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Testing the memory reconsolidation hypothesis in a fear extinction paradigm: The effects of ecological and arbitrary stimuli

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Abstract
Various studies demonstrated that extinction training taking place shortly after the activation of the acquired fear could weaken the conditioned fear. The procedure is called post-retrieval extinction (PRE). However, from the time it emerged, it has suffered from inconsistencies in the ability of researchers to replicate the seemingly established effects. Extant literature implies that conditioned fear might be differentially sensitive to the nature of conditioned stimuli (CS) used. The aim of the present study, therefore, is threefold. First, we aimed to replicate Schiller et al. (*Nature, 463*, 49–53. 2010) procedure in which the PRE had produced positive results with arbitrary CSs only. Also, we examined the PRE as a function of CS type (ecological-fear-relevant (images of spider and snake) vs. arbitrary (images of yellow and blue circles)). Finally, we aimed to investigate the long-term effects of the PRE (i.e., 24 h, 15 d, and 3 mo). The study consisted of acquisition, re-activation and extinction, and re-extinction phases. Dependent measure was the recovery of fear responses as indexed by the skin conductance responses (SCRs) and arousal ratings of the participants at the last trial of the extinction and the first trial of the re-extinction. All groups showed significant acquisition and extinction patterns, compared to the other two groups (i.e., 6 h after the activating CS and without an activating stimulus) only the group that undertook extinction trials 10 min after the activating CS showed a sustained extinction. Thus, our findings provided further evidence for the robustness of the PRE paradigm in preventing the recovery of extinguished fears behaviorally, both with ecological and arbitrary stimuli.

Keywords Reconsolidation · Fear conditioning · Extinction · Spontaneous recovery · Ecological vs. arbitrary CSs · SCR

Introduction

Fear learning is of great adaptive importance because it motivates organisms to identify threat signals in their environment and, thus, cope with the source of threat more effectively by forming a fear memory. Fear memory represents acquired associations between initially neutral stimuli (e.g., a visual stimulus) and intrinsically aversive consequences (e.g., electrical shock, unconditioned stimuli (US)). Because the response is conditional on the contingency between the two stimuli, the visual stimulus becomes a conditioned stimulus (CS). Thus, the fear elicited by the CS is called the conditioned response (CR) (Fendt & Fanselow, 1999).

Equally crucial for adaptive behavior is learning the change in contingency between the stimuli. Since the fear memory is necessary for the maintenance of conditioned fear, repeated presentations of the CS without any adverse consequence should lead to new learning that the stimulus is innocuous. Hence, extinction occurs when the CS occurs in the absence of the US, and the CS elicits decreasing amounts of conditioned fear as extinction trials progress (e.g., Bouton, 1988; Delgado, Olsson, & Phelps, 2006; Field, 2006; Kindt, Soeter, & Vervliet, 2009).

Although extinction produces substantial behavioral and emotional effects, the loss of CS-elicited fear is usually transient. Even after comprehensive extinction training, there may be much recovery from the extinguished fear (Bouton, 2002; Delamater, 2004; Rescorla, 2001). Extinction has several defining phenomena of relapse. The first is spontaneous recovery. The return of extinguished fear may be spontaneous (Rescorla, 2004) as a function of the length

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of the retention interval, i.e., the time passed since the last presentation of CS. Generally, the longer the delay, the more rigorous the CR (Quirk, 2002). The second phenomenon is renewal. Extinguished CRs may reappear when animals are tested in a context different from the context of the extinction performed (Bouton, 1993; Bouton & Woods, 2008). The third phenomenon is reinstatement. Extinguished conditioned fear responses may relapse by unsignaled presentations of the US (Dirikx et al., 2004; Rescorla & Heth, 1975). Thus, the violation of the expected contingency between the CS and the US formed during the acquisition training seems to be a key factor for extinction. In addition, the extinction process does not imply the reversal of acquisition but rather, promotes the development of new learning. Several inhibitory associations describe the learning motivated by the extinction process (e.g., inhibitory CS-US association, inhibitory CS-CR association, or CS-NoUS association) (Bouton, 2002; Rescorla, 1993). Empirical data obtained from the variety of preparations on various species, including humans, widely supported these analyses of extinction (for detailed reviews, see Bouton, 2002; Delamater, 2004).

Given the significance of extinction in both basic and translational research, a substantial effort has been dedicated to finding ways to enhance extinction learning (Chen et al., 2022; Craske, Hermans, & Vervliet, 2018; Fitzgerald, Seemann, & Maren, 2014; Keller & Dunsmoor, 2020; Laborda & Miller, 2013; Leung, Reeks, & Westbrook, 2012; Monfils et al., 2009). These efforts include, but are not limited to, increasing the number of extinction trials (e.g., Leung et al., 2007), increasing the intertrial interval (e.g., Urcelay, Wheeler, & Miller, 2009), extinction in various contexts (e.g., Bandarian Balooch & Neumann, 2011), providing reminder cues for extinction (e.g., Laborda & Miller, 2012), and extinction shortly after conditioning (Myers et al., 2006). However, most of these efforts were attempts to improve the inhibitory effects in the competition between the excitatory association promoted by acquisition training and the inhibitory association promoted by extinction training. If the inhibitory association is stronger than the original excitatory fear association, the animal shows no fear of the CS; however, if the inhibitory association is not sufficiently strong to suppress fear responses, the animal responds fearfully (Auchter et al., 2017). Of course, this does not weaken the theoretical and translational significance of efforts that enhance extinction. Instead, they mark the ubiquity of recovery from extinction, available only under restricted conditions (Chan et al., 2010).

Alternatively, if the acquired fear association is altered by interfering with the memory upon retrieval, the subject would be less vulnerable to the return of fear. This interference could be achieved by retrieval of the fear memory after the initial consolidation, because previously formed fear associations are not necessarily permanent, but can become transiently labile and open to modification when directly retrieved by the presentation of a CS (Miller & Matzel, 2000; Misanin, Miller, & Lewis, 1968; Schafe, Nader, & Le Doux, 2000; Tronson & Taylor, 2007). In line with this concept, Monfils et al. (2009) devised a method in which a single CS, as the reminder of fear association, was presented shortly before introducing the extinction training in fear-conditioned rats. The procedure, called post-retrieval extinction (PRE), was found to be consistently effective in reducing conditioned fear in rats. Likewise, Schiller et al. (2010) trained three groups of human participants in a discriminative fear conditioning procedure. Two circles, one painted blue and one yellow, served as CSs. One circle (CS+) was repeatedly paired with an aversive electric stimulus (US), while the other (CS-) was not. The next day, all groups underwent extinction training, in which both CSs occurred without the US. In two groups, a single presentation of CS+ served as a reminder of the fear association. However, one group received the reminder trial 10 min before extinction, and the other, 6 h before. On the third day of the study, they reintroduced the extinction trials to obtain an assay of spontaneous fear recovery. The group receiving their initial extinction trials 10 min after the reminder (in the reconsolidation window) showed significantly less recovery, as indicated by skin conductance measures. The study also provided some evidence of the long-term nature of the effect. However, a significant amount of fear returned in the groups that received traditional extinction and extinction outside the reconsolidation window, as typically observed across extinction studies (Bouton, 2002).

This early success of the PRE procedure encouraged many researchers to replicate these findings with humans (e.g., Agren et al., 2012a, Johnson & Casey, 2015; Oyarzún et al., 2012; Schiller et al., 2013; Sizhen et al., 2022; Steinfurth et al., 2014) and non-human animals (e.g., Flavell & Lee, 2011; Jones & Monfils, 2016; Mugnaini et al., 2022; Nader et al., 2000; Sara, 2000; Schafe & LeDoux, 2000). However, subsequent research has not yielded very consistent results. In human studies, some were successful in replicating the PRE effect (e.g., Agren et al., 2012a; Asthana et al., 2015; Bjorkstrand et al., 2015; Johnson & Casey, 2015; Liu et al., 2014; Oyarzún et al., 2012; Schiller et al., 2010, 2013; Thompson & Lipp, 2017), while others failed (e.g., Fricchione et al., 2016; Golkar et al., 2012; Kindt & Soeter, 2013; Klucken et al., 2016; Kredlow, Unger, & Otto, 2016; Meir Drexler et al., 2014; Soeter & Kindt, 2011).

Successful reactivation and destabilization of memory are crucial prerequisites for memory reconsolidation (Gisquet-Verrier & Riccio, 2012; Piñeyro et al., 2014). Thus, for the memory to enter a reconsolidation process, a reminder cue should successfully destabilize it in the first place. Although not all reactivations are successful in destabilizing the consolidated memory, it seems a necessary step. Consequently,

efforts were made to identify a series of conditions that keep the memory from reconsolidation, called "boundary conditions of reconsolidation," such as individual differences, memory strength, memory age, retrieval strength, prediction error, and genetic polymorphism (for reviews, see Agren et al., 2012b; Auber et al., 2013; Auchter et al., 2017; Finnie & Nader, 2012; Kredlow et al., 2016; Oyarzún et al., 2012; Schiller & Phelps, 2011; Soeter & Kindt, 2011, 2013; Zuccolo & Hunziker, 2019).

One critical boundary condition of PRE is the nature of the CS used. Since the first demonstration of PRE in humans (Schiller et al., 2010), in which arbitrary stimuli served as CSs, there has been both success and failure in replicating the PRE with CSs of different nature. Generally, visual preparations of potentially dangerous humans and other animals (frightening male faces, snakes, spiders, tigers, and dogs) have served as the fear-relevant or ecological CSs (e.g., Fricchione et al., 2016; Golkar et al., 2012; Kindt & Soeter, 2013; Meir-Drexler et al., 2014; Soeter & Kindt, 2011), and potentially safe cues (the pictures of colored squares or circles, mugs, different colored photo lamps, and various geometric shapes) as the fear-irrelevant or arbitrary CSs (e.g., Bjorkstrand et al., 2016; Golkar et al., 2012; Liu et al., 2014; Schiller et al., 2010; Steinfurth et al., 2014).

Considering the apparent significance of the PRE in translational research, the effects of fear-relevant events on acquisition and extinction have been studied and compared to the fear-irrelevant events. In a recent review, Zuccolo and Hunziker (2019) examined 28 studies on the PRE of fear, of which seven aimed to investigate the effects of fear-relevant CSs on the PRE. Four explicitly compared the impact of fear-relevant and fear-irrelevant CSs on the PRE. Half of the studies failed to obtain diminished conditioned fear responses in tests. However, a meta-analysis (Kredlow et al., 2016) indicated that the fear-relevance of the CS significantly moderated the effect of PRE in humans in favor of the fear-irrelevant stimuli. Still, the authors noted the relatively limited number of studies using fear-related stimuli, emphasizing the need to further validate these findings. Because of the inconclusive results observed in testing the PRE hypothesis, replication efforts are still valuable since the effect has not been successfully shown in non-pharmacological behavioral studies with ecologically relevant stimuli. However, several lines of work revealed the greater potency of naturalistic stimuli on various learning phenomena (for a review, see Domjan, 2005).

Naturalistic learning paradigms often predict that conditioning phenomena would be more readily available with ecologically-relevant events compared to their ecologically-irrelevant counterparts (e.g., Domjan, 2005, 2008; Domjan, Cusato, & Krause, 2004; Domjan & Galef 1983; Fanselow & Lester, 1988; Garcia, Hankins, & Rusiniak, 1974; Hollis, 1982, 1997; Öhman & Mineka, 2001; Rozin & Kalat, 1971; Seligman, 1970; Seligman & Hager, 1972; Shettleworth, 1998; Timberlake, 1983). Indeed, Domjan's (1994, 2000) research program on an animal model of sexual conditioning in Japanese quail provided further insights into the ecological relevance of learning. Domjan's ecological approach predicts that learning is more likely where the CS has a pre-existing relationship with the US. Thus, stimuli and responses forming part of a given ecology will more effectively activate the learning process (Domjan & Krause, 2017). Several studies in his sexual learning laboratory have explicitly compared the effectiveness of ecologically relevant stimuli on conditioned behavior, showing that ecological CSs were more effective in acquiring sexually conditioned behavior, producing second-order conditioning, and in resistance to blocking and extinction. Also, these studies show persistence in conditioned behavior through lengthy CS-US intervals and lower I/T ratios (for review, see Domjan, 2005). In addition, naturalistic learning paradigms define ecological and arbitrary stimuli by their inherent relations with US occurring in an animal's ecological niche (Domjan, 2000; Domjan & Galef, 1983; Rozin & Kalat, 1971). An arbitrary CS is unrelated to the US, and it rarely occurs in conjunction with a particular US under natural circumstances. However, ecological stimuli are cues that reliably precede biologically significant events (e.g., a US) commonly encountered by animals in their evolutionary histories. Thus, a natural precursor of a US is regarded as a naturalistic stimulus given its inherent relationship with the US (Çetinkaya, 2018; Domjan et al., 2004). An ecological relationship between CS and US is usually due to complementarity (e.g., sex-specific plumage on the head and neck (CS) of female quail (US)) or natural contingency (e.g., contextual cues reliably signaling a sexual encounter with the female quail) between CS and US. Moreover, this approach establishes a continuum extending between highly naturalistic stimuli to purely arbitrary stimuli. Many studies provided evidence that fading ecological features of a CS resulted in a change in its effectiveness (e.g., in acquisition: Cusato & Domjan, 1998; Domjan, Akins, & Vandergriff, 1992; Hilliard et al., 1998; Köksal et al., 1994; in blocking: Köksal et al., 1994; in extinction: Krause, Cusato, & Domjan, 2003). Although fear conditioning studies have provided results similar to the fear-relevant stimuli, they regarded the effects of fear-related stimuli from phylogenetic and ontogenetic perspectives. Audio-visual presentations of life-threatening animals such as snakes and spiders served as phylogenetic or ecological CSs (e.g., Fricchione et al., 2016; Golkar et al., 2012), while acquired fear stimuli such as guns and electrical outlets functioned as ontogenetic CSs (e.g., Hugdahl & Jonsen, 1988).

This paradigm, by and large, is compatible with the findings of fear learning. The 40 million years of co-existence with snakes and spiders created selection pressure on our

ancestors for survival, and it presumably favored those who associate threat cues (e.g., the sight of a dangerous spider or snake) with the danger itself. A natural consequence of interacting with a deadly spider or snake is likely a venomous bite. That constitutes the basis for the pre-existing relationship between a CS and an aversive US. As a result, presumably, we have evolved mechanisms making us more likely to develop a fear of these ancestral threats (Hoehl et al., 2017). In case of fear-relevant stimuli, fear is acquired more readily (e.g., Cook & Mineka 1987; Öhman et al., 1976; Öhman & Mineka, 2001; Öhman, Erixon, & Lofberg, 1975) and is more resistant to extinction (e.g., McNally 1987; Mineka & Öhman, 2002; Prokasy & Kumpfer, 1973). For example, people are more likely to associate an electric shock with fear-relevant stimuli (images of snakes, spiders, or angry faces) than with fear-irrelevant stimuli (flowers, mushrooms, or happy faces).

Considering the mixed findings from studies using PRE, and in order to obtain more comparable results, we employed Schiller et al.'s (2010) experimental strategy, which had successfully prevented the return of acquired fear, albeit only with arbitrary CSs. Consequently, the present study was designed to include the ecological fear-related CSs.

Therefore, the present study aimed to investigate the effects of the stimulus type (ecological vs. arbitrary) and memory activation before the extinction (within or outside of the reconsolidation window) on the return of conditioned fear after successful extinction. We used a human version of the reconsolidation update paradigm, adapted by Schiller et al. (2010), from the version initially developed for animal studies by Monfils and his colleagues (2009). The ecological and arbitrary stimuli eliciting comparable SCRs were predetermined in a separate study conducted with an independent sample (see *Methods* section for the details). Accordingly, the blue and yellow circles served as arbitrary CSs, and spider and snake pictures as ecological-fear relevant stimuli. The paradigm consisted of a three-phase procedure: acquisition, extinction (with or without reminder), and re-extinction phases. In the first phase, participants acquired conditioned fear through differential fear conditioning; CS+ was paired intermittently with an electrical shock while CS- was presented unpaired. Half of the participants were trained with an ecological CS+ and CS-, and the other half, with an arbitrary CS+ and CS-. The next day, all groups underwent extinction training, in which both CSs occurred without the US. In two groups, a single presentation of CS+ served as a reminder of the fear association. However, one group received the reminder trial 10 min before extinction (during the reconsolidation window); the other did 6 h before it (after it closed). The remaining participants received the extinction without reactivation. The last phase was conducted 24 h, 15 d, or 3 mo following the extinction phase to test the persistence of the extinguished fear responses at different retention intervals. SCRs and CS+ arousal ratings were recorded to index the recovery of fear responses. We assessed spontaneous recovery of the fear by comparing the SCR and arousal measurements obtained from the last trial of extinction and the first trial of re-extinction.

We hypothesize less effective recovery from fear when extinction occurred within the reconsolidation window (10 min after reminder) compared to outside (6 h after reminder) or with no reminder treatment. In the face of the previous compelling evidence, we also predict that ecological CSs, even though they elicit initially comparable fear responses, will lead to the differences in acquisition and extinction of conditioned fear between ecological and arbitrary CSs. Finally, we expect sustained effects of the PRE across different retention intervals.

Materials and methods

Participants

The participants consisted of volunteer students and staff from the Izmir University of Economics. We first administered an evaluation form including questions about participants' past and current physiological/ psychological well-being and previous research participation experience to decide on eligibility. Healthy volunteers with no prior experience of fear or anxiety-related studies participated in the study (see a complete list of initial eligibility criteria in the Online Supplementary Material (OSM)). Although a sample of 326 participated initially, further elimination criteria were set based on the participants' attendance and performance. Attrition ($n = 13$), technical problems ($n = 3$), and failures of participants in following the instructions ($n = 4$) resulted in exclusion of 20 participants in total. Successful acquisition and extinction (as indexed by differential SCRs to CSs, or dSCRs) were prerequisites to assess the recovery of fear, therefore, a total of 87 participants were excluded from the study because they failed either in forming CR (dSCR < .10 μS for acquisition, $n = 55$) or in extinguishing CR (dSCR > .10 μS for extinction, $n = 32$), as assessed by SCR. Importantly, the type of CS had no relationship with the number of participants excluded; therefore, the performance-based exclusion criteria cannot introduce a bias to our conclusion regarding the type of CS (see Table 1 in the OSM for distribution of excluded participants by stimulus type). The data from the remaining 219 participants (137 female, aged between 18 and 53; *mean* ± *SD*, 21.70 ± 5.71) were included in the statistical analysis. The adequacy of the sample size was determined by a power analysis using PANGEA (Power ANalysis for GEneral Anova designs, v0.2; Westfall, 2016). The analysis showed that the current experimental design provides a power of .93 with 219 participants

for medium effect size ($d = .45$). The number of participants across experimental conditions was almost equal; there were 14, 13, 12, and 11 participants in one, three, 12, and two groups, respectively (see Table 2 in the OSM for distribution of participants across 18 experimental conditions). If applicable, participants were either paid a small amount or given partial course credit for a psychology course. The research was approved by the IRB of the Izmir University of Economics, where the study was carried out. All participants gave their written consent before participating in the study.

Stimuli

Arbitrary and ecological stimuli that were used as CSs in the main study were determined by a preliminary study conducted on a separate sample ($n = 50$). No pre-screening for participation was implemented at this stage, and all volunteers were accepted as participants. Twenty pictures containing ecological and arbitrary figures comprised the initial stimuli pool. The snake and spider pictures (five of each) were obtained from the internet as the candidates of ecological stimuli, and blue and yellow circles in various sizes (five of each) were created on a visual processing software. The pictures appeared on a 1,024 × 768 pixels display for 4 s with a 10–12 s variable inter-trial interval (ITI) in a randomized order. Equal numbers of participants were randomly assigned to five presentation conditions, and their SCRs elicited by the stimulus pictures were recorded. Amplitudes of SCR (base to peak difference) evoked by each stimulus presentation were calculated. The average SCR was 8.44 μS regardless of stimuli. One picture from each category that elicited comparable levels of SCR to the average SCR and each other ($H(3) = .54$, $p > .05$) was chosen as ecological (snake: 8.30 μS, spider: 8.57 μS) and arbitrary (blue circle: 7.89 μS, yellow circle: 8.22 μS) stimuli for the main study. While the pictures of snake and spider were 760 × 760 pixels, the diameters of yellow (R = 255, G = 255, B = 0) and blue (R = 0, G = 0, B = 255) circles were 540 pixels (see OSM Fig. 1 for the stimuli used in the main study).

The chosen pictures were presented at the center of a 20-in. computer screen with a black background in the main study. From each category, one of the stimuli was used as CS+ (positive CS-US contingency), and the other was used as CS- (negative CS-US contingency). Stimuli serving as CS+ were counterbalanced across the participants. In all phases, the duration of the CS presentation was 4 s.

An electrical current generated by an isolated linear stimulator (Model: STMISOLA; BIOPAC Systems, Inc.), serving as US, was delivered through a bar electrode (Model: EL350; BIOPAC Systems, Inc.) attached to the right inner wrist. The electrode site was cleaned, and an amount of electrode cream (Model: EC2; Grass Technologies) was applied to the electrode prior to its placement on the wrist. All participants determined the level of the electrical stimulation themselves with the assistance of the experimenter at the beginning of the first session, starting from a mild level (around 20V) and gradually increasing over three trials to a maximum of 60V, until the shock reached a level which the participant considered as "uncomfortable but not painful" (e.g., Schiller et al., 2010).

In the acquisition phase, US presentations started 3,800 ms after the CS+ onset, lasted for 200 ms, and co-terminated with the CS+. The stimulator was kept in the "on" position with the bar electrode attached across the phases, even though no electrical stimulation was delivered after the acquisition.

Skin conductance response

SCR results from electrodermal activity were measured with an MP150WSW-G Data Acquisition System coupled with the Bionomadix Wireless Pulse and EDA Amplifier BN- PPGED via a Universal Interface Module UIM100C (BIOPAC Systems, Inc.). In addition, an isolated digital interface (Model: STP100C; BIOPAC Systems, Inc.) module was used to connect the MP system to the computer running stimulus presentation programs to isolate digital inputs and outputs to and from the MP system. Disposable snap electrodes pre-gelled with isotonic gel (Model: EL507; BIOPAC Systems, Inc.) were affixed to the palm of the left hand (thenar and hypothenar eminence). The AcqKnowledgeTM (Model: 4.2; BIOPAC Systems, Inc.) software was used to record and offline analyze the electrodermal activity.

The SCR magnitude (in μS) for each CS was measured as the base-to-peak difference (i.e., amplitude) in the 500 ms–5 s time interval following the stimulus onset and normalized using square root transformation. Then the normalized SCR values for CSs were corrected by dividing each response by the participant's average US response. The value of 0.02 μS was used as the minimum response criterion (see Shiller et al., 2010). The dSCR (SCR to CS- subtracted from SCR to CS+) was the principal unit for calculating acquisition, extinction, and spontaneous recovery scores (see *Calculation of SCR Scores* in the OSM for details).

Arousal scale

As the second dependent variable, the spontaneous recovery of the fear responses was measured with the Self-Assessment Manikin (SAM) arousal scale (Lang, Bradley, & Cuthbert, 2005). The scale was particularly appropriate considering the significant relationship between arousal ratings and SCR (Lang et al., 1993). It consisted of five manikin pictures depicting different levels of arousal (see OSM Fig. 2), ranging from 1 (very low) to 5 (very high). The arousal scale was used by the participants in the last trial of the extinction

session and the first trial of the re-extinction session to indicate their feelings on seeing the CS+.

Procedure

Experimental sessions were conducted in two adjacent soundproof (experimental and control) rooms. Participants sat in front of a screen in the experimental room and received stimulus presentations (designed in SuperlabTM 4.5). Another computer in the control room recorded SCR data. Experimental sessions were videotaped to ensure that the participants followed the basic instructions (e.g., not moving their arms during the experimental session).

Before the first experimental session, the stimulator was set to the "ON" position, and an electrical stimulation electrode was attached to the participants' right inner wrist. The intensity of the electrical stimulation was adjusted to a level defined by each individual participant as "uncomfortable, but not painful." Participants were informed that this predetermined level of electrical stimulation would be delivered to their right inner wrist whenever required throughout experimental sessions. It is important to note that even if there was no electrical stimulation during the extinction and re-extinction stages, the electrical stimulation electrode remained attached, the electrical stimulator was set to the "ON" position, and the stimulation level was adjusted to the level previously decided by the participant. Disposable electrodes were placed on the palm of the left hand connected to the system to collect SCR data.

Participants were requested to sit still, attend to the computer screen and try to understand the association between the picture on the screen and the delivery of electrical stimulation. All experimental sessions began with a 5-min habituation period. Hence participants were expected to adapt to the experimental environment while electrodermal activity levels stabilized at baseline levels.

The reconsolidation update procedure (as described in Schiller et al., 2010) consisted of three consecutive phases: (1) acquisition, (2) extinction, and (3) re-extinction (see Fig. 1). Stimulus type (ecological vs. arbitrary), reconsolidation treatment prior to extinction (10 min, 6 h, no reminder), and retention interval prior to re-extinction (24 h, 15 d, 3 mo) were all between-group manipulations.

Acquisition

In the first phase, participants underwent a differential Pavlovian fear conditioning procedure in which the designated CS+ was paired with the electrical stimulation in 37.5% of CS+ trials, while CS- was always presented alone. Participants were assigned randomly to one of the two groups depending on stimulus type. For half the participants, the CSs were arbitrary (images of blue and yellow circles), and for the other half, ecological (snake and spider pictures). Within both stimulus type groups, the stimulus serving as a CS+ was counterbalanced, such that half of the participants saw one of the two stimuli within a stimulus category as CS+, and half saw the other. The acquisition phase contained 26 trials (presentations of 16 CS+ and ten CS- in pseudo-random order), of which six CS+ presentations were paired with shocks. Each CS was presented for 4 s followed by a 10- to 12-s variable ITI. The US was delivered during the last 200 ms of the CS+ presentation.

Extinction

Twenty-four hours after acquisition, participants from each stimulus type group were randomly divided into three reconsolidation treatment groups. A single CS+ presentation for 4 s without US served as the reminder in two of these groups for memory reactivation (reactivation groups). The first group received the extinction trials 10 min after the reminder (i.e., extinction within the reconsolidation window). During this 10-min break, participants remained seated in the experiment room and watched a video clip (from a TV show, Joy of Painting) and were reassured that they would not receive any electrical stimulation. The second group received extinction trials 6 h after the reminder (i.e., extinction outside the reconsolidation window). The third group did not receive a reminder cue and went through the extinction immediately (extinction without reminder). While the extinction phase contained 10 CS+ and 11 CS- presentations in reactivation groups, the no reminder group received 11 CS+ and 11 CS- presentations to keep the number of CS presentations equal across participants. All CSs were presented without US in a pseudorandom order for 4 s, followed by a 10- to 12-s variable ITI.

Re-extinction

Spontaneous recovery of conditioned responses after extinction was measured through the re-extinction process. The time interval between extinction and re-extinction was manipulated into three levels as a retention interval variable. Re-extinction took place 24 h, 15 d, or 3 mo after extinction. One-third of each reconsolidation treatment group was randomly assigned to one of these retention interval groups. This phase was the same as the extinction phase with no reminder condition, including 4-s presentations of 11 CS+ and 11 CS- without the US, and ITI was 10–12 s.

At the end of all experimental sessions, we checked with participants to ensure that electrical stimulation was correctly delivered during acquisition, and not delivered during extinction and re-extinction. They were also instructed to report which picture was seen on the screen during the stimulation.

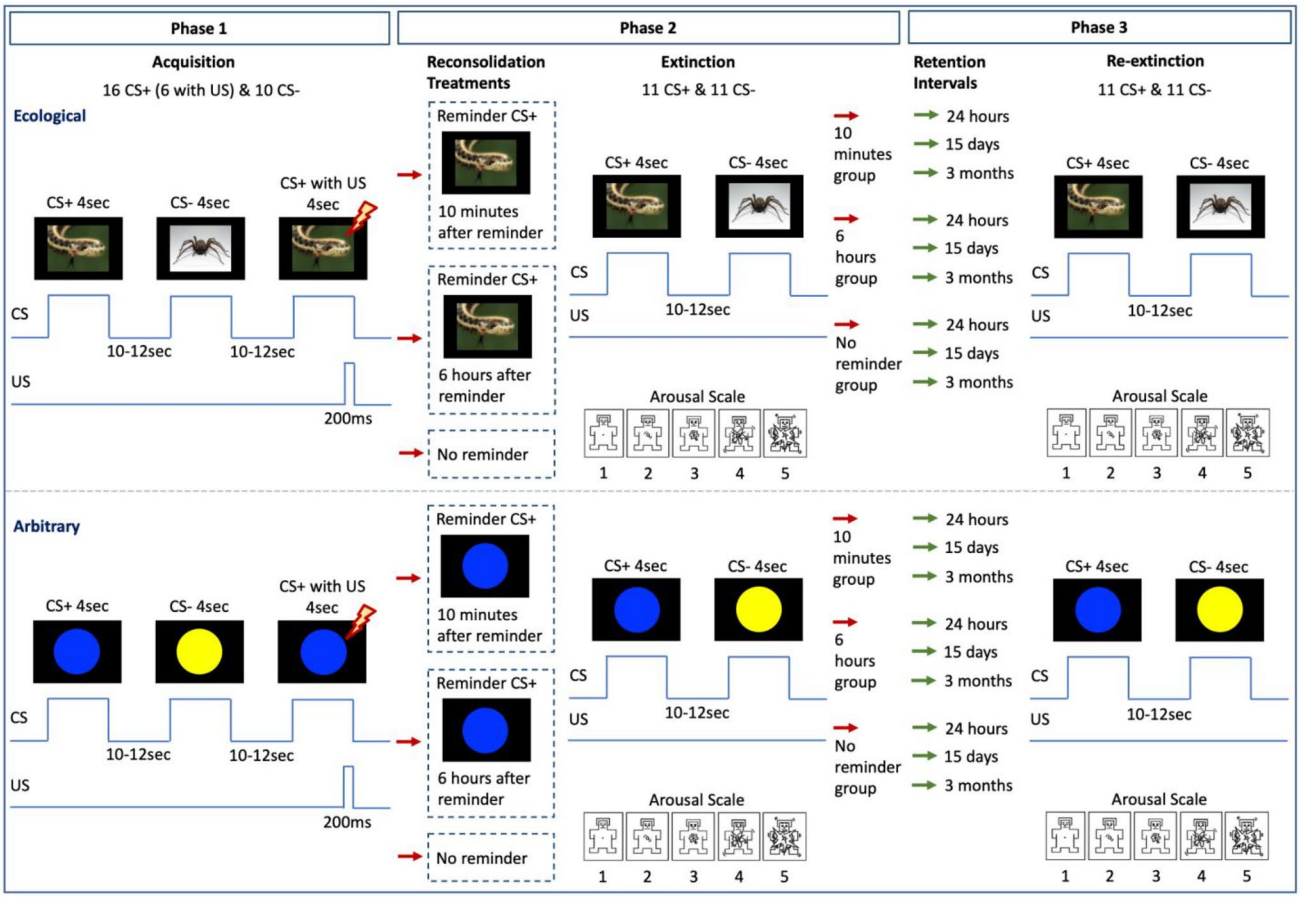

Fig. 1 Schema of experimental design. The study consisted of three phases. *Phase 1 (Acquisition)*: A discriminative fear conditioning procedure was employed. Ecological and arbitrary stimuli served as CS+ and CS- in a counterbalanced fashion. Each group received 26 trials (16 CS+ and 10 CS-, in a pseudo-random order). The participants received a brief wrist shock in six of 16 CS+ trials (37.5% of CS+ trials). *Phase 2 (Extinction)*: Participants underwent extinction training 24 h after the acquisition. In two groups, a single presentation of a 4-s CS+ served as a reminder of the fear association. However, one group received the reminder 10 min before the extinction trials, and the other, 6 h before. The remaining participants underwent extinction directly without the reminder trial. An arousal measurement was taken from all participants using the Arousal Scale of Self-Assessment Manikin immediately after the last CS+ presentation of the extinction procedure. *Phase 3 (Re-extinction)*: The extinction trials were repeated after different retention intervals: 24 h, 15 d, or 3 mo after the extinction phase. Arousal measurements were taken soon after the presentation of the first CS+. The SCRs were recorded across the phases as the main dependent measure. As an index of spontaneous recovery, difference scores of conditioned fear were calculated between the first trial of Phase 3 and the last trial of Phase 2

Results

Stimulus control

As stated at the outset, ecological (snake vs. spider) and arbitrary (yellow circle vs. blue circle) stimuli had served as CS+ and CS- in a counterbalanced fashion across the experimental phases. In order to control the counterbalance variable, first, we calculated the acquisition, extinction, and re-extinction scores, as described in Schiller et al. (2010) (see *Calculation of SCR Scores* in the OSM for details). Then we compared SCR differences elicited by ecological and arbitrary CSs separately, by running six independent t-tests in each stimulus category (i.e., snake vs. spider and yellow circle vs. blue circle) across the experimental phases.

We found that receiving snake or spider as CS+ in acquisition ($t(108) = .79$, $p > .05$), extinction ($t(108) = 1.07$, $p > .05$), and re-extinction ($t(108) = 1.02$, $p > .05$) or receiving blue or yellow circle as CS+ in acquisition ($t(107) = .92$, $p > .05$), extinction ($t(107) = 1.77$, $p > .05$), and re-extinction ($t(107) = .91$, $p > .05$) made no difference in dSCRs of the participants. Therefore, in subsequent analyses, all participants who received the snake or spider as CS+ were collapsed into a single ecological stimulus group, and all those who received blue or yellow circles, into a single arbitrary stimulus group.

Acquisition and extinction

To compare acquisition and extinction patterns across the trials for the reconsolidation treatment groups, we conducted two separate mixed ANOVAs, one for acquisition and one for extinction trials. In both analyses, the trial number was a within-subject factor, and stimulus type (ecological and arbitrary), reconsolidation treatment (10 min, 6 h, and no reminder), and retention interval (24 h, 15 d, and 3 mo) were between-group factors.

Figure 2 shows mean dSCRs throughout acquisition and extinction trials for reconsolidation treatment groups. Comparison of dSCRs during acquisition trials revealed a significant linearly increasing trend, $F(1, 201) = 188.83$, $p < .05$, partial $\eta^2 = .48$, indicating conditioned autonomic fear responses to CS+ increased as acquisition trials proceeded. Moreover, the observed increase was comparable between stimulus types ($F(1, 201) = .98$, $p > .05$), reconsolidation treatment groups ($F(2, 201) = 1.13$, $p > .05$), and retention intervals ($F(2, 201) = .24$, $p > .05$). Similar analyses for extinction showed that the linearly decreasing trend observed in dSCR over extinction trials was significant, $F(1, 201) = 40.36$, $p < .05$, partial $\eta^2 = .17$, with no significant difference between stimulus types ($F(1, 201) = 1.43$, $p > .05$), reconsolidation treatment groups ($F(2, 201) = .19$, $p > .05$), or retention intervals ($F(2, 201) = 2.66$, $p > .05$), indicating a similar pattern of decreasing differential conditioned autonomic fear responses towards the end of the extinction session among all experimental conditions. Supplementary analyses showed that the decrease observed in dSCR during extinction was result, not of generalization to CS-, but a decreased SCR to CS+ (as expected) both for ecological and arbitrary stimuli (for detail see Tables 3–4, and Figs. 3 and 4 under *Additional Analyses* in the OSM). These findings provided evidence that the acquisition and the extinction occurred in all groups regardless of the experimental conditions (i.e., stimulus type, reconsolidation treatment, and retention interval).

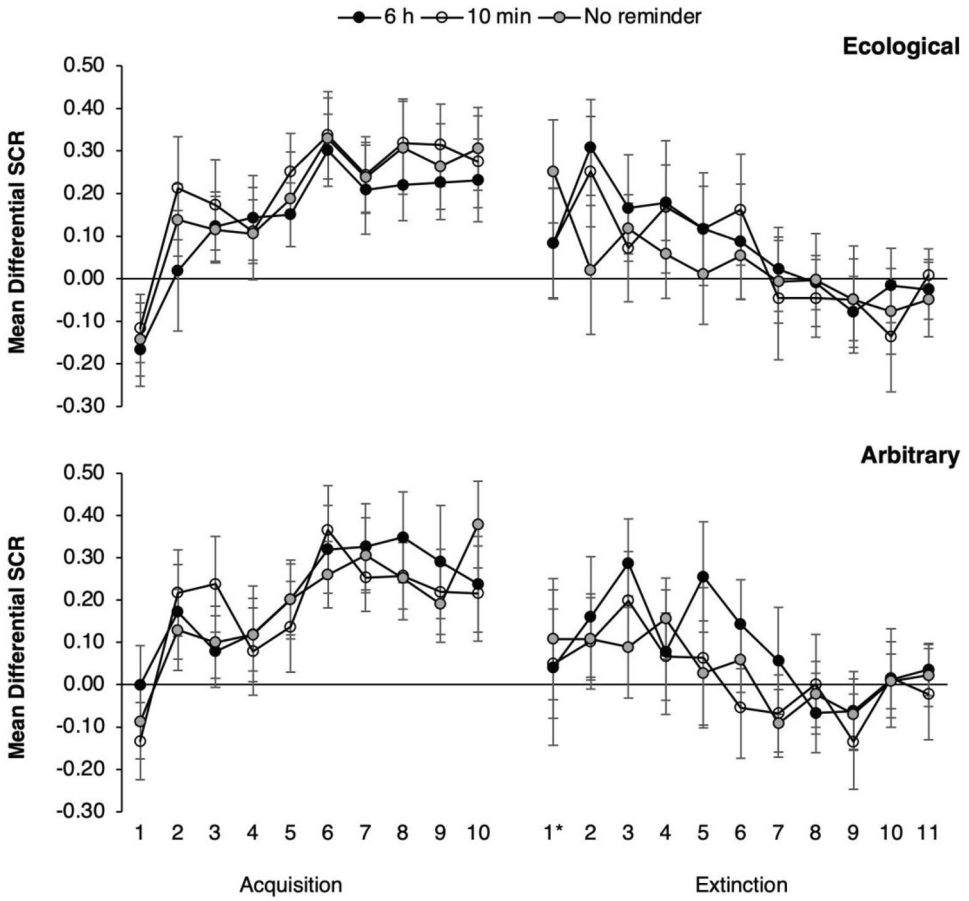

Fig. 2 Differential SCRs (CS+ minus CS-) for ecological (upper panel) and arbitrary (lower panel) stimuli during acquisition and extinction trials by reconsolidation treatment groups (10 min, 6 h, and no reminder). For all groups, extinction trials began with a CS+. For the reactivation groups (6 h and 10 min conditions), this CS+ presentation served as the reminder (1*), and the extinction trials were continued either 10 min or 6 h after the reminder. However, the no-reminder group underwent extinction directly with the CS+. Error bars represent SEM

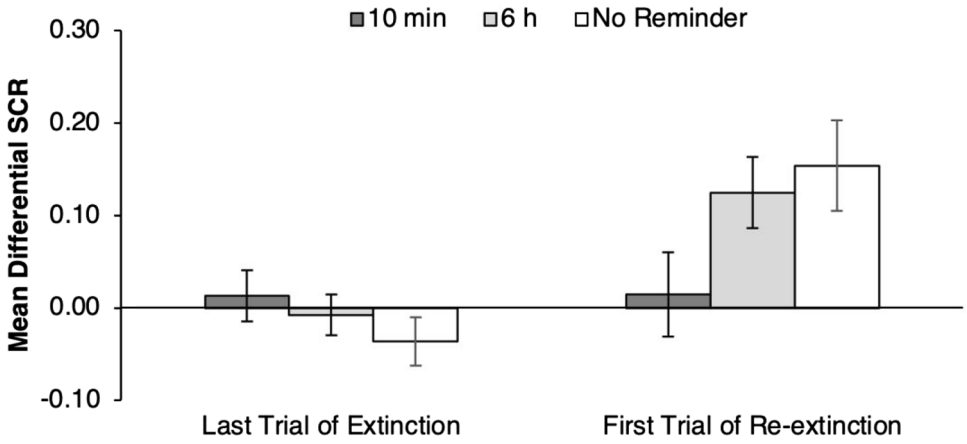

Fig. 3 The mean dSCRs (CS+ minus CS-) for the last trial of extinction and the first trial of re-extinction across reconsolidation treatment groups (10 min, 6 h, and no reminder). Error bars represent SEM

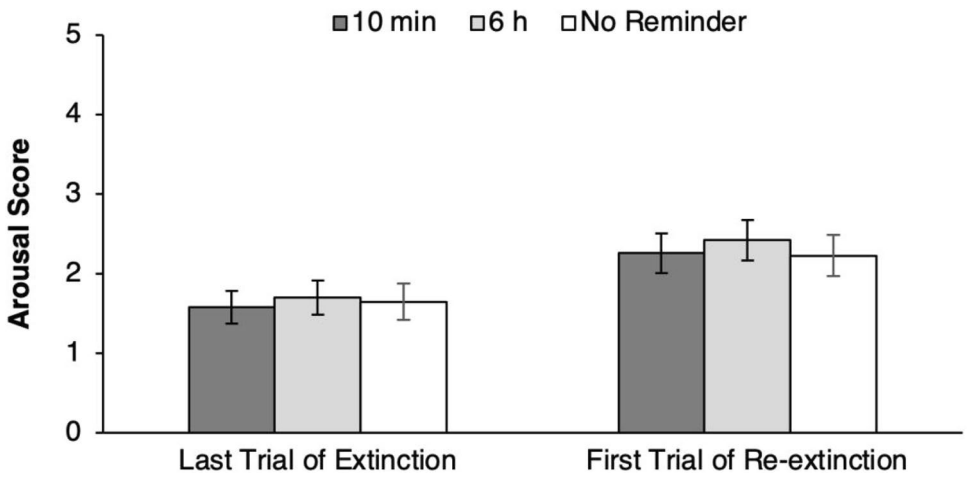

Fig. 4 Arousal levels of the participants for the last trial of extinction and the first trial of re-extinction across reconsolidation treatment groups (10 min, 6 h, and no reminder). Error bars represent SEM

Spontaneous recovery

Differential SCRs and arousal scores were analyzed utilizing a 2 (recovery: last trial of extinction and the first trial of re-extinction) × 2 (stimulus type: ecological and arbitrary) × 3 (reconsolidation treatment: 10 min, 6 h, and no reminder) × 3 (retention interval: 24 h, 15 d, and 3 mo) mixed ANOVA with "recovery" as within-subject factor. Follow-up comparisons were performed with separate two-tailed t-tests with Bonferroni adjusted alpha level of .017 per test (.05/3).

Differential SCRs

A comparison between the last trial of extinction (M = -.01, SEM = .02) and first trial of re-extinction (M = .10, SEM = .03) indicated a significantly higher dSCRs for the latter, suggesting a significant spontaneous recovery from fear, $F(1, 201) = 13.59$, $p < .001$, $\eta^2 = .06$. Importantly, this finding varied as a function of the reconsolidation treatment, $F(2, 201) = 3.74$, $p < .05$, $\eta^2 = .04$ (Fig. 3). Follow-up tests to investigate this interaction revealed that the difference between dSCRs for last trial of extinction and first trial of re-extinction was statistically significant both for the 6-h group ($t(70) = 3.51$, $p < .001$, $r = .39$) and no-reminder group ($t(71) = 3.48$, $p < .001$, $r = .38$). However, the dSCRs obtained in the first trial of re-extinction did not differ from the last trial of extinction in the 10-min group ($t(75) = .03$, $p > .05$), and while the participants in both the 6-h group and no-reminder group showed recovery from fear, the participants in 10-min group showed none. This interaction was affected neither by the stimulus type ($F(2, 201) = .53$, $p > .05$), nor the retention interval ($F(4, 201) = .53$, $p > .05$).

There was no statistical significance in the main effects of stimulus type ($F(1, 201) = .25$, $p > .05$), reconsolidation treatment ($F(2, 201) = 1.10$, $p > .05$), retention interval ($F(2, 201) = .11$, $p > .05$), and stimulus type × reconsolidation treatment ($F(2, 201) = 1.30$, $p > .05$), reconsolidation treatment × retention interval ($F(4, 201) = 1.05$, $p > .05$), stimulus type × retention interval ($F(2, 201) = 1.04$, $p > .05$), recovery × stimulus type ($F(1, 201) = 2.19$, $p > .05$), recovery × retention interval ($F(2, 201) = .33$, $p > .05$), stimulus type × reconsolidation treatment × retention interval ($F(4, 201) = 1.23$, $p > .05$), recovery × stimulus type × retention interval ($F(2, 201) = .83$, $p > .05$), recovery x stimulus type × reconsolidation treatment x retention interval ($F(4, 201) = .83$, $p > .05$) interactions (see Table 5 in the OSM for mean and standard deviation values in last trial of extinction and first trial of re-extinction by stimulus type, reconsolidation treatment, and retention interval).

Arousal scores

The comparison of the arousal scores obtained in the last trial of extinction ($M = 1.64$, $SEM = .06$) and the first trial of re-extinction ($M = 2.24$, $SEM = .08$) revealed a significant spontaneous recovery from fear, $F(1, 201) = 48.01$, $p < .05$, $\eta^2 = .19$ (Fig. 4). However, this recovery did not vary according to stimulus type ($F(1, 201) = .24$, $p > .05$), reconsolidation treatment ($F(2, 201) = 1.47$, $p > .05$), or retention interval ($F(2, 201) = 2.94$, $p > .05$).

There was no statistical significance in the main effects of stimulus type ($F(1, 201) = .21$, $p > .05$), reconsolidation treatment ($F(2, 201) = 1.48$, $p > .05$), retention interval ($F(2, 201) = .29$, $p > .05$) and stimulus type × reconsolidation treatment ($F(2, 201) = .41$, $p > .05$), reconsolidation treatment × retention interval ($F(4, 201) = 1.02$, $p > .05$), stimulus type × retention interval ($F(2, 201) = .95$, $p > .05$), stimulus type × reconsolidation treatment × retention interval ($F(4, 201) = .31$, $p > .05$), recovery × stimulus type × reconsolidation treatment ($F(2, 201) = .94$, $p > .05$), recovery × reconsolidation treatment × retention interval ($F(4, 201) = 1.26$, $p > .05$), recovery × stimulus type × retention interval ($F(2, 201) = 2.48$, $p > .05$), and recovery × stimulus type × reconsolidation treatment × retention interval ($F(4, 201) = 2.42$, $p > .05$) interactions (see Table 6 in the OSM for mean and standard deviation values in the last trial of extinction and first trial of re-extinction by stimulus type, reconsolidation treatment, and retention interval).

The mean dSCRs obtained during acquisition, extinction, and re-extinction trials by stimulus type (ecological and arbitrary), reconsolidation treatment (10 min, 6 h, and no reminder), and retention interval (24 h, 15 d, and 3 mo) were presented in the OSM (see OSM Fig. 5 for acquisition trials, OSM Fig. 6 for extinction trials, and OSM Fig. 7 for re-extinction trials).

Discussion

The present study aimed to investigate the effects of the reconsolidation treatment, stimulus type, and the retention interval on the recovery of extinguished conditioned fear in human participants. Our findings provided further evidence for the efficacy of the PRE approach (Monfils et al., 2009; Schiller et al., 2010), which proposes that acquired associations are not permanent, but rather, are labile when activated (for review, Sara, 2000).

The robustness of the PRE effect is much influenced by the success of acquisition and extinction attained in the fear conditioning procedures (Steinfurth et al., 2014), and thus the associative strength obtained. Animal studies of PRE have already demonstrated the interfering effects of the associative strength on the PRE (Chen et al., 2021; Suzuki et al., 2004; Wang et al., 2009; Winters et al., 2009). Laboratory preparations of human PRE provide a valuable opportunity for controlling the strength of fear associations as the boundary conditions relevant to the acquisition and extinction. The asymptotic associative level supported by the conditioned stimulus during the acquisition phase of PRE studies will affect subsequent extinction and re-extinction performance, thus the recovery levels. In this respect, the differential effects of the variables on acquisition, extinction, and re-extinction may be confounding in the recovery of extinction. Thus, the present study obtained similar patterns of acquisition and extinction regardless of the experimental condition, even though the reconsolidation manipulation resulted in significant spontaneous recovery differences in favor of the group undergoing extinction trials 10 min after the reminder. The similar acquisition and extinction patterns across the experimental phases suggested that the observed lack of the recovery of fear evidenced in the 10 min group should be attributed to the PRE.

The reinforcement schedules utilized during acquisition may affect the vigor of behavioral and emotional effects of an extinction (Domjan, 2018). According to a well-exploited notion, a CS that is paired intermittently with a US will show greater resistance to extinction compared to one that is continuously paired (e.g., Fitzgerald, 1963; Gibbon et al., 1980; Gibbs et al., 1978; Grady et al., 2016; Ishida & Papini, 1997; Pearce et al., 1997; Slivka & Bitterman, 1966). In other words, extinction will progress more rapidly after partial compared to continuous reinforcement (Bouton, 2014; Horsley et al., 2012; Maren & Holmes, 2016; Rescorla, 1999; Todd et al., 2014). This classic phenomenon is known as the partial reinforcement extinction effect (PREE), implying that more robust learning occurs under partial reinforcements compared to under continuous reinforcements.

Although we used a partial reinforcement schedule (i.e., 37.5% of the CS+ were paired with the wrist-shock US)

during fear acquisition, we obtained acquisition patterns with discernible asymptotes reflecting the strength of the fear association. Thus, the partial reinforcement schedule we used in fear acquisition trials should be an appropriate procedure for producing a reasonably strong fear memory. In addition, extinction effects were evident by the significant decreases in dSCRs elicited by the CS+ for all groups. As the extinction trials progressed, the SCRs differences produced by the CS+ and the CS- approached zero, yielding the typical extinction curves. In addition, in a recent review, Zuccolo and Hunziker (2019) concluded that there was no clear relation between the number of CS-US pairings and fear reduction after PRE.

One of our dependent variables was related to SCRs, which are the measures of the changes in autonomic fear responses produced by the central nucleus of the amygdala. Therefore, our findings are potentially compatible with the previous neurobiological studies on the involvement of amygdaloid structures in the update of the fear associations through the interventions of the reconsolidation process (e.g., Agren et al., 2012). For all three groups of the reconsolidation treatment, a single presentation of the reminder CS+ set the stage for the subsequent inhibitory response to the CS+. This was presumably achieved by the CS+, creating a prediction error and subsequent destabilization in the amygdaloid structures of the acquired association of fear (Chan et al., 2010; Craske et al., 2014; Myers & Davis, 2007). Moreover, the re-extinction tests revealed an enhanced extinction only in the group that had taken the extinction trials within the reconsolidation window (i.e., 10 min after the reminder), and this effect lasted at least three months. Therefore, this piece of evidence provided support for the notion that fear memories maintained by the CS+-US excitatory association could be updated with the memory of inhibitory association (CS+-noUS) formed during the reconsolidation window (Lee et al., 2017; Monfils et al., 2009; Schiller et al., 2010).

On the other hand, we found that regardless of whether or not the extinction trials had taken place in the reconsolidation window, the participants showed a significant spontaneous recovery in their self-reported fear-related arousal measures. The self-reported arousal levels generally rely on the participant's explicit knowledge about the CS-US contingency. Thus, this finding is consistent with the analysis that reconsolidation update procedures of fear memories target only fear associations stored in the amygdala, leaving intact explicit knowledge of the CS-US contingency stored in the hippocampus (Agren et al., 2012a; Bechara et al., 1995; Phelps et al., 2001; Schiller et al., 2013), which in turn results in a discrepancy between the autonomic and self-report measures.

We obtained typical acquisition and extinction patterns of dSCRs with both ecological and arbitrary stimuli. In addition, contrary to our predictions, we found no significant difference between the differential electrodermal responses to ecological and arbitrary CS pairs during spontaneous recovery. The ecological and arbitrary conditioned fear stimuli elicited similar levels of differential autonomic fear responses both in the acquisition and extinction phases. Although these findings replicate several previous works with null ecological-arbitrary stimuli differences on the PRE (e.g., (Björkstrand et al., 2015, 2016; Golkar et al., 2012; Thompson & Lipp, 2017), many others reported difficulties in replicating the findings from Schiller et al., (2010) with fear-relevant-ecological stimuli such as the images of spiders, snakes, tigers, dogs, or frightening male faces (Fricchione et al., 2016; Golkar et al., 2012; Kindt & Soeter, 2013; Meir Drexler et al., 2014; Soeter & Kindt, 2011). Various hypotheses have been proposed to elucidate these failures. For example, according to Mineka and Öhman (2002), the acquisition trials with ecological-fear-related stimuli may have led to relatively stronger conditioned fear. Indeed, this is a plausible idea that should be tested. However, it seems circular to suggest that ecological-fear-related stimuli are more resistant to extinction (Zuccolo & Hunziker, 2019) to explain this "strong fear hypothesis". In addition, as well as the present study, many empirical attempts for testing the PRE include only participants who passed the extinction phase successfully (Golkar et al., 2012; Liu et al., 2014; Oyarzún et al., 2012; Schiller et al., 2013, 2010; Steinfurth et al., 2014). It is interesting that Golkar et al. (2012) were unable to replicate the PRE effect with either ecological-fear-relevant stimuli or the arbitrary, suggesting that PRE might work on both types. Lastly, we would be in a better position to understand these failures and offer better solutions had previous works obtained measurements of the levels of autonomic arousal that these two types of stimuli elicit before beginning laboratory acquisition experiments.

It is crucial to measure the associative strengths of the different CSs serving in the various experimental conditions of a PRE study. Without integrating such a procedure into the PRE paradigm, it becomes challenging to identify which parameter or process was responsible for the observed conditioning effects. In this regard, the current study incorporated a preliminary study conducted on a separate sample to determine the base levels of autonomic arousal elicited by the ecological (images of a spider and a snake) and the arbitrary (images of the yellow and blue circle) before the introduction of acquisition trials, which allowed the selection of ecological and arbitrary stimuli with comparable levels of SCR. Spider and snake pictures were determined as the ecological stimuli because of their inherent relevance to the danger and fear, and because they have become a “standard” in fear studies.

Another source of variation between the PRE studies often pertains to the participant variables, such as genetic,

demographic, or psychiatric status. For example, compared to non-fearful normal participants, stronger conditioned responses and resistance to extinction were shown in spider-fearful participants by Mertens et al. (2019), and in individuals with anxiety disorders by Lissek et al. (2005). We therefore deliberately excluded individuals with such tendencies, disorders, and experiences of fear in our study sample, as well as individuals who failed to fulfill acquisition and extinction criteria.

The present study also investigated the longevity of the PRE effect in the prevention of acquired fear responses. We performed three consecutive spontaneous recovery tests (24 h, 15 d, and 6 mo after the re-extinction). The data did not indicate any significant change in dSCRs across these retention intervals. Thus, the findings seem to provide further evidence that the PRE taking place during the reconsolidation of the fear memory (10 min after the reminder) may have long-lasting fear reduction (Schiller et al., 2010). However, we tend to interpret this finding more cautiously. An alternative analysis would go as follows: the positive PRE effect was observed for the first time in the re-extinction phase, and spontaneous recovery levels were measured in subsequent retention tests by presenting the CSs alone. During which, CSs were never paired with the US-shock. Therefore, the long-term positive PRE effect observed can also be explained by an inhibitory CSs-context association that might have developed across the retention tests (Bouton, 2002). We hope future research may shed light on this issue.

Although this study provided evidence for the efficacy of PRE with both ecological and arbitrary stimuli, it is worth mentioning three important issues regarding the stimulus type variable. First, the PRE paradigm produces more robust results in animal studies than in human studies (Kredlow et al., 2016). One possible reason for these observations may be the differences between these species in terms of the mismatch between their evolutionary dispositions and their contemporary ecology. In their ecological niche, compared to their animal peers, humans are exposed to a much higher frequency audio-visual instances (CSs) of ecological fear-related stimuli (e.g., snake pictures or videos); however, these CSs are very rarely paired with the aversive US. According to the World Health Organization (WHO), the number of snake-encounter occurrences per annum per person is only 0.0002% (WHO, 2021). Therefore, there are many more opportunities for humans to deal with the fear of snakes. Perhaps the inconclusive results of previous human PRE studies using images of snakes and spiders as CSs could be explained by human exposure to a significantly greater number of CS-noUS associations. Through audio-visual media and social interactions, people frequently encounter images of dangerous animals in everyday life. However, the same cannot be said for other animals in their current ecology. The number of "safe" pre-experimental encounters a laboratory rat experiences with these dangerous animals is almost zero. Therefore, the frequency of people's exposure to images of dangerous animals without a subsequent danger might weaken the strength of the fear association. Second, describing CS dichotomously as fear-relevant and fear-irrelevant may have serious drawbacks. For example, previous studies seem to rely on the assumption that the images of snakes and spiders are invariably fear-related. However, the present study has shown that there may be little difference between pictures of snakes and yellow circles in terms of the levels of autonomic arousal they elicit, leaving the inherent relation of snake-venomous bite intact. Finally, since it is problematic to consider CSs dichotomously, it is crucial to quantify fear-related stimuli in terms of their predictive values before any conditioning is taken into effect. Although various authors addressed the importance of the measurement of memory strength (Wang et al., 2009) and conditioning strength (Golkar et al., 2012; Suzuki et al., 2004; Wang et al., 2009), both seemed to be greatly correlated to the base level of fear responses to the CS of interest in PRE studies.

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Data Availability The data and materials used in the experiment are available from the corresponding author upon request.

Declarations

Conflict of Interest The authors have no financial or nonfinancial interests to disclose.

Ethics Approval This study was approved by the Institutional Review Board of the Izmir University of Economics.

Consent to Participate Informed consent was obtained from all individual participants included in the study.

References

Agren, T., Engman, J., Frick, A., Björkstrand, J., Larsson, E. M., Furmark, T., & Fredrikson, M. (2012a). Disruption of reconsolidation erases a fear memory trace in the human amygdala. *Science, 337*, 1150–1552.

Agren, T., Furmark, T., Eriksson, E., & Fredrikson, M. (2012b). Human fear reconsolidation and allelic differences in serotonergic and dopaminergic genes. *Translational Psychiatry, 2*(2), e76–e76.

Asthana, M. K., Brunhuber, B., Mühlberger, A., Reif, A., Schneider, S., & Herrmann, M. J. (2015). Preventing the return of fear using reconsolidation update mechanisms depends on the met-allele of the brain derived neurotrophic factor Val66Met polymorphism.

International Journal of Neuropsychopharmacology. https://doi.org/10.1093/ijnp/pyv137

Auber, A., Tedesco, V., Jones, C. E., Monfils, M. H., & Chiamulera, C. (2013). Post-retrieval extinction as reconsolidation interference: Methodological issues or boundary conditions? *Psychopharmacology, 226*(*4*), 631–647.

Auchter, A., Shumake, J., Gonzalez-Lima, F., et al. (2017). Preventing the return of fear using reconsolidation updating and methylene blue is differentially dependent on extinction learning. *Scientific Reports, 7*, 46071. https://doi.org/10.1038/srep46071

Bandarian Balooch, S., & Neumann, D. L. (2011). Effects of multiple contexts and context similarity on the renewal of extinguished conditioned behavior in an ABA design with humans. *Learning and Motivation, 42*, 53–63. https://doi.org/10.1016/j.lmot.2010.08.008

Bechara, A., Tranel, D., Damasio, H., Adolphs, R., Rockland, C., & Damasio, A. R. (1995). Double dissociation of conditioning and declarative knowledge relative to the amygdala and hippocampus in humans. *Science, 269*, 1115–1118.

Björkstrand, J., Agren, T., Åhs, F., Frick, A., Larsson, E.-M., Hjorth, O., Furmark, T., & Fredrikson, M. (2016). Disrupting reconsolidation attenuates long-term fear memory in the human amygdala and facilitates approach behavior. *Current Biology, 26*, 2690–2695. https://doi.org/10.1016/j.cub.2016.08.022

Björkstrand, J., Agren, T., Frick, A., Engman, J., Larsson, E. M., Furmark, T., & Fredrikson, M. (2015). Disruption of memory reconsolidation erases a fear memory trace in the human amygdala: An 18-month follow up. *PloS One., 10*, e0129393.

Bouton, M. E. (1988). Context and ambiguity in the extinction of emotional learning: Implications for exposure therapy. *Behavior Research and Therapy, 26*(*2*), 137–149.

Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin, 114*, 80–99. https://doi.org/10.1037/0033-2909.114.1.80

Bouton, M. E. (2002). Context, ambiguity, and unlearning: sources of relapse after behavioral extinction. *Biological Psychiatry, 52*, 976–986. https://doi.org/10.1016/S0006-3223(02)01546-9

Bouton, M. E. (2014). Why behavior change is difficult to sustain. *Preventive Medicine, 68*, 29–36. https://doi.org/10.1016/j.ypmed.2014.06.010

Bouton, M. E., & Woods, A. M. (2008). Extinction: Behavioral mechanisms and their implications. In J. H. Byrne (Ed.), *Learning theory and behavior*, *Learning and memory: A comprehensive reference* (Vol. *1*, pp. 151–172). Elsevier.

Çetinkaya, H. (2018). Naturalistic stimuli. In J. Vonk, T. Shackelford (Eds.), *Encyclopedia of animal cognition and behavior*. Springer. https://doi.org/10.1007/978-3-319-47829-6_2019-1

Chan, W. Y., Leung, H. T., Westbrook, R. F., & McNally, G. P. (2010). Effects of recent exposure to a conditioned stimulus on extinction of Pavlovian fear conditioning. *Learning and Memory. 30, 17*(10), 512-21. https://doi.org/10.1101/lm.1912510

Chen, W., Li, J., Xu, L., Zhao, S., Fan, M., & Zheng, X. (2021). Destabilizing different strengths of fear memories requires different degrees of prediction error during retrieval. *Frontiers in Behavioral Neuroscience, 14*, 598924. https://doi.org/10.3389/fnbeh.2020.598924

Chen, Y., Lin, X., Ai, S., Sun, Y., Shi, L., Meng, S., Lu, L., & Shi, J. (2022). Comparing three extinction methods to reduce fear expression and generalization. *Behavioural Brain Research, 420*, 113714.

Cook, M., & Mineka, S. (1987). Second-order conditioning and overshadowing in the observational conditioning of fear in monkeys. *Behaviour Research and Therapy, 25*(5), 349–364. https://doi.org/10.1016/0005-7967(87)90013-1

Craske, M. G., Hermans, D., & Vervliet, B. (2018). State-of-the-art and future directions for extinction as a translational model for fear and anxiety. *Philosophical Transactions of the Royal Society B, 373*, 20170025. https://doi.org/10.1098/rstb.2017.0025

Craske, M. G., Treanor, M., Conway, C. C., Zbozinek, T., & Vervliet, B. (2014). Maximizing exposure therapy: an inhibitory learning approach. *Behaviour Research and Therapy, 58*, 10–23.

Cusato, B., & Domjan, M. (1998). Special efficacy of sexual conditioned stimuli that include species typical cues: Tests with a conditioned stimuli preexposure design. *Learning and Motivation, 29*(2), 152–167. https://doi.org/https://doi.org/10.1006/lmot.1997.0988

Delamater, A. R. (2004). Experimental extinction in Pavlovian conditioning: Behavioural and neuroscience perspectives. *Quarterly Journal of Experimental Psychology, 57*, 97–132.

Delgado, M. R., Olsson, A., & Phelps, E. A. (2006). Extending animal models of fear conditioning to humans. *Biological Psychology, 73*, 39–48.

Dirikx, T., Hermans, D., Vansteenwegen, D., Baeyens, F., & Eelen, P. (2004). Reinstatement of extinguished conditioned responses and negative stimulus valence as a pathway to return of fear in humans. *Learning & Memory, 11*(*5*), 549–554.

Domjan, M. (1994). Formulation of a behavior system for sexual conditioning. *Psychonomic bulletin & review, 1*, 421–428. https://doi.org/10.3758/BF03210946

Domjan, M. (2000). General process learning theory: Challenges from response and stimulus factors. *International Journal of Comparative Psychology, 13*, 101–118.

Domjan, M. (2005). Pavlovian conditioning: A functional perspective. *Annual Review of Psychology, 56*, 179–206.

Domjan, M. (2008). Adaptive specializations and generality of the laws of classical and instrumental conditioning. In J. Byrne (Ed.) *Learning and Memory: A comprehensive reference*. (Vol. 1, *Learning and Behavior Theory*, R. Menzel, Ed., pp. 327-340.) Oxford: Elsevier. https://doi.org/10.1016/B978-0123705090-9.00183-2

Domjan, M. (2018). *The essentials of conditioning and learning*. American Psychological Association.

Domjan, M., & Galef, B. G. (1983). Biological constraints on instrumental and classical conditioning: Retrospect and prospect. *Animal Learning & Behavior, 11*, 151–161.

Domjan, M., & Krause, M. (2017). Generality of the laws of learning: From biological constraints to ecological perspectives. In J. Byrne (Ed.), *Learning and Memory: A Comprehensive Reference* (Second ed., pp. 189–201). Academic Press.

Domjan, M., Akins, C., & Vandergriff, D. H. (1992). Increased responding to female stimuli as a result of sexual experience: Tests of mechanisms of learning. *The Quarterly Journal of Experimental Psychology B: Comparative and Physiological Psychology, 45B*(2), 139–157. https://doi.org/https://doi.org/10.1080/14640749208401014.

Domjan, M., Cusat, B., & Krause, M. (2004). Learning with arbitrary versus ecological conditioned stimuli: Evidence from sexual conditioning. *Psychonomic Bulletin & Review, 11*(2), 232–246.

Fanselow, M. S., & Lester, L. S. (1988). A functional behavioristic approach to aversively motivated behavior: Predatory imminence as a determinant of the topography of defensive behavior. In R. C. Bolles & M. D. Beecher (Eds.), *Evolution and Behavior* (pp. 185–212). Erlbaum.

Fendt, M., & Fanselow, M. S. (1999). The neuroanatomical and neurochemical basis of conditioned fear. *Neuroscience and Biobehavioral Reviews, 23*, 743–760.

Field, A. P. (2006). Is conditioning a useful framework for understanding the development and treatment of phobias. *Clinical Psychology Review, 26*, 857–875.

Finnie, P. S., & Nader, K. (2012). The role of metaplasticity mechanisms in regulating memory destabilization and

reconsolidation. *Neuroscience Biobehavior Review, 36*(7), 1667–1707. https://doi.org/10.1016/j.neubiorev.2012.03.008

Fitzgerald, P. J., Seemann, J. R., & Maren, S. (2014). Can fear extinction be enhanced? a review of pharmacological and behavioral findings. *Brain Research Bulletin, 105*, 46–60.

Fitzgerald, R. D. (1963). Effects of partial reinforcement with acid on the classically conditioned salivary response in dogs. *Journal of Comparative and Physiological Psychology, 56*, 1056–1060.

Flavell, C. R., & Lee, J. L. (2011). Behavioural memory reconsolidation of food and fear memories. *Nature Communications, 2*, 504.

Fricchione, J., Greenberg, M. S., Spring, J., Wood, N., Mueller-Pfeiffer, C., Milad, M. R., Pitman, R. K., & Orr, S. P. (2016). Delayed extinction fails to reduce skin conductance reactivity to fear-conditioned stimuli: Delayed extinction fails to reduce reactivity. *Psychophysiology, 53*, 1343–1351. https://doi.org/10.1111/psyp.12687

Garcia, J., Hankins, W. G., & Rusiniak, K. W. (1974). Behavioral regulation of the milieu interne in man and rat. *Science, 185*, 824–831.

Gibbon, J., Farrell, L., Locurto, C. M., Duncan, H. J., & Terrace, H. S. (1980). Partial reinforcement in autoshaping with pigeons. *Animal Learning and Behavior, 8*, 45–59.

Gibbs, C. M., Latham, S. B., & Gormezano, I. (1978). Classical conditioning of the rabbit nictitating membrane response: Effects of reinforcement schedule on response maintenance and resistance to extinction. *Animal Learning and Behavior, 6*, 209–215.

Gisquet-Verrier, P., & Riccio, D. (2012). Memory reactivation effects independent of reconsolidation. *Learning and Memory, 19*, 401–409.

Golkar, A., Bellander, M., Olsson, A., & Öhman, A. (2012). Are fear memories erasable? Reconsolidation of learned fear with fear-relevant and fear-irrelevant stimuli. *Frontiers in Behavioral Neuroscience, 6*, 1–10.

Grady, A. K., Bowen, K. H., Hyde, A. T., Totsch, S. K., & Knight, D. C. (2016). Effect of continuous and partial reinforcement on the acquisition and extinction of human conditioned fear. *Behavioral Neuroscience, 130(1)*, 36.

Hilliard, S., Domjan, M., Nguyen, M., et al. (1998). Dissociation of conditioned appetitive and consummatory sexual behavior: Satiation and extinction tests. *Animal Learning & Behavior, 26*, 20–33. https://doi.org/10.3758/BF03199159

Hoehl, S., Hellmer, K., Johansson, M., & Gredebäck, G. (2017). Itsy bitsy spider…: Infants react with increased arousal to spiders and snakes. *Frontiers in Psychology*. https://doi.org/10.3389/fpsyg.2017.01710

Hollis, K. L. (1982). Pavlovian conditioning of signal-centered action patterns and autonomic behavior: a biological analysis of function. *Advances in the Study of Behavior, 12*, 1–64.

Hollis, K. L. (1997). Contemporary research on Pavlovian conditioning: a "new" functional analysis. *American Psychologist, 52*, 956–965.

Horsley, R. R., Osborne, M., Norman, C., & Wells, T. (2012). High frequency gamblers show increased resistance to extinction following partial reinforcement. *Behavioural Brain Research, 229*, 438–442. https://doi.org/10.1016/j.bbr.2012.01.024

Hugdahl, K., & Jonsen, B. H. (1988). Preparedness and electrodermal fear-conditioning: Ontogenetic vs phylogenetic explanations. *Behaviour Research and Therapy, 27*(3), 269–278.

Ishida, M., & Papini, M. R. (1997). Massed-trial overtraining effects on extinction and reversal performance in turtles (*Geoclemys reevesii*). *The Quarterly Journal of Experimental Psychology B: Comparative and Physiological Psychology, 50B*(1), 1–16.

Johnson, D. C., & Casey, B. J. (2015). Extinction during memory reconsolidation blocks recovery of fear in adolescents. *Scientific Reports, 5*, 8863. https://doi.org/10.1038/srep08863

Jones, C. E., & Monfils, M. H. (2016). Post-retrieval extinction in adolescence prevents return of juvenile fear. *Learning & Memory, 23*, 567–575.

Keller, N. E., & Dunsmoor, J. E. (2020). The effects of aversive-to-appetitive counterconditioning on implicit and explicit fear memory. *Learning and Memory, 27*, 12–19.

Kindt, M., & Soeter, M. (2013). Reconsolidation in a human fear conditioning study: A test of extinction as updating mechanism. *Biological Psychology, 92(1)*, 43–50.

Kindt, M., Soeter, M., & Vervliet, B. (2009). Beyond extinction: Erasing human fear responses and preventing the return of fear. *Nature Neuroscience, 12(3)*, 256–258.

Klucken, T., Kruse, O., Schweckendiek, J., Kuepper, Y., Mueller, E. M., Hennig, J., & Stark, R. (2016). No evidence for blocking the return of fear by disrupting reconsolidation prior to extinction learning. *Cortex, 79*, 112–122. https://doi.org/10.1016/j.cortex.2016.03.015

Köksal, F., Domjan, M., & Weisman, G. (1994). Blocking of the sexual condiyioning of differentially effective conditioned-stimulus objects. *Animal Learning and Behavior*. https://doi.org/10.3758/BF03199962

Krause, M. A., Cusato, B., & Domjan, M. (2003). Extinction of conditioned sexual responses in male Japanese quail (Coturnix japonica): role of species-typical cues. *Journal of Comparative Psychology, 117*(1), 76–86. https://doi.org/https://doi.org/10.1037/0735-7036.117.1.76

Kredlow, M. A., Unger, L. D., & Otto, M. W. (2016). Harnessing reconsolidation to weaken fear and appetitive memories: A meta-analysis of post-retrieval extinction effects. *Psychological Bulletin, 142*(3), 314–336. https://doi.org/10.1037/bul0000034

Laborda, M. A., & Miller, R. R. (2012). Reactivated memories compete for expression after Pavlovian extinction. *Behavioural Processes, 90*, 20–27. https://doi.org/10.1016/j.beproc.2012.01.012

Laborda, M. A., & Miller, R. R. (2013). Preventing return of fear in an animal model of anxiety: additive effects of massive extinction and extinction in multiple contexts. *Behavior Therapy, 44*, 249–261.

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2005). *International affective picture System (IAPS): affective ratings of pictures and instruction manual*, *Technical Report A-5*. University of Florida.

Lang, P. J., Greenwald, M. K., Bradley, M. M., & Hamm, A. O. (1993). Looking at pictures: Affective, facial, visceral, and behavioral reactions. *Psychophysiology, 30*, 261–273. https://doi.org/10.1111/j.1469-8986.1993.tb03352.x

Lee, J. L. C., Nader, K., & Schiller, D. (2017). An update on memory reconsolidation updating. *Trends in Cognitive Sciences, 21*(7), 531–545. https://doi.org/10.1016/j.tics.2017.04.006

Leung, H. T., Reeks, L. M., & Westbrook, R. F. (2012). Two ways to deepen extinction and the difference between them. *Journal of Experimental Psychology. Animal Behavior Processes, 38*, 394–406.

Leung, H. T., Bailey, G. K., Laurent, V., & Westbrook, R. F. (2007). Rapid reacquisition of fear to a completely extinguished context is replaced by transient impairment with additional extinction training. *Journal of Experimental Psychology: Animal Behavior Processes, 33*, 299–313. https://doi.org/10.1037/0097-7403.33.3.299

Lissek, S., Powers, A. S., McClure, E. B., Phelps, E. A., Woldehawariat, G., Grillon, C., & Pine, D. S. (2005). Classical fear conditioning in the anxiety disorders: a meta-analysis. *Behaviour Research and Therapy, 43*, 1391–1424. https://doi.org/10.1016/j.brat.2004.10.007

Liu, J., Zhao, L., Xue, Y., Shi, J., Suo, L., Luo, Y., Chai, B., Yang, C., Fang, Q., Zhang, Y., Bao, Y., Pickens, C. L., & Lu, L. (2014). An unconditioned stimulus retrieval extinction procedure to prevent

the return of fear memory. *Biological Psychiatry, 76*, 895–901. https://doi.org/10.1016/j.biopsych.2014.03.027

Maren, S., & Holmes, A. (2016). Stress and fear extinction. *Neuropsychopharmacology, 41*, 58–79. https://doi.org/10.1038/npp.2015.180

McNally, R. J. (1987). Preparedness and phobias: A review. *Psychological Bulletin, 101*, 283–303.

Meir Drexler, S., Merz, C. J., Hamacher-Dang, T. C., Marquardt, V., Fritsch, N., Otto, T., & Wolf, O. T. (2014). Effects of post retrieval-extinction learning on return of contextually controlled cued fear. *Behavioral Neuroscience, 128*, 474–481. https://doi.org/10.1037/a0036688

Mertens, G., Wagensveld, P., & Engelhard, I. M. (2019). Cue conditioning using a virtual spider discriminates between high and low spider fearful individuals. *Computers in Human Behavior, 91*, 192–200.

Miller, R. R., & Matzel, L. D. (2000). Memory involves far more than "consolidation". *Nature Reviews Neuroscience, 1*, *214–216*. https://doi.org/10.1038/35044578

Mineka, S., & Öhman, A. (2002). Phobias and preparedness: The selective, automatic, and encapsulated nature of fear. *Biological Psychiatry, 52*(10), 927–937.

Misanin, J. R., Miller, R. R., & Lewis, D. J. (1968). Retrograde amnesia produced by electroconvulsive shock after retrieval of a consolidated memory trace. *Science, 80*(160), 554–555. https://doi.org/10.1109/LASCAS.2014.6820259

Monfils, M.-H., Cowansage, K. K., Klann, E., & LeDoux, J. E. (2009). Extinction-reconsolidation boundaries: Key to persistent attenuation of fear memories. *Science, 324,* 951–955. https://doi.org/10.1126/science.1167975.

Mugnaini, M., Alfei, J. M., Bueno, A. M., Monti, R. I. F., Urcelay, G. P., & Gonzalo, P. (2022). Fear memory modulation by incentive down and up-shifts. *Behavioural Brain Research, 422*, 113766. https://doi.org/10.1016/j.bbr.2022.113766

Myers, K. M., & Davis, M. (2007). Mechanisms of fear extinction. *Molecular Psychiatry, 12*, 120–150.

Myers, K. M., Ressler, K. J., & Davis, M. (2006). Different mechanisms of fear extinction dependent on length of time since fear acquisition. *Learning and Memory, 13*, 216–223.

Nader, K., Schafe, G. E., & Le Doux, J. E. (2000). Fear memories require protein synthesis in the amygdala for reconsolidation after retrieval. *Nature., 406*, 722–726.

Öhman, A., & Mineka, S. (2001). Fears, phobias, and preparedness: Toward an evolved module of fear and fear learning. *Psychological Review, 108*(*3*), 483.

Öhman, A., Erixon, G., & Lofberg, I. (1975). Phobias and preparedness: Phobic versus neutral pictures as conditioned stimuli for human autonomic responses. *Journal of Abnormal Psychology, 84*, 41–45.

Öhman, A., Fredrikson, M., Hugdahl, K., & Rimmo, P. A. (1976). The premise of equipotentiality in human classical conditioning: Conditioned electrodermal responses to potentially phobic stimuli. *Journal of Experimental Psychology: General, 103*, 313–337.

Oyarzún, J. P., Lopez-Barroso, D., Fuentemilla, L., Cucurell, D., Pedraza, C., Rodriguez-Fornells, A., & de Diego-Balaguer, R. (2012). Updating fearful memories with extinction training during reconsolidation: A human study using auditory aversive stimuli. *PloS One, 7*(*6*), e38849.

Pearce, J. M., Redhead, E. S., & Aydin, A. (1997). Partial reinforcement in appetitive Pavlovian conditioning with rats. *Quarterly Journal of Experimental Psychology, 50B*, 274–294.

Phelps, E. A., O'Connor, K. J., Gatenby, J. C., Grillon, C., Gore, J. C., & Davis, M. (2001). Activation of the left amygdala to a cognitive representation of fear. *Nature Neuroscience, 4*, 437–441.

Piñeyro, M. E., Monti, R. I. F., Alfei, J. M., Bueno, A. M., & Urcelay, G. P. (2014). Memory destabilization is critical for the success of the reactivation–extinction procedure. *Learning & Memory, 21*, 46–54. https://doi.org/10.1101/lm.032714.113

Prokasy, W. F., & Kumpfer, K. L. (1973). Classical conditioning. In W. F. Prokasy & D. C. Raskin (Eds.), *Electrodermal activity in psychological research*. Academic Press.

Quirk, G. J. (2002). Memory for extinction of conditioned fear is long-lasting and persists following spontaneous recovery. *Learning and Memory, 9*, 402–407.

Rescorla, R. A. (1993). Inhibitory associations between S and R in extinction. *Animal Learning & Behavior, 21*, 327–336. https://doi.org/10.3758/BF03197998

Rescorla, R. A. (1999). Partial reinforcement reduces the associative change produced by nonreinforcement. *Journal of Experimental Psychology: Animal Behavior Processes, 25*, 403–414.

Rescorla, R. A. (2001). Retraining of extinguished Pavlovian stimuli. *Journal of Experimental Psychology: Animal Behavior Processes, 27*(2), 115–124. https://doi.org/https://doi.org/10.1037/0097-7403.27.2.115

Rescorla, R. A. (2004). Spontaneous Recovery. *Learning and Memory, 11*, 501–509.

Rescorla, R. A., & Heth, C. D. (1975). Reinstatement of fear to an extinguished conditioned stimulus. *Journal of Experimental Psychology: Animal Behavior Processes, 1*, 88–96.

Rozin, P., & Kalat, J. W. (1971). Specific hungers and poison avoidance as adaptive specializations of learning. *Psychological Review, 78*, 459–486.

Sara, S. J. (2000). Retrieval and reconsolidation: toward a neurobiology of remembering. *Learning & Memory, 7*, 73–84.

Schafe, G. E., & LeDoux, J. E. (2000). Memory consolidation of auditory pavlovian fear conditioning requires protein synthesis and protein kinase A in the amygdala. *Journal of Neuroscience, 20*, RC96.

Schafe, G. E., Nader, K. E., & Le Doux, J. (2000). The labile nature of consolidation theory. *Nature, 406*, 722–726. https://doi.org/10.1038/35044580

Schiller, D., & Phelps, E. A. (2011). Does reconsolidation occur in humans? *Frontiers in Behavioral Neuroscience, 5*, 24.

Schiller, D., Kanen, J. W., LeDoux, J. E., Monfils, M. H., & Phelps, E. A. (2013). Extinction during reconsolidation of threat memory diminishes prefrontal cortex involvement. *Proceedings of the National Academy of Sciences, 110*(*50*), 20040–20045.

Schiller, D., Monfils, M. H., Raio, C. M., Johnson, D. C., LeDoux, J. E., & Phelps, E. A. (2010). Preventing the return of fear in humans using reconsolidation update mechanisms. *Nature, 463*, 49–53.

Seligman, M. E. P. (1970). On the generality of the laws of learning. *Psychological Review, 77*, 406–418.

Seligman, M. E. P., & Hager, J. L. (1972). *Biological boundaries of learning*. Appleton-Century-Crofts.

Shettleworth, S. J. (1998). *Cognition, evolution, and behavior*. Oxford University Press.

Sizhen, S., et al. (2022). Continuous theta-burst stimulation over the right dorsolateral prefrontal cortex disrupts fear memory reconsolidation in humans. *iScience, 25*(1), 103614.

Slivka, R. M., & Bitterman, M. E. (1966). Classical appetitive conditioning in the pigeon: Partial reinforcement. *Psychonomic Science, 4*, 181–182.

Soeter, M., & Kindt, M. (2011). Disrupting reconsolidation: pharmacological and behavioral manipulations. *Learning & Memory, 18*(*6*), 357–366.

Soeter, M., & Kindt, M. (2013). High trait anxiety: A challenge for disrupting fear memory reconsolidation. *PloS One, 8*(*11*), e75239. https://doi.org/10.1371/journal.pone.0075239

Steinfurth, E. C., Kanen, J. W., Raio, C. M., Clem, R. L., Huganir, R. L., & Phelps, E. A. (2014). Young and old Pavlovian fear memories can be modified with extinction training during reconsolidation in humans. *Learning & Memory, 21(7),*338–341. http://dx.doi.org/https://doi.org/10.1101/lm.033589.113

Suzuki, A., Josselyn, S. A., Frankland, P. W., Masushige, S., Silva, A. J., & Kida, S. (2004). Memory reconsolidation and extinction have distinct temporal and biochemical signatures. *Journal of Neuroscience, 24*, 4787–4795. 10.1523/jneurosci.5491–03.2004

Thompson, A., & Lipp, O. V. (2017). Extinction during reconsolidation eliminates recovery of fear conditioned to fear-irrelevant and fear-relevant stimuli. *Behaviour Research and Therapy, 92*, 1–10. https://doi.org/10.1016/j.brat.2017.01.017

Timberlake, W. (1983). The functional organization of appetitive behavior: Behavior systems and learning. In M. D. Zeiler & P. Harzem (Eds.), *Advances in analysis of behaviour: Vol. 3. Biological factors* (pp. 177–221). Wiley.

Todd, T. P., Vurbic, D., & Bouton, M. E. (2014). Behavioral and neurobiological mechanisms of extinction in Pavlovian and instrumental learning. *Neurobiology of Learning and Memory, 108*, 52–64. https://doi.org/10.1016/j.nlm.2013.08.012

Tronson, N. C., & Taylor, J. R. (2007). Molecular mechanisms of memory reconsolidation. *Nature Reviews Neuroscience, 8(4)*, 262–275.

Urcelay, G. P., Wheeler, D. S., & Miller, R. R. (2009). Spacing extinction trials alleviates renewal and spontaneous recovery. *Learning & Behavior, 37*, 60–73. https://doi.org/10.3758/LB.37.1.60

Wang, S. H., de Oliveira Alvares, L., & Nader, K. (2009). Cellular and systems mechanisms of memory strength as a constraint on auditory fear reconsolidation. *Nature Neuroscience, 12*, 905–912. https://doi.org/10.1038/nn.2350

Westfall, J. (2016). *PANGEA (v0.2): Power ANalysis for GEneral Anova designs* [Computer software]. https://jakewestfall.shinyapps.io/pangea/

WHO. (2021). *Snakebite envenoming*. https://www.who.int/news-room/fact-sheets/detail/snakebite-envenoming

Winters, B. D., Tucci, M. C., & DaCosta-Furtado, M. (2009). Older and stronger object memories are selectively destabilized by reactivation in the presence of new information. *Learning & Memory, 16*(9), 545–553. https://doi.org/10.1101/lm.1509909

Zuccolo, P. F., & Hunziker, M. H. L. (2019). A review of boundary conditions and variables involved in the prevention of return of fear after post-retrieval extinction. *Behavioural Processes, 162*, 39–54. https://doi.org/10.1016/j.beproc.2019.01.011