SHORT TITLE: INSTRUMENTAL LEARNING AND REINSTATEMENT

Reinstatement of Instrumental Actions in Humans: Possible Mechanisms and their Implications to Prevent it

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Abstract

The study of post-extinction recovery effects in humans has received significant attention. For instance, research on reinstatement has increased in the last decade. However, most of the studies focus on the return of fear responses. In the present experiments, we used a videogame task to explore the reinstatement of operant behavior in human participants. In Experiment 1, after participants learned to shoot at enemies, they received an extinction procedure that eliminated the shooting behavior. However, the mere reintroduction of the outcome reinstated the original response. Experiment 2 showed that the reinstatement of instrumental behavior is contextually modulated. Finally, in Experiment 3 we found that presenting a reminder for extinction attenuated the response recovery effect. The overall pattern of results suggests that reinstatement of voluntary actions in humans could be explained by an interference memory framework. In addition, the present data suggest that therapies that use brief reminders of therapeutic intervention could help prevent the reinstatement of unhealthy instrumental behaviors.

Key words: Context; Extinction-Cue; Human Participants; Instrumental Learning; Reinstatement.

Reinstatement of Instrumental Actions in Human Beings: Possible Mechanisms and their Implications to Prevent it

1. Introduction

It is widely accepted that learned behaviors such as overeating and cigarette smoking are linked to human diseases (Houben & Jansen, 2011; Schroeder, 2007). It is also accepted that those behaviors involve instrumental conditioning (e. g., eating a midnight snack [instrumental response] is reinforced by its high palatability). Although cognitive behavior therapies successfully reduce unhealthy behaviors, several data show that those behaviors are not eliminated (e. g., Craske & Mystkwoski, 2006) and reappear relatively easily (Kirshenbaum, Olsen & Bickel, 2009). Given that instrumental extinction (i. e., response decrement when reinforcers are withdrawn) is involved in many clinical procedures that eliminate behaviors, some authors have proposed that the study of instrumental extinction could provide some insights for the development of more enduring therapeutic strategies that prevent or reduce relapsing (e. g., Bouton, Winterbauer & Todd, 2012).

Instrumental extinction is not permanent (e. g., Todd, Vurbic & Bouton, 2014). For instance, in spontaneous recovery, an extinguished behavior reappears after introducing a retention interval (Rescorla, 1997; after a period of abstinence the urge to seek a beer might return), whereas testing the subject outside the extinction context *renews* the original performance (e. g., Bouton, Todd, Vurbic & Winterbauer, 2011; Nakajima, Tanaka, Urushihara & Imada, 2000; the background provided by a family party may produce the craving for drinking soda). Finally, free delivery of reinforcers *reinstates* the instrumental performance (e. g., Reid, 1958; a person who recently quit smoking might begin smoking

again after she smells someone else's cigarette). Because it has been suggested that those effects might explain the high rates of relapse after having a therapeutic treatment (e. g., Crombag, Bossert, Koya & Shaham, 2008), several researchers have proposed the development of new behavioral ways to prevent relapse of unhealthy voluntary actions based on the study of the aforementioned response recovery effects (e. g., Bouton, 2011; Crombag, Grimm, & Shaham, 2002).

Although there is evidence of renewal (e. g., Vila, Romero & Rosas, 2002) and spontaneous recovery (e. g., Lopez-Romero, García-Barraza & Vila, 2010) of instrumental responses in humans, to the best of our knowledge all the available data about reinstatement of instrumental behavior has been conducted with nonhuman animals (e. g., Bouton, Winterbauer &Vurbic, 2011). Hence, exploring the effect in humans seems necessary in order to: a) to aid the research field to fully understanding the mechanisms underlying the reinstatement of voluntary responses, b) to provide a potential explanation for why individuals relapse and c) to improve behavioral techniques that thwarts relapse after psychological therapy.

Thus, the main goal of this experimental series was to study the reinstatement of voluntary behaviors in healthy humans. In Experiment 1, we explored whether the reinstatement of instrumental actions could be found using a videogame task with college students. The purpose of the second experiment was to assess whether the context used during the re-exposure of the outcome had any impact on reinstatement. Finally, in Experiment 3 we explored whether the reinstatement of instrumental actions was attenuated in the presence of the cue that accompanied the extinction of the action.

2. Experiment 1

Since its very first report with dogs (Pavlov, 1927), reinstatement has been observed using Pavlovian (e. g., Bouton & Bolles, 1979; Rescorla & Heth, 1975; Schachtman, Brown, & Miller, 1985; Westbrook, Iordanova, McNally, Richardson & Harris, 2002), and instrumental procedures with rats (e. g., Baker, 1990; Delamater, 1997; Rescorla & Skucy, 1969). In humans, this phenomenon has been found in contingency judgment tasks (García-Gutiérrez & Rosas, 2003a, 2003b; Vila & Rosas, 2001), fear conditioning procedures (e.g., Dirikx, Hermans, Vansteenwegen, Baeyens, & Eelen, 2004; Hermans, et al., 2005; LaBar & Phelps, 2005) and in a conditioned suppression task (Neumann, 2008). To this date, no evidence of reinstatement of instrumental responses in human participants has been reported. As we previously stated, this response recovery effect has been reported with rats (e.g., Rescorla & Skucy, 1969). For example, Baker, Steinwald and Bouton (1991) trained two groups of hungry rats to press a lever for food (Response, R). Following the extinction of the instrumental response, both groups were exposed to the experimental chambers with no levers. During that day, only rats in Group Food received non-contingent food presentations (Outcome, O). On the next day, all rats were tested with the levers present. Baker et al. (1991) found a reinstatement of the lever-pressing behavior because rats in Group Food showed the most response recovery.

Experiment 1 aimed to test whether the recovery of an extinguished instrumental behavior can be observed in a reinstatement procedure with healthy humans. In a within-subject design, participants played a computer game (Gámez & Rosas, 2005, 2007) in which they were requested to defend Andalusia against invasion by shooting missiles at tanks or planes by clicking on their respective pictures (i. e. R1 or R2 counterbalanced). The explosion of the enemies (tanks, O1 or planes, O2) served as reinforcer for the shooting behavior (i. e., instrumental response). Then, both responses (shooting at tanks or

at planes) underwent extinction (the shooting did not produce the destruction of any enemies). After the last extinction trial, participants saw only one enemy destroyed by an ally (e. g., the tanks). It was hypothesized that reinstatement of the extinguished instrumental response would be observed only for shooting at tanks (R1). It should be noted that all participants experienced all responses, stimulus, and reinforcers throughout the experiment, so, it would seem more likely that the difference between R1 and R2 during testing should be attributed to the reinstatement effect (i. e., watching the destruction of the enemy) than to any other factor (i.e, differences between participants, preferences for a particular enemy or response).

2.1. Method

2.1.1. Participants

Sixteen undergraduate students from the Universidad de Cádiz participated in this experiment in exchange for course credit (12 women, 4 men; M_{age} = 21.81years; age range= 21-28 years). They had no previous experience with this task. All individuals participated voluntarily and gave their informed consent before starting the experiment, being free to abandon the task at any point of the process, although it did not happen.

2.1.2. Apparatus and stimuli

Participants were trained individually in ten adjacent cubicles. Each cubicle had a Pentium PC on which the task was presented. The procedure was implemented using the SuperLab Pro (Cedrus Corporation) software. The task was similar to the one used by León, Abad and Rosas (2010). Participants played a computer game in which they had to defend Andalusia from air and land attacks. The main screen represented a viewer simulating a participant's view from a hypothetical bunker in which they were supposed to be. Contexts were presented within the viewer's viewing area. Scenes of different beaches

in Andalusia, Puerto Banús (urban beach) and Tarifa (natural beach) were counterbalanced as contexts A and B. The two attackers were a plane and a tank. The plane was presented in the sky, at the top right area of the context, while the tank was presented on the sand, at the bottom left area of the context. Both attackers could appear in one of two different positions within their respective areas on the context so that it would give the impression of movement to the participant. The instrumental response consisted of clicking on either the plane or the tank (R1 and R2, counterbalanced). The destruction of the tank and the plane was counterbalanced asoutcomes O1 and O2 across participants.

2.1.3. Procedure

The instructions and all the necessary information were presented in participants' native language (Spanish) on the computer screen. Participants interacted with the computer using the mouse (left button). Instructions were presented in three screens using a black Times New Roman 26 bold font against a light-yellow background to emulate the appearance of an old document. To advance through the instruction screens, participants had to click on a button labeled as "next" placed on the bottom right corner of the screen. Each participant was initially asked to read the following instructions:

> "(Screen 1) Andalusia is being attacked. Different parts of Andalusia are being assaulted by land and air. You are placed in the only bunker able to face the attackers. Use the mouse to launch missiles at the targets. Your goal is to destroy the attackers before they take over Andalusia. (Screen 2) The monitor represents the bunker's viewer, in which the different attackers you should facewill appear. To shoot, click the left button on the mouse while the pointer is on top of the target. Your technology and weapons are older than theirs, so you will need to shoot several times to be able to destroy them. (Screen 3)

The battle begins! You have to destroy tanks and planes before they take the Andalusian coast. We are in your hands! GOOD LUCK!"

In each trial the tank or the plane was presented. Giving the appropriate response (i.e., clicking on the plane) was reinforced with the destruction of the attacker (outcome) on a variable interval (VI) 2-s schedule in which the availability of reinforcement varied randomly between 1 s and 3 s. So, in each trial the participant should make multiple clicks on the enemy to destroy it. The trial ended only after the participant gave the correct response and, hence, the enemy was destroyed (O1 or O2).

The experiment was conducted in four phases (see the experimental design in the first row of Table 1).

Table 1

Experimental Designs

Experiment	Acquisition	Extinction	Re-exposure	Test
1	A: R1-O1 B: R2-O2	A: R1- B: R2-	A: O1	A: R1- B: R2-
2	A: R1-O1 B: R2-O2	A: R1- B: R2-	A: O1	C: R1- B: R2-
3	A: R1-O1 B: R2-O2	A*: R1- B*: R2-	A: O1 B: O2	A*: R1- B: R2-

Note: Contexts A and B (and C in experiment 2) were Beaches of Puerto Banús and Tarifa (and Cabo de Gata in experiment 2), counterbalanced. "R1" and"R2" stands for clicking on the plane or the tank, counterbalanced. "O1" and "O2" means plane or tank destruction, counterbalanced."*" Stands for the extinction-cue. See text for details.

Acquisition. A screen displaying the message "Your detachment has been posted to… (name of the beach where the battle continued)" was presented for 2 s before starting

training in each context. Participants received 10 training trials with each attacker. R1-O1 trials were conducted in two blocks of 5 trials in Context A, whereas R2-O2 trials were conducted in two blocks of 5 trials in Context B. Trial order within each context was random. Context order for half of the participants was ABAB and BABA for the other half.

Extinction. After the acquisition phase, all participants received 30 extinction trials with duration of 4 seconds, identical to the acquisition trials except that responses were never reinforced. R1 underwent extinction in Context A and R2 in Context B.

Re-exposure. This phase began with the following instruction: "You have no fuel! You need to refuel for some seconds. While you do this you can see how your allies destroy some of your enemies". Then, the screen with the sentence "Your detachment has been posted to… (name of the beach where the battle continued)" was presented for 2 s. After that, all participants received a session of 20 seconds in which just one of the two attackers went off 12 times within the training context (i. e., A: O1 or B:O2, counterbalanced), while the other attacker was not destroyed.

Test. This phase began with the following instruction: "Refuelling has ended! You are ready to fight. The battle continues. Good luck!". Next, all participants received a test trial in extinction in each context. Each trial lasted 4 seconds and the order in which the contexts were presented was counterbalanced across participants.

2.1.4. Dependent Variable and Statistical Analysis

For all experiments presented here, the total number of mouse clicks on each enemy were recorded and transformed to responses per minute. Responding was evaluated by analysis of variance (ANOVA). The rejection criterion was set at $p<.05$, and effect sizes

were reported using partial eta-squared (η_p^2). Additionally, 90% confidence intervals for the effect sizes were calculated and reported for each analysis.

2.2. Results and Discussion

Figure 1 shows the mean response per minute for both responses during 2-trial blocks of acquisition (left panel) and during 3-trial blocks of extinction (right panel). A 2 (Response) x 5 (Block) ANOVA conducted with the data from acquisition confirmed that both responses were acquired similarly by all participants and that the responding increased as acquisition progressed, only finding a significant main effect of Block, $F(4, 60) = 16.50$, $p < .001$, $\eta_p^2 = .52$ [CI: .34-.61]. The main effect of Response and Response x Block interaction did not reach significance, $F<.88$, $p>.48$, $\eta_p^2 < .05$, showing that there was no difference in acquisition between R1 and R2.

A 2 (Response) x 10 (Block) ANOVA conducted on the extinction data only found a significant main effect of Block, $F(9, 135)= 34.83$, $p < .001$, $\eta_p^2 = .70$ [CI: .61-.73]. More importantly, the main effect of Response and the interaction did not reach significance, $F<1.47$, $p>.24$, $\eta_p^2 < .08$, indicating that extinction proceeds similarly for both responses.

Although the responses rate was quite high in the beginning of the training, particularly due to the simplicity of the task, we found a significant increase for both responses at the end of the acquisition phase. Moreover, the lack of reinforcement during extinction led participants to reduce their response rate in the presence of both contexts.

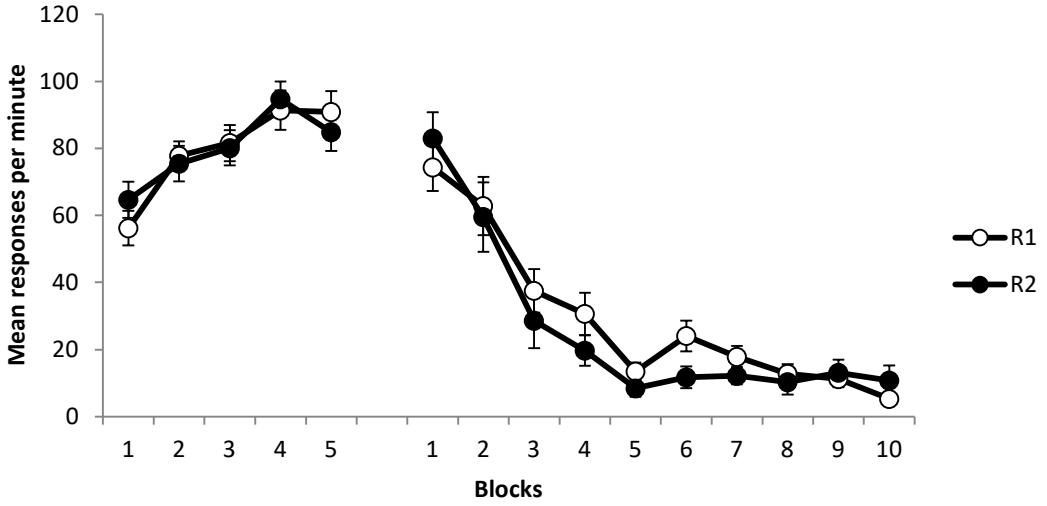

Figure 1. Mean responding of R1 and R2 during acquisition and extinction in Experiment 1. Error bars denote standard errors of the mean.

The effect of the outcome delivery on extinguished responses was then assessed. The response rate data, expressed as the mean responses per minute for R1 and R2 during the last extinction trial and the test trial, are presented in Figure 2. If the outcome delivery leads to the recovery of the response associated with that outcome, then higher response rate of R1 would be expected in the test trial than in the last extinction trial. This is precisely what we found. An ANOVA conducted with the data from the last extinction trial and the test trial found a significant main effect of Response (R1 vs. R2), F (1, 15) = 15.25, p= .001, η_p^2 = .50 [CI: .17- .67] and Trial (last extinction trial vs. test trial), F (1, 15) = 23.22, p< .001, η_p^2 = .61 [CI: .28- .74]. Most importantly, Response x Trial interaction was significant as well, F (1, 15) = 22.98, p< .001, η_p^2 = .60 [CI: .28- .74]. Follow-up comparisons showed an increase in responding from the last extinction trial to test trial for R1, F (1, 15) = 40.15, p< .001, η_p^2 = .73 [CI: .45- .82], but not for R2, F (1, 15) = 4.21,

p=.058, η_p^2 = .21 [CI: .00- .46]. Given that the rate of responding at the end of extinction is too low and that clicking on the mouse is a very easy response, it would be expected an increase of performance after the re-exposure phase (note that the instructions encourage the participant to shoot again). However, if the exposure to the outcome leads to the reappearance of the instrumental behavior, then a higher responding rate should be found on R1 than on R2 in test trial. As you can see on Figure 2, that is what we found. This was confirmed by the analysis conducted with the data of Test trial, $F(1, 15) = 25.19$ p< .001, η_p^2 = .63 [CI: .31- .75].

The present data is consistent with prior reports of reinstatement in Pavlovian and instrumental learning with nonhuman animals (e.g. Bouton & Woods, 2008). In addition, it is important to note that the present results extended the findings of reinstatement in humans to an instrumental learning situation.

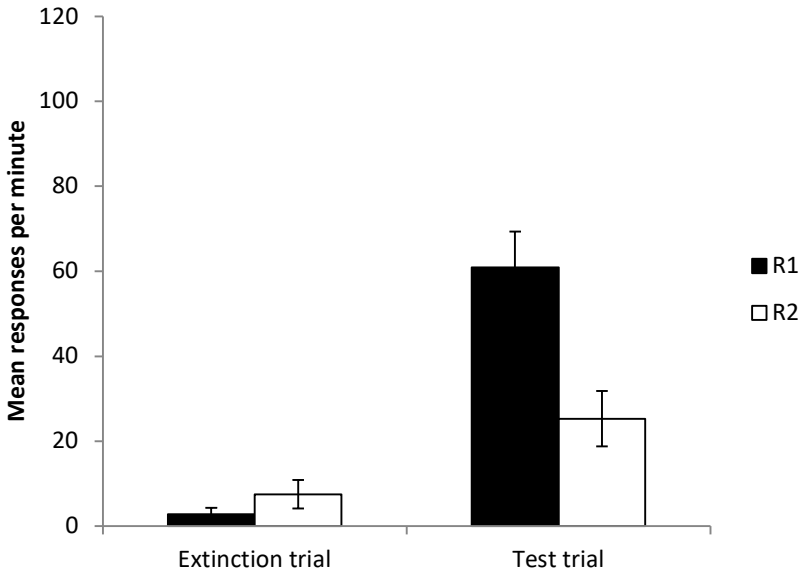

Figure 2. Mean responding per minute of R1 and R2 during the last extinction trial and the test trial in Experiment 1. Error bars denote standard errors of the mean.

3. Experiment 2

Along with spontaneous recovery and renewal, reinstatement has been used as evidence against conceiving instrumental extinction as unlearning. Although those three phenomena have been explained using different theoretical perspectives, Bouton has proposed that all three recovery effects might share a common mechanism (see Bouton, 2014; Bouton & Woods, 2008).

According to the retrieval theory of forgetting during extinction, instead of eliminating the original learning, a new and inhibitory learning is established, which creates two different memories (Bouton, 1993, 1994, 1997). The context helps participant to choose between those memories. Given that the theory assumes that it is harder to remember extinction outside the extinction context, it clearly predicts a retrieval of the original memory when testing takes place in anywhere except the extinction context. In the particular case of reinstatement (although physical contexts do not change), the theory proposes that delivering the outcome after extinction produces changes in the associative value of the context which promotes the return of the extinguished response (García-Gutiérrez, Rosas & Nelson, 2005). Furthermore, Bouton's proposal predicts that reinstatement would be observed only when outcome delivery and testing occur in the same context.

Experiment 2 was designed to evaluate whether the findings of Experiment 1 can be accounted through the mechanism proposed by the retrieval theory of forgetting. As in the previous experiment, we used a within-subject design (see the second row of Table 1). Participants learned to defend Andalusia from two attackers (R1 or R2 counterbalanced). Then, participants experienced extinction for both responses. Next, participants saw one enemy destroyed by an ally (O1). Finally, testing of R1 was conducted in a novel context.

If reinstatement is contextually modulated then no response recovery should be observed for R1.

3.1. Method

3.1.1. Participants

Sixteen undergraduate students from the Universidad de Cádiz participated in this experiment (15women, 1 man; M_{age} = 22.62 years; age range = 21-33 years). The rest of characteristics are the same as those in the previous experiment.

3.1.2. Apparatus and stimuli

We conducted the present experiment in the same conditions of Experiment 1, with the exception that a third context was added. Thus, different beaches of Andalusia, Puerto Banús (urban beach), Tarifa (natural beach), and Cabo de Gata (natural beach with a lighthouse) were counterbalanced as contexts A, B and C.

3.1.3. Procedure

Except as noted, we used the same procedure as in Experiment 1.

Test. This session was conducted in the same manner as in the previous experiment, except in this case participants received a test trial in context B, in which re-exposure to the reinforcer did not take place, and in a novel context (C). The order of presentation of the contexts B and C was counterbalanced across participants.

3.2. Results and Discussion

The left panel of Figure 3 depicts the mean response per minute for R1 and R2 throughout 2-trial blocks of acquisition, while the right panel shows 3-trial blocks of extinction performance for both responses. A 2 (Response) x 5 (Block) ANOVA conducted with the data from acquisition confirmed that both responses were acquired similarly by all participants and that the responding increased as acquisition progressed, only finding a

significant main effect of Block, $F(4, 60) = 4.93$, $p = .002$, $\eta_p^2 = .25$ [CI: .07-.35]. The main effect of the Response and the interaction did not reach significance, $F<1.08$, $p>.37$, $\eta_p^2 < .06$, showing that there was no difference in acquisition between R1 and R2.

A 2 (Response) x 10 (Block) ANOVA conducted on the extinction data only found a significant main effect of Block, $F(9, 135) = 25.69$, $p < .001$, $\eta_p^2 = .63$ [CI: .52-.67]. Given that neither the main effect of Response nor the Response x Session interaction reached significance, $F<1.38$, $p>.26$, $\eta_p^2 < .08$, ANOVA confirmed that R1 and R2 were extinguished in a similar manner.

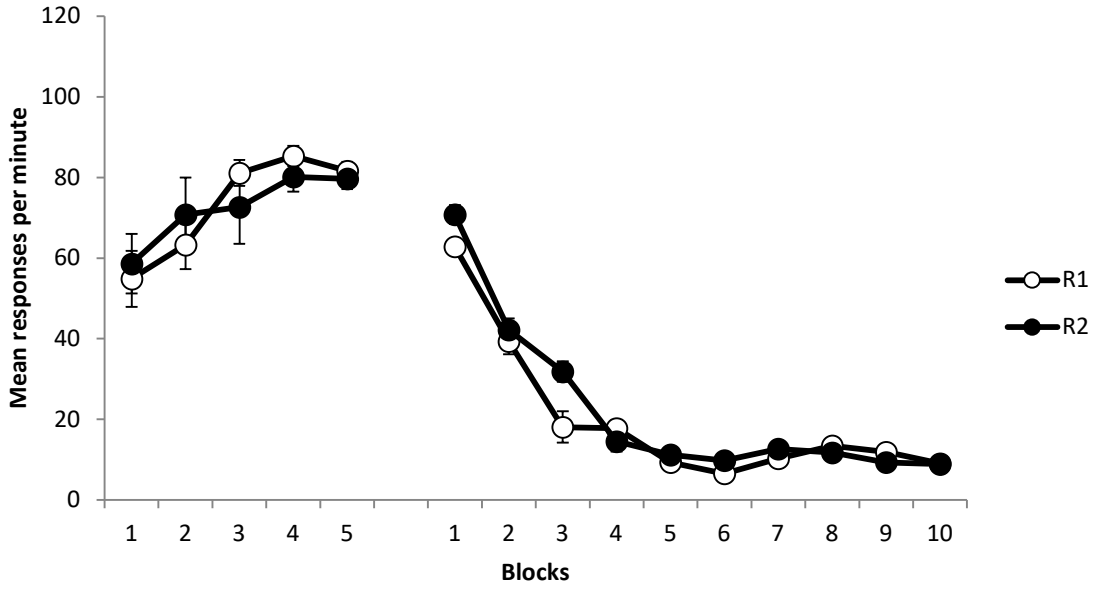

Figure 3. Mean responding of R1 and R2 during acquisition and extinction in Experiment 2. Error bars denote standard errors of the mean.

As in experiment 1, these results show a significant increase of both responses at the end of the acquisition phase in context A and context B and a decrease in those responses' rate at the end of the extinction phase in the presence of both contexts.

Figure 4 shows mean responses per minute for R1 and R2 responses in the last extinction trial and in the test trial. An ANOVA conducted with those data yielded only a significant main effect of Trial (last extinction trial vs. test trial), $F\,(1, 15) = 8.31$, $p = .011$, $\eta_p^2 = .36$ [CI: .05- .56]. The main effect of Response (R1 vs. R2) and the interaction were not significant, $F < .53$, $p > .48$, $\eta_p^2 < .03$ [CI: .00- .25]. Post-hoc comparisons to assess the reinstatement effect in both R1, that has been tested in a novel context, and R2 showed an increase in responding from the last extinction trial to test trial for R1, $F\,(1, 15) = 11.91$, $p < .004$, $\eta_p^2 = .44$ [CI: .11- .63], but not for R2, $F\,(1, 15) = 3.85$, $p = .069$, $\eta_p^2 = .20$ [CI: .00- .44].

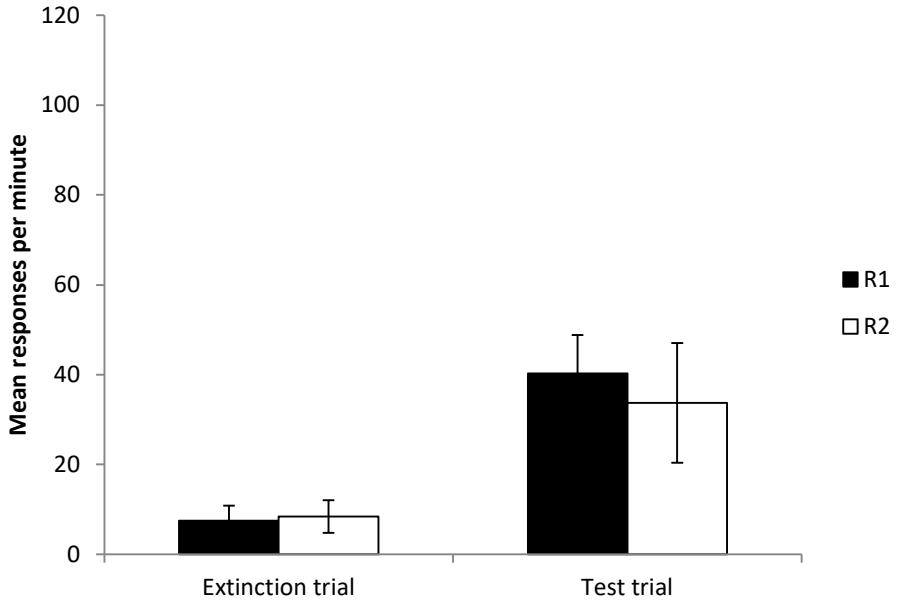

Figure 4. Mean responding per minute of R1 and R2 during the last extinction trial and the test trial in Experiment 2. Error bars denote standard errors of the mean.

The analyses showed a general enhancement for both responses. However, we should be cautious about claiming that the mechanism underlying the instrumental reinstatement in humans is different to the one proposed by Bouton's perspective. Although it might seem a reinstatement effect for R1, it is important to note that the rate of responding (approximately 40) is lower than the one reported in Experiment 1 (approximately 60). In addition, as we stated above, if reinstatement of R1 took place, it could be expected a higher response rate on R1 than on R2 (which outcome was not presented during pre-exposure phase). However, given that the analysis showed no difference between the rate of responding for R1and R2 during testing, F (1, 15) = .40, p= .530, the mechanism of this reinstatement effect is not clear.

Given that testing for R1 took place in a novel context, the present result might be explained by a contextual effect of renewal (i. e, an AAB-like renewal), in the meantime the present data suggest that reinstatement of voluntary actions in humans may depend on some kind of contextual modulation. This finding is consistent with other data both with nonhuman animals (e. g., Bouton & Woods, 2008; c.f. Westbrook et al., 2002) and humans (e. g., García-Gutiérrez & Rosas, 2003a) that might suggest that the mechanism underlying reinstatement is context change.

4. Experiment 3

One might interprete the results from Experiment 2 as consistent with the retrieval theory of forgetting (i. e., contextual modulation, Bouton, 1993, 1994). Given the clinical implications of the reinstatement of instrumental responses for understanding relapse after therapy, it seems adequate to use a behavioral strategy to prevent the reinstatement of voluntary behaviors based on Bouton' proposal. According to this theoretical perspective,

relapsing is a failure to retrieve the therapeutic abilities (extinction memory) outside the therapeutic setting (extinction context). Thus, presenting a reminder of the therapy (i. e., extinction-cue) should improve the retrieval of the clinical treatment. The purpose of Experiment 3 was to explore whether an extinction-cue had any impact on the reinstatement of instrumental responses in human beings. After participants learned to perform R1 and R2, they received an extinction procedure for both responses. During this phase, all participants experienced the presence of an extinction-cue. Then, all participants saw both attackers destroyed by allies (O1 and O2). Finally, testing took place; only R1 was tested in the presence of the extinction-cue. Following Bouton's proposal, performance of R1 should be lower than R2.

4.1. Method

4.1.1. Participants

Sixteen undergraduate students from the Universidad de Cádiz participated in this experiment (14 women, 2 men; M_{age} = 23.12 years; age range = 21-30 years). The rest of characteristics are the same as those in the previous experiment.

4.1.2. Apparatus and stimuli

We used the same apparatus and stimuli from Experiment 1.

4.1.3. Procedure

Except as noted, the same procedure as in Experiment 1 was used.

Extinction. All participants received 30 extinction trials identical to the previous experiment's extinction phase, except that in each of those trials we presented on top of the screen a red-colored rectangle (extinction-cue).

Re-exposure. This phase was conducted in the same manner as in the previous experiments, except that in this case participants were re-exposed to outcomes 1 and 2 (i. e.,

all participants experienced the destruction of the two attackers in their respective contexts).

Test. As in previous experiments, in this phase, we carried out one trial for testing R1 in Context A and R2 in Context B. During the trial for testing R1 the red-colored rectangle (extinction-cue) was presented. In Context B, no extinction-cue was presented. The order of testing was fully counterbalanced, as in Experiment 2. Refer to the experimental design in the third row of Table 1.

4.2. Results and Discussion

Figure 5 shows the mean response per minute for both responses during 2-trial blocks of acquisition (left panel) and during 3-trial blocks of extinction (right panel). A 2 (Response) x 5 (Block) ANOVA conducted with the data from acquisition only found a significant main effect of Block, $F(4, 60) = 9.92$, $p < .001$, $\eta_p^2 = .40$ [CI: .20-.49]. The main effect of Response and the interaction were not significant, $F<1.29$, $p>.35$, $\eta_p^2 < .07$, showing that both responses were acquired similarly by all participants and that the responding increased as acquisition progressed.

A 2 (Response) x 10 (Block) ANOVA conducted on the extinction data only found a significant main effect of Block, $F(9, 135) = 29.24$, $p < .001$, $\eta_p^2 = .66$ [CI: .56-.70]. Moreover, the main effect of Response and the interaction did not reach significance, $F<1.75$, $p>.15$, $\eta_p^2 < .10$, indicating that extinction proceeds similarly for both responses.

As in previous experiments, these results show a significant increase of both responses at the end of the acquisition phase in context A and context B and a decrease in those response rates at the end of the extinction phase in the presence of both contexts.

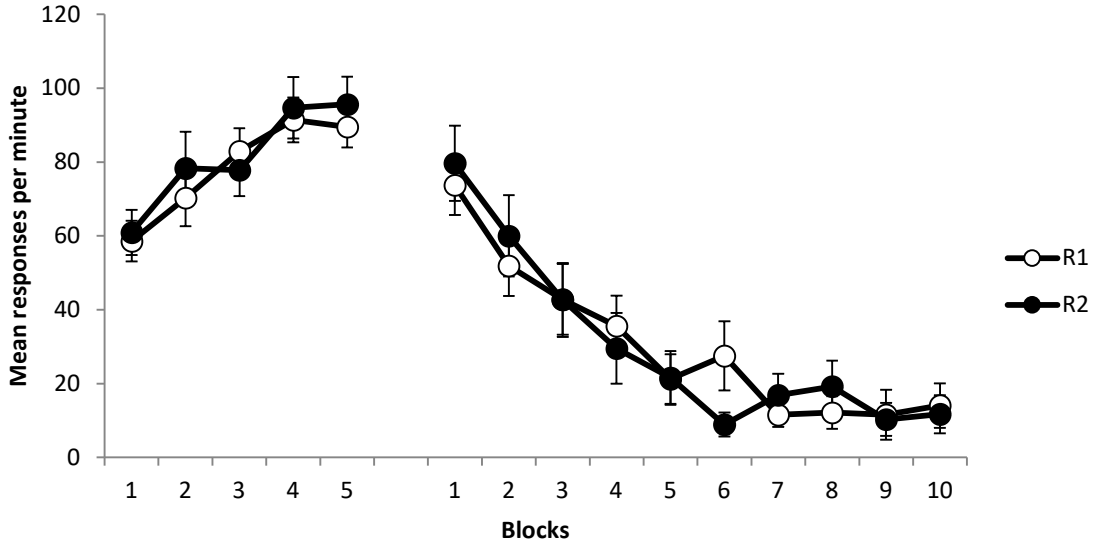

Figure 5. Mean responding of R1 and R2 during acquisition and extinction in Experiment 3. Error bars denote standard errors of the mean.

Figure 6 shows mean responses per minute for R1 and R2 during testing. An ANOVA conducted with data from the last extinction trial and the test trial found a significant main effect of Response (R1 vs. R2), F (1, 15) = 8.60, p= .010, η_p^2= .36 [CI: .06- .57] and Trial (last extinction trial vs. test trial), F (1, 15) = 27.05, p< .001, η_p^2= .64 [CI: .33- .76]. Interaction did not reach significance, F (1, 15) = 3.45, p= .083, η_p^2= .19 [CI: .00- .43]. Post-hoc comparisons to explore the reinstatement of the responses showed an increase from last extinction trial to test trial for both R1, F (1, 15) = 16.13, p= .001, η_p^2= .52 [CI: .18- .68], and R2, F (1, 15) = 22.70, p< .001, η_p^2= .60 [CI: .27- .74]. Moreover, in order to assess the effect of the extinction-cue, we conducted a comparison between R1 and R2. This comparison showed a higher responding for R2 than for R1, F(1, 15) = 10.26, p= .006, η_p^2= .41 [CI: .08- .60]. This demonstrates that the presence of the

extinction-cue reduced the performance of R1. In summary, the present data strongly suggests that the reinstatement of human instrumental learning can be reduced by using a reminder from the extinction phase.

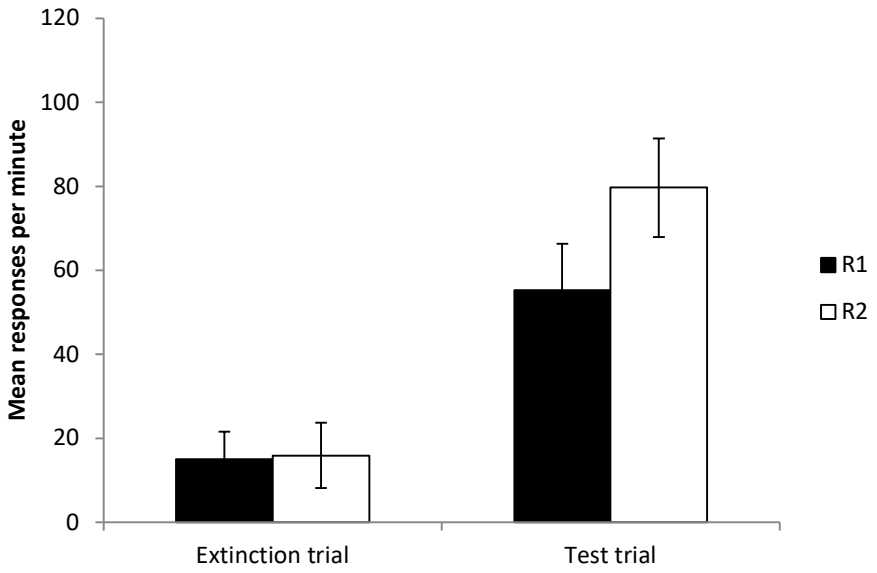

Figure 6. Mean responding per minute of R1 and R2 during the last extinction trial and the test trial in Experiment 3. Error bars denote standard errors of the mean.

5. General Discussion

The present experimental series evaluated the reinstatement of instrumental behaviors in human beings. Using a video game task, we found unprecedented evidence of reinstatement of instrumental learning in a within-subject design with college students (Experiment 1). Moreover, our findings show that performance of an extinguished instrumental response depends notably on the context's current value (Experiment 2). Most importantly, we found that reinstatement of voluntary responses was attenuated in the presence of a stimulus associated with extinction (Experiment 3).

Reinstatement of instrumental responses has been reported with rats using food reinforcers (e. g., Baker, 1990; Delamater, 1997; Ostlund & Balleine, 2007), drug reinforcers (e. g., De Wit & Stewart, 1981; Stewart & De Wit, 1987) and with monkeys, by using drug reinforcers (Gerber & Stretch, 1975). Our findings in Experiment 1 show a procedural parallelism in a videogame task with healthy humans, which suggests that despite the fictional trait of the task, it could be considered as an adequate procedure to study the learning mechanisms underlying relapse of voluntary actions in humans. Regarding to this novel methodology to study reinstatement of instrumental responses in humans, it is important to briefly discuss a part of the procedure that might raises some doubts. Before the reinstatement test took place, participants read: "Refuelling has ended! You are ready to fight." After this kind of instruction, it might be tempting to think that the reinstatement effect reported in Experiment 1 could be due to the instruction and not to the re-exposure of the outcome. However, note that the instruction provides participants information about starting the shooting, but, it did not specify what button should be pressed nor how many times they should press the button. So, if the instructions were producing the reinstatement we should have observed reinstatement for both responses, nevertheless, given that we only found reinstatement for the response that was re-exposure to the outcome, it is hard to suggest that the result obtained in Experiment 1 is due to the instructions.

As we stated earlier, the reinstatement effect is a well-known and studied phenomenon in human beings (e. g., Haaker, Golkar, Hermans, & Lonsdorf, 2014; Vila & Rosas, 2001). However, the emphasis on those studies has been on Pavlovian learning (i. e., participants learn relationships between events or cues), with a recent interest on human fear conditioning (e. g., Vervliet, Craske & Hermans, 2013). Therefore, our results from

Experiment 1 extend the generality of the reinstatement effect to an instrumental learning task (i.e. voluntary behaviors that are controlled by their consequences).

Although there are different theoretical views to account for reinstatement (e. g., Dunsmoor, Niv, Daw & Phelps, 2015), evidence from Experiment 2 suggests the context plays a key role. However, given that this is the first study that assessed the mechanisms underlying the reinstatement of voluntary actions in humans, it is necessary to conduct more research.

Given that the reoccurrence of the eliminated (extinguished) voluntary unhealthy behavior is highly undesirable, reducing or preventing reinstatement of instrumental responses might be of value from a clinical standpoint. In Experiment 3, we found that presenting a reminder from extinction reduced reinstatement of instrumental actions. The very same finding has been reported with rats. Bernal-Gamboa, Gámez and Nieto (2017) trained hungry rats to perform two operant responses for food (R1 and R2). Then, both R1 and R2 received an extinction treatment. Throughout this phase, all rats received brief presentations of a tone (extinction-cue). Following extinction, a single re-exposure to the food session was conducted. Testing of R1 took place in the presence of the tone, whereas testing of R2 was conducted without the tone. Bernal-Gamboa et al. (2017) observed a reduction of reinstatement produced by the extinction reminder because performance of R1 was lower than R2.

The extinction-cue strategy has shown to be a reliable technique to attenuate other response recovery effects. For example, there are studies that demonstrate that using a stimulus associated with extinction diminishes renewal of extinguished fear responses with humans (Dibbets, Havermans, & Arntz, 2008, Vansteenwegen et al., 2006), appetitive Pavlovian conditioning with rats (Brooks & Bouton, 1994) and instrumental responses with

rats (Nieto, Uengoer & Bernal-Gamboa, 2017; Willcocks & McNally, 2014). In addition, the effectiveness of extinction-cue has been reported in animal research for decreasing the spontaneous recovery of appetitive Pavlovian conditioning (Brooks & Bouton,1993), conditioning taste aversion (Brooks, Palmatier, García & Johnson, 1999), conditioned alcohol tolerance (Brooks, Vaughn, Freeman & Woods, 2004) and operant performance (Bernal-Gamboa et al, 2017). The overall pattern of results suggests that all response recovery effects shared a common mechanism (Bouton, 2014). They also suggest that in order to prevent relapse, a long-lasting treatment might integrate a memory retrieval component from therapy.

Our findings in Experiment 3 demonstrate the impact of extinction-cues on the reinstatement of voluntary actions in humans. However, is important to note two important points. The first is related to an alternative explanation. Given that the extinction-cue was presented throughout the extinction trials, participants could encode the context and the extinction-cue as a configural pattern (Pearce, 1994). Thus, the findings for R2 (testing was conducted without the extinction-cue) might be explained as a generalization decrement. The second issue concerns the mechanisms underlying the extinction-cue. The reduction of reinstatement observed in Experiment 3 could be explained by three possible accounts. One possibility is that an extinction-cue may directly inhibit the representation of the outcome (e. g., Rescorla & Wagner, 1972). A second approach could be that the extinction-cue modulates the response-outcome association (Bouton, 1997). And a third possibility could be that a specific response is directly inhibited by the extinction-cue (Rescorla, 1993). Unfortunately, the present design could not discern which of the three aforementioned accounts is correct. However, future research should clarify the underlying mechanisms,

because it would be helpful to understand the strengths and weaknesses of extinction reminders in therapeutic settings.

6. References

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