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Temporal context cues in human fear conditioning: Unreinforced conditional stimuli can segment learning into distinct temporal contexts and drive fear responding

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ABSTRACT

In associative learning, if stimulus A is presented in the same temporal context as the conditional stimulus (CS) - outcome association (but not in a way that allows an A–CS association to form) it becomes a temporal context cue, acquiring the ability to activate this context and retrieve the CS-outcome association. We examined whether a CS- presented during acquisition or extinction that predicted the absence of the unconditional stimulus (US) could act as a temporal context cue, reducing or enhancing responding, in differential fear conditioning. Two groups received acquisition (CSx–US, CSa–noUS) in phase 1 and extinction (CSx–noUS; CSe–noUS) in phase 2 (AE groups), and two groups received extinction in phase 1 and acquisition in phase 2 (EA groups). After a delay, participants were presented with either CSa (AEa and EAa groups) or CSe (AEe and EAe groups). Responding to CSx was enhanced after presentation of CSa but reduced after presentation of CSe, suggesting that training was segmented into two learning episodes and that the unreinforced CS present during an episode retrieved the CSx–US or CSx–noUS association. These findings suggest that temporal context cues may enhance or reduce fear responding, providing an exciting new avenue for relapse prevention research.

Anxiety researchers and clinicians have a common problem – anxiety disorders are particularly susceptible to relapse. Although treatments are efficacious in the short-term, between one and two thirds of successfully treated patients will relapse within eight years (Craske, 1999). Understanding what triggers relapse, how treatments can be made more robust against these triggers, and what aspects of fear acquisition make relapse more likely to occur is crucial. We have moved well past the assumption that extinction, or exposure, simply erases the original fear memory. Bouton's theory of relapse revolutionised the field – treatment does not erase the original fear learning but instead creates a context specific inhibitory learning – in this place, at this time, the original fear learning does not hold (Bouton, 2002). Context, however, is a complex concept – while a change in physical context is relatively concrete, a change in temporal context is not. Time is always moving and changing, being segmented into distinct temporal episodes. It is not clear what is encoded in these temporal episodes and whether stimuli that are present during a particular temporal episode can promote or reduce fear relapse.

Differential fear conditioning provides a reliable paradigm to study fear acquisition, extinction, and relapse (Vervliet, Craske, & Hermans, 2013). During differential fear acquisition, one neutral conditional stimulus (CS+; e.g., a picture of a circle) is paired with an aversive unconditional stimulus (US; e.g., an electro-tactile stimulus), while, a second neutral stimulus (CS-; e.g., a picture of a square) is presented alone. Throughout acquisition, differential physiological responding develops, such that the CS+ elicits larger physiological responses than the CS-. During fear extinction, the CS+ and the CS- are both presented alone, in the absence of the US, and the differential responding acquired throughout acquisition gradually reduces (Lipp, 2006). Extinction training creates an inhibitory association (CS+–noUS) which suppresses the excitatory fear association (CS+–US). After extinction, the CS+ becomes ambiguous and context can be used to disambiguate it, i.e., context cues determine whether conditional fear returns (Bouton, 2002). In the laboratory, return of fear after successful extinction can be induced via three manipulations: unpaired presentations of the US alone (reinstatement), a context change after extinction (renewal), and

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testing after a delay (spontaneous recovery). Bouton suggests that reinstatement and spontaneous recovery could be regarded as special cases of renewal. Spontaneous recovery may occur because the CS+ is presented in a different temporal context and reinstatement may occur because presenting the US alone activates the CS+–US memory which triggers the acquisition context (Bouton, 2002; for a comprehensive review of return of fear mechanisms see; Vervliet et al., 2013).

As context is critical in disambiguating the CS+ when two competing associations are present, researchers have tried presenting cues from extinction to increase the likelihood that participants will retrieve the inhibitory association. Presenting a cue (e.g., an '&' symbol) on the screen during extinction (Dibbets & Maes, 2011; Dibbets, Havermans, & Arntz, 2008) or pairing another stimulus with the CS+ during extinction (Vansteenwegen et al., 2006) have been shown to attenuate renewal when these cues are also present during test. Retrieval cues have also been examined in clinical studies. Shin and Newman (2018) showed that using retrieval cues from exposure therapy (e.g. a puffer ball and a peppermint diffuser) could attenuate spontaneous recovery when participants had access to the cue at test. Culver, Stoyanova, and Craske (2011) and Dibbets, Moor, and Voncken (2013) examined the use of retrieval cues during exposure therapy, but both found that they did not attenuate fear renewal. Retrieval cues[1] are trained in a way that permits the formation of a direct association between the cue and the CS+. This direct association is problematic because the cues may function as conditioned inhibitors, protecting the CS+ from undergoing extinction learning altogether (Lovibond, Davis, & O'Flaherty, 2000; Rescorla & Wagner, 1972) and return of fear may occur when the CS+ is presented without them.

Evidence from the memory literature suggests that the content of temporal episodes can be triggered by stimuli that were present during the episode but not in a way that permitted the formation of a direct association with any other event from that episode. The absence of a direct association among events means that the stimulus used to retrieve a temporal episode will not act as a conditioned inhibitor or an occasion setter for other associations. Howard and Kahana's (2002) temporal context model proposes that during training, stimuli become associated with the current state of a gradually changing representation of the temporal context. This temporal context also enters into an association with the training stimuli such that subsequent presentation of a training stimulus can activate the temporal context. Based on this theory, Matute, Lipp, Vadillo, and Humphreys (2011) examined whether temporal context cues could enhance or reduce responding acquired during a causal learning task. During phase 1 of their experiments, stimulus X was repeatedly paired with outcome 1 and stimulus A with outcome 2; whereas in phase 2, stimulus X was repeatedly paired with outcome 2 and stimulus E with outcome 1. This training should render stimulus X ambiguous in a delayed test and, according to associative learning theories, should not permit a direct association between stimulus X and A, or stimulus X and E. Interestingly, the meaning of stimulus X was disambiguated when participants were presented with A followed by outcome 2 or E followed by outcome 1 prior to test. Participants behaved as if stimulus X was followed by outcome 1 after the A-outcome 2 pairing and by outcome 2 after the E-outcome 1 pairing. These results are interesting as they suggest that temporal contexts can be defined not only by the mere passage of time but also by discrete stimuli present during a learning episode.

This result is especially relevant to anxiety researchers and clinicians as it would suggest that renewal can occur under a broader set of conditions than previously thought. Changes in context could be cued not only by physical changes in external and internal environments or by the passage of time, but also by any other stimulus that had been present during acquisition or extinction training. This would suggest that the presentation of stimuli that are associated with the treatment context could reduce relapse without becoming conditioned inhibitors and interfering with the extinction or exposure treatment. It would also suggest that stimuli that were present when the fear was acquired could activate the temporal context of acquisition and lead to relapse. Understanding whether temporal context cues can influence the retrieval of previously acquired or extinguished fear learning could aid the development of anxiety treatments and help us to understand, and prevent, instances of relapse. We examined whether the findings of Matute et al. (2011) in a causal learning task would transfer to fear conditioning involving the measurement of physiological fear responses. Using a differential fear conditioning design, half of the participants received acquisition training in phase 1, in which stimulus X was followed by an aversive US and stimulus A was presented alone, and extinction training in phase 2 in which both stimulus X and E were presented alone (AE groups). The other half of the participants received the same training but the order of the phases was reversed (extinction then acquisition; EA groups[2]). After a delay phase, participants were presented with one temporal context reminder trial of either stimulus A (AEa and EAa groups) or stimulus E (AEe and EAe) and physiological responding to X was tested. We hypothesized that presentation of the acquisition reminder cue would enhance responding to X, and presentation of the extinction reminder cue would reduce responding to X in comparison to the last presentation of X during phase 2, regardless of whether phase 2 was acquisition or extinction.

1. Method

1.1. Participants

Sixty-eight undergraduate students aged between 17 and 41 years (M = 21.29, SD = 4.20 years) volunteered participation in exchange for course credit (46) or AU$10 (22). Participants provided informed consent and were randomly assigned to one of four groups (AEa, AEe, EAa, EAe; n = 19, 16, 16, 17, respectively). The experimental procedure was approved by the local ethical review committee (approval number 2011001267). Data from 2 additional participants were lost due to a computer error.

1.2. Apparatus/Stimuli

The conditional stimuli were pictures of geometric shapes (black outlines on a white background; circle, square, diamond, upward pointing triangle, downward pointing triangle). Conditional stimuli were displayed on a 17-inch colour CRT screen and took up an area of approximately 6.5 cm × 6.5 cm. Three shapes were used as conditional stimuli during the main experiment and two as conditional stimuli during the delay phase. The CS+ from the main training phase will be referred to from now on as the CSx. CSx+ denotes that the CSx is reinforced, CSx- denotes that the CSx is not reinforced, and CSx is used when referring to the stimulus per se. The CS- from acquisition and the CS- from extinction will be referred to as CSa- and CSe-, respectively. Two different shapes were used as the CS+ and CS- during the delay and are referred to as CSg+ and CSh-, respectively. The square, circle, and diamond were used as CSx, CSa-, and CSe- and the two triangles were used as the unrelated CSg+ and CSh- stimuli in the delay phase. The allocation of image to stimulus condition was counterbalanced

[1] In this paper we refer to retrieval cues as cues that have been trained in a way that permits the formation of a direct association between the cue and the CS+ and to temporal context reminder cues (or just reminder cues) as cues that are trained in a way that does not allow the formation of a direct association between the cue and the CS+.

[2] The extinction phase in this group could also be conceptualized as habituation training rather than extinction. The goal was to create two training phases that made the meaning of CSx ambiguous (i.e. trained competing CSx–US and CSx–noUS associations) and to ensure that the results held regardless of the order in which the associations were acquired. Therefore, we included this as a factor in the experiment. For simplicity, we have called the phases 'acquisition' and 'extinction' but they could also be referred to as the 'CSx–US' and CSx–noUS' phases.