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Reappraising fear: is up-regulation more efficient than down-regulation?

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Abstract

Catastrophizing thoughts may contribute to the development of anxiety, but functional emotion regulation may help to improve treatment. No study so far directly compared up- and down-regulation of fear by cognitive reappraisal. Here, healthy individuals took part in a cued fear experiment, in which multiple pictures of faces were paired twice with an unpleasant scream or presented as safety stimuli. Participants (N = 47) were asked (within-subjects) to down-regulate, to up-regulate and to maintain their natural emotional response. Valence and arousal ratings indicated successful up- and down-regulation of the emotional experience, while heart rate and pupil dilation increased during up-regulation, but showed no reduction in down-regulation. State and trait anxiety correlated with evaluations of safety but not threat stimuli, which supports the role of deficient safety learning in anxiety. Reappraisal did not modulate this effect. In conclusion, this study reveals evidence for up-regulation effects in fear, which might be even more efficient than down-regulation on a physiological level and highlights the importance of catastrophizing thoughts for the maintenance of fear and anxiety.

Keywords Fear conditioning · Cognitive reappraisal · Pupil diameter · Heart rate · Anxiety

Introduction

Feelings of fear and anxiety are hard to control. Looking down from a skyscraper, for example, can make our knees shake, even if we know that we are safe in the building. For patients suffering from panic attacks, it often takes more than an hour in a feared situation until their anxiety dissolves (Gloster et al. 2011). However, there is convincing research suggesting that humans can regulate their emotional responses by the way they evaluate a situation. Gross (1998b) defines such cognitive reappraisal as "cognitively transforming the situation so as to alter its emotional impact". Most research on cognitive reappraisal effects is based on cognitively reframing emotional pictures and negative affect in general. A picture of a gun directed at your head, for example, can be appraised as life threatening or as an unreal movie scene. Cognitive reappraisal was shown to effectively reduce the experience of negative affect in response to unpleasant pictures (Webb et al. 2012), as indicated by reduced reports of negative affect and reduced physiological arousal reflected in skin conductance responses (McRae et al. 2012). However, a meta-analysis suggests that there is no significant impact of cognitive reappraisal on peripheral physiological responses (Webb et al. 2012). Yet, more recent studies documented reappraisal effects on brain responses, startle responses and facial expressions typically associated with emotion (Baur et al. 2015; Buhle et al. 2014; Conzelmann et al. 2015; Wu et al. 2012). Also, pupil dilation has been shown to vary with cognitive reappraisal (Kinner et al. 2017; Martins et al. 2018).

From a clinical perspective, cognitive reappraisal might be a useful strategy to improve the treatment of anxiety disorders. However, studies about reappraisal effects on anxiety are relatively rare. One reason might be the common view of an encapsulated fear module that is relatively independent of cognitive processes (see Mineka and Öhman 2002), strict independence however is questioned repeatedly (e.g. Pessoa 2008). Indeed, Goldin et al. (2009) found that both patients with social anxiety disorder and healthy controls are able to use reappraisal to

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reduce negative affect and amygdala activity in response to negative self-beliefs, yet the effect of acute threat was not assessed. Hofmann et al. (2009) created a more acute anxiety-eliciting situation by asking participants to give a speech in front of a camera. Participants who reappraised this situation as non-threatening and as only an experiment reported less anxiety than those who suppressed their feelings. In addition, reappraisal and the acceptance of feelings led to lower heart rate responses than suppression. However, since there was no neutral control condition, we cannot infer if these effects were due to a beneficial effect of reappraisal or a dysfunctional effect of suppression (see Gross 1998a).

First indications that emotion regulation may dampen conditioned fear responses exist, which is interesting since fear conditioning is assumed to play a major role in the development of anxiety disorders. Delgado et al. (2008) who found that thinking about something calming in nature while viewing a conditioned stimulus (CS+) predicting an aversive electric shock (unconditioned stimulus, US) reduces the triggered conditioned responses, i.e. skin conductance and amygdala activity. Although effective, this regulation strategy involves attentional distraction from the situation and may prevent adequate coping in a real situation. Shurick et al. (2012) experimentally manipulated cognitive reappraisal after the acquisition of conditioned fear towards spider stimuli by asking participants to see the CS+ and the US as separate stimuli and to focus on less negative aspects of the CS+ and found reduced fear ratings and skin conductance responses. Finally, Blechert et al. (2015) used social stimuli as CS+ and asked participants to reappraise negative expressions about oneself. They found that such reappraisal reduced self-reported negative valence, and socially anxious individuals were able to compensate stronger negative affect. All studies so far used cognitive reappraisal to down-regulate anticipatory anxiety as this is of therapeutic relevance. However, it might also be interesting to test the effects of up-regulating anxiety by reappraisal, since this mimics catastrophizing thoughts, which are considered crucial for the development of anxiety disorders (Domschke et al. 2010). If fear has more of an encapsulated nature, both up- and down-regulation should have little effect. If fear is susceptible to cognitive modulation, it may be increased or decreased in both ways. However, also an asymmetric pattern would make sense since an increase of fear in a situation of potential threat should improve chances of survival compared to a decrease of fear. While responding inadequately to a non-threatening situation with high fear should have little costs, responding to a threatening situation with little fear might lead to fatal consequences. By this logic, emotional processes should be affected by a negativity bias (Vaish et al. 2008).

Besides these basic questions about the convertibility of fear and anxiety, the question arises how anxiety as an individual trait is related to it. Trait anxiety is associated with anxiety disorders (Sylvers et al. 2011; Taylor et al. 1991) and other forms of psychopathology (Muris and Meesters 2004; Schneider et al. 2010), implying a potential disruption of the cognitive reappraisal of fear in highly anxious individuals. Recent meta-analyses suggest that anxiety may be especially related to increased responses to safety stimuli (Lissek et al. 2005; Duits et al. 2015). So, we tested the impact of trait anxiety on the evaluation of threat and safety stimuli separately.

With the present study, we advanced these lines of research by using an associative fear learning paradigm in which healthy participants applied cognitive reappraisal to down- or up-regulate negative affect or responded naturally when seeing cues (faces) predicting an aversive unconditioned stimulus (aversive screams). Unlike previous studies, we combined the anticipation of unconditioned threat with both up- and down-regulation and a neutral condition. Moreover, we used the combination of cues and aversive screams instead of sole threatening pictures to evoke fear and anxiety with an anticipatory and acute, intense quality. In addition to self-reported emotion ratings, we measured heart rate responses and pupil dilation as physiological indicators of emotion. In previous studies, heart rate and pupil dilation were successfully used as indicators of aversive conditioning and emotional arousal. Pupil dilation is closely related to neural activity in the locus coeruleus in the brainstem (Joshi et al. 2016) and increases during the anticipation of an US (Reinhard and Lachnit 2002) indicating emotional arousal (Bradley et al. 2008). Heart rate decelerations are usually observed in anticipatory orienting responses and sensory intake (Bradley 2009), while fear can trigger defensive heart rate accelerations depending on the imminence of threat (Lang et al. 2000). Moreover, we investigated whether emotion regulation has an impact on associative fear memory by later asking participants about CS-US associations. Biased associative fear memory is often found in anxiety disorders (Wiemer et al. 2015; Wiemer and Pauli 2016), but the impact of emotion regulation on covariation estimates is unknown.

We hypothesized that relative to a neutral maintain condition, (1) up-regulating the conditioned fear leads to more negative and arousing emotion ratings, to an increase in pupil dilation and to stronger heart rate responses; the reverse effects were expected for the down-regulation condition. (2) We tested the relationship between trait anxiety and the evaluation of the CS+ and the CS−, and how cognitive reappraisal impacts this relationship. We expected highly anxious individuals to rate the stimuli as more negative and arousing than low anxious individuals, and this relationship should be stronger for CS− than CS+. (3) Finally, emotion regulation should also bias CS-US memory; up-regulation should enhance memory of CS-US-associations while down-regulation should have the opposite effect.

Methods

Participants

Forty-seven participants (34 females) took part in this within-subjects designed experiment. Mean age was $M = 24.04$ years ($SD = 4.75$). The sample size was chosen in order to detect a medium sized effect ($d = 0.5$) with a power of 0.80 and an alpha of 0.05, taking possible dropouts into account. An according power analysis for two-sided *t* tests for dependent means suggested at least 34 participants (G*Power 3.1.9.7; Faul et al. 2007). Participants were recruited among students and via local and online advertisements. They were compensated with course credit or 10 euros. Participants had normal or corrected-to-normal vision, and by self-report, had not suffered from any psychiatric or neurological disease within the past ten years, nor did they take any psychoactive drugs or medication. All but four participants indicated German as their native language (one Italian, one Polish, one Bulgarian, one Korean). All participants had good German language skills.

Stimuli

Visual stimuli

We used black and white pictures of female neutral and fearful facial expressions as learning material, in order to evoke anticipatory anxiety and fear in our participants. All 38 female portraits were obtained from picture sets that have been used previously by other researchers to study fear conditioning and emotion processing (Karolinska Directed Emotional Faces, Lundqvist et al. 1998; Radboud Faces Database, Langner et al. 2010; NimStim Set of Facial Expressions, Tottenham et al. 2009). We used a neutral and a fearful expression of each of the 38 models. The neutral expressions served as the conditioned stimuli (CS), while the fearful expressions served as a part of the unconditioned stimuli (US). In particular, half of the neutral conditioned stimuli (CS+) were followed by a fearful expression and a loud and aversive scream (US). The other half of the conditioned stimuli was not followed by a US and served as safety stimuli (CS−). Two of the 38 faces were used for the practice trials, the remaining 36 faces were divided into three sets of 12 faces each, which were used in the three different emotion regulation conditions. The three sets were composed in a way that the average luminance (measured with a picture editing software) did not differ significantly between them ($M = 154.44$, $M = 155.36$, $M = 155.24$, $ps > 0.94$). All visual stimuli were presented on a white background. In addition, the attribution of pictures to threat or safety stimuli and to the emotion regulation conditions was counter-balanced across participants. This ensured that effects on pupil dilation were not confounded with physical features of the pictures.

Auditory stimulus

The US consisted of a fearful picture and a 1.5 s lasting 95 dB loud and unpleasant female scream applied over headphones.

Procedure

After arrival in the laboratory, participants were informed about the procedure of the experiment, signed informed consent, filled out a questionnaire about demographic data, as well as the state and trait versions of the STAI. Then, the experimenter attached the electrodes for skin conductance (SCR) and heart rate measurement. SCR results are not reported here due to technical failure and data loss.

The participants read the instructions onscreen how to regulate their emotional response to pictures of faces and loud and aversive screams. Participants were asked to think about the situation in a way that enhances or reduces their emotion, or to just maintain the emotion. For the *enhance* condition, they should interpret the scream as an indicator of a catastrophic event, such as a terrible accident, in which a close friend or family member or themselves were involved. In addition, it was acceptable to think negatively about the situation of the experiment. The participants were asked to apply a strategy that worked best for them. For the *reduce* condition, participants were asked to imagine that nothing harmful happened to a person that they do not know, such as the woman encountered a mouse and was only mildly shocked. Participants were also given the opportunity to interpret the experimental situation as useful and transient. For the *maintain* condition, participants were asked to behave naturally and to experience their emotion without trying to change it. Following written instructions, the experimenter made sure that the participants had understood their task and initiated two practice trials for each condition involving two faces that did not reoccur later.

Following the six practice trials, participants completed two blocks of the emotion regulation task. In each block, they were confronted with three mini-blocks, one for each emotion regulation condition. Each mini-block contained six CS− trials and six CS+ trials in randomized order with the restriction of no more than four stimuli of the same type in a row. The order of emotion regulation mini-blocks was counter-balanced across participants, also within the practice phase.[1] One trial started with a fixation cross (3–5 s), followed by a short reminder (2 s) of the emotion regulation condition (enhance, reduce, or maintain written on the screen) and another fixation cross (3–5 s). Then the CS+ or CS− appeared (8 s). The CS+ was immediately followed by a US (1.5 s scream and fearful face). After another fixation cross (6 s), participants rated valence and arousal of their overall emotional experience in the trial on visual analogue scales. The order of ratings was counter-balanced order across participants and ratings were assessed with a computer mouse. Every CS+ and CS− was shown twice, once in the first block and once in the second block.

After the emotion regulation phase, the participants again saw all pictures in a randomized order and were asked to indicate whether a scream had been associated with a given picture or not, and how confident they are with their decision. In addition, they rated valence and arousal, in counterbalanced order across participants. Trials were separated by a random interval of 1–2 s. The design and trial set-up are summarized in Fig. 1.

Psychometric data acquisition

State Trait Anxiety Inventory (STAI)

The German version of the STAI (Laux et al. 1981) was used in order to assess trait anxiety as well as state anxiety prior to the start of the experiment. The STAI is one of the most widely used questionnaire assessing anxiety in research and clinical practice. It involves two scales with 20 items each, one assessing anxiety as a situational variable (state) and one assessing anxiety as a more enduring personality characteristic (trait). A higher total score indicates higher anxiety. One participant did not fill out the questionnaire; for one participant one item was missing and replaced by the mean item score of the sample. Cronbach's alpha for the present sample was $\alpha = 0.88$ for state anxiety and $\alpha = 0.90$ for trait anxiety, which is comparable to previous reports of reliability of this test (Laux et al. 1981).

Valence and arousal ratings

During the learning phase, valence ("How UNPLEASANT or PLEASANT did you just feel?") and arousal ratings ("How CALM or AROUSED did you just feel?") were assessed with a computer mouse on visual analogue scales ranging from 0 to 100. Low values indicated very unpleasant emotional valence, respectively very calm arousal. High values indicated very pleasant emotional valence resp. very exciting arousal. These poles, as well as a value of 50 as neutral valence were labelled. Values were averaged for each condition, resulting in mean valence and arousal ratings for each CS and each regulation condition. The same procedure was followed in ratings after the learning phase, except emotional experience of seeing a CS was assessed ("How UNPLEASANT or PLEASANT do you feel seeing this picture?"; "How CALM or AROUSED do you feel seeing this picture?"), and rating scales were presented simultaneously with pictures.

Memory ratings

Memory ratings were assessed for each picture ("Did a scream follow this picture?"). They were asked to choose a number from − 4 to + 4 (without zero), depending on whether they thought there had been a scream (positive number) or not (negative number), and how confident they were (1—not confident, 4—absolutely confident). Rating scales were presented until participants gave a response.

Psychophysiological data acquisition and preprocessing

Pupil dilation

Pupil diameter was measured with an iViewX Hi Speed System (SensoMotoric Instruments; Berlin, Germany) at a sampling rate of 120 Hz. A chin and forehead rest helped the participants to keep their head still, while the eye was illuminated by an infrared light. Horizontal pupil diameter was used for further analysis. Horizontal pupil diameter was cleaned from artifacts, such as blinks and other rapid changes in diameter. Blinks and artifacts were interpolated via linear interpolation. In addition, the data were low-pass filtered at 10 Hz, and baseline corrected to 500 ms before stimulus onset. Trials with more than two consecutive seconds of interpolated data were discarded from the analysis. On average, 5.76 of six trials were left per cell. One participant had 44% of artifact-affected trials and was discarded from the current analysis (average 5.6%). Another participant had no trials left in one cell and was discarded, too. Due to technical failure, we had to discard additional five participants, leaving 40 participants for the final analysis. For statistical analysis, mean pupil dilation was calculated for four consecutive two-second-intervals during picture presentation.

[1] In order to rule out that regulation effects were still driven by order effects, we also conducted linear mixed models with regulation as a fixed factor and the order of a regulation block as a covariate. For all dependent variables (emotion ratings, pupil diameter and heart rate), the regulation effect remained significant.

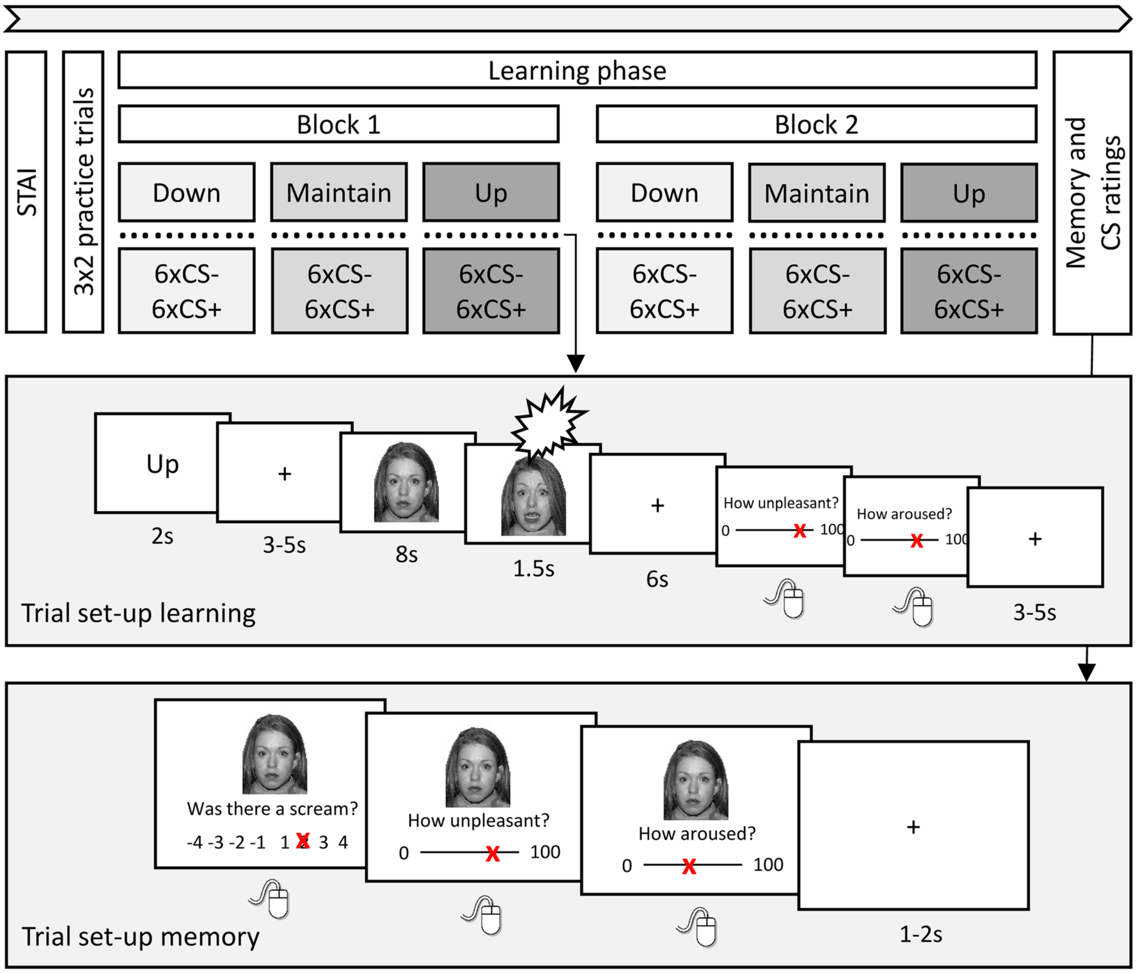

Fig. 1 The experimental procedure started with the assessment of state and trait anxiety (State Trait Anxiety Inventory, STAI), followed by the instruction for emotion regulation and six practice trials (one CS+ and one CS− per regulation condition). The main part involved two blocks of emotion regulation. Each block involved three mini-blocks for the three regulation conditions in a pseudo-randomized order counter-balanced across participants. Every dot in the learning phase represents a single trial, which is depicted in detail in the center of the figure. After a short reminder of the regulation condition, a fixation cross was presented followed by the picture of a neutral face (CS). CS+ faces were followed by a fearful expression synchronized with a loud and aversive scream (US), CS− faces by no consequence. Valence and arousal ratings were collected after each trial, before a fixation cross led to the next trial. Thirty-six faces were used in total, so every face was only presented twice, i.e. once per block. Finally, associative memory and emotion ratings were assessed (bottom of the figure). First, participants indicated whether they thought that a scream was associated with a face or not, and how certain they were with their decision (−4: no scream, high certainty; +4: scream, high certainty). Then, they rated valence and arousal of the face. The presentation of ratings is simplified for display purposes

Heart rate

Heart rate was measured by means of electrocardiogram (ECG). Electrodes (Ag/AgCl) were placed in a 3-lead-system with positive and negative poles on the thorax diagonally over the heart and a ground electrode on the back. The ECG was recorded with a V-Amp 16 amplifier and the software Vision Recorder (Brain Products, Munich, Germany) at a sampling rate of 500 Hz. Heart rate was analyzed by transforming inter-beat-intervals into beats per minute for every time point of R-peak occurrence. Trials with remaining artifacts were manually removed from further analysis, while the analyzers were blind to conditions. On average, 5.69 of six trials were left per cell. Due to artifacts and measurement failure, we had to discard nine participants, leaving 38 participants for the final analysis. Trials were averaged for each condition, segmented into four 2-s-intervals during picture presentation and baseline corrected to one second before picture onset.

Data analysis

The data were analyzed using SPSS Statistics V25.0 (IBM). All dependent variables were analyzed with

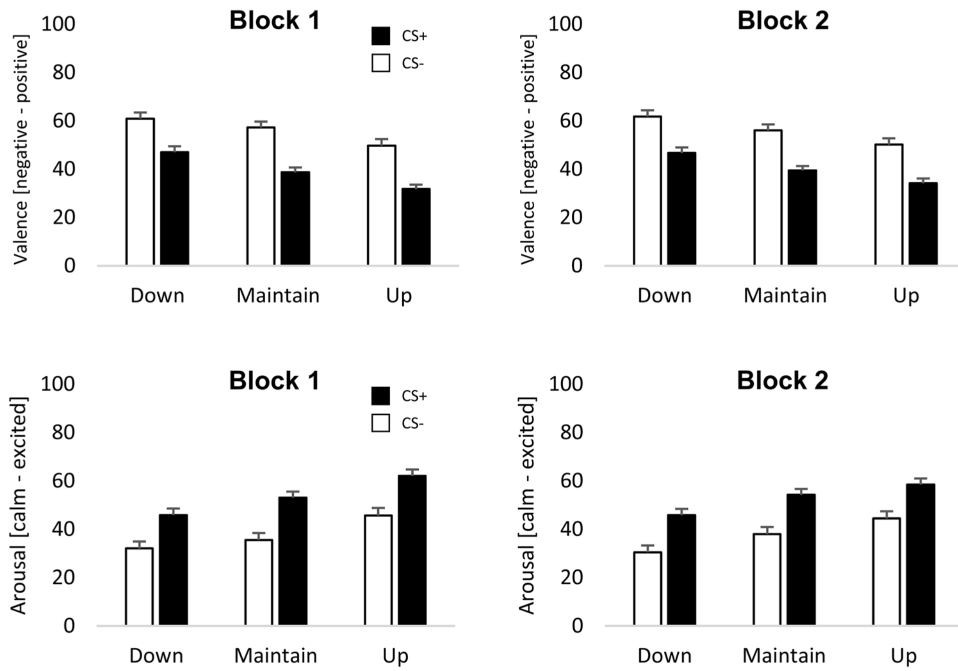

Fig. 2 Mean valence and arousal ratings assessed after each trial of the learning phase. Participants rated CS− less negative and less arousing than CS+. Emotion regulation led to more negative ratings and higher arousal in the up-regulation condition and less negative ratings and lower arousal in the down-regulation condition, compared with the maintain condition. Error bars indicate standard errors of the mean

repeated-measures ANOVAs. For each variable, the number of factors and levels is described in the results section. If sphericity was violated, we used Greenhouse–Geisser corrected *p* values. *T* tests (two-tailed if not otherwise specified) were run as follow-up tests in order to further resolve significant effects. Means are reported ± standard deviations. In addition, the 95% confidence intervals (CI) are reported for difference values. Finally, we tested Pearson correlations (one-tailed, since we always expected positive correlations for arousal and negative correlations for valence) between anxiety (state and trait) and emotional experience (valence and arousal) for the CS+ and the CS− separately. In order to reduce the number of tests, we first ran ANCOVAs with the factors *regulation*, *block* and *CS*, and included state, resp. trait anxiety as covariates. Then, we checked for significant interactions between factors and anxiety and calculated separate correlations only if a significant interaction was present. For all analyses, *p* values below an α-level of 0.05 were considered as statistically significant. Data are available at 10.6084/m9.figshare.7700669.

Results

Valence and arousal ratings[2]

Valence and arousal ratings (Fig. 2) were analyzed with repeated-measures ANOVAs containing the factors *regulation* (up, down, maintain), *CS* (CS+ vs. CS−) and *block* (first, second). For valence ratings, there was a significant effect of *regulation*, $F(2, 92) = 31.71$, $p < 0.001$, $\eta_p^2 = 0.41$, $\varepsilon_{GG} = 0.83$, and a significant effect of *CS*, $F(2, 46) = 48.37$, $p < 0.001$, $\eta_p^2 = 0.51$. Ratings were relative to the maintain condition ($M = 47.89 \pm 11.49$) more negative in the up-regulation condition ($M = 41.44 \pm 12.39$), $t(46) = 5.50$, $p < 0.001$, $d = 0.80$, 95% CI [4.09, 8.81], and more positive in the down-regulation condition ($M = 54.10 \pm 13.99$), $t(46) = 3.56$, $p = 0.001$, $d = 0.52$, 95% CI [2.70, 9.72]. Besides, the CS+ ($M = 39.63 \pm 11.65$) was rated as more negative than the CS− ($M = 55.99 \pm 15.36$), $t(46) = 6.96$, $p < 0.001$, $d = 1.01$, 95% CI [11.63, 21.10].

For arousal ratings, there was a significant effect of *regulation*, $F(2, 92) = 37.64$, $p < 0.001$, $\eta_p^2 = 0.45$, $\varepsilon_{GG} = 0.82$, a significant effect of *CS*, $F(2, 46) = 45.38$, $p < 0.001$, $\eta_p^2 = 0.50$, and a significant interaction of *Regulation × Block*, $F(2, 92) = 3.48$, $p = 0.035$, $\eta_p^2 = 0.07$, $\varepsilon_{GG} = 0.98$. Arousal ratings were higher in the up-regulation ($M = 52.67 \pm 16.33$) versus the maintain condition ($M = 45.21 \pm 15.37$), $t(46) = 4.56$, $p < 0.001$, $d = 0.67$, 95% CI [4.17, 10.76], and higher in the maintain versus the down-regulation condition ($M = 38.54 \pm 16.55$), $t(46) = 4.28$, $p < 0.001$, $d = 0.62$, 95% CI [3.53, 9.81]. However, the difference between up-regulation and maintain was greater in the first ($M = 9.56 \pm 12.06$) than in the second block ($M = 5.37 \pm 12.71$), $t(46) = 2.73$, $p = 0.009$, $d = 0.40$, 95% CI [1.10, 7.28], while the down-regulation relative to the maintain condition did not differ between blocks, $p = 0.135$. Finally, the CS+ ($M = 53.25 \pm 15.75$) was rated as more

[2] The reported results refer to all available rating data (N = 47). The main effects of ***CS*** and ***regulation*** remained significant (***p*** < 0.001) without the participants who had to be discarded from the analysis of physiological data.

arousing than the CS− ($M = 37.70$, $SD = 17.66$), $t(46) = 6.74$, $p < 0.001$, $d = 0.98$, 95% CI [10.90, 20.19].

In sum, these results indicate successful conditioning and successful regulation of emotions on an experiential, verbal level.

Pupil dilation

Pupil dilation was analyzed with a repeated-measures ANOVA containing the factors *regulation* (up, down, maintain), *CS* (CS+, CS−), *block* (first, second) and *time* (0–2, 2–4, 4–6, 6–8 s). This analysis revealed a significant effect of *regulation*, $F(2, 78) = 6.04$, $p = 0.004$, $\eta_p^2 = 0.13$, a significant effect of *time*, $F(3, 117) = 47.82$, $p < 0.001$, $\eta_p^2 = 0.55$, $\varepsilon_{GG} = 0.41$, a significant interaction of *Regulation* × *Time*, $F(6, 234) = 4.63$, $p = 0.003$, $\eta_p^2 = 0.11$, $\varepsilon_{GG} = 0.55$, a significant interaction of *Time* × *Block*, $F(7, 117) = 9.24$, $p < 0.001$, $\eta_p^2 = 0.19$, $\varepsilon_{GG} = 0.56$, a significant three-way interaction of *Regulation* × *Time* × *Block*, $F(6, 234) = 2.61$, $p = 0.04$, $\eta_p^2 = 0.06$, $\varepsilon_{GG} = 0.64$, and a significant three-way interaction of *CS* × *Time* × *Block*, $F(3, 117) = 3.25$, $p = 0.047$, $\eta_p^2 = 0.77$, $\varepsilon_{GG} = 0.63$.

Emotion regulation effects

Since we were primarily interested in the effects of regulation, we resolved the *Regulation* × *Time* × *Block* interaction with two separate *Time* × *Regulation* ANOVAs for the two blocks. Both blocks showed main effects of *regulation* (first block: $p = 0.035$, second block: $p = 0.010$), *time*, *p*s < 0.001, and significant *Time* × *Regulation* interactions (first block: $p = 0.020$, second block: $p = 0.006$).

In the first block (Fig. 3, upper left panel), follow-up one-factorial ANOVAs for each time interval revealed *regulation* effects for 2–4 s, $F(2, 78) = 5.23$, $p = 0.007$, $\eta_p^2 = 0.12$, and for 6–8 s $F(2, 78) = 3.84$, $p = 0.026$, $\eta_p^2 = 0.09$. In both intervals, up-regulation and down-regulation led to larger pupil dilations than the maintain condition. From 2 to 4 s: up-regulation ($M = 0.40 \pm 0.40$) > maintain ($M = 0.25 \pm 0.43$), $p = 0.005$, 95%, $d = 0.47$, CI [0.05, 0.26], down-regulation ($M = 0.36 \pm 0.39$) > maintain, $p = 0.034$, $d = 0.37$, 95% CI [0.01, 0.20]. From 6 to 8 s: up-regulation ($M = 0.63 \pm 0.58$) > maintain ($M = 0.47 \pm 0.62$), $p = 0.034$, $d = 0.35$, 95% CI [0.01, 0.31], down-regulation ($M = 0.62 \pm 0.54$) > maintain, $p = 0.022$, $d = 0.38$, 95% CI [0.02, 0.28].

In the second block (Fig. 3, upper right panel), follow-up one-factorial ANOVAs revealed *regulation* effects for 4–6 s, $F(2, 78) = 4.65$, $p = 0.012$, $\eta_p^2 = 0.11$ and for 6–8 s $F(2, 78) = 6.12$, $p = 0.003$, $\eta_p^2 = 0.14$. In both intervals, up-regulation evoked larger pupil dilations than maintain and down regulation. From 4 to 6 s: up-regulation ($M = 0.46 \pm 0.40$) > maintain ($M = 0.30 \pm 0.45$), $p = 0.004$, $d = 0.49$, 95% CI [0.05, 0.26], up-regulation > down-regulation ($M = 0.35 \pm 0.38$), $p = 0.034$, $d = 0.33$, 95% CI [0.004, 0.22]. From 6 to 8 s: up-regulation ($M = 0.56 \pm 0.54$) > maintain ($M = 0.34 \pm 0.51$), $p = 0.002$, $d = 0.53$, 95% CI [0.09, 0.36], up-regulation > down-regulation ($M = 0.39 \pm 0.50$), $p = 0.027$, $d = 0.36$, 95% CI [0.02, 0.33].

Conditioning effect

Moreover, we resolved the *CS* × *Time* × *Block* interaction by calculating two *CS* × *Time* ANOVAs for the two blocks (Fig. 4). In the first block, there was only a significant *time* effect, $p < 0.001$, which was expected, since participants did not know the contingencies, yet. However, in the second block, there was a significant *time* effect, $p < 0.001$, and a significant *Time* × *CS* interaction, $F(3, 117) = 3.73$, $p = 0.026$, $\eta_p^2 = 0.09$, $\varepsilon_{GG} = 0.71$. Follow-up one-sided *t* tests revealed a larger pupil dilation for CS+ ($M = 0.41 \pm 0.35$) than for CS− ($M = 0.33 \pm 0.42$) both in the 4–6 s interval, $p = 0.017$, $d = 0.35$, 95% CI [0.006, 0.16], and in the 6–8 s interval ($M = 0.47 \pm 0.45$ vs. $M = 0.39 \pm 0.50$), $p = 0.026$, $d = 0.30$, 95% CI [0.001, 0.17].

Overall, these results on pupil dilation indicate significant conditioning effects in the second learning trial for each CS and linear emotion regulation effects with up-regulation enhancing pupil dilatation the most, while down-regulation led to larger pupil dilations relative to maintenance in the first block only.

Heart rate

Heart rate was analyzed in a repeated-measures ANOVA containing the factors *regulation* (up, down, maintain), *CS* (CS+, CS−), *block* (first, second) and *time* (0–2, 2–4, 4–6, 6–8 s). The analysis of heart rate responses resulted in a significant effect of *regulation*, $F(2, 74) = 3.15$, $p = 0.048$, $\eta_p^2 = 0.08$, and a significant effect of *time*, $F(3, 111) = 15.02$, $p < 0.001$, $\eta_p^2 = 0.29$, $\varepsilon_{GG} = 0.46$. Only up-regulation ($M = -0.40 \pm 1.53$) led to a higher heart rate relative to the maintain condition ($M = -0.94 \pm 1.57$), $t(37) = 2.06$, $p = 0.047$, $d = 0.33$, 95% CI [0.009, 1.07], and relative to down-regulation ($M = -0.98 \pm 1.72$), $t(37) = 2.32$, $p = 0.026$, $d = 0.38$, 95% CI [0.07, 1.09]. The course of heart rate can be seen in Fig. 3 (lower panels).

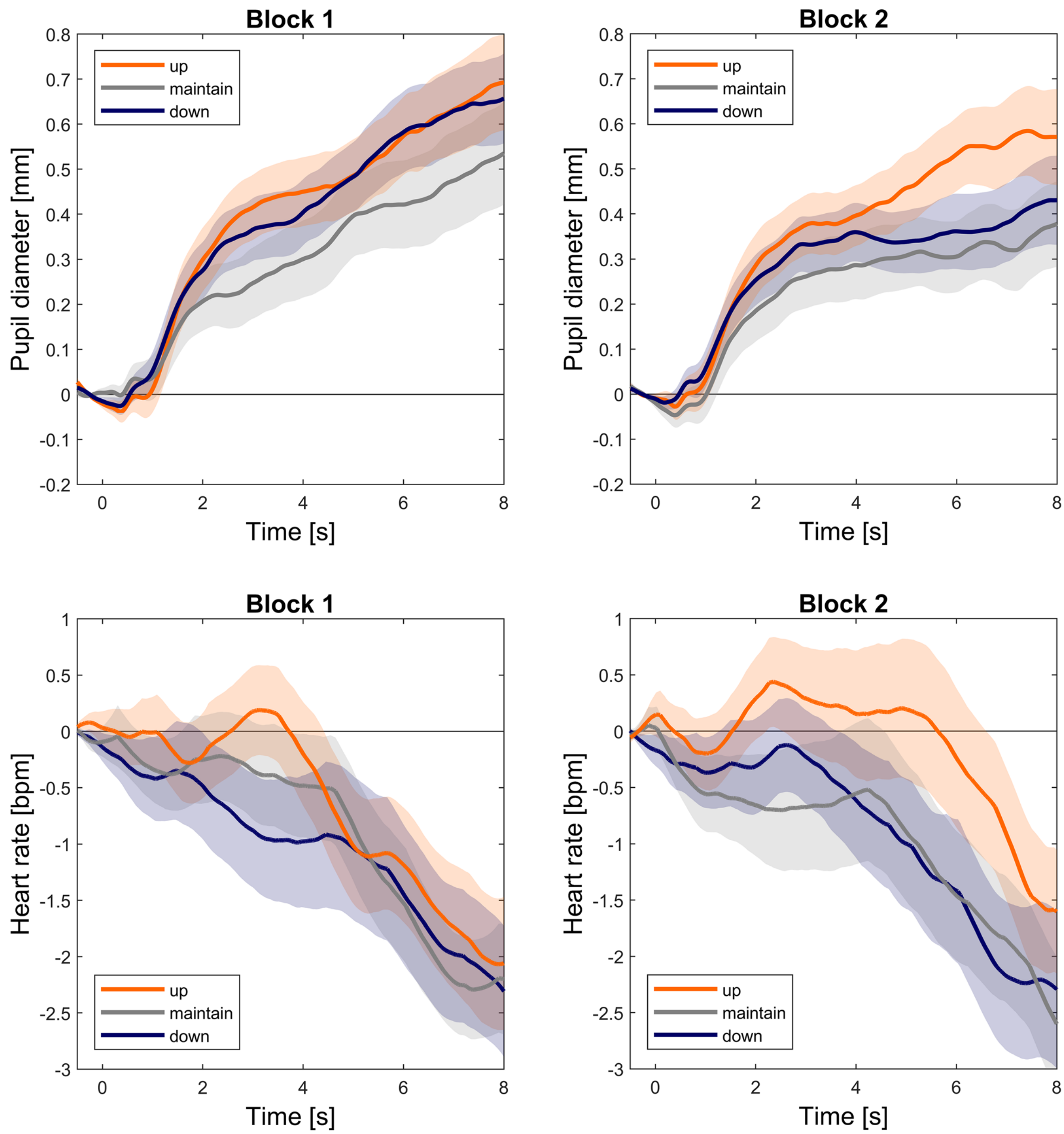

Fig. 3 Mean pupil diameter (in mm; upper graphs) and heart rate (in beats per minute, lower graphs) while viewing the CS+/CS−. The graphs depict general emotion regulation effects (CS+ and CS− combined) as there was no interaction between emotion regulation and CS. In the first block, pupil dilation (upper graphs) was higher in both regulation conditions than in the maintain condition. In the second block, this effect was only present for up-regulation. Heart rate (lower graphs) was generally higher during up-regulation than during maintenance and down-regulation. No significant difference between maintenance and down-regulation was found. Shades indicate standard errors of the mean

Correlations between anxiety and emotion ratings

State anxiety

For both valence and arousal, ANCOVAs with *state anxiety* as a covariate and *regulation*, *block* and *CS* as independent variables were run. We checked for interactions between *state anxiety* and independent variables and found a significant interaction between *state anxiety* and *CS* for valence ratings, $p = 0.027$, and for arousal ratings, $p = 0.007$. No significant interactions between *state anxiety* and *regulation* or *block* were found. So, we calculated correlations between *state anxiety* and CS+ and CS− separately across all other conditions. *State anxiety* significantly correlated with CS− ratings of *valence*, $r = -0.42$, $p = 0.002$, 95% CI [−0.14, −0.63], and arousal, $r = 0.36$, $p = 0.006$, 95% CI [0.08, 0.59]. No such correlations were found for the CS+, $ps > 0.21$.

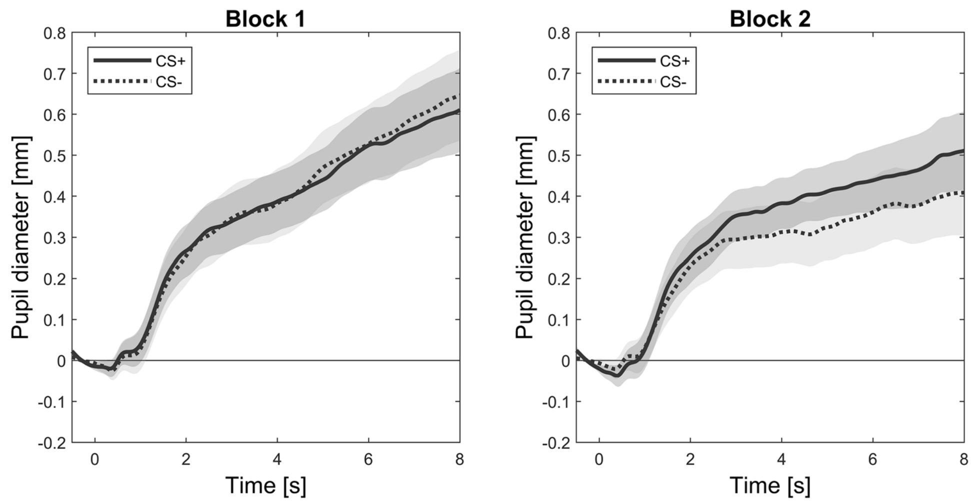

Fig. 4 Mean pupil diameter (in mm) while viewing the CS+ and the CS−. There was no significant difference in the first block, when participants saw each of the CSs once for the first time. In the second block, when each of the CSs were shown for the second time, the CS+ evoked a stronger pupil dilation than the CS− indicating a successful conditioning effect on pupil dilation

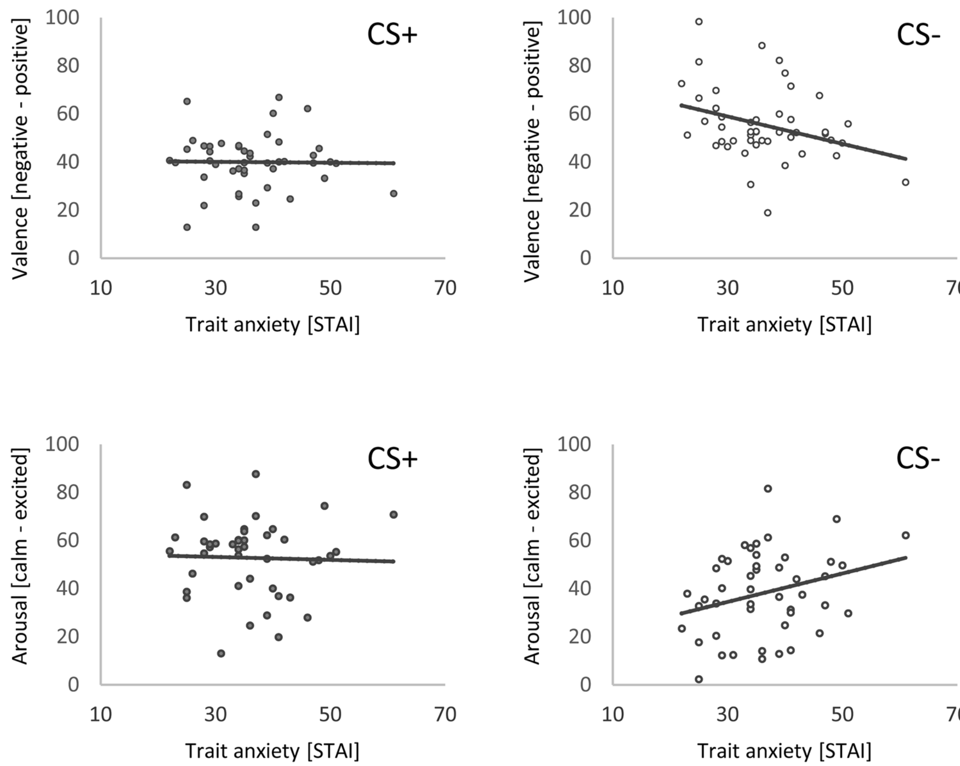

Fig. 5 Correlations between trait anxiety and CS+ and CS− ratings. There was, on the one hand, a significant correlation between trait anxiety and evaluating the CS− as negative and arousing. On the other hand, there was no relationship between trait anxiety and CS+ ratings. The same pattern of correlations was found for state anxiety. Note that ratings were assessed after the presentation of both the CS+ and the US

Trait anxiety

Here, we checked for interactions between *trait anxiety* and independent variables in ANCOVAs and found a significant interaction between *trait anxiety* and *CS* for valence ratings, $p = 0.035$, and for arousal ratings, $p = 0.009$. No significant interactions between *trait anxiety* and *regulation* or *block* were found. Like for state anxiety, we calculated correlations between *trait anxiety* and CS+ and CS− separately across all other conditions revealing that *trait anxiety* significantly correlated with CS− ratings of *valence*, $r = -0.32$, $p = 0.014$, 95% CI [−0.03, −0.59], and arousal, $r = 0.29$, $p = 0.028$, 95% CI [−0.00033, 0.54], but not with CS + ratings, $ps > 0.41$ (Fig. 5).

Memory and emotion ratings after learning

We also measured whether participants could remember which picture was associated with a scream and which was not. Memory was analyzed in a repeated-measures ANOVA containing the factors *regulation* (up, down, maintain) and *CS* (CS+, CS−). We found a significant effect of *CS*, *F*(1,

46) = 93.97, $p < 0.001$, $\eta_p^2 = 0.67$, but no effect of *regulation*. That is, CS+ ($M = 0.99 \pm 0.84$) were rated as more associated with the scream than CS− ($M = -0.92 \pm 1.08$), $t(46) = 9.69$, $p < 0.001$, $d = 1.41$, 95% CI [1.51, 2.31], thus participants could overall remember which CSs were associated with the scream, but emotional regulation did not affect this memory. Values could range from −4 (certainly not associated with scream) to +4 (certainly associated with scream).

Likewise, valence and arousal ratings after learning reflected an effect of learning, but no enduring emotion regulation effect. For valence ratings, there was a significant main effect of *CS*, $F(1, 46) = 14.70$, $p < 0.001$, $\eta_p^2 = 0.24$, and no effect of *regulation*; CS+ ($M = 42.91 \pm 7.50$) were rated more negative than CS− ($M = 47.80 \pm 8.75$), $t(46) = 3.83$, $p < 0.001$, $d = 0.56$, 95% CI [2.33, 7.47]. For arousal, there was also a significant effect of *CS*, $F(1, 46) = 15.42$, $p < 0.001$, $\eta_p^2 = 0.25$, and no *regulation* effect; CS+ ($M = 47.69 \pm 16.05$) were rated as more arousing than CS− ($M = 41.83 \pm 14.83$), $t(46) = 3.93$, $p < 0.001$, $d = 0.57$, 95% CI [2.86, 8.87].

Discussion

In the present study, we investigated the impact of cognitive reappraisal on associative fear learning and conditioned fear responses. While previous emotion regulation research suggests that negative affect can be reduced by cognitive reappraisal (Webb et al. 2012), the concept of an encapsulated fear module states that fear is relatively independent of cognition (Mineka and Öhman 2002). We tested the hypothesis that humans can down- and up-regulate conditioned fear responses by reappraisal. Participants were confronted twice with 36 faces, half of them were always followed by a loud and aversive scream. Ratings of valence and arousal, pupil dilation and heart rate served as verbal and physiological indicators of emotional reactions.

Supporting previous research (Blechert et al. 2015; Delgado et al. 2008; Shurick et al. 2012), we found reduced self-reported negative valence and arousal in the down-regulation condition. In addition, we revealed, to our knowledge for the first time, that cued fear can be up-regulated by cognitive reappraisal, too. Physiological responses even suggest that fear can be more readily up-regulated than down-regulated because pupil dilation and heart rate were increased in the up-regulation condition only, but not reduced in the down-regulation condition, both relative to the maintain condition. One explanation may be that self-reported emotion ratings only reflect one level of the participants' fear responses, but emotions are based on multi-dimensional affect programs, in which divergent responses can be observed on different levels, such as experiential, physiological and behavioral (e.g. Andreatta et al. 2010). Thus, on the physiological level up-regulation of conditioned fear responses through reappraisal seems to be more effective than down-regulation.

Our interpretation that the up-regulation of conditioned fear is more effective than the down-regulation is in accordance with the assumption of a negativity bias in human emotion processing (Vaish et al. 2008). This theory, which is widely supported by empirical evidence, assumes that humans attend to and make more use of negative than positive information. For instance, three-month-old infants displayed an aversion to anti-social actors, but no comparable attention to pro-social actors (Kiley Hamlin et al. 2010). Taking an evolutionary perspective, the survival costs of missing negative information are higher than the costs of missing positive information. Accordingly, cognitive reappraisal may increase fear and anxiety more easily than decrease it. These results could also have important implications for the treatment of anxiety disorders, suggesting that refraining from catastrophic thoughts is more effective than using calming thoughts.

The notion that the down-regulation of acute and intense anxiety is less susceptible to cognitive reappraisal is also in line with findings in highly anxious individuals. Moscovitch et al. (2013) found that undergraduates with high trait social anxiety perceive negative mental images in feared situations as less controllable than less anxious students. Also, a brief training in cognitive reappraisal for social anxiety patients with more severe symptoms turned out to be inefficient (Cristea et al. 2014). Maybe a more extensive training is needed for high levels of fear and anxiety, or emotion regulation should set in at earlier stages of the regulation process, such as trying to prevent negative imagery to unfold by paying less attention to them, accepting them from a distance and concentrating on the task. Alternatively, since the present study only focused on negative emotion, it may be possible that it is also easier to up-regulate positive emotion, which may be another efficient strategy.

However, we have to consider that up-regulation and down-regulation differ in a specific aspect, which affects pupil dilation and heart rate but not verbal responses. Indeed, we observed a stronger pupil dilation for down-regulation than for the maintain condition in the first block which may reflect increasing cognitive effort in the former condition (Kahneman and Beatty 1966). Thus, down-regulation may be associated with both reduced emotional arousal and increased cognitive effort, and both effects may cancel out each other regarding changes in pupil dilation. In this way, our results for conditioned fear are in line with previous emotion regulation studies, which did not find a decrease or even found an increase in pupil diameter during the down-regulation of negative affect (Kinner et al. 2017; Urry et al. 2009; Strauss et al. 2016). The present results suggest that repeated presentation throughout the experiment (and thus practice) might be an important moderator of this effect. While pupil dilation was increased for down- and up-regulation in the first block, it was only increased for up-regulation in the second block. Similarly, heart rate may also increase as a function of cognitive demands (Kennedy and Scholey 2000), perhaps accompanied by stress which also may blur physiological down-regulation effects. However, in the context of cognitive reappraisal, previous studies rather suggest a decrease than an increase in heart rate during down-regulation (Driscoll et al. 2009; Williams et al. 2009). In any case, we assume that cognitive reappraisal can more easily up-regulate than down-regulate physiological fear and anxiety responses, although underlying mechanisms need to be explored by future studies which may assess or control cognitive effort.

Our results also indicate that pupil dilation is an excellent measure of threat conditioning. Despite the fact that participants saw each face only once in the first block, they displayed a significantly larger pupil diameter during CS+ than during CS− presentations in the second block, in spite of relatively low explicit certainty ratings for associative fear memory assessed after the experiment. We conclude that pupil dilation is a very sensitive indicator of associative fear memory, reflecting even one-trial-learning. Such one trial learning until now was only demonstrated for event related brain potentials with magnetoencephalography (Rehbein et al. 2014). In respect of the time point at which differential pupil diameter was observed here, our findings concur well with a recent conditioning study that also reported CS+/CS− differences from 6 to 8 s after stimulus onset, but not as early as from 0 to 2 s (Jentsch et al. 2020). A recent study also demonstrated an association between pupil dilation and prediction errors in fear conditioning (Koenig et al. 2018). In contrast to pupil dilation, heart rate did not reveal any conditioning effects, presumably due to only two presentations of CSs. The experiment was not specifically designed to capture conditioned responses, but emotion regulation effects.

Another goal of the present study was to test whether emotion regulation influences associative fear memory. In a former experiment, we found that a higher aversiveness of a consequence leads to an increased expectancy of this consequence, and participants overestimated the association between a highly aversive consequence and a preceding cue (Wiemer et al. 2014). Therefore, we expected that cognitive reappraisal might increase or decrease the aversiveness of the feared consequence and thus lead to a stronger or weaker associative memory for the CS-US association, respectively. However, this was not the case. Maybe cognitive reappraisal had little or no influence on the aversiveness of the used US and therefore did not affect associative memory. It should be considered, though, that this might depend on the consolidation interval after learning. In this study, we tested the participants fear memory right after the learning phase. In previous research, it was demonstrated that the memory enhancing effect of emotional arousal may become stronger with an ongoing consolidation process (Andreatta et al. 2017; McGaugh 2018). During consolidation, the basolateral amygdala seems to be involved in transferring learned information from the hippocampus-dependent memory to long-term memory depending more on neocortical activity. For example, one study showed that participants could remember an emotional version of a short story better than a non-emotional version of a story one week after learning, but one hour after learning there was no difference in memory performance (Quevedo et al. 2003). Possibly, emotion regulation still modulates long-term memory of fear relevant associations, and therefore future studies should consider testing memory one day after learning.

Finally, we found a significant correlation between state and trait anxiety and the evaluation of the CS− only. Those participants with more self-reported state or trait anxiety rated the CS− as more negative and more arousing. No such correlation was found for the CS+/US. This finding further supports and extends meta-analytic reports of enhanced fear responses to the CS− in patients with anxiety disorders during acquisition (Duits et al. 2015). It is assumed that people with anxiety disorders suffer from deficient inhibition of fear responses to safety cues and/or generalize their fear to neutral or safety cues. The present results confirm this idea and add to this research as we observed no interaction between subclinical anxiety and emotion regulation on the negative evaluation of the CS−. That is, highly anxious participants were not less efficient in emotion regulation than less anxious participants. Thus, cognitive reappraisal may compensate in part for the enhanced responses to safety cues. However, this may only be true for trait anxiety and generalizations to anxiety disorders should be made with caution, since we only studied a non-clinical sample here. A recent review came to the conclusion that patients with social anxiety disorders are less efficient in cognitive reappraisal (Dryman and Heimberg 2018).

Overall, some limitations of the present study should be considered. First, an issue already discussed is that cognitive effort of the regulation strategies was not assessed in the present experiment. Future studies may ask participants to rate cognitive effort and use further potential indicators of cognitive effort and emotional responding, such as fMRI. Second, some participants had to be excluded from the physiological data analysis, because of technical failures and artifacts. However, verbal ratings were similar to the whole sample in the remaining participants and the aimed statistical power was still achieved. Finally, the ratings of the CS+/US during the learning phase were not designed to distinguish between CS+ and US, so participants could fully concentrate on the emotion regulation task without being interrupted by too many rating prompts. In addition, CS-specific ratings were assessed separately after the learning phase.

In conclusion, the present study supports previous findings that humans can use cognitive reappraisal to down-regulate conditioned fear. It further adds to research that conditioned fear can also be up-regulated and that this may even be more efficient than down-regulation, as physiological responses suggest. However, cognitive reappraisal had no impact on immediate associative memory. Still, future studies may further explore the potential of cognitive reappraisal in improving safety learning, especially in patients with anxiety disorders and by considering consolidation intervals.

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Compliance with ethical standards

Conflict of interest Julian Wiemer, Milena Rauner, Yannik Stegmann, and Paul Pauli declares that they have no conflict of interest to disclose.

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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