Full title: Should we keep some distance from distancing? Regulatory and post-regulatory effects of emotion downregulation.

Short title: Regulatory and post-regulatory effects of emotion downregulation.

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21 **Abstract**

22 Emotion regulation is an indispensable part of mental health and adaptive behavior. Research
23 into emotion regulation processes has largely focused on the concurrent effects of volitional emotion
24 regulation. However, there is scarce evidence considering post-regulatory effects with regard to
25 neural mechanisms and emotional experiences. Therefore, we compared concurrent effects of
26 cognitive emotion regulation with effects at different (immediate, short- and long-term) time
27 intervals. In an fMRI study with N=46 (N=30 at re-exposure) young healthy adults, we compared
28 neuronal responses to negative and neutral pictures while participants had to distance themselves
29 from or to actively permit emotions in response to these pictures. We investigated the temporal
30 dynamics of activation changes related to regulation in cognitive control brain networks as well as in
31 the amygdala during stimulation (concurrent effects, timepoint 1) and post-stimulation (immediate,
32 timepoint 2), as well as during re-exposure with the same pictures after short (10 minutes, timepoint
33 3) and long (1 week, timepoint 4) time intervals. At timepoint 1, negative pictures (versus neutral
34 pictures) elicited a strong response in regions of affective processing, including the amygdala.
35 Distancing (as compared to permit) led to a decrease of this response, and to an increase of activation
36 in the right middle frontal and inferior parietal cortex. We observed an interaction effect of time
37 (stimulation vs. post-stimulation) and regulation (distance vs. permit), indicating a partial reversal of
38 regulation effects during the post-stimulation phase (timepoint 2). Similarly, after 10 minutes
39 (timepoint 3) and after 1 week (timepoint 4), activation in the amygdala was higher during pictures
40 that participants were previously instructed to distance from as compared to permit. These results
41 show that the temporal dynamics are highly variable both within experimental trials and across brain
42 regions. This can even take the form of paradoxical aftereffects at immediate and persistent effects at
43 prolonged time scales.

44 Introduction

45 Research on emotion regulation is based on the basic tenet that subjective experience and
46 physiological reactions are susceptible to voluntary regulation efforts, and that this constitutes an
47 adaption to complex and changing environments [1]. While there are different strategies of emotion
48 regulation, according to the Process Model of Emotion Regulation [2], they all have in common that
49 they alter the subjective experience of an emotion by means of (cognitive) top-down influences.

50 The Process Model of Emotion Regulation [2] distinguishes five strategies of emotion
51 regulation according to the timepoint in the emotion generation process at which they are
52 implemented: Situation selection, situation modification, attentional deployment, cognitive change
53 (often referred to as reappraisal), and response modulation. A recent taxonomy [3] builds on this
54 model and further specifies the terminology (to be) used in past and future emotion regulation
55 research. Each strategy comprises different tactics. For instance, situation selection might be achieved
56 by behavioral avoidance, modification by problem solving, attentional deployment via distraction,
57 and response modulation by suppression of the emotional expression. In this study, we focus on
58 cognitive change, or reappraisal, that has been repeatedly reported as adaptive emotion regulation
59 strategy in terms of both (short-term) effectiveness and relation to psychopathology [3-6]. Reappraisal
60 appears early in the emotion generation process (antecedent-focused) and refers to altering the value
61 of the emotion eliciting stimulus. It has been assumed that reappraisal is advantageous because the
62 emotional response has not fully unfolded and the affective value of an event itself is altered [6, 7].
63 Reappraisal can be further divided into different tactics, as well [3]: Reinterpretation, i.e. changing
64 the meaning of a stimulus [8], and distancing (previously often referred to as detachment) [see also
65 our own work, 9, 10]. The meta-analysis by Webb, Miles and Sheeran (4) showed that while
66 reappraisal has been proven effective overall, distancing ($d_+ = 0.45$) was more advantageous than

reinterpretation ($d_+ = 0.36$). According to Powers and LaBar (3), distancing can take different forms: Emotion downregulation by taking a perspective a) that is more spatially distant from the stimulus (spatial), b) that is more distant in time (temporal), c) in which the stimulus represents a hypothetical scenario as opposed to reality (hypothetical), or d) by taking an objective perspective (objective). Most (neuroimaging) studies investigating distancing including our own, so far, implemented experimental designs using the objective form: Participants are instructed to take the perspective of a non-involved, objective observer in order to downregulate emotional responses [9, 11]. Objective distancing has been shown to effectively downregulate negative emotions and activate brain regions implied in cognitive control [3, 4, 12], offering an effective form of emotion regulation to investigate neural correlates and temporal dynamics of successful emotion regulation.

At a neural level, emotion regulation, including cognitive change and attentional deployment, is implemented by cortical regions that exercise influence over emotion-generating subcortical regions [13]. Specifically, emotion-generating regions such as the amygdala have been shown to be responsive to both up- and down-regulation; conversely, regions within the dorsal and ventral frontal cortex, the inferior parietal cortex, and the cingulate cortex are regarded as parts of a common cognitive emotion regulation network [12, 14, 15]. These two systems are assumed to be negatively coupled [16, 17], although there have been conflicting findings [18]. Further research has shown that cortical regions are selectively recruited for the regulation of different kinds of stimuli, for example positive vs. negative [19], for different regulation goals such as up- vs. down-regulation [8], and for different of regulation strategies, e.g. distancing, expressive suppression, or distraction [10, 17, 20, 21]. Taken together, this suggests that while a common and potentially indispensable control network of cognitive emotion regulation can be identified, additional structures are selectively recruited only under certain circumstances, leading to highly context-dependent patterns of co-activation of different brain structures.

91 The effects of these networks, however, are not consistently stable over time and cannot be
 92 fully understood without the consideration of their evolution across multiple time scales. The idea is
 93 that regulation processes act differently at distinct temporal stages of the emotion-generating process
 94 and even beyond, that is, after the cessation of the stimulus. Most studies so far have focused on
 95 concurrent effects of active emotion regulation. However, it has been shown that emotion regulation
 96 effects are also observed beyond the active regulation period, that is during the subsequent post-
 97 stimulation phase [immediate effects, see for distancing 9]. In detail, the authors showed an
 98 immediate increase of amygdala signal once active regulation via distancing had ended. This was
 99 described as a rebound, or paradoxical aftereffect. To qualify as such, the signal needs to demonstrate
 100 a crossed interaction effect between time and task, that is decreased concurrent amygdala activation
 101 during the stimulation (picture presentation) period and increased activation during the immediate
 102 post-stimulation period for a comparison of regulation vs no-regulation conditions. This concept has
 103 been extended to a number of brain regions and timepoints. Lamke and colleagues [22] observed
 104 decreased activation during emotion regulation in the amygdala and in visual cortex regions in the
 105 stimulation phase but increased activation in the subsequent post-stimulation phase. Yet, increased
 106 activation was observed during both stimulation and post-stimulation period in the dorsolateral
 107 prefrontal cortex and other cortical regions, leading to a distinction between reverse and concordant
 108 task-rest interactions.

109 One study [9] demonstrated not only immediate aftereffects, but also effects across an even
 110 more extended period of time up to several minutes (short-term effects). Specifically, upon re-
 111 encountering previously regulated negative stimuli in a passive viewing task ten minutes later, the
 112 authors observed a persisting down-regulation of the amygdala. This re-exposure effect was
 113 negatively correlated to the paradoxical aftereffect that was observed immediately after the
 114 stimulation phase; i.e., a higher immediate aftereffect was associated with a smaller short-term

115 regulation effect. A similar study [23] investigated concurrent and long-term effects (1 day) of both
 116 emotional up- and down-regulation. After one day, lasting experiential and neural effects were only
 117 observed for down-regulation of negative feelings via reinterpretation, but not for other tactics
 118 (distraction) or other goals of regulation (up-regulation). Further, the lasting neural effects were
 119 confined to prefrontal regions, and were not observed in the amygdala. Independently, it has been
 120 shown that regulation effects are also present on long-term time scales of more than one day:
 121 Amygdala responses remained attenuated after one week for images that had previously been
 122 reappraised [using objective distancing, 24]. This, however, was only observed within the amygdala,
 123 but not the frontal cortex, and only happened when the images had been presented and reappraised
 124 repeatedly. Another example of long-term effects has been established for episodic memory
 125 processes: Down-regulation via distancing during encoding led to prefrontal cortical activation during
 126 recognition after one year, whereas lack of regulation during encoding led to activation of rather
 127 affective brain regions after the same interval [25].

128 As systematic investigations of the temporal dimension of distancing including several time
 129 intervals are still lacking, the present research aims at replicating and extending previous results on
 130 the temporal dynamics of distancing, that is its concurrent, immediate, short- and long-term
 131 consequences. We implement a full two-by-two design and compare negative and neutral pictures,
 132 achieving a joint maximization of both arousal and valence differences under two task conditions: to
 133 distance from (regulation) and to actively permit (no-regulation) all emotions that might arise from
 134 negative and neutral pictures. We use multiple timepoints to disentangle the temporal dynamics: 1) a
 135 stimulation phase to measure concurrent activation differences between regulation and no-regulation,
 136 2) a post-stimulation phase to investigate immediate aftereffects, 3) a re-exposure phase after 10
 137 minutes (short-term) as well as 4) a re-exposure phase after one week (long-term) to investigate
 138 prolonged aftereffects of distancing.

139 We expected that this experimental design would lead to activation increases within the
 140 amygdala in response to negative pictures, as compared to neutral ones, and that these activation
 141 increases would be subject to modulation by the concurrent condition: During the stimulation phase
 142 (timepoint 1), we expected relatively less activation in the amygdala when participants were
 143 instructed to distance from negative pictures as compared to permitting all upcoming emotions. This
 144 should be accompanied by activation increases within several cortical regions, in particular within
 145 the frontal and parietal cortex as an indicator of processes associated with cognitive emotion
 146 regulation, more specifically objective distancing. Besides the replication of these expected canonical
 147 results, we sought to investigate possible paradoxical aftereffects within the amygdala: We expected
 148 that the lower amygdala activation in the distance condition as compared to the permit condition in
 149 the stimulation phase reverses in the post-stimulation phase (immediate aftereffect, timepoint 2). We
 150 further aimed at characterizing the amygdala response during re-exposure with the same pictures after
 151 short (10 minutes, timepoint 3) and long (1 week, timepoint 4) time intervals [9, 22].

152 **Materials and methods**

153 This study presents data collected within a larger project on neural correlates and individual
 154 differences in emotion regulation and its aftereffects (SFB 940 Project A5). Specifically, the project
 155 aimed at elucidating the effectiveness and potential costs of volitional emotion regulation. Different
 156 cognitive regulation strategies (acceptance, up- and down-regulation) were compared with respect to
 157 their behavioral and neural effectiveness, i.e., emotion regulation success, but operationalized along
 158 a prolonged time scale. This allowed to examine potential costs of volitional emotion regulation as
 159 indexed by paradoxical immediate and delayed regulatory after-effects. Further aims of the overall
 160 project were to investigate associations of emotion regulation success with personality traits and
 161 genetic polymorphisms. A detailed overview of the project and its subprojects is given in the

Supplementary Materials (Fig S1). Therefore, some of the data reported in this article have been reused in three follow-up studies within the scope of this project: in accordance with the a priori specified analysis plan (<http://gepris.dfg.de/gepris/projekt/223659428> and <https://tu-dresden.de/bereichsuebergreifendes/sfb940/research/a-mechanismen/a5>), associations with genetic polymorphisms were investigated [26], as well as the relation between emotion regulation and personality [27]. Additionally, associations of emotion regulation success and dispositional emotion regulation with resting-state cortico-limbic connectivity have been analyzed [18]. Results from the present sample on the research questions of this publication have not been reported in any of these publications. We report how we determined our sample size, all data exclusions (if any), all manipulations, and all measures in our study, as recommended by transparency guidelines [28]. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The experimental protocol was approved by the ethics committee of the Technische Universität Dresden (EK10012012). Data and materials are provided at the Open Science Framework (<https://osf.io/mg5ac/>).

Participants

Sample size was defined based on feasibility considerations. This resulted in a target sample size of over 48 participants. The sample size that we considered feasible to collect, enabled us with the possibility to at least detect medium-sized effects at a significance level of 0.05 and a power of 0.80. Forty-eight volunteers (16 male, age range 18 – 38 years, age mean $\pm$ *SD* = 24.6 $\pm$ 4.1 years) were recruited from the university community. All participants were right-handed and did not report any current or prior neurological or psychiatric illness or treatment. All participants provided written informed consent and received financial compensation. One participant did not complete the

185 experiment, and another participant withdrew from the study. MRI data were therefore available for
186 46 (out of 48) participants. Out of these 46 participants, 30 returned after 1 week for their second
187 MRI measurement and were included in the analyses of the follow-up measurements (re-exposure,
188 timepoint 4), while 10 returned at an earlier or later time (after 6 to 30 days) and were hence not
189 included in the present analysis, and 6 did not return at all for the second session.

190 **Experimental paradigm and procedure**

191 The study consisted of two sessions, one week apart [for detailed descriptions see 18, 27].
192 During the first session (60 min), participants performed a preparatory scan (5 min), four runs of an
193 emotion regulation task (36 min), an anatomical scan (8 min) and a re-exposure task (10 min). During
194 the second session (25–35 min), participants performed a preparatory scan (5 min), a resting state
195 measurement (8 min) and repeated the re-exposure task (10 min). Additionally, participants were
196 asked to fill in questionnaires with regard to individual differences in emotion regulation and their
197 subjective experience during the fMRI measurement as well as provided a blood sample, which are
198 not focused on in the present publication [for a detailed description see 26, 27].

199 **Emotion regulation task (timepoints 1 and 2)**

200 During the emotion regulation task, participants were asked to either permit the emotions
201 arising in response to a set of negative and neutral pictures, or to down-regulate them by means of
202 objective distancing. During the “permit” condition, participants were asked to take a close look at
203 the picture and permit any emotions that might arise as a result. They were encouraged to imagine
204 that they were immediately witnessing the depicted situation, and instructed not to voluntarily
205 intensify their emotions, to re-interpret the situation, or to distract themselves. During the “distance”
206 condition, they were asked to “take the position of a non-involved observer, thinking about the picture
207 in a neutral way”. This could be achieved, for example, by reducing the personal involvement with

208 the depicted situation, for instance by assuming a personal or physical distance; again, participants
209 were instructed to refrain from interpreting the situation as not real, attaching a different meaning to
210 the situation, or distracting themselves. The “distance” and “permit” instructions were chosen based
211 on previous work, which demonstrated their efficacy [10, 29]. All participants received written
212 instructions including examples, completed a training session outside the MR scanner, which took
213 about 10-15 min and consisted of 16 trials, and were subsequently interviewed about how they
214 implemented the proposed emotion regulation tactic.

215 Each of the four runs of the emotion regulation task consisted of 16 trials, encompassing four
216 trials for each condition. At the beginning of each trial, a picture was presented for 10 s (stimulation
217 phase, timepoint 1). During the initial 2 s of this period, a semi-transparent overlay was presented
218 across the center of the picture, which contained, as a single word, the instruction for either the
219 “permit” or the “distance” condition. Following the offset of the picture, a fixation cross was
220 presented for a variable period of 16–24 s (post-stimulation phase, timepoint 2). This rather long
221 period was inserted into the trial to provide the participants with a relaxation phase, and to allow the
222 return of the BOLD response to baseline levels. Altogether, the total duration of a single trial was, on
223 average, 30 s. At the end of each run, participants were asked to give a rating of their retrospective
224 subjective arousal. For each experimental condition, participants rated on a continuous scale, how
225 much aroused they felt during the presentation of the negative and neutral images and the “distance”
226 and “permit” instructions, respectively. The scale for the continuous arousal scale ranged from –200
227 to 200 for technical reasons (screen coordinates). However, the particular choice of scale units and
228 limits did not affect the participants’ ratings, since only verbal anchors were provided at either end of
229 the scale and participants had to move a slider to a position between those anchors that resembled
230 their arousal (“not at all aroused” vs. “very much aroused”).

231 **Re-exposure task (timepoints 3 and 4)**

232 The re-exposure tasks at the end of session 1 (timepoint 3, 10 minutes later) and during session
233 2 (timepoint 4, 1 week later) consisted of the presentation of exactly those negative and neutral
234 pictures that participants had seen during the emotion regulation task. Since we wanted to investigate
235 emotional reactivity, the presentation duration was shortened to 1000 ms, in accordance with the
236 emotional reactivity paradigm in the study by Walter and colleagues [9]. In contrast to the emotion
237 regulation task, each presentation was followed by a variable inter-trial interval of 2 s to 12 s, and
238 participants should passively view the pictures. Specifically, they were instructed not to voluntarily
239 change their emotional experience as they had done during the main experiment.

240 **Stimuli**

241 Stimuli were selected from the International Affective Picture System [IAPS, 30] and the
242 EmoPicS picture set [31]. We used two sets of negative pictures and two sets of neutral pictures (16
243 pictures per set) matched for content, arousal, and valence (mean valence negative pictures: set 1 =
244 2.71, set 2 = 2.65; mean arousal negative pictures: set 1 = 5.85, set 2 = 5.69; mean valence neutral
245 pictures: set 1 = 5.17, set 2 = 5.13; mean arousal neutral pictures: set 1 = 2.94, set 2 = 2.96). The
246 negative pictures consisted primarily of depictions of animals, bodies, disaster, disgust, injuries,
247 suffering, or violence, while the neutral pictures depicted various scenes, objects and people. The
248 negative and neutral picture sets were matched with regard to depictions of faces, other parts of the
249 body, single or multiple persons, animals, and inanimate objects. The assignment of the pictures to
250 either the “distance” or “permit” conditions was counterbalanced. In order to rule out any further
251 stimulus- or content-related confounds, two sets of negative and neutral pictures were used for one
252 half of the participants, and the other two negative and neutral sets were used for the other half of the
253 participants. Each set of pictures was arranged in two different sequences assigned to participants in

254 an alternating fashion. For the emotion regulation task (timepoints 1 and 2), the order of stimuli was
255 pseudo-randomized within each sequence with the constraint that all experimental conditions
256 appeared equally within each experimental run and that no more than three presentations of the same
257 experimental condition occurred in succession. For the re-exposure tasks (timepoints 3 and 4), the
258 order of stimulus presentation was randomly shuffled. All pictures were projected to a screen located
259 at the rear end of the scanner and were viewed through a mirror attached to the head coil.

260 **Data acquisition**

261 Magnetic resonance (MR) imaging was done on a 3 Tesla scanner (Siemens Trio; Siemens
262 Erlangen, Germany), using a 12-channel head coil. Functional (T2*) MR images were acquired using
263 an EPI sequence with 42 axial slices (slice thickness 2 mm) per volume (TR 2410 ms; TE 25 ms; flip
264 angle 80°; slice gap 1 mm; field of view 192 × 192 mm; matrix size 64 × 64). In addition, anatomical
265 (T1) images were acquired using an MPRAGE sequence consisting of 176 sagittal slices of 1 mm
266 thickness (TR 1900 ms; TE 2.26 ms; flip angle 9°; FOV 256 mm × 256 mm; matrix size 256 × 256).

267 **Data analysis**

268 **Behavioral data analyses**

269 Analysis of the subjective ratings and possible relations between subjective and physiological
270 measures was performed with R 3.0.2 (<http://r-project.org>) including the ggplot2 package [32], and
271 consisted of a two-way repeated-measures ANOVA with the factors picture (negative, neutral) and
272 regulation (permit, distance) with subsequent post-hoc *t*-tests for dependent samples. Due to technical
273 issues and incomplete measurements, ratings were not available from ten participants.

274 **fMRI analyses**

275 Imaging data analysis for all tasks was performed using Matlab 7.4 (MathWorks, Natick, MA)
 276 and SPM 8 (<http://www.fil.ion.ucl.ac.uk/spm/software/spm8>). After discarding the first 4 volumes of
 277 each run, preprocessing consisted of motion correction, coregistration of individual functional and
 278 anatomical data, spatial normalization of the anatomical images to the MNI template, application of
 279 the estimated transformation parameters to the coregistered functional images using a resampling
 280 resolution of $2 \times 2 \times 2 \text{ mm}^3$, and spatial smoothing of the functional images (FWHM 8 mm).

281 First-level statistical analysis of the emotion regulation task was performed using a general
 282 linear model with the experimental conditions (detailed below) as regressors and six additional
 283 motion regressors of no interest. To account for the notion that “rest” is not necessarily a true rest,
 284 especially not in emotionally challenging paradigms [22], we included not only the stimulation but
 285 also the post-stimulation phase in our model, starting with the offset of each picture and lasting for
 286 the same duration as the stimulation phase. This resulted in a first-level model with eight regressors
 287 of interest: we modeled the “permit neutral”, “permit negative”, “distance neutral”, and “distance
 288 negative” conditions both for the stimulation (onset of picture presentation, timepoint 1) and post-
 289 stimulation (offset of picture presentation, timepoint 2) phase. As the temporal dynamics of amygdala
 290 activation may differ from those in cortical regions, we conducted an additional sensitivity analysis
 291 for the amygdala, where activation was modeled by a stick function (transient response) in addition
 292 to a boxcar function (sustained response). This resulted in two different first-level models for the
 293 amygdala, whereas a single first-level model was used for all other brain regions. All regressors of
 294 interest were convolved with the canonical hemodynamic response function, and the default high-
 295 pass filter for SPM8 (128s) was used. The imaging runs of the emotion regulation task were combined
 296 within one fixed-effects model. Parameter estimates for the contrasts of interest were averaged across
 297 runs, submitted to a second-level, random-effects analysis and evaluated using one-sample *t*-tests.

298 The emotion regulation task follows a 2*2*2 factorial design with the factors “picture”
 299 (negative vs. neutral), “regulation” (permit vs. distance), and “time” (stimulation phase vs. post-
 300 stimulation phase). For the stimulation phase, we analyzed the main effects of “picture” and
 301 “regulation” as well as the interaction of “picture” and “regulation”, which were the contrasts of
 302 primary interest. Next, we repeated this analysis for the post-stimulation phase. Finally, we included
 303 “time” as an additional factor into the model and computed the three-way interaction contrast for
 304 “picture”, “task”, and “time” in order to characterize the changes in emotional regulation from
 305 stimulation to post-stimulation. Additionally, the comparisons were restricted to either neutral or
 306 negative pictures.

307 The first-level model of the re-exposure tasks (timepoints 3 and 4) included four regressors
 308 for “negative permit”, neutral permit”, “negative distance”, and “neutral distance” (assignment to
 309 these conditions was based on the preceding emotion regulation task). The duration of all events was
 310 set to 1000 ms as this was the duration of picture presentation. For statistical analysis, contrasts were
 311 computed for the main and interaction effects of the “picture” and “preceding regulation” conditions,
 312 and evaluated in a second-level analysis using one-sample t-tests.

313 Based on our a priori hypotheses, we employed two regions of interest (ROI), the left and
 314 right amygdala as defined by the Harvard-Oxford Subcortical Structural Atlas within the FSL
 315 software package (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases>). Masks were created from the
 316 probabilistic segmentations at a threshold of 50%. For statistical analyses within the amygdala, we
 317 applied a threshold of $p = .05$ FWE after correction for small volume. For all other analyses, a voxel-
 318 wise threshold of $p = .05$ FWE across the whole brain was applied. Activations were labeled using
 319 the Harvard-Oxford Structural Atlases as well as the Anatomy Toolbox for SPM8 [33].

320 Since voxel-wise analyses are limited in integrating data across a predefined anatomical
 321 structure, we additionally obtained summary measures of activation within the left and right amygdala

for all tasks. For this purpose, we extracted parameter estimates for all experimental conditions from the individual first-level analyses using SPM8's `spm_summarise()` function and further analyzed these data using repeated-measures ANOVAs with the factors picture, strategy, and/or time. In addition, for the emotion regulation task, we extracted the activation time courses from these regions by using the `rfxplot` toolbox (Gläscher 2009) to provide an illustration of the results of the model-based analyses.

Results

Behavioral analysis of the stimulation phase (concurrent effects, timepoint 1)

The retrospective subjective arousal ratings after each run of the emotion regulation task demonstrated an interaction between picture and regulation ($F(1,37) = 16.38, p < .001, \eta^2 = .016$) as well as main effects of picture ($F(1,37) = 118.12, p < .001, \eta^2 = .456$) and regulation ($F(1,37) = 107.15, p < .001, \eta^2 = .160$). On average, negative pictures were associated with higher subjective arousal ratings than neutral pictures. Pictures during “permit” were rated as more arousing than pictures during “distance” and this effect was more pronounced for negative than for neutral pictures. On a scale ranging from -200 to 200, the experimental conditions had the following Mean±SD values: permit negative: 50.1±54.4; distance negative: -17.7±58.1; permit neutral: -75.4±71.0; distance neutral: -112.6±59.2.

Neuronal activation differences during the stimulation phase (concurrent effects, timepoint 1)

For both, the emotion regulation and the re-exposure tasks, we report the comparison of pictures (“negative > neutral” and vice versa) and regulation tactic (“distance > permit” and vice

343 versa) as well as the interaction effects between picture and regulation. During the emotion regulation
 344 task, we consider these effects for both the stimulation phase (timepoint 1) and the post-stimulation
 345 phase (timepoint 2), separately. For simplicity, we only report interaction effects between regulation
 346 and time (stimulation to post-stimulation phase) in a joint analysis of the stimulation and post-
 347 stimulation phase. Regarding the two analytic strategies for amygdala activation (transient and
 348 sustained responses), we point out when the choice of the analytical model matters; if not indicated
 349 otherwise, results hold for both strategies. Finally, we report effects of picture and regulation during
 350 re-exposure after 10 min (timepoint 3) and after 1 week (timepoint 4), separately.

351 **Activation differences between negative and neutral pictures**

352 Results of the analysis of activation differences during the stimulation phase are depicted in
 353 Fig 1. During the regulation phase, negative pictures elicited greater activation than neutral pictures
 354 in a large temporo-occipital cluster as well as a few additional brain regions (Table 1). Specifically,
 355 activation peaks were observed in the right fusiform gyrus, the left and right inferior temporal, right
 356 inferior frontal, left insula, posterior cingulate cortex as well as in the left and right amygdala. Greater
 357 activation during neutral than negative pictures was also observed, primarily in left and right superior
 358 temporal as well as left precentral regions.

359 - Insert Fig 1 here -

Fig 1. Whole-brain analysis of concurrent main effects of regulation (stimulation phase, timepoint 1). A. Permit > Distance during the stimulation phase. B. Distance > Permit during the stimulation phase.

Table 1. Activation maxima in the emotion regulation task during the stimulation phase (concurrent effects, timepoint 1).

k	p_{FWE}	t	$p_{unc.}$	x	y	z	label
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Main effect picture							
<i>Neutral Stim Phase > Negative Stim Phase</i>							
248	0.001	6.52	<0.001	-32	-30	62	Left Precentral Gyrus
129	0.002	6.23	<0.001	-58	-16	2	Left Superior Temporal Gyrus
38	0.004	6.08	<0.001	58	-4	-4	Right Superior Temporal Gyrus
32	0.005	5.99	<0.001	12	-20	48	Right SMA
47	0.005	5.95	<0.001	44	-64	50	Right Angular Gyrus
39	0.005	5.94	<0.001	42	-14	20	Right Rolandic Operculum
42	0.011	5.69	<0.001	-34	-20	48	Left Precentral Gyrus
<i>Negative Stim Phase > Neutral Stim Phase</i>							
6265	<0.001	13.63	<0.001	42	-46	-14	Right Fusiform Gyrus
5965	<0.001	12.28	<0.001	-40	-46	-16	Left Inferior Temporal Gyrus
1876	<0.001	10.23	<0.001	44	18	24	Right Inferior Frontal Gyrus
1963	<0.001	10.15	<0.001	14	-20	-10	N/A
339	<0.001	7.96	<0.001	-32	18	-18	Left Insula Lobe
134	0.001	6.62	<0.001	-2	-50	26	Left Posterior Cingulate Cortex
163	0.001	6.61	<0.001	2	-56	-36	Cerebellar Vermis
25	0.006	5.91	<0.001	6	48	-20	Right Gyrus Rectus
36	0.016	5.56	<0.001	0	-54	44	Left Precuneus
164	<0.001	6.91	<0.001	-24	-8	-14	Left Amygdala (ROI)
183	<0.001	7.70	<0.001	20	-6	-12	Right Amygdala (ROI)
190	<0.001	7.63	<0.001	-20	-8	-12	Left Amygdala (ROI, stick model)
211	<0.001	7.86	<0.001	18	-6	-12	Right Amygdala (ROI, stick model)
Main effect regulation							
<i>Distance Stim Phase > Permit Stim Phase</i>							
2957	<0.001	9.73	<0.001	36	28	40	Right Middle Frontal Gyrus
1967	<0.001	9.65	<0.001	54	-52	38	Right Inferior Parietal Lobule
274	<0.001	7.35	<0.001	-40	22	34	Left Middle Frontal Gyrus
302	<0.001	7.07	<0.001	12	-72	38	Right Cuneus
858	<0.001	6.88	<0.001	-42	-50	44	Left Inferior Parietal Lobule

214	<0.001	6.81	<0.001	-12	-76	46	Left Precuneus
111	0.001	6.42	<0.001	6	-38	24	Right Posterior Cingulate Cortex
119	0.001	6.41	<0.001	66	-20	-10	Right Middle Temporal Gyrus
173	0.002	6.26	<0.001	36	20	0	Right Insula Lobe
129	0.003	6.23	<0.001	-32	46	8	Left Middle Frontal Gyrus
71	0.003	6.17	<0.001	10	-34	42	Right Middle Cingulate Cortex
70	0.009	5.80	<0.001	44	48	-4	Right Inferior Frontal Gyrus
67	0.011	5.74	<0.001	-58	24	6	Left Inferior Frontal Gyrus
<i>Permit Stim Phase > Distance Stim Phase</i>							
159	0.001	6.43	<0.001	-22	-96	-8	Left Inferior Occipital Gyrus
122	0.002	6.25	<0.001	28	-94	0	Right Middle Occipital Gyrus
27	0.016	3.40	0.001	-18	-10	-12	Left Amygdala (ROI)
28	0.015	3.50	0.001	18	-8	-12	Right Amygdala (ROI)
122	0.001	4.33	<0.001	-18	-6	-12	Left Amygdala (ROI, stick model)
115	0.002	4.22	<0.001	22	-10	-14	Right Amygdala (ROI, stick model)
Interaction effect picture X regulation							
<i>(DistanceNeutral Stim Phase > PermitNeutral Stim Phase) > (DistanceNegative Stim Phase > PermitNegative Stim Phase)</i>							
13	0.044	3.05	0.002	-18	-10	-12	Left Amygdala (ROI, stick model)
10	0.031	3.29	0.001	32	-2	-22	Right Amygdala (ROI, stick model)
<i>(PermitNeutral Stim Phase > DistanceNeutral Stim Phase) > (PermitNegative Stim Phase > DistanceNegative Stim Phase)</i>							
5	0.023	3.33	0.001	22	-4	-26	Right Amygdala (ROI)
Regulation effect negative pictures only							
<i>DistanceNegative Stim Phase > PermitNegative Stim Phase</i>							
1590	<0.001	8.76	<0.001	52	-48	36	Right Angular Gyrus
2116	<0.001	8.71	<0.001	42	26	38	Right Middle Frontal Gyrus
478	<0.001	6.89	<0.001	-52	38	-8	Left Inferior Frontal Gyrus
147	0.001	6.62	<0.001	-42	22	34	Left Middle Frontal Gyrus
102	0.001	6.43	<0.001	62	-36	-20	Right Inferior Temporal Gyrus
294	0.003	6.21	<0.001	-48	-50	44	Left Inferior Parietal Lobule
113	0.004	6.11	<0.001	42	18	-10	Right Insula Lobe

149	0.004	6.06	<0.001	-30	44	8	Left Middle Frontal Gyrus
74	0.005	6.04	<0.001	12	-66	40	Right Precuneus
<i>PermitNegative Stim Phase > DistanceNegative Stim Phase</i>							
5	0.041	3.06	0.002	18	-8	-12	Right Amygdala (ROI)
148	0.001	4.68	<0.001	-20	-8	-14	Left Amygdala (ROI, stick model)
100	0.006	3.94	<0.001	22	-10	-14	Right Amygdala (ROI, stick model)
Regulation effect neutral pictures only							
<i>PermitNeutral Stim Phase > DistanceNeutral Stim Phase</i>							
205	0.001	6.45	<0.001	36	40	32	Right Middle Frontal Gyrus
192	0.002	6.36	<0.001	60	-42	30	Right Supramarginal Gyrus
<i>PermitNeutral Stim Phase > DistanceNeutral Stim Phase</i>							
267	0.001	6.69	<0.001	-20	-96	-6	Left Inferior Occipital Gyrus
182	0.003	6.21	<0.001	26	-88	6	Right Middle Occipital Gyrus
12	0.038	3.02	0.002	-18	-8	-18	Left Amygdala (ROI)
20	0.045	3.02	0.002	20	-8	-16	Right Amygdala (ROI)
12	0.014	3.50	0.001	-16	-4	-14	Left Amygdala (ROI, stick model)
50	0.02	3.42	0.001	18	-8	-18	Right Amygdala (ROI, stick model)

Abbreviations: k = spatial extent, p_{FWE} = p -values corrected for multiple comparisons (FWE), $p_{unc.}$ = uncorrected p -values, t = t -statistics, x, y, z = MNI coordinates. ROI indicates that an activation peak was observed within the left or right amygdala region of interest.

Activation differences between distancing and permitting emotions

Besides the main effect of picture, there was also a main effect of regulation (Table 1): Clusters of greater activation during distance as compared to permit were observed in the left and right inferior and middle frontal gyrus, left and right inferior parietal lobe and the precuneus, among others. Reverse effects, i.e. greater activation during permit than during distance, were exclusively observed in the left and right amygdala and the occipital cortex. When comparing responses to negative pictures (Table 1), greater activation for distance vs. permit was primarily observed in the right frontal and parietal cortex. Conversely, greater activation for permit vs. distance was present in the left and right

371 amygdala and occipital cortex. Interestingly, similar activation patterns also emerged when only
372 neutral pictures were considered (Table 1).

373 **Interaction effects between picture and regulation**

374 Finally, interaction effects of picture and regulation were observed: the distance vs. permit
375 difference was greater for negative than for neutral pictures in the left and right amygdala for transient
376 responses, while contradictory results were observed for sustained responses (Table 1).

377 In order to further characterize the effects observed during the voxel-based analysis, we
378 conducted an additional analysis of summary statistics based on the left and right amygdala ROIs (see
379 Fig 2Fehler! Verweisquelle konnte nicht gefunden werden.). We observed greater activation for
380 negative than neutral pictures as well as a decrease of this activation during distance vs. permit. That
381 is, there were significant picture and regulation main effects during the stimulation phase, but no
382 interaction effects (left amygdala: picture: $F(1,45) = 30.56, p < .001, \eta^2 = .112$; strategy: $F(1,45) =$
383 $10.08, p = .003, \eta^2 = .046$; picture $\times$ strategy: $F(1,45) = 3.33, p = .075, \eta^2 = .006$; right amygdala:
384 picture: $F(1,45) = 26.65, p < .001, \eta^2 = .109$; strategy: $F(1,45) = 9.02, p = .004, \eta^2 = .037$; picture $\times$
385 strategy $F(1,45) = 1.62, p = .210, \eta^2 = .003$).

386 - Insert Fig 2 here -

387 **Fig 2. Summary statistics for the activation of the amygdala ROI during the stimulation**
388 **phase (concurrent effects, timepoint 1)**

Neuronal activation differences during the post-stimulation phase (immediate effects, timepoint 2)

Picture and regulation effects were also present during the post-stimulation phase (Table 2): For both, the permit and distance condition, there was a greater activation for negative than neutral pictures in the amygdala ROI, but not in any other brain region. Across picture conditions, greater activation was observed after distance than after permit in brain regions such as the occipital cortex, the precuneus, and also the amygdala (for sustained responses). Similar effects emerged when the comparison was restricted to negative pictures and even neutral picture (primarily for sustained responses). Conversely, we did not observe any activation difference for the reverse contrast, that is there was no greater activation after permit vs. after distance in the post-stimulation phase. No interaction effects between picture and strategy were present during the post-stimulation phase.

Table 2. Activation maxima in the emotion regulation task during the post-stimulation phase (immediate effects, timepoint 2).

k	p_{FWE}	t	$p_{unc.}$	x	y	z	label
Main effect picture							
<i>Neutral Post-Stim Phase > Negative Post-Stim Phase</i>							
No results							
<i>Negative Post-Stim Phase > Neutral Post-Stim Phase</i>							
49	0.028	3.16	0.001	-22	-12	-12	Left Amygdala (ROI)
27	0.033	3.16	0.001	28	-6	-14	Right Amygdala (ROI)
75	0.004	3.94	<0.001	-26	-6	-18	Left Amygdala (ROI, stick model)
105	0.007	3.82	<0.001	24	-6	-14	Right Amygdala (ROI, stick model)
Main effect regulation							
<i>Distance Post-Stim Phase > Permit Post-Stim Phase</i>							
75	0.004	6.03	<0.001	-42	-68	4	Left Middle Occipital Gyrus

46	0.006	5.87	<0.001	-44	-52	-24	Left Inferior Temporal Gyrus
37	0.014	5.59	<0.001	-4	-76	48	Left Precuneus
53	0.024	5.39	<0.001	-42	-54	54	Left Inferior Parietal Lobule
18	0.028	3.12	0.002	-26	-12	-14	Left Amygdala (ROI)
93	0.002	4.21	<0.001	32	-2	-20	Right Amygdala (ROI)

Permit Post-Stim Phase > Distance Post-Stim Phase

No results

Interaction effect picture X regulation

(DistanceNeutral Post-Stim Phase > PermitNeutral Post-Stim Phase) > (DistanceNegative Post-Stim Phase > PermitNegative Post-Stim Phase)

No results

(PermitNeutral Post-Stim Phase > DistanceNeutral Post-Stim Phase) > (PermitNegative Post-Stim Phase > DistanceNegative Post-Stim Phase)

No results

Regulation effect negative pictures only

DistanceNegative Post-Stim Phase > PermitNegative Post-Stim Phase

6	0.026	3.15	0.001	-26	-10	-16	Left Amygdala (ROI)
41	0.015	3.44	0.001	24	-8	-18	Right Amygdala (ROI)
6	0.059	2.94	0.003	24	-8	-18	Right Amygdala (ROI, stick model)

PermitNegative Post-Stim Phase > DistanceNegative Post-Stim Phase

No results

Regulation effect neutral pictures only

DistanceNeutral Post-Stim Phase > PermitNeutral Post-Stim Phase

7	0.012	3.54	<0.001	-32	0	-18	Left Amygdala (ROI)
49	0.033	3.16	0.001	32	-2	-22	Right Amygdala (ROI)

PermitNeutral Post-Stim Phase > DistanceNeutral Post-Stim Phase

No results

Abbreviations: k = spatial extent, p_{FWE} = p -values corrected for multiple comparisons (FWE), $p_{unc.}$ = uncorrected p -values, $t = t$ -statistics, x, y, z = MNI coordinates. ROI indicates that an activation peak was observed within the left or right amygdala region of interest.

Neuronal interaction effects of regulation (permit, distance) and time (stimulation, post-stimulation)

When time was included as additional factor in the analysis (Table 3), that is, when considering changes from stimulation to post-stimulation phase, interaction effects between regulation and time were observed in several regions. In the right occipital cortex as well as the left and right amygdala, the effect permit vs. distance was greater during stimulation than during post-stimulation. Conversely, in the right superior frontal gyrus and the right inferior parietal lobe, the reverse effect, that is distance vs. permit, was greater during stimulation than during post-stimulation. Similar patterns emerged when the analysis was restricted to negative pictures and even neutral pictures (for the latter, only in sustained responses).

This analysis was complemented by an additional analysis of summary statistics based on the left and right amygdala ROIs in order to further characterize the voxel-based effects. Specifically, we conducted an analysis for negative pictures that also took the effect of time into account. We found significant regulation-by-time interactions in the left and right amygdala (Fig 3), indicating greater activation in the permit condition than the distance condition during the stimulation phase, but not during the post-stimulation phase (left amygdala: strategy: $F(1,45) = 2.13, p = .151, \eta^2 = .008$; Time: $F(1,45) = 0.55, p = .461, \eta^2 = .004$; strategy $\times$ Time: $F(1,45) = 11.86, p = .001, \eta^2 = .029$; right amygdala: strategy: $F(1,45) = 1.33, p = .254, \eta^2 = .005$; Time: $F(1,45) = 0.94, p = .338, \eta^2 = .008$; strategy $\times$ Time: $F(1,45) = 11.51, p = .001, \eta^2 = .025$).

Table 3. Immediate aftereffects of emotion regulation (interaction effects of regulation (permit, distance) and time (stimulation/timepoint 1, post-stimulation/timepoint 2)).

k	p_{FWE}	t	$p_{\text{unc.}}$	x	y	z	label
Interaction effect regulation X time							

<i>(Distance Stim Phase > Permit Stim Phase) > (Distance Post-Stim Phase > Permit Post-Stim Phase)</i>							
95	0.001	6.48	<0.001	60	-50	46	Right Inferior Parietal Lobule
31	0.006	5.94	<0.001	20	8	64	Right Superior Frontal Gyrus
<i>(Permit Stim Phase > Distance Stim Phase) > (Permit Post-Stim Phase > Distance Post-Stim Phase)</i>							
148	0.003	6.22	<0.001	-18	-96	-10	Left Inferior Occipital Gyrus
127	0.005	6.00	<0.001	14	-100	0	Right Calcarine Gyrus
31	0.007	5.90	<0.001	0	2	-10	Subcallosal Cortex
39	0.008	5.84	<0.001	34	-86	-14	Right Inferior Occipital Gyrus
161	0.002	4.29	<0.001	-18	-12	-14	Left Amygdala (ROI)
226	<0.001	4.97	<0.001	32	-2	-20	Right Amygdala (ROI)
134	<0.001	4.97	<0.001	-26	-12	-14	Left Amygdala (ROI, stick model)
144	0.001	4.64	<0.001	24	-8	-18	Right Amygdala (ROI, stick model)
Interaction effect regulation X time, negative pictures only							
<i>(DistanceNegative Stim Phase > PermitNegative Stim Phase) > (DistanceNegative Post-Stim Phase > PermitNegative Post-Stim Phase)</i>							
68	0.001	6.6	<0.001	18	12	62	Right Superior Frontal Gyrus
<i>(PermitNegative Stim Phase > DistanceNegative Stim Phase) > (PermitNegative Post-Stim Phase > DistanceNegative Post-Stim Phase)</i>							
77	0.004	3.98	<0.001	-24	-12	-14	Left Amygdala (ROI)
163	0.003	4.12	<0.001	24	-12	-12	Right Amygdala (ROI)
114	<0.001	5.40	<0.001	-28	-10	-16	Left Amygdala (ROI, stick model)
146	<0.001	5.22	<0.001	24	-8	-18	Right Amygdala (ROI, stick model)
Interaction effect regulation X time, neutral pictures only							
<i>(DistanceNeutral Stim Phase > PermitNeutral Stim Phase) > (DistanceNeutral Post-Stim Phase > PermitNeutral Post-Stim Phase)</i>							
No results							
<i>(PermitNeutral Stim Phase > DistanceNeutral Stim Phase) > (PermitNeutral Post-Stim Phase > DistanceNeutral Post-Stim Phase)</i>							
57	0.006	5.92	<0.001	-20	-96	-8	Left Inferior Occipital Gyrus
69	0.013	3.49	0.001	-16	-10	-16	Left Amygdala (ROI, stick model)
187	0.001	4.41	<0.001	32	-2	-20	Right Amygdala (ROI, stick model)

Abbreviations: k = spatial extent, p_{FWE} = p -values corrected for multiple comparisons (FWE), $p_{unc.}$ = uncorrected p -values, $t = t$ -statistics, x, y, z = MNI coordinates. ROI indicates that an activation peak was observed within the left or right amygdala region of interest.

- Insert Fig 3 here -

Fig 3. Summary statistics for the amygdala ROI during the stimulation phase (timepoint 1) and the post-stimulation phase (immediate aftereffects, timepoint 2). This analysis is limited to negative stimuli.

Activation time-courses during the stimulation- and post-stimulation phase (timepoint 1, timepoint 2)

The temporal course of activation in the left and right amygdala was investigated in a post-hoc analysis (Fig 4). It is noteworthy that in this descriptive analysis, an initial peak during the regulation period was followed by a second peak during the post-stimulation period. While the first peak is most pronounced for the permit negative condition, this is no longer the case for the second peak, which shows roughly similar activation levels for all four conditions.

- Insert Fig 4 here -

Fig 4. Activation time-courses in the left and right amygdala during stimulation (timepoint 1) and post-stimulation phase (immediate aftereffects, timepoint 2). The shaded area indicates the stimulation phase

Neuronal activation differences during the re-exposure tasks

Re-exposure after 10 minutes (short-term effects, timepoint 3)

During re-exposure after 10 minutes, picture main effects were observed in the posterior cingulate gyrus, the fusiform gyrus, the right temporal gyrus, the left occipital gyrus, and the left amygdala (all negative > neutral, Table 4). There was also a regulation effect (distance > permit) within the left and right amygdala when the analysis was restricted to negative pictures (Fig 5; Table 4). No other effects of interest in this analysis were significant.

Re-exposure after 1 week (long-term effects, timepoint 4)

Re-exposure after 1 week led to greater activation for negative than for neutral pictures in several brain regions, including the right inferior temporal gyrus, left occipital, fusiform, and inferior frontal gyrus, and the left and right amygdala (Table 5). Again, there was an effect of the previous regulation condition: greater activation for previously distanced pictures was present in the right amygdala (Fig 5). Restricting this comparison to negative pictures did not yield any significant effect, but a small effect of the same kind appeared for neutral pictures (Table 5). No other effect of interest in this analysis exceeded the whole-brain threshold.

- Insert Fig 5 here -

Fig 5. Summary statistics for the amygdala ROI during re-exposure after 10 min (short-term effects, timepoint 3) and after 1 week (long-term effects, timepoint 4).

Table 4. Activation maxima during re-exposure after 10 minutes (short-term effects, timepoint 3).

k	p_{FWE}	t	$p_{unc.}$	x	y	z	label
Main effect picture							
<i>Neutral > Negative</i>							
No results							
<i>Negative > Neutral</i>							
148	<0.001	8.21	<0.001	-8	-18	30	Left Posterior Cingulate Cortex
428	<0.001	7.96	<0.001	42	-50	-16	Right Fusiform Gyrus
366	<0.001	7.16	<0.001	-42	-48	-22	Left Fusiform Gyrus
167	0.001	6.83	<0.001	50	-70	12	Right Middle Temporal Gyrus
85	0.006	6.23	<0.001	-44	-80	-2	Left Middle Occipital Gyrus
8	0.005	3.97	<0.001	-16	-8	-14	Left Amygdala (ROI)
Main effect regulation							
<i>Distance > Permit</i>							

No results

Permit > Distance

No results

Interaction effect picture X regulation

(Distance Neutral > Permit Neutral) > (Distance Negative > Permit Negative)

No results

(Permit Neutral > Distance Neutral) > (Permit Negative > Distance Negative)

No results

Regulation effect negative pictures only

DistanceNegative > PermitNegative

	k	p_{FWE}	t	$p_{unc.}$	x	y	z	label
	9	0.011	3.68	<0.001	-20	-10	-12	Left Amygdala (ROI)
	43	<0.001	5.74	<0.001	26	-6	-14	Right Amygdala (ROI)

PermitNegative > DistanceNegative

No results

Regulation effect neutral pictures only

DistanceNeutral > PermitNeutral

No results

PermitNeutral > DistanceNeutral

No results

Abbreviations: k = spatial extent, p_{FWE} = p -values corrected for multiple comparisons (FWE), $p_{unc.}$ = uncorrected p -values, $t = t$ -statistics, x, y, z = MNI coordinates. ROI indicates that an activation peak was observed within the left or right amygdala region of interest.

Table 5. Activation maxima during re-exposure after 1 week (long-term effects, timepoint 4).

k	p_{FWE}	t	$p_{unc.}$	x	y	z	label
Main effect picture							
<i>Neutral > Negative</i>							
No results							
<i>Negative > Neutral</i>							
347	<0.001	8.97	<0.001	44	-46	-14	Right Inferior Temporal Gyrus

122	<0.001	8.68	<0.001	-32	-76	20	Left Middle Occipital Gyrus
85	<0.001	8.01	<0.001	18	-6	-14	Right Hippocampus
150	0.004	6.99	<0.001	-40	-50	-12	Left Fusiform Gyrus
84	0.005	6.90	<0.001	-30	22	-20	Left Inferior Frontal Gyrus
79	<0.001	5.23	<0.001	-24	-4	-14	Left Amygdala (ROI)
149	<0.001	8.01	<0.001	18	-6	-14	Right Amygdala (ROI)

Main effect regulation*Distance > Permit*

23	0.005	4.28	<0.001	24	0	-22	Right Amygdala (ROI)
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Permit > Distance

No results

Interaction effect picture X regulation*(Distance Neutral > Permit Neutral) > (Distance Negative > Permit Negative)*

No results

(Permit Neutral > Distance Neutral) > (Permit Negative > Distance Negative)

No results

Regulation effect negative pictures only*DistanceNegative > PermitNegative*

No results

PermitNegative > DistanceNegative

No results

*Regulation effect neutral pictures only**DistanceNeutral > PermitNeutral*

16	0.016	3.76	<0.001	24	-4	-20	Right Amygdala (ROI)
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PermitNeutral > DistanceNeutral

No results

Abbreviations: k = spatial extent, p_{FWE} = p -values corrected for multiple comparisons (FWE), $p_{unc.}$ = uncorrected p -values, $t = t$ -statistics, x, y, z = MNI coordinates. ROI indicates that an activation peak was observed within the left or right amygdala region of interest.

456 Discussion

457 This study presents a systematic investigation of emotional processing and regulation across
458 two picture types and regulation conditions and immediate as well as short- and long-term time scales.
459 Its main results can be summarized as follows: During stimulation (at timepoint 1) negative pictures
460 elicited a strong response in affective regions of the brain, most prominently the amygdala, but also
461 the insula and cingulate cortex. Volitional emotion regulation, as implemented by objective
462 distancing, led to a decrease of this response, and to an increase of activation in the right middle
463 frontal and inferior parietal cortex. During the stimulation phase, distancing-related activation in
464 cortical regions appeared as a sustained response, whereas the reverse effect, that is the down-
465 regulation of the amygdala, appeared mainly as a transient response, in particular for negative
466 pictures. Regarding paradoxical immediate aftereffects in the amygdala (at timepoint 2), statistically
467 significant interaction effects between time and regulation indicate that higher levels of amygdala
468 activation in the permit condition during the stimulation phase reversed to higher activation in the
469 distance condition during the post-stimulation phase. Further (paradoxical) task-rest interactions for
470 negative pictures were observed in the occipital cortex and the ventromedial frontal / subgenual
471 cingulate cortex. Previous emotion regulation had an impact on amygdala activation both at timepoint
472 3 (after 10 minutes) and timepoint 4 (after one week): Activation within the amygdala was higher if
473 the participants had previously (in the emotion regulation task) been instructed to distance from the
474 picture as compared to permit all upcoming emotion.

475 **Effects of emotional processing and regulation at timepoint 1**

476 **Concurrent emotion regulation effects – Replication and extension**

477 A key result of the present study is the replication of canonical emotion regulation effects, in
478 particular the down-regulation of the amygdala and the concurrent activation of a right frontoparietal
479 control network during distancing from negative pictures. This confirms several previous reports [10,
480 20, 34]. This pattern of replications hints at the robustness of our experimental paradigm and can
481 serve as a basis for a systematic extension, as will be discussed below, for the exploration of activation
482 changes in other cortical and subcortical regions, and for the incorporation of additional experimental
483 variables such as time.

484 A second result of this study is that the observed effects extend beyond the regions that are
485 commonly implicated in emotion regulation. Specifically, negative pictures were not only associated
486 with amygdala and insula activation, but also with activation in the inferior temporal gyrus and the
487 occipital cortex, the latter was also observed during the permit condition. During the distance negative
488 condition, left- (instead of right-) hemispheric activation in the inferior and middle frontal gyrus
489 specifically was an unexpected observation with respect to our hypotheses and previous results [10].

490 Other authors have noted that emotion regulation – as any complex psychological function –
491 does not rely on single brain regions [for network analyses see for instance 17, 35, 36]. Emotion
492 regulation is a heterogeneous construct that overlaps to a certain extent with other cognitive domains:
493 for example, Messina, Bianco, Sambin and Viviani (37) distinguish between executive and semantic
494 processes during reappraisal; they suggest that executive functions serve a general role, while
495 semantic regions in the temporal and parietal cortex should be exclusively activated during
496 reappraisal via perspective-taking. With regard to our finding of additional left-hemispheric frontal
497 cortical activation, it is possible that inner speech is a component of distancing via self-instruction

that results in selective recruitment of left frontal regions [38] in addition to a more general, right-hemispheric control network. Further support for the idea that higher-level regulation strategies recruit additional neural resources to effectively cope with an emotion-eliciting event is provided by a meta-analysis [39]. This analysis shows that ventromedial prefrontal cortex activation is present in diverse, but related experimental domains such as fear extinction, cognitive emotion regulation (reappraisal), and placebo-mediated changes in negative affect. Only during reappraisal and placebo-mediated changes, however, insular and cingulate regions were activated as well, indicating that these two regions specifically support more complex functions as compared to basic extinction processes, for which less distributed activation, primarily of the ventromedial prefrontal cortex, seems to be sufficient.

A third notable result is that a principled approach to experimental design and data analysis allows for further insights beyond the canonical results. On the one hand, as detailed below, we were able to identify different temporal response profiles for the sources and targets of emotional regulation. On the other hand, we were also able to differentiate between main and interaction effects for the picture and regulation conditions.

The first insight regards a dissociation between transient/sustained responses and the targets/sources of emotional regulation. During the stimulation phase, but not necessarily during the post-stimulation phase, we observed a primarily transient response pattern within the amygdala, considering the statistical significance, spatial extent, and consistency across hemispheres. This pattern is consistent with its presumed alerting function [40]. In that sense, the amygdala initiates a response, but its activation does not represent the emotional response *per se*, which also includes down-stream activation in for example motor systems [41]. As long as the environment does not change any further, as it is the case for static pictures, continued activation of such an alerting structure is not needed, and hence the transient response. These results are compatible with Paret, Kluetsch,

522 Ruf, Demirakca, Kalisch, Schmahl, et al. (42), who found that primarily the anterior insula, but also
523 the left amygdala, exhibits a transient response pattern in event-related designs with longer picture
524 durations. Both studies underscore that results crucially depend on the analytical model, and that
525 modeling choices must be made consciously, based on a priori evidence.

526 **Concurrent emotion regulation effects in different picture conditions**

527 Another insight concerns the question whether or not emotion regulation is a domain-general
528 or a domain-specific process; that is, whether regulation strategies and their effectiveness generalize
529 across stimulus characteristics. Morawetz, Bode, Derntl and Heekeren (43) already showed, that
530 activation of brain areas during emotion regulation generalizes across stimulus categories (IAPS
531 pictures versus faces, film clips, reward, pain, scripts, and shapes). Our results point to a
532 generalization across stimulus characteristics (in this case: valence), which is also in line with
533 domain-general views on the brain basis of emotional reactivity [44]. The observation of decreased
534 amygdala activation for neutral pictures during the distancing condition as compared to the permit
535 condition may indicate that the distinction between negative and neutral pictures is a gradual one: we
536 speculate that the mere presentation of (bright) pictures in the dark environment of the scanner elicits
537 an unspecific alerting/arousing response – and that this response can be the target of emotional
538 regulation.

539 Although, in our experiment, the difference between distance and permit was greater for
540 negative than neutral pictures, the interaction effect between picture and regulation was relatively
541 small, for example with regard to its spatial extent, and not as consistent as for the main effects.
542 Similar results were also reported by Walter and colleagues [9] with a similar experimental design,
543 indicating that there is a minor (quantitative), but no fundamental (qualitative) difference between
544 distancing oneself from a negative or a neutral stimulus. The overall activation patterns of the neutral

545 and negative pictures and the joint analysis are also similar in that they all lead to activation of the
546 right middle frontal gyrus and inferior parietal lobe. This supports the idea of a core network
547 consisting of middle frontal and inferior parietal regions involved in general regulation efforts, and
548 that additional components are added to this network depending on the particular task at hand. From
549 a conceptual point of view, we suggest that it is therefore not just either domain-general or just
550 domain-specific processing that characterizes emotion regulation, but both - depending on the
551 particular region.

552 **Effects of time**

553 The second major focus of our study was on the temporal aspects of emotion regulation. We
554 implemented a slow event-related design to achieve a balance between stimulation (timepoint 1) and
555 post-stimulation (timepoint 2) periods, and also investigated the response to previously regulated and
556 non-regulated pictures after short (10 min, timepoint 3) and long (one week, timepoint 4) intervals.

557 **Immediate emotion regulation aftereffects at timepoint 2**

558 We observed paradoxically increased amygdala activation after regulation at timepoint 2.
559 However, these did not appear as a fully crossed interaction and were dependent on the statistical
560 activation model: In the voxel-based analysis, we found greater activation during distance than during
561 permit in the post-stimulation phase only for sustained responses and interaction effects between time
562 and regulation for both the transient and sustained responses. These results can be regarded as partial
563 replications of the paradoxical rebound effect reported by Walter and colleagues [9]. They confirm
564 the original proposition of post-stimulation activation differences across conditions as well as
565 activation increases and decreases within conditions, but disagree with respect to the exact nature of
566 this effect. For example, the original effect was found using the activation obtained from extracted
567 time courses, whereas we used a model-driven approach. On the one hand, the effects depended on

568 how the amygdala responses were modeled, and on the other hand, they did not necessarily occur at
 569 precisely the same locations (in terms of MNI coordinates), although all of them occurred within the
 570 amygdala ROI. Although this implies that a functional interpretation of this effect needs to be made
 571 in a more careful way, both studies support the notion of an interdependence of stimulation and post-
 572 stimulation periods. One could argue that the amount of cortical engagement during reappraisal is
 573 reduced as a function of time spent on implementing a certain reappraisal strategy [45]. This in turn
 574 might lead to an increase of amygdala activation after initial down-regulation.

575 Previous studies proposed that the concept of emotional aftereffects be extended to other
 576 regions apart from the amygdala, and to other types of interaction besides paradoxical, or crossed,
 577 ones. In this regard, a key result of Lamke and colleagues [22] is that reverse task-rest interactions
 578 (decreased activation during regulation but increased activation during relaxation/rest) were present
 579 in the amygdala after emotion down-regulation, whereas concordant task-rest interactions (increased
 580 activation during both regulation and relaxation/rest periods) were apparent in the prefrontal cortex.
 581 Comparable results were obtained in our study. We also observed task(stimulation)-rest(post-
 582 stimulation) interactions for negative pictures in regions beyond the amygdala, for example in the
 583 occipital cortex and the ventromedial frontal / subgenual cingulate cortex.

584 **Short- and long-term emotion regulation effects (timepoints 3 and 4)**

585 In our study, previous regulation had also an impact on amygdala activation during the re-
 586 exposure sessions: both after 10 min and after 1 week: Previously down-regulated items showed
 587 greater activation within the left and right amygdala than previously non-regulated items. This effect
 588 was, however, not limited to negative pictures, but also appeared for neutral ones. These findings
 589 differ from previous results [9, 24] indicating that emotion regulation effects persisted over time, that
 590 is that previously down-regulated items were associated with decreased amygdala activation.

591 Hermann and colleagues [46] also investigated re-exposure to previously (one week) regulated
592 stimuli and found not difference between previously distanced and permitted stimuli in amygdala
593 activation nor in ratings of emotional experience. However, the authors reported an effect of previous
594 reinterpretation, another reappraisal tactic, of negative stimuli leading to increased amygdala
595 activation and reduced emotional experience during re-exposure. Additionally, there was no
596 difference in re-exposure effects between reinterpretation and distancing. Since we did not record
597 arousal ratings during re-exposure, we cannot conclude that being confronted with negative situations
598 that have been previously regulated via distancing leads to reduced emotional experience.
599 Nevertheless, the findings by Hermann and colleagues [46] might suggest, that this is a possible
600 consequence of reappraisal, albeit at least for reinterpretation.

601 All of the aforementioned studies show that regulation effects persist over time, albeit in
602 different ways. Although it has previously been shown that re-exposure effects also depend on the
603 regulation strategy [47], this is no explanation for the specific pattern of results in our study, and why
604 there are differences with regard to the Walter et al. study, given the similarity of the experimental
605 setup. This remains an open question and needs to be the subject of further replication efforts.

606 **Limitations**

607 We will now address the limitations of our study, which primarily concern the experimental
608 design and the generality of our results. First, for reasons of design efficiency we only investigated
609 negative vs. neutral pictures. This did not allow us to disentangle the impact of different levels of
610 arousal and valence, since negative and neutral pictures simultaneously differ in both dimensions. It
611 has been shown, though, that this is a relevant distinction with regard to amygdala [48]and prefrontal
612 activation [49]. Including positive pictures would have allowed for a more comprehensive
613 investigation in this regard. Further, a comparison of negative and neutral pictures alone does not

614 allow conclusions about different kinds of emotion, if a discrete model of emotions is assumed. Again,
615 there is evidence that different negative emotions such as fear, anxiety, sadness, and anger, and also
616 positive vs. negative emotions are differentially susceptible to emotional regulation [50-52].

617 Second, this experiment was not designed to investigate the effects of different reappraisal
618 tactics. While there is a common core network of emotion regulation, which we also found in our
619 study, this does not necessarily mean that our results hold for different regulation tactics or even other
620 strategies. Similar to the inclusion of further stimulus categories, the inclusion of further strategies
621 would have been desirable, but would have necessitated the presentation of trials in a more rapid
622 succession, which conflicted with our decision for a slow event-related experimental design. In that
623 sense, there is a trade-off between design choices that cannot be resolved within a single study.

624 Third, the interpretation of our results rests on the assumption that participants on average
625 could successfully implement the distance and permit instructions. Although we took effort to control
626 for this by means of detailed instructions, training, and subsequent self-reports, it is possible that
627 alternative strategies, involuntarily regulation, or mind-wandering were applied by the participants.
628 We assume, though, that the impact of such regulation variants is random and just increases error
629 variance in the data. However, to investigate whether such variability can lead to any systematic bias,
630 further targeted studies are needed, e.g. to distinguish voluntary vs. involuntary emotion regulation.

631 Fourth, the interpretation of results for the re-exposure session is impacted by the drop-out of
632 participants, which led to a reduced sample size for this part of the experiment. Also, additional
633 arousal ratings during this phase could have provided additional information on the short- and long-
634 term effects of emotion regulation. Finally, more variables than those considered for the present study
635 play a role in emotion regulation: on the one hand, variation among individuals, be it clinical or non-
636 clinical, will impact cognitive emotion regulation in a sense that different strategies will have different

637 efficacies for different individuals. This could, for example, take the form of an association of
638 successful reappraisal with less trait anxiety and more positive daily emotion as well greater
639 activation in medial and lateral prefrontal regions [53]. On the other hand, successful vs. deficient
640 emotion regulation will lead, in a developmental perspective, to different clinical trajectories; for
641 example, emotion regulations skills predict the severity of anxiety symptoms across an interval of 5
642 years [54], and improving emotion regulation skills has been shown to enhance the efficacy of
643 psychotherapeutic interventions [55]. Emotion regulation deficits are present in almost all clinical
644 psychological disorders, which in turn are characterized by differential strategies of unsuccessful
645 emotion regulation. Especially in the clinical context, comparing short term beneficial vs long term
646 dysfunctional emotion regulation attempts appears very promising. To extend the study design to
647 other populations than young and healthy students is therefore a necessary step for translating emotion
648 regulation research into application contexts.

649 **Conclusions**

650 Many of the issues central to this study have already been investigated, but not necessarily in
651 a single study, and indeed, often in isolation. Further integration within the field requires some “firm
652 ground”, that is canonical results of established and replicable findings that can be derived from
653 systematic reviews and quantitative meta-analyses, but also from replication efforts such as the
654 present study. A key motivation of our study was to replicate and refine some core and emerging
655 results in cognitive emotion regulation. Its main contribution is the joint and coherent consideration
656 of a subset of relevant experimental factors – emotional processing and regulation as well as their
657 temporal trajectories – and their effects on the activation patterns of known emotion generating and
658 regulating networks. Our results confirm and extend previous characterizations of these networks,
659 but also call for further investigation especially of their temporal dynamics.

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662 Materials.

663 **Data Availability Statement**

664 Data and materials are provided at the Open Science Framework (<https://osf.io/mg5ac/>).
665 Specifically, we provide data for first- and second-level fMRI analyses, thee respective SPM code,
666 ROI masks, behavioral data (arousal ratings, age, sex), the emotion regulation experiment, and R-
667 code for reproducing the analyses and results. We are not able to provide raw and preprocessed fMRI
668 data due to data privacy reasons.

669

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