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Exposure to a novel context after extinction causes a renewal of extinguished
conditioned responses: Implications for the treatment of fear

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Abstract

Renewal gives an experimental model for the relapse of fear symptoms following exposure therapy. While renewal of extinguished fear in humans has been observed following a return to the original context in which fear was acquired (ABA design), it has been more difficult to show upon presentation of a novel context (ABC design). The present experiment used a particularly strong context manipulation in a fear conditioning procedure. Context was manipulated by using large photographs of real environments taken from various angles and was present throughout the entire experiment. A renewal of cognitive expectancy was found in both ABA and ABC renewal designs, although it was larger in the former than in the latter. Response times in making the expectancy judgments increased when there was a change to a new context. The results demonstrate consistency in fear renewal effects between human and animal studies and suggest that relapse following exposure therapy via renewal remains a danger when people encounter a previously feared object in a novel context.

Keywords: Pavlovian conditioning; extinction; renewal; fear learning

Introduction

Relapse of fear symptoms following exposure-based therapy for anxiety disorders is a significant issue for behaviour therapists. In a comprehensive review of treatment outcomes for specific phobia in adults, for example, Choy, Fyer and Lipsitz (2007) found that relapse rates can be as high as 30% to 50% at 6 months to 3.5 years following treatment. Contemporary conditioning accounts for clinical fears (e.g., Craske & Waters, 2005; Field, 2006) underlie learning-based explanations for relapse (Bouton, 2002). These explanations are based on the premise that fears can be acquired by associating a neutral stimulus (conditional stimulus or CS) with an aversive event (unconditional stimulus or US), leading to conditioned fear of the CS. Fears can be extinguished by repeated presentations of the feared CS alone, a procedure that forms the basis of exposure therapy.

One learning-based explanation for relapse following exposure therapy is termed renewal (Bouton, 2002). In renewal, a return of fear to an extinguished CS occurs when the context is changed from that experienced in extinction. For instance, suppose a person acquires a fear in one context (e.g., at a shopping centre). If they receive exposure therapy in a different context (e.g., office of therapist), s/he is prone to show a return of fear if re-exposed to the CS in the context in which the fear was first acquired (ABA renewal) or in a novel context (ABC renewal).

The effect of context changes on the return of fear has been validated in semi-clinical research using spider fearful individuals (Mineka, Mystkowski, Hladek, & Rodriguez, 1999; Mystkowski, Craske, & Echiverri, 2002; Mystkowski, Craske, Echiverri, & Labus, 2006; Mystkowski, Mineka, Vernon, & Zinbarg, 2003). Renewal can also explain past failures to maintain long-term treatment outcomes. One example noted by Otto (2002) is that of a panic treatment trial (Barlow, Gorman, Shear, & Woods,

2000). The study examined the efficacy of a cognitive behaviour therapy (CBT) program that included exposure therapy. Immediately after treatment, outcomes were better in a CBT group that also got the drug imipramine than in a CBT+placebo or CBT alone group. However, in a long-term follow up, outcomes were worse in the CBT+imipramine group than the others. These seemingly confusing findings make sense with reference to state-dependent learning (Raffa et al., 2008), as exemplified by renewal. The withdrawal of the drug caused a change in context that promoted the return of fear. In this case, the changing context would have implicated internal physiological states in addition to external cues (e.g., sight of pill bottle). In cases when the relapse of panic following therapy occurred in a novel context, the relapse mechanism can be explained via an ABC renewal effect

ABC renewal suggests that relapse has the potential to occur whenever the feared stimulus is encountered in a novel situation. Moreover, relapse via an ABA renewal effect represents an exceptional circumstance because the acquisition context is often not known. ABC renewal is thus particularly important as a potential model of relapse in clinical practice. However, a major criticism against the relevance of ABC renewal is a comparative lack of evidence for it in human experimental research (for reviews of human research on renewal see Boschen, Neumann, & Waters, 2009; Hermans, Craske, Mineka, & Lovibond, 2006; Vansteenwegen et al., 2005). Three experimental studies using human participants and physical context changes did not find ABC renewal (Effting & Kindt 2007; Havermans, Keuker, Lataster, & Jansen, 2005; Neumann 2006). In contrast, ABA renewal has been observed in several fear conditioning experiments with humans (Alvarez, Ruben, Johnson, & Grillon, 2007; Effting & Kindt, 2007; Milad, Orr, Pitman, & Rauch, 2005; Neumann & Longbottom, 2008; Vansteenwegen et al., 2005, 2006).

The lack of evidence for ABC renewal in human experimental studies is not necessarily a decisive argument for or against its relevance to explaining relapse. Animal research has shown that ABC renewal is smaller than ABA renewal (Harris, Jones, Bailey, & Westbrook, 2000). Stronger contextual manipulations may be required to detect its presence in humans. A particularly powerful contextual manipulation was recently demonstrated by Neumann and Longbottom (2008) in a fear conditioning procedure. Rather than using changes in the background color of the computer screen (Havermans et al., 2005) or lighting in the room (Effting & Kindt 2008; Neumann 2006) as seen in past failures to find ABC renewal, they used photographs of real objects and environments that were projected as large images. A strong ABA renewal effect was observed.

The present experiment adapted the contextual manipulation used by Neumann and Longbottom (2008) to test for ABA and ABC renewal in a fear conditioning procedure. Control groups (AAA and ABB groups) and control CSs were used to assess the strength of renewal. The measure of learning was based on that recently reported in this journal by Lissek et al. (2008). Participants were prompted during the CS presentations to rate the likelihood of the US. Importantly, this measure also recorded the time taken to make this judgment. The examination of response time may thus give additional information about the processing of the CS in a renewal procedure. It was hypothesised that the contextual manipulations would lead to both ABA and ABC renewal and that a slowing of response time would be observed when the extinguished CS was presented in the test context due to the ambiguity surrounding the meaning of the CS (Bouton, Westbrook, Corcoran, & Maren, 2006).

Method

Participants

Sixty first-year psychology students (11 males and 49 females) with a mean

age of 23.4 years (range of 17 to 50) participated for partial course credit. Participants provided informed consent to an experimental protocol approved by the Institutional Research Ethics Committee. Participants were allocated at random to one of the four groups of AAA, ABA, ABB, and ABC such that the experiment was primarily based on a between subject randomized design.

Apparatus

The participant sat facing a white screen on which a Panasonic Model PT-L557E LCS projector presented 1.8 m x 1.2 m images of the CSs and contexts. The three CSs were photographs of a hammer, screwdriver, and adjustable wrench. Each CS was photographed in three distinct contexts (an office, living room, and undercover foyer with vending machines). Ten photographs were taken from various angles and with the CS in different locations in each context to ensure that no specific feature of the background functioned as a cue. Photographs of the context alone were also taken from the same angles. The US shock was a 200 ms electrotactile stimulus generated by an IWORX SI100 stimulus isolator and delivered via two disposable Ag/AgCl electrodes to the participant's inner preferred forearm. Ratings of US shock expectancy were recorded from a computer keyboard. The keys v, b, n, and m were labeled 1 = very low, 2 = low, 3 = moderate, and 4 = high, respectively. Skin conductance responses were also measured using methods described previously (Neumann & Longbottom, 2008), but are not reported because the speeded expectancy judgments interfered with the elicitation of the response.

Procedure

After the participant was seated, the intensity of US shock was set at a level the participant determined was 'unpleasant but not painful'. A 3-min acclimatization period followed. The participant was next instructed that photographs with different

objects would be shown and they may receive presentations of the electrotactile shock stimulus. The participant was further told that they would be prompted to indicate the likelihood of receiving the shock by pressing a button corresponding to its rating as “quickly and accurately as possible” when the probe text *Likelihood of shock?* appeared.

Following the instructions, the experiment proper began and consisted of pre-exposure, acquisition, extinction, and test phases. In the pre-exposure phase, one presentation each of the CS_{a+}, CS_{b+} and CS⁻ were made. In the acquisition phase, there were 10 presentations each of the CS_{a+}, CS_{b+}, and CS⁻. The shock US was presented at the offset of the CS_{a+} and CS_{b+}. Next, the extinction phase had 10 presentations of the CS_{a+} and CS⁻ and no presentations of CS_{b+} or shock US were made. The extinction trials were presented in two blocks of five CS_{a+} and CS⁻ presentations such that after each block there was an equivalent duration of time in which the participant was exposed to a different context alone to control for context-US learning effects. Finally, the test phase consisted of one presentation each of the CS_{a+}, CS_{b+}, and CS⁻ and no shock US was presented. The US expectancy probe appeared 2 s post CS onset concurrently at the top and bottom of the screen in white text on trials 1, 4, 7, and 10 during acquisition and extinction phases, and during the test trials for each CS. The CS order within each phase was randomized such that the first three presentations in acquisition included all three CSs, and the first two trials in extinction were the CS_{a+} and CS⁻. The nature of the first stimulus in each phase was counterbalanced across participants.

The nature of the contexts used across the experimental phases varied across the four groups ($n = 15$ in each). The CSs in the ABA group occurred in context A for pre-exposure, acquisition, and test phases, and in context B for the extinction phase.

The context alone presentations during extinction consisted of context A and were used to control for the possibility that context A would serve as the cue for the shock during the test phase (Neumann, 2007). The CSs were always in context A across phases for the AAA group, except during context alone where context B was used. The CS presentations in the ABC group were made in context A for pre-exposure and acquisition, context B for extinction, and context C for the test phase. The context alone presentations were of context A. Finally, the CSs in the ABB group occurred in context A for pre-exposure and acquisition, and in context B for extinction and test phases. The context alone presentations were of context A. The nature of which environment served as context A, B, and C were distributed evenly across groups and phases.

The presentations of the CS and context were made in a specific way within each phase. The context appeared first, followed by the CS superimposed onto the context for 8 s. After the CS offset the context remained for a further 5 s, whereupon another photograph of the same context from a different angle or location appeared. This technique created an impression of the context being present throughout the entire experiment, yet did not allow any specific object in the context to become associated with shock absence or shock presence. The CS offset to next CS onset interval was randomly varied between 10 to 14 s.

Results

Unconditional stimulus expectancy ratings

As shown in Figure 1, a high expectancy of the shock US developed during the CS_a+ and CS_b+ in acquisition and a low expectancy of the shock US developed during the CS_a+ in extinction. A renewal of shock US expectancy during test emerged for the CS_a+ in both renewal design groups, although the size of the renewal was larger in the ABA

group than in the ABC group. The expectancy ratings during acquisition were examined with a 4 x 3 x 4 (Group x CS x Trial) ANOVA. The analyses confirmed the development of an expectation of the shock US during the CS_{a+} and CS_{b+} and not during the CS₋ with a CS x Trial interaction, $F(6, 336) = 36.23$, $\epsilon = .79$, $p < .001$, $\eta_p^2 = .39$.

Insert Figure 1 about here

To examine the transfer of expectancy for the CS_{a+} and CS₋ following the context change from acquisition to extinction, a 2 x 2 x 2 (Context change x CS x Trial) ANOVA compared the last acquisition trial and first extinction trial. The Context change factor was formed on the basis of whether there was a change of context (ABA, ABB, and ABC groups) or not (AAA group). The analyses showed a main effect for CS, $F(1, 58) = 116.25$, $p < .001$, $\eta_p^2 = .67$. However, no main effects or interactions involving the Context Change or Trial factors were significant, indicating a transfer of acquisition learning across contexts.

The expectancy ratings to the CS_{a+} and CS₋ during extinction were examined with a 4 x 2 x 4 (Group x CS x Trial) ANOVA. The analyses resulted in a CS x Trial interaction, $F(3, 168) = 40.53$, $\epsilon = .69$, $p < .001$, $\eta_p^2 = .42$. As shown in Figure 1, expectancy of the shock US during the CS_{a+} declined across trials to result in a similarly low level of shock expectancy during the CS_{a+} and CS₋ on the last extinction trial.

Two strategies were used to test for renewal. The first compared expectancy to the CS_{a+} and CS₋ on the last extinction trial and the test trial with a 4 x 2 x 2 (Group x CS x Trial) ANOVA. The change in expectancy ratings across the two trials for each group is shown in Figure 2. The main effects and two-way interactions that resulted from the statistical analyses were subsumed by a Group x CS x Trial interaction, $F(3, 56) = 9.09$,

$p < .001$, $\eta_p^2 = .33$. Separate 2 x 2 (CS x Trial) ANOVAs conducted for each group showed a significant two-way interaction for the ABA and ABC groups, both $F_s > 5.51$, $p < .05$, $\eta_p^2 > .28$, indicating the presence of a renewal effect. Pairwise analyses using Sidak's correction compared across trials separately for each CS. A significant increase in US expectancy across trials was found in the ABA group for the CS_{a+}, $t = 10.01$, $p < .001$, $d = 2.63$, and not the CS₋, $t = .94$, $p > .05$. Likewise, significant increase in expectancy was found in the ABC group for the CS_{a+}, $t = 4.69$, $p < .001$, $d = 1.06$, and not the CS₋, $t = .94$, $p > .05$. Inspection of the means suggested that the renewal effect was larger in the ABA group than the ABC group. To provide a more direct comparison between the groups, the change in expectancy from the last extinction trial to the first test trial for the CS_{a+} was calculated (a positive change indicates an increase in shock expectancy). The increase in expectancy was significantly larger in the ABA group ($M = 2.13$, $SD = 1.13$) than in the ABC group ($M = 1.00$, $SD = 1.07$), $t(28) = 2.83$, $p = .009$.

Insert Figure 2 about here

The second test for renewal compared the three CSs during the test trial with a 4 x 3 (Group x CS) ANOVA and it produced a Group x CS interaction, $F(6, 112) = 4.51$, $\epsilon = .97$, $p < .001$, $\eta_p^2 = .19$. In the AAA and ABB groups, expectancy was significantly lower for the CS_{a+} than the CS_{b+}, both $t_s > 4.62$, $p < .001$, $d > 1.43$, and expectancy for the CS_{a+} and CS₋ did not differ, both $t_s < 1.97$, $p > .05$. In the ABA group, renewal was found in that expectancy did not differ for the CS_{a+} and CS_{b+}, $t = .01$, $p > .05$, but was higher for the CS_{a+} than the CS₋, $t = 6.82$, $p < .001$, $d = 2.39$. In the ABC group, renewal was found in that expectancy for the CS_{a+} was significantly higher than for the CS₋, $t = 2.64$, $p = .007$, $d = 0.76$, although it was lower than for the CS_{b+}, $t = 2.87$, $p = .005$, $d =$

1.91. To again test for the strength of renewal effects observed in the ABA and ABC groups, the expectancy rating to the CS_a+ was compared. Expectancy of shock for the test trial was significantly higher in the ABA group ($M = 3.40$, $SD = 0.99$) than in the ABC group ($M = 2.33$, $SD = 1.05$), $t(28) = 2.87$, $p = .008$.

Response time to make expectancy ratings

The response time to make the US expectancy ratings are shown in Figure 3. The results showed a pattern in which response times declined across trials within acquisition and extinction. Response time also differed between the CSs during test in some groups. To examine response time during acquisition, a 4 x 3 x 4 (Group x CS x Trial) ANOVA was conducted. The decline in response time across trials was confirmed by a main effect for Trial, $F(3, 168) = 41.85$, $\epsilon = .74$, $p < .001$, $\eta_p^2 = .43$. Further comparisons showed that response time on Trial 4 was faster than on Trials 1 to 3, and faster on Trial 2 than on Trial 1, all $t_s > 6.01$, $p < .001$.

Insert Figure 3 about here

To test for any change in the transfer from acquisition to extinction, a 2 x 2 x 2 (Context change x CS x Trial) ANOVA was conducted to compare the last acquisition trial and the first extinction trial. A significant Context change x Trial interaction was found, $F(1, 56) = 4.99$, $p = .029$, $\eta_p^2 = .08$. The interaction reflected that response time increased from acquisition ($M = 1069$ ms, $SD = 479$) to extinction ($M = 1465$ ms, $SD = 940$) in participants that received a context change, $t = 2.87$, $p < .006$, whereas the difference between the acquisition ($M = 1425$ ms, $SD = 678$) and extinction ($M = 1317$ ms, $SD = 662$) trials was not significant for participants that received no context change, $t = 0.78$, $p = .44$.

The response times during extinction were examined with a 4 x 2 x 4 (Group x CS x Trial) ANOVA. The analyses resulted in a CS x Trial interaction, $F(3, 168) = 4.33$, $\epsilon = .94$, $p = .007$, $\eta_p^2 = .07$. The interaction reflected different rates of response time shortening in each CS. For the CS_{a+}, response time was faster on Trial 4 than on Trials 1 to 3, all $t_s > 4.67$, $p < .001$ and for the CS₋, response time was faster on Trial 4 than on Trial 1, $t = 4.32$, $p < .001$.

Two strategies were used to examine response time during the test trials. The 4 x 2 x 2 (Group x CS x Trial) ANOVA to examine the change from the last extinction trial to the first test trial showed a Group x CS x Trial interaction, $F(3, 56) = 3.80$, $p = .015$, $\eta_p^2 = .17$. Separate 2 x 2 (CS x Trial) ANOVAs yielded a significant interaction only in the ABC group, $F(1, 14) = 6.44$, $p = .024$, $\eta_p^2 = .31$. Pairwise comparisons showed that response time was slower on the test trial than on the last extinction trial for the CS_{a+} only, $t = 3.63$, $p = .001$. In the second strategy the response times during the three CSs on the test trial were compared with a 4 x 3 (Group x CS) ANOVA. The analyses resulted in a Group x CS interaction, $F(6, 112) = 3.52$, $\epsilon = .94$, $p = .004$, $\eta_p^2 = .16$. Response time was slower for the CS_{a+} and CS_{b+} than for the CS₋ in the ABC group, both $t_s > 3.20$, $p < .002$, whereas all other comparisons were not significant, all $t_s < 2.57$, $p > .01$.

Discussion

The present experiment showed a renewal of self-reported likelihood of the shock US in both ABA and ABC renewal designs. The renewal was observed as an increase in the perceived likelihood of shock during the CS_{a+} from extinction to test and as a higher likelihood of the shock US during the CS_{a+} than the CS₋ on the test trial. ABA renewal has been observed in prior experiments using a fear conditioning procedure (Alvarez et al., 2007; Effting & Kindt, 2007; Milad et al., 2005; Neumann & Longbottom, 2008; Vansteenwegen et al., 2005, 2006). The present results, however, provide the first

conclusive demonstration of ABC renewal in a human fear conditioning procedure.

The observation of ABC renewal in the present experiment is consistent with observations found in animal research (e.g., Bouton & Bolles 1979; Harris et al., 2000), but contrasts with some prior studies with human participants (Effting & Kindt 2007; Havermans et al., 2005; Neumann 2006). Havermans et al. (2005) did not find ABC renewal in a single cue conditioning procedure. Neumann (2006) and Effting and Kindt (2007) did not find ABC renewal in a differential conditioning procedure similar to that used here, although only a CS+ and CS- stimulus was used. The reason for the contrasting results may reflect differences in methodology. The stronger contextual manipulation employed in the present experiment may have enhanced context-specific learning, resulting in a stronger effect of the context change during test.

Although ABC renewal was observed in the present experiment, it was not as strong as that found for ABA renewal. In the ABA renewal group, ratings of the likelihood of the shock did not differ between the CS_{a+} and the control stimulus CS_{b+}. In contrast, ratings of the likelihood of the shock were significantly lower for the CS_{a+} than the CS_{b+} in the ABC group. One explanation for this difference between groups is that it reflects contextual conditioning of context A forming an association with the US, although the exposures to context A alone during extinction in the ABA group would have somewhat negated this effect. Another explanation is that acquisition learning, in addition to extinction learning, shows some degree of context specificity (Bouton, 2004; Bouton et al., 2006; Harris et al., 2000). The clinical implication of these findings is that while relapse seems to be particularly prone to occur when an individual is exposed to the feared object in the original learning context, it remains as a potential source of relapse even when the feared objects is encountered in a novel context.

The observation of ABC renewal in the present experiment highlights that the

renewal procedure provides a viable experimental analogue for relapse following exposure therapy for anxiety disorders (Bouton, 2002; Vansteenwegen et al., 2005). Relapse can remain as an ever present danger whenever the client is re-exposed to the feared object in a different context to which therapy was undertaken. The results support prior research in which participants were selected on the basis of pre-existing fears or dependencies for which the context during the presumed acquisition phase is not known. For instance, Mystkowski et al. (2002) pre-selected a group of spider fearful individuals and gave them one session of graded, exposure-based treatment in a specific treatment location. Renewal of self-reported fear was observed when the individuals were exposed to a tarantula in a location that was different to that in which the treatment session was given (i.e., likened to ABC renewal).

Although shock US expectancy has been measured in a renewal procedure before (e.g., Neumann, Lipp, & Cory, 2007; Neumann & Longbottom, 2008), the time taken to make the judgment has not yet been examined. Response times to excitatory CSs increased from acquisition to extinction and from extinction to test, but only following a change to a novel context. Lissek et al. (2008) interpreted expectancy response times as reflecting the amount of threat ambiguity of the stimulus. This interpretation would suggest that exposure to an excitatory CS in a novel context creates uncertainty about the level of threat associated with the CS. As a result, there is a more extensive evaluation of the CS and a longer time is taken to make an expectancy judgment.

An alternative interpretation of the response time results may be derived from prior research in which reaction time to an irrelevant probe is examined during a CS (e.g., Dirikx, Hermans, Vansteenwegen, Baeyens, and Eelen, 2007). Reaction times are typically slower to a probe presented during a CS+ than during a CS- in an acquisition phase. The slowing is taken as evidence of a greater allocation of processing resources

during the CS+ than during the CS-. In the present experiment, the slowing of response times may reflect a similar increase in the allocation of processing resources. Participants may have allocated more resources when processing an excitatory CS in a novel context. If this is the case, it is unclear as to whether attentional resources were allocated to the CS itself, the features of the novel context, or to a combination of both. Moreover, it remains to be determined whether the increased allocation is due to the ambiguity associated with the threat value of the CS and context or the threat value per se. Further research is required to separate these potential influences on response time to determine what implications this measure might have for our understanding of fear renewal in humans.

A limitation of the present findings is that ABC renewal was observed in a self-report measure (shock expectancy judgements). Replication of the present results are required using a non-verbal measure known to be associated with fear learning, such as skin conductance responses or the startle reflex (e.g., Lipp, Neumann, & Mason, 2001; Neumann, Lipp, & Siddle, 1997; Neumann, Waters, & Westbury, 2008). In any study that measures autonomic nervous system activity, it would be recommended that expectancy judgments are either omitted or that they are not measured using the methods employed in this experiment. We found that the need to make a speeded button-press response interfered with the skin conductance measure. This is likely because the message that prompted participants to make a judgement elicited an orienting response that confounded the elicitation of the autonomic conditioned response. Prior research has successfully measured expectancy judgments and skin conductance responses concurrently (e.g., Effting & Kindt, 2007, Neumann & Longbottom, 2008). These studies did not require participants to make a speeded response, but measured expectancy judgments continuously through the use of a dial-and-pointer. Such a measure should be preferred in any research that seeks to measure subjective ratings and autonomic responses in

parallel.

In conclusion, the present experiment has shown a renewal of shock expectancy when participants are exposed to a novel context after extinction treatment (i.e., ABC renewal). The implication for clinical practice is that it greatly extends the potential for relapse to occur following successful exposure therapy. One might be tempted to take comfort in the fact that the magnitude of ABC renewal was not as large as that found with ABA renewal. However, even one lapse has the potential to lead to a full-blown relapse. Future research is required to develop novel approaches to minimize the chance of relapse via a renewal effect regardless of the context in which a previously feared object is encountered (Bouton, 2002).

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Figure Legends

Figure 1. Mean unconditional stimulus (US) expectancy ratings for the AAA and ABA groups (top panel) and ABB and ABC groups (bottom panel) in each phase of the experiment. Expectancy ratings were probed on trials A1, A4, A7, and A10 in acquisition, on trials E1, E4, E7, and E10 in extinction, and the single test trial. Error bars depict the standard error of the mean. The means for the CS_{a+} and CS_{b+} on the test trial were identical in the ABA group.

Figure 2. Mean unconditional stimulus (US) expectancy ratings for the AAA, ABA, ABB, and ABC groups on the last extinction trial (E10) and the test trial for the CS_{a+} and CS₋. Error bars depict the standard error of the mean.

Figure 3. Mean response time to make the expectancy ratings for the AAA and ABA groups (top panel) and ABB and ABC groups (bottom panel) in each phase of the experiment. Expectancy ratings were probed on trials A1, A4, A7, and A10 in acquisition, on trials E1, E4, E7, and E10 in extinction, and the single test trial. Error bars depict the standard error of the mean.