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Opialla, Sarah ; Lutz, Jacqueline ; Scherpiet, Sigrid ; Hittmeyer, Anna ; Jäncke, Lutz ; Rufer, Michael ; Grosse Holtforth, Martin ; Herwig, Uwe ; Brühl, Annette B

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Neural circuits of emotion regulation: a comparison of mindfulness-based and cognitive reappraisal strategies

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Abstract Dealing with one's emotions is a core skill in everyday life. Effective cognitive control strategies have been shown to be neurobiologically represented in prefrontal structures regulating limbic regions. In addition to cognitive strategies, mindfulness-associated methods are increasingly applied in psychotherapy. We compared the neurobiological mechanisms of these two strategies, i.e. cognitive reappraisal and mindfulness, during both the cued expectation and perception of negative and potentially negative emotional pictures. Fifty-three healthy participants were examined with functional magnetic resonance imaging (47 participants included in analysis). Twenty-four subjects applied mindfulness, 23 used cognitive reappraisal. On the neurofunctional level, both strategies were

associated with comparable activity of the medial prefrontal cortex and the amygdala. When expecting negative versus neutral stimuli, the mindfulness group showed stronger activations in ventro- and dorsolateral prefrontal cortex, supramarginal gyrus as well as in the left insula. During the perception of negative versus neutral stimuli, the two groups only differed in an increased activity in the caudate in the cognitive group. Altogether, both strategies recruited overlapping brain regions known to be involved in emotion regulation. This result suggests that common neural circuits are involved in the emotion regulation by mindfulness-based and cognitive reappraisal strategies. Identifying differential activations being associated with the two strategies in this study might be one step towards a better understanding of differential mechanisms of change underlying frequently used psychotherapeutic interventions.

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Introduction

Successful emotion regulation has been associated with adaptive levels of general health, mental health as well as psychosocial functioning [1–4]. Emotion regulation can be defined as “processes by which individuals influence which emotions they have, when they have them, and how they experience and express these emotions” [5]. Such processes can be applied consciously, but various automatic and effortless methods to regulate emotions have also been investigated [4, 6].

Most research on the neural mechanisms of emotion regulation has concentrated on cognitive emotion-regulation strategies such as cognitive reappraisal (e.g. [7, 8], for a review: [9]). Meta-analyses suggest a regulatory influence of prefrontal cortical areas (PFC)—specifically dorsolateral (DLPFC), ventrolateral (VLPFC) and dorsomedial (DMPFC) parts—on subcortical regions such as the amygdala, parahippocampal gyrus, anterior cingulate and the thalamus (see meta-analyses: [9–12]; see also animal models: [13]).

Another approach to dealing with challenging emotional situations is the concept of mindfulness, which has its roots in ancient eastern traditions and meditation [14]. Within the last 20 years, mindfulness practice has found its way into “Western” psychotherapy, for example in programs such as mindfulness-based stress reduction (MBSR [15]) or mindfulness-based cognitive therapy (MBCT [16]). Mindfulness has been defined “as paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally” ([14], p. 4). Neurobiological research on mindfulness has investigated distinct aspects of mindfulness in diverse samples, ranging from participants without any experience in mindfulness over inexperienced learners of mindfulness practices (e.g. MBCT) to long-term meditation practitioners [17]. These studies investigated neural correlates with different forms of meditation [18, 19] as well as the influence of trait mindfulness on performance in stressful or emotionally challenging tasks [20, 21].

Studies with meditation experts meditating during functional magnetic resonance imaging (fMRI) identified increased recruitment of DMPFC and lateral PFC ([17, 18], reviews: [22, 23]). Similarly, trained subjects showed increased recruitment of viscerosensitive networks (e.g. insula) and lateral PFC during negative valence processing and sadness provocation [20, 21]. However, these findings in prefrontal regions seem to be strongly mediated by meditation experience: Tang et al. [24] showed that early- and middle-stage meditators needed *more* effortful control to achieve a meditative state compared to expert

meditators: the early stages were accompanied by *increased* recruitment of ventral and dorsal ACC, lateral PFC and parietal areas, whereas in *n* expert meditators, lateral prefrontal and parietal areas were *less* active. A similar pattern was found in another study in expert meditators [25]. Farb et al. [19] demonstrated that MBSR training resulted in *decreased* ventral and dorsal MPFC activity and increased recruitment of viscerosensitive networks (e.g. insula) as well as increased lateral prefrontal areas in a focused-attention task.

Only few studies, however, have investigated the neural mechanisms of short mindfulness interventions in meditation-naïve subjects. In one of these studies, focused breathing activated parietal and prefrontal structures (e.g. DMPFC, dACC) as well as the insula [26]. Studies on emotional introspection (comparable to mindful awareness of one’s feelings) [27] and on labelling of emotions [28] were both associated with reduced activity in the left amygdala and increased activation in the VLPFC.

From a theoretical and clinical perspective, studies on short emotion-regulation interventions are valuable as they could contribute to advancing models of emotion regulation and furthermore support the development of personalized treatment strategies in psychotherapy by establishing neurobiological criteria for the selection of emotion regulation strategies for individual patients.

In the present study, we compared the application of short mindfulness-based strategies to reality checking as cognitive reappraisal technique, both during the cued expectation and perception of emotional stimuli. Previous studies have shown that merely expecting emotional stimuli already may function as an emotion eliciting stimulus itself [29, 30], possibly even enhancing the subsequent emotional response to perceiving an emotional stimulus [31]. The neural circuits involved in cognitive emotion regulation during the expectation period have been investigated before [8], identifying MPFC and left DLPFC as regulating and diminishing left amygdala activation [8]. Studies on the effect of a cognitive emotion regulation on the perception of emotional pictures found a similar regulatory network [7, 32, 33].

In the current study, we expected comparable effects of mindfulness-based and cognitive reappraisal strategies during the expectation and the perception of emotional stimuli.

The reviewed literature suggests that at least in early to middle stages of mindfulness training, mindfulness-based strategies recruit similar prefrontal brain regions as cognitive reappraisal strategies. As the direct comparison of these strategies has not been done before, it is difficult to generate specific hypotheses regarding differences in prefrontal activations between these strategies.

Therefore, we hypothesize for the comparison of mindfulness-based and cognitive reappraisal strategies, that

- (a) brain regions associated with emotion regulation show similar activations with both strategies (i.e. DMPFC, MPFC) as well as the amygdala as the main structure known to be targeted by these regions [11]. To adhere to the logic of hypothesis testing, we hypothesized that the two groups would differ significantly in these structures.
- (b) in contrast to cognitive reappraisal, mindfulness-based strategies are associated with stronger activity in attention-related networks, particularly in parietal and lateral prefrontal regions [26] and in the insula, given the possible body focus in mindfulness instructions (e.g. [26, 34]). We tested this hypothesis by conducting a whole-brain analysis.

Materials and methods

Subjects

Fifty-three healthy subjects (31 females; ages 20–55, $M = 29.25$, $SD = 7.51$; all right-handed according to the Annett hand preference scale [35]) without any history of neurological or psychiatric illness participated in the study. Exclusion criteria were excessive consumption of alcohol, nicotine or caffeine, intake of medication (except oral contraceptives) or psychotropic drugs, current neurological or psychiatric illness and fulfilling contraindications against magnetic resonance imaging (MRI) examinations as assessed by a semi-structured clinically oriented interview (based on the SCID [36], administered by an experienced psychiatrist [ABB]). To obtain a naturalistic variation in the amount of experience with mindfulness practice and to study effects of the mindfulness instruction independent of training, experience with meditation or mindfulness was neither an inclusion nor an exclusion criterion. Meditation experience was only assessed in the mindfulness group; an overview is given in supplementary Table S1 (previously published in [37]). Participants were recruited via mailing lists and personal contacts. All subjects gave written informed consent according to the Declaration of Helsinki [38] and received a financial compensation of 50 Swiss Francs. The study was approved by the local ethics committee of the Canton of Zurich.

Experimental design

Task and stimuli

During functional MRI (fMRI), subjects performed an emotional expectation task (Fig. 1, described in [8]). They expected and perceived emotional pictures of known and

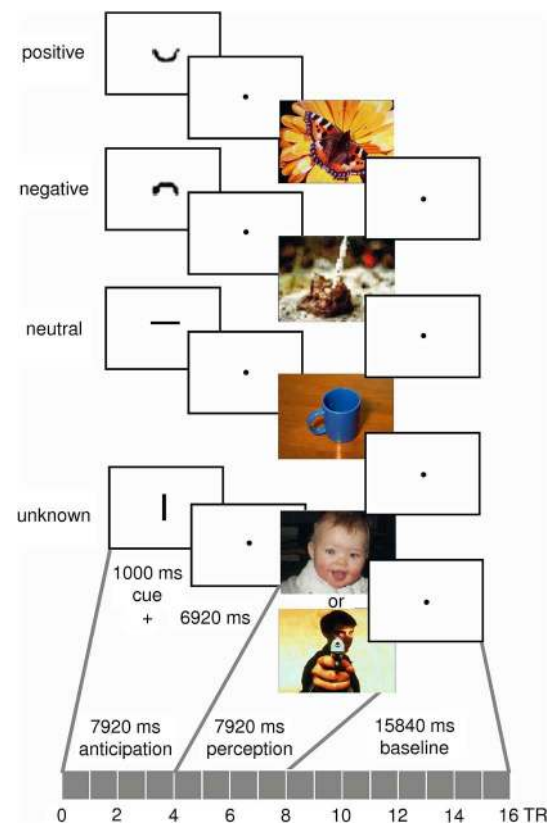


Fig. 1 Task and duration, cues are enlarged for presentation reasons (actual height about 1/40 screen size)

unknown valence (International Affective Picture System [39]; list of pictures available upon request from the authors) that were presented via digital video goggles (Resonance Technologies, Northridge, CA). Each trial started with a short cue (duration 1,000 ms) indicating, after an expectation period of 6,920 ms, the appearance of pictures of positive “U” (ps), negative “∩” (ng), neutral “–” (nt) or of unknown valence “|” (uk), which were either positive or negative (50/50). During expectation, a blank screen with a small fixation cross was shown followed by the full-screen presentation of a picture of the respective valence (7,920 ms). A baseline period with a blank screen shown for 15,840 ms allowed the blood oxygen level-dependent signal to level off before the next trial. Participants were instructed to expect the pictures indicated by the cue and to perceive them accordingly.

The task was programmed with Presentation™ (Neurobehavioral Systems, USA) and consisted of one run (total duration: 30 min) with 56 pseudo-randomized trials comprising 14 trials for each condition of known valence (positive, negative, neutral) and 14 trials for unknown valence. The cues were intuitively understandable and used only few cognitive resources. Pictures were matched for valence difference from neutral, for complexity of content

and, as far as possible, for arousal, based on a prior behavioural study in which subjects rated a set of IAPS pictures (for a discussion of arousal matching, see [8]). Furthermore, the task did not require any motor reaction that could have interfered with the subjects' performance.

After scanning, participants were shown the pictures as printouts again and rated the emotional valence of the presented stimuli on a 9-point-Likert scale (1 = most negative; 9 = most positive). Additionally subjects completed a structured interview about their general ability to perform the task, and in the mindfulness group, about the regulation strategies they had employed (focusing on feelings, thoughts or bodily sensations).

Task instructions

Subjects were assigned to the cognitive reappraisal group or the mindfulness group. For organizational reasons, assignment to the two groups/interventions was not randomized, as the two groups were recruited after each other (separate ethical approvals). The data of the mindfulness group has been previously published [37], but the data of the cognitive control group has not been analysed before. The assignment to the groups was age- and gender-matched. All participants were instructed to apply the respective strategy only during the negative and the “unknown” expectation and perception trials, assuming that in real life these situations are most stressful and more likely require emotion-regulation strategies. In pleasant and neutral conditions, participants in both groups were instructed to expect and observe the pictures. The pleasant conditions were primarily used for assuring a balanced emotional valence of the stimuli and to avoid any negative mood induction.

Participants were given written instructions that were orally recapitulated by the main investigators and participant's questions were answered. Subsequently, participants summarized the instructions in their own words and were given as much time as they needed until the investigators decided that a participant had fully understood the instruction. Afterwards, subjects underwent a training session until they felt comfortable with the task and their instruction during the task. Instruction and training session usually lasted for 10–15 min. Pictures shown in the training session were not presented in the main task.

Participants in the mindfulness group were given an instruction on mindful awareness, in which the terms “mindfulness” and “regulation” were not mentioned. Instead, common aspects of mindfulness definitions—nonjudgmental awareness of the present moment and openness to experience [14, 40]—were used: “Try to consciously be aware of yourself, of what happens to you and within you at this moment. Do this while expecting the

picture and while looking at it. Do not judge; remain conscious of and attentive to your present state. You may focus on thoughts, on emotions, or on bodily sensations” [37]. The cognitive reappraisal group was instructed to perform a mental operation that was called “reality checking” during the unpleasant and unknown expectation conditions. This mental operation is comparable to standard interventions used in cognitive behavioural therapy [41–43]. Subjects were instructed to realistically evaluate the context of their current situation during the expectation of the emotional picture, to think e.g. “I am lying in a scanner”, “They will show me a picture, this is part of the study” [8].

FMRI acquisition

Imaging was performed using a General Electric 3.0 T Signa™ HD Scanner equipped with an 8-channel head coil (GE Medical Systems, Milwaukee, USA). Across a single functional run, 908 functional volumes (16 per trial) were obtained from 22 sequential axial slices covering whole brain (repetition time/echo time (TR/TE) 1,980/32 ms, slice thickness 3.5 mm with 1 mm gap, voxel size $3.125 \times 3.125 \times 4.5$ mm, field of view 200 mm, flip angle 70°). The first four volumes were discarded to allow for T1* equilibration effects. High resolution anatomical volumes were acquired for co-registration with functional data (TR/TE 9.2/2.1; $1 \times 1 \times 1$ mm³ resolution, axial orientation). T2-weighted functional magnetic resonance images were obtained to exclude possible T2-sensitive brain abnormalities.

FMRI data analysis and statistics

FMRI Data were analysed using BrainVoyager™ QX 2.4 (Brain Innovation, Maastricht, The Netherlands, [44]). The functional data were pre-processed to maximize signal-to-noise contrast. Pre-processing included motion correction, slice scan time correction, high frequency temporal filtering and linear detrending. Functional images were superimposed on the 2D anatomical images and incorporated into 3D data sets. Each data set was converted to Talairach space [45], resulting in a voxel size of $3 \times 3 \times 3$ mm³, followed by spatial smoothing with an 8-mm Gaussian kernel for subsequent group analysis.

The design matrix consisted of eight predictors representing the expectation (exp) and perception (per) periods of each valence (ng, ps, nt, uk) and the additional factor “group”. These conditions were modelled as epochs using a two-gamma haemodynamic response function. FMRI data analysis comprised the following steps according to the general linear model (GLM). First, we calculated fixed-effects analyses for each subject for the three contrasts

Table 1 ROI group analysis in the mindfulness group versus the cognitive control group

ROI Coordinates <i>x/y/z</i>	Cluster size (mm ³)	Exp ng > nt		Exp uk > nt		Per ng > nt	
		<i>t</i>	<i>p</i> (<i>d</i>)	<i>t</i>	<i>p</i> (<i>d</i>)	<i>t</i>	<i>p</i> (<i>d</i>)
Amygdala R 19/−8/−15	729	.14	.89 (.04)	.93	.36 (.28)	−.87	.39 (−.26)
Amygdala L −19/−8/−15	729	.345	.73 (.10)	.59	.56 (.18)	−.59	.56 (−.18)
MPFC R 7/57/23	3,375	−.975	.33 (−.29)	−.807	.42 (−.24)	−1.798	.08 (−.54)
MPFC L −7/57/23	3,375	−.686	.50 (−.21)	−.702	.49 (−.21)	−1.517	.14 (−.45)
V1 R 5/−86/−3	729	1.08	.29 (.32)	−.25	.80 (−.07)	.67	.50 (.20)
V1 L −5/−86/−3	729	1.05	.30 (.31)	.20	.84 (.06)	.25	.81 (.07)
DMPFC R 6/6/50	1,728	1.29	.21(.38)	1.30	.20 (.39)	−.77	.44(−.23)
DMFPC L −6/6/50	1,728	1.88	.07 (.56)	1.18	.24 (.35)	−.51	.61 (−.15)

ROI analysis of emotion expectation negative versus neutral (exp ng > nt), expectation unknown versus neutral (exp uk > nt) and perception negative versus neutral (per ng > nt) in the mindfulness group compared to the cognitive control group. There were no significant differences ($p < .05$). Effect sizes are indicated in brackets
V1 primary visual cortex, MPFC medial prefrontal cortex, DMPFC dorsal medial prefrontal cortex, R right, L left

comparing the emotion regulation conditions to the respective neutral conditions: The emotion expectation conditions “exp ng > nt” and “exp uk > nt” and the perception condition “per ng > nt”. Second, we calculated a random effects group comparison on the “mindful” and the “cognitive control” group for the brain activation in the selected contrasts on the whole-brain level. Results are reported on a voxel-wise statistical level of $p < .005$. To avoid alpha error accumulation, Monte-Carlo-Correction [44] was applied, resulting in cluster thresholds of 918 mm³ (exp ng > nt), 701 mm³ (per ng > nt) and 665 mm³ (exp uk > nt), each resulting in a cluster-wise $p < .05$. Due to the focus on regulating and regulated structures, we performed ROI-analyses on the three contrasts in bilateral anterior MPFC, DMPFC and bilateral amygdala using cubic ROIs with an edge-length of 15, 12 and 9 mm, respectively (details in Table 1). For further details on the ROI definitions, we referred to Lutz et al. [37]. We controlled for general attention and performance by examining individual brain activity in the primary visual cortex, as brain activity would have decreased as a result of closed eyes or diverted gaze. ROI analyses investigating haemodynamic differences in V1 (cubic ROI, 9 mm edge length, Table 1) revealed no significant differences between both groups. Identification of anatomical regions was based on Talairach atlas [45] and Talairach daemon [46].

Questionnaires

Prior to scanning all participants completed German versions of self-report questionnaires assessing depression

(Self-Rating Depression Scale, SDS [47]), anxiety (State-Trait Anxiety-Inventory, STAI [48]), as well as neuroticism and extraversion (Eysenck Personality Inventory, EPI [49]), and emotion regulation (Emotion Regulation Questionnaire, ERQ [43]). The mindfulness group additionally completed two self-report questionnaires assessing trait mindfulness (Mindfulness Attention and Awareness Scale, MAAS [40]; Freiburg Mindfulness Inventory, FMI [50]). Statistical analyses were performed by SPSS18.0 using student's t test and χ^2 -tests, statistical significance level $p < .05$.

Results

Participants

Twenty-seven subjects were assigned to the cognitive reappraisal group (four excluded due to excessive head movements with more than 3 mm in translation and/or rotation), and 26 subjects were assigned to the mindfulness group (1 subject excluded due to reported drowsiness, 1 due to excessive head movements). The final analysis included 23 subjects in the cognitive reappraisal group and 24 in the mindfulness group, totalling 47 subjects (ages 20–55, $M_{\text{age}} = 29.06$, $SD = 7.83$, 30 females). The two groups did not differ significantly in terms of age ($t(45) = -.42$, $p = .67$), gender distribution ($\chi^2(1) = .17$, $p = .68$) and education ($\chi^2(3) = 1.15$, $p = .76$), with mostly students in both groups (mind = 14, cog = 15).

Psychometric assessment revealed no clinically relevant degrees of depression or anxiety in any of participants ([51], supplementary Table S2), and the two groups did not differ significantly in their levels of depression, anxiety, neuroticism and extraversion. The mindfulness scores (MAAS, FMI) in the mindfulness group were highly intercorrelated ($r = .52$, $p = .01$; $N = 24$).

Behavioural data

The mean ratings of emotional valence for positive ($M = 7.26$, $SD = .72$; $p = .98$), negative (3.01 , $SD = .72$, $p = .72$) and neutral pictures ($M = 5.20$, $SD = .22$, $p = .37$) did not differ significantly between the two groups (supplementary Table S2). Internal consistencies for positive (Cronbach's $\alpha = .91$) and negative valences ($\alpha = .90$) showed very good reliabilities. Only the neutral valence demonstrated a poor internal consistency ($\alpha = .43$). The valence ratings of our sample did not differ significantly from IAPS standard values ($t_{nt} = .40$, $p = .69$; $t_{neg} = 35$, $p = .73$; $t_{pos} = .50$, $p = .62$).

After scanning, subjects in both groups confirmed their ability to follow the instructions of cognitive reappraisal or

of mindfulness, respectively. Subjects' primary focus of attention in the mindfulness group was almost evenly distributed on feelings ($n = 10$), thoughts ($n = 7$) and bodily sensations ($n = 7$).

FMRI results

The hypothesis-driven ROI analysis in bilateral amygdala, MPFC and DMPFC revealed no differences between the two groups in the investigated contrasts (Table 1). However, the whole-brain group comparison for the expectation of negative >neutral stimuli (Table 2A) revealed significantly higher activations in the mindfulness group compared to the reappraisal group in bilateral inferior frontal gyrus (IFG, Fig. 2a–c) as part of the VLPFC, extending into the anterior insula on the left side, as well as bilateral supramarginal gyrus (SMG) and the left DLPFC. During the expectation of unknown announced >neutral pictures, the mindfulness group had significantly higher activations in the left DLPFC (Table 2B). The perception of negative >neutral pictures was associated with significantly decreased activations in the mindfulness group compared to the reappraisal group in the caudate head (Fig. 3).

Table 2 Whole-brain group comparison mindfulness >cognitive control

Anatomic region	Brodmann area	Cluster size (mm ³)	Talairach coordinates			<i>t</i> -max	<i>p</i> -max
			<i>X</i>	<i>Y</i>	<i>Z</i>		
A. Expectation of negative emotional stimuli (negative >neutral)							
MidFG/DLPFC L	8	3,942	−37	34	45	4.30	.00009
IFG/PreCentG R, divided into	45/44	4,557	56	16	3	6.00	.00000
(a) IFG/VLPFC R	43/4	1,989	50	−5	12	3.99	.00024
(b) IFG/VLPFC R	45/44	2,397	56	16	3	6.00	.00000
IFG L, divided into	47	11,177	−34	31	−15	4.86	.00002
(a) IFG/VLPFC L	46/10	3,077	−37	40	3	4.47	.00005
(b) Insula/IFG L	13	5,126	−34	25	12	4.09	.00018
IFG L	6/4	2,162	−61	−2	21	4.73	.00002
PreCentG R	4	1,013	14	−26	60	3.80	.00043
SMG R	13/40	1,100	47	−26	24	3.93	.00029
SMG L	40/42	1,984	−64	−23	21	3.84	.00038
B. Expectation of possibly negative emotional stimuli (unknown >neutral)							
SFG/MidFG L	8	1,324	−37	25	51	4.56	.00004
C. Perception of negative emotional stimuli (negative >neutral)							
Caudate head R		1,123	17	22	9	−3.79	.00045

Activated areas in a random effects analysis (rfx) with a voxel-wise threshold of $p < .005$ of the contrast mindfulness > cognitive control group. Minimum cluster size (for cluster-wise threshold of $p < .05$ in contrast A): 896 mm³ (34 functional voxel). Contrast B): 665 mm³ (26 functional voxel). Contrast C): 707 mm³ (27 functional voxel)

Larger clusters with several local maxima were manually split into anatomically separate sub-clusters

Given are the Talairach coordinates of the peak voxel

IFG inferior frontal gyrus, PreCentG precentral gyrus, VLPFC ventrolateral prefrontal cortex, SMG supramarginal gyrus, MidFG middle frontal gyrus, DLPFC dorsolateral prefrontal cortex, SFG superior frontal gyrus, R right, L left

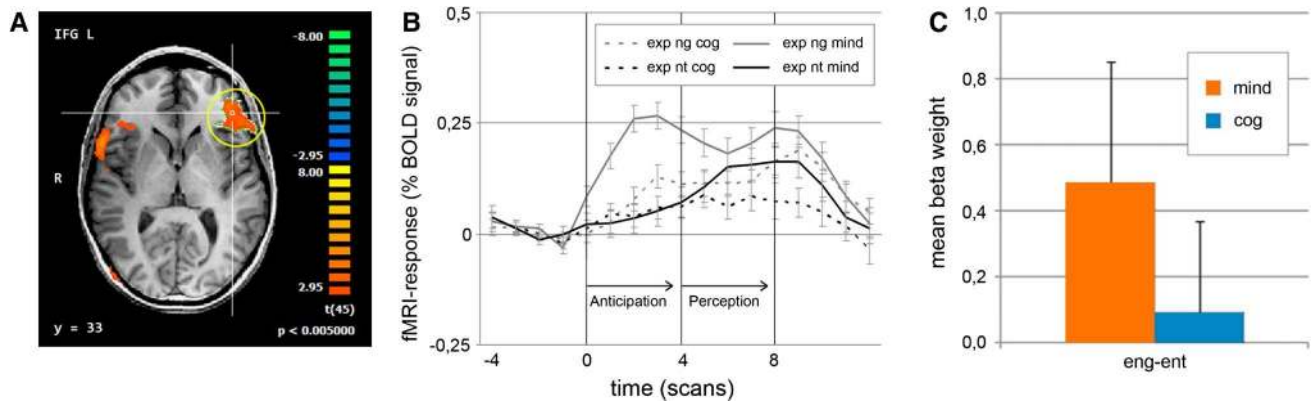


Fig. 2 Group comparison mindful >cognitive control during the expectation of negative versus neutral pictures (exp ng > nt). **a** Increased brain activity in the left inferior frontal gyrus in the mindful group ($p < .005$ voxel-wise, $p < .05$ clusterwise). **b** Average time courses of activation in this region. *Error bars* indicate standard error (consider the delay of the haemodynamic response function).

c Mean beta weights within the IFG ($x = -39, y = 33, z = 3$) in the mindfulness group (*mind*) compared to the cognitive reappraisal group (*cog*), error bars indicate standard deviations. *Mind* mindfulness group, *cog* cognitive reappraisal group, *exp ng* expectation of negative pictures, *exp nt* expectation of neutral pictures

Discussion

We compared the neural correlates with a mindfulness-based and a cognitive reappraisal strategy during the expectation and perception of emotionally arousing stimuli. The application of mindfulness-based and cognitive reappraisal strategies in an emotional context showed comparable effects on the level of activation in the amygdala as the central emotion-processing structure. Whereas the neural circuits partly overlapped between these two strategies, they also showed differences, suggesting the employment of partly distinct psychological mechanisms with distinct neural representations for emotion regulation.

Shared circuits between mindfulness-based and cognitive reappraisal strategy

Both groups did not differ in their activations in the DMPFC, anterior MPFC and the amygdala in nearly all investigated contrasts. This suggests that the regulating structures as well as the target regions (amygdala) are shared by the two strategies. Differences, however, might be based on differential time courses of the two strategies. It could be argued that mindfulness, once activated, has a slightly more sustained effect, thus subsequently requiring less mental effort for maintaining regulation in contrast to a more rapidly fading effect of the cognitive reappraisal strategy. However in the present study as in the literature, there are overall comparable activations of the DMPFC, MPFC and amygdala in mindfulness-based and cognitive reappraisal strategies [10, 11, 13]. This could reflect a common regulatory network generally activated by several emotion regulation strategies [11].

Differential mechanisms of mindfulness-based and cognitive reappraisal strategies

In summary, the use of mindfulness-based strategies for emotion regulation as compared to cognitive reappraisal during the expectation of negative stimuli was associated with *stronger* activations in left DLPFC, bilateral VLPFC and bilateral SMG. Differences between the two strategies were similar, but less pronounced during the expectation of previously announced unknown, possibly negative pictures. During the perception of negative stimuli, the application of mindfulness was associated with *reduced* activation in right caudate head compared to cognitive reappraisal.

The VLPFC/IFG region has previously been activated bilaterally with cognitive reappraisal (compared to no explicit control [8]) and with regulatory functions in other domains such as response inhibition [52, 53] and affect labelling [28]. A prior study on affect labelling (which could be considered as a reduced mindfulness intervention) found similar activation in the right VLPFC [28]. Furthermore, several studies implicated the IFG in self-awareness and self-referential processing, particularly when emotions were involved [54–56].

In the current study, the stronger activation of the VLPFC during emotional expectation in the mindfulness group could either reflect the involvement of different neural circuits for mindful emotion regulation in comparison to cognitive reappraisal or it could be related to a stronger involvement of brain structures associated with self-referential information processing [57, 58].

Stronger activation of the insula has been found (in parallel to activation in the VLPFC) in studies investigating

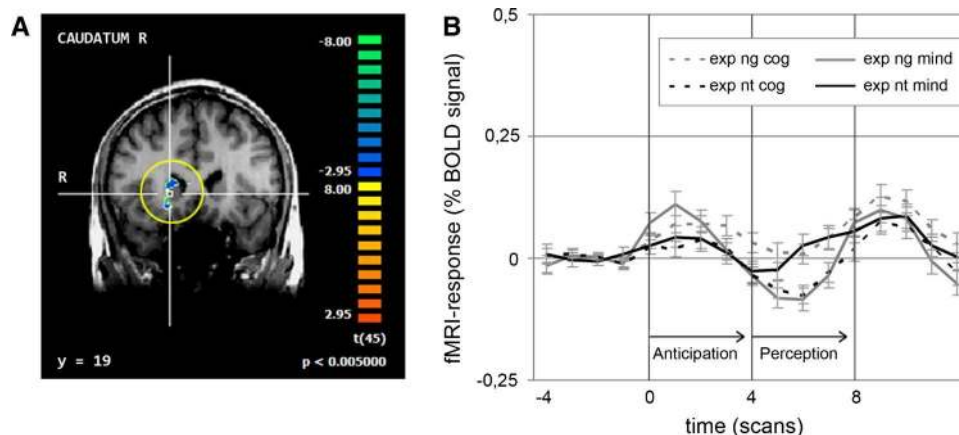


Fig. 3 Group comparison during the perception of negative versus neutral pictures (per ng > nt). **a** Lower brain activity in the right caudate in the mindfulness group compared to the cognitive reappraisal group. **b** Average time courses of activation in this

region. *Error bars* indicate standard error (consider the delay of the haemodynamic response function). *Mind* mindfulness group, *cog* cognitive reappraisal group, *per ng* perception of negative pictures, *per nt* perception of neutral pictures

expressive suppression [9], mindful affect labelling of negative affective stimuli [34], and also cognitive reappraisal during the expectation of negative events [59], pointing to the insula playing a role in regulatory processes. Additionally, the insula has been found to be associated with awareness of one's own body [60] as in focused breathing [26] and with viscerosensitive processing [61], potentially reflecting a focus on bodily sensations in mindfulness meditation [57]. In our study, increased insula activity might represent either the allocation of more regulatory resources in the mindfulness-based strategy or a response to the focus on bodily sensations in the mindfulness-based instruction. However, we cannot separate these two processes in the current study.

In the mindfulness group, stronger activation in the bilateral SMG during the expectation of negative emotional stimuli could be related to emotion regulation, comparable as to what has been shown for reappraisal [7, 62], for focused attention and meditation states [63]. These findings suggest that increased neural resources are required for the initial phase of mindful regulation.

In the current study, the mindfulness-based strategy was associated with increased activity in the left DLPFC during expecting negative emotional stimuli compared to the cognitive reappraisal strategy. Left DLPFC was more active also when comparing cognitive reappraisal to no control in prior studies [7, 8]. As cognitive reappraisal and mindfulness-based strategies have not been compared directly before, it may be tentatively concluded that DLPFC resources are likely to be important in both strategies. However, the early phase of mindfulness seems to require more DLPFC resources.

Interestingly, the differences between mindfulness-based and cognitive reappraisal-based emotion regulation

were less pronounced during the expectation of stimuli being announced as “unknown”. In this study, we found an increased activity in the left DLPFC (and at an exploratory level in left VLPFC and right SMG) only when mindfulness was applied. This finding stands in contrast to a large body of literature on uncertainty (for example [64–66]), and may suggest higher levels of arousal in uncertain situations, consequently requiring more regulatory efforts. Further research is needed to clarify this apparent contradiction.

During the perception of negative versus neutral stimuli, mindfulness-based and cognitive reappraisal strategies differed solely in the activation of one region, i.e. the caudate head. Compared to mindfulness, activity in the caudate was *increased* in the cognitive reappraisal group. The caudate as part of the striatum has been associated with motor control [67], with learning and memory functions [68], with response inhibition [69] as well as with cognitive and emotional processing [70, 71]. Furthermore, the caudate has been found to be modulated by regulatory strategies [9]. Graybiel summarized the general role of the caudate as playing a major role in optimal motor function and cognitive reappraisal [72], particularly in automated or habitual motor and cognitive processes [70, 73].

With regard to the comparison between mindfulness and cognitive reappraisal, the activation in the caudate in the cognitive reappraisal group is not obviously clear. On the one hand, subcortical structures including the caudate were more active during focused breathing [26], and a meta-analysis revealed stronger activations in the left caudate body and the MPFC during meditation when compared with rest or control conditions [74]. Considering the previously shown relevance of the caudate particularly in well-learned cognitive circuits, our results might eventually

be explained with the assumption that cognitive reappraisal might constitute a better established routine as opposed to mindfulness. This especially in a sample of participants from a “Western” cultural background with mostly no or very little mindfulness experience. On the other hand, the caudate was not activated stronger in beginners during a short mindfulness task when compared to experienced meditators [75]. Therefore, our results await replication in future studies and further research is needed for clarifying the caudate’s role in processes involving mindfulness and emotion-regulation strategies.

Limitations

One possible limitation of this study is that no behavioural control was used. We intentionally chose this approach to prevent potential interference due to preparatory and executive processes during task performance as suspected in previous studies using this paradigm (e.g. [8]). Nevertheless, it is difficult to draw conclusions concerning the subjectively experienced efficiency of the applied strategies.

Another limitation is that subjects were not homogeneous in their experience with mindfulness. This approach was chosen to study the neural correlates with the initialization of mindfulness at a more general level. However, this heterogeneity within the sample might have influenced some neural responses.

Additionally, the stimuli were only rated on subjective valence, but not on evoked arousal after the scan, so that an experience of arousal in the scanner can only be assumed. The choice of a between-groups-design with no randomization and the probability of unaccounted group differences have to be regarded as a limitation. In the current study, we wanted to prevent possible mixing of strategies by participants and therefore decided to instruct the participants in separate groups. Future studies could implement within-group-comparisons to address this concern.

Future perspectives

In future applications, our results might contribute to the development of individualized therapy plans for people presenting with mental disorders. The neurobiological markers linked to distinct emotion regulation strategies could assist therapists in choosing emotion-regulation strategies that optimally match the patient’s strengths and deficits. For example, the results of an fMRI scan may help to choose between mindfulness-focused strategies versus cognitive reappraisal strategies for emotion regulation.

In addition, future research may vary the length of the expectation period or may subdivide this period, to see if distinct activations can be identified with different time courses. Furthermore, it would be of interest to compare

trained with untrained meditators, as trained meditators may need lesser resources to initiate a mindful state and may be more effective in applying mindfulness-based strategies without facing concrete negative stimuli at all.

Concluding remarks

To summarize, the results of this study demonstrate that mindfulness strategies during emotional stimulation seem to recruit similar brain circuits as cognitive strategies. Also, mindful emotion regulation appears to exert a similar effect as cognitive emotion regulation onto the amygdala, figuring as a main brain region for emotional processing. These commonalities between mindfulness and cognitive reappraisal support prior findings of an emotion regulating effect of mindfulness without requiring an explicit regulatory intention or needing intensive training. The more pronounced activation of VLPFC, left DLPFC, SMG and insula with mindfulness as compared to cognitive reappraisal during the expectation, but not the perception of negative stimuli lead to the following tentative conclusion: Whereas at the outset, the early initiation of a mindful state may claim more cognitive resources than cognitive reappraisal in this expectant situation, once activated, mindful processing may not require more prefrontal activation than cognitive reappraisal does. This reasoning is consistent with the proposition that, particularly in untrained participants, mindfulness could be considered a top-down emotion-regulation process involving an increased activation of PFC areas [76].

Implications of our study for clinical practice may be seen in the use of the individual’s neurobiological activation pattern associated with different emotion regulation strategies for a differential diagnosis of strengths and deficits of the patients and for adapted therapy indications.

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