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Assessing behavioral control across reinforcer solutions on a fixed-ratio schedule of reinforcement in rats

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Instrumental behavior can shift from flexible, goal-directed actions to automatic, stimulus-response actions. The satiety-specific devaluation test assesses behavioral flexibility by evaluating reward seeking after temporary devaluation of the reinforcer via satiety; a decrease in responding compared to control conditions indicates goal-directed behavior. We have observed variability in the outcome of this test that may be dependent on the reinforcer. Another test of habit, contingency degradation, involves changing the action-outcome association over the course of retraining and determines whether reward seeking is sensitive to changing contingencies. We hypothesized that the outcome of the contingency-degradation test would remain consistent across reinforcers, while the satiety-specific devaluation test may vary across reinforcers because it depends on the ability of the reinforcer to induce satiety. Therefore, we trained rats to self-administer 1.5% sucrose, 10% sucrose, 10% ethanol, or 10 mM monosodium glutamate (MSG) on a fixed-ratio (FR5) schedule that has been shown to promote long-term, goal-directed responding. Next, behavioral flexibility was evaluated in three satiety-specific devaluation tests over 6 weeks. Finally, we investigated reward seeking after contingency-degradation training. All groups displayed sensitivity to satiety-specific devaluation in the first test, indicating goal-directed behavior. While the 10% sucrose and ethanol groups remained goal-directed, the 1.5% sucrose and MSG groups exhibited habit-like behavior in later tests. Nevertheless, all groups displayed decreased responding in an extinction session after contingency-degradation training, indicating goal-directed behavior. These results demonstrate that tests of behavioral flexibility can yield dissimilar results in the same rats. Next, rats from the 1.5% sucrose group underwent the entire experiment again, now self-administering 10% sucrose. These rats showed pronounced goal-directed behavior in satiety-specific and contingency-degradation tests under 10% sucrose conditions, further suggesting that the reinforcer solution affected the outcome of the satiety-specific devaluation test. We conclude that reinforcer characteristics should be considered when investigating habit-like behavior in alcohol research.

Introduction

Flexible, outcome-driven behaviors may shift to more inflexible, environmentally driven habits with repeated performance. Such a transition in the locus of control is implicated in individuals with alcohol use disorder, whose drinking persists despite significant negative consequences. A behavior may be described as either goal- or habit-directed by its sensitivity to changes in expectation. Accordingly, these behaviors can be evaluated in animal models of reinforcement by manipulating an aspect of reward expectation, typically the subjective value of the outcome or the contingency between behavior and outcome (Dickinson, 1985; Dickinson, Wood, & Smith, 2002; Yin & Knowlton, 2006; Yin, Knowlton, & Balleine, 2006). Since the rate of reinforcement in fixed or random ratio schedules is proportional to the rate of responding, these schedules provide immediate feedback and drive flexible, "goal-directed" behaviors. Conversely, in variable or random interval schedules, reinforcement is additionally dependent on the passage of time; as a result, the correlation between responding and reinforcement is weakly perceived and yields more inflexible, "habit-like" behaviors. Indeed, the degree of "goal" or "habit"-directedness is often determined by the change in responding under extinction conditions following manipulation of either the outcome value or the action-outcome contingency, with larger and smaller changes reflecting goal-directed and habit-like seeking, respectively.

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The outcome value in instrumental conditioning may be either increased or decreased, but is typically decreased to test for goal-directed behavior. Conditioned taste aversion, a technique that pairs the reinforcer with a lithium chloride injection, can be an effective method of devaluation but often produces reductions in self-administration lasting days to weeks (Foy & Foy, 2009; Nolan et al., 1997). In contrast, satiety-specific devaluation transiently decreases the value of a reinforcer by inducing satiety via free access. Because consumed foods are subsequently both less desired and consumed relative to other palatable foods when given free access (Rolls, Rolls, Rowe, & Sweeney, 1981), satiety is to a large degree taste-specific. Reward-seeking can be tested after free access to the reinforcer (satiety) and compared to seeking after access to an alternative solution. In such reward devaluation tests, decreased responding after reinforcer devaluation relative to control conditions would indicate "goal-directed" behavior, while comparable responding across conditions would indicate "habitual" behavior.

Alternatively, contingency-degradation tests assess flexibility by evaluating reward-seeking behavior after degradation of the action-outcome contingency (Bradfield, Bertran-Gonzalez, Chieng, & Balleine, 2013; Yin & Knowlton, 2006). Degradation may be accomplished via uncoupling of reward delivery from responses, or even reversal of the contingency via omission, in which the withholding of a response results in reinforcement. The animal's behavior is assessed in extinction sessions before and after the contingency-degradation training. Again, decreases in seeking behavior after contingency degradation indicate "goal-directed" behavior, while insensitivity to the new training is considered "habit."

Despite initial differences in behavioral flexibility, both low and high contingency schedules can reflect habit-like behavior with repeated performance as animals become "overtrained" (Dickinson, 1985). Additionally, the properties of the reinforcer have been shown to influence the rate of habit formation, as ethanol reinforcement appears to promote habit formation as compared to non-drug reinforcers (Corbit, Nie, & Janak, 2012; Dickinson et al., 2002; Mangieri, Cofresí, & Gonzales, 2012) (but see Samson et al., 2004). However, low doses of ethanol may be insufficient to accelerate habit formation, as rats self-administering ~0.5 g/kg ethanol daily retained goal-directed behavior on an FR5 reinforcement schedule over several weeks (Hay, Jennings, Zitzman, Hodge, & Robinson, 2013). Moreover, in that study and unpublished observations from our laboratory, we found that rats self-administering ethanol or 10% sucrose on an FR5 reinforcement schedule appeared more sensitive to satiety-specific devaluation (i.e., more goal-directed) than rats self-administering 1.5% sucrose on the same schedule, suggesting that reinforcer properties may contribute to the assessment of behavioral flexibility. Since satiety-specific devaluation as a test of habit is dependent upon the ability of the solution to induce satiety and since our reinforcing solutions differ across short-term satiety signals like caloric load, it follows that the outcome of the devaluation test may vary across reinforcer solutions. However, as contingency degradation depends only upon the experience of changing contingencies, it is plausible this method would be more consistent across reinforcers.

The goal of the present study was to determine the congruency between satiety-specific devaluation and contingency-degradation tests of behavioral flexibility in rats trained to self-administer one of four solutions on an FR5-reinforcement schedule. The solutions were 1.5% sucrose (w/v), 10% sucrose (w/v), 10 mM monosodium glutamate (MSG), and 10% ethanol (w/v) faded with either sucrose or MSG. MSG was chosen as a non-sweet, alternative reinforcer (McCool & Chappell, 2012; Shibata, Kameishi, Kondoh, & Torii, 2009) that has been used as an ethanol-fading solution (McCool & Chappell, 2012). We hypothesized that the outcome of the satiety-specific devaluation test would be influenced by the reinforcer, whereas contingency degradation would not.

Materials and methods

Animal subjects

Adult, male Long-Evans rats ($n = 83$) were obtained from Harlan Laboratories (Frederick, MD) at a starting weight range of 250–275 g. Rats were individually housed in a controlled vivarium (12-h light/dark schedule with lights on at 7:00 AM; 25 °C) and had food and water *ad libitum* except as noted below. Rats were given 5 days upon arrival to adapt to the vivarium before training began (5 days/week, Monday-Friday). All procedures were compliant with the NIH Guide for the Care and Use of Laboratory Animals and approved by the Institutional Animal Care and Use Committee of the University of North Carolina at Chapel Hill.

FR5 self-administration training

Self-administration training occurred in operant boxes within sound-attenuating chambers (Med Associates, St. Albans, VT). Each box contained two retractable levers on one wall, with a circular cue light located above each lever and two metal fluid cups in between the levers. A house light was located on the upper portion of the opposite wall, and an exhaust fan and white noise generator were on during training sessions. Each training session began with a 5-min waiting period, followed by illumination of the house light and, after 30 s, extension of the levers. At each reinforced lever-press response, the activated lever's cue light turned on, the house light turned off, both levers were retracted, and 0.1 mL fluid was dispensed into the activated lever's cup. After 5 s, the levers extended, the cue light extinguished, the house light resumed, and the rat was able to again press the lever for reinforcement. Cups were checked at the end of each session to verify that the rat consumed the reinforcer and any remaining volume was recorded.

Rats were trained to respond for either 1.5% sucrose (w/v; 1.5-SUC), 10% sucrose (w/v; 10-SUC), 10 mM MSG (10-MSG), or 10% ethanol (w/v; 10-E); 10-E self-administration was accomplished either by a typical sucrose fade (S-10-E) (Hay et al., 2013; Samson, 1986) or by an analogous MSG fade (M-10-E) (McCool & Chappell, 2012). The training schedules for the five resulting experimental groups are shown in Table 1. For the first 5 days of training, animals were water-deprived up to 23 h per day to facilitate learning of the operant task, with 1-h water access immediately following the operant session. Sessions 1 and 2 were run on an FR1 reinforcement schedule, with sessions 3–8 run on an FR3 schedule before moving to the FR5 schedule that was maintained thereafter.

During the initial three training sessions, responding on either lever resulted in a fluid reward and the session lasted up to 3 h. On the fourth day of training, the rats' least preferred side was used as the rewarded lever and on subsequent days the active lever alternated daily; these sessions were limited to 30 m. For the S-10-E and M-10-E groups, concentration of ethanol gradually increased while the concentration of sucrose or MSG concurrently decreased. The 10-MSG and 1.5-SUC groups followed the M-10-E and S-10-E groups' fading procedures through the first 20 sessions but without the inclusion of ethanol. Finally, rats in the 10-SUC group were maintained for the duration of the experiment at the 10% w/v concentration from session 4 onwards. To equate the number of fluid deliveries earned across groups, sessions were limited to 50 or 25 reinforcements as shown in Table 1.

Satiety-specific devaluation

Beginning at week 5 of training, rats underwent a satiety-specific devaluation test each Friday for 6 weeks (control versus test solution across groups at weeks 5–6, 7–8, and 9–10), resulting