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Lasting effects of cognitive emotion regulation: neural correlates of reinterpretation and distancing

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Abstract

Reinterpretation and distancing are two cognitive reappraisal tactics, used to regulate one's emotions in response to emotion-eliciting stimuli or situations. Relatively less is known about their (differential) lasting effects on emotional responding and related neural correlates. This functional magnetic resonance imaging study investigated 85 healthy females, participating in a 2-day cognitive emotion regulation experiment. On the first day, participants were instructed to passively look at, reinterpret or distance from repeatedly presented aversive pictures. One week later, they were re-exposed to the same stimuli without regulation instruction, in order to assess lasting effects. The main outcome measures comprised ratings of negative feelings and blood-oxygen-level-dependent responses. Lasting effects for reinterpretation compared with looking at aversive pictures during passive re-exposure 1 week later were reflected in stronger activation of the left amygdala, the ventromedial prefrontal cortex (vmPFC) and reduced negative feelings. Neither distancing compared with looking at aversive pictures nor reinterpretation compared with distancing did result in significant effects during re-exposure. These findings indicate that reinterpretation leads to reduced negative feelings 1 week later, which might be mediated by inhibitory vmPFC activation or stronger positive emotions during re-exposure. However, the missing difference compared with distancing questions the specificity of the results and the mechanisms underlying these two cognitive reappraisal tactics.

Key words: reinterpretation; distancing; vmPFC; amygdala; cognitive reappraisal

Introduction

Cognitive emotion regulation is of central importance for changing emotional responses toward emotino-eliciting stimuli and situations in daily life. (Gross and John, 2003). Moreover, it is a crucial part of cognitive behavioral therapy (Beck, 1979) and has been shown to be related to therapy success in anxiety disorders (Smits *et al.*, 2012). One of the most prominent strategies—cognitive reappraisal—is defined as reinterpreting a potentially emotional stimulus or situation in a way that changes its emotional impact (Gross and John, 2003). Neuroimaging stud-

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ies investigating cognitive reappraisal particularly revealed an interaction of regulatory lateral and medial prefrontal, anterior cingulate and parietal and temporal cortex areas with brain regions associated with bottom-up processing of emotions (e.g. amygdala) during regulation (Ochsner et al., 2012).

There are two main tactics by which cognitive reappraisal is implemented in experimental studies (Ochsner et al., 2012), namely reinterpretation and distancing. Reinterpretation is defined as changing one's interpretation of an emotion-eliciting stimulus or situation (e.g. imagining that the situation has a better ending) and distancing is defined as changing one's personal or psychological distance from an emotional stimulus or situation (e.g. taking the detached perspective of an observer/a third person). Both tactics are able to effectively regulate emotions (Webb et al., 2012), while the neural correlates derived from studies mainly investigating only one of both tactics differ somehow (Ochsner et al., 2012): reinterpretation seems to activate more ventral lateral prefrontal regions while distancing is associated with the activation of parietal regions. So far, there are only two published studies directly comparing the neural correlates of distancing and reinterpretation. Ochsner et al. (2004) specifically found enhanced activation of cingulate gyrus and inferior parietal cortex in a subject group using distancing and stronger activation of lateral prefrontal cortex (PFC), temporal, parietal, occipital and cerebellar regions in the group using reinterpretation. A more recent between-subject study (Dörfel et al., 2014) showed enhanced activation in several areas including orbitofrontal cortex (OFC), inferior frontal cortex, anterior insula, superior frontal cortex, supplementary motor area, precentral gyrus and temporal gyrus for reinterpretation compared with distancing, while distancing more strongly increased angular gyrus activation. Moreover, activation in the supramarginal gyrus, rolandic operculum and left posterior insula was reduced for reinterpretation compared with the passive look condition. Furthermore, activation in the temporal gyrus and left amygdala was decreased for distancing relative to the passive look condition.

Despite the general and clinical relevance of cognitive reappraisal, relatively less is known about lasting effects (Ochsner et al., 2012). Previous experimental studies indicate the lasting effects of distancing on emotional experience during re-exposure (Kross and Ayduk, 2008; Ayduk and Kross, 2009; MacNamara et al., 2011; Ahn et al., 2015). In our own previous study, we could also show that repeated reinterpretation leads to reduced negative feelings during passive re-exposure to the same stimuli 1 day after the active regulation condition (Hermann et al., 2017).

Moreover, one neuroimaging study demonstrated reduced amygdala activation during re-exposure after 15 min to previously reappraised stimuli via distancing in healthy participants (Walter et al., 2009), while this effect was not found in patients with major depressive disorder (Erk et al., 2010b). Reduced amygdala activation also appeared in another study during re-exposure after 1 week, but only when emotions were repeatedly (four times) regulated via distancing in response to the same stimuli 1 week before (Denny et al., 2015). Moreover, dorsolateral PFC activation during distancing predicted better recognition of negative pictures after one year (Erk et al., 2010a). In our own study (Hermann et al., 2017), we furthermore found a negative association of negative feelings and ventromedial prefrontal cortex (vmPFC) activation during re-exposure to previously reinterpreted stimuli 1 day later. The vmPFC is an important region for regulating negative emotions through cognitive strategies and during extinction (Diekhof et al., 2011) and might therefore be crucial for the interaction of cognitive reappraisal with clinically relevant emotional memory processes. However, there are no neuroimaging studies directly comparing the lasting effects of reinterpretation and distancing. In a previous behavioral study, repeated training of the cognitive reappraisal tactic distancing led to reduced negative affect on non-instructed baseline trials, while reinterpretation did not (Denny and Ochsner, 2014). Further studies moreover indicate that either direct or indirect training of emotion regulation has beneficial (lasting) effects (Cohen and Ochsner, 2018).

In the current study, 85 healthy females participated in a 2-day functional magnetic resonance imaging (fMRI) study with an active regulation task on the first day and re-exposure to the same pictures without regulation instructions 1 week later. In total, this study is part of a larger project, comprising one diagnostic session, one behavioral testing session and three magnetic resonance imaging (MRI) sessions. During the active regulation task, participants were instructed to repeatedly look at aversive and neutral stimuli, as well as to repeatedly distance themselves from or reinterpret the meaning of aversive stimuli. We were especially interested in the (differential) (i) effects of reinterpretation and distancing during active regulation, (ii) lasting effects of reinterpretation and distancing during passive re-exposure to the same stimuli 1 week after active emotion regulation as well as (iii) prediction of long-term emotion regulation success from active emotion regulation. For reinterpretation, we intended to replicate and extend our previous findings (Hermann et al., 2017) and therefore expected reduced negative feelings and stronger vmPFC activation compared with the passive look condition during re-exposure. We suppose distancing compared with reinterpretation to be a less stimulus bound tactic and therefore expected a stronger rebound of negative emotions and related neural response (reduced vmPFC and enhanced amygdala and insula activation) during re-exposure to stimuli previously presented in the distancing compared with the reinterpretation condition. In addition, each strategy compared with the look condition is expected to lead to reduced amygdala and insula activation during re-exposure. Moreover, reduced negative feelings for previously regulated stimuli should be predicted from reduced negative feelings, reduced amygdala and reduced insula activation, as well as increased vmPFC activation during the active regulation phase.

Methods and materials

Subjects

Ninety-four healthy female students, recruited via mailing lists at the local university, took part in this fMRI study. This study was part of a larger project investigating the predictive value of emotion regulation and fear conditioning for the development of analog intrusions in the trauma film paradigm. After the interview session, the participants took part in a behavioral testing session (pattern separation task and neuropsychological testing) 1 to 3 days later. The first phase of the emotion regulation task was conducted 7 to 10 days after the interview session, followed by the second emotion regulation session 6–8 days later. After the emotion regulation task, the participants left the scanner, gave ratings for the emotion regulation task and were prepared for the following fMRI fear-conditioning task (shock workup procedure, instruction) including fear acquisition and immediate extinction training. One day later, participants came back for the

recall and renewal phase of the fear-conditioning task during scanning and afterward conducted the trauma film paradigm (outside the scanner). The development of analog intrusions was assessed in the following 7 days as well as after 3 months via online survey. A further study appointment was conducted to investigate film memory and Posttraumatic Stress Disorder (PTSD) symptoms in reaction to the film. Moreover, the participants filled in several questionnaires not related to the question of this study. The results for the other tasks (besides emotion regulation) and for the questionnaires will be reported elsewhere. We confirm that we have reported, for the experiment in this study, all measures, conditions, data exclusions and determination of sample size.

An a priori power analysis was conducted for the main question of the project, namely the prediction of intrusions from fear conditioning. Due to the lack of previous studies regarding these associations, we assumed a medium effect of $\rho = 0.3$ for power analysis, leading to a minimum sample size of $N = 67$ for linear regression analysis with one predictor (power $(1\text{-}\beta) = 0.80$, $\alpha = 0.05$), with a final planned sample size of $N = 83$ participants (compensating for a drop-out rate of 20%). Further drop-outs, e.g. for skin conductance responses during the fear-conditioning task, ultimately led to the final sample size of 94 females for all tasks and measures.

To screen for study inclusion and exclusion criteria, a short telephone interview and a comprehensive examination appointment were conducted with each participant. In order to check for any mental disorders and traumatic experiences, participants were screened with the Diagnostic Interview for mental disorders (DIPS) for DSM-5 (Margraf *et al.*, 2017a,b) and the German version of the Clinician-Administered PTSD Scale (Cwik and Would, 2015) in combination with the Life Events Checklist. They were excluded from the study if they fulfilled criteria for any mental disorder, or if they had experienced a traumatic event within the last 4 weeks, or physical or sexual violence in the past. Further exclusion criteria consisted of self-reported neurological disorders, color blindness, severe or chronical medical diseases, current or past psychological treatment, MRI contraindications and the use of psychoactive or other potentially confounding substances (currently and/or regular drug use in the past). All participants were right-handed as assessed by the Edinburgh Inventory of Handedness (Oldfield, 1971), were aged between 18 and 35 years, had normal or corrected-to-normal vision and spoke German fluently. Participants were reimbursed with course credits or 10€/h for their participation. Nine females were excluded because of early termination of the study ($n = 5$), technical problems during scanning ($n = 2$) and excessive head movement during scanning ($n = 2$; see below for details), leaving a final sample of $n = 85$ women (age: $M = 23.15$ years; s.d. = 2.65 years; range = 18–31 years). The participants gave written informed consent according to the guidelines of the ethical standards of the Declaration of Helsinki and were told that they could terminate the experiment at any time. All procedures were approved by the local ethical review board of the Faculty of Psychology and Sports Science at the Justus Liebig University Giessen, Germany. As this project also comprises very sensitive clinical information, the data are not publicly available but can be received on request from the authors.

Stimuli

Sixteen aversive pictures (12 on day 1 and additional 4 on day 2) and eight neutral pictures (4 on day 1 and additional 4 on day 2) were used as stimuli for the emotion regulation paradigm, consisting of an active emotion regulation training phase on day 1 and a re-exposure phase on day 2. Additionally, four unpleasant pictures and one neutral picture were used for regulation training. Pictures of the aversive category showed one or more people suffering (four subcategories containing four pictures each: homeless person, domestic violence, ill person in hospital, and accident scene), while neutral pictures displayed everyday scenes (e.g. two people in a conversation). At least one person was depicted in each picture. Stimuli were selected either from the International Affective Picture System (Lang *et al.*, 1997) or from the Internet and used in a previous study (Hermann *et al.*, 2017). Valence and arousal ratings (pictures used in the main experiment) assessed in a pre-study ($n = 36$; age: $M = 26.19$ years, s.d. = 4.01 years, range: 20–37 years; 41.7% females, 58.3% males) indicated aversive pictures to be less pleasant ($M = 2.50$, s.d. = 0.84) and more arousing ($M = 5.13$, s.d. = 1.58) than neutral pictures (valence: $M = 5.58$, s.d. = 0.77; arousal: $M = 2.00$, s.d. = 0.99). Stimuli were presented on a 32″ LCD monitor (NordicNeuroLab Inc., Milwaukee, WI, USA) located at the end of the scanner (visual field = 28°), and the monitor was viewed through a mirror mounted to the head coil.

Procedure

Active emotion regulation was performed on a first day, and re-exposure to the same stimuli took place 6–8 days later ($M = 6.88$ days, s.d. = 0.42 days). The participants got written instructions concerning the emotion regulation paradigm. They were informed about seeing neutral and unpleasant pictures and having three different tasks during picture viewing. An instruction word before the picture presentation indicated which task to perform during picture viewing. Moreover, they were instructed to watch all stimuli attentively, and to avoid focusing on single details of the presented scene. In order to decrease their negative feelings via reinterpretation, they were asked to imagine the displayed situation to have a better ending or to be better than expected. During distancing, they should view the presented scene from a detached observer perspective, in order to reduce negative feelings. For the look condition, participants were instructed to look at aversive and neutral pictures, respectively, to respond naturally and to permit all upcoming feelings and thoughts without actively changing them. After participants read the written instruction, the experimenter went through the complete instruction together with them, whereby the correct understanding of the strategies was ensured and practiced with sample pictures. Afterward, participants completed a computer-based training phase outside the scanner consisting of 13 trials with different stimuli (4 aversive pictures each paired once with the instruction reinterpretation, distancing, and look, and 1 neutral picture shown once with the instruction look). The conditions 'reinterpretation', 'distancing' and 'look aversive' were performed four times, 'look neutral' one time. Following this, the experimenter checked the correct implementation of the strategies and all resulting questions were clarified. The same training (13 trials with the same stimuli) was conducted inside the scanner again, in order to familiarize them with the task in the scanning environment.

The experimental paradigm (see Figure 1) was adapted from a previous study (Hermann *et al.*, 2017). The emotion regulation phase on the first day consisted of altogether 64 trials, with 16 trials for each of the experimental conditions ('reinterpretation', 'distancing', 'look aversive', 'look neutral'). For the aversive picture category, one picture of each subcategory (homeless person,

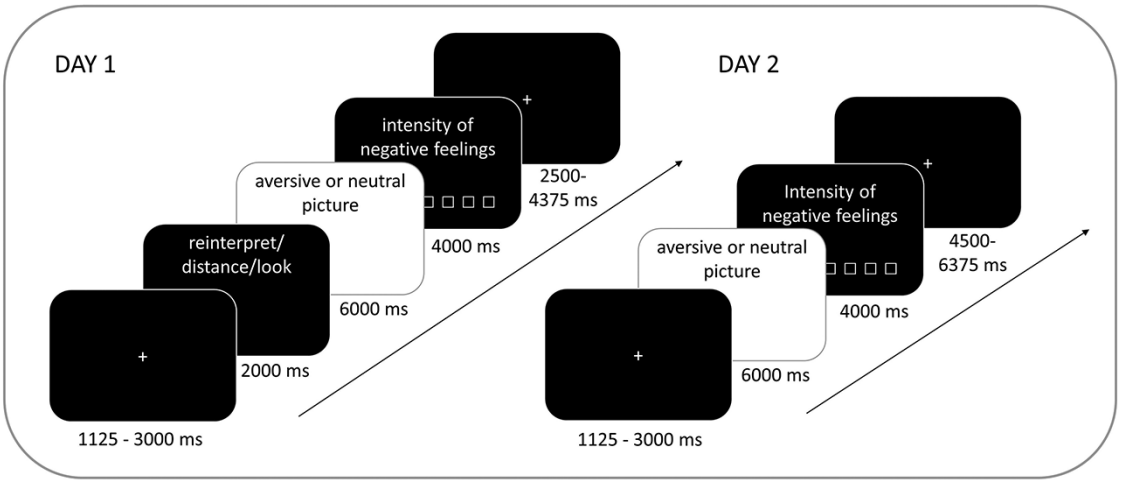

Fig. 1. Schematic illustration of the trial structure for the emotion regulation experiment on day 1 and day 2.

domestic violence, ill person in hospital and accident scene) was used for each condition in order to have comparable stimuli over conditions. The assignment of specific pictures of each subcategory to conditions was randomized across participants.

A white fixation cross on a black background jittered between 1125 and 3000 ms was shown at the beginning of each trial. Afterward, an instruction word (in German; white letters on a black background) was presented for 2000 ms, indicating the different tasks ('reinterpret'/'umdeuten' for 'reinterpretation', 'distance'/'distanzieren' for 'distancing', 'look'/'betrachten' for 'look aversive' or 'look neutral'). Subsequently, an aversive or neutral picture was presented for 6000 ms and participants should perform the instructed task during picture presentation. Immediately afterward, the question 'How strong are you experiencing negative feelings right now?' appeared on the screen above a seven-point Likert scale (ranging from 1 = 'not at all' to 7 = 'very strong') for a maximum of 4000 ms or until participants finished their input by pressing the OK button on the button box. Each trial ended with a white fixation cross on a black background (2500–4375 ms), leading to a total trial duration of 17.5 s.

The active emotion regulation phase on the first day comprised four blocks. During the first block, 4 different pictures were shown in each of the 4 conditions (16 trials). This was the same for all blocks. Each picture was again shown with the same regulation instruction in each block (four times in total). The trials were presented in pseudo-randomized order within and across blocks, with no more than twice the same instruction in sequence. After the experimental paradigm on day 1, participants rated their success and effort for the implementation of the regulation conditions as well as the frequency of daily use of these strategies on nine-point Likert scales outside the scanner.

The re-exposure phase took place 6–8 days later (day 2), and participants were instructed to attentively look at the pictures without any specific regulation task (no presentation of instruction words). The 16 pictures of the emotion regulation phase on day 1 (12 aversive and 4 neutral) were presented again, in addition to 4 new aversive and 4 new neutral pictures, resulting in altogether 6 conditions: aversive pictures with reinterpretation on day 1 ('previous reinterpretation'), aversive pictures with distancing on day 1 ('previous distancing'), aversive pictures passively looked at on day 1 ('previous look aversive'), neutral pictures passively looked at on day 1 ('previous look neutral'), new aversive pictures ('new aversive') and new neutral pictures ('new neutral'). The 24 different pictures were presented in each of two blocks (48 trials altogether). As on day 1, all 24 pictures were presented in pseudo-randomized order with a maximum of two presentations of the same condition in sequence. Each trial started with the presentation of a white fixation cross on a black background jittered between 1125 and 3000 ms, followed by an aversive or a neutral picture for 6000 ms. Afterward, participants were presented with the same rating screen as on day 1 for a maximum of 4000 ms, and subsequently with a fixation cross for 4500–6375 ms, leading to a total trial duration of 17.5 s.

After the re-exposure phase on day 2, recognition of pictures and strategy-awareness were assessed for each picture starting with the question 'Did you see this picture during the experiment last week?' ('yes', 'no') and if so the following questions should be answered: 'Which instruction did you receive for this picture last week?' ('look', 'reinterpret', 'distance', 'I don't know'), and 'Did you use this strategy again today?' ('yes', 'no').

MRI

A 3-T whole-body scanner (Siemens Prisma) with a 64 channel head/neck coil was used for the acquisition of brain images. A total of 832 volumes was registered (active emotion regulation phase on day 1: 472 volumes, re-exposure phase on day 2: 360 volumes) using a T2*-weighted gradient echo-planar imaging sequence with 42 slices covering the whole brain (slice thickness = 3 mm; 0.75 mm gap; descending slice order; TE = 30 ms; TR = 2.5 s; flip angle = 81°; field of view = 220 × 220 mm; matrix size = 110 × 110; PAT mode GRAPPA, acceleration factor PE 2). The first three volumes were discarded as the steady state of magnetization was incomplete. An anatomical scan (MPRAGE; 0.94 mm slice thickness) was conducted before the functional runs on day 1 in order to get highly resolved structural information for the normalization procedure. A gradient echo field map sequence was measured in order to get information for unwarping B0 distortions. Statistical Parametric Mapping software (SPM12, r7219, Wellcome Department of Cognitive Neurology, London, UK; 2009) implemented in MATLAB (R2018b, Mathworks Inc., Sherborn, MA, USA) was used for data analysis. Following preprocessing steps were done in this order: unwarping and realignment (b-Spline interpolation), slice time

correction, co-registration of functional data to each participant's anatomical image, segmentation of the anatomical image into the different tissue types, normalization to the standard space of the Montreal Neurological Institute (MNI) brain and smoothing with an isotropic three-dimensional Gaussian filter with a full width at half maximum of 6 mm. Participants ($n = 2$) were excluded from further analyses for both days if a framewise displacement (Power *et al.*, 2012) of >0.5 mm was detected in at least 15% of the volumes of one scanning session.

In the first level models, the following regressors were included separately for each block (day 1: 4 blocks; day 2: 2 blocks) with a duration of 6 s for each event (day 1: reinterpretation, distancing, look aversive, look neutral; day 2: previous reinterpretation, previous distancing, previous look aversive, previous look neutral, new aversive, new neutral). Additionally, one regressor for the instruction period on day 1 (duration: 2 s) and one regressor for the rating period on day 1 and day 2, respectively, were implemented in one first-level model separately for each session (day 1 and day 2). The regressors were each modeled by a boxcar function convolved with the canonical hemodynamic response function in the general linear model. Six movement parameters of the realignment procedure for each day as well as one regressor for each volume with a framewise displacement >0.5 mm (Power *et al.*, 2012) were included as regressors of no interest. A high-pass filter of 128 s was applied to filter voxel-based time series. Contrasts between the different conditions (look aversive minus look neutral, reinterpretation minus look aversive, distancing minus look aversive, reinterpretation minus distancing, previous look aversive minus previous look neutral, previous reinterpretation minus previous look aversive, previous distancing minus previous look aversive, previous reinterpretation minus previous distancing, new aversive minus previous look aversive) were calculated on an individual level, and analyzed in one-sample *t*-tests and multiple regression (for the prediction question) during second-level analyses as implemented in SPM12.

For exploratory whole brain analyses, the intensity and significance thresholds were set to $P < 0.05$ on voxel-level corrected for multiple testing (family-wise error [FWE] correction); the minimal cluster size (*k*) was 10 voxels. Region of interest (ROI) analyses were conducted by using the small volume correction option of SPM12. For ROI analyses, the significance threshold was set to $\alpha = 0.05$ on voxel level, corrected for multiple testing (FWE correction), and the intensity threshold was set to $P = 0.001$ (uncorrected). Analyses for a priori defined ROIs were done for amygdala, insula and vmPFC. Probability masks taken from the current 'Harvard-Oxford Cortical and Subcortical Structural Atlases' provided by the Harvard Center for Morphometric Analysis (http://www.cma.mgh.harvard.edu/) with a probability threshold of 0.50 included in the FSL software package (http://www.fmrib.ox.ac.uk/fsl/) were used for bilateral amygdala and insula. In line with our previous study (Hermann *et al.*, 2017), the vmPFC mask was constructed by adding a sphere (radius: 9 mm) around the peak voxel (MNI: $x = 0$, $y = 40$, $z = -18$) of regulation-related vmPFC activation, as identified in a meta-analysis (Diekhof *et al.*, 2011).

Statistical analysis (behavioral data)

All statistical analyses were performed in IBM SPSS Statistics for Windows 27.0 with Greenhouse–Geisser correction if needed, and the statistical significance level was set to $P \leq .05$. Statistical comparisons between negative feelings for the different conditions were done separately for the active regulation as well as for the re-exposure phase. For active regulation, look aversive and look neutral were compared by conducting a *t*-test for dependent samples, in order to investigate emotional reactivity. For the analysis of emotion regulation effects, comparisons of reinterpretation, distancing and look aversive on day 1 were investigated by means of Analysis of Variance (ANOVA); significant main or interaction effects were followed by appropriate post hoc tests. During re-exposure, planned comparisons (previous

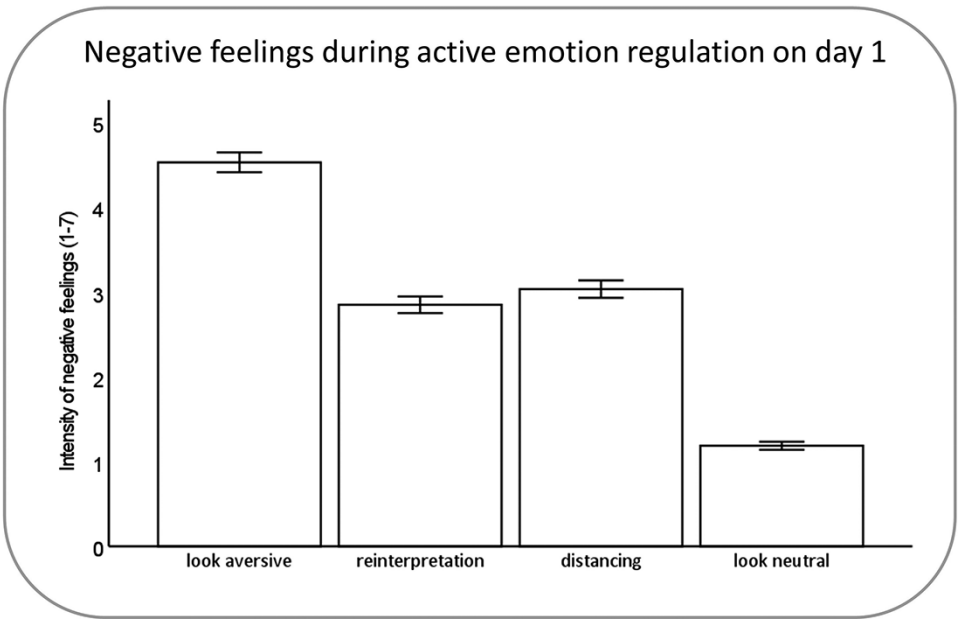

Fig. 2. Ratings of the intensity of negative feelings during the active regulation task on day 1 for the different conditions. All conditions differed significantly from each other (all $P \leq 0.016$). Error bars depict SEM.

reinterpretation *vs* previous look aversive, previous distancing *vs* previous look aversive, previous reinterpretation *vs* previous distancing) were analyzed via *t*-tests for dependent samples. Post hoc, we moreover conducted *t*-tests for dependent samples for the comparison of new aversive *vs* previous look aversive and previous look aversive *vs* previous look neutral. Differences between reinterpretation and distancing regarding regulation success, effort and daily use (day 1), as well as explicit memory for the regulation tactic (which regulation tactic was used for each picture) and pictures (picture shown during the active regulation phase 1 week before) (day 2) were investigated via *t*-tests for dependent samples. Pearson correlations were used for investigating the association of negative feelings for reinterpretation/distancing minus look aversive (day 1) with negative feelings for previous reinterpretation/previous distancing minus previous look aversive (day 2).

Results

Emotional reactivity (day 1)

Passively looking at negative compared with neutral pictures led to increased self-reported negative feelings ($t(84) = 28.499$, $P < 0.001$) (see Figure 2), as well as activation of several brain regions (see Supplementary Tables S1 and S2), including the a priori defined ROIs amygdala, insula and vmPFC, and indicating successful induction of negative emotions.

Active emotion regulation (day 1)

ANOVA revealed a significant main effect of regulation condition (reinterpretation, distancing, look aversive) during active emotion regulation on day 1 ($F(1,84) = 3.208$, $P = 0.043$). Post hoc *t*-tests (Bonferroni corrected) showed that both reappraisal tactics reduced negative feelings (distancing: $t(84) = 13.731$, $P < 0.001$, Cohen's $d = 1.49$; reinterpretation: $t(84) = 17.200$, $P < 0.001$, Cohen's $d = 1.87$), while reinterpretation was even more effective in down-regulating negative feelings than distancing ($t(84) = 2.450$, $P = 0.049$, Cohen's $d = 0.27$) (see Figure 2). On the neural level, reinterpretation compared with look aversive led to stronger activation of angular gyrus and temporal gyrus/pole, cerebellum and several frontal brain regions, including inferior, superior and middle frontal gyrus, as well as frontal pole (see Table 1). Moreover, reinterpretation compared with look aversive diminished activation in bilateral insula (ROI), vmPFC (ROI) and lingual gyrus. Distancing compared with look aversive more strongly activated middle temporal gyrus, and inferior frontal gyrus, while activation was reduced in bilateral amygdala (ROI), vmPFC (ROI) and intracalcarine cortex (see Table 2). Stronger activation for reinterpretation compared with distancing was found for bilateral insula (ROI), left amygdala (ROI) and middle temporal gyrus (see Table 3). Post hoc ratings indicated no differences between reinterpretation and distancing in regulation success ($t(83) = 1.627$, $P = 0.108$, Cohen's $d = 0.18$), regulation effort ($t(83) = -0.523$, $P = 0.603$, Cohen's $d = -0.06$) and frequency of use of the specific tactic in daily life ($t(83) = -0.037$, $P = 0.970$, Cohen's $d = -0.004$).

Re-exposure 1 week later (day 2)

Previous reinterpretation compared with previous look aversive led to less negative feelings ($t(84) = 2.429$, $P = 0.017$; Cohen's $d = 0.48$) (see Figure 3) and enhanced activation in the left amygdala (ROI; MNI: $x = -32$, $y = 0$, $z = -18$; $T = 3.25$, $p_{fwe} = 0.043$; Cohen's $d = 0.35$) and vmPFC (ROI; MNI: $x = 4$, $y = 38$, $z = -18$; $T = 4.08$, $p_{fwe} = 0.006$; Cohen's $d = 0.44$) (see Figure 4) during re-exposure. Previous distancing compared with previous look aversive only marginally significantly reduced negative feelings during re-exposure ($t(84) = 1.896$, $P = 0.061$; Cohen's $d = 0.47$) (see Figure 3), while no significant activation differences were found. Previous reinterpretation and previous distancing did not result in significant differences during re-exposure on the behavioral level ($t(84) = .576$, $P = 0.566$) or on the neural level.

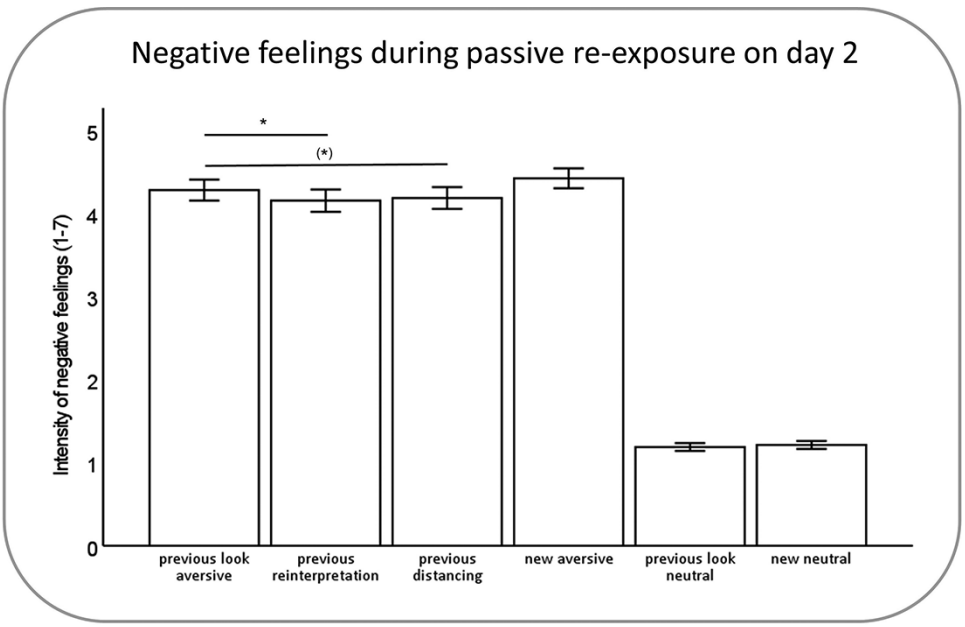

Fig. 3. Ratings of the intensity of negative feelings during re-exposure to the stimuli on day 2 previously presented with different instructions on day 1. Significant differences for the planned comparisons (previous reinterpretation *vs* previous look aversive; previous distancing *vs* previous look aversive; previous reinterpretation *vs* previous distancing) are marked with * ($P < 0.05$), trends ($P < 0.1$) with $^{(*)}$. Error bars depict SEM.

Table 1. Neural activation for reinterpretation compared with look aversive during the active regulation phase on day 1

Brain region	H	x	y	z	T_{max}	p_{fwe}	d
Reinterpretation minus look aversive							
Temporal gyrus (posterior division)	L	−48	−40	2	7.65	<0.001	0.83
Frontal pole	L	−48	36	−6	7.34	<0.001	0.80
Angular gyrus	L	−54	−58	20	7.10	<0.001	0.77
Temporal pole	R	50	12	−22	7.06	<0.001	0.77
Superior frontal gyrus	L	−4	12	64	6.51	<0.001	0.71
Frontal pole	R	48	38	−12	6.40	0.001	0.69
Cerebellum (right crus II)	R	18	−82	−40	6.17	0.001	0.67
Temporal pole	L	−52	8	−22	6.06	0.002	0.66
Inferior frontal gyrus, pars triangularis	L	−52	22	10	6.06	0.002	0.66
Middle frontal gyrus	L	−38	4	50	5.84	0.005	0.63
Middle temporal gyrus, anterior division	R	56	−4	−24	5.81	0.006	0.63
Inferior frontal gyrus, pars triangularis	R	54	24	16	5.61	0.012	0.61
Angular gyrus	R	56	−54	24	5.43	0.023	0.59
Insula (ROI)	L	−30	22	−2	3.73	0.042	0.40
Look aversive minus reinterpretation							
Lingual gyrus	R	14	−78	−2	6.67	<0.001	0.72
Insula (ROI)	L	−38	−2	10	4.82	0.001	0.52
Insula (ROI)	R	42	2	6	4.80	0.001	0.52
vmPFC (ROI)		−2	36	−24	3.36	0.043	0.36
vmPFC (ROI)		4	34	−18	3.32	0.047	0.36

The significance threshold was set to $P = 0.05$ (FWE corrected). Results from the region of interest analysis are labeled with '(ROI)'. All coordinates (x, y, z) are given in MNI space. H = hemisphere, L = left, R = right.

Table 2. Neural activation for distancing compared with look aversive during the active regulation phase on day 1

Brain region	H	x	y	z	T_{max}	p_{fwe}	d
Distancing minus look aversive							
Middle temporal gyrus, posterior division	L	−52	−38	0	5.86	0.005	0.64
Inferior frontal gyrus, pars triangularis	L	−48	30	−4	5.57	0.014	0.60
Look aversive minus distancing							
Intracalcarine cortex	R	12	−84	0	5.55	0.015	0.60
Amygdala (ROI)	L	−20	−4	−12	4.15	0.003	0.45
Amygdala (ROI)	R	24	−4	−12	4.53	0.001	0.49
vmPFC (ROI)		4	34	−16	4.61	0.001	0.50

The significance threshold was set to $P = 0.05$ (FWE-corrected). Results from region of interest analysis are labeled with (ROI). All coordinates (x, y, z) are given in MNI space. H = hemisphere, L = left, R = right.

There were no significant results for exploratory whole brain analyses for previous reinterpretation and previous distancing compared with each other and compared with previous look aversive.

New aversive compared with previous look aversive led to stronger negative feelings ($t(84) = 2.715$, $P = 0.008$; Cohen's $d = 0.48$), stronger activation of left insula, bilateral amygdala and vmPFC and further activation differences in several brain regions as shown by whole brain exploratory analyses (see Supplementary Table S3). Moreover, findings for previous look aversive minus previous look neutral showed stronger negative feelings ($t(84) = 24.34$, $P < 0.001$; Cohen's $d = 1.17$), stronger activation in bilateral insula (ROI) and vmPFC (ROI), reduced activation in the right insula (ROI) and activation differences in several regions as revealed by whole brain exploratory analyses (see Supplementary Table S4).

Post hoc ratings indicated better memory for the regulation tactic applied on day 1 for previous reinterpretation compared with previous distancing ($t(84) = 3.948$, $P < 0.001$, Cohen's $d = 0.43$) and for previous reinterpretation compared with previous look aversive ($t(84) = 7.423$, $P < 0.001$, Cohen's $d = 0.81$), as well as for previous distancing compared with previous look aversive ($t(84) = 4.031$, $P < 0.001$, Cohen's $d = 0.44$). However, there were no differences between these three categories regarding the memory for having seen the respective picture in the week before (all $P > 0.43$).

Prediction of re-exposure effects (day 2) from active emotion regulation (day 1)

Neither ratings of negative feelings ($r = 0.019$, $P = 0.866$) nor neural correlates on the first day (reinterpretation minus look aversive) significantly predicted lasting effects for reinterpretation compared with look aversive.

Negative feelings for distancing minus look aversive predicted negative feelings for previous distancing minus previous look aversive ($r = 0.270$, $P = 0.012$), indicating stronger down-regulation of negative feelings during active regulation to predict reduced negative feelings during re-exposure. Moreover, stronger activation in vmPFC (ROI; MNI: $x = -2$, $y = 38$, $z = -12$; $T = 3.63$, $p_{fwe} = 0.021$; $r^2 = 0.137$) during distancing *vs* look aversive during active regulation predicted reduced

Table 3. Neural activation for reinterpretation compared with distancing during the active regulation phase on day 1

Brain region	H	x	y	z	T_{max}	p_{fwe}	d
Reinterpretation minus distancing							
Middle temporal gyrus, anterior division	R	56	2	−20	5.92	0.004	0.64
Insula (ROI)	L	−30	20	−4	6.01	<0.001	0.65
Insula (ROI)	R	34	22	−4	4.63	0.003	0.50
Insula (ROI)	R	38	16	−12	3.81	0.033	0.41
Amygdala (ROI)	L	−18	−4	−12	3.44	0.028	0.37
Distancing minus reinterpretation							
No significant results							

The significance threshold was set to $P = 0.05$ (FWE-corrected). Results from region of interest analysis are labeled with (ROI). All coordinates (x, y, z) are given in MNI space. H = hemisphere, L = left, R = right.

negative feelings for previous distancing minus previous look aversive (see Figure 5).

Discussion

This is the first study investigating the differential lasting effects of reinterpretation and distancing—two widely known cognitive reappraisal tactics—on subjective and neural responses to aversive stimuli. The main results showed that both strategies were effective immediately, while reinterpretation compared with passively looking at aversive stimuli even led to a stronger reduction of negative feelings and enhanced vmPFC activation during re-exposure 1 week later. Distancing only showed a marginally significant effect on negative feelings during re-exposure. For distancing, both a stronger reduction of negative feelings and a stronger activation of vmPFC during active emotion regulation predicted reduced negative feelings during re-exposure.

During emotion regulation on the first day, both tactics led to reduced negative feelings and activation of a widespread network of brain regions, including temporal, parietal (only reinterpretation) and lateral PFC regions. This activation pattern might represent processes related to emotion regulation, as, e.g. selective attention/working memory, selection of goal-appropriate responses and information from semantic memory, and representation of relevant perceptual and semantic features (Ochsner et al., 2012). Reduced activation in vmPFC and occipital cortex during active regulation for both tactics might relate to diminished affective value and salience of the stimuli due to the regulation of their affective value. Insula activation was reduced for reinterpretation, whereas amygdala activation was reduced for distancing. According to a review of emotion regulation studies, the amygdala, vmPFC and insula have been the most prominent regions showing reduced activation during down-regulation of negative feelings via cognitive reappraisal (Ochsner et al., 2012). The results of the current study are largely

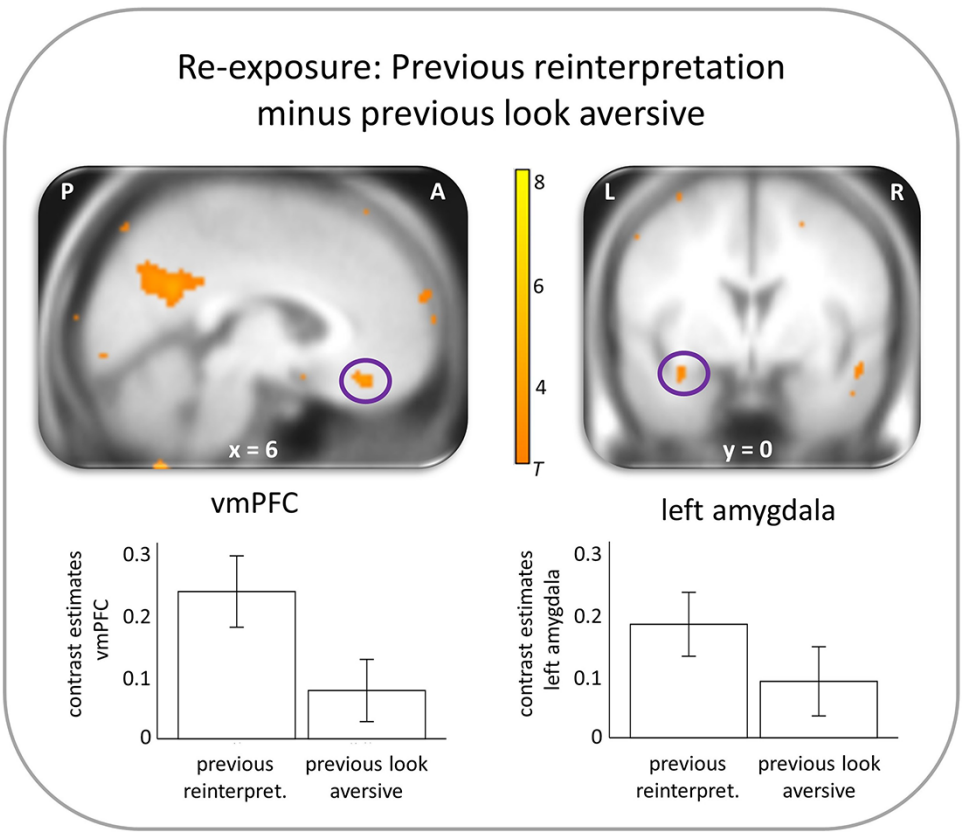

Fig. 4. Enhanced activation in the vmPFC and left amygdala for previous reinterpretation minus previous look aversive during re-exposure on day 2. The intensity threshold was set to $P = 0.005$ (uncorrected) for illustration purposes; activations were superimposed on the MNI305 T1 template. All coordinates (x, y, z) are given in MNI space. The color bar depicts T-values. R = right, L = left, A = anterior, P = posterior.

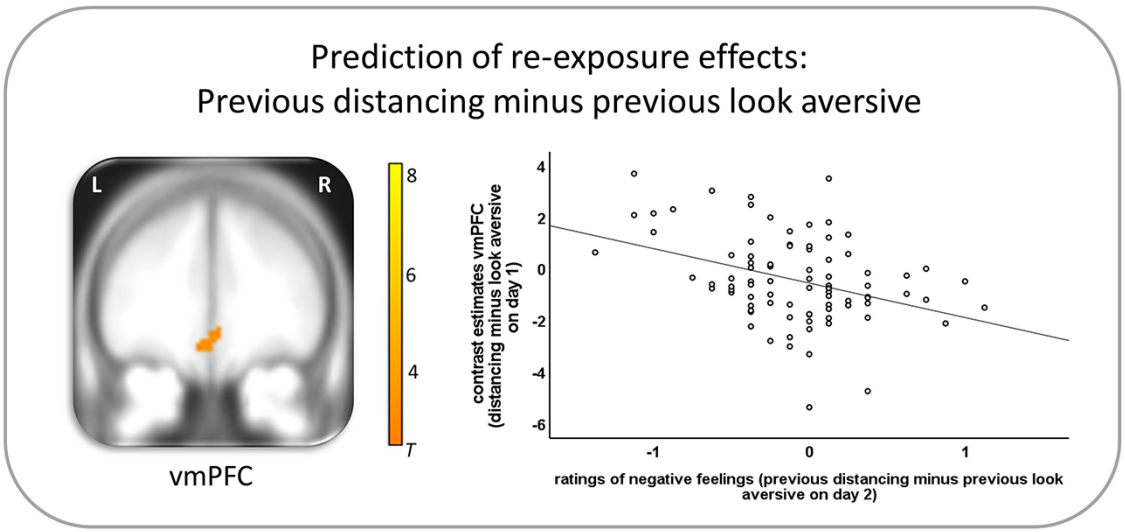

Fig. 5. Neural activation in the vmPFC for distancing minus look aversive on day 1 predicting reduced negative feelings for this contrast (previous distancing minus previous look aversive) on day 2. The intensity threshold was set to P = 0.005 (uncorrected) for illustration purposes; activations were superimposed on the MNI305 T1 template. All coordinates (*x*, *y*, *z*) are given in MNI space. The color bar depicts *T*-values. L = left, R = right, A = anterior, P = posterior.

in line with previous findings, showing activation in a similar fronto–temporo–parietal network for both reappraisal tactics, reduced insula activation for reinterpretation and reduced amygdala activation for distancing in a between-subject study (Dörfel *et al.*, 2014). In the current study, reinterpretation compared with distancing led to a stronger reduction of negative feelings and no differences in neural activation, while distancing compared with reinterpretation led to reduced activation of left amygdala and a more anterior part of the insula. Moreover, anterior insula activation was also increased for reinterpretation compared with look aversive, but did not show reduced activation for distancing *vs* look aversive. In line with a previous meta-analysis (Picó-Pérez *et al.*, 2019), decreased amygdala activation was found specifically for distancing but not for reinterpretation. The down-regulation of amygdala activation by distancing but not reinterpretation might be due to the elicitation of positive emotions during reinterpretation (e.g. the situation is better than expected or will have a positive ending), also leading to enhanced amygdala activation (Dörfel *et al.*, 2014).

Our results of reinterpretation reducing posterior and increasing anterior insula activation are in correspondence with previous findings showing the same activation pattern for affective stimuli from pre to post cognitive reappraisal by reinterpretation (Zhang *et al.*, 2020). These findings are also interpreted with regard to Craig's posterior to anterior distinction of the insula (Craig, 2009). While posterior insula activation might reflect reduced experience of negative feelings, increased anterior insula activation might more likely be associated with enhanced cognitive processing after reinterpretation. Moreover, our study is also in line with a recent meta-analysis showing enhanced anterior insula activation during reappraisal, indicating a general regulatory function of this region (Picó-Pérez *et al.*, 2017).

In contrast to the abovementioned previous study (Dörfel *et al.*, 2014), we could not observe the unique activation of ventrolateral prefrontal cortex (vlPFC) and OFC for reinterpretation, but instead both tactics activated vlPFC. Additionally, we also did not find a stronger left-lateralized activation pattern for reinterpretation, indicating that both tactics as investigated in our study do not substantially differ (at least in the neural correlates) of linguistic and semantic processes, as indicated by previous findings (Ochsner *et al.*, 2012; Dörfel *et al.*, 2014).

In our previous study (Hermann *et al.*, 2017), reinterpretation led to reduced negative feelings 1 day after active regulation. In the current study, this lasting effect could be replicated for a 1 week re-exposure delay. Furthermore, vmPFC activation was enhanced for previously reinterpreted stimuli (*vs* look aversive). In association with reduced negative feelings, this stronger vmPFC activation was also found in the abovementioned previous study (Hermann *et al.*, 2017). While two meta-analyses indicate the vmPFC as an important region for the cognitive regulation of emotions (Diekhof *et al.*, 2011; Yang *et al.*, 2020), other meta-analytic investigations could not replicate this finding (Buhle *et al.*, 2014; Morawetz *et al.*, 2017). In a previous study, vmPFC activation mediated the association of vlPFC and amygdala activation during emotion regulation (Johnstone *et al.*, 2007), indicating a more indirect role of this region. Besides cognitive regulation, the vmPFC has frequently been associated with (successful) extinction recall of conditioned fear (Phelps *et al.*, 2004; Kalisch *et al.*, 2006; Milad *et al.*, 2007; Hermann *et al.*, 2016; Fullana *et al.*, 2018). During extinction learning, an inhibitory memory trace is assumed to develop, which inhibits the original fear memory trace during successful extinction recall (Quirk and Mueller, 2008). The results from the current and our former study (Hermann *et al.*, 2017) indicate that the vmPFC might similarly be involved in recalling the memory for emotion regulation via reinterpretation 1 week after initial regulation. This effect might also be due to the development of an inhibitory memory trace, which dampens the natural response to these emotional stimuli. A further study is in line with our finding, demonstrating that the vmPFC is involved in the association of habitual cognitive reappraisal usage and fear extinction recall (Hermann *et al.*, 2014), moreover emphasizing the relevance of this region for the interaction of cognitive reappraisal with emotional learning and memory processes.

In contrast to our expectations, we additionally found stronger amygdala activation for previous reinterpretation *vs* previous look aversive during re-exposure. As already mentioned above, stronger amygdala activation during encoding might be associated with positive emotions elicited by positive reinterpretation (Dörfel *et al.*, 2014). This interpretation was also confirmed by previous findings, showing reinterpretation to specifically increase positive feelings and distancing to decrease arousal or negative feelings (Shiota and Levenson, 2012; Qi *et al.*, 2017), which was also evident during re-exposure after 30 min (Qi *et al.*, 2017). In our study, reinterpretation might have led to enhanced and lasting positive feelings in association with increased amygdala activation for the specific stimulus, and, as a consequence, to reduced negative feelings during re-exposure. This interpretation, however, challenges the interpretation of vmPFC activation during previous reinterpretation as an indicator for its regulatory/inhibitory function. A previous meta-analysis reveals different subregions of the vmPFC to be related to positive (anterior vmPFC) and negative (posterior vmPFC) affect (Yang *et al.*, 2020). Moreover, a further activation focus in posterior vmPFC was found for the regulation of negative emotions. Therefore, the vmPFC finding in our study, as mentioned above, might reflect regulatory activity or increased positive emotions due to the positive reinterpretation tactic. However, the activation locus in our study more likely reflects posterior vmPFC activation and associated regulatory function as indicated by Yang *et al.* (2020). Further studies are needed to investigate the specific role of the vmPFC in emotional processing and emotion regulation.

For distancing, negative feelings during re-exposure tended to be lower compared with previous look aversive, while no significant activation differences appeared. This is not in line with previous studies, showing reduced amygdala activation during re-exposure after 15 min (Walter *et al.*, 2009), or 1 week (Denny *et al.*, 2015), which might be due to methodological differences (picture presentation time, repeated/onetime active emotion regulation, different instructions). There were also no significant differences in neural correlates or affective self-report between reinterpretation and distancing during re-exposure, questioning the specificity of the results for reinterpretation. The only difference was found for explicit memory for the previously applied regulation strategy, showing better memory for reinterpretation compared with distancing and for each regulation tactic compared with passively looking at pictures. Despite our relatively large sample, these sparse differences between regulation strategies regarding lasting effects might, however, be due to small between-tactic effects or further methodological details and should be considered in future studies.

For distancing, enhanced vmPFC activation as well as a stronger reduction of negative feelings predicted lower negative feelings during re-exposure 1 week later. As described above, the vmPFC is important for emotional processing as well as the regulation of emotions (Yang *et al.*, 2020). In relation with reduced negative feelings, it is more likely that regulatory vmPFC activation predicts reduced negative feelings during re-exposure 1 week later.

The current study has some limitations: as we only investigated females, the generalizability to males is questionable. Additionally, individual differences in hormonal status might have contributed to more variability in the results and should be considered in future studies. As emotion regulation success and effort ratings were only assessed once after the active emotion regulation phase, we could not predict lasting emotion regulation effects on a trial-by-trial basis. Future studies should include these measures in order to have more detailed information for prediction. Moreover, future studies should use valence and arousal ratings instead of ratings of negative feelings, as well as valence-sensitive physiological measures (e.g. startle response), in order to better understand the relevance of positive feelings for immediate and lasting effects of positive reinterpretation. Furthermore, we used stimuli depicting very specific contents, also compromising the generalizability of the results. As we only used four different stimuli per condition and a limited number of stimuli in total, this might, on the one hand, have restricted the reliability and generalizability of the parameter estimates, and on the other hand, the generalizability of the results.

In summary, the findings of the current study show that reinterpretation indeed leads to reduced negative feelings during re-exposure 1 week later. This effect is accompanied by enhanced vmPFC activation, probably associated with enhanced inhibition of the natural emotional response or increased positive feelings, as also indicated by stronger amygdala activation. Distancing, however, did not result in significant lasting effects. Nevertheless, reduced negative feelings and stronger vmPFC activation during active regulation predicted reduced negative feelings for distancing during re-exposure. These findings might contribute to a better understanding of the mechanisms underlying lasting effects of emotion regulation.

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Conflict of interest

None declared.

Supplementary data

Supplementary data is available at *SCAN* online.

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