3,840 s = 64 min).

If a rat did not choose the large reinforcer on at least 80% of trials (e.g., five out of six free choice trials per block) the large reinforcer amount was raised from two to three pellets, which was sufficient to establish this degree of choice. Sessions continued under these conditions until five consecutive sessions were completed with no more than one omission per block each session. After reliable responding on the general procedure was established, shock was added as an outcome for responses on the lever that produced the large reinforcer (the "dual-valence" lever).

Shock Introduction and Adjustment

The first block of each session was a no-shock block, in which rats chose between the small and large reinforcers. In the subsequent five blocks of each session, a delayed shock was delivered contingent upon a response on the dual-valence lever. Shocks were delivered 10-s after the end of the reinforcement cycle, that is, after the end of the 2- or 3-s tone that accompanied the large reinforcer. During the delay to shock a 2000 Hz tone played continuously and the cue light above the chosen lever flashed (0.5 s on, 0.5 s off). The intertrial interval began immediately after shock delivery.

During this phase, shock intensity was adjusted individually across rats to ensure that delayed shock functioned as a punisher but did not completely suppress responding. Initially, a 0.5 mA shock lasting 500 ms was delivered. Across sessions, the shock intensity was adjusted in 0.05 mA increments or decrements until the following criteria were met for five consecutive sessions: (a) percent choice of the dual-valence lever in the last five blocks of each session was

approximately 50% (±17%) and (b) no more than four omissions occurred per session. Once a shock intensity was selected for each rat, the experiment proper began.

Conflicting-Choice Procedure

Under the conflicting-choice procedure, the delay to shock was varied across blocks within each session. Responses on the single-valence lever resulted in one pellet – the small, immediate reinforcer. Alternatively, responses on the dual-valence lever resulted in two or three pellets – the large, immediate reinforcer – and a delayed shock. The delay to shock was lowered across blocks 2-6 in the following sequence: 40, 20, 10, 5, 1 s. Each delay to shock was accompanied by a different tone of 1000, 1500, 2000, 2500, or 3000 Hz.

Parameter Adjustments. Additional adjustments to the procedural parameters were made, on an individual rat basis, if (a) more than four omissions occurred per session in three consecutive sessions or (b) more than 80% of free-choice responses occurred on one lever in three consecutive sessions. These requirements were imposed to ensure that each session was completed with a minimal number of omissions and that choice changed to some minimum degree within each session (i.e., as a function of delay to shock). Shock intensity was changed in 0.5 mA increments or decrements for all rats. Shock duration was lowered, from 500 to 400 ms, for Rat E18. A modified delay sequence was used for Rat E18 because choice of the single-valence lever changed drastically between the 10- and 20-s delays. In an attempt to generate more graded changes in choice, the following delay sequence was used in blocks 2-6: 40, 20, 15, 10, 5 s. The assignment of the single- and dual-valence levers, left or right, was reversed for Rat C25 because near-exclusive responding occurred on the dual-valence and choice was insensitive to changes in shock intensity. The limited hold to respond was raised from 10 to 15 s for Rat C26

because omissions reliably occurred during the 1- and 5-s delay blocks. The terminal parameter values are listed in Table 1.

Stability Criteria. Responding on the conflicting-choice procedure was judged stable when the following criteria were met. First, 15 sessions had to be completed with no parameter changes. Second, of the last 15 sessions, the mean percent choice of the dual-valence lever at each delay, averaged in groups of three sessions, could not be highest or lowest in the last three-session group compared to the other four groups. Third, the dual-valence lever had to be selected in at least 80% of free-choice trials during the no-shock block across the last three sessions.

No-Shock Probe Sessions. Intermittent no-shock probe sessions were included to demonstrate that changes in responding across blocks were controlled by delay to shock on the dual-valence lever and not other factors (e.g., perseverative responding). During no-shock probe sessions, responses on the single-valence lever resulted in the small, immediate reinforcer and responses on the dual-valence lever resulted in the large, immediate reinforcer without a delayed shock. If choice of the large reinforcer was less than 80% in any block, another no-shock probe session was conducted; however, no more than three no-shock probe sessions were conducted consecutively.

Pharmacological Procedure

The pharmacological procedure began after responding on the conflicting-choice procedure was judged stable. Injections, either drug or saline, were administered two to three times a week (e.g., Tuesday, Thursday, and Sunday). To ensure that responding recovered between drug administrations, an injection was given only if data from the preceding (non-injection control) session was consistent with data collected from other non-injection sessions.

Specifically, the area under the curve (AUC) for the control session had to be within the range of AUC values from the preceding 10 non-drug sessions.

Injections were administered subcutaneously and there was a 15-min pretreatment time between the injection and the start of the session for all drugs. The rat was put in the chamber shortly after each injection and the 5-min blackout was started 10 min after the injection. This route of administration is based on the literature (Beardsley et al., 2004; Hunt et al., 2020; Perry et al., 2008). Before assessing drug effects, saline was administered, under the conditions described above, until no discriminable effects of the injection procedure occurred for a minimum of two consecutive saline injections.

Effects of varying doses of two drugs were assessed: oxycodone hydrochloride (0.1, 0.3, 0.56, and 1.0 mg/kg) and methylphenidate hydrochloride (1.0, 3.0, 5.6, and 10.0 mg/kg). All drugs were initially dissolved in 0.9% sodium chloride solution and injected at a volume of 1.0 ml/kg. For each drug, doses were administered in ascending order; effects of each dose were determined at least twice. For some rats, a smaller dose (0.03 mg/kg oxycodone or 0.3 mg/kg methylphenidate) was given if the lowest dose tested produced substantial changes in choice. The order in which oxycodone or methylphenidate was administered was counterbalanced across rats (see Table 1). At least two weeks separated the administration of different drugs. In three cases, Rats C24, C25 and C26, within-session patterns of choice shifted between drug regimens. Procedural adjustments were made in an attempt to recover patterns of responding under the initial conditions; these changes are noted in the footnotes of Table 1. For Rat C26, oxycodone was not administered because this rat was approximately 2.5 years old after completion of the methylphenidate regimen and initial parameter changes were insufficient to recover baseline patterns of responding.

Data Analysis

The primary dependent measure was the allocation of responding, expressed as a percentage of responses to the single-valence lever within each block. The shape of the function relating choice and delay to shock was characterized in two ways: *k* (by fitting Eq. 1 to the data) and AUC. Additional dependent measures included the latency to respond during forced-choice trials and the frequency of omissions each session.

Results

Two rats failed to show sensitivity of responding to within-session changes in the delay to shock. Rats C23 and E19 typically developed exclusive, or near exclusive, responding on one lever despite changes in the procedural parameters and lever assignment. Data for these rats are not included in subsequent descriptions of analyses and no drugs were administered to these rats.

Pre-Drug Baseline

Choice. Figure 2 shows the percent of choice of the single-valence lever as a function of the delay to shock arranged on the dual-valence lever. Each data point shows the mean (±*SD*) for each block from the last 10 (stable) sessions. Overall, choice of the single-valence lever decreased as delay to shock was raised on the dual-valence lever. When the delay to shock on the dual-valence lever was short (e.g., 1-5 s), all rats chose the single-valence lever on the majority of trials. As the delay to shock was raised, choice of the single-valence lever decreased. The single-valence lever was seldom selected when shock was delayed by 40 s and never selected during the no-shock block. A hyperbolic-discounting function (Eq. 1) was fit to the data to obtain parameter values for *k* and overall model fit. Individual estimates for *k* and R^2 are shown in each panel. Overall, the hyperbolic model provided a reasonably good fit for all rats: R^2 ranged from .74 to .93 (*M* = .87).

AUC was also calculated to describe the discounting function for each rat; AUC provides a useful summary statistic for describing overall choice within a session. An AUC value of 1 would indicate that the rat exclusively chose the single-valence lever across all blocks of the session. Alternatively, an AUC value of 0 would indicate that the rat never chose the single-valence lever. The mean AUC (*SD*) from the last 10 stable sessions for each rat is shown in the top portion of Table 2. When interpreted in conjunction with Figure 2, it can be seen how AUC relates to the steepness of the discounting function: higher AUC values indicate a shallower discounting function (see Rat C25 in Figure 2) and lower AUC values indicate steeper discounting (see Rat C26). This measure will be useful for describing drug effects on overall changes in choice in subsequent sections.

Latencies. Another measure to quantify the strength of responding is latency (de Villiers & Herrnstein, 1976; Mackintosh, 1974). Generally, responses that are maintained by highly effective reinforcers occur with a short latency. Alternatively, as behavior is weakened (e.g., by delaying reinforcement or adding punishment), the response latency increases. Figure 3 shows the mean (±*SD*) latency to respond on each lever during forced-choice trials across each block from the last 10 stable sessions. Latencies to respond on the single-valence lever (filled triangles) were relatively short, generally less than 2 s, in every block. Latencies to respond on the dual-valence lever (unfilled triangles) were also short when the delay to shock was long (10-40 s) and during the no-shock block for all rats. Longer latencies on the dual-valence lever were evident for Rats C24 and C25 when the delay to shock was short (1-5 s). Note that the present measure of response latency is constrained by the 10-s limited hold: if more than 10-s elapsed (15-s for Rat C26) before a response was made the trial would be scored as an omission.

Omissions. Trials that were scored as omissions occurred infrequently. The middle portion of Table 2 shows the mean omissions per block, out of the six free-choice trials, and the range of omissions each session across the last 10 stable sessions. In most cases, no omissions occurred. At most, one omission occurred per block in any given session. Omissions occurred most frequently in the 5-s block (three out of four rats).

No-Shock Probe Sessions

In no-shock probe sessions, responses on the single-valence lever produced the small reinforcer and responses on the dual-valence lever produced only the large reinforcer (i.e., no shocks were delivered). The bottom portion of Table 2 shows the mean (*SD*) percent choice of the large reinforcer from the last three no-shock probe sessions prior to the start of the pharmacological procedure. If consecutive no-shock probe sessions occurred, only the final session was used as one of the three sessions in these calculations. Although there is a slight decrease in choice of the larger reinforcer during blocks 3-5 (particularly for Rat C24), overall, all rats clearly showed a strong preference for the larger reinforcer. These findings increase the believability that the changes in choice in the baseline procedure (see Figure 2) resulted from manipulation of the delay to shock as opposed to other factors (e.g., satiation on food pellets, perseverative responding, etc.).

Effects of Oxycodone

Choice

Figure 4 shows mean percent choice of the single-valence lever at selected doses of oxycodone. The 1.0 mg/kg dose was excluded because this dose typically produced general disruptions in responding (e.g., shifts in choice during the no-shock control block or an increase in omissions); choice data for all doses are shown in Table 3. Each panel in Figure 4 shows

within-session changes in choice at saline (white circles) and one dose of oxycodone (black circles). At saline, choice of the single-valence decreased as the delay to shock (on the dual-valence lever) was raised. As in the baseline conditions, Eq. 1 provided a good fit for this relation for all rats, R^2 ranged from .70 to .98 (M = .84).

Effects of oxycodone on choice depended on the dose. For Rats C24 and E18, low doses (0.1 and 0.3 mg/kg) of oxycodone shifted the function down relative to saline: oxycodone decreased choice of the single-valence lever. Low doses of oxycodone did not produce any reliable changes in choice for Rat C25 at low doses. Higher doses (particularly 0.56 mg/kg) of oxycodone shifted the function up for Rats C24 and C25: oxycodone increased choice of the single-valence lever. However, both Rats C24 and C25 also show an increase in choice of the single-valence lever during the no-shock block at the 0.56 mg/kg dose. The highest dose tested, 1.0 mg/kg oxycodone (displayed in Table 3), produced irregular, and idiosyncratic, patterns of responding. For example, Rats C25 and E18 show a decrease in choice of the single-valence lever when the delay was long, but an increase at shorter delays (i.e., the functions relating choice and delay to shock were bitonic at this dose).

Estimates for k and R^2 are shown for all doses in Table 4. Recall that in Eq. 1, k scales the rate at which the value of an outcome is discounted by its delay: the steepness of the discounting function. That is, k quantifies how sensitive changes in choice are to changes in delay to shock. Rats C24 and E18 show more extreme changes in choice at 0.1 and 0.3 mg/kg compared to saline, indicated by steeper discounting in Figure 4 and an increase in k values. (Because the lowest dose produced an effect, a lower dose – 0.03 mg/kg – was administered to Rat E18 to demonstrate that changes in choice occurred as a function of dose). Rats C24 and C25 show the opposite effect at higher doses: changes in choice became less extreme as a function of dose,

resulting in a shallower discounting function and a smaller *k*. Fits of Eq. 1 did a reasonably good job accounting for variance in choice across all doses except 1.0 mg/kg, at which R^2 decreased substantially.

AUC. Figure 5 shows the mean AUC from control and injection sessions as a function of dose of oxycodone. As shown in Figure 5, low doses of oxycodone decreased choice of the single-valence lever for Rats C24 and E18 (compared to saline). This shift in choice is reflected by a decrease in AUC at the 0.1 and 0.3 mg/kg doses in Figure 5. Higher doses of oxycodone tended to increase choice of the single-valence lever for all rats, shown by the dose-related increases in AUC. Overall, there was a strong, negative correlation between *k* and AUC across doses, *r* ranged from -.99 to -.82 across rats (*M* = -0.93).

Latencies

Response latencies are of interest for two reasons. First, dose-related changes in the latency to press the dual-valence lever could indicate drug-related changes in the efficacy of shock. For example, shorter response latencies might result from oxycodone-related attenuation of the aversive function of shock. Of course, latency is not a pure measure of the aversive function of shock, and shorter latencies could also indicate an increase in the reinforcing value of the food pellet. Second, dose-related increases in latencies to respond (particularly on the single-valence lever) might indicate that the drug has disrupted general behavioral processes (e.g., motor control, discrimination of reinforcer amounts) rather than specific behavioral mechanisms (sensitivity to delayed shock). Figure 6 shows the mean latency to respond on each lever during forced-choice trials from select doses of oxycodone. At saline (black bars), latencies to press the dual-valence lever were longer when the delay to shock was short and decreased at longer delays and during the no-shock block. Effects of oxycodone on this relation were idiosyncratic across

both delays and rats. Only Rat E18 shows a reliable shortening of latencies under drug sessions (at the 5, 10, and 15 s delays). Latencies to press the single-valence lever were uniformly short (less than 2 s) across delays and did not reliably change as a function of dose of oxycodone.

Omissions

The mean number of omissions on free-choice trials (per block) for each rat at all doses of oxycodone are shown in Table 5. Omissions occurred infrequently, generally less than one omission per block across delays and doses. Bolded values in Table 5 indicate instances in which omissions occurred in more than two out of six (or >33%) free-choice trials per block. Note that omissions occurred at this high frequency for two out of three rats (Rats C25 and E18) and for these rats only occurred at the highest dose of oxycodone that was tested (1.0 mg/kg).

Effects of Methylphenidate

Choice

Figure 7 shows the mean percent choice of the single-valence lever at select doses of methylphenidate (data for all doses are shown in Table 6). At saline, choice of the single-valence lever decreased as the delay to shock was raised. Methylphenidate typically shifted the function up relative to saline: dose-dependent increases in choice of the single-valence lever are clearly shown across all doses for Rats C26 and E18 and at higher doses (5.6 and 10.0 mg/kg) for Rats C24 and C25. Increased choice of the single-valence lever occurred at a dose, or doses, that did not affect choice in the no-shock block for Rats C25 (at 5.6 mg/kg), C26 (at 1.0 and 3.0 mg/kg), and E18 (at 3.0, 5.6, and 10.0 mg/kg).

Estimates for k and R^2 based on fits of Eq. 1 at each dose of methylphenidate are shown in Table 7. Generally, k decreased as a function of dose: methylphenidate decreased sensitivity to changes in delay to shock. Eq. 1 provided a reasonably good fit to the data across rats and doses

with only a few exceptions. Typically, R^2 was lower at doses in which choice was insensitive to within-session changes in delay to shock (e.g., Rat C24 at 3.0 mg/kg, Rat C25 at 5.6 mg/kg).

AUC. Figure 8 shows the mean AUC from control and injection sessions as a function of dose of methylphenidate. Generally, methylphenidate increased choice of the single-valence lever. Overall changes in choice resulted in dose-dependent increases in AUC for Rats C24, C25, and E18 (with the exception of 3.0 mg/kg for C25). Rat C26 shows a drastic increase in AUC at the lowest dose, 0.3 mg/kg, and only minimal changes at higher doses (although note that responding is at the ceiling). Overall, there was a strong, negative correlation between *k* and AUC across doses, *r* ranged from -.95 to -.83 across rats (*M* = -0.89).

Latencies.

Figure 9 shows the mean latency to respond during forced-choice trials from select doses of oxycodone. Latencies to press the dual-valence lever are shown in the left column of panels. At saline (black bars), latencies were generally longest at the shorter delays (1-10 s) and were short (<2 s) at longer delays (20 and 40 s) and in the no-shock block. Methylphenidate did not reliably change latencies at any delay within or across rats. Latencies to press the single-valence lever are shown in the right column of panels. Single-valence latencies were generally short. Although methylphenidate produced the occasional increase in latency, there were no systematic changes across delays.

***Omissions*.**

The mean number of omissions on free-choice trials (per block) for each rat at all doses of methylphenidate are shown in Table 8. Omissions occurred with a low frequency across all doses and delays. Methylphenidate never produced more than one omission per block on average.

Discussion

In Experiment 1, rats responded under a discrete-trial choice procedure in which responding on the single-valence lever produced a small reinforcer immediately and responding on the dual-valence lever produced a larger reinforcer and a delayed shock. The delay to shock on the dual-valence lever was lowered across blocks of trials each session. Under baseline conditions, choice changed as a function of this within-session manipulation in a manner well-described by a hyperbolic discounting function (Eq. 1). These findings replicate prior research (Liley et al., 2019; Rodriguez et al., 2018). Indeed, fits of Eq. 1 to the baseline choice data in the present study (for R^2, M = .87, SEM = 0.05) were comparable to those obtained by Rodriguez et al. in the descending-delay group (for R^2, M = .81, SEM = 0.03) and provide additional evidence that hyperbolic discounting is a valid framework for describing how the efficacy of aversive outcomes are modified by their delay.

Interestingly, Rodriguez et al. (2018) found much steeper discounting (i.e., higher k, M = 0.32, SEM = 0.07) compared to the rats in the present study (M = 0.10, SEM = 0.01): choice of the single-valence outcome decreased more rapidly as the delay to shock on the dual-valence lever was raised. One conspicuous difference between the two procedures, the reinforcement amounts, could potentially account for this discrepancy in the rate of discounting. In Rodriguez et al., the dual-valence lever always produced four pellets, whereas in Experiment 1 the dual-valence lever produced only two or three pellets. It is possible that changes in the efficacy of a delayed shock depend on the magnitude of the competing reinforcer (Hineline & Rozales-Ruiz, 2013). The discrepancy in discounting rates between Rodriguez et al. and Experiment 1 suggests a potentially fruitful area for subsequent research on delayed aversive events (see also, Estle et

al., 2006); however, it is also worth considering how other variables (e.g., strain of rat used) could have contributed to these differences in discounting.

Two drugs were administered to determine their effects. Changes in choice produced by oxycodone depended on the dose. At low doses, oxycodone tended to decrease choice of the single-valence lever. This shift in responding is consistent with the limited findings in the literature that suggest opioids decrease self-control (Eppolito et al., 2013; Kieres et al., 2004; Maguire et al., 2016; Pattij et al., 2009). Higher doses of oxycodone produced the opposite effect: an increase in choice of the single-valence lever (i.e., an increase in self-control). However, changes in choice at higher doses of oxycodone were accompanied by an increase in choice of the single-valence lever during the no-shock block – potentially indicating a disruption of control by reinforcement amount – and/or an increase in omissions (particularly at 1.0 mg/kg) – potentially indicating general disruption of behavior. Thus, interpreting these results is difficult because it seems likely that oxycodone's effects on choice were not selective to the behavioral mechanism of interest: sensitivity to the delay to shock.

Given the mixed effects of oxycodone on choice, it is worth considering other behavioral mechanisms that may determine drug effects in the conflicting-choice arrangement. For example, oxycodone could increase the degree to which choice is controlled by the reinforcer amount associated with each outcome (thereby shifting choice toward the dual-valence outcome). The purpose of including the no-shock block was to identify drug-related changes in control by reinforcement amount, but because responding in the no-shock control block occurred exclusively on the dual-valence lever under non-drug conditions this control is only sensitive to detect decreases in control by reinforcement magnitude. Nonetheless, oxycodone-related

increases in control by reinforcement magnitude seem unlikely. Hunt et al., (2020) showed that oxycodone *decreased* sensitivity to reinforcement amount in rats.

Effects of methylphenidate were generally more consistent across rats: methylphenidate increased choice of the single-valence outcome. This increase in self-control is consistent with effects of methylphenidate on self-control in reinforcement-only paradigms (i.e., increased choice of a larger, later reinforcer). One interpretation of these common findings is that methylphenidate increases control by delayed outcomes. In the present results, an increase in the efficacy of delayed shock (an aversive stimulus) would result in a shift in responding away from the dual-valence option and toward the single-valence option. Alternatively, in the delay-discounting paradigm with reinforcement, an increase in the efficacy of delayed reinforcement would result in a shift in responding away from the smaller, sooner option and toward the larger, later option. Consistency in the finding that methylphenidate increases self-control across different paradigms strengthens the case that increased sensitivity to delayed outcomes is a relevant behavioral mechanism by which methylphenidate affects choice.

In the present study, a descending sequence of delays was arranged each session. It is possible that the effects of either drug on choice depended on this delay sequence. For example, Tanno et al. (2014) arranged for rats to choose between smaller, sooner and larger, later reinforcers under a within-session choice procedure (see Evenden & Ryan, 1996). Under baseline conditions, the sequence of delays within the session (ascending or descending) did not substantially affect patterns of responding: choice of the larger reinforcer decreased as its delay was raised. However, drug effects on choice did depend on the delay sequence: amphetamine and methylphenidate (two stimulant drugs) increased choice of the larger, later reinforcer in the ascending group and decreased choice of the larger, later reinforcer in the descending group.

Tanno et al. suggest that these shifts in choice could be due to behavioral perseveration. In the ascending group, the delay to the large reinforcer is shortest in the first block of the session, and thus it is strongly preferred. Both stimulants increased choice of the larger, later reinforcer in the ascending condition: rats persisted in this preference even as the delay was raised (see also, Maguire et al., 2014; Slezak & Anderson, 2009).

Because only a descending sequence was used in the present study, the possibility of drug-by-delay sequence interactions cannot be ruled out; however, if the delay sequence did influence drug effects, it seems unlikely that it was due to behavioral perseveration. The first block of each session was the no-shock block, in which all rats typically showed exclusive, or near-exclusive, choice of the dual-valence lever. If methylphenidate increased behavioral perseveration, this should have resulted in an increase in choice of the dual-valence lever, the opposite effect was observed: methylphenidate increased choice of the single-valence lever.

Although the discrete-trial procedure has been the standard approach for studying impulsive choice in behavioral pharmacology, there are a few limitations worth noting. First, indications of general behavioral disruption are limited to latencies and omissions. In the present study, neither measure reliably changed as a function of dose. Second, gradations of changes in choice are constrained by the number of free-choice trials each block. Alternative procedures are worth considering as a means of improving the sensitivity of these measures.

Experiment 2

The procedure used in Experiment 1 served as a sufficient baseline for studying drug effects on self-control involving conflicting outcomes; however, some limitations of this procedure specifically, and discrete-trial choice procedures generally, make it worthwhile to consider alternative approaches. The concurrent-chains procedure shows promise as an

experimental preparation for isolating the variables involved in self-control and characterizing how choice changes as a function of changes in delay to shock under drug and nondrug conditions. Indeed, concurrent-chains procedures have been used extensively to study determinants of choice, including reinforcement amount (Hunt et al., 2020; Neuringer, 1967; Pitts et al., 2016, Experiment 2), reinforcement delay (e.g., Chung & Hernnstein, 1967; Grace et al., 2003; Grace & Nevin, 1999; Ito & Asaki, 1982; Oliveira et al., 2014; Orduña et al., 2013; Pitts et al., 2016, Experiment 1), and punishment frequency (Farley & Fantino, 1978; Green & Rachlin, 1996; Schuster & Rachlin, 1968). The matching law consistently accounts for changes in response allocation as a function of changes in outcomes across numerous dimensions of both positive and negative valence.

However, pilot testing in our lab suggests that the conventional, steady-state concurrent-chains procedure (e.g., Herrnstein, 1964; Squires & Fantino, 1971) may not be optimal for studying effects of delayed shock on choice. We arranged for four rats to respond under a concurrent-chains procedure in which choices made in the initial link produced one of two mutually exclusive terminal links: one with one food pellet alone (single-valence outcome) and the other with three food pellets and a delayed shock (dual-valence outcome). Responding in the initial link had to satisfy a VI 10-s schedule to produce access to the terminal link. Changes in response allocation in the initial link were measured in a no-shock baseline and several delay conditions (in which shock in the dual-valence terminal link was delayed by 5, 10, 20, 40, or 60 s). Conditions lasted a minimum of 20 sessions and until responding was judged stable over 10 sessions based on visual inspection. The 20-s delay condition was first for all rats; within this condition, adjustments were made to shock intensity, in 0.1 mA increments or decrements, until the mean number of responses made on the dual-valence lever was 75% of the mean number of

responses made on that lever during the no-shock baseline. The remaining delay conditions were arranged in an irregular order.

For each session, the ratio of responses (dual-valence lever/single-valence lever) was calculated. This ratio was converted to a suppression ratio to show changes in overall response allocation compared to the no-shock baseline. To calculate the suppression ratio, the response ratio from the last six sessions of each delay condition was divided by the sum of that ratio and the mean response ratio from the last six stable sessions of the no-shock baseline. Although this analysis does not show absolute changes in responding on each lever, it does permit comparison of effects of delay in each condition relative to the no-shock baseline. Suppression ratios from the last six stable sessions in each condition are shown in Figure 10. Note that a suppression ratio of .5 (shown by the horizontal dashed line in each panel) indicates no change in response allocation compared to the no-shock baseline. Values less than .5 indicate a decrease in the relative response ratio – a shift toward indifference – which could result from a decrease in responding on the dual-valence lever and/or an increase in responding on the single-valence lever. However, based on visual analysis of the absolute responses made on each lever across conditions, changes in responding on the single-valence lever were small and non-systematic (data not shown).

Changes in response ratios as a function of delay to shock were idiosyncratic. For Rats P1 and P2 suppression ratios were lowest in the 20-s condition and increased at longer delays (40 and 60 s); however, this trend reversed at the 5 and 10-s delays. For P4, suppression ratios were lowest in the 5-s condition and near .5 at longer delays. Rat P3 shows no systematic changes in responding across conditions but only two delays were studied.

Pilot testing was conducted for two reasons. The first was to identify some of the procedural parameters (e.g., initial-link schedule duration, changeover-delay duration, and shock intensity) necessary to maintain responding and detect changes in response allocation across conditions. The second was to find out how many sessions were required to reach steady state after the start of a new condition. The plan was to continue each condition for a minimum of 20 sessions and until responding was stable. However, in most conditions, responding was stable by the tenth session. The extended duration of each condition could have contributed to the insensitivity of responding to changes across conditions. In a study by Deluty (1976), a concurrent schedule was used to study how response allocation changed as a function of relative shock frequency with rats (responding was maintained by a concurrent random interval 1.5 min random interval 1.5 min schedule and conjointly punished on random interval schedules ranging from 1 to 12 min). Each condition lasted only five sessions.

It was of particular interest in Experiment 2 to further develop the concurrent-chains procedure to better characterize the functional relation between response allocation and delay to shock in a choice context. The degree to which behavior is controlled by aversive outcomes, despite their delay, is critical to understanding self-control. Matching-based analyses (with VI schedule initial links) show promise as an approach to characterizing this behavior-environment relation; however, the best version of the generalized matching law (Eq. 3; Baum, 1974) for incorporating aversive outcomes remains a topic of debate (see Klapes et al., 2018). One model, the direct suppression version of the matching law, does a reasonably good job of accounting for choice under conditions that involve both reinforcing and aversive outcomes. This punishment-based model of the matching law was first described in its generalized form by Critchfield et al. (2003; see also, de Villiers, 1980, Farley, 1980):

$$\log(B_L/B_R) = S_P \log\left(\frac{R_L - P_L}{R_R - P_R}\right) + \log(b), \quad (4)$$

in which B_L/B_R is the ratio of behavior on the left and right alternatives, R_L and R_R are the reinforcers available on the left and right alternatives, and P_L and P_R are the aversive outcomes on the left and right alternatives. Note that the aversive outcomes are simply subtracted from the reinforcers in the ratio. The parameter S_P is the slope of the function and describes *sensitivity* to changes in delay to shock. The parameter *b* is the y-intercept which describes a *bias* for either outcome that is not accounted for by the reinforcer amount or delay to shock ratios.

An illustration of how Eq. 4 can be used to interpret drug-related changes in response allocation is shown in Figure 11. On the *y*-axis of each panel is the log ratio of behavior in the initial link: left-lever responses divided by right-lever responses. Positive values indicate that relatively more responses occurred on the left lever (i.e., more choice of the left outcome) and negative values indicate that relatively more responses occurred on the right lever (i.e., more choice of the right outcome). On the *x*-axis is the log punishment ratio. For simplicity, the relative availability of reinforcement is held constant in this example, thus, only the relative immediacy (1/delay) to shock arranged in each of the terminal links influences choice; negative values indicate that the relative delay to shock is *longer* on the right terminal link and positive values indicate that the relative delay to shock is *longer* in the left terminal link. Recall that longer delays to shock (an aversive outcome) are preferred over shorter delays to shock (Hineline & Rosales-Ruiz, 2013). Thus, Eq. 4 predicts a positive linear relation between response ratios and delay to shock ratios: more responding will occur on the lever that produces the relatively longer delay to shock (assuming the relative rate of reinforcement does not change). Each function in Figure 11 shows a function based on Eq. 4 that differs in terms of either slope –

indicative of changes in the sensitivity of responding to changes in delay to shock—or the y-intercept – indicative of changes in bias for the left or right lever.

The top panel of Figure 11 shows how changes to the sensitivity parameter affect the matching function. The solid line shows data when sensitivity (S_P) = 1: response allocation is directly proportional to the delays to shock arranged in the left and right terminal links, a relation called *strict matching*. The dashed and dotted functions show two deviations from strict matching. For example, if a drug increases the effectiveness of delayed shock, response ratios may become more extreme; that is, the rat may allocate relatively more responses to the lever that produces the longer delay to shock. This more sensitive pattern of responding, shown by the dashed function would be indicated by an increase in sensitivity (S_P). Alternatively, a drug could decrease the degree to which delayed shock affects choice (shown by the dotted function), resulting in less extreme response ratios and a decrease in sensitivity.

The bottom panel of Figure 11 shows changes in bias for each lever. Compared to the solid function, in which bias (B) = 0, positive values for bias indicate a preference for the left lever and negative values for bias indicate a preference for the right lever. Although bias is not of particular interest in the present study (*cf.* Rasmussen & Newland, 2008), it is important to parse out preference for one option that is not related to reinforcement or delay to shock ratios. Further, drug-related changes in bias may indicate that the drug has produced general disruption of behavior, as opposed to the specific behavioral mechanism of interest: sensitivity to delayed shock.

The goal of Experiment 2 was to further develop the concurrent-chains procedure for use as a baseline to study drug effects on delayed punishment. Three variations of the concurrent-chains procedure were arranged, described in Experiments 2A, B, and C below. Each procedure

was evaluated based on the degree to which response allocation during the initial links – the choice phase – was sensitive to changes in the relative delay to shock arranged in the terminal links – the outcome phase. Based on these variations, a final version was arranged, Experiment 2D, which was used as a baseline for studying drug effects. It was of particular interest to characterize how two drugs, oxycodone and methylphenidate, affected sensitivity to delayed shock.

General Method

Subjects & Apparatus

Eight experimentally naïve, male Sprague Dawley rats were maintained as in Experiment 1, and they were studied in the same operant-conditioning chambers.

Procedure

Preliminary training occurred using the same procedures as described for Experiment 1.

General Concurrent-Chains Procedure

Sessions were normally conducted seven days per week at about the same time of day. To mitigate effects of handing the rats, each session was preceded by a 5-min blackout, in which the chamber was dark and silent. The session was divided into chains. Each chain included an initial link – the choice phase –and terminal link – the outcome phase. Unless specified otherwise, sessions ended after 60 chains were completed or 75 min had elapsed, whichever came first.

A diagram of the general concurrent-chains procedure is shown in Figure 12 (note that the parameter values of the diagram may not reflect the specific parameter values used in the procedures described below). At the outset of the initial link the houselight was turned on, one (on forced-choice chains) or both (on free-choice chains) levers were extended into the chamber, and white noise was played. The white noise played continuously throughout each session unless

noted otherwise (e.g., during reinforcement). A VI 10-s schedule was arranged, such that the first response after 10-s, on average, satisfied the schedule. A response had to meet three criteria to produce access to the terminal link. First, the response had to occur after the current interval in the VI schedule had elapsed. Second, the response had to occur on the *preassigned* lever. The preassigned lever for each chain was determined randomly, with a probability of .5 and the constraint that the same lever was assigned in no more than three consecutive chains; the preassigned lever was not differentially signaled in the initial links. This method ensured equal exposure to the two terminal links in each session (Stubbs & Pliskoff, 1969) and prevented exclusive responding on one lever. (Note that this method of dependent scheduling is approximately equivalent to arranging an independent, concurrent VI 20-s VI 20-s schedule, because each schedule could be completed on average of every 20 s). Third, the response had to occur at least 2 s after a changeover. A changeover is defined as response that is preceded by a response on the other lever. The purpose of the changeover delay (COD) was to reduce the likelihood of adventitious reinforcement for switching between levers (Herrnstein, 1970; Shull & Pliskoff, 1967).

The first two chains of each session were forced-choice chains. These were included to ensure exposure to the contingencies arranged in the terminal links prior to the free-choice chains. Note that these forced-choice chains were not necessary, one of the benefits of using dependent scheduling in the initial links is that it ensures equal exposure to each terminal link; however, forced-choice chains were included to bring responding under control of the terminal-link delays earlier in the session.

A response that satisfied all three initial-link criteria produced entry to the corresponding terminal link, which was signaled by turning on the cue light above the chosen lever and

retracting the other lever. In the terminal link, a single response (FR 1) resulted in the delivery of the terminal link outcome(s). Reinforcement was delivered immediately after the terminal-link response; the delivery of each pellet was accompanied by a 1-s, 500-Hz tone. If multiple pellets were delivered, they were dispensed in rapid succession (0.1 s intervals) and the tone sounded for 1 s per pellet delivered. After reinforcement, either a signaled delay to shock or the interchain interval occurred. During the interchain interval, all lights were turned off and the levers were retracted. At the end of the interchain interval, the start of the next chain began.

In most of the procedures described below, both terminal links included immediate reinforcement and a delayed shock. The goal of this approach was to identify changes in initial-link responding as a function of changes in the relative immediacy (1/delay) to shock arranged in the terminal links. Further, this approach permits analysis of changes in choice using punishment-based version(s) of the matching law (Eq. 4; see also Klapes et al., 2018). One lever was designated the *variable lever* because the delay to shock arranged in the terminal link associated with this lever changed either within or across sessions. The terminal-link delay associated with the other lever, the *standard lever*, remained fixed within and across sessions. Lever assignments were initially counterbalanced across rats; however, in some cases the lever assignments were reversed for individual rats if the development of bias was evident.

Stability Criteria. Responding was considered sensitive to the terminal-link delays if sensitivity (calculated using Eq. 4) was greater than 0.3 in four out of six consecutive sessions. Responding on those six sessions was considered stable if the mean sensitivity from the first three sessions and the last three sessions were each within 15% of the grand mean of sensitivity across all six sessions. The conditions described below were exploratory, and many of the procedures were insufficient to generate sensitivity greater than 0.3. If increases in sensitivity

seemed unlikely after a minimum of 20 sessions, the condition was terminated. The number of sessions in each condition is included below.

Data Analysis

In the initial link, responding was characterized by three different measures. The primary measure was the ratio of responses on the two levers during initial links (e.g., variable lever/standard lever). Generally, response ratios were $\log_{10}$ transformed, and proportional changes in response allocation were plotted as a function of proportional changes in the delay to shock. This approach permits analysis of choice using Eq. 4 and interpretation of changes in responding as described in Figure 11.

A second measure, overall response rate (total initial link responses/initial link time), was calculated for each session as an index of general disruption of behavior (e.g., generalized punishment effects or drug-related suppression). Third, the number of completed chains was recorded each session.

Experiment 2A: Within-Session Procedure

The initial approach to establishing a concurrent-chains baseline for characterizing control by delayed shock was to develop a procedure that arranged multiple delays to shock within each session (see Aparicio et al., 2019; Hughes et al., 2022). One advantage of this approach is its efficiency; in each session response allocation was measured under three different ratios of delay to shock. As a result, a function relating response allocation and delay to shock was generated, and sensitivity calculated, within each session.

Procedure and Results

Phase 1: Initial Within-Session Procedure

Each session consisted of three blocks of 20 chains: 2 forced-choice chains and 18 free-choice chains. Each chain was separated by a 3-s interchain interval. The criteria required to satisfy the initial link of each chain were as described in the General Procedure (i.e., a dependent VI 10-s schedule, levers preassigned with p = .5, 2-s COD). Both terminal links resulted in food and shock. Shocks were initially delivered at an intensity of 0.4 mA for 400 ms. Responses on the *standard lever* produced the same terminal-link outcome within and across sessions: one pellet followed by a shock after 20 s. Responses on the *variable lever* produced three pellets and a shock after a delay that changed across blocks within each session (10, 20, or 40 s). The order of delays was decided for each session by randomly selecting without replacement from a list of six possible sequences until each sequence had occurred once across six sessions. This was to ensure that the relative delay to shock (short, equal to standard, or long) in the variable terminal link was equally likely to occur in each block (first, second, or third) every six sessions. These conditions were continued for 40 sessions.

The filled circles in Figure 13 show mean log response ratios (±*SD*) as a function of the relative delay to shock in the terminal links from the last six stable sessions (the figure also shows results for Phase 2 and 3, described below). All six rats showed greater choice of the variable lever: log response ratios were greater than 0 in all cases. This is not surprising, however, because responding on the variable lever produced three pellets while responding on the standard lever produced one pellet.

Of primary interest was the sensitivity of responding to changes in the relative delay to shock arranged in the terminal link. When the variable delay was 10 s, it was predicted that the standard lever, with its 20-s delay, would be chosen more; this change in response allocation would result in a decrease in the log response ratio. Alternatively, when the variable delay was

40 s, it was predicted that the variable lever would be chosen more, shown by an increase in the log response ratio. The net results would be a positive sensitivity parameter—that is, a positive slope. To test these predictions, Eq. 4 was fit to the data from Phase 1. Estimates for sensitivity (the slope of the function) and bias (the y-intercept) were calculated for each rat; these estimates and overall model fit are shown in the top section of Table 9. The sensitivity parameter, $S_{P,}$ was near 0 for five rats and slightly negative for Rats E11, E16, and E17 (overall M = -0.06, SD = 0.16). The Phase 1 conditions failed to generate responding that showed sensitivity to within-session changes in the delay to shock. Most rats showed a slight bias for the variable lever, indicated by a positive value for bias: more responding occurred on the variable lever than was accounted for by reinforcement magnitude or the relative delay to shock (M = 0.15, SD = 0.14). Overall model fits were poor and varied considerably across rats; R^2 ranged from .21 to .93 (M = .60).

Phase 2: Pellet and Delay Sequence Adjustments

Three adjustments were made to the procedure in Phase 2. First, the number of pellets produced by the variable lever was reduced from three to one. Responding in Phase 1 was controlled by the relative reinforcement magnitude and perhaps this overshadowed the relative effects of delayed shock. Second, different shock delays were used. Shock was delivered 5, 15, or 45 s after the end of the reinforcement cycle in the variable terminal link and after 15 s in the standard terminal link. This change was made to increase the relative difference between the delays arranged on the variable and standard levers (i.e., the delay ratios were 1:3, 1:1, or 3:1 versus 1:2, 1:1, and 2:1 in Phase 1). Third, the delays on the variable lever were arranged in a fixed, descending sequence. The delay to shock on the variable lever was always 45 s in the first block, 15 s in the second block, and 5 s in the third block. By comparison, the sequence of delays

varied unpredictably across sessions in Phase 1, and this source of variability could have contributed to the insensitivity of responding to changes in the delay to shock.

Phase 2 ended after 35 sessions. Data from the last 6 sessions are shown with the unfilled circles in Figure 13 along with results from Phases 1 and 3. The most striking difference from Phase 1 is that response ratios shifted toward indifference (0) for all rats. This shift may have resulted from equating the reinforcement magnitude between the variable and standard levers. As in Phase 1, the slope of all of the functions approximate 0 indicating that choice in the initial link did not change as a function of changes in the terminal link delays to shock. Estimates for S_P, shown in the middle section of Table 9, were close to 0 (M = -.07, SD = 0.09). Compared to Phase 1, bias in Phase 2 was reduced – closer to 0 – for six out of eight rats (all except Rats E11 and E15; overall M = 0.05, SD = 0.17). Overall, responding on the variable and standard levers did not systematically differ based on factors other than the reinforcement and delay to shock ratios. Model fits in Phase 2 were comparable to Phase 1, R^2 ranged from 0.19 to .95 (M = .66).

Phase 3: Delay-Specific Signals

In Phase 3, a tone was played continuously during the delay to shock. Delay-correlated stimuli have been shown to increase the efficacy of delayed outcomes, both reinforcers (e.g., Lattal 1984; see Lattal 1987 for a review) and punishers (e.g., Trenholme & Baron, 1975). In Phase 3, each delay to shock was accompanied by a distinctive tone of either 1500, 2000, or 2500 Hz, counterbalanced across rats.

Phase 3 ended after at least 14 sessions. Mean log response ratios from the last 6 sessions are shown with the grey triangles in Figure 13. Adding tones to the terminal links did not produce a reliable change in response ratios for six of the eight rats. Response ratios did shift downward for both Rats E14 and E15. For Rat E14 this indicates greater choice of the standard

lever and for Rat E15 responding shifted toward indifference. Estimates for S_P, bias, and model fit are shown in the bottom section of Table 9. Sensitivity remained near 0 for all rats (M = -0.07, SD = 0.09), indicating that adding delay-specific stimuli to the procedure did not increase the degree to which response ratios changed as a function of those delays. There was no systematic bias, for the variable or standard lever, across rats (M = -0.04, SD = 0.16). Overall model fits remained poor, R^2 ranged from .10 to .99 (M = .58).

Experiment 2B: Rapid-Acquisition Procedure

In Experiment 2B, within-session changes in the delay to shock were removed and instead the delay associated with the variable lever was changed across sessions. This type of procedure was originally developed to study the acquisition of preference within a session (Christensen & Grace, 2009; see Grace et al., 2003) and has been used as a preparation for studying how drugs affect sensitivity to different dimensions of reinforcement, such as delay (Pitts et al., 2016, Exp. 1; TA et al., 2008), magnitude (Maguire et al., 2007, 2009; Pitts et al., 2016, Exp. 1) and probability (Rankin, 2014). The initial link was identical to that arranged in Experiment 2A. Satisfying the initial-link criteria resulted in entry to one of the two terminal links, which were still designated *variable* and *standard*. Responses on the variable lever resulted in one pellet and a shock after 5 or 45 s: the delay to shock varied across sessions but remained constant within each session. Responses on the standard lever always resulted in one pellet and a shock after 15 s.

Initially, each session consisted of 60 initial link-terminal link chains; however, this was reduced to 48 chains per session after the first 20 sessions. In either case, the first two chains of each session were forced-choice chains, in which only one lever was extended into the chamber during the initial link, and the remaining chains were free-choice chains, in which both levers

were available during the initial-link. The delay arranged in the variable terminal link was selected using a pseudo-random sequence with the constraints that each delay (5 or 45 s) was arranged an equal number of sessions over every eight sessions, and the same delay could not be used for more than three consecutive sessions. Each chain was separated by a 15-s interchain interval (note that this is longer than the 3-s interchain interval in Experiment 2A). Parameters for each rat are listed in Table 10.

Experiment 2B ended after 21 to 23 sessions. Log response ratios from the last six sessions of each type are shown in Figure 14. The *x*-axis shows the log delay ratio (variable/standard); data points at -0.48 are from sessions in which the variable delay was 5 s and data points at 0.48 are from sessions in which the variable delay was 45 s. Overall, response allocation did not drastically change across the different delays to shock. For all rats, sensitivity was near 0 or slightly negative (M = -0.17, SD = 0.11), however, the R^2 values are so low (M = .16, SD = .13) that sensitivity estimates should be interpreted cautiously as descriptions of changes in behavior. Three rats (Rats E13, E14, and E16) clearly show a negative bias; that is, more responding occurred on the standard lever. This bias may result from a preference for a predictable delay to shock compared to the variability in delays in the variable terminal link (see Badia et al., 1979). This seems unlikely, however, given that only two delays were arranged on the variable lever and the delays within each session did not change.

Experiment 2C: Conflicting-Choice Procedure

Experiments 2A and 2B failed to produce changes in response allocation as a function of the relative delays to shock arranged in the terminal links. Insensitivity of responding to changes in shock persisted despite the addition of several procedural changes to increase the discriminability of the terminal links or increase exposure to the outcomes arranged in each

terminal link. A different approach was taken in Experiment 2C. As in Experiments 2A and 2B, a concurrent-chains procedure was used; responding in the initial link granted access to one of two, mutually exclusive terminal links. Unlike the previous procedures, shock was only arranged as an outcome for responding in one of the terminal links. Responses on the *dual-valence* lever initially produced a large, immediate reinforcer – three pellets – and a shock after 40, 20, 10, or 5 s in the terminal link. Responses on the *single-valence* lever produced a small, immediate reinforcer – one pellet – alone. (Note that this arrangement shares many procedural features with Experiment 1).

Each session consisted of four blocks of 12 chains: 4 forced-choice chains and 8 free-choice chains. In the initial link, an independent VI 10-s VI 10-s schedule was arranged with a 2-s COD. Because response allocation in Experiments 2A and 2B was typically near indifference the dependent schedule was removed to try to mitigate the extent to which patterns of responding were controlled by procedural variables instead of delay to shock. Thus, on free-choice chains, access to both terminal links was available in each initial link. The additional two forced-choice chains per block were added to ensure adequate exposure to both terminal links.

At the outset, the dual-valence lever produced three pellets. Within each session, the delay to shock was lowered across blocks in a descending sequence. The intensity of shock was initially set at 0.4 mA and lasted 400-500 ms (duration varied across rats). Adjustments to the number of pellets, shock intensity, and/or shock duration were made if (a) more than four omissions occurred per session in three consecutive sessions or (b) more than 80% of free-choice responses occurred on one lever in three consecutive sessions. The terminal parameters for each rat in Experiment 2C are shown in Table 11.

Figure 15 shows the mean percent choice of the single-valence lever (±*SD*) as a function of the delay to shock on the dual-valence lever from the last six sessions. Data are expressed as a percentage of total responses instead of a response ratio because in some cases exclusive responding occurred within a block and the response ratio could not be calculated. The reference line at 50% indicates responding at indifference. Three rats (Rats E13, E16, and E17) responded near indifference (50%) and the remaining five rats showed greater choice of the dual-valence lever (<50%). Overall, changes in choice as a function of delay to shock were minimal: the range of percent choice was less than 30% for most rats. Further, choice of the single-valence lever tended to increase as the delay to shock on the dual-valence lever increased (this effect is most clearly shown by Rats E10 and E17). This pattern of responding is the opposite of that shown in Experiment 1, in which choice of the single-valence lever decreased as the delay to shock on the dual-valence lever increased.

Experiment 2D: Drug Effects under the Within-Session Procedure

All three of the concurrent-chains procedures described above failed to maintain responding that showed sensitivity to differences in the delay to shock arranged in the terminal link(s). However, the procedure used in Experiment 2A would have made the most efficient baseline for studying drug effects and it permitted analysis of changes in choice from a matching law framework. Thus, in Experiment 2D, a within-session concurrent chains procedure, like that described in Experiment 2A was used as a baseline for studying drug effects.

The procedure used in Experiment 2D differed from Experiment 2A in three ways. First, the initial-link (VI) schedule requirement was shortened. Under concurrent-chains procedures, the relative durations of the initial and terminal links have been shown to affect sensitivity to the terminal-link outcomes. Christensen & Grace (2008) showed that this relation is bitonic,

response ratios increased as the initial-link duration was raised up to 10 s and decreased at longer initial-link durations. However, shortening the initial-link duration also decreases the sampling period in which responding can occur. In Experiment 2D the VI-schedule value was lowered from 10 to 5 s. To ensure a sufficient sample of responses was made each chain, a minimum of five responses was also required in the initial link (i.e., an FR 5 schedule). Thus, the first response after the interval elapsed produced the terminal link, as long as that response was preceded by at least four responses during the interval (i.e., a conjunctive VI 5-s FR 5 schedule). Second, the block of chains in which the variable and standard delays were equivalent was removed. Instead, the delay values arranged in each terminal link were always shorter or longer than the standard delay. This was done to improve the discriminability of the delays in each terminal link. Third, the reinforcement amount was raised to three pellets in both terminal links.

Behavioral Procedure

Each session consisted of four blocks of 10 chains; each block contained 2 forced-choice chains and 8 free-choice chains. A response in the initial-link only produced entry to the terminal link if (1) the VI-5 s schedule was satisfied, (2) at least five responses had occurred, distributed across either lever, (3) the response occurred on the preassigned lever, and (4) a 1-s COD was satisfied. The delay to shock in the variable terminal link changed across blocks within each session. For four rats (Rats E10, E11, E12, and E13) only two delay values were used: 4 and 64 s. For the other four rats (Rats E14, E15, E16, and E17) four delay values were used: 3, 6, 24, and 48 s. The delay to shock in the *standard* terminal links was the geometric mean of the delay values in the variable terminal link -- 16 s for Rats E10-13 and 12 s for Rats E14-17-- and was held constant within and across sessions. The terminal parameters for each rat are shown in Table 12.

The pharmacological procedure began once responding was judged sensitive and stable across six consecutive sessions or after 40 sessions on the baseline procedure, whichever came first.

Pharmacological Procedure

The pharmacological procedure was similar to that described in Experiment 1. Both oxycodone hydrochloride (0.1, 0.3, 0.56, and 1.0 mg/kg) and methylphenidate hydrochloride (1.0, 3.0, 5.6, and 10.0 mg/kg) were injected subcutaneously 15-min prior to select sessions. Unlike in Experiment 1, each rat only received injections of one drug. Oxycodone was administered to Rats E10, E11, E16, and E17 and methylphenidate was administered to Rats E12, E13, E14, and E15. Each dose was administered at least twice, with the exception of the highest dose (1.0 mg/kg oxycodone and 10.0 mg/kg methylphenidate) which was not re-administered if the first injection of this dose resulted in a substantial reduction in responding, indicated by completion of less than 50% of the session.

Results

Baseline Responding

Rat E13 met the sensitivity and stability criteria after 35 sessions on the baseline procedure, for the remaining seven rats the baseline procedure was ended after 40 sessions. Log response ratios (variable lever/standard lever) from the last six sessions of the baseline procedure are shown in Figure 16. Each data point represents a response ratio from one block of a session. Generally, response ratios did not change as a function of the relative delay to shock arranged in the terminal links: most rats showed no substantial change in response allocation throughout the session. Estimates for sensitivity – the slope of each function – ranged from -0.17 to 0.48 (M = 0.08). Only Rat E13 clearly shows changes in responding that could be described as sensitive to

the terminal link delays to shock: response ratios favored the variable lever when the variable delay was long (64 s vs 16 s on the standard lever) and favored the standard lever when the variable delay was short (4 s vs 16 s on the standard lever). Rats E16 and E17 show slight changes in response ratios across delay to shock ratios (sensitivity was 0.10 for Rat E16 and 0.18 for Rat E17); however, these changes are accompanied by considerable overlap of response ratios across blocks. For the remaining five rats (Rats E10, E11, E12, E14, and E15) response ratios did not change as a function of the terminal-link delays: sensitivity was near 0 or negative.

Bias, indicated by the y-intercept of each function in Figure 16, differed unsystematically across rats. Bias ranged from -0.25 to 0.15 (M = -.05), indicating that slightly more responses were made on the standard lever on average. Fits of Eq. 4 to the data were poor: R^2 ranged from .00 to .65 (M = .20).

Effects of Oxycodone

Figure 17 shows effects of oxycodone on mean response ratios from sessions in which saline (white circles) and select doses (0.1, 0.3, and 0.56 mg/kg; black circles) were administered. The degree of change was quantified using Eq. 4, and estimates for sensitivity (the slope of the line of best fit) are shown in each panel. At saline, there are three different patterns of responding across rats. Rat E10's responding indicates an increase in choice of the shorter delay to shock, as shown by a negative sensitivity (slope). Rats E11 and E17 show no change in response allocation across delays to shock: sensitivity is near 0. Rat E16 shows a preference for the option that produced the longer delay to shock, indicated by a positive sensitivity of 0.27. Oxycodone did not reliably change these patterns of responding for Rats E10 or E11 at any dose. Interestingly, oxycodone produced a modest increase in sensitivity at 0.56 mg/kg for Rat E16 and a substantial increase in sensitivity at 0.3 and 0.56 mg/kg for Rat E17. That is, for Rats E16

and E17, oxycodone increased the degree to which changes in responding changed as a function of delay to shock: relatively more responding occurred on the option with the longer delay compared to at saline.

Figure 18 shows changes in sensitivity, bias, and overall initial-link response rates as a function of dose of oxycodone. The top row of panels shows sensitivity. For Rats E10, E11, and E12, 0.1-0.56 mg/kg oxycodone did not produce any substantial changes in sensitivity; however, 1.0 mg/kg oxycodone did produce an increase in sensitivity for Rat E11 and a decrease in sensitivity for Rat E16. Conversely, oxycodone increased sensitivity of responding for Rat E17 across multiple doses (particularly 0.3 and 0.56 mg/kg).

The middle row of panels in Figure 18 shows bias as a function of dose of oxycodone for each rat. Recall that positive values indicate relatively more responses occurred on the variable lever and negative values indicate that relatively more responses occurred on the standard lever, regardless of the delay to shock ratio. Oxycodone did not dose-dependently affect bias for any rat. Changes in bias either only occurred at one dose (e.g., the slight increase in bias for the variable lever at 0.56 mg/kg for Rat E10) or did not change across doses (e.g., the slight reversal of bias from variable to standard at all doses for Rat E17). In both cases, absolute changes in bias were relatively small.

The bottom row of panels shows initial-ink response rates as a function of dose of oxycodone. For all rats there was at least one dose that did not affect response rates compared to control and saline (typically, 0.1 and/or 0.3 mg/kg). Higher doses of oxycodone tended to decrease response rates; these changes were gradual and dose-dependent for Rats E10 and E11 and abrupt for Rat E16 (between 0.56 and 1.0 mg/kg). Rat E17 showed no substantial changes in

rates across doses. Despite these decreases in response rates, sessions were consistently completed by all rats at all doses, with the exception of Rat E10 at 1.0 mg/kg (see Table 13).

It was of particular interest to identify selective effects of oxycodone on sensitivity, that is, changes in sensitivity that occurred at a dose, or doses, of oxycodone that did not affect bias or response rates. For example, Rat E11 shows an increase in sensitivity at 1.0 mg/kg; however, this dose also substantially reduced response rates (from 84.33 responses a min at saline to 34.00 responses per min at 1.0 mg/kg). Alternatively, for Rat E16, 0.56 oxycodone produced a slight increase in sensitivity but did not affect bias or response rates. Similarly, for Rat E17, 0.56 and 1.0 mg/kg increased sensitivity but did not affect response rates (although note the slight reversal of bias from the variable to the standard lever; however, bias did not change dose-dependently). Overall, the evidence of selective effects of oxycodone on sensitivity to delayed shock is limited. Only two out of four rats showed selective changes in sensitivity, although in both cases oxycodone produced an increase in sensitivity (at 0.56 mg/kg for Rat E16 and 0.3-1.0mg/kg for Rat E17).

Effects of Methylphenidate

Figure 19 shows effects of methylphenidate on mean response ratios from sessions in which saline and select doses of methylphenidate were administered. After saline administration, Rats E12 and E14 show no changes in response ratios across delays to shock: sensitivity was near 0. Alternatively, Rats E13 and E15 show changes in responding that track changes in the response ratio, sensitivity was 0.41 and 0.15, respectively. Effects of methylphenidate varied across rats. For Rat E12, there were no substantial changes in response ratios across doses of methylphenidate. For Rat E13 all doses of methylphenidate shifted responses ratios toward the standard lever and decreased the degree to which response ratios changed as a function the delay

to shock compared to at saline, resulting in a decrease in sensitivity and bias. For Rats E14 and E15, methylphenidate produced an increase in the degree to which response ratios changed as a function of delay to shock at 5.6 mg/kg only (sensitivity increased); however, for Rat E14 there was also a substantial increase in responding on the standard lever overall (bias decreased).

Figure 20 shows dose-effect functions for sensitivity, bias, and initial-link response rates. Rat E12 showed no dose-related or substantial changes in sensitivity, bias, or initial-link response rates. For Rat E13, responding became less sensitive to the delay to shock at all doses of methylphenidate that were tested; however, these changes were also accompanied by an increase in bias for the standard lever and a modest decrease in initial-link response rates. Conversely, for Rats E14 and E15 responding became more sensitive to the delay to shock at higher doses of methylphenidate (5.6 and 10.0 mg/kg). For Rat E14 these changes were accompanied by decreased response rates; however, for Rat E15, methylphenidate increased sensitivity at doses that did not substantially affect bias or response rates. Thus, only one out of four rats show what could be described as dose-related, selective effects of methylphenidate on sensitivity to delayed shock.

The percent of cycles completed each session at each dose is shown in Table 14. Every session was completed for all rats at control, saline, and low doses of methylphenidate. Only one rat, Rat E12, showed a decrease in the percentage of chains completed at 5.6 mg/kg and three rats (Rats E12, E13, and E14) showed a substantial decrease in the percentage of chains completed at 10.0 mg/kg.

Discussion

In Experiment 2 an exploratory approach was taken to develop a concurrent-chains procedure suitable for studying changes in choice as a function of delayed shock. In total, three

versions of the concurrent-chains procedures were arranged. The first procedure (Experiment 2A) was a within-session procedure, in which the delay to shock associated with one of the terminal links changed across blocks within each session. The second procedure (Experiment 2B) was a rapid-acquisition procedure, in which the delay to shock associated with one of the terminal links was changed across sessions but remained constant within each session. The third procedure (Experiment 2C) was a concurrent-chains version of the conflicting choice procedure used in Experiment 1, in which one terminal link produced a large reinforcer plus a delayed shock and the other terminal link produced a small reinforcer alone. All three variations of the concurrent-chains procedure were insufficient to generate a baseline of responding that showed sensitivity to changes in the delay to shock arranged within or across sessions.

In Experiment 2D, the within-session procedure from Experiment 2A was adapted in a final attempt to bring choice under control of the relative delays to shock. A within-session procedure was used in which the delay to shock associated with one of the terminal links changed across blocks within each session. Overall, sensitivity to delay to shock was low in Experiment 2D. Similar procedures have been used with rats to characterize sensitivity to different dimensions of reinforcement, including amount (Hunt et al., 2020; van Heukelom, 2021) and delay (Aparicio et al., 2019; Blejewski et al., 2023; Orduna et al., 2013) in isolation and in combination (Hughes et al., 2021; Ito & Asaki, 1982; Pope et al., 2020). Generally, these studies demonstrate a minimum sensitivity of 0.4, regardless of the dimension(s) of reinforcement involved (note that sensitivity is typically even higher in studies with pigeons; e.g., Pitts et al., 2016).

The procedures used throughout Experiment 2 failed to generate changes in initial-link response allocation that tracked changes in the relative delays to shock in each terminal link.

This insensitivity persisted despite manipulation of numerous variables that have been shown to affect choice on concurrent-chains procedures, including changes to the initial links (e.g., mean initial link duration, COD duration), terminal links (e.g., the relative and absolute delays to shock in the terminal link, inclusion of delay-correlated stimuli), interchain interval (e.g., interchain interval duration), and shock intensity (e.g., mA and duration).

One potential source of interference with the development of sensitive responding could have been the dependent scheduling arranged in the initial links (Stubbs & Pliskoff, 1969). One benefit of using a dependent schedule is that it ensures equal exposure to each of the terminal-link outcomes; however, this type of scheduling also requires the rat to respond on both levers to complete the session. Thus, perhaps the dependent schedule produced a pattern of responding that resulted in response ratios near indifference (e.g., bouts of responding that alternated between levers). This explanation seems insufficient given the numerous published studies that have demonstrated sensitivity of responding under procedures that have used dependent schedules (e.g., Hughes et al., 2021; Yates et al., 2019).

Despite the lack of sensitivity shown in the baseline procedure of Experiment 2D, oxycodone and methylphenidate were administered to determine their effects. It was possible that even with patterns of baseline responding that showed no sensitivity to delayed shock, drugs could dose-dependently affect sensitivity. Of course, this was not the ideal baseline, as only increases in sensitivity could be detected for most rats. Administration of oxycodone increased sensitivity to delay under at least one dose for three out of four rats. Alternatively, administration of methylphenidate decreased sensitivity for one (out of four) rats and increased sensitivity for two rats. However, effects of both drugs should be interpreted cautiously: in many cases, drug-

related changes in sensitivity were accompanied by disruptions in other measures of behavior (e.g., response rates).

The baseline of Experiment 2 was perhaps in the unique position to test baseline-dependent effects of oxycodone and methylphenidate. The notion that drug effects on behavior depend on the baseline characteristics of responding is not new (see Branch, 1984 for an discussion of *rate dependency*); however, it has gained recent attention as a relevant determinant when studying drug effects on variables related to self-control. Pope et al., (2020) arranged a concurrent-chains procedure in which mice responded to produce smaller, sooner and larger, later reinforcers. Effects of *d*-amphetamine on sensitivity to each of the manipulated dimensions – reinforcement amount and reinforcement delay – depended on the baseline sensitivity for each. *d*-Amphetamine increased sensitivity to both amount and delay of reinforcement when baseline sensitivity was low (<0.40) and decreased sensitivity when it was high (baseline sensitivity was controlled by adding or removing delay-correlated stimuli). Under the baseline conditions in Experiment 2D, sensitivity to delayed shock was less than 0.4 for all rats. Thus, it might be predicted that methylphenidate would increase sensitivity to delayed shock. There is limited evidence to support this prediction. Rat E13 showed the highest sensitivity of responding under baseline conditions, and methylphenidate typically decreased sensitivity for this rat. Alternatively, Rats E12, E14, and E15 showed no sensitivity of responding under baseline conditions and methylphenidate produced an increase in sensitivity under at least one dose for Rats E14 and E15. At the very least, these findings suggest that researchers interested in drug effects on self-control should consider how baseline characteristics of responding interact with drug effects on choice.

General Discussion

Two experiments were conducted with rats to study how choice between outcomes that produced both reinforcing and aversive outcomes changed as a function of the delay to the aversive outcome. In Experiment 1, a discrete-trial, conflicting-choice procedure was used. Rats chose between a small reinforcer alone (the single-valence outcome) and a large reinforcer plus a delayed shock (the dual-valence outcome). The delay to shock was lowered across blocks of each session. Discrete-trial procedures like this one have been commonly used in behavioral pharmacology to study drug effects on delay discounting (de Wit & Mitchell, 2010) and the conflicting-choice version of the procedure showed promise as a baseline for studying the sensitivity of choice to delayed aversive outcomes (Liley et al., 2019; Rodriguez et al., 2018). Under this procedure, responding was well-described by a hyperbolic discounting function (Eq. 1; Mazur, 1987). Effects of oxycodone on choice of the single-valence lever (the self-control option) were modest and depended on dose. Low doses of oxycodone slightly decreased choice of the single-valence lever and high doses increased choice of the single-valence lever, even in the no-shock block. Effects of methylphenidate were much more robust and reliable across rats: methylphenidate increased choice of the single-valence lever (i.e., increased self-control).

In Experiment 2, an exploratory approach was taken to develop a concurrent-chains procedure for studying drug effects on choices that produced immediate reinforcement and delayed shock. None of the variations of the concurrent-chains procedure were sufficient to generate changes in responding that were sensitive to changes in the relative delays to shock arranged in the terminal links. Drug effects on sensitivity to delayed shock varied across rats and were typically accompanied by disruption of other dimensions of behavior (e.g., response rates).

A different quantitative approach was taken to describe changes in choice in each experiment. In Experiment 1, a hyperbolic discounting function (Eq. 1; Mazur, 1987) was fit to the data. Under baseline conditions, Eq. 1 provided a good fit overall: R^2 was > 80% for three out of four rats. Fits of Eq. 1 remained good after drug administration under at least one dose of each drug. In Experiment 2, a version of the generalized matching law (Eq. 4) was fit to the data. Across all procedures used in Experiment 2, Eq. 4 provided a poor fit to the data: R^2 rarely exceeded 80%; however, this is not surprising given that control of response allocation by the relative delays to shock was not clearly demonstrated in Experiment 2.

Drug Effects on Self-Control with Aversive Events

Oxycodone. Across both experiments, effects of oxycodone on choice remain difficult to interpret. In Experiment 1, oxycodone produced bitonic changes in choice: low doses decreased choice of the single-valence lever and high doses increased choice of the single-valence lever; however, drug-related changes in choice were relatively small given the variability under baseline. In Experiment 2, oxycodone did not produce selective, or systematic changes in sensitivity for three out of four rats. One interpretation of these findings is that oxycodone does not directly affect sensitivity to delayed shock and that any effects of oxycodone resulted from the disruption of control by other behavioral mechanisms (e.g., sensitivity to reinforcement amount). Indeed, in one study with human participants, oxycodone did not affect choice on any hypothetical discounting tasks (Zacny & de Wit, 2009). It does seem surprising that oxycodone would not affect sensitivity to delayed shock, a noxious stimulus, especially considering the growing evidence that oxycodone does produce systematic changes in sensitivity to different dimensions of reinforcement, including amount (Hunt et al., 2020; Van Heukelom, 2021) and delay (Blejewski et al., 2023).

Methylphenidate. In Experiment 1, methylphenidate increased choice of the single-valence lever (i.e., increased self-control). In Experiment 2, effects of methylphenidate varied, but two out of four rats showed an increase in sensitivity to delayed shock (although this effect was only selective for one rat). These findings seem consistent and provide cursory evidence that methylphenidate increases self-control with aversive events.

Determinants of Choice with Aversive Outcomes

There are several variables that could have contributed to changes in responding that may have interfered with the ability to detect orderly drug effects in both experiments.

Habituation. It is possible that with repeated exposure to the procedures described in Experiments 1 and 2 habituation to the shock occurred for some rats (Chen & Amsel, 1982). That is, the aversive function of shock could have decreased due to repeated exposure. In Experiment 1, shifts in patterns of responding across sessions were evident, and adjustments to the parameters of shock were frequently required to re-establish a behavioral baseline. These shifts in baseline responding are not ideal and limit the validity of within-subject comparisons across drugs. In Experiment 2, if habituation to shock occurred it could not be readily detected. Changes in response rates were not evident after adjustments were made to shock intensity (data not shown). It is possible that delayed shock did not function as an aversive stimulus for some rats and thus response allocation remained near indifference because each lever produced an equivalent number of pellets.

Schedule Requirements. In Experiment 1, only a single response was required to produce the outcomes associated with each lever. The benefit of this approach is that it maintains the temporal contiguity between the response and its consequences. However, the limitation of only requiring a single response is that response rates cannot be measured as a dependent

variable. Conversely, in Experiment 2, responding had to satisfy an interval schedule to produce the terminal links (during which the outcomes were delivered). There are a number of benefits to this approach. First, interval schedules allow the experimenter to control the rate of entry into the terminal links (assuming a minimum rate of responding). Second, response rates can be interpreted as an indication of generally disruption to responding. However, using an interval schedule also introduces an additional delay between the initiation of responding (the first response in the initial link) and the eventual delivery of the consequence (in the terminal link). Indeed, the relative durations of the initial and terminal links have been shown to affect choice (the initial link effect) and thus the initial link interval was kept short (initially 10 s, which was then lowered to 5 s in Experiment 2D).

Conclusions

The study of self-control has typically overlooked sensitivity to delayed, aversive outcomes as a critical variable. Many socially significant issues involve an insensitivity to delayed aversive outcomes: they bear little impact at the time a choice is made. It is difficult to fault researchers for neglecting this area of research: the experimental analysis of punishment requires careful consideration of numerous variables. The experiments described above highlight at least one procedure that may be useful for advancing the study of self-control with aversive events and at least several procedures that should be abandoned.

References

Ainslie, G. (1974). Impulse control in pigeons. *Journal of the Experimental Analysis of Behavior, 21,* 485–489.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*. https://doi.org/10.1176/appi.books.9780890425596

Anderson, K. G., Woolverton, W. L. (2005). Effects of clomipramine on self-control choice in Lewis and Fischer 344 rats. *Pharmacology Biochem Behavior, 80,* 387–393.

Aparicio, C. F., Hennigan, P. J., Mulligan, L. J., & Alonso-Alvarez, A. (2019) Spontaneously hypertensive (SHR) rats choose more impulsively than Wistar-Kyoto (WKY) rats on a delay discounting task. *Behavioural Brain Research, 364*, 480-493. https://doi.org/10.1016/j.bbr.2017.09.040.

Autor, S. M. (1969). The strength of conditioned reinforcers as a function of frequency and probability of reinforcement. In D. P. Hendry (Ed.), *Conditioned reinforcement* (pp. 127–162). Homewood, IL: Dorsey Press.

Azrin, N. H. (1960). Effects of punishment intensity during variable interval reinforcement. *Journal of the Experimental Analysis of Behavior*, *3*, 123-142. doi: 10.1901/jeab.1960.3-123

Badia, P., Culbertson, S., & Harsh, J. (1973). Choice of longer or stronger signalled shock over shorter or weaker unsignalled shock. *Journal of the Experimental Analysis of Behavior, 19*, 25-32.

Banks, R. K., & Vogel-Sprott, M. (1965). Effect of delayed punishment on an immediately rewarded response in humans. *Journal of Experimental Psychology, 70*(4), 357–359. https://doi.org/10.1037/h0022233

Baron, A. (1965). Delayed punishment of a runway response. *Journal of Comparative and Physiological Psychology, 60,* 131-134.

Baum, W. M. (1974). On two types of deviation from the matching law: Bias and undermatching. *Journal of the Experimental Analysis of Behavior, 22*, 231-242.

Beardsley, P. M., Aceto, M. D., Cook, C.D., Bowman, E. R., Newman, J. L., Harris, L. S. (2004). Discriminative stimulus, reinforcing, physical dependence, and antinociceptive effects of oxycodone in mice, rats, and rhesus monkeys. *Experimental and Clinical Psychopharmacology, 12*, 163–172.

Bickel, W. K., Odum, A. L., & Madden, G. J. (1999). Impulsivity and cigarette smoking: Delay discounting in current, never, and ex-smokers. *Psychopharmacology, 146,* 447-454.

Blejewski, R. C., Van Heukelom, J. T., Langford, J. S., Hunt, K. H., Rinkert, I. R., Wagner, T. J., ... & Hughes, C. E. (2023). Behavioral mechanisms of oxycodone's effects in female and male rats: Reinforcement delay and impulsive choice. *Experimental and Clinical Psychopharmacology*.

Bouzas, A. (1978). The relative law of effect: Effects of shock intensity on response strength in multiple schedules. *Journal of the Experimental Analysis of Behavior, 30,* 307–314.

Bradley, C. (1937). The behavior of children receiving benzedrine. *American Journal of Psychiatry,* 94, 577–585.

Branch, M. (2006). How research in behavioral pharmacology informs behavioral science. *Journal of the Experimental Analysis of Behavior*, *85*(3), 407-423. https://doi.org/10.1901/jeab.2006.130-04

Branch, M. N., Nicholson, G., & Dworkin, S. I. (1977). Punishment-specific effects of pentobarbital: dependency on the type of punisher. *Journal of the Experimental Analysis of Behavior, 28*(3), 285–293. https://doi.org/10.1901/jeab.1977.28-285

Byrne, T. & Poling, A. (2017). Behavioral effects of delayed timeouts from reinforcement. *Journal of the Experimental Analysis of Behavior, 107,* 208-217.

Camp, D. S., Raymond, G. A., & Church, R. M. (1967). Temporal relationship between response and punishment. *Journal of Experimental Psychology, 74,* 114-123.

Cardinal, R. N., Robbins, T. W., & Everitt, B. J. (2000). The effects of *d*-amphetamine, chlordiazepoxide, □-flupenthixol and behavioural manipulations on choice of signalled and unsignalled delayed reinforcement in rats. *Psychopharmacology, 152*, 362-375.

Carlson, R. G., Nahhas, R. W., Martins, S. S., Daniulaityte, R. (2015). Predictors of transition to heroin use among initially non-opioid dependent illicit pharmaceutical opioid users: A natural history study. *Drug Alcohol Depend, 160,* 127-134. doi:10.1016/j.drugalcdep.2015.12.026.

Carroll, M.E., Anker, J.J., Mach, J.L, Newman, J.L, & Perry, J.L. (2010). Delay discounting as a predictor of drug abuse. In G.J. Madden & W.K. Bickel (Eds.) *Impulsivity: The behavioral and neurological science of discounting* (pp. 243-272). Washington, DC: APA.

Coffey, S. F., Gudleski, G. D., Saladin, M. E., & Brady, K. T. (2003). Impulsivity and rapid discounting of delayed hypothetical rewards in cocaine-dependent individuals. *Experimental and Clinical Psychopharmacology, 11,* 18-25.

Chen, J.-S., & Amsel, A. (1982). Habituation to shock and learned persistence in preweanling, juvenile, and adult rats. *Journal of Experimental Psychology: Animal Behavior Processes, 8*(2), 113.

Christensen, D. R., & Grace, R. C. (2009). Response allocation in a rapid-acquisition concurrent-chains procedure: Effects of overall terminal-link duration. *Behavioural Processes, 81*(2), 233-237. https://doi.org/ 10.1016/j.beproc.2008.01.006

Chung, S-H., & Herrnstein, R. J. (1967). Choice and delay of reinforcement. *Journal of the Experimental Analysis of Behavior, 10*, 67–74.

Critchfield, T. S., Paletz, E. M., MacAleese, K. R., & Newland, M. C. (2003). Punishment in human choice: Direct or competitive suppression? *Journal of the Experimental Analysis of Behavior, 80*, 1–27. https://doi.org/10.1901/jeab.2003.80-1

Davison, M. C. (1987). The analysis of concurrent-chain performance. In M. L. Commons, J. E. Mazur, J. A. Nevin, & H. Rachlin (Eds.), *Quantitative analyses of behavior: The effect of delay and of intervening events on reinforcement value* (Vol. 5, pp. 225-241). Erlbaum. https://doi.org/10.4324/9781315825502

Davison, M., & Baum, W. M. (2000). Choice in a variable environment: Every reinforcer counts. *Journal of the Experimental Analysis of Behavior, 74*, 1–24.

Davison, M., & Baum, W. M. (2003). Every reinforcer counts: Reinforcer magnitude and local preference. *Journal of the Experimental Analysis of Behavior, 80*, 95–129.

Davison, M., & Baum, W. M. (2007). Local effects of delayed food. *Journal of the Experimental Analysis of Behavior, 87*, 241–260.

Davison M, McCarthy D (1988). *The Matching Law: A Research Review*. Hillsdale: Lawrence Erlbaum Associates, Inc.

de Villiers, P. (1977). Choice in concurrent schedules and a quantitative formulation of the law of effect. In W. K. Honig, & J. E. R. Staddon (Eds.), *Handbook of operant behavior*, Englewood Cliffs, NJ: Prentice Hall.

de Wit, H. & Mitchell, S. H. (2010). Drug Effects on Delay Discounting. In G.J. Madden & W.K. Bickel (Eds.) *Impulsivity: The behavioral and neurological science of discounting* (pp. 213-242). Washington, DC: APA.

Deluty, M. Z. (1976). Choice and the rate of punishment in concurrent schedules. *Journal of the Experimental Analysis of Behavior, 25*, 75–80.

Deluty, M. Z. (1978). Self-control and impulsiveness involving aversive events. *Journal of Experimental Psychology: Animal Behavior Processes, 4*, 250–266.

Deluty, M. Z., Whitehouse, W.G., Mellitz, M., & Hineline, P.N. (1983). Self-control and commitment involving aversive events. *Behaviour Analysis Letters, 3*, 213-219.

Dumas, A. D. (2014). *Choice between reinforcers with and without delayed shock*. Unpublished master's thesis, West Virginia University, Morgantown, West Virginia.

Eppolito, A. K., France, C.P., Gerak, L. R. (2013). Effects of acute and chronic morphine on delay discounting in pigeons. *Journal of the Experimental Analysis of Behavior, 99*, 277–289.

Epstein, R. (1984). An effect of immediate reinforcement and delayed punishment, with possible implications for self-control. *Journal of Behavior Therapy and Experimental Psychiatry, 15*, 291-298.

Estes, W. K. (1944). An experimental study of punishment. *Psychological Monographs, 57* (Serial No. 3).

Estle, S. J., Green, L., Myerson, J., & Holt, D. D. (2006). Differential effects of amount on temporal and probability discounting of gains and losses. *Memory & Cognition, 34*(4), 914–928.

Evenden, J., & Ryan, C. (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.

Fantino, E. (1969). Choice and rate of reinforcement. *Journal of the Experimental Analysis of Behavior, 12*(5), 723- 730. https://doi.org/10.1901/jeab.1969.12-723

Farley, J., & Fantino, E. (1978). The symmetrical law of effect and the matching relation in choice behavior. *Journal of the Experimental Analysis of Behavior, 29*(1), 37–60. https://doi.org/10.1901/jeab.1978.29-37

Fleshler, M., & Hoffman, H. S. (1962). A progression for generating variable-interval schedules. *Journal of the Experimental Analysis of Behavior, 5*, 529–530.

Fox, A. E., Visser, E. J., Nicholson, A. M. (2019). Interventions aimed at changing impulsive choice in rats: Effects of immediate and relatively long delay to reward training. *Behavioral Processes, 158*, 126-136. https://doi.org/10.1016/j.beproc.2018.11.009

Geller, I., Kulak, J. T., Seifter, J. (1962). The effects of chlordiazepoxide on a punishment discrimination. *Psychopharmacologia, 3*, 374-385. https://doi.org/10.1007/BF00408322

Giordano, L. A., Bickel, W. K., Loewenstein, G., Jacobs, E. A., Marsch, L., Badger, G. J. (2002) Mild opioid deprivation increases the degree that opioid-dependent outpatients discount delayed heroin and money. *Psychopharmacology, 163*, 174–182.

Gonçalves, F. L., & Silva, M. T. A. (2015). Comparing individual delay discounting of gains and losses. *Psychology & Neuroscience, 8*(2), 267.

Grace, R. C. (1994). A Contextual Model of Concurrent-Chains Choice. *Journal of the Experimental Analysis of Behavior, 61,* 113-129.

Grace, R. C., Bragason, O., & McLean, A. P. (2003). Rapid acquisition of preference in concurrent chains. *Journal of the Experimental Analysis of Behavior, 80,* 235–252. http://dx.doi.org/10.1901/jeab.2003.80-235

Grace, R. C., & Nevin, J. A. (1999). Timing and choice in concurrent chains. *Behavioural Processes, 45*(1-3), 115-127.

Green, L., & Rachlin, H. (1996). Commitment using punishment. *Journal of the Experimental Analysis of Behavior, 65*(3), 593-601.

Harvey-Lewis, C., Perdrizet, J., & Franklin, K. B. J. (2012). The effect of morphine dependence on impulsive choice in rats. *Psychopharmacology, 223*(4), 477-487.

Herman, R. L., &: Azrin, N. H. (1964). Punishment by noise in an alternative response situation. *Journal of the Experimental Analysis of Behavior, 7,* 185-188. doi: 10.190 l/jeab.1964. 7-185

Herrnstein, R. J. (1961). Relative and absolute strength of response as a function of frequency of reinforcement. *Journal of the Experimental Analysis of Behavior, 4,* 267–272.

Herrnstein, R. (1964). Aperiodicity as a factor in choice. *Journal of the Experimental Analysis of Behavior, 7*(2), 179-182. https://doi.org/10.1901/jeab.1964.7-179

Herrnstein, R. J. (1970). On the law of effect. *Journal of the Experimental Analysis of Behavior, 13,* 243-266.

Hineline, P. N., & Rosales-Ruiz, J. (2012). Behavior in relation to aversive events: Punishment and negative reinforcement. In G. J. Madden, W. V. Dube, T. Hackenberg, G. Hanley, &

K. A. Lattal (Eds.), *APA handbook of behavior analysis* (pp. 483–512). Washington, DC: American Psychological Association

Holz, W. C. (1968). Punishment and rate of positive reinforcement. *Journal of the Experimental Analysis of Behavior, 11*, 285-292.

Hughes, C. E., Langford, J. S., Van Heukelom, J., Blejewski, R., Pitts, R. C. (2022). A method for studying reinforcement factors controlling impulsive choice for use in behavioral neuroscience. *Journal of the Experimental Analysis of Behavior*, *117* (3), 363-383. https://doi.org/10.1002/jeab.751

Hunt, K. H., Hughes, C. E., & Pitts, R. C. (2020). Effects of oxycodone on sensitivity to reinforcement magnitude: Implications for effects of opioids on impulsive and risky choice. *Behavioural Pharmacology*, *31*(2-3), 221-232. https://doi.org/10.1097/FBP.0000000000000543

Ito, M., & Asaki, K. (1982). Choice behavior of rats in a concurrent-chains schedule: Amount and delay of reinforcement. *Journal of the Experimental Analysis of Behavior, 37*(3), 383-392. https://doi.org/10.1901/jeab.1982.37-383

Jeffery, D. R. & Barrett, J. E. (1979). Effects of chlordiazepoxide on comparable rates of punished and unpunished responding. Psychopharmacology, 64, 9-11. https://doi.org/10.1007/BF00427337

Johnson MW, Bickel WK, Baker F (2007) Moderate drug use and delay discounting: a comparison of heavy, light, and never smokers. *Experimental and Clinical Psychopharmacology, 15*, 187–194.

Kahneman, D., & Tversky, A. (1979). Prospect theory: An analysis of decision under risk. *Econometrica, 47*, 263– 292. doi: 10.2307/1914185

Kamin, L. J. (1959). The delay-of-punishment gradient. *Journal of Comparative and Physiological Psychology, 52,* 44-51.

Kendall, T., Taylor, E., Perez, A., & Taylor, C. (2008). Diagnosis and management of attention-deficit/hyperactivity disorder in children, young people, and adults: summary of NICE guidance. *Bmj*, 337.

Kieres, A. K., Hausknecht, K. A., Farrar, A. M., Acheson, A., de Wit, H., Richards, J. B. (2004). Effects of morphine and naltrexone on impulsive decision making in rats. *Psychopharmacology, 173*, 167-174.

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,* 78-87.

Kirby, N. L., & 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.

Klapes B, Riley S, & McDowell JJ (2018). Toward a contemporary quantitative model of punishment. *Journal of the Experimental Analysis of Behavior*, 109(2), 336–348.

Krebs, C. A., Reilly, W. J., Anderson, K. G. (2016) Reinforcer magnitude affects delay discounting and influences effects of d-amphetamine in rats. *Behavioral Processes, 130*, 39-45. doi:10.1016/j.beproc.2016.07.004

Kuroda, T., Cançado, C. R. X., & Podlesnik, C. A. (2018). Relative effects of reinforcement and punishment on human choice. *European Journal of Behavior Analysis, 19:1*, 125-148, DOI: 10.1080/15021149.2018.1465754

Kyonka, E. G. E., & Grace, R. C. (2008). Rapid acquisition of preference in concurrent chains when alternatives differ on multiple dimensions of reinforcement. *Journal of the Experimental Analysis of Behavior, 89,* 49–69. http://dx.doi.org/10.1901/jeab.2008.89-49

Lattal, K. A. (1984). Signal functions in delayed reinforcement. *Journal of the Experimental Analysis of Behavior, 42*(2), 239-253.

Lattal, K. A. (1987). Considerations in the experimental analysis of reinforcement delay. In M. L. Commons, J. Mazur, J. A. Nevin, & H. Rachlin (Eds.), *Quantitative studies of operant behavior: The effect of delay and of intervening events on reinforcement value* (pp. 107–123). New York: Erlbaum.

Lerman, D. C., & Vorndran, C. M. (2002). On the status of knowledge for using punishment implications for treating behavior disorders. *Journal of Applied Behavior Analysis, 35(4),* 431-464.

Liley, A. E., Gabriel, DBK, Sable, HJ, Simon, NW. (2019) Sex Differences and Effects of Predictive Cues on Delayed Punishment Discounting. *eNeuro*,6(4). doi: 10.1523/ENEURO.0225-19.2019.

Logue, A. W. (1988). Research on self-control: An integrating framework. *Behavioral and Brain Sciences, 11*, 665–679.

Logue, A. W., Tobin H, Chelonis JJ, Wang RY, Geary N, Schachter S (1992) Cocaine decreases self-control in rats: a preliminary report. *Psychopharmacology, 109,* 245–247

Madden, G. J., Bickel, W. K., & Jacobs, E. A. (1999). Discounting of delayed rewards in opioid dependent outpatients: Exponential or hyperbolic discounting functions? *Experimental and Clinical Psychopharmacology, 3,* 284-293.

Madden, G. J., Petry, N. M., Badger, G. J., & Bickel, W. K. (1997). Impulsive and self-control choices in opioid-dependent patients and non-drug-using control participants: Drug and monetary rewards. *Experimental and Clinical Psychopharmacology, 5,* 256-262.

Madden, G. J., & Johnson, P. S. (2010). A delay-discounting primer. In G. J. Madden & W. K. Bickel (Eds.), *Impulsivity* (pp. 11–37). Washington, DC: American Psychological Association.

Magoon, M. A., & Critchfield, T. S. (2008). Concurrent schedules of positive and negative reinforcement: Differential-impact and differential-outcomes hypotheses. *Journal of the Experimental Analysis of Behavior, 90,* 1–22. doi: 10.1901/jeab.2008.90-1

Maguire, D. R., Gerak, L. R., France, C. P. (2016). Effect of daily morphine administration and its discontinuation on delay discounting of food in rhesus monkeys. *Behavioral Pharmacology, 27,* 155–164.

Maguire, D. R., Henson, C., & France, C. P. (2014). Effects of amphetamine on delay discounting in rats depend upon the manner in which delay is varied. *Neuropharmacology, 87,* 173-179. https://doi.org/10.1016/j.neuropharm.2014.04.012

Manwaring, J. L., Green L, Myerson J, Strube MJ, Wilfley DE. (2011). Discounting of various types of rewards by women with and without binge eating disorder: Evidence for general rather than specific differences. *Psychological Record, 61*(4), 561–582.

Mazur, J. E. (1987). An adjusting procedure for studying delayed reinforcement. In: Commons ML, Mazur JE, Nevin JA, Rachlin H, editors. *Quantitative Analyses of Behavior: The Effect of Delay and of Intervening Events on Reinforcement Value* (pp. 55–73). Vol. 5. Erlbaum; Hillsdale, NJ.

Mazur, J. E. (2013) *Learning and Behavior, 7th Edition*. New York, NY: Pearson.

McDowell, J. J. (1988). Matching theory in natural human environments. *The Behavior Analyst, 11*, 95-109.

McMillan, D. E. (1973). Drugs and punished responding I: Rate-dependent effects under multiple schedules. *Journal of the Experimental Analysis of Behavior, 19*(1), 133-145. https://doi.org/10.1901/jeab.1973.19-133

Miczek, K. A. (1973). Effects of scopolamine, amphetamine and chlordiazepoxide on punishment. *Psychopharmacologia, 28*(4), 373-389. https://doi.org/10.1007/BF00422757

Mischel, W. & Ebbesen, E. E. (1970). Attention in delay of gratification. *Journal of Personality and Social Psychology, 16*, 329-337.

Mischel, W., Grusec, J., & Masters, J. C. (1969). Effects of expected delay time on the subjective value of rewards and punishments. *Journal of Personality and Social Psychology, 11*(4), 363–373. https://doi.org/10.1037/h0027265.

Monterosso, J., Ainslie, G. (1999). Beyond discounting: possible experimental models of impulse control. *Psychopharmacology, 146*, 339–347. https://doi.org/10.1007/PL00005480

Myer, J. S., Ricci, D. (1968). Delay of punishment gradients for the goldfish. *Journal of comparative and physiological psychology, 66*(2), 417.

National Institute on Drug Abuse (2021) Opioid Overdose Crisis. https://nida.nih.gov/drug-topics/opioids/opioid-overdose-crisis. Accessed: 12/11/21

Odum, A. L. (2011). Delay discounting: I'm a k, you're a k. *Journal of the Experimental Analysis of Behavior, 96*, 427–439.

Oliveira, L., Green, L., & Myerson, J. (2014). Pigeons' delay discounting functions established using a concurrent-chains procedure. *Journal of the Experimental Analysis of Behavior, 102*, 151–161. http://dx.doi.org/10.1002/jeab.97

Orduña, V., Valencia-Torres, L., Cruz, G., Bouzas, A. (2013) Sensitivity to delay is affected by magnitude of reinforcement in rats. *Behavioural Processes, 98*, 8–24. https://doi.org/10.1016/j.beproc.2013.04.011

Orduña,V. (2015). Impulsivity and sensitivity to amount and delay of reinforcement in an animal model of ADHD, *Behav. Brain Res. 294*, 62–71.

Paine, T. A., Dringenberg, H. C., Olmstead, M. C. (2003). Effects of chronic cocaine on impulsivity: Relation to cortical serotonin mechanisms. *Behavioural Brain Research, 147*(1–2), 135–147.

Pattij, T., Schetters D, Janssen MC, Wiskerke J, Schoffelmeer AN (2009). Acute effects of morphine on distinct forms of impulsive behavior in rats. *Psychopharmacology (Berl) 205*:489–502.

Perone, M. (1991). Experimental design in the analysis of free-operant behavior. In I. Iverson & K. A. Lattal (Eds.), *Experimental analysis of behavior* (Part 1, pp. 135-168). Elsevier. https://doi.org/10.1007/978-1-4899-1947-2_1

Perry, J. L., & Carroll, M. E. (2008). The role of impulsive behavior in drug abuse. *Psychopharmacology*, *200*, 1–26.

Perry, J. L., Stairs, D. J., & Bardo, M. T. (2008). Impulsive choice and environmental enrichment: effects of d-amphetamine and methylphenidate. *Behavioural brain research, 193*(1), 48-54.

Pierce, W. D., & Cheney, C. D. (2008). *Behavior Analysis and Learning* (4th ed.). Psychology Press. p. 193

Pitts, R. C. (2014). Reconsidering the concept of behavioral mechanisms of drug action. *Journal of the Experimental Analysis of Behavior, 101*, 422–441. http://dx.doi.org/10.1002/jeab.80

Pitts, R. C., Cummings, C. W., Cummings., C., Woodcock, R. L., & Hughes, C. E. (2016). Effects of methylphenidate on sensitivity to reinforcement delay and to reinforcement amount in pigeons: Implications for impulsive choice. *Experimental and Clinical Psychopharmacology*, *24*, 464-476.

Pitts, R. C., & Febbo, S. M. (2004). Quantitative analyses of methamphetamine's effects on self-control choices: Implications for elucidating behavioral mechanisms of drug action. *Behavioural Processes, 66*, 213–233. http://dx.doi.org/10.1016/j.beproc.2004.03.006

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*, 297-314.

Pope, D. A., Hutsell, B., & Newland, M. C. (2020). Baseline-dependency: How genotype and signaled delays influence amphetamine's effects on delay discounting. *Pharmacology Biochemistry and Behavior, 199*, 173070.

Rachlin, H. (1974). Self-control. *Behaviorism, 2*, 94- 107.

Rachlin, H., Raineri, A., & Cross, D. (1991). Subjective probability and delay. *Journal of the Experimental Analysis of Behavior, 55*, 233–244.

Rankin, K. S. (2014). *Effects of d-amphetamine on probabilistic choice.* (Unpublished master's thesis). University of North Carolina Wilmington.

Rasmussen, E. B., & Newland, M. C. (2008). Asymmetry of reinforcement and punishment in human choice. *Journal of the Experimental Analysis of Behavior, 89*, 157–167. doi: 10.1901/jeab.2008.89-15

Renda, C. R., Rung, J. M., Peck, S., Madden, G. J. (2020). Reducing impulsive choice VII: effects of duration of delay-exposure training. *Animal Cognition*. doi:10.1007/s10071-020-01412-0

Renner, K. E. (1966). Temporal Integration: The relative utility of immediate versus delayed reward and punishment. *Journal of Experimental Psychology, 72(*6), 901-903.

Reynolds, B. (2006). A review of delay-discounting research with humans: Relations to drug use and gambling. *Behavioural Pharmacology, 17*, 651–667.

Reynolds, B., Patak, M., Shroff, P., Penfold, R., Melanko, S., Duhig, A. (2007). Laboratory and slef-report assessments of impulsive behavior in adolescent daily smokers and nonsmokers. *Experimental and Clinical Psychopharmacology, 15*(3), 264-271.

Rodewald, A. M., Hughes, C. E., & Pitts, R. C. (2010). Development and maintenance of choice in a dynamic environment. *Journal of the Experimental Analysis of Behavior, 94*, 175–195.

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

Schuster, R., & Rachlin, H. (1968). Indifference between punishment and free shock: evidence for the negative law of effect 1. *Journal of the Experimental Analysis of Behavior, 11*(6), 777-786.

Shull, R. L. and Pliskoff, S. S. (1967). Changeover delay and concurrent schedules: some effects on relative performance measures. *Journal of the Experimental Analysis of Behavior, 10,* 517-527.

Simon, N. W., Mendez, I. A., Setlow, B. (2007). Cocaine exposure causes long-term increases in impulsive choice. *Behavioral Neuroscience, 121,* 543–549.

Skinner, B. F. (1953). *Science and human behavior* (pp. 230-241). New York: Macmillan.

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

Slezak, J. M., & Anderson, K. G. (2011). Effects of acute and chronic methylphenidate on delay discounting. *Pharmacology Biochemistry and Behavior, 99*, 545–551. http://dx.doi.org/10.1016/j.pbb.2011.05.027

Slezak JM, Ricaurte GA, Tallarida RJ, Katz JL (2014). Methylphenidate and impulsivity: a comparison of effects of methylphenidate enantiomers on delay discounting in rats. *Psychopharmacology, 231*, 191–198.

Smith, A.P., Marshall, A.T., Kirkpatrick, K., 2015. Mechanisms of impulsive choice: II. Time-based interventions to improve self-control. *Behavioral Processes, 112*, 29–42. https://doi.org/10.1016/j.beproc.2014.10.010.

Stubbs, D. A., & Pliskoff, S. S. (1969). Concurrent responding with fixed relative rate of reinforcement. *Journal of the Experimental Analysis of Behavior*, *12*, 887–895. http://dx.doi.org/10.1901/jeab.1969.12-887

Squires, N., & Fantino, E. (1971). A model for choice in simple concurrent and concurrent-chains schedules. *Journal of the Experimental Analysis of Behavior, 15*, 27-38.

Ta, W.-M., Pitts, R.C., Hughes, C.E., McLean, A.P., Grace, R.C., 2008. Rapid acquisition of preference in concurrent chains: effects of d-amphetamine on sensitivity to reinforcement delay. *Journal of the Experimental Analysis of Behavior, 89,* 71-91.

Tanno, T., Maguire, D. R., Henson, C., & France, C. P. (2014). Effects of amphetamine and methylphenidate on delay discounting in rats: Interactions with order of delay presentation. *Psychopharmacology, 231*, 85-95.

Toegel, C., Holtyn, A. F., Toegel, F., Perone, M. (2022). The aversiveness of timeout from response-dependent and response independent food deliveries as a function of delivery rate. *Journal of the Experimental Analysis of Behavior, x*, 1-39.

Toegel, F. (2018). *Effects of Delay and Signals on Choice between Delayed Food Alone and Immediate Food with Delayed Shock*. Unpublished Dissertation. West Virginia University.

Trenholme, I. A. & Baron, A. (1975). Immediate and delayed punishment of human behavior by loss of reinforcement. *Learning and Motivation, 6,* 62-79.

van Gaalen, M.M., van Koten, R., Schoffelmeer, A.N.M., Vanderschuren, L.J.M.J. (2006). Critical involvement of dopaminergic neurotransmission in impulsive decision making. *Biol. Psychiatry, 60,* 66-73.

Van Heukelom, J. (2021). *Effects of oxycodone on sensitivity to reinforcement magnitude in female/male rats: implications for impulsive/risky choice*. (Unpublished master's thesis). University of North Carolina Wilmington.

Van Zee A (2009). The promotion and marketing of oxycontin: commercial triumph, public health tragedy. *American Journal of Public Health, 99,* 221–227.

Vogel-Sprott, M. D. (1966). A classical conditioning procedure to control suppression of a rewarded response punished after delay. *Psychological Reports, 19,* 91-98.

Vowles, K. E., McEntee, M. L., Julnes, P. S., Frohe, T., Ney, J. P., van der Goes, D. N. (2015). Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis. *Pain, 156*(4), 569-576. doi:10.1097/01.j.pain.0000460357.01998.f1.

Weafer. J., Mitchell, S. H., de Wit, H. (2014). Recent translational findings on impulsivity in relation to drug abuse. *Curr Addict Rep, 1,*289–300.

Woolverton, W. L., Freeman, K. B., Myerson, J., & Green, L. (2012). Suppression of cocaine self-administration in monkeys: Effects of delayed punishment. *Psychopharmacology, 220*, 509-517.

Woolverton, W. L., Meyerson, J. & Green, L. (2007). Delay discounting of cocaine by rhesus monkeys. *Experimental Clinical Psychopharmacology, 15,* 238-244.

Yates, J. R., Prior, N. A., Chitwood, M. R,, Day, H. A., Heidel, J. R., Hopkins SE, et al. (2019). Using a dependent schedule to measure risky choice in male rats: effects of d-amphetamine, methylphenidate, and methamphetamine. *Exp Clin Psychopharmacology*.

Yi, R., Mitchell, S.H., & Bickel, W.K. (2010). Delay discounting and substance abuse-dependence. In G.J. Madden & W.K. Bickel (Eds.) *Impulsivity: The behavioral and neurological science of discounting* (pp. 67-92). Washington, DC: APA.

Zacny JP, de Wit H (2009). The prescription opioid, oxycodone, does not alter behavioral measures of impulsivity in healthy volunteers. *Pharmacology Biochemistry Behavior, 94*, 108–113.

Table 1

Experiment 1: Parameters

Rat ID	Dual-Valence				Drug Sequence	
			Shock			
	Lever	Pellets	mA	ms	Drug 1	Drug 2
C24	Left	3/2	0.55/0.65	500	OXY	MPH*
C25	Left	2	0.55	500	OXY	MPH
C26	Right	2	0.45	500	MPH	--
E18	Right	2	0.65	400	MPH	OXY

Note. Assignment and outcomes associated with the dual-valence lever are listed above. In the right side of the table is listed the sequence in which each drug, oxycodone (OXY) and methylphenidate (MPH), was administered for each rat.

* Due to shifts in baseline responding after administration of oxycodone, the following parameter adjustments were made before methylphenidate was administered: dual-valence pellets lowered from 3 to 2, shock intensity raised from 0.55 to 0.65 mA.

Table 2

Experiment 1: Baseline Measures for AUC, Omissions, and No-Shock Choice

Rat ID	**Area Under the Curve**
C24	0.36 (0.10)
C25	0.49 (0.18)
C26	0.27 (0.16)
E18	0.25 (0.10)

	Omissions x Delay					
Rat ID	NS	40	20	10	5	1
C24	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.02 (0, 1)	0.02 (0, 1)	0.00 (0, 0)
C25	0.00 (0, 0)	0.02 (0, 1)	0.00 (0, 0)	0.00 (0, 0)	0.02 (0, 1)	0.00 (0, 0)
C26	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.02 (0, 1)	0.03 (0, 1)
E18	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)

	No-Shock Probe Sessions: Percent Choice of the Larger Reinforcer x Block					
Rat ID	1	2	3	4	5	6
C24	94.44 (9.62)	83.33 (28.87)	72.22 (25.46)	77.78 (38.49	83.33 (28.87)	83.33 (16.67)
C25	100.00 (0.00)	100.00 (0.00)	94.44 (9.62)	100.00 (0.00)	94.44 (9.62)	83.33 (28.87)
C26	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	88.88 (9.62)	100.00 (0.00)
E18	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	94.44 (9.62)	88.89 (9.62)	100.00 (0.00)

Note. Top portion shows area under the curve (*SD*) from the 10 stable baseline sessions. The middle portion shows the mean (range) number of omissions each block from the 10 stable baseline sessions. The bottom portion shows mean percent choice (*SD*) of the larger reinforcer across blocks of the no-shock probe sessions.

Table 3

Experiment 1: Effects of Oxycodone on Choice

	Delay to Shock (s)					
Rat C24	1	5	10	20	40	NS
Control (20)	79.17 (26.67)	60.83 (36.16)	44.00 (36.81)	35.83 (35.14)	15 (20.07)	2.50 (6.24)
Saline (9)	90.74 (14.70)	74.07 (12.58)	46.30 (48.43)	35.19 (45.98)	20.37 (36.11)	3.70 (7.35)
0.1 mg/kg (3)	66.67 (28.87)	55.56 (24.06)	0.00 (0.00)	0.00 (0.00)	5.56 (9.62)	0.00 (0.00)
0.3 mg/kg (2)	91.67 (11.79)	58.33 (5.89)	30.00 (42.43)	25.00 (11.79)	8.33 (11.79)	0.00 (0.00)
0.56 mg/kg (3)	94.44 (9.62)	100.0 (0.00)	61.11 (34.69)	44.44 (48.11)	33.33 (44.10)	22.22 (38.49)
1.0 mg/kg (3)	55.56 (25.46)	55.56 (25.46)	55.56 (50.92)	61.11 (53.58)	44.44 (50.92)	46.67 (50.33)
Rat C25	1	5	10	20	40	NS
Control (13)	97.44 (9.25)	88.46 (19.7)	52.56 (35.25)	14.10 (26.22)	2.56 (6.26)	0.00 (0.00)
Saline (4)	100.0 (0.00)	87.50 (7.98)	66.67 (45.13)	12.50 (15.96)	8.33 (9.62)	0.00 (0.00)
0.1 mg/kg (3)	100.0 (0.00)	100.0 (0.00)	66.67 (44.1)	22.22 (38.49)	5.56 (9.62)	0.00 (0.00)
0.3 mg/kg (2)	100.0 (0.00)	91.67 (5.89)	41.67 (58.93)	16.67 (23.57)	8.33 (11.79)	8.33 (11.79)
0.56 mg/kg (2)	100.0 (0.00)	100.0 (0.00)	58.33 (35.36)	41.67 (58.93)	25.00 (35.36)	18.33 (2.36)
1.0 mg/kg (2)	83.33 (23.57)	62.50 (26.52)	20.00 (0.00)	91.67 (11.79)	100.0 (0.00)	100.0 (0.00)
Rat E18	5	10	15	20	40	NS
Control (11)	88.46 (23.94)	61.54 (39.9)	21.79 (34.95)	6.41 (12.8)	5.13 (10.51)	0.00 (0.00)
Saline (3)	100.0 (0.00)	82.22 (8.39)	38.89 (53.58)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
0.03 mg/kg (2)	100.0 (0.00)	75.00 (35.36)	25.00 (35.36)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
0.1 mg/kg (2)	91.67 (11.79)	58.33 (29.46)	8.33 (11.79)	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)
0.3 mg/kg (2)	83.33 (23.57)	33.33 (11.79)	0.00 (0.00)	0.00 (0.00)	8.33 (11.79)	0.00 (0.00)
0.56 mg/kg (2)	91.67 (11.79)	75.00 (5.89)	0.00 (0.00)	0.00 (0.00)	8.33 (11.79)	0.00 (0.00)
1.0 mg/kg (2)	75.00 (11.79)	83.33 (0.00)	50.00 (23.57)	16.67 (23.57)	80.00 (0.00)	--

Note. Mean percent choice (*SD*) of the single-valence lever across blocks (columns) and doses (rows) of oxycodone. The parenthetical values next to each dose indicate the total number of sessions included in the calculations for each row.

Table 4

Experiment 1: k and R^2 as a Function of Dose of Oxycodone

	k	**R^2**
Rat C24		
Control	0.07	0.98
Saline	0.08	0.97
0.1 mg/kg	0.23	0.73
0.3 mg/kg	0.15	0.98
0.56 mg/kg	0.04	0.84
1.0 mg/kg	0.00	0.29
Rat C25		
Control	0.10	0.84
Saline	0.09	0.83
0.1 mg/kg	0.08	0.80
0.3 mg/kg	0.11	0.85
0.56 mg/kg	0.06	0.88
1.0 mg/kg	0.00	-0.17
Rat E18		
Control	0.14	0.81
Saline	0.11	0.70
0.03 mg/kg	0.14	0.75
0.1 mg/kg	0.21	0.79
0.3 mg/kg	0.36	0.90
0.56 mg/kg	0.17	0.65
1.0 mg/kg	0.01	-0.03

Table 5

Experiment 1: Effects of Oxycodone on Omissions

	Delay to shock (s)					
Rat C24	1	5	10	20	40	NS
Control (20)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.15 (0, 1)	0.05 (0, 1)	0.05 (0, 1)
Saline (9)	0.00 (0, 0)	0.00 (0, 0)	0.11 (0, 1)	0.11 (0, 1)	0.00 (0, 0)	0.00 (0, 0)
0.1 mg/kg (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.3 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.50 (0, 1)	0.00 (0, 0)	0.50 (0, 1)
0.56 mg/kg (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
1.0 mg/kg (3)	0.33 (0, 1)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
Rat C25	1	5	10	20	40	NS
Control (13)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.08 (0, 1)
Saline (4)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.1 mg/kg (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.33 (0, 1)	0.00 (0, 0)	0.00 (0, 0)
0.3 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.56 mg/kg (2)	0.50 (0, 1)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
1.0 mg/kg (2)	**3.50 (2, 5)**	**2.50 (2, 3)**	0.50 (0, 1)	**3.50 (1, 6)**	**3.50 (2, 5)**	0.50 (0, 1)
Rat E18	5	10	15	20	40	NS
Control (13)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.10 (0, 1)	0.00 (0, 0)
Saline (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.03 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.1 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.3 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.56 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
1.0 mg/kg (2)	**6.00 (6, 6)**	**3.50 (1, 6)**	0.50 (0, 1)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)

Note. Mean omissions (range) per block at control, saline, and each dose of oxycodone. The parenthetical values next to each dose indicate the total number of sessions included in the calculations for each row. Bolded values indicate instances in which omissions occurred in more than two out of six (or >33%) free-choice trials per block.

Table 6

Experiment 1: Effects of Methylphenidate on Choice

	Delay to Shock (s)					
Rat C24	1	5	10	20	40	NS
Control (11)	50.61 (40.6)	43.64 (42.7)	33.33 (33.33)	18.79 (23.72)	19.7 (16.36)	1.52 (5.03)
Saline (3)	55.56 (38.49)	33.33 (28.87)	33.33 (44.1)	16.67 (28.87)	22.22 (25.46)	0.00 (0.00)
1.0 mg/kg (2)	100.0 (0.00)	73.33 (4.71)	58.33 (58.93)	25.00 (35.36)	25.00 (11.79)	0.00 (0.00)
3.0 mg/kg (2)	66.67 (47.14)	66.67 (23.57)	66.67 (47.14)	58.33 (58.93)	58.33 (58.93)	25.00 (11.79)
5.6 mg/kg (2)	100.0 (0.00)	83.33 (11.79)	91.67 (11.79)	83.33 (23.57)	75.00 (35.36)	25.00 (35.36)
10.0 mg/kg (2)	100.0 (0.00)	100.0 (0.00)	100.0 (0.00)	100.0 (0.00)	91.67 (11.79)	50 (70.71)
Rat C25	1	5	10	20	40	NS
Control (16)	96.88 (6.72)	58.33 (40.37)	22.92 (34.89)	4.17 (9.62)	3.13 (6.72)	0.00 (0.00)
Saline (3)	100.0 (0.00)	83.33 (8.33)	27.78 (48.11)	11.11 (9.62)	11.11 (9.62)	0.00 (0.00)
0.3 mg/kg (2)	100.0 (0.00)	83.33 (11.79)	8.33 (11.79)	8.33 (11.79)	8.33 (11.79)	0.00 (0.00)
1.0 mg/kg (2)	75.00 (35.36)	41.67 (5.89)	8.33 (11.79)	33.33 (0.00)	16.67 (0.00)	0.00 (0.00)
3.0 mg/kg (4)	16.67 (23.57)	4.17 (4.17)	12.5 (15.96)	4.17 (8.33)	4.17 (8.33)	0.00 (0.00)
5.6 mg/kg (3)	94.44 (9.62)	83.33 (8.33)	83.33 (28.87)	66.67 (57.74)	55.56 (25.46)	11.11 (9.62)
10.0 mg/kg (2)	100.0 (0.00)	100.0 (0.00)	100.0 (0.00)	91.67 (11.79)	75.00 (11.79)	25.00 (11.79)
Rat C26	1	5	10	20	40	NS
Control (11)	94.44 (10.86)	97.22 (6.49)	83.33 (18.8)	55.28 (38.94)	43.06 (25.08)	0.00 (0.00)
Saline (2)	100.0 (0.00)	91.67 (5.89)	83.33 (0.00)	66.67 (23.57)	25 (11.79)	0.00 (0.00)
0.3 mg/kg (2)	100.0 (0.00)	100.0 (0.00)	100.0 (0.00)	100.0 (0.00)	50 (16.67)	11.11 (19.25)
1.0 mg/kg (2)	91.67 (11.79)	100.0 (0.00)	91.67 (11.79)	83.33 (23.57)	83.33 (23.57)	8.33 (11.79)
3.0 mg/kg (2)	91.67 (11.79)	91.67 (5.89)	83.33 (23.57)	100.0 (0.00)	66.67 (23.57)	8.33 (11.79)
5.6 mg/kg (2)	100.0 (0.00)	91.67 (5.89)	100.0 (0.00)	100.0 (0.00)	83.33 (0.00)	66.67 (47.14)
10.0 mg/kg (2)	90.00 (14.14)	83.33 (0.00)	91.67 (11.79)	83.33 (0.00)	100.0 (0.00)	83.33 (23.57)
Rat E18	5	10	15	20	40	NS
Control (11)	95.45 (15.08)	63.64 (34.01)	36.36 (34.82)	12.12 (15.08)	7.58 (11.46)	1.52 (5.03)
Saline (3)	94.44 (9.62)	77.78 (12.73)	38.89 (53.58)	11.11 (9.62)	5.56 (9.62)	0.00 (0.00)
1.0 mg/kg (2)	91.67 (11.79)	66.67 (23.57)	16.67 (23.57)	16.67 (23.57)	8.33 (11.79)	0.00 (0.00)
3.0 mg/kg (2)	83.33 (23.57)	50.00 (23.57)	50.00 (47.14)	58.33 (35.36)	0.00 (0.00)	0.00 (0.00)
5.6 mg/kg (2)	100.0 (0.00)	100.0 (0.00)	91.67 (11.79)	66.67 (23.57)	75.00 (11.79)	0.00 (0.00)
10.0 mg/kg (2)	83.33 (23.57)	100.0 (0.00)	91.67 (11.79)	50.00 (70.71)	41.67 (58.93)	0.00 (0.00)

Note. Mean percent choice (*SD*) of the single-valence lever across blocks (columns) and doses (rows) of methylphenidate. The parenthetical values next to each dose indicate the total number of sessions included in the calculations for each row.

Table 7

Experiment 1: k and R^2 as a Function of Dose of Methylphenidate

	k	**R^2**
Rat C24		
Control	0.05	0.93
Saline	0.08	0.83
1.0 mg/kg	0.09	0.96
3.0 mg/kg	0.00	0.75
5.6 mg/kg	0.01	0.57
10.0 mg/kg	0.00	0.67
Rat C25		
Control	0.24	0.93
Saline	0.15	0.85
0.3 mg/kg	0.19	0.78
1.0 mg/kg	0.18	0.74
3.0 mg/kg	0.13	0.53
5.6 mg/kg	0.02	0.97
10.0 mg/kg	0.01	0.84
Rat C26		
Control	0.03	0.87
Saline	0.03	0.87
0.3 mg/kg	0.01	0.59
1.0 mg/kg	0.00	0.43
3.0 mg/kg	0.01	0.39
5.6 mg/kg	0.00	0.47
10.0 mg/kg	0.00	0.00
Rat E18		
Control	0.16	0.95
Saline	0.13	0.88
1.0 mg/kg	0.18	0.89
3.0 mg/kg	0.07	0.68
5.6 mg/kg	0.01	0.69
10.0 mg/kg	0.02	0.57

Table 8

Experiment 1: Effects of Methylphenidate on Omissions

	Delay to shock (s)					
Rat C24	1	5	10	20	40	NS
Control (11)	0.00 (0, 0)	0.00 (0, 0)	0.27 (0, 1)	0.09 (0, 1)	0.09 (0, 1)	0.18 (0, 1)
Saline (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.33 (0, 1)
1.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.50 (0, 1)	1.00 (1, 1)
3.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
5.6 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
10.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.50 (0, 1)	0.50 (0, 1)
Rat C25	1	5	10	20	40	NS
Control (16)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
Saline (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
1.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
3.0 mg/kg (4)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
5.6 mg/kg (3)	0.00 (0, 0)	0.00 (0, 0)	0.33 (0, 1)	0.00 (0, 0)	0.00 (0, 0)	1.00 (0, 3)
10.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	1.00 (0, 2)	0.50 (0, 1)	0.50 (0, 1)
Rat C26	1	5	10	20	40	NS
Control (9)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.22 (0, 1)	0.00 (0, 0)	0.11 (0, 1)
Saline (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
0.3 mg/kg (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.33 (0, 1)	0.00 (0, 0)	0.67 (0, 1)
1.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
3.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
5.6 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.50 (0, 1)
10.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.50 (0, 1)	0.00 (0, 0)	0.50 (0, 1)
Rat E18	5	10	15	20	40	NS
Control (11)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
Saline (3)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
1.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
3.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
5.6 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)
10.0 mg/kg (2)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)	0.00 (0, 0)

Note. Mean omissions (range) per block at control, saline, and each dose of methylphenidate. The parenthetical values next to each dose indicate the total number of sessions included in the calculations for each row.

Table 9

Experiment 2A: Estimates for Sensitivity, Bias, and Overall Model Fit Based on Eq. 4

Phase 1: Initial Within-Session Procedure								
Rat ID	E10	E11	E12	E13	E14	E15	E16	E17
S_P	-0.02	-0.18	-0.03	0.09	0.12	0.04	-0.32	-0.21
Bias	0.33	0.02	0.14	0.24	-0.11	0.10	0.18	0.28
R^2	0.28	0.71	0.55	0.65	0.62	0.21	0.86	0.93

Phase 2: Pellet and Delay Adjustments								
Rat ID	E10	E11	E12	E13	E14	E15	E16	E17
S_P	-0.05	-0.13	-0.12	0.13	-0.02	-0.14	-0.12	-0.08
Bias	0.13	-0.08	0.05	-0.16	-0.06	0.39	0.07	0.04
R^2	0.27	0.42	0.91	0.70	0.19	0.92	0.88	0.95

Phase 3: Delay-Specific Signals								
Rat ID	E10	E11	E12	E13	E14	E15	E16	E17
S_P	-0.22	-0.22	-0.04	-0.09	0.03	0.00	-0.06	0.03
Bias	0.09	-0.12	-0.03	-0.26	-0.28	0.14	0.07	0.02
R^2	0.99	0.96	0.24	0.61	0.66	0.11	0.98	0.10

Note. Estimates for sensitivity (SP) bias, and model fits of Eq. 4 are shown across Phase 1(top section), Phase 2 (middle section) and Phase 3 (bottom section) of Experiment 2A.

Table 10

Experiment 2B: Parameters

Rat ID	Sessions	Variable Lever	Shock: mA	Shock: ms
E10	-	-	-	-
E11	-	-	-	-
E12	21	Left	0.35	500
E13	21	Right	0.30	400
E14	23	Right	0.40	500
E15	22	Right	0.40	500
E16	23	Left	0.35	400
E17	23	Left	0.30	400

Note. Number of sessions, lever assignment and shock-intensity parameters are shown above. Note that Rats E10 and E11 were excluded from this condition.

Table 11

Experiment 2C: Parameters

		Dual-valence Lever		Shock	
Rat ID	**Sessions**	**Assignment**	**Pellets**	**mA**	**ms**
E10	31	Right	3	0.65	400
E11	31	Left	2	0.50	500
E12	31	Left	2	0.50	400
E13	33	Left	2	0.50	400
E14	34	Left*	3	0.45	400
E15	34	Right	3	0.40	300
E16	33	Left	3	0.40	400
E17	33	Left	3	0.40	400

Note. Parameters and lever assignments that differed across rats are shown above. All other parameters were held constant across rats, including: changeover delay = 2 s, interchain interval = 20 s, single-valence pellets = 1, delay sequence = 40, 20, 10, 5 s.

*The lever assignment for Rat E14 was reversed after 16 sessions into Experiment 2C.

Table 12

Experiment 2D: Parameters

		Variable Lever:		Shock Intensity	
Rat ID	**Pellets**	Assignment	Delays to shock (s)	mA	ms
E10	3	Left	64, 64, 4, 4	0.40	400
E11	3	Right	4, 4, 64, 64	0.45	250
E12	2	Right	64, 64, 4, 4	0.55	300
E13	2	Left	4, 4, 64, 64	0.50	250
E14	2	Left	3, 6, 24, 48	0.50	200
E15	2	Right	48, 24, 6, 3	0.45	250
E16	2	Right	48, 24, 6, 3	0.35	250
E17	2	Right	3, 6, 24, 48	0.35	250

Note. The number of pellets delivered was the same in the variable and standard terminal links. The delay to shock in the standard terminal link was always 16 s for Rats E10, E11, E12, and E13 and 12 s for Rats E14, E15, E16, and E17. For all rats, a 1-s changeover delay had to be satisfied in the initial link and a 15-s interchain interval separated each chain of the session.

Table 13

Experiment 2D: Percent Cycles Completed at each Dose of Oxycodone

	Rat ID			
	E10	**E11**	**E16**	**E17**
Control	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
Saline	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
0.1 mg/kg	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
0.3 mg/kg	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
0.56 mg/kg	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
1.0 mg/kg	75.00 (-)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)

Note. Mean (*SD*) chains completed, shown as a percent, each session as a function of dose of oxycodone.

Table 14

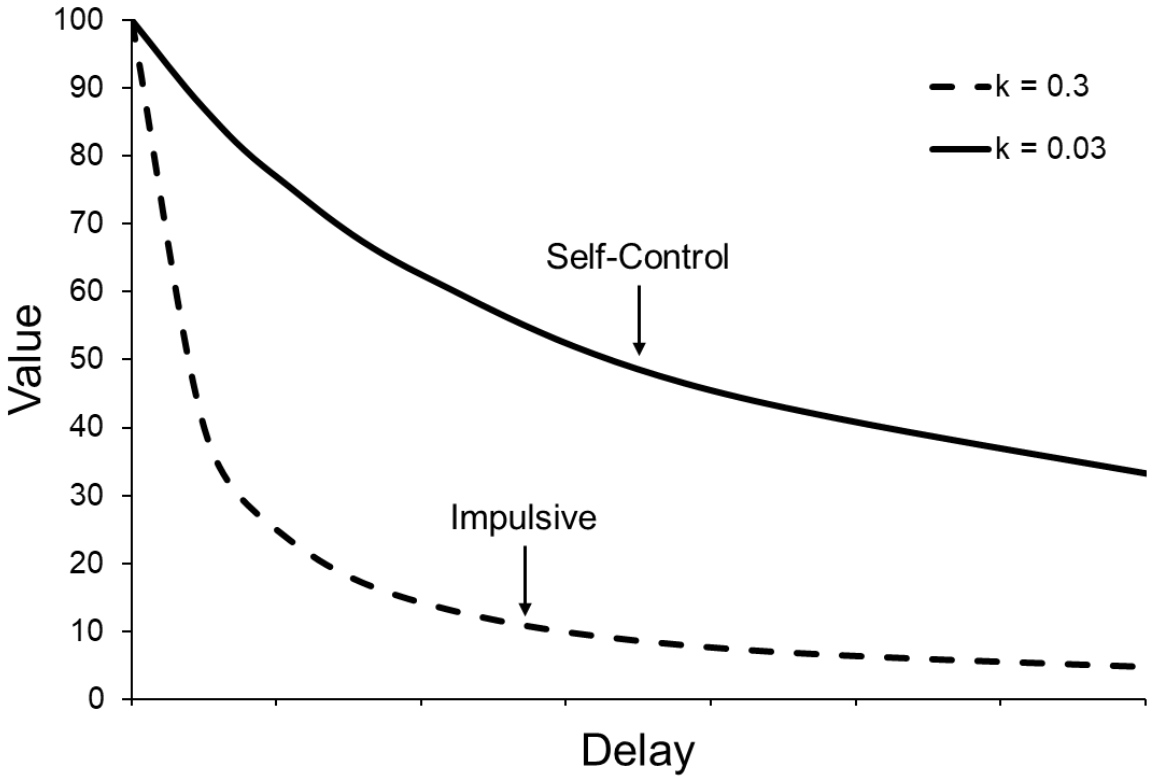
Experiment 2D: Percent Cycles Completed at each Dose of Methylphenidate

	Rat ID			
	E12	**E13**	**E14**	**E15**
Control	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
Saline	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
1.0 mg/kg	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
3.0 mg/kg	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
5.6 mg/kg	88.75 (15.91)	100.00 (0.00)	100.00 (0.00)	100.00 (0.00)
10.0 mg/kg	51.25 (68.94)	20.00 (24.75)	54.75 (65.41)	100.00 (0.00)

Note. Mean (*SD*) chains completed, shown as a percent, each session as a function of dose of methylphenidate.

Figure 1

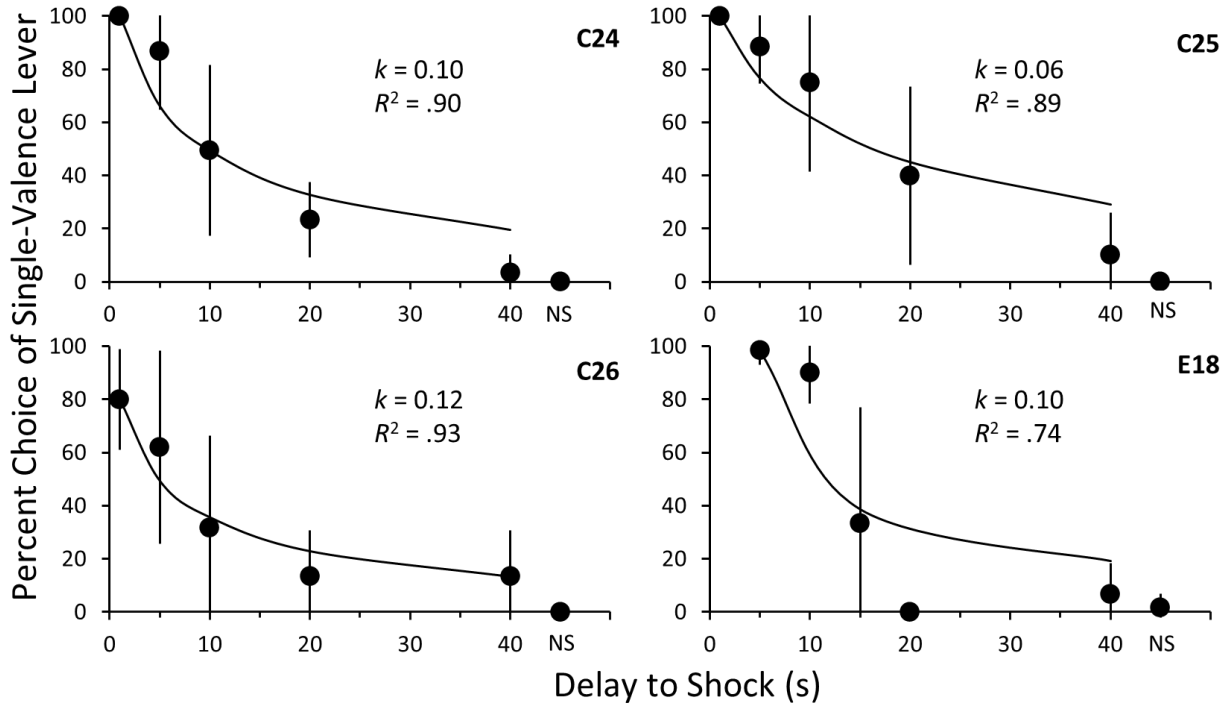
Hypothetical Delay-Discounting Functions



Note. Each hypothetical discounting function is based on Equation 1 and shows a different rate of discounting, scaled by the parameter *k*.

Figure 2

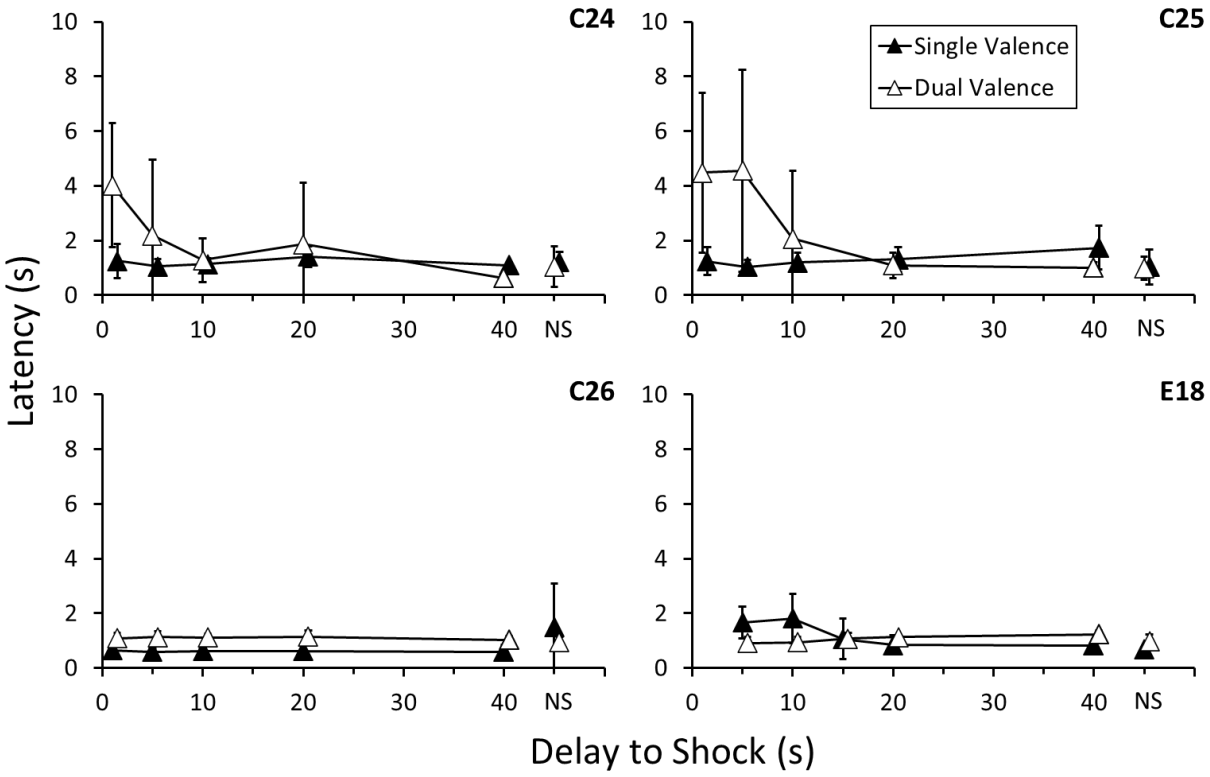
Experiment 1: Pre-Drug Baseline – Choice



Note. Mean (±*SD*) percent choice of the single-valence lever shown as a function of delay to shock on the dual-valence lever and during the no-shock (NS) block. Means are from the last 10 stable sessions of the baseline phase. Estimates for *k* and overall model fit (R^2) are based on Eq. 1.

Figure 3

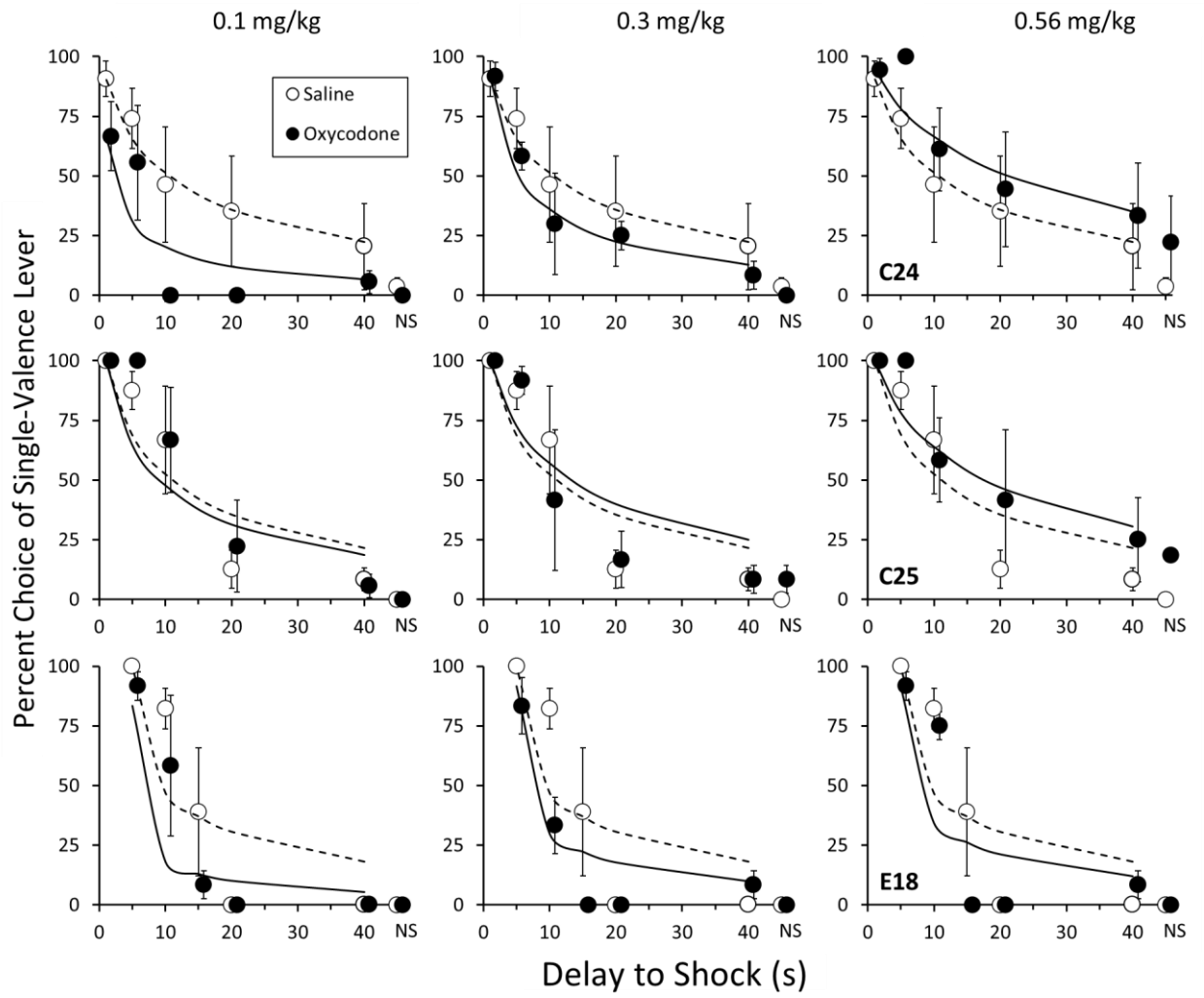
Experiment 1: Pre-Drug Baseline – Latencies



Note. Mean (±*SD*) latencies to respond on the single-valence (filled triangles) and dual-valence (unfilled triangles) levers during forced-choice trials as a function of delay to shock and in the no-shock (NS) block.

Figure 4

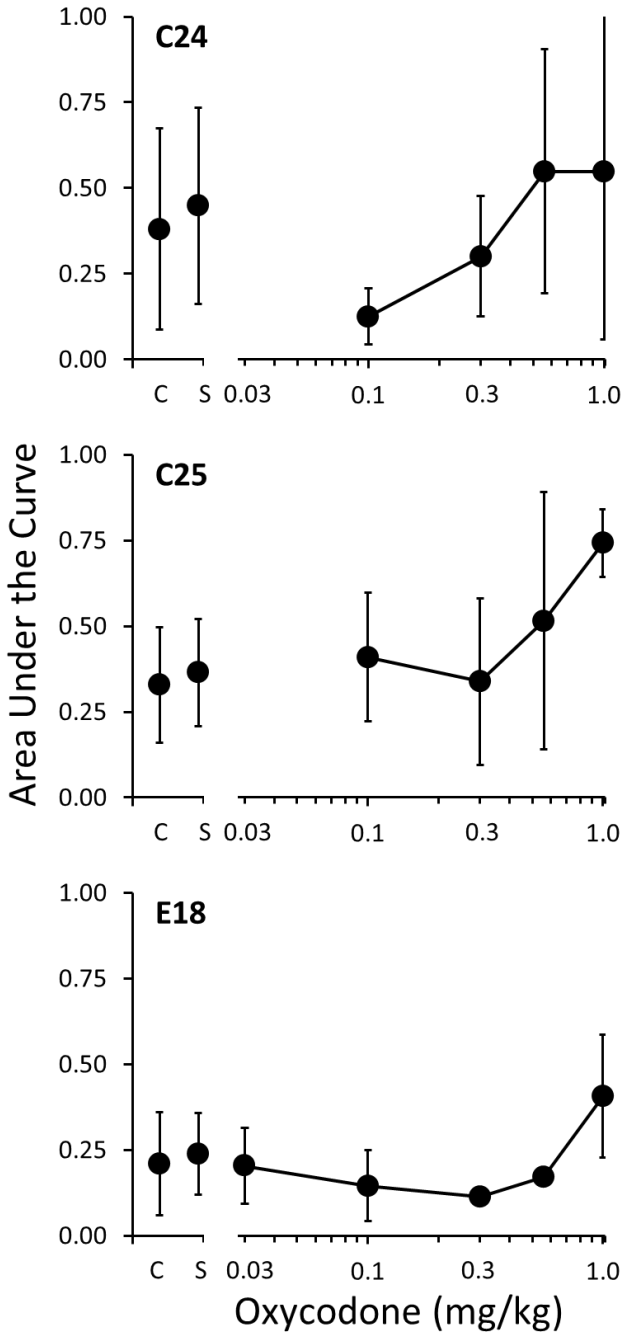
Experiment 1: Effects of Oxycodone on Within-Session Choice



Note. Mean percent choice of the single-valence lever is shown as a function of the delay to shock on the dual-valence lever. Data points show data from sessions in which saline (white data points) and select doses of oxycodone (black data points) were administered. For clarity, error bars show ± half of one standard deviation around the mean. Estimates for *k* and model fit based on Eq. 3 are shown on each panel, the predicted function based on Eq. 3 is shown by the dashed (saline) and solid (oxycodone) data paths. Note that the saline function is repeated across each row.

Figure 5

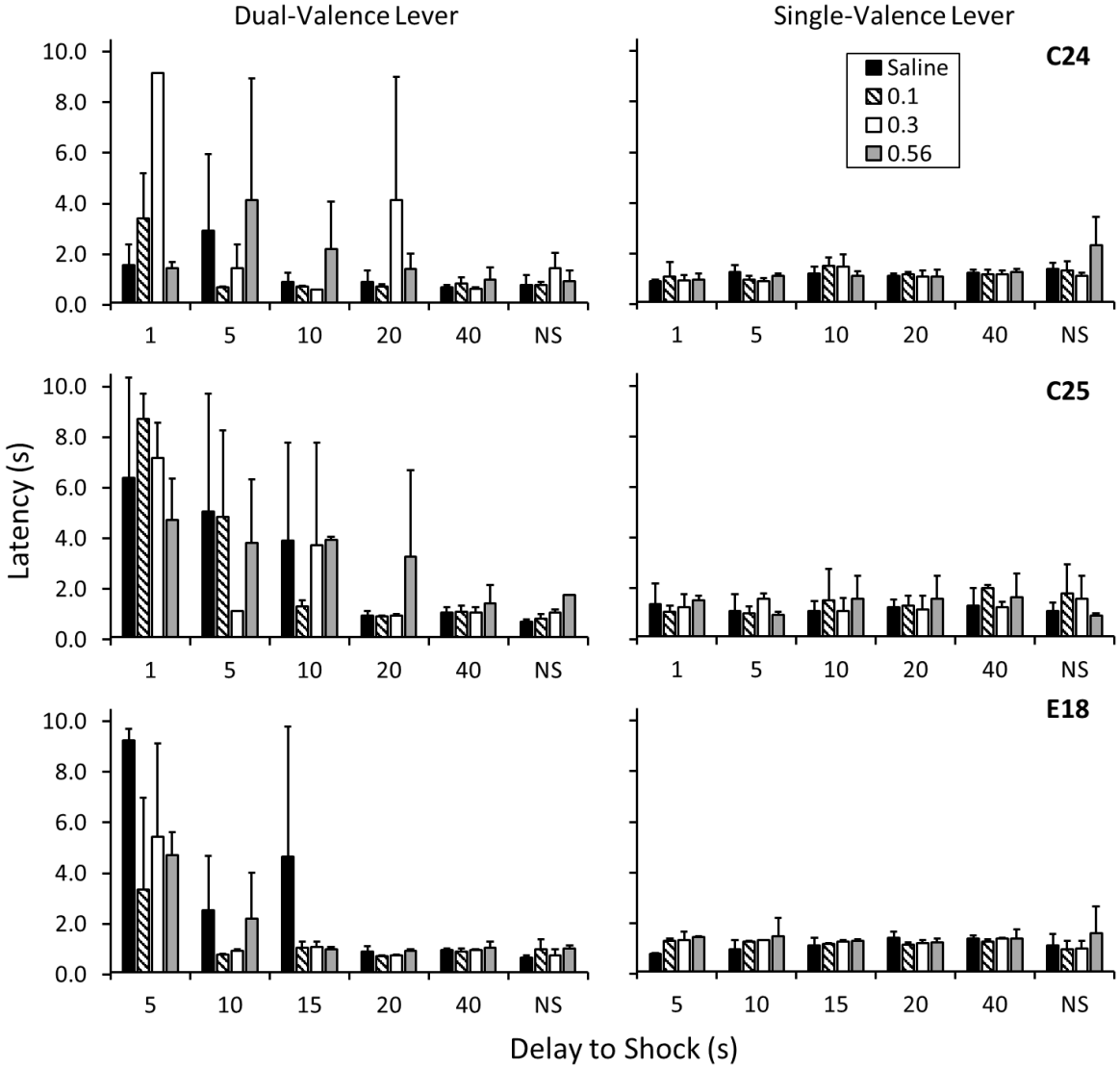
Experiment 1: Dose-Effect Function of Area Under the Curve – Oxycodone



Note. Mean (±*SD*) area under the curve at control (C) and sessions in which saline (S) or oxycodone was administered.

Figure 6

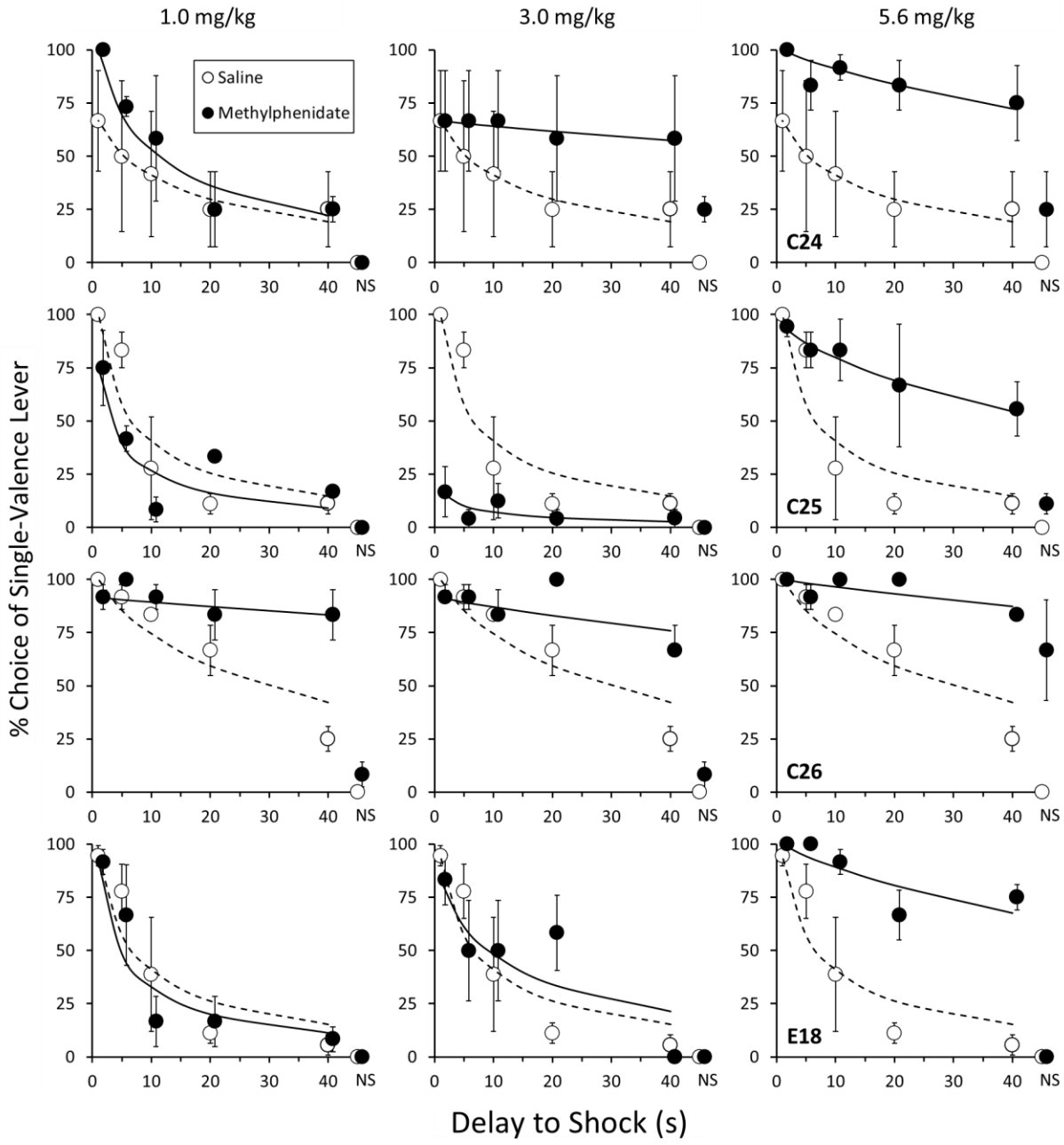
Experiment 1: Effects of Oxycodone on Forced-Choice Response Latencies



Note. Mean (*SD*) latency to press the dual-valence (left panels) and single-valence (right panels) lever during forced-choice trials at saline (black bars) and 0.1 mg/kg (striped bars), 0.3 mg/kg (white bars), and 0.56 mg/kg (grey bars) oxycodone. Latencies are shown as a function of the delay to shock (*x*-axis) and in the no-shock (NS) block.

Figure 7

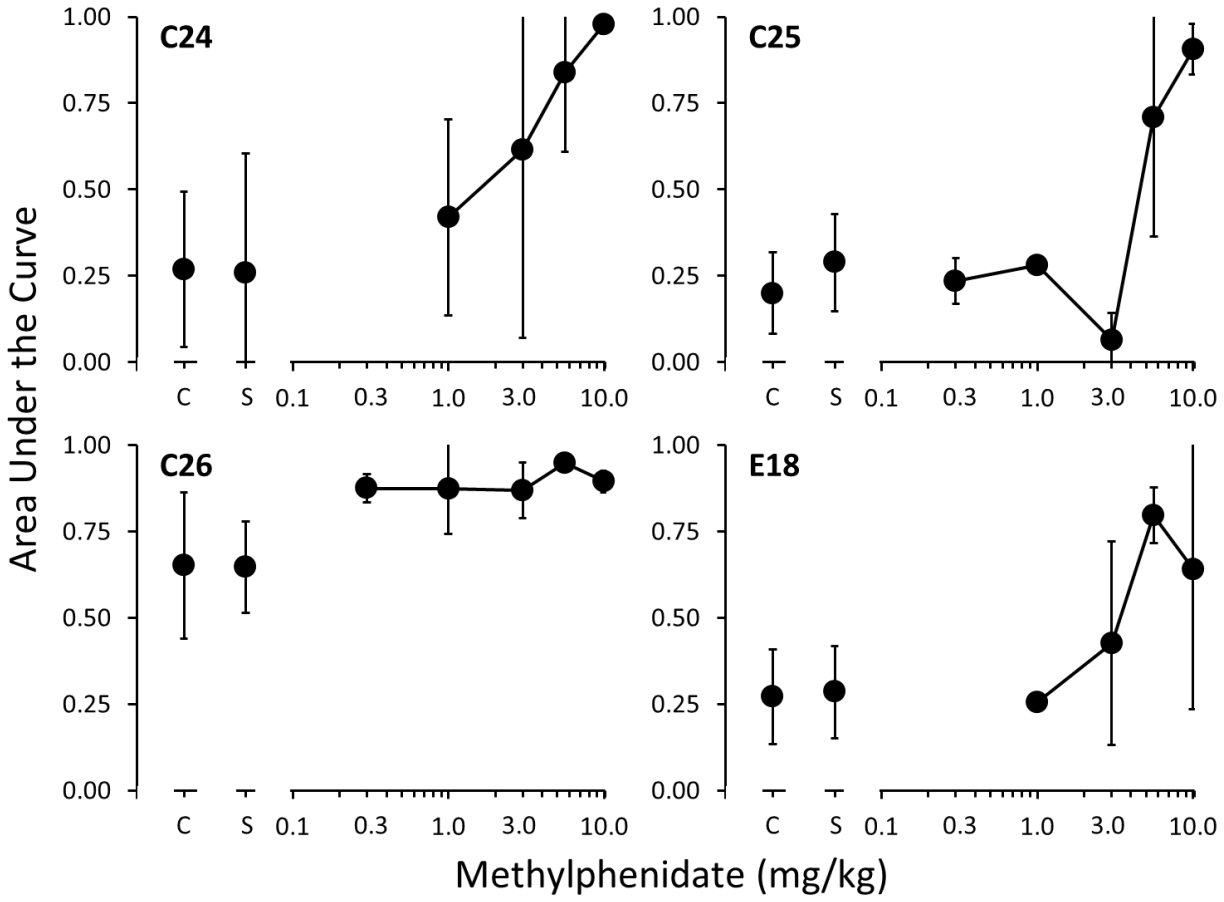
Experiment 1: Effects of Methylphenidate on Within-Session Choice



Note. Mean percent choice of the single-valence lever is shown as a function of the delay to shock on the dual-valence lever. Data points show data from sessions in which saline (white data points) and select doses of methylphenidate (black data points) were administered. For clarity, error bars show ± half of one standard deviation around the mean. Estimates for *k* and model fit based on Eq. 3 are shown on each panel, the predicted function based on Eq. 3 is shown by the dashed (saline) and solid (oxycodone) data paths.

Figure 8

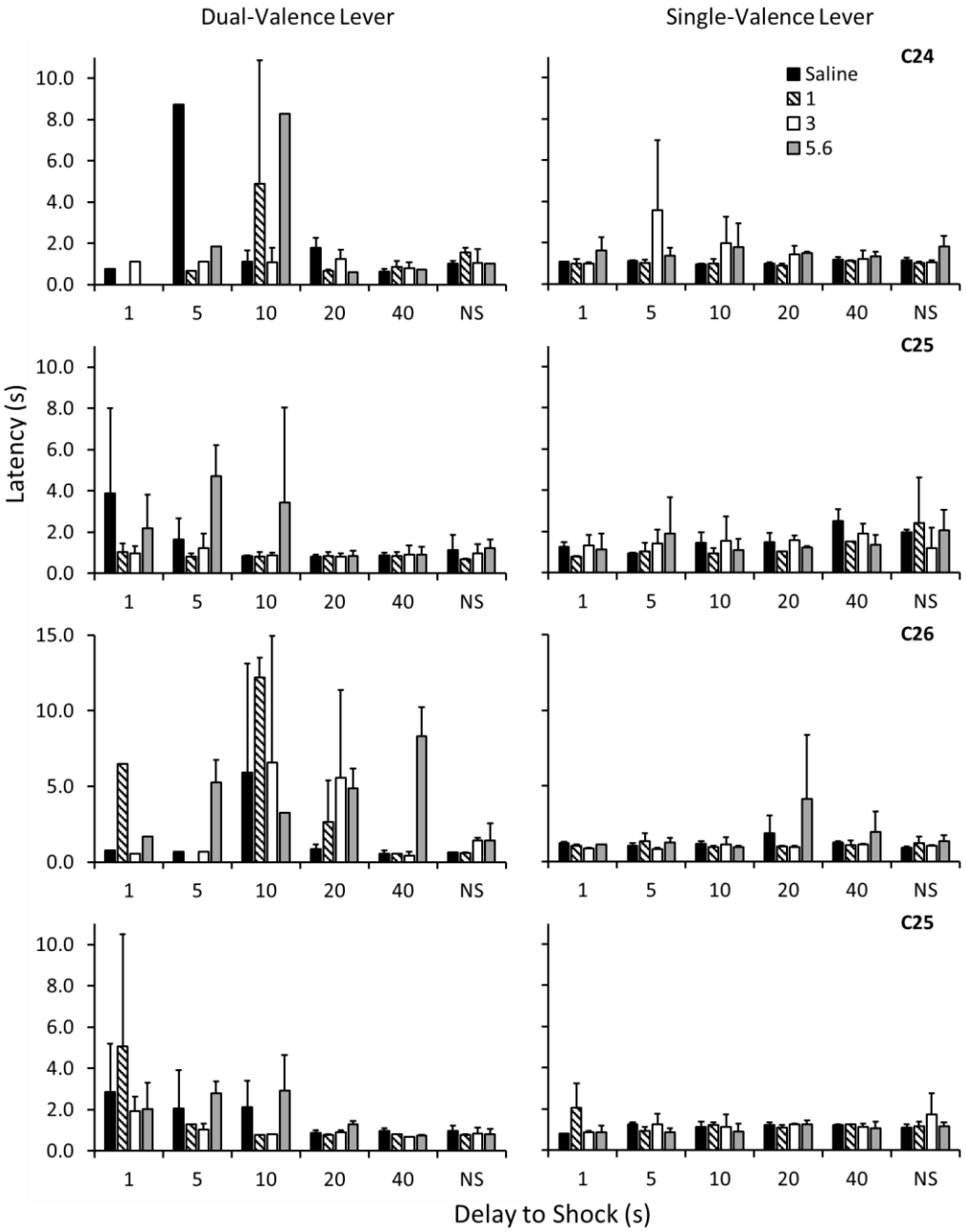
Experiment 1: Dose-Effect Functions for Area Under the Curve – Methylphenidate



Note. Mean (±*SD*) area under the curve at control (C) and sessions in which saline (S) or oxycodone was administered.

Figure 9

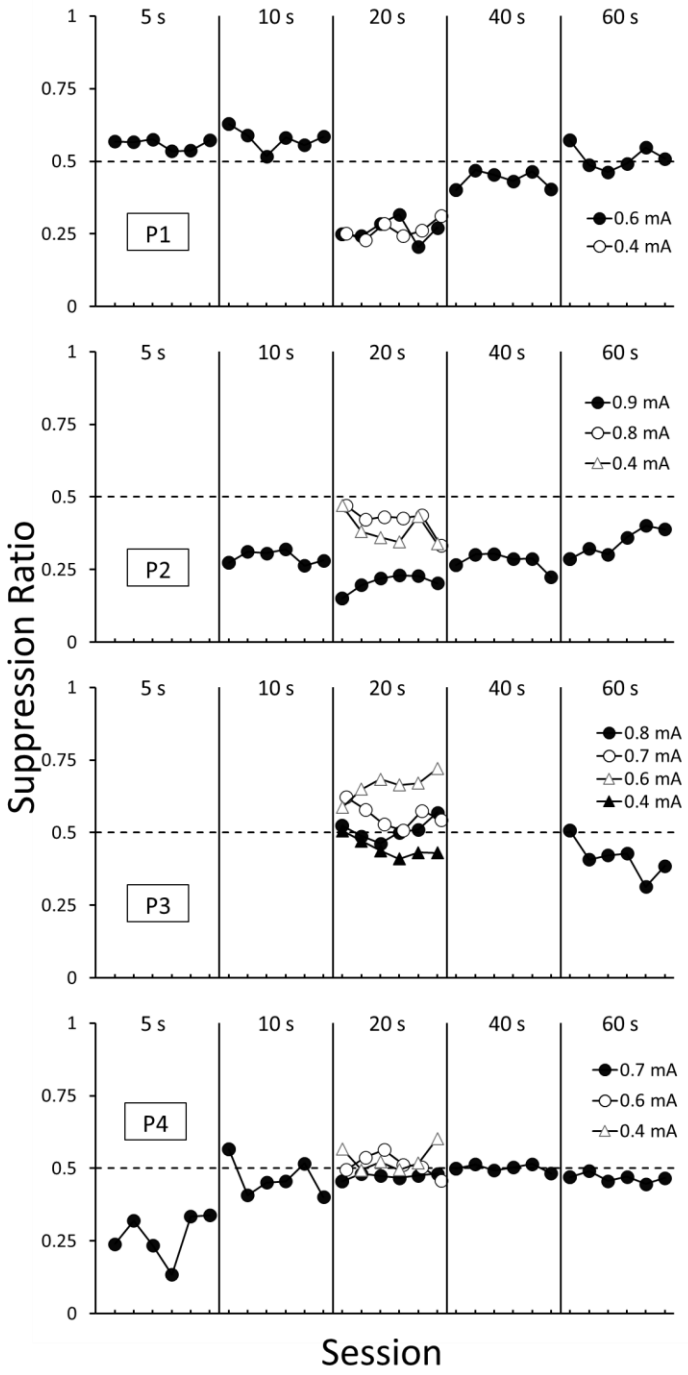
Experiment 1: Effects of Methylphenidate on Forced-Choice Response Latencies



Note. Mean (*SD*) latency to press the dual-valence (left panels) and single-valence (right panels) lever during forced-choice trials at saline (black bars) and 1.0 mg/kg (striped bars), 3.0 mg/kg (white bars), and 5.6 mg/kg (grey bars) methylphenidate. Latencies are shown as a function of the delay to shock (*x*-axis) and in the no-shock (NS) block.

Figure 10

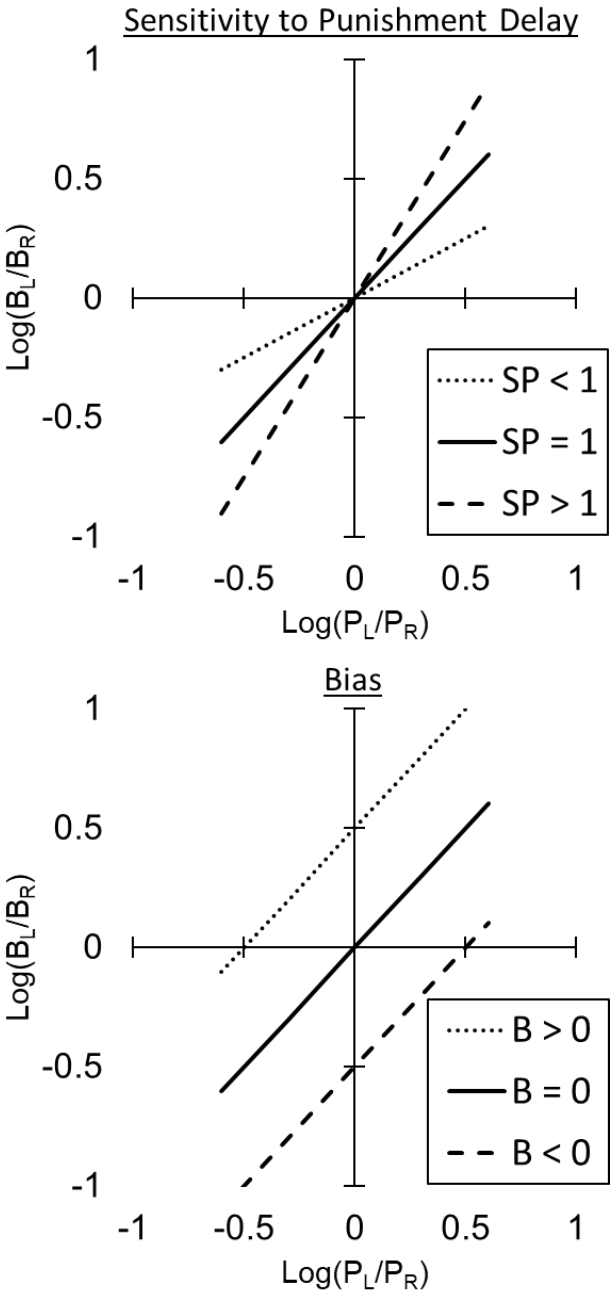
Pilot Test Data: Steady-State Concurrent-Chains



Note. Suppression ratios show the degree to which response ratios changed compared to an unpunished baseline. Changes in suppression ratios are shown as a function of different delays to shock (5-60 s) and shock intensity (indicated by different symbols).

Figure 11

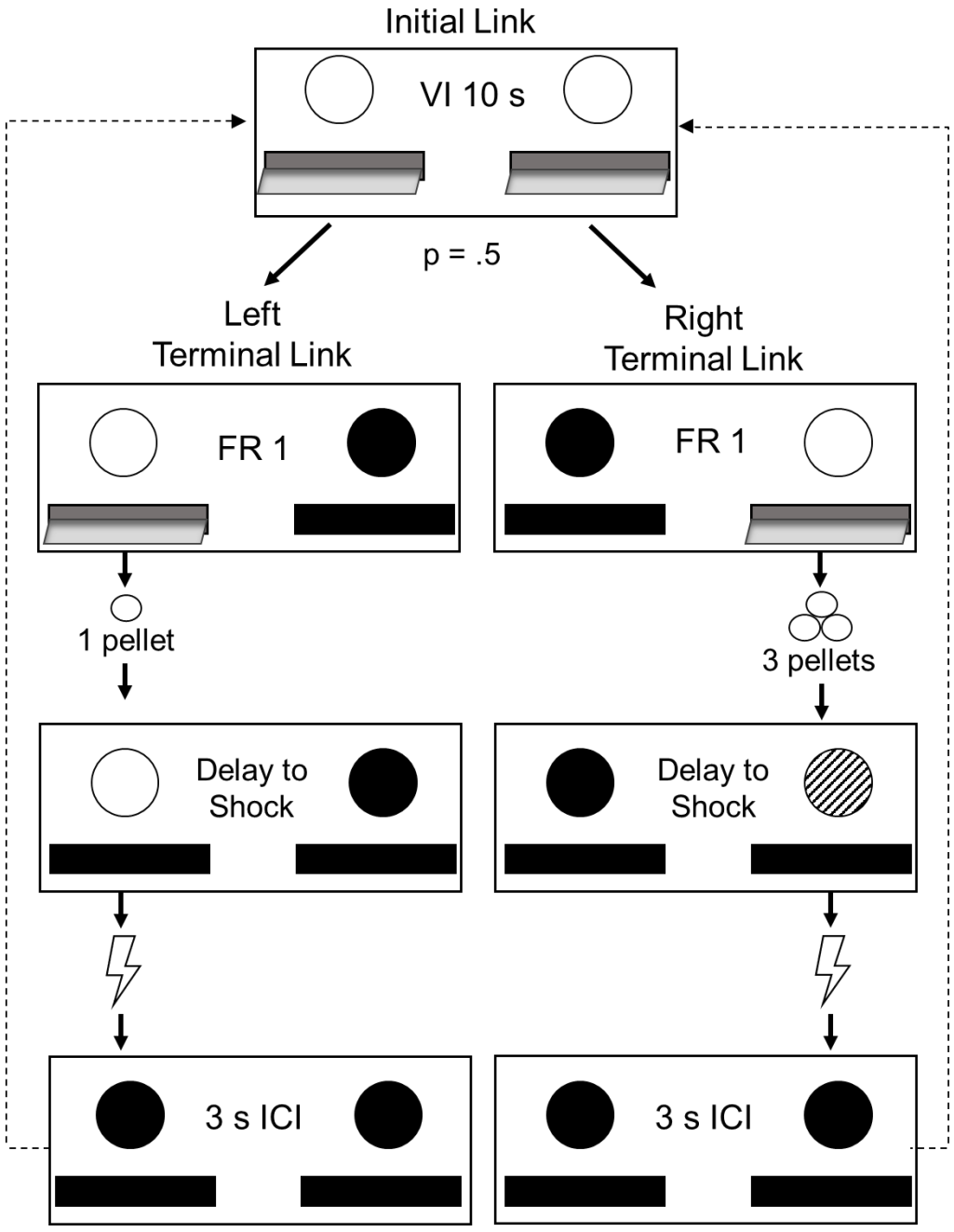
Hypothetical Changes in Response Ratios based on Different Sensitivity Estimates



Note. Each hypothetical matching function is based on Equation 4. The top panel shows how changes in sensitivity to delayed shock affect the slope. The bottom panel shows how changes in bias affect the y-intercept.

Figure 12

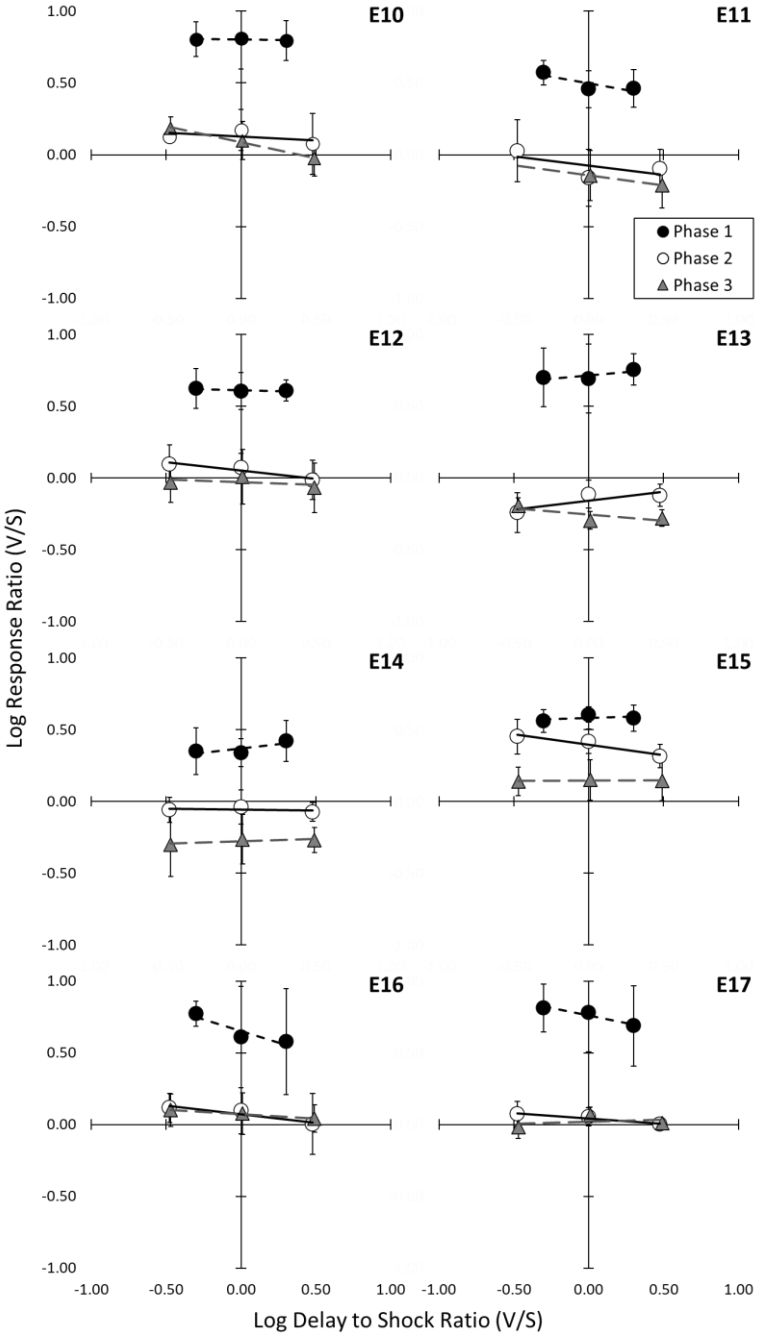
Diagram of Concurrent-Chains Procedure



Note. The terminal link outcomes are mutually exclusive. White circles indicate the cue light is on, black circles indicate the light is off, and the striped circle indicates the light is flashing. Black rectangles indicate retracted levers. ICI = intercomponent interval.

Figure 13

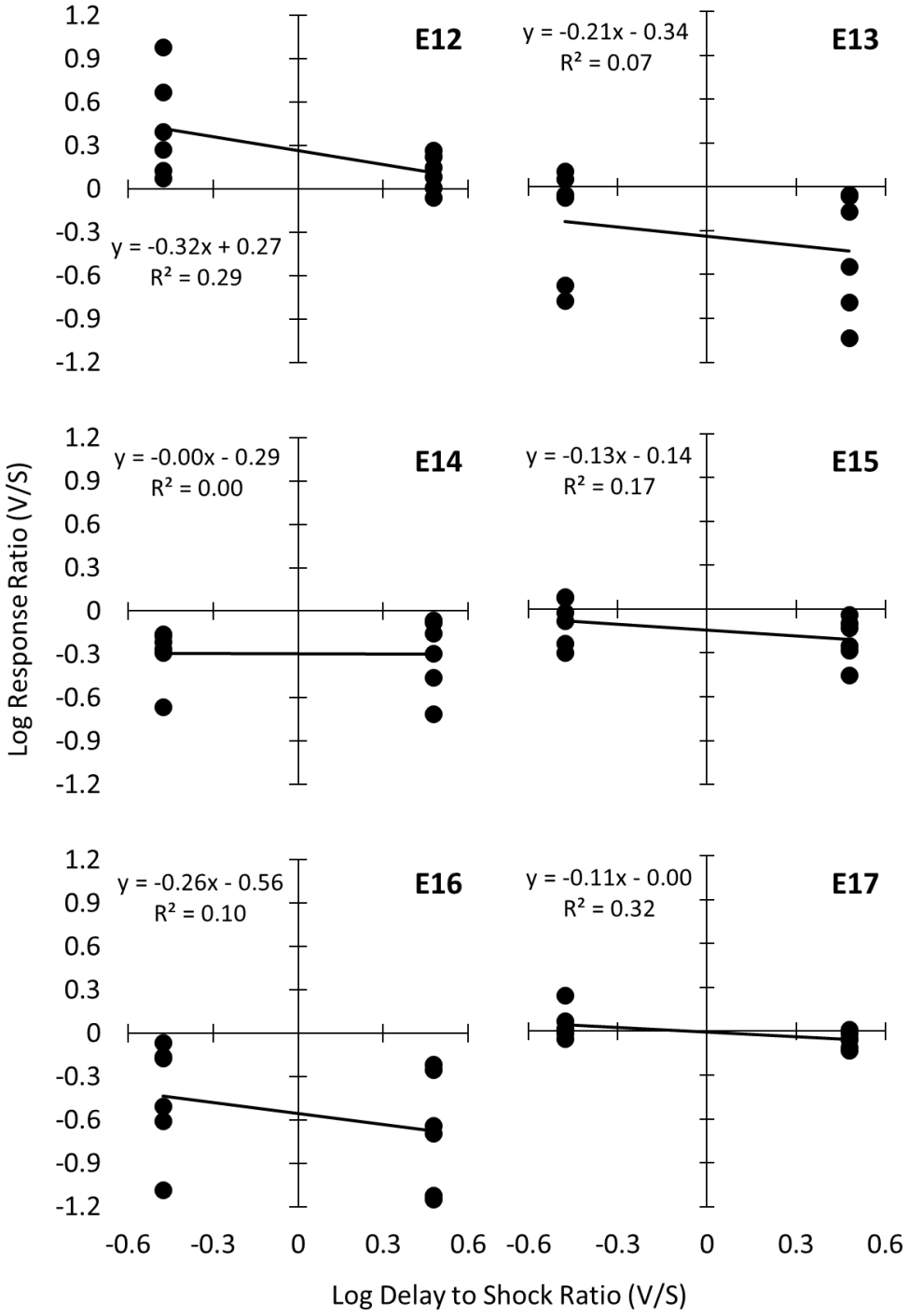
Experiment 2A: Log Response Ratios



Note. Mean (±*SD*) log response ratios from the last six sessions of Phase 1 (black circles), Phase 2 (white triangles), and Phase 3 (grey triangles) of Experiment 2A. Fits of Eq. 4 for each phase are shown by the black dashed (Phase 1), black solid (Phase 2), and grey dashed (Phase 3) lines.

Figure 14

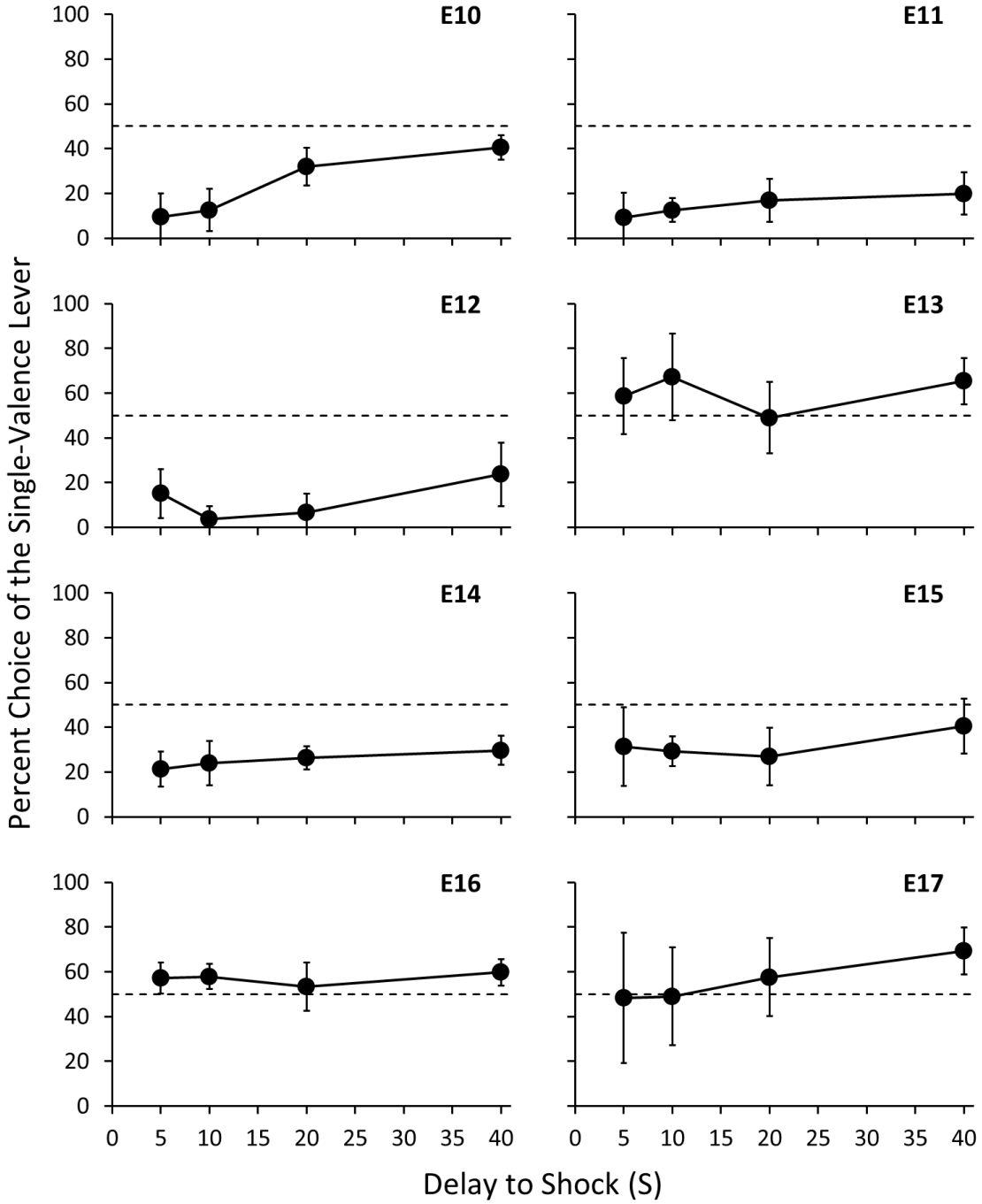
Experiment 2B: Response Ratios under the Rapid-Acquisition Procedure



Note. Log response ratios from the last six sessions of each session type are shown as a function of the ratio of the delay to shock from those sessions. Parameters for line of best fit and R^2 are shown on each panel.

Figure 15

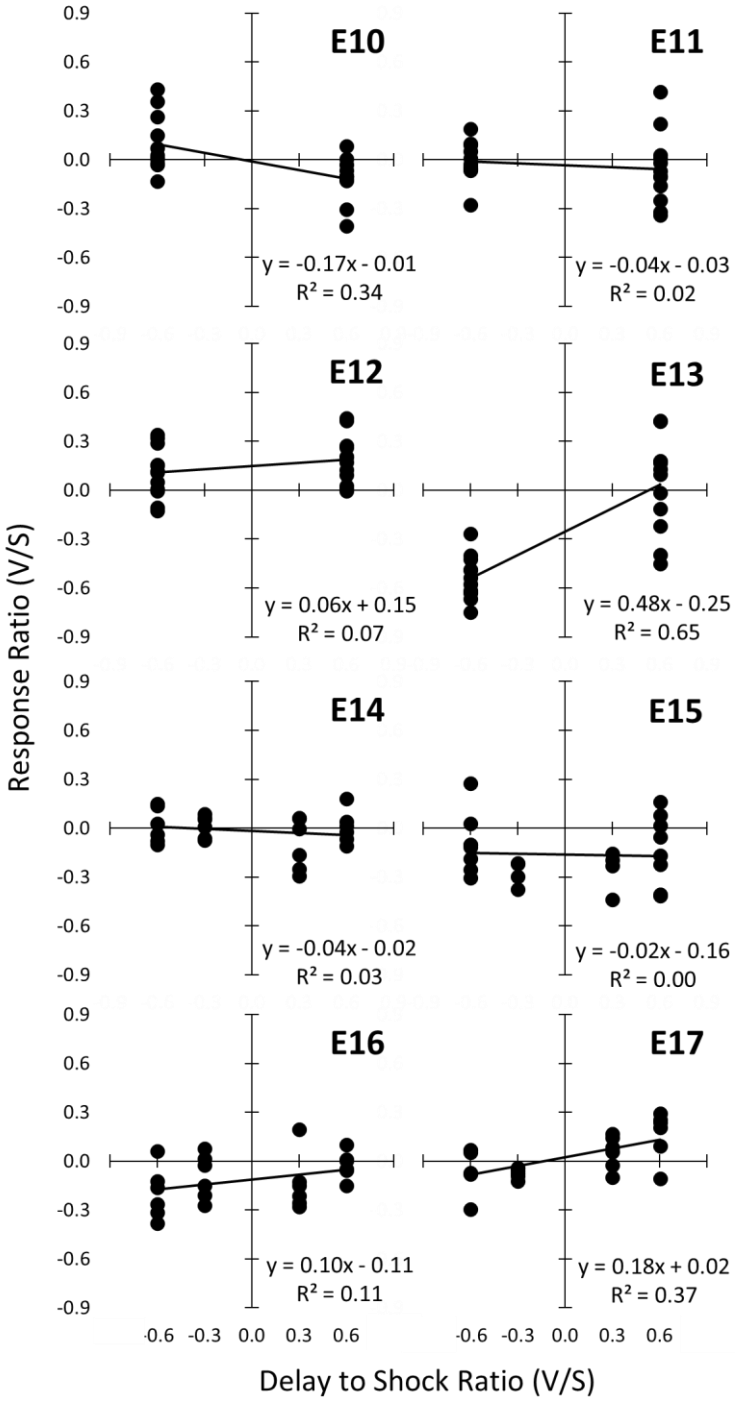
Experiment 2C: Percent Choice on the Concurrent-Chains Conflicting Choice Procedure



Note. Mean (±*SD*) percent choice of the single-valence lever from the last six sessions of Experiment 2C. The dashed reference line at 50% indicates choice at indifference.

Figure 16

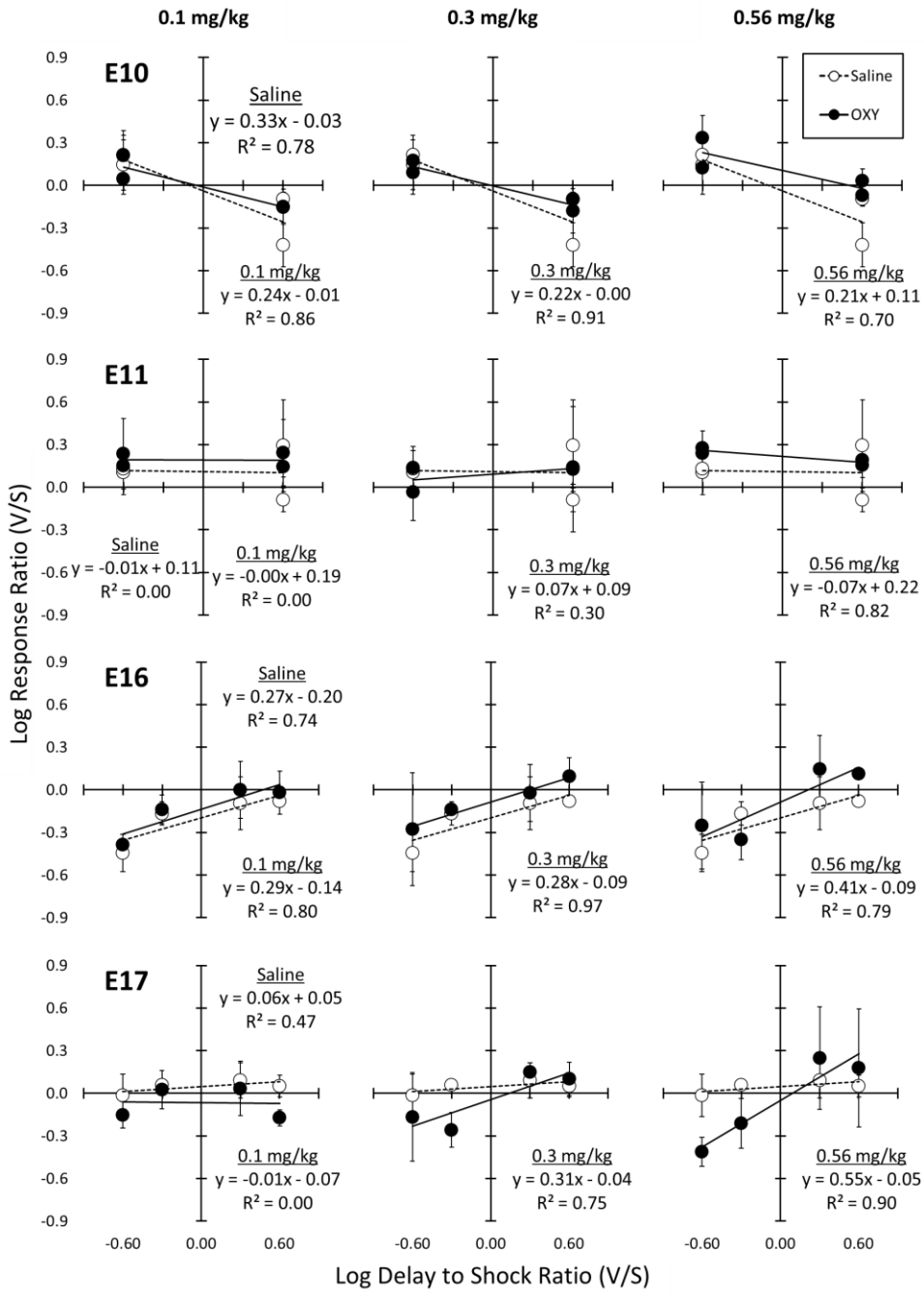
Experiment 2D: Response Ratios as a function of Delay to Shock Ratios (Baseline)



Note. Log response ratios (variable lever/standard lever) as a function of the delay to shock ratio (variable/standard) arranged in the terminal link. Each data point shows the response ratio from one block from the last six stable sessions prior to the Pharmacological Procedure. Line of best fit is based on Eq. 4.

Figure 17

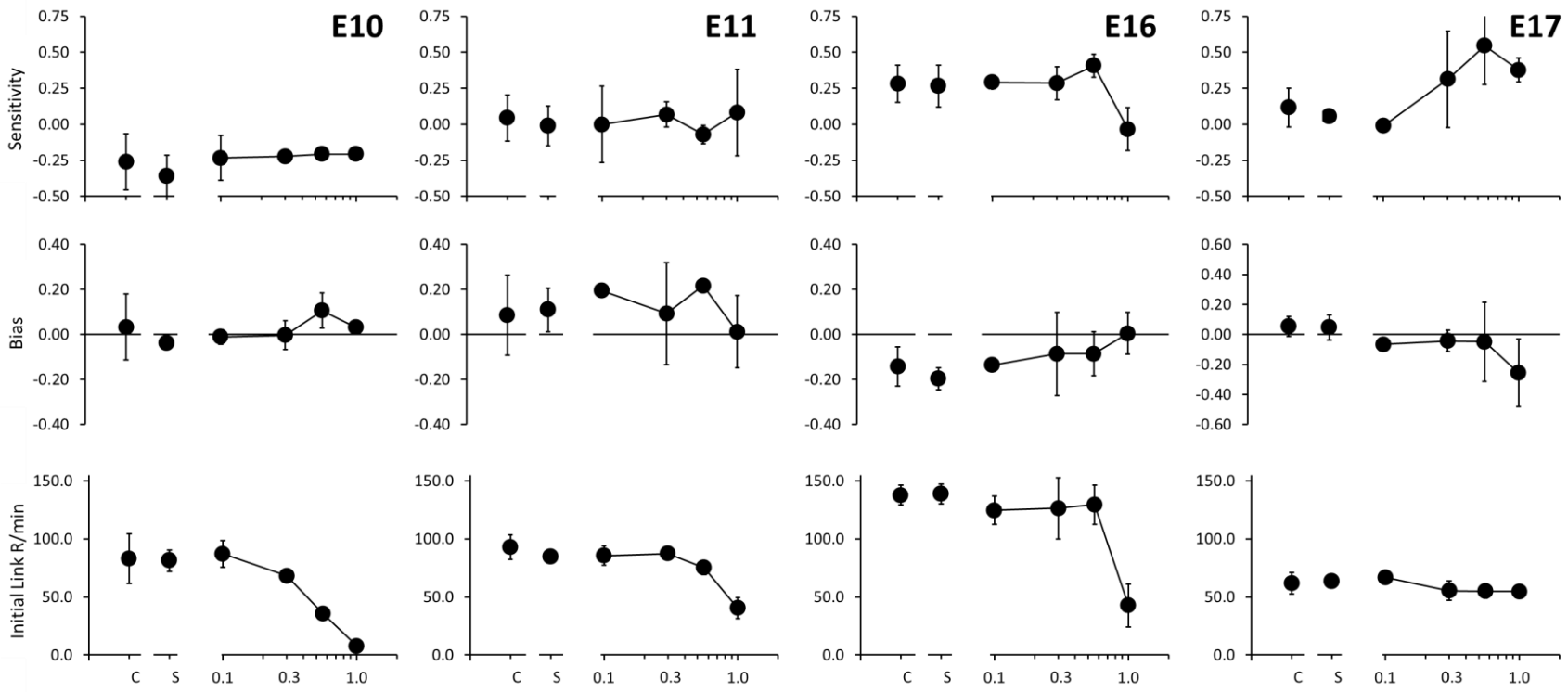
Experiment 2D: Effects of Oxycodone on Response Ratios



*Note***.** Mean (±*SD*) log response ratios (variable lever/standard lever) as a function of the log delay to shock ratio in the variable and standard terminal links. Data for each rat are shown in rows of panels; data from sessions in which saline (white circles) and select doses of oxycodone (OXY; black circles; 0.1, 0.3, and 0.56 mg/kg) were administered are shown in columns of panels.

Figure 18

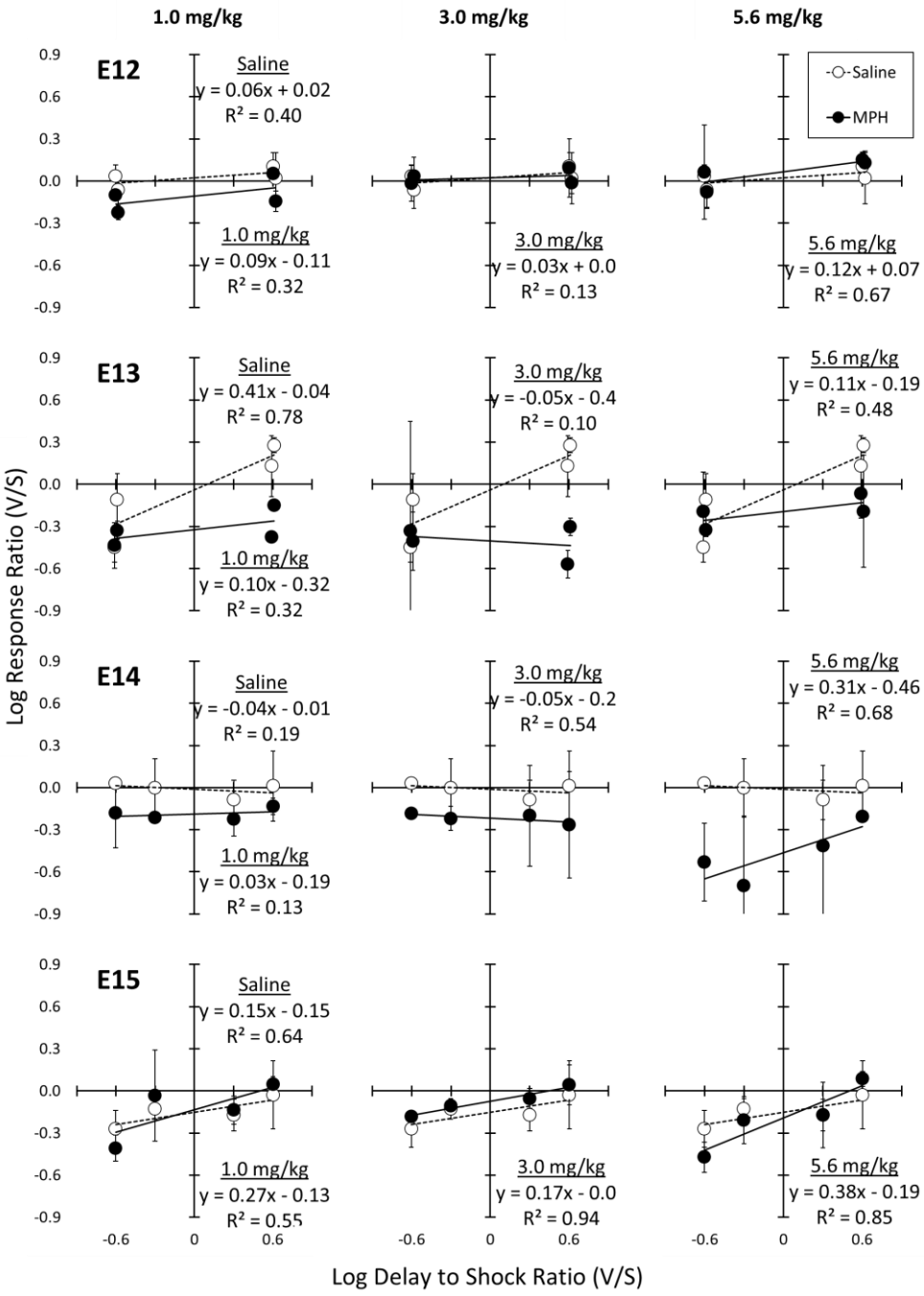
Experiment 2D: Effects of Oxycodone on Sensitivity, Bias, and Initial-Link Response Rates



Note. Mean (±*SD*) estimates for sensitivity (top row of panels), bias (middle row of panels), and initial-link response rates (bottom row of panels) from control sessions (C) and sessions in which saline (S) or oxycodone was administered. Data for individual rats are shown in columns.

Figure 19

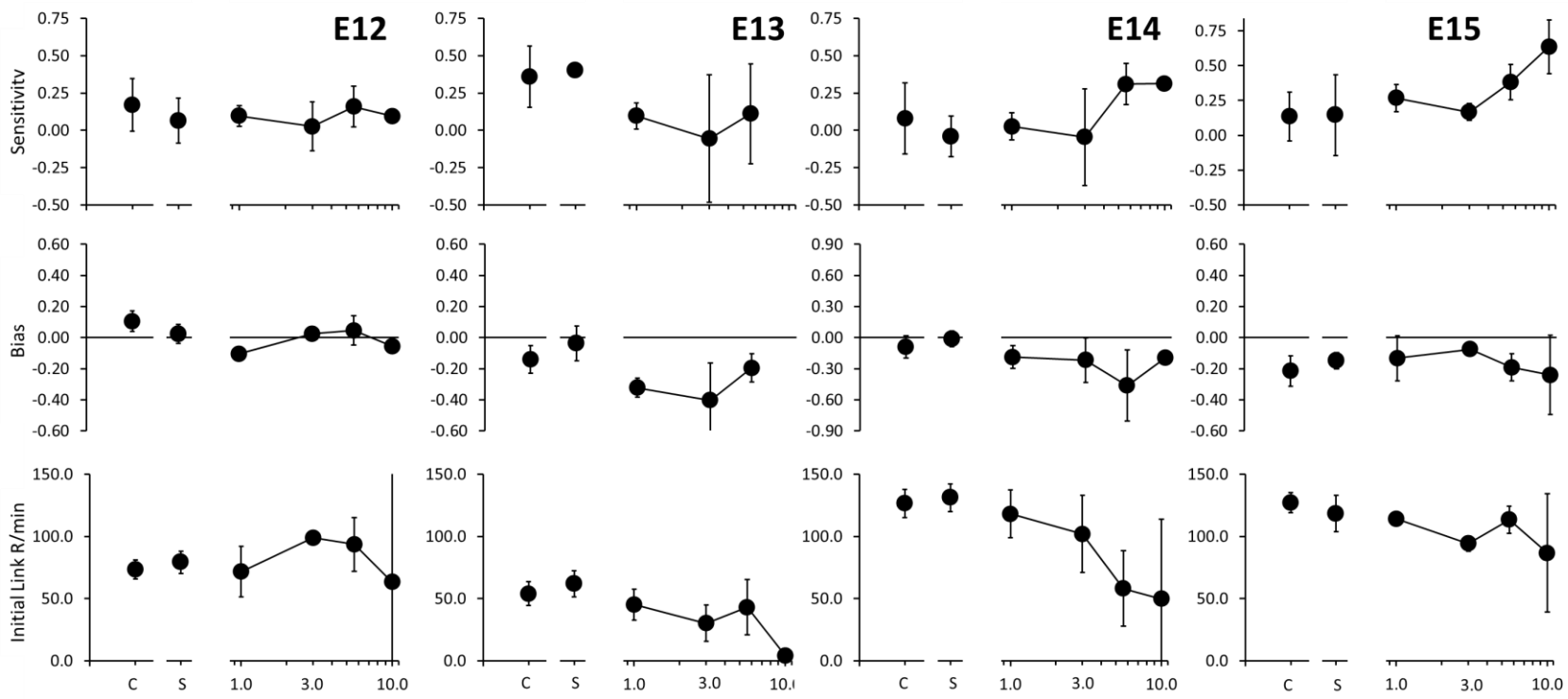
Experiment 2D: Effects of Methylphenidate on Response Ratios



*Note***.** Mean (±*SD*) log response ratios (variable lever/standard lever) as a function of the log delay to shock ratio in the variable and standard terminal links. Data for each rat are shown in rows of panels; data from sessions in which saline (white circles) and select doses of methylphenidate (black circles; 0.1, 0.3, and 0.56 mg/kg) were administered are shown in columns of panels.

Figure 20

Experiment 2D: Effects of Methylphenidate on Sensitivity, Bias, and Initial-Link Response Rates



Note. Mean (±*SD*) estimates for sensitivity (top row of panels), bias (middle row of panels), and initial-link response rates (bottom row of panels) from control sessions (C) and sessions in which saline (S) or methylphenidate was administered. Data for individual rats are shown in columns.