Plasticity of fear memory: a search for relapse prevention

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Contextual control of human fear associations in a renewal paradigm

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Abstract

The original model of behaviour change suggests that extinction is context dependent whereas fear acquisition is context independent (Bouton & Ricker, 1994). Supportive evidence stems mainly from animal studies, showing that after acquisition (CS-US) in Context A and extinction in Context B, fear is renewed by presenting the CS in acquisition Context A (ABA *renewal*) or in a novel Context C (ABC *renewal*). By implication, the model predicts equal ABA and ABC renewal. However, there is also evidence to suggest that the context dependency of extinction and the context independency of acquisition may be less stringent than originally proposed. The present study investigated renewal in humans using a differential fear conditioning paradigm with a shock US and online shock expectancy ratings and electrodermal responses as dependent variables. Experiment 1 compared an ABA condition with an AAA condition. Experiment 2 compared three conditions: ABA, ABC, and AAA. Both experiments demonstrated ABA renewal. Most importantly, Experiment 2 showed larger ABA than ABC renewal. In line with the extinction model, the present findings support the context dependency of extinction in humans. In contrast to the model, the findings suggest that in humans not only extinction learning, but also fear acquisition is controlled by its current context.

Introduction

Simple Pavlovian conditioning in animals (Pavlov, 1927) has provided major clinical applications for humans. Conditioning refers to the process of pairing an initially neutral conditioned stimulus (CS) (e.g., a tone) with an intrinsically aversive unconditioned stimulus (US) (e.g., an electric shock). The learned association between the CS and the occurrence of the aversive event generates a robust conditioned fear response to the CS on its own. Pavlovian fear conditioning has been considered as an important experimental model for the etiology of anxiety disorders for at least 80 years (Mowrer, 1939; Watson & Rayner, 1920). Of even greater clinical relevance is that extinction, that is, attenuation of Pavlovian conditioned fear by repeated presentations to the CS in absence of the US, has been the explicit model for behaviour therapy (Eysenck, 1981; Marks, 1978).

Although CS alone presentations may extinguish conditioned fear responses, it is well established that an extinction procedure does not erase the original learned fear association (Bouton, 2000; Pearce & Hall, 1980; Rescorla, 2001). Retention of the original CS-US association has been uncovered following extinction by a variety of factors including a context change (*renewal*), presenting unsignalled USs (*reinstatement*), or simply the passage of time (*spontaneous recovery*) (Bouton & Bolles, 1979; Bouton & King, 1983; Pavlov, 1927). Instead of erasure, Bouton and colleagues assert that extinction involves new learning that competes with the original learning (see for reviews Bouton, 2000, 2002). The implication is that, once an aversive association has been learned, the memory trace for this association will be forever.

Assuming that the original association (CS-US) remains intact, extinction is thought to provide the CS with a second association (CS-noUS) that is available along with the first. A central tenet of the theory of Bouton is that these conflicting "meanings" supply the CS with ambiguity and that the context determines which meaning or association prevails in a certain situation (Bouton, 2002). This is represented in the original model of extinction learning (Bouton & Ricker, 1994). In this model it is hypothesized that merely elicitation of the CS-noUS association depends on the context whereas elicitation of the CS-US association is context independent. That is, in all contexts the original learned association is activated unless the extinction context turns it off. This hypothesis is derived from findings that a context change after simple acquisition has little impact on conditioned behaviour (e.g., Bouton & King, 1983; Swartzentruber & Bouton, 1992), while the same context change after extinction often produces a loss of the new learned

behaviour (i.e., renewal) (e.g., Bouton & Bolles, 1979; Bouton & Peck, 1989). By implication, the model predicts that "renewed responding should occur whenever an extinguished CS is tested in a context that differs from the extinction context" (Bouton & Ricker, 1994, p. 317). Extrapolating to clinical practice, someone may acquire a spider phobia at home (Context A), which is treated by exposure in a therapeutic setting (Context B). Outside the treatment context, either at home (Context A) or in a new situation (Context C), the patient might suffer relapse when confronted with a spider (CS) due to a context change following exposure.

Evidence of the context dependency of extinction has been provided by studies on renewal in both animals and humans. When conditioned responding is acquired in Context A and extinguished in Context B, rodents demonstrate robust recovery of conditioned responding upon testing the CS in the original Context A, that is, ABA renewal (Bouton & King, 1983; Harris, Jones, Bailey, & Westbrook, 2000; Thomas, Larsen, & Ayres, 2003), or in a new Context C, that is, ABC renewal (Bouton & Bolles, 1979; Bouton & Brooks, 1993; Gunther, Denniston, & Miller, 1998). Renewal is also found when acquisition and extinction take place in the same context and testing occurs in a different context, that is, AAB renewal (Bouton & Ricker, 1994; Tamai & Nakajima, 2000). In humans, however, evidence of the renewal effect is relatively scarce. Most studies have been conducted in anxious individuals who were treated for their pre-existing fear by a short exposure treatment. Such studies show that fear returns when these individuals are tested in a context different from the treatment context (e.g., Mineka, Mystkowski, Hladek, & Rodriguez, 1999; Mystkowski, Craske, & Echiverri, 2002; Mystkowski, Mineka, Vernon, & Zinbarg, 2003). Only recently, renewal in humans has been investigated in which fear was experimentally induced (Milad, Orr, Pitman, & Rauch, 2005; Vansteenwegen et al., 2005). For instance, in a differential fear conditioning paradigm, Vansteenwegen et al. showed participants during acquisition two neutral slides of pictorial faces of which one (CS+) was paired with a loud noise (US), whereas the other (CS-) was never paired with the US. Extinction of conditioned fear was established by presenting both slides without the US in a different context. Conditioned fear responding to the CS+ renewed when returning to the acquisition context (i.e., ABA renewal). The abovementioned findings strengthen the idea that effects of exposure therapy may be lost when the previously feared object is encountered outside the treatment context.

Despite convincing evidence of the renewal effect, also several anomalies in the literature are available suggesting that the proposed model on extinction learning might be unnecessarily defeatist. First of all, the frequently reported

absence of AAB renewal in animal laboratory studies is difficult to reconcile with the current model of extinction (Bouton & King, 1983; Bouton & Swartzentruber, 1989; Goddard, 1999; but see Bouton & Ricker, 1994). Furthermore, the observation by Denniston, Chang, and Miller (2003) that massive relative to moderate extinction training can attenuate the ABA renewal effect in rodents can not be explained by the original model on extinction. If extinction were restricted to its context, no difference in the strength of renewal would be expected between massive and moderate extinction. Also, the recent demonstration of weaker ABC renewal compared to ABA renewal (Harris et al., 2000; but see Thomas et al., 2003) can be considered as an anomaly for the model. That is, from the view that extinction, but not acquisition, depends on the context, it would follow that a return of the conditioned response in the original context (ABA) should be as strong as in a novel context (ABC).

In sum, several findings in the literature suggest that the hypothesized context dependency of extinction and context independency of acquisition may be less stringent than originally supposed. In contrast to the original model on extinction, we assume that contexts are not only relevant for extinction learning but also for fear associations. If so, it may be expected that after acquisition in Context A and extinction in Context B, presenting the CS in a novel Context C would result in less renewal than in the original acquisition Context A. Conversely, as the original model on extinction learning ascribes no importance to the acquisition context, no difference between ABC and ABA renewal would be predicted. The present study was designed to test these opposing predictions. Since demonstrations of ABA renewal of extinguished fear responding in humans are rare (e.g., Vansteenwegen et al., 2005), Experiment 1 addressed the replication of ABA renewal. Experiment 2 tested the prediction of smaller ABC than ABA renewal.

Experiment 1

In Experiment 1, ABA renewal was examined using a differential fear conditioning procedure (Vansteenwegen et al., 2005) with an electric shock as US. In the ABA condition, participants received acquisition in one context (Context A), extinction in another context (Context B), and a test for renewal in the original acquisition context (Context A). In the AAA condition, acquisition, extinction, and testing took place in one and the same context (Context A). Expectancy ratings of shock and autonomic arousal (skin conductance) were measured online as indices of

respectively causal knowledge and conditioned responding, which are suggested to be closely related (Lovibond & Shanks, 2002). It was predicted that participants in both conditions would show a gradual increase of differential responding to CS+ and CS- during acquisition trials (expectancy ratings and skin conductance), which was expected to gradually decrease during extinction trials. Of most interest to our hypothesis was the response pattern between the last extinction trial and the first test trial as an index of renewal. It was predicted that upon a context change after extinction, the ABA condition would show an increase in responding to CS+ relative to CS-. No increases were expected in the AAA condition.

Method

Participants

Fifty-four undergraduate students (13 men, 41 women) participated in return for course credits. Participants did not have heart complaints or an epileptic disorder. They were randomly assigned to one of the conditions with the restriction that conditions were matched on sex as close as possible: AAA (n = 27: 6 men, 21 women) and ABA (n = 27: 7 men, 20 women).

Stimuli

The two neutral line drawings of pictorial faces used by Vansteenwegen et al. (2005) served as CSs. The slides were 267 mm high and 220 mm wide and were presented in the middle of a black screen on a 19-inch computer monitor. One of the slides (CS+) was followed by an US, while the other slide (CS-) was not. Assignment of the slides as CS+ and CS- was counterbalanced across participants. An electric shock, delivered to the wrist of the non-preferred hand, served as US (e.g., Vervliet, Vansteenwegen, Baeyens, Hermans, & Eelen, 2005).

Context manipulation

Contexts were manipulated by illuminating the experimental room in either a pink or a yellow light. Lighting was supplied by a frame with six fluorescent tubes of 36 W (two pink and four yellow tubes) located on the ceiling of the room, resulting in a slightly dimmed coloured illumination of the whole room. The experimenter controlled the lighting from an adjacent room.

Apparatus

Delivery of the electric shock was controlled by a Digitimer DS7A constant current stimulator (Hertfordshire, UK) via a pair of Ag electrodes of 20 mm by 25 mm with a fixed inter-electrode mid-distance of 45 mm. A conductive gel (Signa, Parker) was applied between the electrodes and the skin.

Rated expectations of the US were measured online during CS presentation using a pointer on a continuous scale placed within reach of the preferred hand. The scale consisted of 11 points labelled from 'certainly no shock' (0) through 'uncertain' (5) to 'certainly a shock' (10). The scale and participant's rating were continuously presented at the bottom of the computer screen in order to encourage participants to focus their attention to CSs.

Electrodermal activity was measured using an input device with a sine shaped excitation voltage (± 0.5 V) of 50 Hz, which was derived from the mains frequency. The input device was connected to two Ag/AgCl electrodes. The use of an electrode gel was omitted to prevent the gel forming a capacitive load for the signal. Optimal electrode contact area was ensured by using preformed electrodes of 20 mm by 16 mm, which were attached with adhesive tape to the medial phalanges of the second and third fingers of the non-preferred hand. The signal from the input device was led through a signal-conditioning amplifier and the analogue output was digitized at 100 Hz by a 16-bit AD-converter (National Instruments, NI-6224).

The experiment was run on a Pentium IV 3 GHz PC. A software program (VSSRP98 v5.4), which managed presentation of CSs and the expectancy rating scale and employed a trigger signal to initiate US delivery, recorded expectancy ratings and electrodermal activity during the whole experiment. Data reduction and analysis were performed offline.

Procedure

During the experiment, participants sat behind a table with a computer monitor at a distance of 70 cm in a sound-attenuated room. After participants had given informed consent, the experimenter attached the skin conductance and shock electrodes. The intensity of the US was determined by gradually increasing the level of the shock. Participants were asked to select a level that was uncomfortable, but not painful. After US selection, both CSs were presented once without the US on the computer screen to habituate participants to the stimuli. Next, participants were instructed about the use of the expectancy pointer. It was explained that the

same slides would be presented to them on the computer. Participants were instructed to look carefully at them, as an electric shock would follow some of the slides. They were told that they should learn to predict on the basis of the slides whether an electric shock would occur or not. Participants were required to rate the expectancy of a shock during the presentation of each slide by shifting the pointer on the scale. Once the slide disappeared, they had to return the pointer to zero. Participants were given the possibility to communicate through an intercom in case of problems.

The conditioning experiment consisted of an acquisition phase, an extinction phase, and a test phase. In the *acquisition phase*, the contingency between CS+ and US was learned. Both CS+ and CS- stimuli were presented 10 times for 8 s. The US occurred immediately after CS+ offset with a duration of 2 ms. Intertrial intervals (ITI) varied between 15 s, 20 s and 25 s with a mean of 20 s. Order of trial and ITI were quasi-random, with the restriction that no more than two consecutive trials or ITI were of the same type. For participants in all conditions acquisition took place in Context A.

In the *extinction phase*, participants learned that the CS+ was no longer followed by the US. Both CS+ and CS- stimuli were presented 10 times without the US. Characteristics of CS, trial order, and ITI were similar to the acquisition phase. For participants in the AAA condition extinction occurred in Context A, while for participants in the ABA condition extinction took place in a different context (Context B). Switching to Context B occurred immediately after presentation of the last acquisition trial.

In the *test phase*, renewal of responding was examined. Participants were exposed to both CS+ and CS- stimuli for three times. None of the CS+ was paired with the US. The same characteristics of CS, trial order, and ITI as during acquisition were applied. Testing occurred for both conditions in the acquisition context (Context A). For Condition ABA, switching to Context A took place immediately after presentation of the last extinction trial. The colours of the lighting that served as Contexts A and B were counterbalanced across participants. Acquisition, extinction, and test phase were presented without interruption.

After removing the electrodes, participants were asked to rate the pleasantness of the US on an 11-point scale ranging from –10 (unpleasant) to +10 (pleasant) and the intensity of the US on a 5-category scale (weak, moderate, intense, enormous, and unbearable).

Scoring, response definition, and statistical analysis

US expectancy ratings were calculated based on the average rating level of the last 2 s of a CS presentation. Skin conductance responses elicited by the CS were scored in two latency windows. First interval responses (FIR) and second interval responses (SIR) were defined as starting within 1-4 s respectively 4-9 s after CS onset (Prokasy & Kumpfer, 1973). Responses initiated between 9-15 s after CS onset were scored as unconditioned responses. A minimum response criterion of 0.05 microSiemens (μS) and a minimum rise time of 400 ms were used. All other responses were scored as zero and were left in the analyses (Dawson, Schell, & Filion, 2000). Responses were range corrected to control for interindividual differences (Lykken & Venables, 1971) using the largest unconditioned response elicited by the US during acquisition trials as the maximum range. Note that no differences were found in maximum ranges across conditions. Range corrected magnitudes were square root transformed to reduce skewness of the distribution.

US characteristics were analyzed by separate 2 (condition: AAA vs. ABA) factorial analyses of variance (ANOVA). Expectancy and electrodermal data during acquisition were subjected to a 2 (CS-type: CS+ vs. CS-) × 10 (trial: 10 acquisition trials) × 2 (condition: AAA vs. ABA) mixed ANOVA with condition as a between-subjects factor and CS-type and trial as within-subjects factors. To confirm an acquisition effect, focused contrasts were used to examine the predicted within-subjects interactions, CS-type × Trial and CS-type × Trial × Condition (Rosenthal & Rosnow, 1985). To explore whether acquisition generalized to another context, data were analyzed on basis of responses to the last acquisition trial (a10) and the first extinction trial (e1), using a 2 (CS-type: CS+ vs. CS-) × 2 (trial: a10 vs. e1) × 2 (condition: AAA vs. ABA) mixed ANOVA.

Like acquisition, a similar analysis was used to examine an extinction effect except that the factor trial consisted of 10 extinction trials. To test for renewal, responding to the last extinction trial (e10) was compared to the first test trial (t1). Therefore, a 2 (CS-type: CS+ vs. CS-) × 2 (trial: e10 vs. t1) × 2 (condition: AAA vs. ABA) mixed ANOVA was performed. The results of most interest to our hypothesis were reported and further examined with post-hoc simple interactions and pairwise comparisons. A Greenhouse-Geisser procedure was applied in case of violation of the sphericity assumption in ANOVAs with more than two levels of the factor trial. An alpha level of .05 was used for all statistical analyses.

Results

Of the 54 participants tested, expectancy data of 2 participants were left out because of failure to comply with US rating instructions. Therefore, the results for US expectancy ratings and skin conductance are based on 52 respectively 54 participants. For reasons as missing rating data (n = 5), speaking (n = 1), and coughing (n = 3) at some point of the experiment, sample sizes for the different analyses varied between 47 and 54.

US characteristics

Selected US intensities ranged from 2 to 24 mA with a mean of 10.80 mA (SD = 5.13). After the experiment, participants rated the US as fairly unpleasant (M = -4.65, SD = 2.39) and rated the intensity of the US as moderate to intense (M = 2.52, SD = 0.51). There were no differences between conditions in selected intensities or in the way participants experienced the US, all Fs < 1.87.

Acquisition

US expectancy ratings. Figure 2.1 summarizes mean expectancy ratings to CS+ and CS- across trials for both conditions separately (AAA, ABA). As expected, the analysis yielded a significant linear CS-type × Trial (a1 to a10) interaction, $F(1, 45) = 200.79$, $p < .01$, indicating a gradual increasing differentiation between CS+ and CS- ratings from the first to the last acquisition trial. This pattern of acquisition did not differ between conditions, as reflected by a non-significant linear CS-type × Trial × Condition interaction, $F < 1$. This suggests that the CS+ and CS- had become valid predictors of the US, respectively, non-occurrence of the US in both conditions.

Skin conductance (FIR). No evidence of an acquisition effect was provided for FIR. Because recovery of conditioned responding cannot be expected when there is no acquisition of conditioned responding, FIR results were not reported for the sake of brevity.

Skin conductance (SIR). Mean SIR on CS+ and CS- trials are shown per condition in Figure 2.2. In contrast to expectancy ratings, the ANOVA for SIR did not reveal the predicted linear CS-type × Trial (a1 to a10) interaction, $F < 1.77$. Also, the linear CS-type × Trial × Condition interaction was not significant, $F < 1.16$. Despite the absence of the expected pattern for SIR across acquisition trials, there was, however, a main effect of CS-type, $F(1, 51) = 16.43$, $p < .01$, and no CS-

type × Condition interaction, $F < 1$, indicating that both conditions emitted larger responses to CS+ than to CS-. Furthermore, there was an unexpected trend for larger responses in the ABA condition than in the AAA condition, $F(1, 51) = 3.30$, $p = .08$. The results are considered as evidence that acquisition of conditioned responding was established, as supplementary analyses revealed differential responding to CS+ and CS- on the last acquisition trial, $F(1, 51) = 4.81$, $p = .03$, but not on the first acquisition trial, $F < 2.76$.

Generalization of acquisition

US expectancy ratings. The ANOVA revealed interactions between CS-type and trial (a10, e1), $F(1, 50) = 17.41$, $p < .01$, and, crucially, between CS-type, trial, and condition, $F(1, 50) = 5.86$, $p = .02$. Simple interactions (CS-type × Trial) within each level of condition yielded only a significant interaction in the ABA condition, $F(1, 24) = 18.80$, $p < .01$, suggesting a loss of differential ratings to CS+ and CS- upon transition from one context (A) to another context (B). Pairwise comparisons showed that from the last acquisition trial to the first extinction trial CS+ ratings decreased marginally significant ($p = .05$), while the increase in CS- ratings was highly significant ($p < .01$). Thus, there was some evidence of decrement of acquisition from one context to another context.

Skin conductance (SIR). Contrary to expectancy ratings, there was no CS-type × Trial (a10, e1) interaction, $F < 1.04$, nor a CS-type × Trial × Condition interaction, $F < 1.15$. However, the analysis revealed overall larger responses to CS+ than to CS-, $F(1, 52) = 6.57$, $p = .01$. These results indicate that a context change did not influence differential responding. Hence, acquisition of conditioned responding seems to have been maintained from one context (A) to another context (B).

Extinction

US expectancy ratings. As expected, the ANOVA showed a significant linear CS-type × Trial (e1 to e10) interaction, $F(1, 50) = 61.33$, $p < .01$, indicating that the difference in rated expectancies between CS+ and CS- gradually decreased across extinction trials, that is, an extinction effect. At the end of extinction, the CS+ no longer predicted the US. An almost significant linear CS-type × Trial × Condition interaction, $F(1, 50) = 3.97$, $p = .05$, reflected a tendency for the ABA condition to show a faster loss of differential ratings to CS+ and CS- during extinction than the AAA condition.

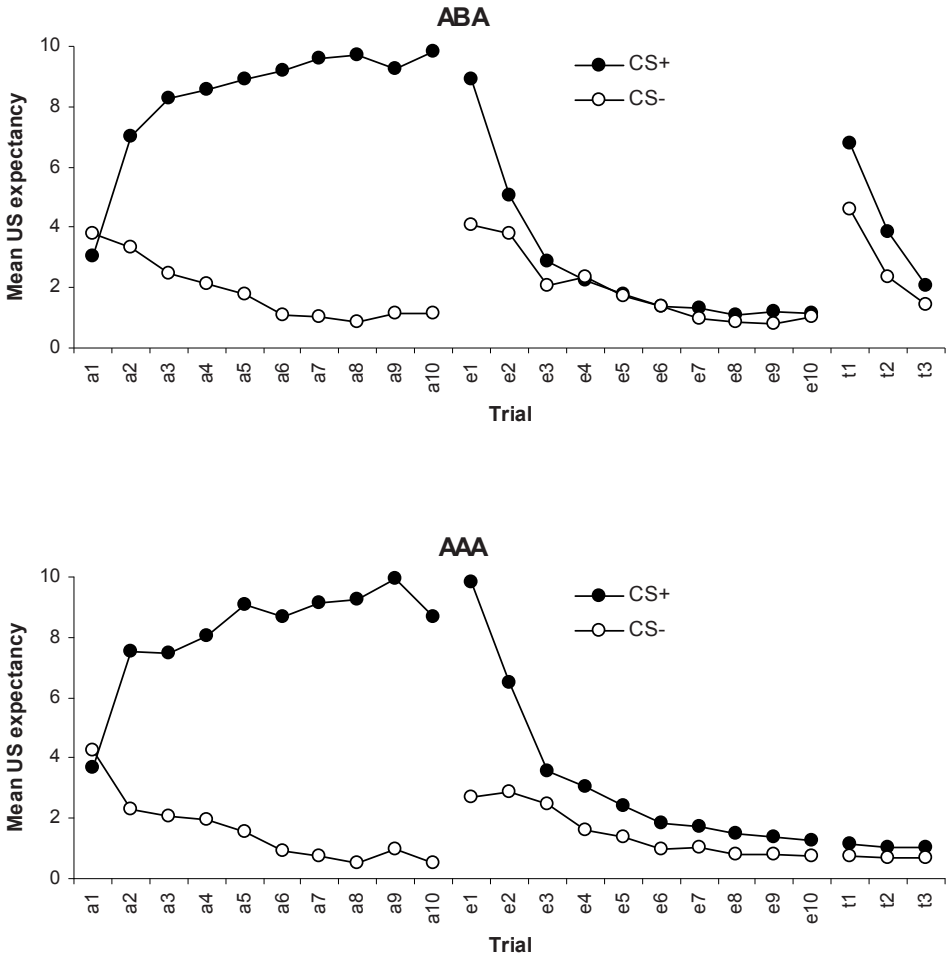

Figure 2.1 Mean US expectancy ratings for CS+ and CS- during 10 acquisition trials (a1 to a10), 10 extinction trials (e1 to e10), and three test trials (t1 to t3) separately for the ABA condition (upper panel) and the AAA condition (lower panel) in Experiment 1. *Note*: Because of varying sample sizes between the different analyses (acquisition, generalization of acquisition, extinction, and renewal) in Experiment 1, some means may slightly differ from means that were used in the analyses.

Skin conductance (SIR). In contrast to rated expectancies, the ANOVA for SIR yielded neither a crucial linear CS-type × Trial (e1 to e10) interaction, $F < 2.14$, nor a linear CS-type × Trial × Condition interaction, $F < 2.53$. Hence, SIR did not reveal the predicted gradual decline between CS+ and CS- responses across extinction trials. However, a trend for the main effect of trial, $F(6.86, 343.03) = 1.75$, $p = .10$, and a significant linear trial main effect, $F(1, 50) = 9.49$, $p < .01$, were

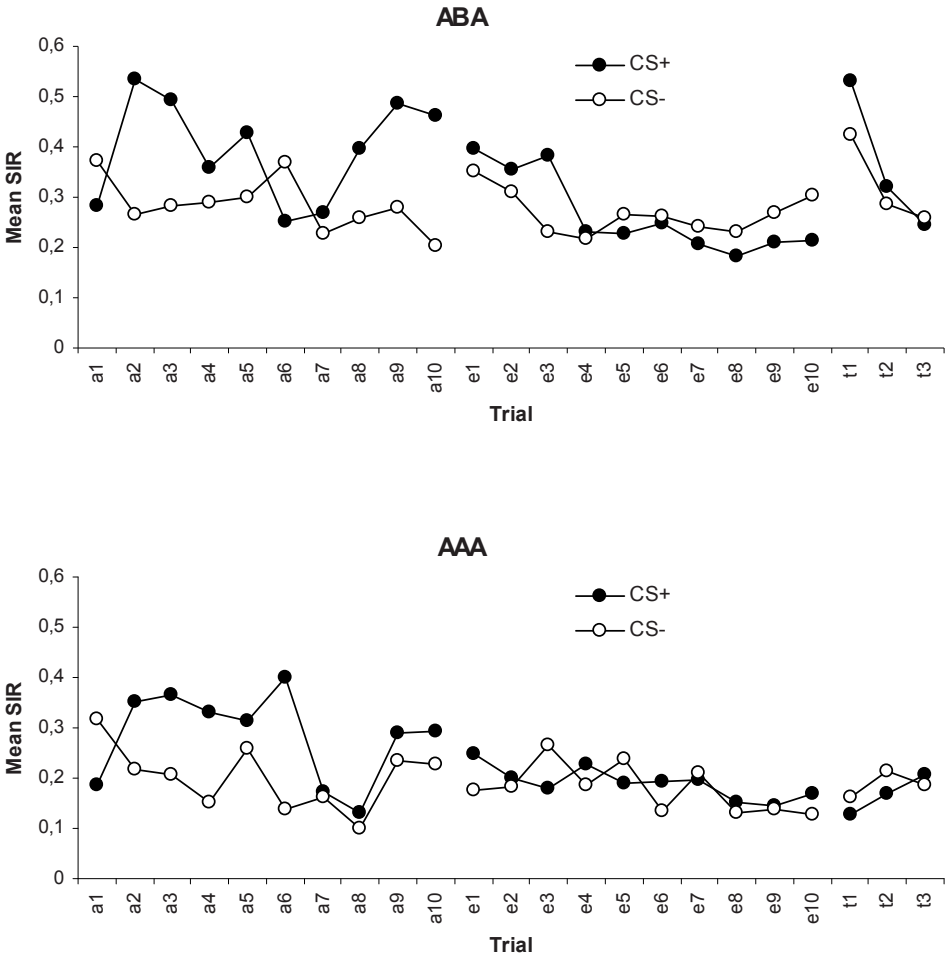

Figure 2.2 Mean square root range-corrected second interval responses (SIR) for CS+ and CS- during 10 acquisition trials (a1 to a10), 10 extinction trials (e1 to e10), and three test trials (t1 to t3) separately for the ABA condition (upper panel) and the AAA condition (lower panel) in Experiment 1. *Note*: Because of varying sample sizes between the different analyses (acquisition, generalization of acquisition, extinction, and renewal) in Experiment 1, some means may slightly differ from means that were used in the analyses.

observed, indicating an overall decline in responses. As an additional analysis showed that no differential responding was present on the last extinction trial, $F < 1$, the results were considered as evidence of the extinction effect.

Renewal

US expectancy ratings. The analysis yielded a CS-type × Trial (e10, t1) interaction, $F(1, 49) = 7.08$, $p = .01$, and, most crucial to our hypothesis, a CS-type × Trial × Condition interaction, $F(1, 49) = 8.05$, $p < .01$. To clarify the latter interaction, simple interactions (CS-type × Trial) were performed within each condition. In the ABA condition, the significant CS-type × Trial interaction, $F(1, 23) = 6.80$, $p = .02$, reflects a larger increase for CS+ ratings than for CS- ratings from extinction to test. Pairwise comparisons showed a significant increase from the last extinction to the first test trial for CS+ ratings ($p < .01$) as well as for CS- ratings ($p < .01$). In line with expectation, in the AAA condition an interaction between CS-type and trial was absent, $F < 1$, indicating a similar decrease in ratings for both CSs. In sum, these results show a clear evidence of the ABA renewal effect.

Skin conductance (SIR). While the analysis revealed a main effect of trial (e10, t1), $F(1, 50) = 4.70$, $p = .04$, indicating an overall increase in responding from extinction to test, there was no CS-type × Trial interaction, $F < 1$. Moreover, the interaction of main interest, CS-type × Trial × Condition, revealed no significance, $F < 1.82$. These results indicate no direct evidence of a renewal effect for electrodermal responses by comparing both conditions and this is in line with findings of Vansteenwegen et al. (2005).

Inspection of Figure 2.2, suggests that the lack of a renewal effect may be explained by unexpectedly large responses to CS- on the last extinction and the first test trial in the ABA condition. Therefore, we additionally conducted a separate 2 (trial: ext10, t1) × 2 (condition: AAA, ABA) mixed ANOVA for only CS+ responses (see also Vansteenwegen et al., 2005). This analysis showed an increase in responding to CS+ from extinction to test for the ABA condition relative to the AAA condition, as reflected by a significant Trial × Condition interaction, $F(1, 51) = 5.94$, $p = .02$. Pairwise comparisons revealed a significant increase in CS+ responses between the last extinction and the first test trial in the ABA condition ($p < .01$), but no significant change in CS+ responses between extinction and test in the AAA condition ($p = .68$). Hence, participants showed a recovery of responding to the CS+ upon changing the context after extinction.

Discussion

Experiment 1 demonstrates a clear ABA renewal effect for US expectancy ratings. There was an obvious recovery of shock expectancy following a context change

after extinction (ABA), whereas no such recovery was observed in the absence of a context change (AAA). The results for the skin conductance data were less convincing. Only analyzing simple conditioning effects, that is, responding to CS+, a context change after extinction (ABA) resulted in recovered conditioned responding in comparison to no context change (AAA). Given that discriminative learning (CS+ vs. CS-) is considered as the golden standard in human fear conditioning research with skin conductance as dependent variable, these results should be interpreted with caution. Although our skin conductance results are in line with the findings reported by Vansteenwegen et al. (2005), only the expectancy ratings showed convincing evidence of a renewal effect.

Several explanations may be given for the lack of a strong renewal effect for the electrodermal data. A well-known problem in measuring electrodermal responses is that they suffer from habituation, that is, they tend to decline over time as a result of repeated stimulus presentation (e.g., Lovibond, Davis, & O'Flaherty, 2000). As such, responses to CS+ on the first test trial in the ABA condition might suffer from a habituation effect. Another explanation may be that responses to CS- on the first test trial were influenced by an US omission effect (see for an extensive discussion Neumann, 2006). In general, this effect refers to the supposed impact of omission of an expected US after a CS+ on the next presentation of a CS-. That is, after an unreinforced CS+ the US is subsequently expected on the CS-. Inspection of stimulus presentation learned that two-third of the participants in the ABA condition had started the test phase with an unreinforced CS+. This may have resulted in elevated CS- responses and, thereby, diminishing a potential renewal effect. The observed increment in rated expectancies to CS- between extinction and test are in line with such an explanation. The second experiment addressed these potential problems by reducing the number of acquisition trials and counterbalancing the order of presentation of the first CS+ and CS- in the test phase.

Experiment 2

The aim of Experiment 2 was to test our prediction of smaller ABC than ABA renewal. This prediction is in contrast with the extinction model since this model predicts that only a context switch between extinction and testing determines the renewal effect (i.e., no difference between ABA and ABC renewal). No renewal was expected in the AAA control condition. Furthermore, Experiment 2 was aimed to replicate the findings of Experiment 1.

Method

Participants

Eighty-one undergraduate students (28 men, 53 women) participated in return for course credits or a small payment. Participants did not report heart complaints, an epileptic disorder or colour blindness. Assignment to one of the three conditions was at random with the restriction that conditions were matched on sex as close as possible. Due to experimenter error, data of 2 participants were not included, reducing the final sample to seventy-nine participants: AAA (n = 28: 11 men, 17 women), ABA (n = 25: 8 men, 17 women), and ABC (n = 26: 8 men, 18 women).

Context manipulation

Contexts were again manipulated by coloured lighting. In the present experiment, three contexts (pink, yellow, or green light) were provided by six tubes (three pink, two yellow, and one green). To meet the loss of intensity of light by using fewer tubes per context, reflective sheets were applied to the wall in front of the participant in order to optimize differentiation between contexts.

Apparatus

The apparatus was identical to that used in Experiment 1, except for the labels of the US expectancy rating scale and electrode attachment. The word 'shock' in the labels of the rating scale was replaced by 'electric stimulus' in order to reduce the negative connotation of the word shock. This time skin conductance electrodes were attached to the medial phalanges of the index and second fingers of the non-preferred hand after cleaning them with tap water.

Procedure

Experiment 2 was conducted in the same laboratory as Experiment 1, using in general the same procedure with some modifications. The US selection procedure was changed in the way that participants in Experiment 2 were asked to select a level that was not painful, but definitely uncomfortable and demanding some effort to tolerate. In Experiment 2, participants did not receive presentation of the CSs prior to the experiment, but instead two unreinforced habituation CSs (1 CS+, 1 CS-) were presented at the beginning of the experiment, preceding the acquisition trials. Order of habituation stimuli was counterbalanced across participants. In Experiment 2, participants were asked to return the US expectancy pointer to the

middle of the rating scale (5), instead of the lower end (0), after a slide was gone. So, its starting point before each rating was the uncertain position.

To prevent habituation of electrodermal responding, the number of acquisition trials was reduced to seven trials for both CSs. Participants in all conditions (AAA, ABC, ABA) received the acquisition trials in Context A. The number of extinction trials was also reduced to eight trials for both stimuli. For the AAA condition extinction was provided in Context A, while for the other two conditions (ABC, ABA) extinction took place in Context B. Unlike Experiment 1, switching to Context B occurred 12 s prior to the onset of the first extinction trial in order to stabilize electrodermal activity after the last acquisition trial. To control for potential US omission effects, the first two extinction trials and the first two test trials consisted of a CS+ and a CS- and were presented in a counterbalanced order. Participants who started with a CS+ in the extinction phase, also started with a CS+ in the test phase and vice versa. Testing occurred either in the acquisition context (Context A) for Conditions AAA and ABA, or in a novel context (Context C) for Condition ABC. Switching to Context A or C was initiated 12 s prior to the onset of the first test trial. The colours of the lighting that served as Contexts A, B, and C were counterbalanced across participants. Habituation, acquisition, extinction, and test phase were presented without interruption.

Scoring, response definition, and statistical analysis

Scoring for US expectancy ratings and skin conductance was identical to Experiment 1. For 1 participant, skin conductance responses could not be range corrected as all her unconditioned responses began within 1 s after US onset. For this participant, range correction was conducted using the maximum range elicited by the US starting between 8-15 s after CS onset. Like in Experiment 1, no differences were found in maximum ranges across conditions.

Analysis of the expectancy and electrodermal data was similar to Experiment 1 with some exceptions. The factor trial in the analyses of acquisition and extinction had seven respectively eight levels. The between-subjects factor order (CS+CS- vs. CS-CS+) was added to the analyses of generalization of acquisition and renewal resulting in four-way mixed ANOVAs. Moreover, in all analyses, the factor condition had three levels (AAA, ABC, ABA). To examine the interactions most pertinent to our hypotheses (CS-type × Trial × Condition), Helmert's contrasts were performed to compare the control condition with the experimental conditions (AAA vs. ABC and ABA) with regard to the CS-type × Trial

interaction. In addition, the experimental conditions were directly contrasted (ABC vs. ABA) for this interaction (Field, 2005).

Results

Of the 79 participants, 3 participants failed to understand instructions for the use of the pointer to rate US expectancies. Their expectancy ratings were left out. Therefore, the results for US expectancy ratings and skin conductance are based on 76 respectively 79 participants.

US characteristics

Selected intensities ranged from 4 to 40 mA with a mean of 12.47 mA (SD = 7.32). After the experiment, participants rated the US as fairly unpleasant (M = -5.77, SD = 2.24) and intense (M = 2.87, SD = 0.88). There were no differences between conditions in selected intensities or in the way participants experienced the US, all Fs < 1.

Acquisition

US expectancy ratings. Figure 2.3 displays mean expectancy ratings to CS+ and CS- across trials for each condition separately (AAA, ABC, ABA). The ANOVA revealed the crucial linear CS-type × Trial (a1 to a7) interaction, $F(1, 73) = 456.96$, $p < .01$. Importantly, the linear CS-type × Trial × Condition interaction was not significant, $F < 1$. This suggests that participants in all conditions showed a gradual increase in differentiation between shock expectancies to CS+ and CS- from the first to the last acquisition trial. Hence, an acquisition effect seemed to be successfully accomplished in all conditions.

Skin conductance (FIR). Figure 2.4 illustrates mean FIR on CS+ and CS- trials per condition. Like for expectancy ratings, the analysis for FIR also yielded the predicted linear CS-type × Trial (a1 to a7) interaction, $F(1, 76) = 12.57$, $p < .01$. The interaction reflects a significantly larger decline in CS- responses than in CS+ responses across acquisition trials and, therefore, a gradual increase in differential responding during acquisition. This pattern of acquisition did not differ between conditions, $F < 1$, indicating a similar acquisition effect in all three conditions.

Skin conductance (SIR). No evidence of an acquisition effect was obtained for SIR. For similar reasons as in Experiment 1 (FIR results), SIR results were not reported.

Generalization of acquisition

US expectancy ratings. There was a CS-type × Trial (a7, e1) interaction, $F(1, 70) = 49.89$, $p < .01$, and, crucially, a CS-type × Trial × Condition interaction, $F(2, 70) = 3.27$, $p = .04$, which was not influenced by the order of the first two extinction trials, $F < 1$. This suggests that the pattern for CS+ and CS- ratings from acquisition to extinction differed between the conditions. In exploring the three-way interaction, a first contrast indicated that the CS-type × Trial interaction was different in the condition without a context change (AAA) compared to the conditions with a context change (ABC and ABA) ($p = .01$). Subsequent simple interactions (CS-type × Trial) revealed a trend for the interaction in the AAA condition, $F(1, 25) = 3.31$, $p = .08$, reflecting a tendency for a larger increase in CS- than CS+ ratings from acquisition to extinction (see Figure 2.3). For the ABA and ABC conditions combined, a significant CS-type × Trial interaction was observed, $F(1, 49) = 33.04$, $p < .01$. Pairwise comparisons showed a significant decrease from the last acquisition trial to the first extinction trial in CS+ ratings ($M_{a7} = 9.52$; $M_{e1} = 9.02$) ($p = .04$) and a significant increase in CS- ratings ($M_{a7} = 0.62$; $M_{e1} = 3.94$) ($p < .01$). A second contrast, which directly compared the CS-type × Trial interaction between the ABC and ABA conditions, was not significant ($p = .76$). Thus, although these results imply some loss of acquired conditioned responding upon a context change, this loss of acquisition was similar for the ABC and ABA conditions.

Skin conductance (FIR). The FIR data partly confirmed the expectancy data. The ANOVA also revealed an interaction between CS-type and trial (a7, e1), $F(1, 73) = 5.36$, $p = .02$, indicating an increase in responses to CS- relative to CS+ between the last acquisition trial to the first extinction trial. In contrast, a context change had no additional effect, as reflected by a non-significant interaction between CS-type, trial and condition, $F < 1$. Furthermore, there was no CS-type × Trial × Condition × Order interaction, $F < 1$. This indicates that acquisition generalized across contexts.

Extinction

US expectancy ratings. As expected, the ANOVA revealed a linear CS-type × Trial (e1 to e8) interaction, $F(1, 73) = 106.16$, $p < .01$, reflecting a gradual decrease in ratings between CS+ and CS- across extinction trials. This extinction effect was similar for all conditions as indicated by a non-significant linear CS-type × Trial × Condition interaction, $F < 1$.

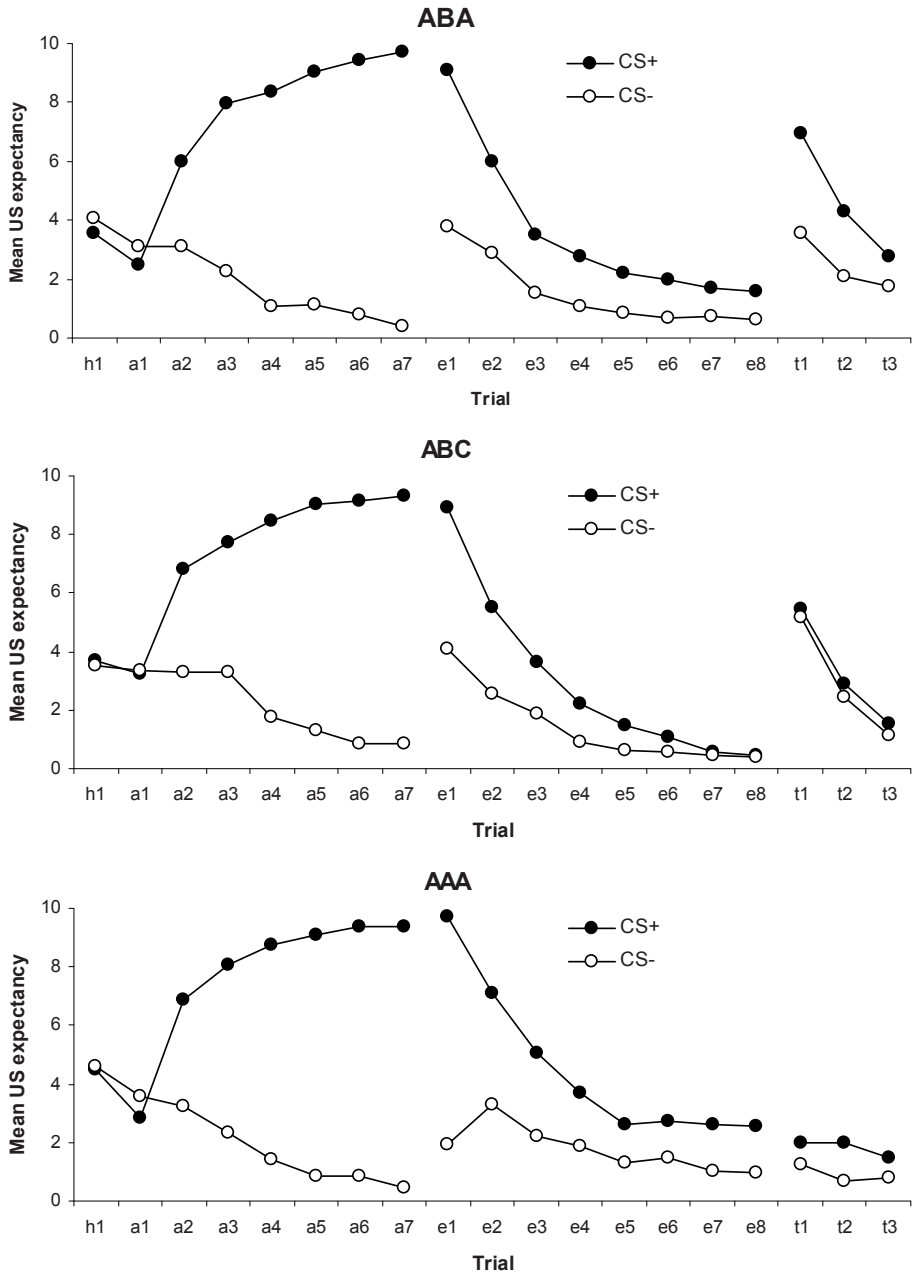

Figure 2.3 Mean US expectancy ratings for CS+ and CS- during one habituation trial (h1), seven acquisition trials (a1 to a7), eight extinction trials (e1 to e8), and three test trials (t1 to t3) across orders (CS+ CS-, CS-CS+) separately for the ABA condition (upper panel), the ABC condition (middle panel), and the AAA condition (lower panel) in Experiment 2.

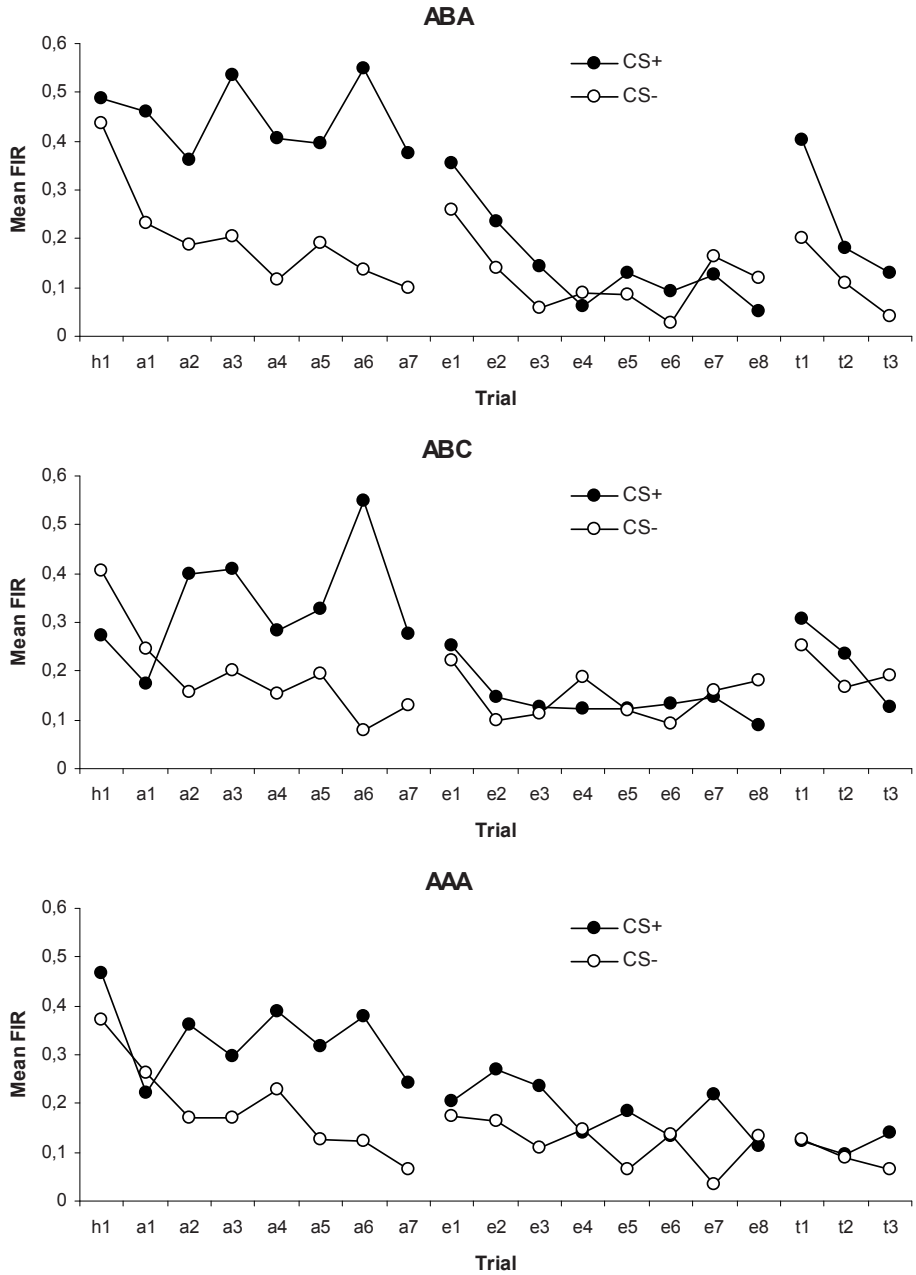

Figure 2.4 Mean square root range-corrected first interval responses (FIR) for CS+ and CS- during one habituation trial (h1), seven acquisition trials (a1 to a7), eight extinction trials (e1 to e8), and three test trials (t1 to t3) across orders (CS+CS-, CS-CS+) separately for the ABA condition (upper panel), the ABC condition (middle panel), and the AAA condition (lower panel) in Experiment 2.

Skin conductance (FIR). Similar to expectancy ratings, the analysis for FIR yielded a linear CS-type × Trial (e1 to e8) interaction, $F(1, 76) = 3.89$, $p = .05$. This indicates that during extinction trials the acquired differentiation between CS+ and CS- responses declined. In addition, no linear CS-type × Trial × Condition interaction was obtained, $F < 1$, indicating that the observed extinction effect did not differ across conditions.

Renewal

US expectancy ratings. The ANOVA yielded a trend for the CS-type × Trial (e8, t1) interaction, $F(1, 70) = 3.08$, $p = .08$, and, most pertinent to our hypothesis on renewal, a significant CS-type × Trial × Condition interaction, $F(2, 70) = 7.07$, $p < .01$. However, the crucial interaction depended on the order of stimulus presentation in the test phase, as reflected by the significant CS-type × Trial × Condition × Order interaction, $F(2, 70) = 5.47$, $p < .01$. To examine this four-way interaction, three-way interactions (CS-type × Trial × Condition) were calculated for both orders separately. For participants who started the test phase with a CS+, the CS-type × Trial × Condition interaction was not significant, $F < 1$, whereas for participants starting the test with a CS-, the interaction yielded significance, $F(2, 36) = 7.83$, $p < .01$. Contrasts were performed to explore whether this latter interaction indicated a difference in a potential renewal effect between the ABA and ABC conditions. A first contrast showed that the CS × Trial interaction was significantly different for the AAA condition compared with the ABC and ABA conditions combined, ($p < .01$). Subsequent simple interactions (CS-type × Trial) revealed no significant results for the AAA condition, Fs < 1.97, reflecting no significant changes in CS+ and CS- ratings from extinction ($M_{CS+} = 2.54$; $M_{CS-} = 1.19$) to test ($M_{CS+} = 1.97$; $M_{CS-} = 1.61$). In contrast, for the ABA and ABC conditions together, the significant CS-type × Trial interaction, $F(1, 23) = 13.71$, $p < .01$, reflects a larger increase in CS+ than CS- ratings upon a context change between extinction ($M_{CS+} = 0.97$; $M_{CS-} = 0.46$) and test ($M_{CS+} = 6.08$; $M_{CS-} = 2.62$) (i.e., renewal). A second contrast indicated that the ABC and ABA conditions differed significantly with regard to the CS-type × Trial interaction, $p < .01$. Simple interactions (CS-type × Trial) within each level of condition revealed a significant interaction for the ABA condition, $F(1, 11) = 20.13$, $p < .01$, demonstrating a larger increase in CS+ than CS- ratings from extinction ($M_{CS+} = 1.56$; $M_{CS-} = 0.72$) to test ($M_{CS+} = 7.39$; $M_{CS-} = 1.26$) (i.e., ABA renewal). Pairwise comparisons showed a significant increase in CS+ ratings ($p < .01$) and a trend for an increase in CS- ratings ($p =$

.06). For the ABC condition, a CS-type × Trial interaction was absent, $F < 1.40$, indicating a similar increase in ratings for both CSs from extinction ($M_{CS+} = 0.39$; $M_{CS-} = 0.21$) to test ($M_{CS+} = 4.77$; $M_{CS-} = 3.98$), $F(1, 11) = 34.33$, $p < .01$. In sum, the analyses suggest that only testing in the original acquisition context (ABA) yielded the predicted renewal effect, whereas renewal was not apparent in a novel context (ABC).

Skin conductance (FIR). Like expectancy data, the ANOVA for FIR revealed a CS-type × Trial (e8, t1) interaction, $F(1, 73) = 6.29$, $p = .01$, reflecting a larger increase in responses to CS+ compared to CS- between the last extinction and the first test trial. Although FIR followed a similar pattern as expectancy ratings, the ANOVA did not reveal the crucial CS-type × Trial × Condition interaction, $F < 1.65$. Thus, contrary to the hypothesis, the skin conductance data indicated no renewal effects comparing all three conditions. This finding was not explained by differences between orders, $F < 1$. Therefore, the electrodermal responses did not support the obtained difference between ABA and ABC renewal for US expectancy ratings.

One issue is that renewal effects for electrodermal responses might not have been strong enough to detect overall differences between conditions. To see whether renewal effects were present in each condition separately (ABA, ABC), and to enable a comparison with Experiment 1, two 2 (CS-type: CS+ vs. CS-) × 2 (trial: e8 vs. t1) × 2 (condition: AAA vs. ABA or ABC) × 2 (order: CS+CS- vs. CS-CS+) mixed ANOVAs were conducted. Comparing Conditions ABA and AAA revealed a trend for the crucial CS-type × Trial × Condition interaction, $F(1, 49) = 3.30$, $p = .08$. This suggests a tendency for an increase in CS+ relative to CS- responses between extinction and test in the ABA condition and a decrease in CS+ relative to CS- responses in the AAA condition. This finding was not influenced by an order effect, $F < 1.05$. Hence, a trend for the ABA renewal effect was obtained. Comparing Conditions ABC and AAA did not reveal the crucial CS-type × Trial × Condition interaction, $F < 1$, or a CS-type × Trial × Condition × Order interaction, $F < 1$, and thus no evidence of ABC renewal was observed.

Discussion

The main finding of Experiment 2 was that, in line with our predictions, the renewal effect in the ABA condition was stronger than in the ABC condition for US expectancy ratings. This effect depended on the order of stimulus presentation in the test phase. Although electrodermal data followed a similar pattern as

expectancy ratings, a difference between ABA and ABC renewal could not be confirmed. However, analyzing separately, electrodermal responses revealed evidence of ABA renewal but not of ABC renewal. This latter provides indirect evidence for the presence of stronger ABA than ABC renewal in autonomic responding. These findings suggest that the specific context change after extinction (ABA or ABC) influenced the degree of renewal. This is at variance with the original model of extinction learning (Bouton & Ricker, 1994).

A renewal effect was strictly taken absent in the ABC condition with regard to US expectancy ratings. Although we predicted that ABC renewal would be smaller than ABA renewal, we did not expect that ABC renewal would be completely absent. This lack of renewal can be explained by equal increases in CS+ and CS- expectancy ratings between extinction and test in the ABC condition. On the first test trial both means were around the middle of the rating scale. It seemed as if participants were uncertain whether to expect a shock on both CSs in the novel context. An US omission effect could not account for this unpredicted high level of CS- ratings because these participants received the unreinforced CS+ after the CS- in the test phase.

Finally, in Experiment 1, conditioned responding was acquired for SIR but not for FIR, while in Experiment 2 the reversed result was observed. No explanation can be given for this difference in electrodermal responding between Experiments 1 and 2. Note, however, that for human conditioning studies, it is not uncommon to find inconsistent results on these indices of conditioned responding (Lipp, Neumann, & Mason, 2001).

General discussion

Experiment 1 replicated the renewal effect in humans within an ABA renewal paradigm previously demonstrated by Vansteenwegen et al. (2005). In an acquisition phase, one slide (CS+) was contingently paired with an US while another slide (CS-) was never followed by the US in Context A. During extinction, both slides were presented without the US in Context B. Changing the context after extinction resulted in a significant increase of US expectancy ratings to CS+ relative to CS- in Context A, that is, ABA renewal. Although no renewal effect was demonstrated for the physiological data with respect to discriminative learning (CS+ vs. CS-), a less stringent method, by analyzing simple conditioning effects (CS+), showed evidence of renewal of conditioned responding (cf. Vansteenwegen et al., 2005). The results of Experiment 2 also demonstrated an ABA renewal effect

for expectancy ratings and, in contrast to Experiment 1, a trend for ABA renewal for autonomic responses. We view these results as supportive of a central feature of Bouton's theory – that an extinction procedure does not erase learned fear associations but instead involves new learning that is context dependent. Moreover, in the current study, renewal was demonstrated with online US expectancy ratings, which are less susceptible to demand effects than the retrospective ratings used in Vansteenwegen et al. (2005). Therefore, the present results may be taken as a further support for the hypothesized context dependency of extinction in humans.

Experiment 2 demonstrated larger renewal of shock expectancy in the original context of fear acquisition (ABA) than in a novel context (ABC). Electrodermal responses showed indirect evidence of a larger return of conditioned responding in the ABA condition than in the ABC condition. Although these findings are in line with our predictions, they are in contrast with the extinction model stating that renewal is only determined by a context change after extinction, irrespective of the specific context change. Note that smaller ABC than ABA renewal has also been found in animals (Harris et al., 2000).

The present design does not allow drawing any conclusions with respect to the mechanisms that may explain the observed difference in renewal between the ABA and ABC conditions. One explanation might be that fear acquisition may have become context dependent as extinction took place in a different context (Context B) than acquisition (Context A). Since extinction involves the CS to be no longer informative for the occurrence or non-occurrence of the US (e.g., Bouton, 2002), human subjects may have retrospectively searched for the best predictor of the CS-US association: the acquisition context. In other words, the acquisition context may have been reconsidered as important for the CS-US fear association. Such explanation would correspond with the present findings that ABA renewal is larger than ABC renewal. Alternatively, it may be that fear associations were already controlled by the acquisition context before extinction started. For instance, the perception of CSs across the different contexts might not have been identical, which may have prevented full generalization of acquisition to another context. In accordance with such an explanation, both experiments demonstrated some loss of acquisition following a context change for US expectancy ratings. Accordingly, renewal of conditioned responding would be larger in a context similar to the acquisition context (ABA) than in a novel context (ABC). Future research is required to investigate whether retrospective contextualization and/or

contextualization during acquisition contribute to the attenuation of ABC renewal in humans.

In sum, the present study provides further support for the contextual control of extinction in humans. In clinical practice, this effect may be observed in the relapse patients experience when leaving the treatment context. In addition, the finding of larger renewal of extinguished fear in the original acquisition context than in a novel context suggests that behaviour change is not easily sustained in the context in which fear was originally acquired. This is in contrast to the current model of extinction learning that predicts equal relapse of fear following any context change after extinction.

The present results may have implications for the development of new treatment methods. Until now, research has mainly focused on reducing relapse after exposure treatment by generalization of extinction to other contexts. For example, conducting extinction in multiple contexts or with multiple stimuli seems to be a promising way to prevent relapse (Chelonis, Calton, Hart, & Schachtman, 1999; Gunther et al., 1998; Rowe & Craske, 1998). The underlying idea is that extinction in multiple contexts or with multiple stimuli enhances the probability that new contexts share features with the extinction situation and, therefore, result in better retrieval of extinction. However, it is not possible to cover all sorts of situations in therapy that patients might encounter in the future. Hence, there will always be a risk for patients to be confronted with the feared object in a new situation. In addition to focusing on the generalization of extinction, the present results suggest that it might also be promising to examine factors that enhance the contextualization of fear associations in order to prevent relapse after successful therapy. It is known that anxiety patients tend to generalize threat to all kind of situations. We propose here that it may be functional to encourage patients with anxiety disorders to contextualize their fear memories (i.e., CS-US associations). A similar approach has recently been put forward as a framework for the treatment of posttraumatic stress disorder in which the contextualization of trauma memories may reduce re-experiencing symptoms (Ehlers & Clark, 2000). Contextualization refers to learning that similar cues (CS) can have different meanings in different contexts. For example, as illustrated by Ehlers and Clark, a rape victim may learn that having sex predicted rape in the trauma-related context but not in the present context with her husband. If, indeed, fear memories can be contextualized, this might open an interesting hypothesis that contextualization within an extinction procedure (i.e., learning that the CS predicted the US only in Context A) might reduce renewal of conditioned fear in novel contexts.