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CUES ASSOCIATED WITH ALTERNATIVE REINFORCEMENT CAN ATTENUATE RESURGENCE OF AN EXTINGUISHED INSTRUMENTAL RESPONSE

A Dissertation Presented

by

Sydney Trask

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ABSTRACT

In resurgence, a target behavior (R1) is acquired in an initial phase and extinguished in a second phase while an alternative behavior (R2) is reinforced. When reinforcement for the second response is removed, however, R1 behavior returns or "resurges." The resurgence paradigm may have implications for understanding relapse after behavioral interventions in humans such as contingency management, or CM, in which (for example) drug users can earn vouchers contingent upon drug abstinence. The present experiments examined the effectiveness of a putative retrieval cue for treatment in attenuating the resurgence effects and determined the likely mechanism by which this cue functions. Experiment 1 established that a 2-second cue associated with delivery of the alternative reinforcer in Phase 2 can attenuate R1 resurgence and promote R2 behavior during testing. Experiment 2 demonstrated that this effect occurs regardless of whether the cue is delivered contingently or noncontingently on responding during the resurgence test, and Experiment 3 demonstrated that for the cue to be effective in reducing resurgence, it must be paired with alternative reinforcement during Phase 2. This might mean that pairing the cue with reinforcement serves to maintain attention to the cue. Experiment 4 suggested that a cue paired with alternative reinforcement did not serve as a conditioned reinforcer in that making it contingent on a new behavior did not increase the likelihood of that behavior. Experiment 5 demonstrated that the cue must be experienced in sessions that also include the extinction of R1. Experiment 6 found that a cue produced by R1 during the second phase of a resurgence paradigm (analogous to a conditioned inhibitor) does not attenuate resurgence of an extinguished instrumental response. Together, the results suggest that a neutral cue can serve as an effective cue that attenuates resurgence if it is first paired with alternative reinforcement and presented in sessions in which R1 is extinguished. One way to view the results is that creating greater generalization between the extinction context and the testing context results in less resurgence.

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Introduction

Operant conditioning is an important process in which animals interact with their environment and learn to perform actions that provide reinforcing outcomes. The behavior that results is lawfully related to its consequences, and its study in the laboratory is thought to provide a model for understanding voluntary behavior more generally. As such, operant conditioning in animals has implications for understanding voluntary behaviors that impact human health, such as overeating, drug-taking, and smoking.

In the laboratory, operant behavior can be reliably reduced by *extinction*, the procedure in which the response no longer produces a reinforcing outcome. The study of extinction has implications for treating behavioral excesses (e.g., Bouton, 2014). However, one major theme of contemporary research is that extinguished operant behavior is not erased and can readily return. Further, it is especially dependent on the context (e.g., operant chambers in the laboratory that differ in tactile, visual, and olfactory properties) for its expression. The most straightforward example of this context-dependency of extinction is the *renewal effect*, the consistent finding that extinguished responding readily recovers when the response is tested outside of the context in which it has been extinguished (Bouton, Todd, Vurbic, & Winterbauer, 2011; Crombag & Shaham, 2002; Nakajima, Urushihara, & Masaki, 2002). This return of responding can occur when the response is acquired in one context, extinguished in a second, and tested back in the acquisition context (ABA renewal), or when the response is tested in a new context (ABC renewal). Extinguished responding can also renew when the response is acquired and extinguished in the same context and tested in a second context (AAB renewal). Together, these renewal effects suggest that simple removal from the context of extinction is enough to cause extinguished responding to return. Most of the evidence suggests that during operant extinction, an inhibitory association between the context and response is formed (Bouton, Trask, & Carranza-Jasso, 2016; Rescorla, 1997; Todd, 2013; see Trask, Thrailkill, & Bouton, 2017, for a detailed review). Removal from the context in which response inhibition is learned weakens its expression, thus causing a return of behavior.

Extinguished operant responding can also recover in a phenomenon known as *resurgence*. In a standard resurgence paradigm, a target response, R1, is reinforced and then extinguished. While R1 is being extinguished, a newly available response, R2, is reinforced. During a testing phase, both responses are available and neither is reinforced. The typical result is that R1 behavior returns or "resurges" when alternative reinforcement for R2 is removed (e.g., Leitenberg, Rawson, & Bath, 1970). One interpretation of this result is that alternative reinforcement creates a context in which extinction learning takes place and that removal of the reinforcers creates a new context. Thus, the resurgence effect can be conceptualized as an ABC-like renewal effect in which the context is created by the presence or absence of alternative reinforcement (Trask, Schepers, & Bouton, 2015; Winterbauer & Bouton, 2010).

We (Bouton & Schepers, 2014; Bouton, Thrailkill, Bergeria, & Davis, in press; Trask et al., 2015; Winterbauer, Lucke, & Bouton, 2013) and others (Craig, Nall, Madden, & Shahan, 2016; Quick, Pyszczynski, Colston, & Shahan, 2011) have noted that the resurgence effect may have implications for contingency management (CM) treatments in humans with health behavior problems such as drug dependence. In a typical contingency management treatment, patients can earn vouchers to be exchanged for goods and services contingent on providing proof of abstinence (e.g., drug-free urine samples). While this treatment effectively reduces the drug-taking behavior (Higgins, Sigmon, & Heil, 2011; Petry & Martin, 2002; Rawson et al., 2005), the behavior can return (or resurge) when the treatment is discontinued and alternative reinforcement ceases (Roll, Chudzynski, Cameron, Howell, & McPherson, 2013; see Davis, Kurti, Skelly, Redner, White, & Higgins, 2016, for a review). Although the resurgence paradigm is not a perfect model of relapse after contingency management (e.g., Bouton & Schepers, 2014; Bouton, et al., in press), it is possible that understanding the mechanisms of resurgence (and from this, how to reduce it) may contribute to our understanding and control of the relapse seen following such treatments.

Progress has already been made toward this goal in that several factors that can reduce resurgence have been identified. In general, higher rates of alternative reinforcement during treatment produce more resurgence, and leaner rates of alternative reinforcement produce less (Bouton & Trask, 2016; Leitenberg, Rawson, & Mulick, 1975; Smith, Smith, Shahan, Madden & Twohig, 2017; Sweeney & Shahan, 2013). Additionally, “thinning” the rate of alternative reinforcement from high rates to lower rates over the treatment phase also weakens the effect (Sweeney & Shahan, 2013; Winterbauer & Bouton, 2012). “Reverse thinning” procedures in which alternative reinforcement rates gradually increase throughout the phase can also reduce resurgence (Schepers & Bouton, 2015; see also Bouton & Schepers, 2014). Further, Schepers and Bouton (2015; Experiment 3) demonstrated that experience with periods of nonreinforcement during Phase 2 can have the same effect. In their experiment, alternating sessions of reinforcement and nonreinforcement for R2 during R1 extinction weakened the resurgence effect relative to animals that received reinforcement at the same average rate throughout R1 extinction. Overwhelmingly, the results support the idea that conditions that encourage generalization between the Phase-2 alternative reinforcement phase and Phase-3 testing (where no reinforcement is available) can reduce resurgence. That is, making the alternative reinforcement context (where reinforcement is typically available) more similar to the context where testing will take place (where reinforcement is typically not available) results in less resurgence (see Trask et al., 2015, for a detailed review of this idea).

Recent work has also demonstrated that the quality, rather than the quantity, of alternative reinforcement can be important in defining the reinforcement context. For example, Bouton and Trask (2016; Experiment 2) demonstrated that resurgence can be completely abolished by presenting the alternative reinforcer during a test. In that experiment, rats learned to perform an R1 leverpress response for a distinct food reinforcer, O1 (counterbalanced as sucrose- or grain-based pellets). In a second phase, R1 was extinguished while responding on a newly inserted lever, R2, produced a different reinforcer, O2. During a testing phase, both responses were inserted in the chamber, and neither was reinforced. For one group, no reinforcers at all were delivered during the test; resurgence was expected. For a second group, O1 outcomes were delivered freely at the same rate as reinforcers had been earned in Phase 2. A third group had a similar treatment, except O2 outcomes were delivered freely at the same rate as they had been earned in Phase 2. The idea was that if alternative reinforcement creates a unique context in which learning takes place (e.g., Trask et al., 2015), then the delivery of O2, but not O1, during testing should maintain the context in which R1 extinction had occurred and reduce resurgence. During the test, rats that had either no reinforcers or free O1 reinforcers demonstrated the standard resurgence effect; that is, R1 responding during the test was elevated compared to the final day of extinction. However, animals that had the free O2 reinforcers showed no increase in responding. The resurgence effect was completely abolished in this group.

Additional research went on to show that a second reinforcer that had been associated with extinction can also reduce operant relapse in the ABA renewal paradigm. In one demonstration of this, Trask and Bouton (2016, Experiment 3) trained rats to lever press for a distinct food outcome (O1) in Context A. The response was then extinguished in a different context, Context B, during sessions in which a second food outcome (O2) was delivered freely throughout the session. Testing manipulated both physical context and the reinforcer context. Animals were thus tested in either Context A (the conditioning context) or Context B (the extinction context) under two conditions. In one condition, O2 reinforcers were delivered freely as they had been during extinction. In the other condition, no reinforcers were delivered. The results showed that while overall responding was higher in Context A than Context B (demonstrating a renewal effect), the O2 reinforcer served to attenuate responding in both Contexts A and B. Further, the suppressive effect of O2 seemed to be both additive and equal in strength to the inhibitory effect of the physical context of extinction, suggesting that the reinforcers were influencing behavior in a way that mirrored the effects of the context. The results of both Bouton and Trask (2016) and Trask and Bouton (2016), as well as others demonstrating greater resurgence with a physical and reinforcement context change (Kincaid, Lattal, & Spence, 2015; but see Sweeney & Shahan, 2015), lend strong support to the idea that reinforcers can have discriminative properties in addition to their reinforcing properties (see also Bouton, Rosengard, Achenbach, Peck, & Brooks, 1993; Ostlund & Balleine, 2007; Reid, 1958).

The current experiments were designed to extend these results. They were mainly designed to ask whether the resurgence- and renewal-attenuating effects of delivering O2 during relapse testing (Bouton & Trask, 2016; Trask & Bouton, 2016) can also be achieved by delivering a more neutral cue during relapse testing. Neutral cues presented during the course of extinction sessions have been shown to be effective in attenuating renewal (Brooks & Bouton, 1994), spontaneous recovery (Brooks & Bouton, 1993; Brooks, 2000), and reinstatement (Brooks & Fava, 2017) of extinguished Pavlovian responding when they are presented during testing. In those experiments, occasionally presenting a neutral cue (e.g., a brief light) as a feature of the extinction context attenuated renewal of Pavlovian conditioned responding when it was also presented during the test. Subsequent analysis determined that the cue was not a conditioned inhibitor. Instead, the authors argued that the cue likely worked to attenuate relapse by enhancing generalization between the extinction and testing phases, making it easier to retrieve extinction. However, unpublished attempts in our laboratory to use analogous neutral cues associated with Phase 2 as a means of reducing resurgence have not been successful. Despite this, retrieval cues have been effective in reducing other forms of operant relapse, including spontaneous recovery, reinstatement (Bernal-Gamboa, Gámez, & Nieto, 2017), and renewal (Nieto, Uengoer, & Bernal-Gamboa, 2017; Willcocks & McNally, 2014), but not reacquisition (Willcocks & McNally, 2014). Thus, retrieval cues seem to be less effective at reducing operant relapse in procedures in which the animal is earning reinforcers during response suppression or relapse testing. In reacquisition, many reinforcers are earned during relapse testing, whereas in resurgence, many reinforcers are earned during the response elimination phase. Given its possible connection to CM treatments, it seems especially important to expand the range of cues that can be used to reduce the resurgence effect beyond presentations of O2 (Bouton & Trask, 2016; Trask & Bouton, 2016). The idea would be to find a salient enough cue that could be presented during treatment that could also be maintained beyond the time when voucher reinforcement ends (which cannot feasibly go on forever) in an attempt to reduce rates of relapse following cessation of CM.

One potential reason that the reinforcing outcomes (O2) used by Bouton and Trask (2016) and Trask and Bouton (2016) were so effective at reducing resurgence (and renewal) is that food pellets are motivationally significant and attention-commanding. Neutral brief visual or auditory stimuli presented in the background are not. However, neutral cues can acquire more significance. One way to give them significance is to increase the animal's attention to them. Mackintosh (1975) suggested that cues paired consistently with reinforcers attract attention as the animal learns the cue is a good predictor of the outcome, and thus an important part of its environment. Further, his model suggests that a stimulus that is highly attended to will be more conditionable. Although this idea is challenged by some who suggest that attention is higher for *poor* predictors (see Kaye & Pearce, 1984; Hall & Pearce, 1979; Pearce & Hall, 1980) several lines of evidence support this claim. Perhaps the most straightforward example is demonstrated by the intradimensional- versus extradimensional-shift effect. For instance, in an experiment by Mackintosh and Little (1969), pigeons learned that key pecking would be reinforced in two of four stimuli that differed on two dimensions: key color (red or yellow) and orientation of stripes projected on the key (0 degrees or 90 degrees). For half the pigeons, line orientation was the relevant predictor (i.e., a 0-degree or a 90-degree orientation predicted reinforcement), regardless of color. For the other half, color was the relevant predictor (i.e., either a yellow or red key was always reinforced) regardless of line orientation. In a second phase, four new stimuli that differed on the same dimensions were trained (either blue or green in color, with line orientations of 45 or 135 degrees). Animals learned either blue-positive or 45 degree-positive associations. Thus, there were four groups labeled according to the relevant predictors in the first and second phase respectively: Color-Color, Color-Orientation, Orientation-Orientation, and Orientation-Color. Importantly, for groups Color-Color and Orientation-Orientation, the same dimension that was predictive in initial training was still relevant in the second phase (a so-called "intradimensional shift"); the same was not true for the Color-Orientation and the Orientation-Color groups (an "extradimensional shift"). The results were clear: Animals that experienced an intradimensional shift learned the new discrimination more quickly than animals that experienced an extradimensional shift. This suggests that previously relevant predictors were learned about more readily than previously irrelevant predictors, as is consistent with the Mackintosh model. The Mackintosh (1975) model seems to explain data resulting from situations in which there is a discrimination to be solved (Pearce & Mackintosh, 2010), as in the intradimensional-shift effect (Mackintosh & Little, 1969).

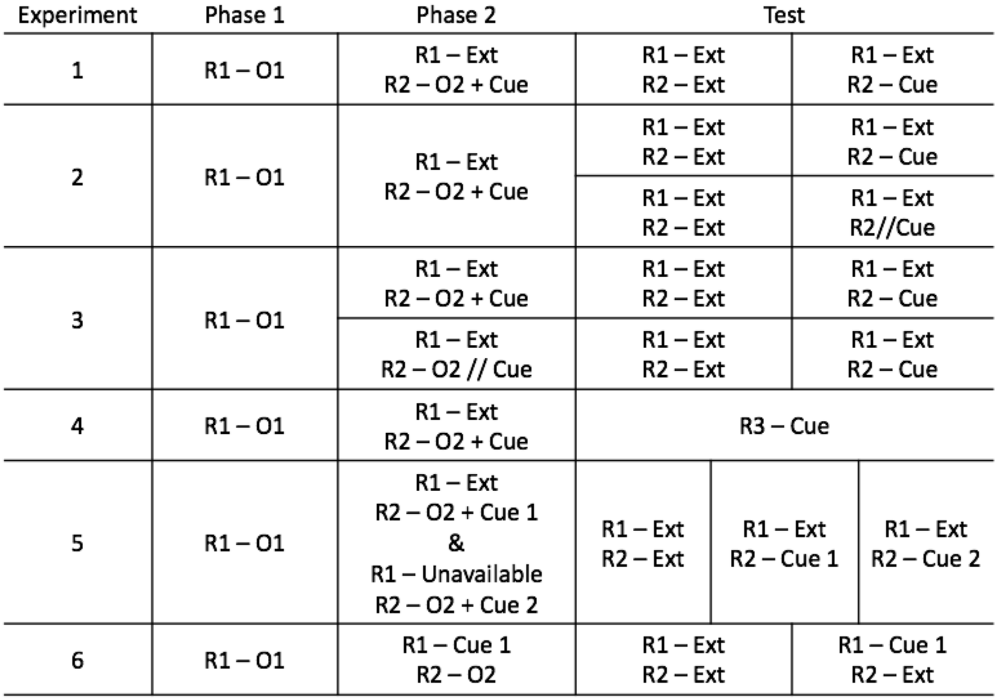
Additional support in human predictive tasks suggests that participants pay more attention (as measured by eye gaze assessed with eye-tracking devices) to stimuli that are good predictors than those that are not (for a review, see Le Pelley, Mitchell, Beesley, George, & Wills, 2016). Further, human participants also show the intradimensional-shift effect, where performance is easier following an intradimensional shift rather than an extradimensional shift (e.g., Roberts, Robbins, & Everitt, 1988), similar to that reported in pigeons by Mackintosh and Little (1969).

Cues that have been paired with reinforcement can of course acquire other types of significance as well. For example, animals will respond to produce a conditioned stimulus (or CS) that has been paired with a reinforcing outcome (Bertz & Woods, 2013; Fantino, 1969; Hyde, 1976). In this way, previously neutral cues can meet criteria for reinforcers in that they can increase the likelihood of an operant response of which they are a consequence. The present experiments therefore began by asking whether cues deliberately associated with the alternative reinforcer during Phase 2 treatment can be used to attenuate response recovery (relapse) by presenting them during testing in the resurgence paradigm.

Experiment 1

Experiment 1 (design depicted in Table 1) was conducted to provide a preliminary test of this possibility. As noted previously, freely presenting a reinforcer during testing that had been associated with Phase-2 response elimination can abolish the resurgence effect (Bouton & Trask, 2016). In the present experiment, all rats were taught to perform an R1 response for an O1 outcome in Phase 1. In Phase 2, R1 responding was extinguished while a newly inserted R2 response produced a different reinforcer, O2. A 2-s tone stimulus was paired with every O2 delivery. During the test, R1 and R2 responding were both extinguished and examined under two conditions administered in a counterbalanced order. In the first condition, R2 responding still produced the 2-s tone. In the second condition, it did not; no reinforcing outcomes were ever delivered. Resurgence was expected in the latter condition, but the hypothesis was that R1 responding would be lower (resurgence would be attenuated) and that R2 responding would be higher in the test in which R2 produced the cue.

Method



Experiment	Phase 1	Phase 2	Test		
1	R1 – O1	R1 – Ext R2 – O2 + Cue	R1 – Ext R2 – Ext	R1 – Ext R2 – Cue	
2	R1 – O1	R1 – Ext R2 – O2 + Cue	R1 – Ext R2 – Ext	R1 – Ext R2 – Cue	
			R1 – Ext R2 – Ext	R1 – Ext R2//Cue	
3	R1 – O1	R1 – Ext R2 – O2 + Cue	R1 – Ext R2 – Ext	R1 – Ext R2 – Cue	
		R1 – Ext R2 – O2 // Cue	R1 – Ext R2 – Ext	R1 – Ext R2 – Cue	
4	R1 – O1	R1 – Ext R2 – O2 + Cue	R3 – Cue		
5	R1 – O1	R1 – Ext R2 – O2 + Cue 1 & R1 – Unavailable R2 – O2 + Cue 2	R1 – Ext R2 – Ext	R1 – Ext R2 – Cue 1	R1 – Ext R2 – Cue 2
6	R1 – O1	R1 – Cue 1 R2 – O2	R1 – Ext R2 – Ext	R1 – Cue 1 R2 – Ext	

Table 1. Experimental design for Experiments 1 through 6. R1 and R2 represent presses on left and right levers (counterbalanced). R3 was pulling a chain suspended from the top of the chamber. O1 and O2 represent sucrose- and grain-based food pellets (counterbalanced). In Experiment 1, the cue was a 2-s tone. In Experiments 2 and 3, the cue was a 2-s tone/light compound. In Experiments 5 and 6, Cue 1 and Cue 2 were counterbalanced as either a 2-s tone or a 2-s light. A + represents two items that occur together whereas a // separates two items that are not explicitly paired.

Subjects

The subjects were 16 female Wistar rats obtained from Charles River, Inc. (St. Constance, Quebec). They were approximately 85–95 days old at the start of the experiment and were individually housed in suspended stainless steel cages in a room maintained on a 16:8-h light:dark cycle. At the beginning of the experiment, all rats were food deprived to 80% of their free-feeding weight and maintained at that level throughout the experiment with a single feeding following each day's session.

Apparatus

Conditioning proceeded in two sets of four standard conditioning boxes (Med-Associates Model Number: ENV-008-VP, St. Albans, VT) that were housed in different rooms of the laboratory. The sets had been modified as described below for use as separate contexts, although they were not used in that capacity here. Boxes from both sets measured 30.5 cm × 24.1 × 21.0 cm (l × w × h), with side walls and ceilings made of clear acrylic plastic and front and rear walls made of brushed aluminum. Recessed 5.1 cm × 5.1 cm food cups with infrared photobeams positioned approximately 1.2 cm behind the plane of the wall and 1.2 cm above the bottom of the cup were centered in the front wall about 3 cm above the grid. In one set of four boxes, the floor was composed of stainless steel rods (0.5 cm in diameter) in a horizontal plane spaced 1.6 cm center to center, while in the other set of four boxes, the floor was composed of identical rods spaced 3.2 cm apart in two separate horizontal planes, one 0.6 cm lower than the other and horizontally offset by 1.6 cm. The boxes with the planar floor grid had a side wall with black panels (7.6 cm × 7.6 cm) placed in a diagonal arrangement, and there were diagonal stripes on both the ceiling and the back panel, all oriented in the same direction, 2.9 cm wide, and about 4 cm apart. The other boxes, with the staggered floor, were not adorned in any way. Retractable levers (1.9 cm when extended) were positioned approximately 3.2 cm to the right and to the left of the food cup and 6.4 cm above the grid. Both sets of boxes were housed in sound-attenuating chambers, and were continuously illuminated by two 7.5-W incandescent light bulbs mounted on the chamber ceiling. A 2-s 4500 Hz, 65dB tone was emitted from a sonalert module mounted directly above the magazine (Med-Associates Model Number: ENV-223HAM). During the conditioned reinforcement test (Experiment 4), a chain-pull manipulandum was used. The response chain (Med Associates model ENV-111C), when in use, was suspended from a microswitch mounted on top (outside) of the ceiling panel of each operant chamber. The chain hung 1.9 cm from the front wall, 3 cm to the right of the food cup, and 6.2 cm above the grid floor.

Food reinforcers consisted of 45-mg MLab Rodent Tablets (5-TUM: 181156; TestDiet, Richmond, IN) and a 45-mg sucrose pellet (5-TUT: 1811251; TestDiet). These were counterbalanced as O1 and O2. The apparatus was controlled by computer equipment located in an adjacent room.

Procedure

Twice-daily sessions were employed throughout the experiment. Each day’s first session began with approximately 15 h of illuminated colony time remaining. Each day’s second session began approximately 2.5 h later. Animals were placed into illuminated conditioning chambers, and the start of each session was indicated by the insertion of the lever(s) as appropriate. All sessions were 30 min in duration, and the end of the session was indicated by retraction of the lever(s).

Magazine training. All animals received magazine training on the day immediately prior to the beginning of Phase 1. At this time, they received two sessions with both levers retracted. During one session, rats received magazine training with their O1 reinforcer. During the other, the O2 reinforcer was delivered to the magazine. Sessions were counterbalanced so that half of the animals received training first with O1 then O2, and half received O2 then O1. On average, 60 food pellets were delivered during each session on a random time 30-s (RT 30-s) schedule of reinforcement.

R1 Acquisition (Phase 1). All animals then received 12 sessions of instrumental conditioning initiated by insertion of the left lever in half animals and the right lever in the other half. In all sessions, presses on the inserted lever (R1) delivered O1 pellets on a VI 30-s schedule of reinforcement. No additional response shaping was necessary.

R1 Extinction and R2 Acquisition (Phase 2). All animals then received eight sessions in which R1 presses were extinguished (i.e., produced no reinforcers) and presses to the second lever (R2) were reinforced with the O2 reinforcer on a VI 30-s schedule. Onset of a 2-s tone sounded from the sonalert module coincided with each delivery of an O2 reinforcer. Both the left and the right levers were inserted throughout each session.

Resurgence Test (Phase 3). On the day following the conclusion of Phase 2, all rats received two 10-min test sessions in which both levers were inserted. R1 and R2 presses were recorded, but neither produced a food outcome. During one test, R2 presses produced only the 2-s tone on a VI 30-s schedule. No cues were presented in the other test. The test order was counterbalanced.

Data Analysis. Analyses of variance (ANOVAs) were used to assess response rates throughout the experiment. The rejection criterion was $p < .05$.

Results

The results of Experiment 1 are displayed in Figure 1. Animals increased their R1 responding in acquisition (Panel A). In Phase 2 (Panel B), R1 responding declined and R2 responding increased. During the testing phase (Panel C), R1 responding was reduced when the cue was present relative to when it was absent, and R2 responding was also elevated when the cue was present relative to when it was not. This was confirmed by statistical analyses.

R1 Acquisition. The animals increased their responding throughout acquisition, as confirmed by an ANOVA on responding over the 12 sessions, which revealed a main effect of session, F (11, 165) = 26.09, MSE = 29.03, $p < .001$, $\eta_p^2 = .64$.

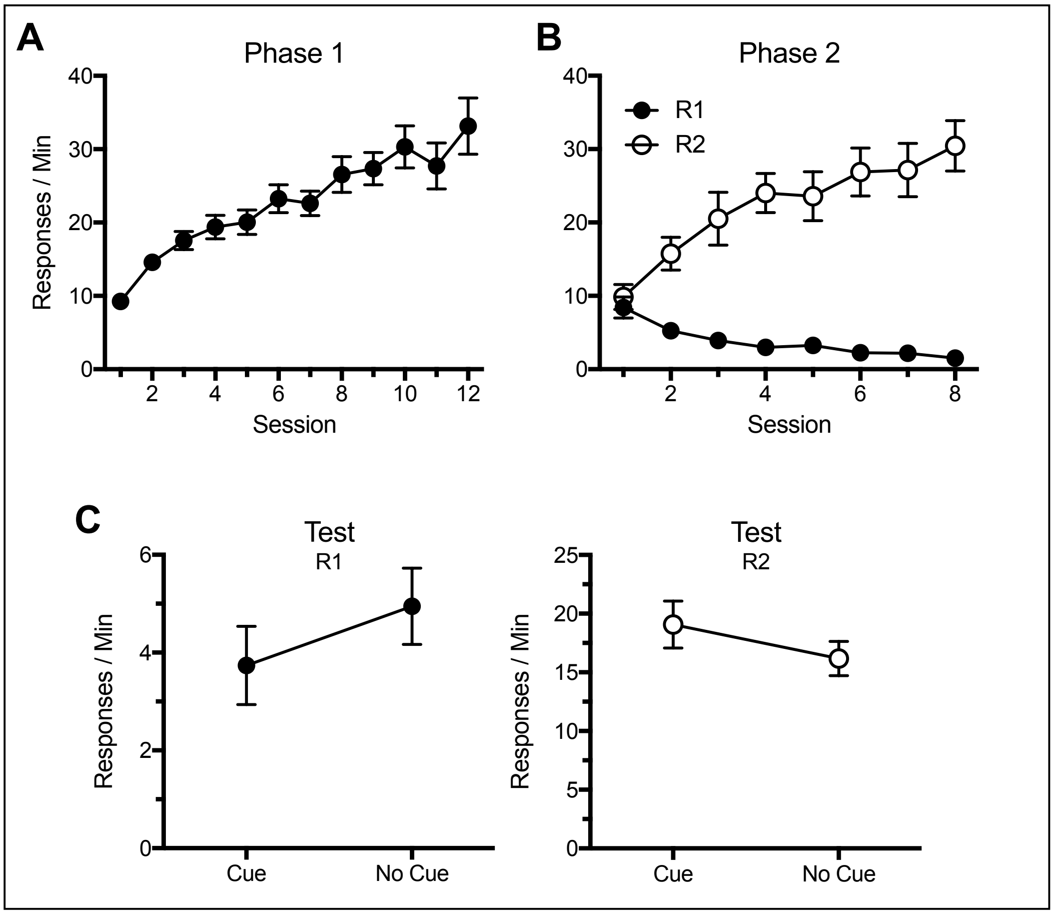


Figure 1. R1 acquisition throughout Phase 1 (Panel A), R1 extinction and R2 acquisition in Phase 2 (Panel B), and responding during the test for R1 and R2 (Panel C) in Experiment 1. Please note that error bars are only appropriate for between-subjects comparisons.

R1 Extinction and R2 Acquisition. Throughout Phase 2, animals decreased their R1 responding. This was confirmed by an ANOVA conducted on R1 responding which revealed a main effect of session, F (7, 105) = 13.06, MSE = 6.03, $p < .001$, $\eta_p^2 = .47$. Animals also increased their responding on R2 throughout Phase 2 as confirmed by an ANOVA assessing responding throughout this phase, F (7, 105) = 17.28, MSE = 41.99, $p < .001$, $\eta_p^2 = .54$.

Test. A 2 (Session: Cue vs. No Cue) x 2 (Response: R1 vs. R2) ANOVA was run to assess responding on both levers throughout the test sessions. This revealed a main effect of response, F (1, 15) = 65.39, MSE = 43.16, $p < .001$, $\eta_p^2 = .81$, but no main effect of session, F (1, 15) = 1.33, $p > .05$. Importantly, the session by response interaction was significant, F (1, 15) = 7.72, MSE = 8.77, $p < .02$, $\eta_p^2 = .34$. Follow-up comparisons revealed that animals responded less on the R1 response during the session when R2 produced the cue than in the session without the cue, F (1, 15) = 9.14, $p < .01$, $\eta_p^2 = .38$. Thus, the cue attenuated the resurgence effect. In addition, R2 responding showed a marginally significant trend in the opposite direction, such that there was more R2 responding in the presence of the cue than without it, F (1, 15) = 4.19, $p = .06$, $\eta_p^2 = .22$.

Discussion

The results of Experiment 1 demonstrated that a cue that is associated with alternative reinforcement during Phase 2 of a resurgence paradigm reduces resurgence of an extinguished instrumental response when it is produced by the R2 response. However, Bouton and Trask (2016) demonstrated that O2 reinforcers delivered freely (i.e., not contingent on responding) reduced resurgence of an instrumental response. We therefore asked in Experiment 2 if a cue delivered noncontingently during the test would have the same effect as a cue that remained contingent on R2 responding.

Experiment 2

The experiment involved two groups. One group received an identical treatment to that of the animals in Experiment 1, and thus provided an opportunity to replicate the main finding. In a first phase, R1 produced O1 reinforcers and R1 was extinguished in a second phase while R2 produced O2 reinforcers and a 2-s cue (this time, a tone-light compound). During the test, rats were tested in a condition in which R2 produced the cue and a condition in which it did not. For the second group, Phases 1 and 2 were identical to that of the first group. However, during the test, R2 did not produce the cue in either condition. Instead, during one condition the cue was presented noncontingently on responding at the same rate it had been presented during Phase 2. In the other condition, the cue was not presented.

Method

Subjects

The subjects were 32 female Wistar rats obtained, housed, and maintained exactly as those in Experiment 1.

Apparatus

The apparatus was the same as was used in Experiment 1. The same sucrose- and grain-based pellets served as reinforcers. As before, a 2-s 4500 Hz, 65dB tone was emitted from a sonalert module mounted directly above the magazine (Med-Associates Model Number: ENV-223HAM). A 2-s illumination of a panel light mounted immediately above the sonalert module occurred at the same time.

Procedure

Twice-daily sessions were used throughout the experiment, as in Experiment 1.

Magazine training and R1 Acquisition (Phase 1). Magazine training and R1 training proceeded identically to Experiment 1.

R1 Extinction and R2 Acquisition (Phase 2). As in Experiment 1, all animals then received eight sessions in which R1 presses were extinguished (i.e., produced no reinforcers) and presses to the second lever (R2) were reinforced with O2 on a VI 30-s schedule. Delivery of each food pellet coincided with presentation of a 2-s tone-light compound. Both the left and the right levers were inserted throughout each session.

Resurgence Test (Phase 3). On the day following the conclusion of Phase 2, all rats received two 10-minute test sessions with both levers inserted. R1 and R2 presses were recorded, but neither produced a food outcome. During one test, the 2-s cue was presented. For the contingent group, this was contingent on R2 responding (as during Phase 2); for the noncontingent group, the cue was presented noncontingently on an RT 30-s schedule. No cues were presented in the second test for either group.

Results

The results are shown in Figure 2. Animals increased their R1 responding throughout Phase 1 (Panel A), and decreased R1 responding throughout Phase 2 (Panel B), when reinforced R2 responding also increased. During the test (Panel C) R1 responding was reduced when the cue was present and R2 responding was increased when the cue was present. This was true regardless of whether or not the cue was contingent on R2 responding.

R1 Acquisition. All animals increased their responding throughout acquisition, as confirmed by a 2 (Group) x 12 (Session) ANOVA. This revealed a main effect of session, F (11, 330) = 66.67, MSE = 26.05, $p < .001$, $\eta_p^2 = .69$, but neither a main effect of group nor a significant interaction, Fs < 1.

R1 Extinction and R2 Acquisition (Phase 2). Throughout Phase 2, animals decreased their R1 responding. This was confirmed by a 2 (Group) x 8 (Session) ANOVA, which found a main effect of session, F (7, 210) = 27.39, MSE = 4.99, $p < .001$, $\eta_p^2 = .48$, but no main effect of group or a group by session interaction, Fs < 1. The rats also increased their responding on R2 throughout the phase. This was confirmed by a

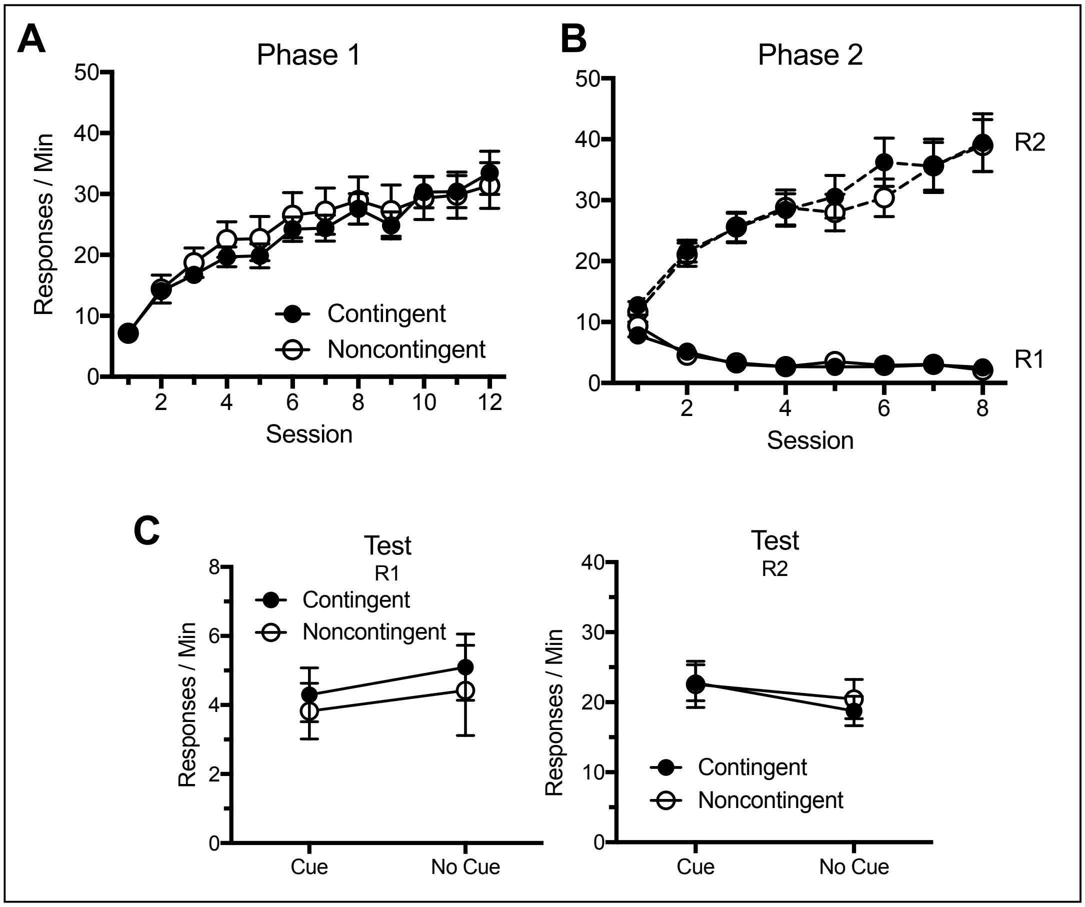


Figure 2. R1 acquisition throughout Phase 1 (Panel A), R1 extinction and R2 acquisition throughout Phase 2 (Panel B), and R1 and R2 responding during the test (Panel C) in Experiment 2. Please note that error bars are only appropriate for between-subjects comparisons.

2 (Group) x 8 (Session) ANOVA, which found a main effect of session, F (7, 210) = 53.64, MSE = 43.63, $p < .001$, $\eta_p^2 = .64$, but no group effect or interaction, Fs < 1.

Test. A 2 (Group) x 2 (Session: Cue vs. No Cue) x 2 (Response: R1 vs. R2) ANOVA was run to assess responding on both levers during the test sessions. This revealed a main effect of response, F (1, 30) = 82.51, MSE = 108.53, $p < .001$, $\eta_p^2 = .73$. Importantly, the session by response interaction was significant, F (1, 30) = 14.30, MSE = 7.89, $p = .001$, $\eta_p^2 = .32$. No other main effects or interactions were significant (largest $F = 2.91$), suggesting that while the cue promoted R2 performance and inhibited R1 performance, this effect did not depend on whether the cue was response-contingent or not. Follow-up comparisons revealed that, when collapsed across group (as there was no significant interaction), animals responded more on the R2 response during the session when R2 produced the cue than in the session without the cue, F (1, 30) = 7.31, $p < .02$, $\eta_p^2 = .20$, while R1 responding showed a trend in the opposite direction, F (1, 30) = 2.92, $p = .098$, $\eta_p^2 = .09$. Based on the findings from Experiment 1, where the cue significantly decreased responding, our a priori hypothesis was that the cue would function similarly here. Thus, a one-tailed t-test was used to examine R1 responding in the test in which the cue was present relative to the test in which it was not. This found that responding was significantly suppressed in the test in which the cue was presented relative to when it was not, t (31) = 1.74, $p < .05$.

Discussion

As in Experiment 1, a retrieval cue associated with alternative reinforcement during Phase 2 of the resurgence paradigm weakened resurgence of an instrumental response. This effect did not depend on whether the cue was contingent on R2 or presented noncontingently during the test. The effectiveness of the noncontingent cue is consistent with findings reported using a reinforcing outcome as a retrieval cue in both resurgence (Bouton & Trask, 2016) and renewal (Trask & Bouton, 2016). One interesting result of this experiment was that the cue was equally effective at promoting R2 behavior whether or not it was presented contingent on responding during the test. This suggests that the cue is not necessarily working as a conditioned reinforcer to promote R2 responding. Instead, its presence might encourage generalization to the test.

Experiment 3

In Experiment 3, we asked whether or not the cue needed to be paired or unpaired with the reinforcer during the treatment phase (Phase 2) in order to attenuate resurgence during testing. We have previously shown that reinforcers delivered both contingently on responding (Bouton & Trask, 2016, Experiment 2) and noncontingently on responding (Trask & Bouton, 2016) during extinction decrease relapse of a target response when presented during testing. That result was further consistent with the view that the events attenuate relapse by increasing the generalization between Phase 2 and testing. However, it has yet to be demonstrated that the cue studied in Experiments 1 and 2 needs to be paired with reinforcement in Phase 2 in order to be effective during the test or if simply being made response contingent is enough. According to some theories of learning, a cue that is not paired with reinforcement will not attract attention (e.g., Mackintosh, 1975) and thus may be ineffective as a retrieval cue.

Method

Subjects and Apparatus

The subjects were 32 female Wistar rats that were obtained, housed, and maintained exactly as those in Experiments 1 and 2. The apparatus and reinforcers was also the same. The compound tone/light cue from Experiment 2 was used here.

Procedure

As usual, animals were run twice a day.

Magazine training and R1 Acquisition (Phase 1). Magazine training on the first day of the experiment proceeded identically to Experiments 1 and 2. Also as before, the rats then received 12 operant acquisition sessions in which R1 produced O1 on a VI 30-s schedule.

R1 Extinction and R2 Acquisition (Phase 2). All animals then received eight sessions in which R1 presses were extinguished (i.e., produced no reinforcers) and presses on the second lever (R2) were reinforced with O2 on a VI 30-s schedule. In one group, delivery of each food pellet was simultaneous with the onset of the 2-s cue. In the second group, Group Unpaired, the cue was also presented in a response-contingent manner, but on a separate VI 30-s schedule than the pellet. In this way, the cue and reinforcer were not explicitly paired. Both the left and the right levers were inserted throughout each session.

Resurgence Test (Phase 3). On the day following the conclusion of Phase 2, all rats received two final 10-minute test sessions with both levers inserted. R1 and R2 presses were recorded, but neither produced a food outcome. During one test, the 2-s cue was presented contingent on R2 responding (on a VI 30-s schedule). No cues were presented in the second test for either group. Testing order was counterbalanced.

Data Analysis. Analyses of variance (ANOVAs) were conducted with a rejection criterion of $p < .05$. Two animals were excluded from Group Paired because they were significant overall outliers on R1 responding during the test (Zs = 2.3, 3.2; Field, 2005). Exclusion of these animals did not change the overall pattern from Phase 1 or Phase 2.

Results

The results are shown in Figure 3. As before, R1 responding increased in Phase 1 (Panel A) and declined in Phase 2 (Panel B), when the newly-available and reinforced R2 response increased. During the test, R1 responding was reduced only in animals that had received the cue paired with O2 in Phase 2.

R1 Acquisition. All animals increased their responding throughout acquisition, as confirmed by 2 (Group) x 12 (Session) ANOVA on responding over Phase 1. This revealed a main effect of session, F (11, 308) = 74.92, MSE = 32.27, $p < .001$, $\eta_p^2 = .73$, but no main effect of group or interaction, Fs < 1.

R1 Extinction and R2 Acquisition. Animals decreased their R1 responding during Phase 2, which was confirmed by a 2 (Group) x 8 (Session) ANOVA that found an effect of session, F (7. 196) = 31.40, MSE = 5.75, $p < .001$, $\eta_p^2 = .53$, but no effect of group or an interaction, Fs < 1. The rats also increased their responding on R2, as confirmed by a 2 (Group) x 8 (Session) ANOVA which found a session effect, F (7, 210) = 54.47, MSE = 44.63, $p < .001$, $\eta_p^2 = .66$, but no group effect or interaction, Fs < 1.

Test. As usual, a 2 (Group) x 2 (Session: Cue vs. No Cue) x 2 (Response: R1 vs. R2) ANOVA was run to assess responding on both levers during testing. This revealed a main effect of response, F (1, 30) = 82.51, MSE = 108.53, $p < .001$, $\eta_p^2 = .73$. Interestingly, because group differences were seen, the usual session by response

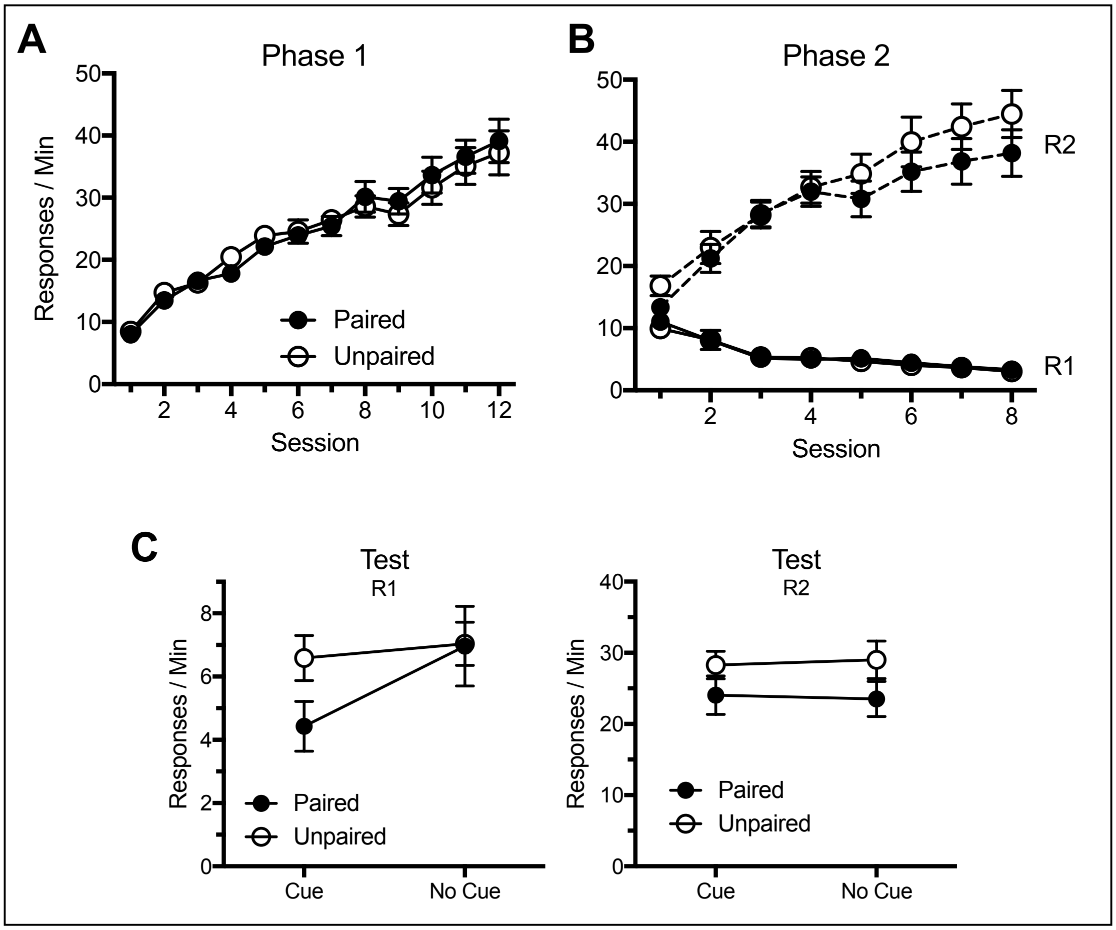


Figure 3. R1 responding throughout Phase 1 (Panel A), R1 and R2 responding throughout Phase 2 (Panel B) and the test (Panel C) in Experiment 3. Please note that error bars are only appropriate for between-subjects comparisons.

interaction was not found, *F* (1, 28) = 1.30, MSE = 11.04, *p* = .18. In order to assess the important group differences, supplementary analyses were run. A separate 2 (Group) x 2 (Session) ANOVA that assessed group differences in R1 responding revealed a main effect of session, *F* (1, 28) = 7.09, MSE = 4.67, *p* < .05, η_p^2 = .20, but no effect of group, *F* = 1.02, *p* = .32. The group by session interaction was marginally significant, *F* (1, 28) = 3.45, MSE = 4.67, *p* = .07. Importantly, Group Paired showed reduced responding during the test in which responding produced the cue relative to the session with no cue, *F* (1, 28) = 9.58, *p* < .01, η_p^2 = .26. There was no corresponding difference in Group Unpaired,

$F < 1$. Further, Group Paired showed suppressed responding relative to Group Unpaired during the test with the cue, F (1, 28) = 4.10, MSE = 8.43, $p = .05$, $\eta_p^2 = .13$, but the groups did not differ during the test without the cue, $F < 1$. In order to more fully examine responding in Group Paired, whose Phase 1 and 2 treatments were identical to animals in Experiments 1 and 2, a 2 (Session: Cue vs. No Cue) x 2 (Response: R1 vs. R2) ANOVA was conducted to assess their responding during the test. Recall that the previous experiments demonstrated a session by response interaction, suggesting that the cue both lowered R1 responding and elevated R2 responding. This ANOVA revealed a main effect of response, F (1, 13) = 57.52, MSE = 7.59, $p < .001$, $\eta_p^2 = .82$, but no effect of session, $F = 1.25$, $p = .28$. The interaction trended towards significance, F (1, 13) = 4.29, MSE = 7.59, $p = .06$, $\eta_p^2 = .25$. While R1 responding was lower in this group when the cue was present (described above), R2 responding did not differ between sessions, $F = 1.45$, $p = .73$, seemingly contrary to Experiments 1 and 2.

Discussion

The results of Experiment 3 demonstrated that a retrieval cue must be associated with alternative reinforcement in Phase 2 for it to be effective at attenuating resurgence during the test. This result is consistent with the view that, without association with a reinforcer, the present audiovisual cue is not sufficiently salient to attenuate resurgence. It must be paired with a reinforcer during Phase 2 in order to serve as an effective cue during the resurgence test. One possible reason this might be the case is that a cue that predicts nothing may not be salient or “attention-grabbing.” The result is predicted by Mackintosh (1975). In his model, stimuli that are poor predictors of outcomes will initially attract attention, but this will fall as the animal effectively learns the stimulus is not important. However, a stimulus consistently paired with reinforcement will acquire increasing levels of attention, as it becomes relevant to the animal. While direct measures of attention (e.g., eye-gaze in humans, Le Pelley et al, 2016, or an orienting response in rats, Kaye & Pearce, 1984) were not explicitly tested in this experiment, this is one possible reason that the cue needs to be paired with a reinforcer in order to serve as an effective retrieval cue; sufficient attention to the cue is not paid otherwise.

Experiment 4

Another potential mechanism through which the cue associated with alternate reinforcement in Phase 2 could both promote R2 behavior and inhibit R1 behavior during the test is that it was acting as a conditioned reinforcer. This could have perhaps engendered some response competition in which R1 behavior was lower simply because R2 was still being reinforced, albeit with a conditioned reinforcer rather than a primary reinforcer. While there was some evidence of this in Experiments 1 and 2 (recall that a cue associated with O2 reinforcers served to increase R2 behavior during the test sessions relative to sessions in which no cue was produced), the cue also supported R2 behavior and reduced resurgence when it was presented noncontingently during the test (Experiment 2). These results, where a conditioned reinforcement mechanism is not immediately evident (as would be more clear in a case in which R2 was consistently elevated when it produced the cue, but only when a response contingency was in place), suggest that the cue might attenuate resurgence by increasing generalization to the testing context rather than through a conditioned reinforcing mechanism. To further probe the possibility that the cue had properties of conditioned reinforcer, in each of the previous experiments, animals that received the Phase 2 treatment of O2 paired with the cue (i.e., all animals except for Group Unpaired of Experiment 3) were given one final session of Phase 2 reacquisition after testing and then a test for conditioned reinforcement. In this test, a new response manipulandum (a chain suspended from the ceiling) was introduced. For half the rats, pulling the chain produced the cue. For the other half, the response produced nothing. It was hypothesized that if the cue was acting as a conditioned reinforcer, then rats whose response produced the cue would respond more than rats whose response did not (see Hyde, 1976; Bertz & Woods, 2013).

Methods

Subjects and Apparatus

The subjects were 64 rats from Experiments 1, 2, and 3.

Procedure

Following the test phase of Experiments 1 – 3 (reported above), all rats had one 30-min retraining session during which Phase 2 contingencies were again in place (i.e., responses on R1 were extinguished while responses on R2 produced an O2 reinforcer along with the 2-s cue). Animals were then given one final test during which the chain pull response manipulandum was introduced to the chamber. For half the rats, chain pull responses produced the 2-s cue (either the tone for those animals from Experiment 1 or the tone/light compound for animals from Experiments 2 and 3) that was paired with the reinforcer during Phase 2 on a VI 30-s schedule. For the other half, chain pulls had no programmed consequences. One animal never made any responses (and thus never experienced the contingency tested) and was therefore excluded from the analysis. This left n = 31 in the cue group and n = 32 in the no cue group.

Results

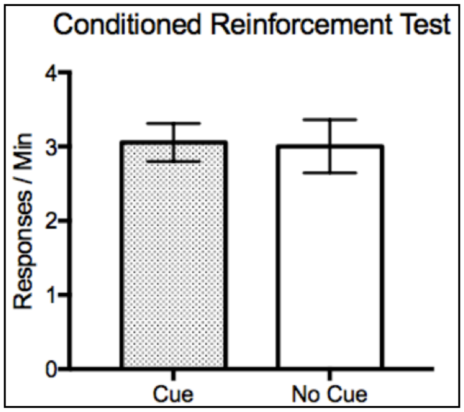


Figure 4. Responding on the chain pull manipulandum during the conditioned reinforcement test (Experiment 4).

Results from the conditioned reinforcement test are shown in Figure 4. A between-subjects t-test was run to test for differences in responding between animals whose responding produced the cue and those whose responding did not produce the cue. This revealed no difference in responding between groups, t (61) = 0.12, p = .91. In order to more fully assess the null hypothesis that there was no difference in responding based on whether or not the response produced the cue, a Bayes factor was calculated according to the scaled Jeffrey-Zellner-Slow prior using the method outlined by Rouder, Speckman, Sun, Morey, and Iverson (2009). The Bayes factor was 5.22, indicating that the obtained results are 5.22 more likely to be obtained under the null hypothesis. Further, the same test given to animals in Group Unpaired from Experiment 3 (whose cue should not have had the opportunity to acquire conditioned reinforcing properties as it was not paired with the outcome) yielded similar results: Animals whose responding produced the cue (M = 3.16 responses per minute) did not differ from animals whose responding produced nothing (M = 3.73 responses per minute), t (14) = 0.74, p = .47.

Discussion

The results of the conditioned reinforcement test produced no evidence that the cue promoted chain pull responding when it was made contingent on this response compared to a no cue condition. This suggests that the cue is not especially effective as a conditioned reinforcer, and thus further suggests that it might not have been acting as a conditioned reinforcer in the resurgence tests. Because conditioned reinforcers are thought to acquire their value through their Pavlovian (i.e., S – O) association with the primary reinforcer (see Williams, 1994), the fact that the cue does not seem to have conditioned reinforcing properties in the present experiments suggests that the cue is not attenuating R1 resurgence by virtue of an excitatory association with the reinforcer. The cue in the present experiments was likely functioning by enhancing generalization between Phase 2 and the testing conditions (see also Experiment 2). If what is learned in instrumental extinction is something akin to response inhibition (Bouton et al., 2016; Rescorla, 1997), the cue might serve to enhance the generalization of response inhibition from the response elimination phase to the test.

Experiment 5

One recent but important finding from our laboratory is that during extinction training, the animal learns to specifically inhibit a response in the presence of certain cues. Extinction is thus thought to result in the formation of an inhibitory S – R association (e.g., Bouton et al., 2016; Rescorla, 1993, 1997; Todd, 2013; Todd, Vurbic, & Bouton, 2014; reviewed in Trask, et al., 2017). Removal of the cues that signal response inhibition results in a return (renewal) of the original behavior. According to this view, if a cue is to reduce resurgence effectively, it might need to be featured in a session in which R1 is directly extinguished. Notice that this was true in Experiments 1-3. Experiment 5 was designed to explicitly test this hypothesis. The experiment utilized a completely within-subject design (detailed in Table 1) in which animals were given alternating Phase 2 sessions following the usual Phase 1 training. In the first such session, R1 was extinguished while R2 produced O2 which coincided with a cue, Cue 1 (either a tone or light counterbalanced). In the second type of session, R1 was unavailable (i.e., the lever remained retracted throughout the entire session) and R2 produced O2, which now coincided with a second cue, Cue 2 (light or tone, counterbalanced). We hypothesized that, due to its presence during R1 extinction sessions, Cue 1, but not Cue 2, would successfully attenuate resurgence when R2 produced it during a resurgence test. Further, animals were then tested for the equivalency of associative strength of each cue by assessing conditioned food cup entries to each stimulus. Foodcup entry is a commonly-used measure of appetitive conditioning to a conditioned stimulus that has been repeatedly paired with an appetitive outcome (e.g., Brooks & Bouton, 1993, 1994). It is worth noting that foodcup entries in response to a CS are not thought to result from instrumental learning and are instead a direct measure of Pavlovian conditioned strength (Harris, Andrew, & Kwok, 2013). Because Cue 1 and Cue 2 were equally paired with the reinforcer in Phase 2, we predicted that they would elicit the same amount of conditioned responding. This test allowed us to dissociate the associative or conditioned strength of Cues 1 and 2 from their ability to suppress resurgence, further demonstrating that its suppressive effects are not due to an excitatory association between the cue and the reinforcer.

Method

Subjects and Apparatus

The subjects were 24 female Wistar rats obtained, housed, and maintained as before. The apparatus was the same as in the previous experiments.

Procedure

Twice-daily sessions were employed throughout the experiment and Phase 2 consisted of four daily sessions. The resurgence testing day consisted of three sessions.

Magazine training and R1 Acquisition (Phase 1). Magazine training and R1 acquisition proceeded as before.

R1 Extinction and R2 Acquisition (Phase 2). All animals then received eight sessions in which R1 presses were extinguished (i.e., produced no reinforcers) and presses to the second lever (R2) were reinforced with the O2 reinforcer on a VI 30-s schedule. Onset of a 2-s tone or 2-s light (counterbalanced as Cue 1) coincided with each O2 delivery. Both the left and the right levers were inserted throughout each session. The R1 extinction sessions were double-alternated with sessions in which only R2 was available and produced O2; R1 was not extinguished. Onset of Cue 2 (counterbalanced as the light or tone) coincided with the delivery of R2 in these sessions. Half of the animals received sessions in the order of Cue1, Cue 2, Cue 2, Cue1, and half received them in the order of Cue 2, Cue 1, Cue 1, Cue 2.

Resurgence Test (Phase 3). On the day following the conclusion of Phase 2, all rats received three 5-minute test sessions in which both levers were inserted. R1 and R2 presses were recorded, but neither produced a food outcome. During one test, R2 presses produced Cue 1. During a second test, R2 presses produced Cue 2. No cues were presented in the other test. Testing order was fully counterbalanced.

Associative Strength Test. Following one session each of reacquisition with Cue 1 and Cue 2 (using the Phase 2 contingencies), animals were subjected to one test in which 30-s presentations of Cue 1, Cue 2, and dummy trials (i.e., no cue) occurred. Stimuli were elongated relative to the cues presented during training in order to provide time for foodcup entry behavior to be assessed. Animals received four presentations of each trial type (separated by a 90-sec ITI). Stimulus order was counterbalanced such that animals experienced Cue 1, Cue 2, and dummy trials equally often as their first, second, or third stimulus in a repeated series.

Data Analysis. Analyses of variance (ANOVAs) were used to assess response rates throughout the experiment. The rejection criterion was $p < .05$.

Results

The results of Experiment 5 are depicted in Figure 5. Animals increased R1 responding throughout Phase 1 (Panel A). During Phase 2 (Panel B), R1 responding decreased in sessions in which it was available (when R2 produced O2 and Cue 1). R2 responding increased in both Cue 1 and Cue 2 sessions. During the test (Panel C), R1 responding was reduced in sessions in which R2 produced Cue 1 relative to both the test in which R2 produced nothing and the test in which R2 produced Cue 2.

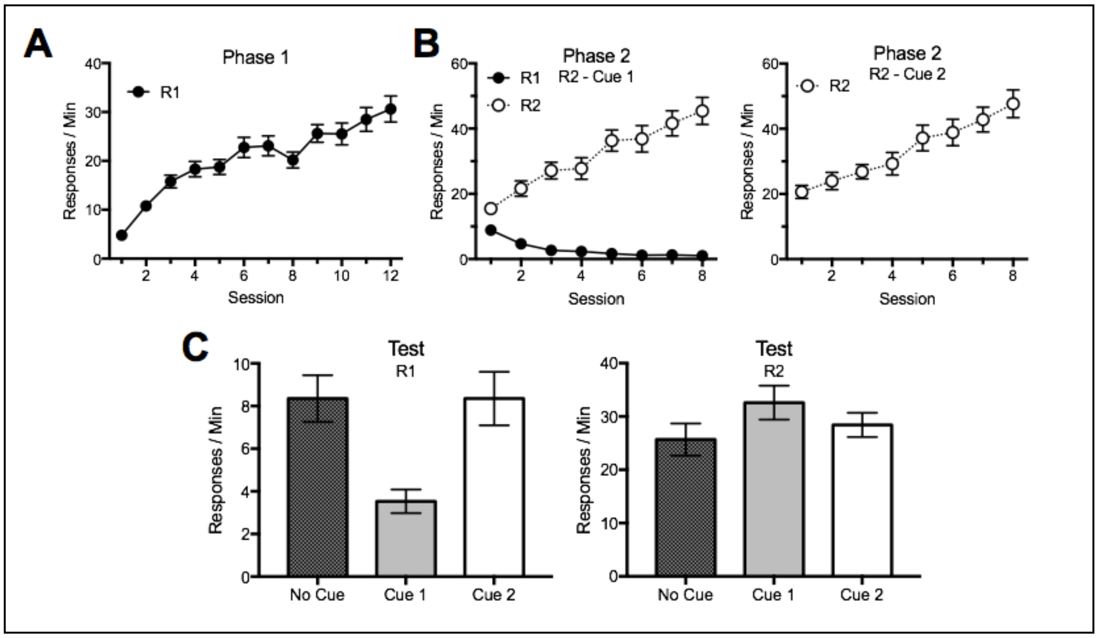


Figure 5. R1 acquisition throughout Phase 1 (Panel A), R1 extinction and R2 acquisition during sessions in which R2 produced Cue 1 and R2 acquisition during sessions in which R2 produced Cue 2 in Phase 2 (Panel B), and responding during the test for R1 and R2 (Panel C) in Experiment 5. Please note that error bars are only appropriate for between-subjects comparisons.

R1 Acquisition. The animals increased their responding throughout acquisition, as confirmed by an ANOVA on responding over the 12 sessions, which revealed a main effect of session, F (11, 253) = 41.38, MSE = 31.71, $p < .001$, $\eta_p^2 = .64$.

R1 Extinction and R2 Acquisition. Throughout Phase 2, animals decreased their R1 responding. This was confirmed by an ANOVA conducted on R1 responding which revealed a main effect of session, F (7, 161) = 55.74, MSE = 3.07, $p < .001$, $\eta_p^2 = .71$. Animals also increased their responding on R2 throughout Phase 2 during both sessions where R2 produced O2 and Cue 1 and sessions where R2 produced O2 and Cue 2 as confirmed by a 2 (Cue 1 vs. Cue 2) x 8 (Session) ANOVA assessing R2 responding throughout this phase. This found a main effect of session, F (7, 161) = 32.02, MSE = 142.89, $p < .001$, $\eta_p^2 = .60$. Responding for O2 and Cue 2 was slightly higher, as revealed by a main effect of cue (1, 23) = 7.67, MSE = 44.45, $p < .05$, $\eta_p^2 = .25$. No interaction was found, F (7, 161) = 1.21, MSE = 24.81, $p = .30$

Test. A 3 (Session: Cue 1 vs. Cue 2 vs. No Cue) x 2 (Response: R1 vs. R2) ANOVA was run to assess responding on both levers throughout the test sessions. This revealed a main effect of response, F (1, 23) = 68.00, MSE = 259.79, $p < .001$, $\eta_p^2 = .75$, but no main effect of session, $F < 1$. Importantly, the session by response interaction was significant, F (2, 46) = 10.94, MSE = 41.31, $p < .001$, $\eta_p^2 = .32$. Follow-up comparisons revealed that animals responded less on the R1 response during the session when R2 produced Cue 1 than in the session without the cue, $p < .001$, and in the session where R2 produced Cue 2, $p = .001$. R1 responding did not differ between Cue 2 and No Cue sessions, $p = 1.00$. Thus, only the cue that had been associated with R1 extinction attenuated the resurgence effect. Follow-up comparisons assessing R2 responding demonstrated that sessions in which R2 produced Cue 1, R2 responding was elevated relative to no cue sessions, $p < .05$, but did not differ from sessions where R2 produced Cue 2, $p = .09$. R2 responding did not differ in sessions where R2 produced Cue 2 or no cue, $p = .21$.

Pavlovian Associative Strength Test. The results from the Pavlovian associative strength test are depicted in Figure 6. Two outliers were removed from the analysis of Pavlovian associative strength. One was a significant outlier (Field, 2005) during the Cue 2 trials (Z = 2.28) and one was a significant outlier during the Dummy trials (Z = 2.02). Overall, there was only modest evidence of excitatory conditioning to the cues. One factor could be a failure to fully generalize between the 2-s cue from Phase 2 and the 30-s cue presented to measure associative strength. Further, the only other time animals had received exposure to the chamber without levers present was during magazine training, causing overall high levels of magazine responding in the pre-S periods. Nevertheless, visually, it appeared as though both Cue 1 and Cue 2 elevated responding above the pre-S baseline, whereas dummy trials did not increase responding above baseline. When pooling the elevation scores for the cue trials, there was a significant increase in responding above baseline (a hypothetical elevation score of 0), t (43) = 1.71, $p < .05$. This was not true of the dummy trials, t (21) = 0.26, $p = .80$. Thus,

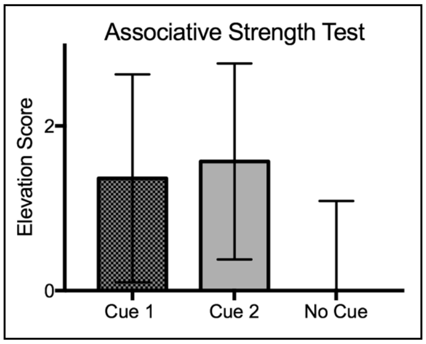


Figure 6. Elevation score (CS – pre-CS periods) of magazine entries during the Pavlovian associative strength test in Experiment 5. Please note that error bars are only appropriate for between-subjects comparisons.

there was modest evidence of excitatory conditioning to the cues. Further, responding did not differ between Cue 1 and Cue 2, *t* (23) = 0.16, *p* = .87.

Discussion

As predicted, Cue 1, but not Cue 2, attenuated R1 resurgence. This suggests that mere pairings between the cue and O2 are not sufficient to account for the finding that a cue associated with alternative reinforcement attenuates the resurgence effect. Instead, the cue must also be a feature of a session in which R1 was extinguished in order reduce resurgence. This experiment provides further support for the idea that any excitatory Pavlovian associations or conditioned reinforcement properties can be dissociated from its ability to reduce resurgence. Further, the finding that a cue has to be associated in some way with extinction of the response accords with several other studies from our laboratory demonstrating that extinction results in new learning in which the animal comes to inhibit a specific response in the extinction context (Bouton et al., 2016; Todd, 2013). While both cues could have entered in excitatory associations with R2 (e.g., Thrailkill & Bouton, 2015; Trask & Bouton, 2014) or O2, only Cue 1 could have signaled any new inhibitory learning about R1, as Cue 2 never occurred in sessions during which R1 was extinguished. Cue 1, however, did. Thus, presenting Cue 1, but not Cue 2, during the test increased the generalization from the context in which rats learned to inhibit R1 responding. Further, while Cue 1 was presented in sessions in which R1 was available and not reinforced, the cue itself was not explicitly linked to R1 extinction in any meaningful way (i.e., R1 responding had no impact on cue presentations). This suggests that the cue likely exerts influence on R1 responding in a similar manner to contextual cues, which also do not have a programmed, direct relationship with the response aside from their presence during learning.

Experiment 6

Experiment 6 then tested an altogether new idea: Namely, how effective at reducing resurgence is a cue that does not signal reinforcement, but is instead presented contingent on R1 when a reinforcer is expected but does not occur? In Pavlovian conditioning, a conditioned inhibitor is conditioned in much this way. In the so-called conditioned inhibition paradigm, one cue is paired with a reinforcing outcome. On other, intermixed, trials, a second cue is added to the first and the compound is not paired with the outcome. Animals come to behave as if the second cue explicitly predicts no outcome (e.g., Rescorla, 1969a). Such results are predicted by most models of associative learning (e.g., Rescorla & Wagner, 1972; Wagner, 1978, 1981). In these models, it is assumed that a conditioned stimulus paired with an unconditioned stimulus will make negatively accelerating gains in associative strength until it comes to predict the unconditioned stimulus perfectly. When the second cue is introduced in compound with the first, the animal therefore expects an outcome. However, when no unconditioned stimulus is presented, there is a discrepancy between what the animal expected and what occurred, generating a negative “prediction error.” In other words, the lack of outcome on these trials is surprising (as it is predicted by the first stimulus) and this surprisingness allows the animal to learn about the second stimulus. This procedure leads to the development of the animal treating the second stimulus as if it explicitly predicts no outcome and it is termed a conditioned inhibitor. The current experiment aimed to create something analogous to a conditioned inhibitor using a similar method to Experiments 1, 2, 3, and 5.

The experiment used a between-subjects design. After the usual conditioning of R1 in Phase 1, during Phase 2, when R1 no longer produced a reinforcer and R2 produced O2, Cue 1 (tone or light, counterbalanced) was presented contingent on R1 on the same schedule (i.e., VI 30-s) as O1 was earned in Phase 1. By being present at moments when a reinforcer might be expected but does not occur, the cue might develop inhibitory properties in the same way the added cue does in the Pavlovian conditioned inhibition procedure described above. In other words, as the outcome is expected following the response, its omission should be surprising. This surprisingness should allow the cue to acquire inhibitory properties. Although to our knowledge an inhibitory cue like this has never been studied using this arrangement in operant conditioning, we hypothesize that this procedure might generate inhibition sufficient to create an attention-grabbing cue that might also be effective at attenuating resurgence. Recall that in Experiment 3, one group of animals received cues and reinforcers that were not explicitly paired. This procedure has also been shown to encourage development of inhibition to the cue (see Rescorla, 1969b). While this cue was not effective at reducing resurgence in that experiment, reports of conditioned inhibition suggest that making the cue contingent on R1 responding when the reinforcer is expected might generate more prediction error, as at the beginning of that phase, a reinforcer is already expected contingent on responding (i.e., the response is at that time the best predictor of the outcome).

For a second group, Cue 1 was presented in a yoked manner during Phase 2, such that when an animal in the first group produced a cue, a matched animal in the second group received a cue presentation regardless of responding. This treatment controlled for cue exposure but removed the response contingency (and thus negative surprise generated to the cue when the reinforcer is expected contingent on responding because the *response* predicts the outcome) that formal models assume is crucial to development of inhibition. In other words, presenting the cue when the outcome is not expected should mean that there is no surprisingness and thus no learning to the cue. For both groups, while R1 was being extinguished, a newly-inserted R2 response produced an O2 reinforcer. During the test, animals were tested in two conditions (order counterbalanced). In the first, both responses were available but produce no programmed consequences. Resurgence on R1 was expected for both groups. In the second condition, both responses were also available and produced no reinforcers. However, as in Phase 2, responding on R1 produced Cue 1. We hypothesize that this cue will serve to suppress resurgence of R1, but only in the animals for whom it was an explicitly conditioned as an inhibitor. In a subsequent, final, test, Cue 1 and a novel cue, Cue 2, were paired with a reinforcer in a Pavlovian preparation. If Cue 1 is an inhibitor for a food reinforcer, it will acquire excitatory properties more slowly than Cue 2 (as in a retardation-of-conditioning test, see, e.g., Rescorla, 1969b), demonstrating that it has the properties of a conditioned inhibitor.

Method

Subjects and Apparatus

The subjects were 32 female Wistar rats obtained, housed, and maintained in exactly the same way as the previous experiments. The apparatus was the same as used in all other experiments.

Procedure

Unless otherwise noted, twice-daily sessions were employed throughout the experiment. All sessions were 30 min in duration, and the end of the session was indicated by retraction of the lever(s).

Magazine training and R1 Acquisition (Phase 1). Magazine training and R1 acquisition proceeded as in the previous experiments.

R1 Extinction and R2 Acquisition (Phase 2). All animals then received eight sessions in which R1 presses were extinguished (i.e., produced no reinforcers) and presses to the second lever (R2) were reinforced with O2 on a VI 30-s schedule. However, R1 produced a 2-s tone or 2-s light (Counterbalanced as Cue 1) on a VI 30-s. Both the left and the right levers were inserted throughout each session.

Resurgence Test (Phase 3). On the day following the conclusion of Phase 2, all rats received two 10-min test sessions in which both levers were inserted. R1 and R2 presses were recorded, but neither produced a food outcome. During one test, R1 presses produced Cue 1 on a VI 30-s schedule. No cues were presented in the other test. The test order was fully counterbalanced.

Pavlovian Conditioning. Following one reacquisition session that returned to the conditions of Phase 2, animals then received two separate Pavlovian conditioning sessions in which Cue 1 and Cue 2 were each separately paired with the O1 reinforcer (counterbalanced so that half received Cue 1 training first and half received Cue 2 training first). Sessions were approximately 35 min and included 32 10-s presentations of each cue separated by a variable ITI that was 60 s on average.

Data Analysis. Analyses of variance (ANOVAs) were used to assess response rates throughout the experiment. The rejection criterion was $p < .05$.

Results

The results of Experiment 6 are shown in Figure 7. As before, R1 increased throughout Phase 1 (Panel A) and decreased in Phase 2 (Panel B) when R2 was acquired.

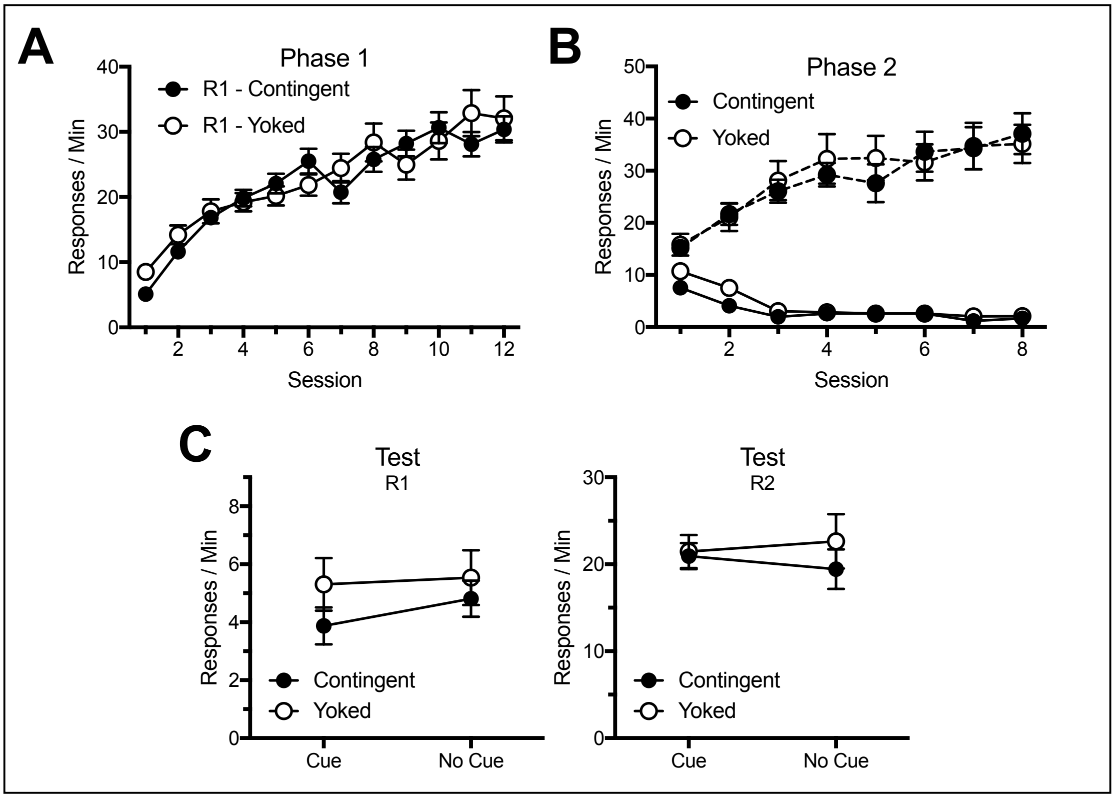


Figure 7. R1 acquisition in Phase 1 (Panel A), R2 acquisition and R1 extinction in Phase 2 (Panel B) and R1 and R2 responding during the test (Panel C) in Experiment 6. Please note that error bars are only appropriate for between-subjects comparisons.

During the test, the presence of the possibly inhibitory cue had no impact on R1 performance for either group.

Acquisition. A 2 (Group) x 12 (Session) ANOVA was run to assess R1 responding throughout acquisition. This found a main effect of session, F (11, 330) = 63.21, MSE = 27.86, $p < .001$, $\eta_p^2 = .68$, as well as a significant group by session interaction, F (11, 330) = 2.39, MSE = 27.86, $p < .01$, $\eta_p^2 = .07$. This interaction is likely due to the fact that groups were different on the first day of acquisition ($p < .05$) as three rats in Group Contingent made less than 1 response per minute, but this difference was not reflected in any other session, including the final. There was no main effect of group, $F < 1$.

R1 Extinction and R2 Acquisition. A 2 (Group) x 8 (Session) ANOVA was run to assess R1 responding throughout Phase 2. This found a main effect of session, F (7, 210) = 74.15, MSE = 2.84, $p < .001$, $\eta_p^2 = .71$, and a significant group by session interaction, F (7, 210) = 5.34, MSE = 2.84, $p < .001$, $\eta_p^2 = .15$. The interaction seemed to stem from differences obtained early in the training that dissipated (recall that only the contingent group received Cue 1 contingent on R1 responding). Group Contingent responded less than Group Yoked on R1 in the first two sessions (Session 1: $p < .01$; Session 2: $p < .05$), but no other sessions. The main effect of group was not significant, F (1, 30) = 2.36, MSE = 36.42, p =.14. A similar 2 (Group) x 8 (Session) assessed R2 responding throughout acquisition. This also revealed a main effect of session, F (7, 210) = 30.84, MSE = 49.80, $p < .001$, $\eta_p^2 = .51$, but no main effect of group or interaction, Fs < 1.

Test. As before, a 2 (Session: Cue vs. No Cue) x 2 (Response: R1 vs. R2) x 2 (Group) ANOVA was run to assess responding in the test. While this found a main effect of response, F (1, 30) = 137.47, MSE = 16.47, $p < .001$, $\eta_p^2 = .82$, no other main effects or interactions approached significance, largest $F = 1.40$, $p = .25$. To isolate the responses, a 2 (Group) x 2 (Session: Cue vs. No Cue) ANOVA was run to assess R1 responding in the test. This revealed no main effect of either session or group, nor an interaction between the two, largest $F = 1.37$, $p = .25$. Follow-up comparisons found no significant differences between responding between or within groups. A similar 2 (Group) x 2 (Session: Cue vs. No Cue) ANOVA assessed R2 responding during the test.

It found no main effect of either group or session, nor an interaction between the two, largest $F = 1.19$, $p = .28$. As in Experiment 3, a 2 (Session: Cue vs. No Cue) x 2 (Response: R1 vs. R2) ANOVA was run to assess responding on the test only in the group we expected the cue to have an impact in, Group Contingent. While this revealed a main effect of response, $F(1, 15) = 81.37$, MSE = 15.50, $p < .001$, $\eta_p^2 = .84$, neither the main effect of session nor the interaction was significant, largest $F = 1.54$, $p = .23$. Thus, a nonreinforced cue produced by R1 during extinction does not behave in a manner similar to a cue paired with alternative reinforcement contingent on R2 (as in Experiments 1 and 2).

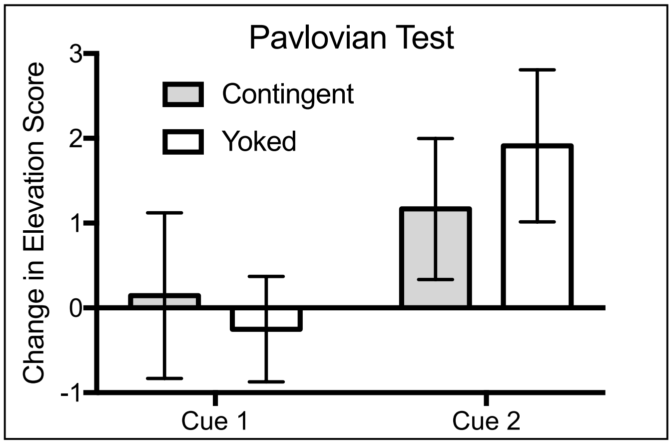


Figure 8. Change in elevation score from the first four-trial block to the final four-trial block during the Pavlovian acquisition test for both Cue 1 and Cue 2 in Experiment 6.

Pavlovian Acquisition. The results of the Pavlovian acquisition test are shown in Figure 8. Due to an equipment failure in which a magazine photocell failed to accurately count entries, 6 animals were excluded from the subsequent analyses, leaving $n = 12$ in Group Contingent, and $n = 14$ in Group Yoked. Pavlovian responding was calculated by binning four-trial blocks of magazine entries both during the 10-s stimulus and during the 10 s immediately prior to stimulus onset. Elevation scores were calculated by subtracting pre-S entries from entries made during the stimulus. To assess the amount of learning that occurred during the Pavlovian training sessions, a change in elevation score was calculated by subtracting the initial elevation score from the final elevation score. A 2 (Group) x 2 (Session: Cue 1 vs. Cue 2) ANOVA was run to assess these scores. This found no main effect of group and no interaction, *F*s < 1, but the main effect of session was marginal, $F(1, 24) = 2.86$, MSE = 11.45, $p = .10$, $\eta_p^2 = .11$. One-sample t-tests were conducted to assess overall changes in learning across both groups to the cues. While the change in learning to Cue 1 was not significantly different than 0, $t(25) = .12$, $p = .90$, indicating no change in performance across the session, learning to Cue 2 did differ significantly from 0, $t(25) = 2.57$, $p < .05$, indicating a change in performance across the session. Thus, both of the groups showed no change in appetitive conditioned approach to Cue 1, but did to Cue 2.

Discussion

This experiment demonstrates that a cue presented when a reinforcer is expected contingent on R1 during extinction does not serve as an effective way to reduce resurgence at testing. Additionally, the cue in this experiment seemed to be more difficult to condition as a Pavlovian conditioned stimulus than a novel cue in both groups. While this could be seen as evidence as conditioned inhibition in Group Contingent, the same finding in Group Yoked (which had less prediction error and therefore less opportunity to develop conditioned inhibition to the cue) suggests that another explanation is likely. Importantly, the groups received an equivalent amount of exposure to the cue throughout Phase-2 training. Overall, it therefore appears that slower conditioning with Cue 1 than Cue 2 is a simple latent inhibition effect. Latent inhibition is the well-documented finding (e.g., Lubow & Moore, 1959) in which pre-exposure to a stimulus weakens its ability to be conditioned as a CS. The Mackintosh (1975) model of attention suggests that the latent inhibition effect results from a loss of attention to a stimulus that is not predictive of anything.

Given a lack of evidence demonstrating that conditioned inhibition had developed to Cue 1 in Group Contingent, it is possible that too little attention was paid to the cue for it to later inhibit the resurgence effect. The Mackintosh (1975) model predicts that presentations of a new cue will initially attract attention, but this effect will decrease quickly on subsequent stimulus presentations in which that stimulus is predictive of nothing (as was the case in the present experiment). In accordance with this, in the present experiment the contingent cue disrupted R1 performance during early sessions of extinction more than did a noncontingent cue. This early disruption might suggest that attention was high to the cue initially, but had diminished by the third session of Phase 2.

One potential way to create a response-contingent stimulus that functions as a better conditioned inhibitor might be to mirror the work done in Pavlovian conditioned inhibition more closely. For example, using a similar design, one might train an R1 behavior to produce an O1 outcome that coincides with a cue (Cue 1). In the second phase, while R2 produces an O2 reinforcer, R1 would now produce a compound of Cue 1 and a novel Cue 2. Based on the (albeit modest) evidence from Experiment 5 that a cue paired with reinforcement gains some excitatory strength, this suggests that Cue 1 might add to the prediction of the outcome by the response (the response, remember, produced the reinforcer on a VI 30-s schedule, meaning that most leverpresses actually went unreinforced). This might consequently generate more negative prediction error on the occasions when Cue 2 is added in Phase 2. The animal might then learn that Cue 2 explicitly predicts no outcome, conditioning it as a stronger inhibitor. Typically, Pavlovian procedures that produce conditioned inhibition additionally use intermixed trials, unlike the switches between Phases in resurgence experiments, where there is less explicit discrimination training. Another possibility would be to condition R1 as before, then, during Phase 2, present Cue 1 alone when R2 was reinforced (such that it coincides with the delivery of O2), but have intermixed trials where the compound of Cue 1 and Cue 2 was presented, contingent on R2, but with no delivery of the reinforcer.

Interestingly, the finding from this experiment that a cue that might have developed an inhibitory relationship with the outcome mirrored the null result reported for Group Unpaired in Experiment 3, whose unpaired cue and reinforcer presentations also could theoretically have developed an inhibitory relationship with the reinforcer (e.g., Rescorla, 1969b). None of these potentially inhibitory cues reduced resurgence. Together, the overall results thus strengthen the argument that the cue must be association with the reinforcer in order to attenuate resurgence.

General Discussion

The current experiments examined the circumstances and mechanisms through which a cue presented in Phase 2 of a resurgence paradigm can come to attenuate resurgence when presented in the final resurgence test. A first experiment demonstrated that a cue paired with the delivery of alternative reinforcement can attenuate resurgence when it is also produced during a test. Experiment 2 demonstrated that this cue attenuated resurgence during a test if it was presented contingently or noncontingently on R2 responding. Experiment 3 demonstrated that the cue had to be paired with the reinforcer during Phase 2 and that simply making the cue separately contingent on R2 responding was not enough. Experiment 4 suggested that a cue paired with alternative reinforcement in this paradigm does not have demonstrable conditioned reinforcing properties. In Experiment 5, it was shown that the cue had to be presented in sessions in which R1 was extinguished in order to be able to attenuate its resurgence. A second cue, not presented in sessions when R1 was extinguished (but with equal history and excitatory strength), was not effective at attenuating resurgence. Finally, Experiment 6 found that a cue made contingent on R1 responding during extinction does not have the same relapse-reducing effects when presented during the test. One caveat is that this experiment found little evidence of conditioned inhibition. There could be other methods that might result in more conditioned inhibition and have a better chance of reducing resurgence during the test. Overall, it appears as though methods that encourage attention to the stimulus result in the greatest likelihood that the cue will be salient enough to reduce resurgence at test if it has been a part of the extinction context.

These results extend previous work from our laboratory demonstrating that a reinforcer associated with sessions in which R1 is extinguished can attenuate both resurgence (Bouton & Trask, 2016) and renewal (Trask & Bouton, 2016) of the instrumental response. Notably, the present resurgence-attenuating effects were dissociated from any conditioned reinforcing properties and demonstrable excitatory Pavlovian associations. This suggests that rather than working through a Pavlovian (S-O) association, the cues reduce resurgence through signaling the new learning that occurs in extinction. A growing literature suggests that in extinction, the contextual cues present come to directly suppress the response through an inhibitory S-R association. In other words, animals learn to inhibit a response in the presence of specific contextual cues in which it was extinguished (Bouton et al., 2016; Rescorla, 1993, 1997; Todd, 2013; Todd et al., 2014; Troisi, LeMay, & Järbe, 2010). Perhaps the present cue operates in a similar manner. In the present Experiment 5, only a cue that was associated with extinction of R1 could be associated with the inhibition of R1. Thus, according to a response inhibition account of extinction, only that cue could successfully signal the inhibition of R1.

However, it should be noted that despite the failure of a cue not associated with alternative reinforcement to attenuate resurgence in the current Experiment 3 and Experiment 6, several studies have shown that neutral cues (e.g., those that have never been paired with alternative reinforcement) on their own can attenuate renewal (Nieto et al., 2017; Willcocks & McNally, 2014), spontaneous recovery, and reinstatement (Bernal-Gamboa et al., 2017) of instrumental behaviors. In one representative study, Nieto et al. (2017) trained animals to perform two responses (R1 and R2) to receive food reinforcement, each in a distinct context (Context A and Context B, respectively). Each was then extinguished in the opposite context (i.e., R1 in B and R2 in A; see Todd, 2013). During extinction of R1, a 5-s tone played approximately twice every minute noncontingent on responding. Animals were then tested for each response back in its original acquisition context and extinction context. For a crucial group, presentations of the extinction cue occurred in both renewal tests for R1 and R2. While an overall renewal effect was seen (e.g., responding was higher on each response in its renewal context than in its extinction context), renewal was weakened on R1 relative to R2. This suggests that the extinction cue served to reduce the renewal effect. According to the authors, these results further demonstrate that extinction learning results in formation of an inhibitory S-R association, as the cue only served to weaken the response that it was extinguished with and failed to transfer to another response. This was further supported by Willcocks and

McNally (2014), who demonstrated that the cue had to be connected with extinction learning in order to effectively attenuate renewal.

As previously stated, in Pavlovian learning, a retrieval cue associated with extinction reduced renewal (Brooks & Bouton, 1994), spontaneous recovery (Brooks & Bouton, 1993), and reinstatement (Brooks & Fava, 2017). Further, in instrumental learning, cues associated with extinction have also attenuated renewal (Nieto et al., 2017; Willcocks & McNally, 2014), reinstatement, and spontaneous recovery (Bernal-Gamboa et al., 2017). One element of the resurgence paradigm that differs from all of the previously mentioned relapse phenomena in both Pavlovian and operant conditioning is that its extinction phase involves reinforcement of an alternative response during extinction of the target response. We have argued (see Trask et al., 2015) that the presence of alternative reinforcement in resurgence paradigms is itself salient enough to act as a context that serves to suppress behavior, and that this alternative reinforcer does seem to have equal and similar ability to control behavior as physical context (e.g., Trask & Bouton, 2016). Including alternative reinforcement for an alternative behavior during extinction could have many effects. The presence of an alternative reinforcer itself could potentially draw attention towards that reinforcer and away from less salient aspects of the context (some might argue that on its own, a cue that predicts nothing or is predictive of nothing might not be competitive for attention, which is a limited resource). That is, a reinforcer is likely to attract more attention and interaction than, for example, a brief illumination of a panel light. Perhaps, in the present experiments, making the cue relevant increased attention to that cue (e.g., Mackintosh, 1975) when limited attention processes would otherwise have been directed towards the reinforcer. It is notable that a neutral cue that has never been paired with a reinforcer also does not serve to weaken rapid reacquisition, a relapse phenomenon that also involves multiple presentations of a reinforcer (Willcocks & McNally, 2014). The current results suggest that in order for a cue to attenuate relapse in situations where alternative reinforcement is present, it has to be both salient enough to attract some attention as well as associated with extinction such that it can signal the new, inhibitory learning.

The results provide more support for the context hypothesis of resurgence (Trask et al., 2015; Winterbauer & Bouton, 2010). According to this view, the cues associated with alternative reinforcement during sessions in which R1 is extinguished increase the generalization between the extinction contexts and testing contexts when they are presented during the test. Other explanations of resurgence, such as the behavioral-momentum based model of resurgence (Shahan & Sweeney, 2011) and the resurgence as choice model of resurgence (Shahan & Craig, in press), fail to account for the present findings because neither invokes mechanisms that would allow a treatment cue to have any impact on responding. The behavioral-momentum based model of resurgence (Shahan & Sweeney, 2011) suggests that removal of the reinforcer during the test should reduce its disruptive effect on R1, thus causing a resurgence of this response. In the current experiments, neither the test with the cue nor the test without the cue have any reinforcers present. Thus, according to this view, there should be no difference in responding as the focus lies solely on the reinforcing properties, rather than discriminative properties, of reinforcers. A possible extension of this model might allow a conditioned reinforcer to act in the place of a primary reinforcer during resurgence testing and thus work similarly to disrupt R1 responding and weaken resurgence. However, given the present results which suggest that the cue associated with alternative reinforcers did not have conditioned reinforcing properties, even this extension seems unlikely to account for the results. The resurgence as choice model (Shahan & Craig, in press) also focuses on the reinforcement rate and its reinforcing (rather than discriminative) properties; this model suggests that resurgence occurs as a function of the recency and cumulative history of reinforcement. Essentially, resurgence of an R1 behavior is thought to occur because placing R2 on extinction increases the relative value of R1 (which was previously an effective way to produce the reinforcer) over R2. However, in the present experiments, if placing R2 on extinction is sufficient to cause behavior to resurge by devaluing that response, R1 responding should be equivalent in the tests regardless of whether the cue was presented or not. That is, the model provides no mechanism that anticipates or accounts for the effects of the cue. Overall, both models fail to account for the current findings. Perhaps their biggest failing is that they give no role to the discriminative effects of cues and reinforcers in controlling extinction, which is the crucial process emphasized by the context view of resurgence.

As previously mentioned, findings from studies of resurgence may have implications for contingency management treatments. While there are several notable differences between CM and resurgence (notably, the lack of a contingency between abstinence and reinforcement [Bouton & Schepers, 2014] and the inability to place human behavior on extinction [Bouton et al., in press]), in general, both the resurgence paradigm and CM are effective at reducing target behavior during the treatment phase and leave the suppressed behavior susceptible to relapse following the cessation of that phase (Davis et al., 2016; Petry, Martin, Cooney, & Kranzler, 2000). These similarities suggest that, despite procedural differences, factors that work to reduce resurgence may also be effective in reducing relapse following the cessation of CM treatments. For example, the present studies suggest that a cue associated with reinforcement in the treatment phase may serve to weaken relapse after CM treatment is terminated. In one potential example of this, Higgins, Budney, Bickel, and Badger (1994) demonstrated that cocaine abstinence was highest in participants whose significant other participated in the treatment. One explanation of this finding is that, like the treatment cues in the current experiments, the presence of the significant other at treatment made the treatment situation generalize better to the situations where relapse was more likely. Further, as noted in the Introduction, thinning procedures during Phase 2 of a resurgence paradigm (in which alternative reinforcement gradually decreases throughout the phase) reduce resurgence of R1 responding. Interestingly, thinning procedures are also effective in CM treatments. For example, Dallery, Raiff, and Grabinski (2013) thinned participants from daily reinforcement (vouchers) contingent on cigarette abstinence to twice-weekly reinforcement contingent on abstinence. At a six-month follow-up, they found that participants who had undergone the thinning procedure had an abstinence rate of 18% whereas a yoked control had an abstinence rate of only 7%. However, this thinning procedure should be compared to participants who receive response-contingent vouchers at a steady rate throughout the treatment in order to demonstrate its effectiveness against a non-thinning control. Other preparations that reduce resurgence (such as the current neutral cue paired with alternative reinforcement) may also function to reduce relapse following contingency management treatments.

In conclusion, the present experiments demonstrate that a cue paired with alternative reinforcement during sessions in which R1 was extinguished can be used to attenuate resurgence of that response when they are presented during the test. Additionally, these cues need to be sufficiently attention-commanding to attenuate resurgence, as cues not paired with the reinforcer (either contingent on R2 or R1 responding) during R1 extinction sessions did not weaken resurgence. Further, the resurgence-attenuating effects seem to not depend on Pavlovian S-O associations (assessed here using both a conditioned reinforcement test and a Pavlovian conditioned approach test). Instead, the cues may work by enhancing generalization between the sessions in which R1 is extinguished and the testing session, increasing the likelihood that animals will retrieve the inhibitory learning acquired during extinction. These are, to our knowledge, the first results demonstrating that cues associated with treatment can attenuate resurgence.

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