



Human fear conditioning and extinction: Timing is everything. . .or is it?

Jason M. Prenoveau^{a,*}, Michelle G. Craske^b, Betty Liao^b, Edward M. Ornitz^c

^a Department of Psychology, Loyola University Maryland, 4501 North Charles Street, Baltimore, MD 21210, USA

^b Department of Psychology, University of California, Los Angeles, 405 Hilgard Ave., Los Angeles, CA 90095-1563, USA

^c Department of Psychiatry & Biobehavioral Science, Center for Neurobiology of Stress, and Brain Research Institute, David Geffen School of Medicine at UCLA, Los Angeles, CA 90095-1759, USA

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ABSTRACT

A differential fear conditioning paradigm was used with 107 healthy undergraduate participants to evaluate the effect of conditioned stimulus (CS) temporal properties on fear acquisition and extinction. Two minute duration CSs were used for Day 1 fear acquisition. Participants were randomized to receive either 1, 2, or 4 min CS durations during Day 2 extinction. Extinction re-test was examined on Day 3 using the original acquisition CS duration (2 min). Findings indicated that participants who were aware of the CS+/unconditioned stimulus (US) contingency ($n = 52$) develop a temporal expectation about when the unconditioned stimulus will be delivered. Although the shorter duration CS resulted in greater fear reduction during extinction, cessation of fear responding at re-test was the same for CS extinction durations ranging from half the CS acquisition duration to twice the CS acquisition duration. Thus, extinction performance did not predict extinction at re-test, which could have important implications for optimizing exposure therapy for anxiety disorders.

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1. Introduction

Although anxiety disorders are effectively treated by exposure therapy (e.g., Norton and Price, 2007) there is room for improvement as not all individuals are appreciably helped by treatment (e.g., Blanchard et al., 2004) and some of those who are helped suffer a relapse of anxiety at a later date (e.g., Rachman, 1989). Because exposure therapy is believed to operate in part through extinction processes (Bouton et al., 2001; Mineka and Zinbarg, 2006), better understanding of fear extinction mechanisms will help to optimize exposure therapy parameters which in turn could lead to more efficacious treatments. Specifically, those with anxiety disorders may develop a temporal expectation about the aversive event they expect in response to their feared stimulus. Understanding the role this temporal expectation plays in extinction of conditioned fear could help therapists to optimize exposure durations. Thus, the present study examined the effect of different duration conditional stimuli (CSs) during extinction on reduction of conditioned fear in humans.

In the present study, extinction will refer to the process underlying fear reduction as well as the experimental phase associated with this process. Reduction of fear observed within the extinction phase will be referred to as extinction *performance*, whereas fear reduction observed at some duration after extinction will be referred to

as extinction *re-test*. Laboratory extinction performance is akin to short-term fear reduction seen during therapy exposures. In addition to short-term relief, exposure therapy also aims to optimize long-term outcomes, such as relapse prevention, which are more akin to extinction re-test. It is important to differentiate between the two because extinction performance does not guarantee extinction at re-test and the absence of extinction performance does not preclude extinction at re-test (Plendl and Wotjak, 2010).

The mechanisms by which extinction occurs are still under investigation. Although early theorists believed that extinction resulted in 'unlearning' of the originally learned relationships (e.g., Rescorla and Wagner, 1972), there is evidence to indicate that original learning still exists after extinction (see Bouton, 2002). Thus, one current associative account proposes that extinction is new, inhibitory learning (CS+/no US) that competes with the original, excitatory CS+/US learning (e.g., Bouton, 1993); an alternative explanation involves an inhibitory association between the CS+ and the particular conditioned response (e.g., Rescorla, 1997).

Although of debatable *necessity* (for a review, see Lovibond and Shanks, 2002), expectancy of the US in response to the CS+ is central to human fear conditioning as conditioned responding only occurs for those aware of the CS+/US contingency (e.g., Prenoveau et al., 2011; Purkis and Lipp, 2001). As excitatory learning is based in part on the expectancy of the US in response to the CS+, inhibitory learning, or extinction, is posited to occur from a violation of this expectancy. Additionally, for fear acquisition, there is evidence that expectancy of the US in response to the CS+ is temporally specific. For example, in fixed delay fear conditioning with animals,

* Corresponding author. Tel.: +1 410 617 5240; fax: +1 410 617 2166.

E-mail address: jmprenoveau@loyola.edu (J.M. Prenoveau).

maximal CRs generally occur at, or around, the time of US delivery (e.g., Drew et al., 2005). Thus, timing likely plays a role in extinction and the violation of US expectancy in response to the CS+. Theories of conditioning differ as to what that role might be.

It is possible that extinction performance and extinction re-test are temporally cue specific. In other words, the less similar the extinction CS+ is to the acquisition CS+, the less generalization of fear there will be from the acquisition to extinction CS+. Thus, the more dissimilar the extinction CS+ duration is to the acquisition CS+ duration (either longer or shorter in duration), the easier it will be to extinguish fear to the CS+ during extinction. Therefore, an enhancement of extinction performance will be observed as the extinction CS+ duration becomes less similar to the acquisition CS+ duration. Under a temporal cue-specificity model although extinction performance would be improved as a result of using a more dissimilar CS+ duration during extinction, extinction re-test would suffer. The use of a different duration CS+ during extinction would result in a generalization gradient at extinction re-test: the less similar the extinction CS+ duration was to the acquisition CS+ duration, the less effective extinction will be at reducing responding at re-test (extinction re-test generalization decrement: attenuated reduction in responding due to generalization). Such generalization gradients for extinction performance and re-test have been shown in appetitive paradigms using auditory tones of different frequencies (as opposed to different durations) (e.g., Dubin and Levis, 1973). A similar pattern has also been observed in human fear conditioning using geometric shapes as CSs (Vervliet et al., 2004).

Componential trace models that view the CS+ as multiple successive cues that can acquire differential associations with the US (see Brandon et al., 2002). Such models posit that the earlier CS cues acquire inhibitory properties whereas later cues which are present for US delivery become excitatory; thus, the earlier CS+ cues would need to be present during extinction in order for the later excitatory cues to be encountered. Such models would predict that the CS+ must be displayed as long, or longer, than that of the acquisition CS+ in order to optimize extinction re-test. An extinction re-test decrement would not be seen for a longer duration CS+, but would be observed for an extinction duration shorter than that of acquisition.

Rate expectancy theory (RET, Gallistel and Gibbon, 2000) posits that extinction is based on a ratio of cumulative time exposed to the CS+ during extinction to the anticipated amount of CS+ exposure per US reinforcement. Thus, the number of extinction trials by itself is unimportant, as is the duration of each individual trial; extinction learning is solely based on prior acquisition learning and cumulative CS+ exposure during extinction. In contrast, other models posit that expectation of US delivery is timed from the CS+ onset, regardless of whether or not the CS+ continues to be displayed (e.g., Grossberg and Schmajuk, 1991). Such models predict that extinction is solely based on the number of extinction CS+ presentations, regardless of duration.

Findings from animal fear conditioning studies have been mixed with some supporting RET for extinction performance (Plendl and Wotjak, 2010) and extinction re-test (Shipley, 1974), and others supporting temporal cue specificity and a generalization decrement at extinction re-test (Plendl and Wotjak, 2010). Findings from animal appetitive paradigms have also been mixed. Some findings have been consistent with cue specificity and generalization decrement for extinction performance (Haselgrove and Pearce, 2003) and extinction re-test (Drew et al., 2004), whereas others have been consistent with componential trace and CS+ onset timing models for extinction performance (Drew et al., 2004). Although such models have not been tested in human fear conditioning paradigms, there is evidence consistent with componential trace models that for phobic samples a few (or a single) long exposure(s) are more effective than multiple short exposures (e.g., Chaplin and Levine,

1981; Marshall, 1985). However, such studies have not specifically manipulated exposure lengths in an attempt to violate temporal expectancies of an aversive outcome.

A better understanding of which model is most applicable to human fear extinction has clear implications for the treatment of anxiety disorders. If extinction is temporally cue specific, therapists would want the temporal properties of exposure to closely match those of the client's learning in order to optimize long-term outcomes. Under this model, exposures that are temporally shorter or longer than a client's learning might appear more efficacious during therapy (enhanced extinction performance), but result in poorer long-term outcomes (extinction re-test generalization decrement). If CS+ onset models were found to predominate, then therapists would be much more concerned about the number of exposures as compared to their duration. Thus, the exposure duration for optimizing long-term therapeutic outcomes would depend on which model is found to best represent extinction processes.

Given the theoretical importance of understanding the effect of CS+ temporal properties on extinction and the clinical impact such understanding could have on exposure therapy, it is surprising how little research has been conducted to elucidate these parameters. Thus, the present study used a human differential fear conditioning paradigm to evaluate temporal CS+/US expectancies and their impact on extinction. Specifically, 2 min duration CSs were used during Day 1 fear acquisition to evaluate if expectancy of the US in response to the CS+ is temporally specific in humans as in animals (e.g., Drew et al., 2005). To evaluate the effects of varying extinction CS duration on extinction performance, participants were randomized to receive either 1, 2, or 4 min CS durations during Day 2 extinction. Two minute CS durations were again used for Day 3 follow-up to evaluate the impact of the manipulation on extinction re-test. Magnitude of associative fear conditioning and subsequent extinction performance and re-test was assessed through both self-report (fear of CSs and online US expectancy during CSs) and physiological indices (skin conductance response and startle reflex).

2. Method

2.1. Participants

One-hundred and seven undergraduates at the University of California at Los Angeles (UCLA) participated for course research credit or payment of sixty dollars. Data from 27 participants were excluded because they discontinued during Day 1 ($n = 3$), did not return for or complete Day 2 ($n = 19$), or there were technical problems ($n = 5$). An additional 28 were excluded from analyses as they were unaware of the CS+/US contingency (see Section 5.1 below for details). The 52 remaining participants ranged in age from 18.3 to 22.8 ($M = 19.7$, $SD = 1.1$) and consisted of 25 females (48.1%). Self-endorsed ethnic breakdown was as follows: 36.5% Asian, 38.5% Caucasian, 15.4% Hispanic/Latin American, and 9.6% reported a mix of ethnicities. All participants were provided with a description of the study and gave written, informed consent that had been approved by UCLA's institutional review board.

3. Materials

3.1. Self-report measures

An 11-point Likert scale was used to obtain subjective fear ratings of the CS+ and CS- (0 = 'not at all fearful of', 10 = 'very fearful of'). Participants' expectancy of receiving the US was rated during CS presentations and intertrial intervals (ITIs) by using a joystick to move an on-screen pointer along an analog scale between the extremes of 0 = 'certain no stimulation' and 10 = 'certain stimulation' with a midpoint of 5 = 'uncertain'. The scale appeared onscreen at specific times (see Section 4 for details) prompting participants to make a rating based on their expectancy of receiving the US in "the next few moments". A short recognition questionnaire (Dawson and Reardon, 1973) was administered after acquisition to assess awareness of the CS+/US contingency: participants were asked what the muscle stimulation was paired with: the green triangle, the purple trapezoid, the movie, there was no pattern, they could not tell, or there were no muscle stimulations. They were then asked how sure they were: completely uncertain, fairly uncertain, fairly certain, or completely certain.

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