



Testing a novelty-based extinction procedure for the reduction of conditioned avoidance

Angelos-Miltiadis Krypotos*, Iris M. Engelhard

Department of Clinical Psychology, Utrecht University, The Netherlands

ARTICLE INFO

Keywords:

Fear
Anxiety
Therapy
Phobias

ABSTRACT

Background and objectives: Excessive avoidance towards non-dangerous cues is a key diagnostic criterion across anxiety-related disorders. Despite current therapies being successful in reducing such avoidance, relapse rates remain high. Based on recent findings, according to which learned fear responses were reduced after the presentation of the fear stimulus with a novel-neutral event (*novel-based extinction*), we tested whether novel-based extinction could diminish conditioned avoidance.

Methods: Forty-six participants completed a Pavlovian acquisition procedure during which two pictures of a spider were presented, one of which (CS⁺) was always followed by a shock (US), while the other (CS⁻) was never followed by a US. Next, participants learned that they could avoid the shock by pressing a computer button. An extinction and response procedure followed. During this phase, the control group was presented with both CSs that were not followed by the US. The experimental group encountered both CSs, but the CS⁺ was followed by a neutral event (i.e., presentation of a tone). Return of avoidance (i.e., button presses) and fear (i.e., US-expectancies and fear-ratings) towards both CSs was tested after three unexpected presentations of the US.

Results: Similar levels of return of avoidance and explicit fear were found for both groups.

Limitations: We collected no physiological measures of fear and we assessed only the short-term effects of our manipulation.

Conclusions: Our results do not support the hypothesis that novelty-based extinction reduces avoidance responses. This study can serve as a first exploration of novelty-based extinction for reducing avoidance and explicit measures of fear.

1. Introduction

Avoidance towards dangerous cues is necessary for adaptive functioning. Alas, often excessive avoidance is expressed towards largely safe cues (e.g., social groups, doorknobs, dizziness). In such cases, avoidance loses its adaptive role and can transform into a symptom of an anxiety-related disorder (e.g., social anxiety disorder, obsessive-compulsive disorder, panic disorder). Given the significant impact of anxiety-related disorders in the lives of the sufferer and the society (Greenberg et al., 1999; Konnopka, Leichsenring, Leibing, & König, 2009), the reduction of pathological avoidance is an issue of high scientific and societal value.

Research and interventions for anxiety-related disorders have mainly focused on Pavlovian processes (Treanor & Barry, 2017). For example, an evidence-based treatment for reducing anxiety symptomatology is exposure therapy. A common laboratory model of this clinical intervention is fear extinction (for a detailed comparison between exposure therapy and extinction, see Scheveneels, Boddez,

Vervliet, & Hermans, 2016). Fear extinction entails the presentation of an initially innocuous stimulus (e.g., a picture of a spider; Conditioned Stimulus or CS) that was previously paired with an evolutionary dangerous stimulus (e.g., a shock; Unconditioned Stimulus or US), without the US. To reduce fear and avoidance, extinction is often combined with response prevention (ExtRP; Voss, Mejta, & Reid, 1974), so as to make sure that the participant is confronted with the fearful stimulus (see Rachman, Radomsky, & Shafraan, 2008 for the role of avoidance in extinction therapy). However, avoidance behavior can persist after extinction (Lovibond, Chen, Mitchell, & Weidemann, 2013) and causes a return of fear (Uijen, Leer, & Engelhard, in press; Vervliet & Indekeu, 2015).

The failure to reduce avoidance in the long term can be explained by referring to the ambiguous meaning of the CS at the end of the ExtRP procedure. Research in both animal and humans (Bouton, 1993, 2000, 2002) suggests that the mere presentation of the CS without the US does not lead to the unlearning of the initial CS-US associations but rather to the formation of a new *extinction memory* (i.e., CS-noUS associations)

* Corresponding author. Heidelberglaan 1, 3584 CS, Utrecht, The Netherlands.
E-mail address: amkrypotos@gmail.com (A.-M. Krypotos).

Table 1

Experimental phases. Fear ratings were collected before and after each phase. The number of trials in each phase is presented in brackets.

Fear Conditioning	Avoidance Conditioning	Response Prevention and Extinction	US (3)	Reinstatement Test	Reextinction Test
CS+ (2)	CS+ (8)	CS+ (12)		CS+ (2)	CS+ (4)
CS- (2)	CS- (8)	CS- (12)		CS- (2)	CS- (4)

that fights for dominance over the initial *acquisition memory* (i.e., CS-US associations). Based on these results, it can be argued that the effects of ExtRP could be enhanced by reducing the ambiguity of the CS meaning at the end of fear extinction.

New research has provided evidence towards this direction. In two experiments, [Dunsmoor, Campese, Ceceli, LeDoux, and Phelps \(2015\)](#) have shown that *novelty-based extinction*, where a CS is associated during an extinction procedure with a novel, neutral event rather than a non-event, is sufficient in reducing the return of extinguished fear responses as were measured in terms of freezing in animals or skin conductance responses in humans. [Dunsmoor et al. \(2015\)](#) argued that the pairing of the CS⁺ with a novel stimulus, rather than just the absence of any event, made the extinction memory stronger, reducing the return of fear.

Inspired by these findings, we sought to investigate whether the combination of the novelty-based extinction procedure with response prevention could block the return of avoidance. Human participants underwent an avoidance learning procedure where they learned to avoid a CS by pressing a computer button. Subsequently, participants were separated into two groups, with one group undergoing a standard ExtRP and the other group undergoing a novelty based extinction in combination with response prevention. The return of avoidance and subjective fear was measured after the presentation of unexpected USs (i.e., *reinstatement* procedure; [Bouton, 2002](#)). We expected that the novelty-based extinction group (NERP) would exhibit less avoidance, indicated by the number of button presses, and less return of fear, as indicated by US-expectancies and fear ratings, during the reinstatement phase compared to the ExtRP group.

2. Materials and methods

2.1. Participants

Forty-six healthy individuals (33 females; mean age, SD: 22.33 years 2.51), participated in the study in exchange of student credits or 8 euros. Participants were randomly and equally assigned to the NERP and the ExtRP group. All procedures have been approved by the Ethics Committee Board of Utrecht University (FETC16-054). Regarding the sample size, we decided that because no prior studies have been conducted with our design, the minimal interesting effect for our study would be a medium effect size. Please note that for a Cohen's *f* of .25 (medium effect size), 2 groups (NERP and ExtRP), 2 measurements (CS⁺ and CS⁻), alpha of 0.05, and power of .80, the minimal total size should be at least 34 individuals. Due to the new experimental paradigm, we had decided to collect more data due to potential participants having to be excluded from further analyses due to unsuccessful manipulation (see below).

2.2. Material

2.2.1. Self reports

Participants rated their expectancy of a US occurrence during each CS presentation on a scale anchored from -5 (certainly no electric stimulus) to +5 (certainly an electric stimulus). Fear levels for each CS were evaluated using a continuous scale anchored from 0 (not afraid at all) to 10 (very afraid). Participants also rated the surprisingness of the neutral tone, in case they had heard it during the computer task, in a continuous scale from -5 (not surprising at all) to 5 (much surprising).

Lastly, participants rated their motivation to complete the computer task and fill in the questionnaires in two different rating scales ranging from -5 (really low) to 5 (really high).

Participants filled in the following questionnaires: STAI-S and STAI-T ([Spielberger, Gorsuch, & Lushene, 1970](#)), Intolerance of Uncertainty (IOU; [Bruin, Rassin, Heiden, & Muris, 2006](#)), the Anxiety Sensitivity Index (ASI; [Peterson & Reiss, 1993](#)), and the neuroticism scale of the Eysenck Personality Questionnaire (EPQ-N; [Eysenck & Rachman, 1975](#)).

2.2.2. Stimuli

Pictures of 2 spiders (items 1200 and 1201 from [Lang, Bradley, and Cuthbert \(1999\)](#); 13 cm × 10.5 cm) served as CSs. A picture of a manikin figure (4 cm × 4 cm) was also presented on each trial (see below).

An electric shock administered to the middle phalange of the index and middle fingers of the participants' non-dominant hand served as a US ([Engelhard, Uijen, Seters, & Velu, 2015](#)). The US was generated by a Coulbourn Transcutaneous Aversive Finger Stimulator (E13-22). The intensity of the shock was individually set to a level that was "highly annoying but not painful" ([Krypotos, Efftig, Arnaudova, Kindt, & Beckers, 2014](#)).

Similar to [Dunsmoor et al. \(2015\)](#), a short bleep sound of 60 db served as the neutral event presented in the NERP (see below).

2.3. Procedure

For a schematic depiction of the experimental procedure see [Table 1](#).

Prior to the beginning of the main experiment, participants read the information brochure, signed the informed consent form, and filled in the STAI-S. Participants were then fitted to the shock electrodes and the shock intensity was determined.

The experiment started with the fear ratings of each CS. Then, on-screen and oral instructions informed participants that they would see pictures of two different spiders, one of which would sometimes be followed by a shock while the other would never be followed by a shock. Instructions stressed that participants had to figure out the contingencies between the CSs and the US. They could rate their expectancy of a US occurring by using the expectancy rating scale that would be presented at the beginning of each trial. They were then asked to put on the headphones. In order to not reveal the future presentation of the surprising tones in the NERP group, instructions mentioned that the headphones served the blocking of any background noise.

During the Pavlovian acquisition phase, each CS was presented twice at the center of the screen, with the manikin presented on the bottom of the screen. The manikin was present throughout the whole experimental task. This number of Pavlovian trials is in line with similar avoidance learning tasks (e.g., [Vervliet & Indekeu, 2015](#)). Also, our prior studies with similar instructions about the CS-US contingencies revealed that Pavlovian differentiation reaches high levels after only 2 trials (e.g., [Krypotos et al., 2014](#)). Each trial started with 3 s presentation of the CS and the manikin. Then, the US-expectancy scale was presented for 8 s. Participants could rate their expectancy in the first 5.5 s. In case of a CS⁺ trial, the US was presented after 7.5 s from the point that the US expectancy scale was presented. After presentation of the US Expectancy scale (11s after trial onset), the CS was presented together with the manikin for 3.75 s. This last period was used for

presenting the manikin moving during the later phases of the experiment (see below). The inter-time intervals (ITIs) ranging from 15 to 25 msec (steps of 5 msec).

Next, participants were informed that in the following phase they could avoid the shock presentation by pressing the spacebar. The avoidance conditioning phase followed. During this phase, participants saw 8 trials per CS (i.e., 16 trials in total). In case participants did not press the spacebar during the first 3 s of the trial (i.e., before the US-expectancy scale was presented), the US was presented at the end of each CS⁺ trial. In case participants pressed the spacebar during the CS⁺ presentation, the manikin gradually walked towards the bottom of the screen, during the last 3.75 s of the trial, while the CS size reduced (width 10.5 cm, 8 cm, 5.30 cm and height 8 cm, 5.30 cm, 2.6 cm respectively). This gave the visual impression that the manikin was actually escaping the CS and, as such, avoiding the US. By having this visual effect, rather than having the no on-screen changes that other human avoidance experiments have used, our task better resembles avoidance learning procedures in animals (e.g., shuttle box experiments; see (J. LeDoux, Moscarello, Sears, & Campese, 2017) for a review), in which animals have to distance themselves from the CS in order to avoid the US. Pressing the button during the CS⁻ trials did not have any effect on the manikin or the CS. Before the beginning of the avoidance conditioning phase, participants were asked to continue rating their US-expectancies, using the same instructions given before the beginning of the Pavlovian phase. At the conclusion of this phase, participants rated their fear for each CS.

The response prevention and extinction phase followed, during which participants were informed that in the coming trials the spacebar would no longer function. Despite these instructions, participants could in principle still press the spacebar. During this phase no US was presented. However, for the NERP group, the presentation of the neutral tone was presented at the end of each CS⁺ trial.

Following the end of the previous phase, participants rated their level of fear for each CS. Then, the US was presented three times on its own preceding the reinstatement test, without any prior notification. The reinstatement test ended after two trials and was followed by the fear evaluation of each CS. Following the CS evaluations, participants completed the reextinction test phase, with four trials per CS with no US presentation, after which participants had to rate their fear for each CS again. The reextinction phase was added in order to explore whether the novel stimulus would result in faster reduction of fear responses after reinstatement (Leslie & Norwood, 2013). Although there were no explicit instruction about the response availability, participants could in principle press the spacebar during both the reinstatement test and reextinction test phase.

After completion of the last phase of the experiment, participants were asked to fill in the STAI-T, ASI, IOU, and EPQ-N scales, a questionnaire on demographics, as well as evaluate the US and the neutral tone – in case they had heard it at any point during the experiment. Upon filling in all questionnaires, participants were debriefed, thanked, and compensated for their time.

2.4. Data analyses

Between-group differences for all self reports were explored using separate independent sample *t*-tests. For the surprisingness scale we ran a one-sample *t*-test, comparing the mean score of the scale to zero.

US-expectancy ratings were analyzed separately for each phase using separate 2 (CS: CS⁺ vs. CS⁻) × (trial) × 2 (group: NERP vs. ExtRP) repeated measures Analyses of Variance (ANOVAs), with the level of the *trial* factor being adjusted to the number of trials on each phase. For each analysis, stimulus and trial served as the within-subject factors, and group as the between-subject factor. For quantifying the level of reinstatement, we used a 2 (CS) × 2 (trial: end of extinction, beginning of reinstatement) × 2 (group: NERP, ExtRP) ANOVA. For this analysis the time factor was created by calculating the mean of the

last two trials of the extinction and response prevention and the first two trials of the reinstatement test phase (Soeter & Kindt, 2011).

Fear ratings were analyzed for each phase using separate 2 (CS: CS⁺ vs. CS⁻) × 2 (group: NERP vs. ExtRP) ANOVAs, with stimulus serving as the within-subject factor, and group as the between-subjects factor. A 2 (CS) × 2 (phase: extinction vs. reinstatement) × 2 (group) ANOVA was run for analyzing the change in fear ratings before and after the reinstatement phase with CS and phase serving as the within-subjects factors, and group as the between-subjects factor.

Avoidance during the reinstatement test phase was quantified by calculating the proportion of avoided trials for each participant and for each CS separately, for both the reinstatement and reextinction phase combined. We decided to combine the reinstatement phase with the reextinction phase trials so that we could compute the proportion of avoidance across 6 trials, rather than only 2 trials. Similar to previous studies (e.g., Vervliet & Indekeu, 2015) we compared the proportion of avoidance responses for each CS during the avoidance conditioning phase to the number of avoidance responses during the reinstatement phase.

We performed all our analyses within both a frequentist and Bayesian framework. This was done as in contrast to null hypothesis significance testing, our Bayesian analyses could provide relative evidence for both the null and alternative hypothesis. Specifically, by using Bayes Factors, we could grade the *relative* evidence of two competing models. In the case of one-sample Bayesian *t*-tests, for example, someone would compare the alternative model (e.g., that the mean difference is different than zero) to the null model (i.e., the mean is close to zero). As such, if a BF_{10} , where the alternative is compared to the null model, is equal to 3, then that would mean that the alternative model is 3 times more probable than the null model. The reverse would be true in case of BF_{01} that is equal to 3. As such, Bayes Factors can provide relative evidence for the null hypothesis, compared to the alternative hypothesis. For interpreting the relative strength of evidence, someone could use the categories suggested in the literature (e.g., Jeffreys, 1961). However, these categories have often been criticized as they often lead to a cut-off logic, similar to that present in traditional *p*-values. Here, we abstain from using these categories, for arguments we have presented previously (Krypotos, Blanken, Arnaudova, Matzke, & Beckers, 2017a; Krypotos, Klugkist, & Engelhard, 2017b). For the Bayesian analyses, we used separate Bayes factor tests as those described in Rouder and Morey (2012) for the ANOVAs, and Rouder, Speckman, Sun, Morey, and Iverson (2009) for reported *t*-tests. The Bayesian analyses were performed in R (R Core Team, 2016), using the BayesFactor package (Morey & Rouder, 2014). We refer to Bayes factors that quantify the evidence of the data under the experimental hypothesis, relative to the null hypothesis, as BF_{10} , and we refer to the reversed as BF_{01} . For primers on Bayesian analyses for fear conditioning research, we refer to Krypotos et al. (2017b, 2017a). The relevant data and analyses scripts are freely available at osf.io/cy2v5.

3. Results

Before conducting our main analyses, we checked whether each participant had successfully acquired the CS-US contingencies by comparing the mean US-expectancy scores for the CS⁺, compared to the CS⁻ trials, during the acquisition phase. The data of four participants who reported higher, or equal, US-expectancy scores for the CS⁻, compared to the CS⁺, were removed from the analyses. All the main analyses were then performed with the remaining 42 participants (22 in the NERP group). This translated in having .88 power in detecting a medium effect size. No significant between-group differences in terms of age, $t(39.65) = 0.4$, $p = 0.688$, $BF_{01} = 3.089$, sex, $\chi^2 = 0.43$, $p = 0.43$, shock level $t(34.83) = 0.57$, $p = 0.574$, $BF_{01} = 2.915$, motivation to complete the computer task, $t(36.45) = 0.49$, $p = 0.626$, $BF_{01} = 2.986$, or fill in the provided questionnaires $t(35.16) = 0.96$, $p = 0.343$, $BF_{01} = 2.258$, were found. The two groups did not also

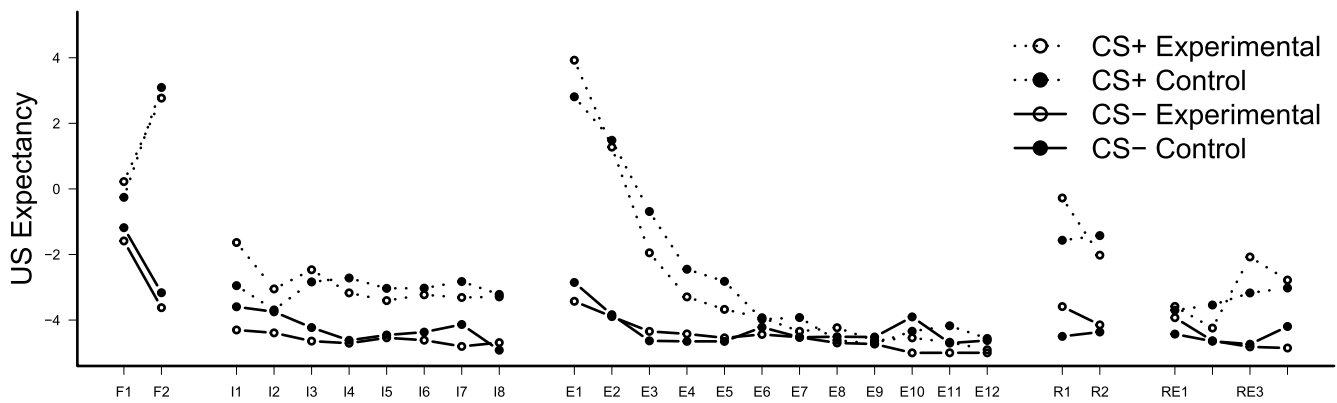


Fig. 1. Mean US-expectancy across all phases for the CS⁺ and CS⁻ for both groups.

differ in terms of any of the questionnaires: STAI-S, $t(38.1) = -1.24$, $p = 0.224$, $BF_{01} = 1.784$, STAI-T, $t(38.07) = -1.23$, $p = 0.225$, $BF_{01} = 1.784$, ASI, $t(38.39) = -1.34$, $p = 0.187$, $BF_{01} = 1.602$, IOU, $t(39.55) = -0.58$, $p = 0.567$, $BF_{01} = 2.892$, EPQ-N, $t(38.01) = -1.1$, $p = 0.28$, $BF_{01} = 2.075$. Lastly, participants in the NERP group rated the sound as surprising $t(21) = 6.72$, $p < 0.001$, $BF_{10} > 1000$.

3.1. Expectancy ratings

For an overview of the mean US expectancies across all phases see Fig. 1.

During the fear conditioning phase participants learned to expect a US after the CS⁺ and not after the CS⁻, CS \times trial, $F(1, 40) = 96.07$, $p < 0.001$, $\eta_G^2 = 0.276$, $BF_{10} > 1000$, an effect that was similar across groups, CS \times trial \times group, $F(1, 40) = 1.51$, $p = 0.226$, $\eta_G^2 = 0.006$, $BF_{01} = 1.942$.

Across the avoidance conditioning phase, the expectancy of a US occurring after the CS⁺ did not differ from the CS⁻, CS \times trial, $F(3.71, 148.4) = 0.6$, $p = 0.647$, $\eta_G^2 = 0.003$, $BF_{01} = 188.624$, across groups, CS \times trial \times group, $F(3.71, 148.4) = 1.12$, $p = 0.346$, $\eta_G^2 = 0.005$, $BF_{01} = 27.106$.

During the response prevention and extinction phase, participants learned to not expect the US after the CS⁺, whereas US-expectancies for the CS⁻ remained the same, CS \times trial, $F(4.4, 176) = 56.38$, $p < 0.001$, $\eta_G^2 = 0.268$, $BF_{10} > 1000$. These results were comparable across groups, CS \times trial \times group, $F(4.4, 176) = 2.13$, $p = 0.073$, $\eta_G^2 = 0.014$, $BF_{01} = 5.49$.

The presentation of the unexpected USs resulted in higher US-expectancies for the CS⁺, CS \times trial; $F(1, 40) = 38.23$, $p < 0.001$, $\eta_G^2 = 0.108$, $BF_{10} > 1000$, a pattern of responses that was similar across groups, CS \times trial \times group, $F(1, 40) = 0.72$, $p = 0.401$, $\eta_G^2 = 0.002$, $BF_{01} = 2.986$.

During the reextinction test phase, the US-expectancies for the CS⁺ decreased, whereas the US expectancies for the CS⁻ remained the same, CS \times trial, $F(2.25, 90) = 4.31$, $p = 0.013$, $\eta_G^2 = 0.027$; $BF_{10} = 3.902$. This effect was comparable across groups, CS \times trial \times group, $F(1, 40) = 0.53$, $p = 0.469$, $\eta_G^2 = 0.002$, $BF_{01} = 2.575$.

3.2. Fear ratings

We summarise the results of fear ratings across all phases in Fig. 2. During the habituation phase, participants in both groups reported similar levels of fear for both CSs, CS, $F(1, 40) = 0.1$, $p = 0.748$, $\eta_G^2 < 0.001$, $BF_{01} = 4.12$, CS \times group, $F(1, 40) = 0.81$, $p = 0.375$, $\eta_G^2 = 0.003$, $BF_{01} = 2.413$.

In the fear conditioning phase, fear ratings were higher for the CS⁺ than the CS⁻, CS, $F(1, 40) = 7.44$, $p = 0.009$, $\eta_G^2 = 0.042$, $BF_{10} = 4.624$, an effect that did not differ across groups, CS \times group, $F(1, 40) = 0.57$, $p = 0.455$, $\eta_G^2 = 0.003$, $BF_{01} = 2.676$. The same pattern

of responses was observed also in the avoidance conditioning phase, CS, $F(1, 40) = 22.78$, $p < 0.001$, $\eta_G^2 = 0.136$, $BF_{10} > 1000$, CS \times group, $F(1, 40) = 0.15$, $p = 0.699$, $\eta_G^2 = 0.001$, $BF_{01} = 2.936$.

For the response prevention and extinction phase, we observed a significant CS \times group interaction, $F(1, 40) = 7.23$, $p = 0.01$, $\eta_G^2 = 0.021$, $BF_{10} = 4.18$, with participants in the NERP group reporting higher fear levels, $t(19) = 4.88$, $p < 0.001$, $BF_{10} = 267.14$ compared to the ExtRP group, $t(21) = 1.49$, $p = 0.15$, $BF_{01} = 1.706$.

The two groups did not seem to differ in the reinstatement test phase, $F(1, 40) = 1.33$, $p = 0.256$, $\eta_G^2 = 0.004$, $BF_{01} = 2.033$, although there was still a CS differentiation across groups, $F(1, 40) = 19.05$, $p < 0.001$, $\eta_G^2 = 0.06$, $BF_{10} = 202.105$.

Lastly, between group differences were observed in the reextinction test phase, $F(1, 40) = 5.95$, $p = 0.019$, $\eta_G^2 = 0.015$, $BF_{10} = 2.427$. Specifically, although participants in both groups showed CS differentiation, this differentiation was stronger for the ExtRP group, $t(19) = 4.16$, $p = 0.001$, $BF_{10} = 63.72$, compared to the NERP group, $t(21) = 2.08$, $p = 0.05$, $BF_{10} = 1.338$.

3.3. Avoidance responses

During the response prevention and extinction phase, participants largely stopped pressing the button, with less than 1% of the trials being avoided in total.

The mean proportions of avoidance responses for the avoidance conditioning and the reinstatement/reextinction test phases are shown on Fig. 3. Participants showed a reduction of differential avoidance from the end of avoidance conditioning phase until the end of reinstatement/reextinction, CS \times trial, $F(1, 40) = 283.18$, $p < 0.001$, $\eta_G^2 = 0.425$, $BF_{10} > 1000$, with the number of avoidance responses being comparable across groups, CS \times trial \times group interaction, $F(1, 40) = 3.5$, $p = 0.069$, $\eta_G^2 = 0.009$, $BF_{01} = 1.646$. Within the reinstatement/reextinction test phases, both groups showed differential avoidance responses, CS, $F(1, 40) = 37.61$, $p < 0.001$, $\eta_G^2 = 0.115$, $BF_{10} > 1000$, CS \times group, $F(1, 40) = 0.19$, $p = 0.662$, $\eta_G^2 < 0.001$, $BF_{01} = 2.947$.

4. Discussion

We investigated if the combination of a novelty-based extinction procedure with response prevention would result in the non-return of conditioned avoidance responses. Contrary to our predictions, the NERP and the ExtRP groups showed similar levels of avoidance during reinstatement. Similar results arose for US-expectancies. Regarding fear ratings, the NERP group showed increased fear responses, compared to the ExtRP group, across the extinction (with response prevention) and reextinction phases. Collectively, our findings suggest that the combination of novelty-based extinction with response prevention does not prevent the return of fear or avoidance and it enhances, rather than

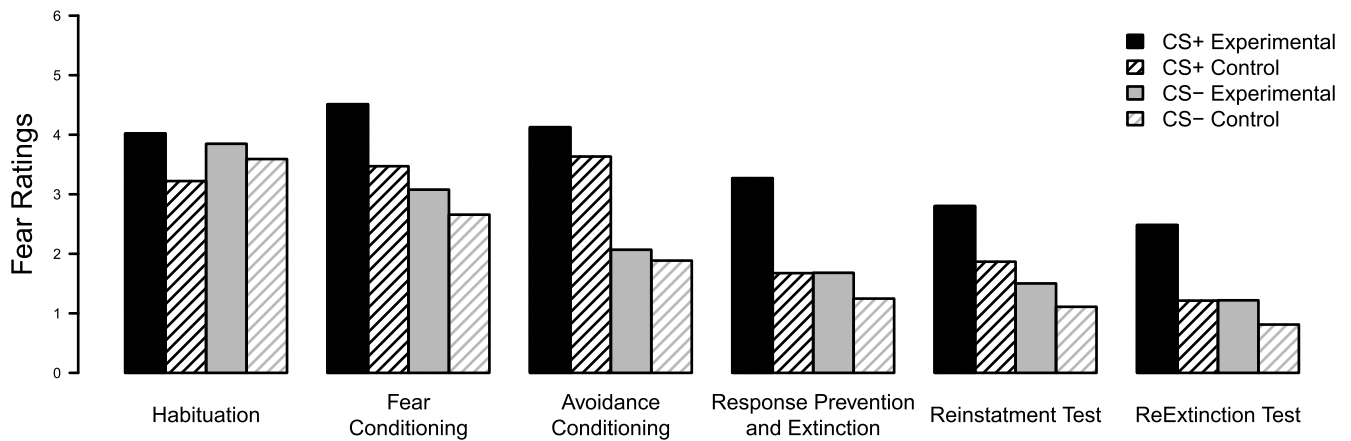


Fig. 2. Fear ratings for each CS and for each group across all phases.

reduces, subjective fear evaluations.

The return of avoidance after ExtRP has been reported previously (but see Boeke, Moscarello, LeDoux, Phelps, & Hartley, 2017; Lovibond et al., 2013; Vervliet & Indekeu, 2015). As mentioned above, these findings are often explained by residual fear evaluations of the CSs after the completion of fear extinction. Alternative explanations also hold. For example, the mere availability of the avoidance response could suggest that threat is impending, with the performance of avoidance being then performed to prevent the US presentation (see Engelhard et al., 2015; Lovibond et al., 2013; and Lovibond, Saunders, Weidemann, & Mitchell, 2008 for relevant findings).

Despite the non-observation of between group differences, we did find a reduction of avoidance from the end of the avoidance conditioning phase to the reinstatement/reextinction test phase. This finding is contrary to some studies (e.g., Lovibond et al., 2008; Vervliet & Indekeu, 2015) but in line with others (e.g., Boeke et al., 2017). Despite this decrease, though, differential avoidance was still observed for both groups at the reinstatement/reextinction test phase. The reduction of avoidance, even for the mere ExtRP group, could be well explained by procedural differences between our study and those of Lovibond et al. (2008) and Vervliet and Indekeu (2015). In both these

experiments, participants were informed on which CS⁺ trials avoidance response was available, and in which CS⁺ trials was not. As such, the mere availability of the avoidance response could have triggered the CS-US fear memory, something that could have resulted in the resurgence of the avoidance responses. In our experiment, we did not give instructions about the availability of the avoidance response after the end of the response prevention and extinction phase. As such, participants were free to initiate an avoidance response, although it was not clear whether such an avoidance response would cancel the US or not. The fear results showed that the unexpected US presentations were adequate for the resurgence of the fear response, as well as for avoidance. However, avoidance responses were expressed in much reduced degree compared to the levels of avoidance in the avoidance conditioning phase.

The failure to prevent the return of fear, or even reduce fear during the response prevention and extinction phase, in the novelty-based group is unexpected. A possible explanation is that the novel neutral tone was not surprising or not neutral. The first explanation seems unlikely given that participants rated the stimulus as surprising. The second explanation also seems unlikely given that similar stimuli had been used in previous experiments (e.g., Dunsmoor et al., 2015).

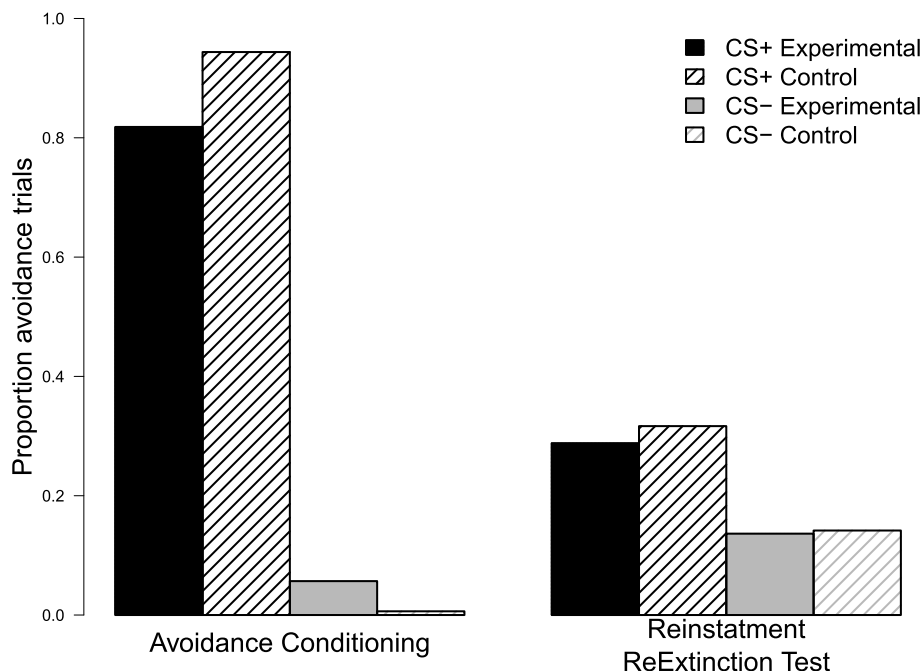


Fig. 3. Proportions of avoidance responses for the CS⁺ and the CS⁻, for both groups, during the Avoidance conditioning and the Reinstatement/Reextinction test phases.

Another unexpected outcome is the elevated fear levels for the NERP group, compared to the ExtRP group. A potential explanation for this result is that the unexpected novel tone increased the uncertainty regarding CS-US associations and as such weakened the fear extinction memory. Please note, though, that this explanation is against the findings of other studies [Dunsmoor et al. \(2015\)](#). Future studies could possibly shed more light on why exactly a novel tone seems to increase explicit fear (such as in our study) but not physiological fear (such as in the study by [Dunsmoor et al., 2015](#)).

Recent discussions (e.g., [De Houwer, Crombez, & Baeyens, 2005](#); [Treanor & Barry, 2017](#)) have brought forward the argument that an avoidance response could operate as a signal that the US does not follow the CS (i.e., *negative occasion setter assumption*). In the present study, during the test phase maybe the participants employed a safe-than-sorry strategy, in which they thought that the CS would not follow the US only if now the available avoidance response was performed. Although this explanation is possible, it should be better addressed in experiments that specifically test the potential function of avoidance as a negative occasion setter. Please note that currently there is evidence for (e.g., [De Houwer et al., 2005](#)) as well as against (e.g., [Declercq & De Houwer, 2011](#)) the idea that avoidance operates as a negative occasion setter.

Our findings could be viewed as contradictory to other studies that novelty-based extinction was used (e.g., [Dunsmoor et al., 2015](#)). However, such a one-to-one comparison would be ill-advised given the key methodological differences between our study and that of [Dunsmoor et al. \(2015\)](#). For example, our study relied mainly on explicit measures of fear, rather than physiology measures. Although from a layman's perspective physiological and subjective levels of fear should correlate, there is strong evidence that this is not the case ([Beckers, Krypotos, Boddez, Eftting, & Kindt, 2013](#); [Evers et al., 2014](#); [Mauss, Levenson, McCarter, Wilhelm, & Gross, 2005](#)). Another crucial difference between our study and that by [Dunsmoor et al. \(2015\)](#) is that in the latter work the authors tested the effects of novelty-based extinction using a two day procedure, something that allowed the test of the long-term effects of extinction learning. In contrast to this study, but in line with other studies of avoidance learning (e.g., [Vervliet & Indekeu, 2015](#)), we used a one-day procedure. As such, we limit all our interpretations to immediate effects of extinction learning, and we do not refer to long-term effects. Future studies could assess whether any between group differences arise when avoidance is tested on another day than that of the initial consolidation day.

A limitation of our study is that we did not account for participants' fear of spiders. Please note though, that due to the randomization procedure, we would expect that any such difference would distribute normally across groups.

An advantage of our article is that we conducted our statistical analyses within both a frequentist and Bayesian framework. Although the former is commonly used in psychology, the Bayesian perspective has recently attracted a lot of attention in our field ([Krypotos et al., 2017b, 2017a](#)). A major advantage of Bayesian analyses, compared to the traditional approach, is that it can provide evidence for the null hypothesis, compared to the alternative one. In the present study, this proved especially helpful for drawing our statistical conclusions as many of our findings provided relative support for the null findings (e.g., that novelty-based extinction does not prevent the return of avoidance responses) compared to the alternative hypothesis (e.g., that novelty-based extinction will result in less return of avoidance compared to standard extinction). We believe that the use of Bayesian statistics in the field of psychology could prove invaluable, especially when novel experimental manipulations are tested.

5. Conclusions

All in all, the combination of a novelty-based extinction procedure with response prevention does not prevent the return of avoidance or

subjective fear. On the contrary, this procedure led to higher subjective fear levels in the NERP compared to the ExtRP group during the response prevention and extinction and reextinction phases. These findings suggest that more evidence of novelty-based procedures should be gathered before they can be potentially translated to clinical settings.

Author note

The research presented in this manuscript was supported by a VICI grant, awarded by the Netherlands Organization for Scientific Research (NWO) (453-15-005), to IME. We would like to thank Emma Deckers, Mark Dubbelman, and Joseline den Hoed for collecting the experimental data and providing helpful remarks during the design of the experimental procedure.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- Beckers, T., Krypotos, A.-M., Boddez, Y., Eftting, M., & Kindt, M. (2013). What's wrong with fear conditioning? *Biological Psychology, 92*, 90–96.
- Boeke, E. A., Moscarello, J. M., LeDoux, J. E., Phelps, E. A., & Hartley, C. A. (2017). Active avoidance: Neural mechanisms and attenuation of Pavlovian conditioned responding. *Journal of Neuroscience, 37*, 4808–4818.
- Bouton, M. E. (1993). Context, time, and memory retrieval in the interference paradigms of Pavlovian learning. *Psychological Bulletin, 114*, 80–99.
- Bouton, M. E. (2000). A learning theory perspective on lapse, relapse, and the maintenance of behavior change. *Health Psychology, 19*, 57–63.
- Bouton, M. E. (2002). Context, ambiguity, and unlearning: Sources of relapse after behavioral extinction. *Biological Psychology, 52*, 976–986.
- Bruin, G. O. de, Rassin, E., Heiden, C. van der, & Muris, P. (2006). Psychometric properties of a Dutch version of the intolerance of uncertainty scale. *Netherlands Journal of Psychology, 62*, 87–92.
- De Houwer, J., Crombez, G., & Baeyens, F. (2005). Avoidance behavior can function as a negative occasion setter. *Journal of Experimental Psychology: Animal Behavior Processes, 31*, 101–106.
- Declercq, M., & De Houwer, J. (2011). Evidence against an occasion setting account of avoidance learning. *Learning and Motivation, 42*, 46–52.
- Dunsmoor, J. E., Campese, V. D., Ceceli, A. O., LeDoux, J. E., & Phelps, E. A. (2015). Novelty-facilitated extinction: Providing a novel outcome in place of an expected threat diminishes recovery of defensive responses. *Biological Psychiatry, 78*, 203–209.
- Engelhard, I. M., Uijen, S. L. van, Seters, N. van, & Velu, N. (2015). The effects of safety behavior directed towards a safety cue on perceptions of threat. *Behavior Therapy, 46*, 604–610.
- Evers, C., Hopp, H., Gross, J. J., Fischer, A. H., Manstead, A. S., & Mauss, I. B. (2014). Emotion response coherence: A dual-process perspective. *Biological Psychology, 98*, 43–49.
- Eysenck, H. J., & Rachman, S. (1975). *Manual of the eysenck personality questionnaire*. San Diego: CA: Educational and Industrial Testing Service.
- Greenberg, P. E., Sisitsky, T., Kessler, R. C., Finkelstein, S. N., Berndt, E. R., Davidson, J. R., ... Fyer, A. J. (1999). The economic burden of anxiety disorders in the 1990s. *Journal of Clinical Psychiatry, 60*, 427–435.
- Jeffreys, H. (1961). *Theory of probability* (3rd ed.). Oxford, UK: Oxford University Press.
- Konnopka, A., Leichsenring, F., Leibing, E., & König, H.-H. (2009). Cost-of-illness studies and cost-effectiveness analyses in anxiety disorders: A systematic review. *Journal of Affective Disorders, 114*, 14–31.
- Krypotos, A.-M., Blanken, T. F., Arnaudova, I., Matzke, D., & Beckers, T. (2017a). A primer on Bayesian analysis for experimental psychopathologists. *Journal of Experimental Psychopathology, 8*, 140–157.
- Krypotos, A.-M., Eftting, M., Arnaudova, I., Kindt, M., & Beckers, T. (2014). Avoided by association acquisition, extinction, and renewal of avoidance tendencies toward conditioned fear stimuli. *Clinical Psychological Science, 2*, 336–343.
- Krypotos, A.-M., Klugkist, I., & Engelhard, I. M. (2017b). Bayesian hypothesis testing for human threat conditioning research: An introduction and the condit R package. *European Journal of Psychotraumatology, 8*.
- Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (1999). *International affective picture system (IAPS): Instruction manual and affective ratings* (Tech. Rep. No. A-4) Gainesville, FL: University of Florida, The Center for Research in Psychophysiology.
- LeDoux, J., Moscarello, J., Sears, R., & Campese, V. (2017). The birth, death and resurrection of avoidance: A reconceptualization of a troubled paradigm. *Molecular Psychiatry, 22*, 24–36.
- Leslie, J. C., & Norwood, K. (2013). Facilitation of extinction and re-extinction of operant behavior in mice by chlordiazepoxide and D-cycloserine. *Neurobiology of Learning and Memory, 102*, 1–6.
- Lovibond, P. F., Chen, S. X., Mitchell, C. J., & Weidemann, G. (2013). Competition

- between an avoidance response and a safety signal: Evidence for a single learning system. *Biological Psychology*, 92, 9–16.
- Lovibond, P. F., Saunders, J. C., Weidemann, G., & Mitchell, C. J. (2008). Evidence for expectancy as a mediator of avoidance and anxiety in a laboratory model of human avoidance learning. *The Quarterly Journal of Experimental Psychology*, 61, 1199–1216.
- Mauss, I. B., Levenson, R. W., McCarter, L., Wilhelm, F. H., & Gross, J. J. (2005). The tie that binds? Coherence among emotion experience, behavior, and physiology. *Emotion*, 5, 175–190.
- Morey, R. D., & Rouder, J. N. (2014). *BayesFactor: Computation of Bayes factors for common designs*. Retrieved from: <http://CRAN.R-project.org/package=BayesFactor>.
- Peterson, R. A., & Reiss, S. (1993). *Anxiety sensitivity index revised test manual*. Worthington, OH: IDS Publishing.
- R Core Team (2016). *R: A language and environment for statistical computing*. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from: <http://www.R-project.org/>.
- Rachman, S., Radosky, A. S., & Shafran, R. (2008). Safety behaviour: A reconsideration. *Behaviour Research and Therapy*, 46, 163–173.
- Rouder, J. N., & Morey, R. D. (2012). Default Bayes factors for model selection in regression. *Multivariate Behavioral Research*, 47, 877–903.
- Rouder, J. N., Speckman, P. L., Sun, D., Morey, R. D., & Iverson, G. (2009). Bayesian t tests for accepting and rejecting the null hypothesis. *Psychonomic Bulletin & Review*, 16, 225–237.
- Scheveneels, S., Boddez, Y., Vervliet, B., & Hermans, D. (2016). The validity of laboratory-based treatment research: Bridging the gap between fear extinction and exposure treatment. *Behaviour Research and Therapy*, 86, 87–94.
- Soeter, M., & Kindt, M. (2011). Noradrenergic enhancement of associative fear memory in humans. *Neurobiology of Learning and Memory*, 96, 263–271.
- Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *Manual for the state-trait anxiety inventory*. Palo Alto, CA: Consulting Psychologists Press.
- Treanor, M., & Barry, T. J. (2017). Treatment of avoidance behavior as an adjunct to exposure therapy: Insights from modern learning theory. *Behaviour Research and Therapy*, 96, 30–36.
- Uijen, S. L. van, Leer, A., & Engelhard, I.M. (in press). Safety behavior after extinction causes a return of threat expectancies. *Behaviour Research and Therapy*.
- Vervliet, B., & Indekeu, E. (2015). Low-cost avoidance behaviors are resistant to fear extinction in humans. *Frontiers in Behavioral Neuroscience*, 9.
- Voss, E., Mejta, C., & Reid, L. (1974). Methods of deconditioning persisting avoidance: Response prevention and counterconditioning after extensive training. *Bulletin of the Psychonomic Society*, 3, 345–347.