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Changes in the neural correlates of self-blame following mindfulness-based cognitive therapy in remitted depressed participants

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ABSTRACT

Mindfulness-Based-Cognitive-Therapy (MBCT) reduces vulnerability for relapse into depression by helping individuals to counter tendencies to engage in maladaptive repetitive patterns of thinking and respond more compassionately to negative self-judgment. However, little is known about the neural correlates underlying these effects. To elucidate these correlates, we investigated fMRI brain activation during a task eliciting feelings of blaming oneself or others. Sixteen participants in remission from major depressive disorder (MDD) completed fMRI assessments before and after MBCT, alongside self-reported levels of self-compassion, mindfulness, and depression symptoms. Analyses of self-blame versus other-blame contrasts showed a reduction in activation in the bilateral dorsal anterior cingulate/medial superior frontal gyrus after MBCT compared to baseline. Further, exploratory analyses showed that increases in self-kindness after MBCT correlated with reduced activation in the posterior cingulate cortex (PCC)/precuneus in self-blame versus rest contrasts. These findings suggest that MBCT is associated with a reduction in activations in cortical midline regions to self-blame which may be mediated by increasing self-kindness. However, this is a small, uncontrolled study with 16 participants and therefore our results will need confirmation in a controlled study.

1. Introduction

Major depression is highly prevalent and, in many of those affected, takes a recurrent course with an increased probability of relapse with each episode: 50% after one, rising to 70 and almost 90% following two and three episodes respectively (Rush et al., 2006; Kupfer, 1991). Thus interventions to prevent relapse are vital. Mindfulness-based Cognitive Therapy (MBCT) is specifically designed to address cognitive vulnerability processes in those currently in remission from depression but who are at high risk of relapse due to their previous history of recurrent depression (Segal et al., 2013) and is recommended for relapse prevention by the UK National Institute for Health and Clinical Excellence (NICE, National Institute for Health and Clinical Excellence, 2017). A meta-analysis of nine randomised controlled trials (RCTs) showed that MBCT is effective in preventing relapse for up to 60 weeks when compared with both maintenance antidepressants and treatment as usual (TAU; Kuyken et al., 2016). In contrast to other psychotherapies, MBCT relies on intensive mental training starting with focussed, sustained attention practices whilst building up to practices that encourage monitoring of all experience, be they positive, negative, or neutral, with increased openness and acceptance (Segal et al., 2013).

Evidence for the beneficial effects of mindfulness meditation on mental capacities comes from studies investigating neuropsychological, brain structural and functional (fMRI) change in long-term meditators and people taking part in structured mindfulness-based interventions (MBIs; for reviews see Young et al., 2018; Lao et al., 2016; Gotink et al., 2016, or Fox et al., 2016). Studies of MBIs (largely MBSR or adaptations) which are similar to MBCT in style and duration have suggested that changes in brain functioning may become visible after only eight weeks of training. Indeed, two systematic reviews of MBI fMRI studies have reported activation changes during functional tasks (including paradigms investigating mindful awareness or responses to emotion stimuli) in the insula (Young et al., 2018) and the prefrontal cortex (PFC), hippocampus, amygdala, and the cingulate cortex (Gotink et al., 2016), regions typically involved in attention, learning, interoception, and self-referential processing. However, to our knowledge, no study has yet investigated fMRI changes following MBCT in remitted depressed individuals.

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A core feature of the cognitive dynamics involved in relapse to and maintenance of depression are negative self-judgments as reflected in self-blame (Zahn et al., 2015). In the context of MBCT, mindfulness training enables remitted depressed participants to develop their capacity to respond to negative self-judgments with a friendly, open, and self-compassionate stance (Kuyken et al., 2010). Self-compassion, a central component of the stance that is cultivated through mindfulness training, is believed to counter the self-blaming thinking that is prevalent in major depression and detectable in previously depressed participants (Zahn et al., 2015). In line with this reasoning, the focus of the current study was specifically on investigating the effects of MBCT on the neural correlates of self-blame. To achieve this aim, individuals with a history of recurrent depression completed a self-blame task both before and after MBCT (Lythe et al., 2015). fMRI findings have linked self-blaming emotions to activation in the subgenual anterior cingulate cortex (sgACC) in both healthy and previously depressed participants (Zahn et al., 2009; Green et al., 2012). The sgACC is one of the key regions involved in the pathophysiology of depression and it has been suggested that increased metabolism in this region during depression, together with reduced coupling with anterior temporal lobe regions involved in differentiation of social concepts, is centrally implicated in tendencies towards overgeneralised self-blame in remitted depression (Green et al., 2012; Drevets et al., 1998; Ebert and Ebmeier, 1996). Furthermore, there is evidence that self-blaming thinking and emotions are associated with activations in a more general network of brain regions, not specific to self-blame, such as those related to emotional salience and guilt (e.g., dorsal and anterior cingulate cortex (d/ACC), dorsolateral and ventrolateral prefrontal cortex (dlPFC; vlPFC), posterior cingulate cortex (PCC), precuneus, and the amygdala (Bastin et al., 2016; Gifuni et al., 2017; Grimm et al., 2009).

Based on the above findings, we expected remitted depressed participants to show increased activation in the sgACC during self-blame compared with other-blame scenarios before MBCT. Given the potential of MBCT to counter tendencies towards self-blaming through the cultivation of an accepting and self-compassionate stance, we hypothesised that following MBCT participants would show decreased neural activation of self-blame, particularly in the sgACC, in this contrast. Furthermore, given the role of self-compassion in countering self-blame, we expected that activation changes following MBCT would correlate with changes in self-compassion.

2. Methods

2.1. Participants

A subset of 23 participants were recruited from a larger controlled study investigating MBCT mechanisms in previously depressed participants (manuscript in preparation). Participants were recruited from departmental study databases, posters and leaflets displayed at local GP and community centres and around the University campus, University research announcements, community websites, and social media. Participants were scanned both times at the NIHR/Wellcome Trust Manchester Clinical Research Facility. Five participants dropped out before (n = 1) or during (n = 4) MBCT, giving 18 complete datasets. Ethical approval was granted by the NHS (North West - Preston Research Ethics Committee) and all participants gave written informed consent in line with the Declaration of Helsinki (World Medical Association, 2001).

2.2. Inclusion and exclusion criteria

Participants had experienced at least two episodes of major depression (MDD) in the last five years and had been in full or partial remission according to DSM-IV criteria for the last three months; this was assessed using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) and scores of 12 or below on the Montgomery & Åsberg Depression Rating Scale (MADRS; Montgomery and Åsberg, 1979). Participants taking antidepressants were recruited if there were no recent (within the last three months) or planned future changes (during the study) to either dosage or medication. Participants were aged 18 to 60, in good physical health, had normal color vision, and were fluent in English to ensure sufficient task understanding. Participants were excluded if they had any other current or previous DSM-IV axis 1 mental health diagnosis (with the exception of anxiety disorders provided this was secondary to a diagnosis of remitted major depression), substance abuse or dependence, self-report physical or neurological disorders, or had previously participated in an MBI, had an ongoing mindfulness practice, or had completed psychotherapy in the last 12 months.

2.3. Design

Participants were assessed at baseline and after the eight week MBCT (post-MBCT). The larger study was a longitudinal, preference choice (MBCT or treatment as usual (TAU)) mechanistic design and is registered on clinicaltrials.gov (NCT02226042). Participants received MBCT free-of-charge and only the MBCT group were scanned.

2.4. Procedure

The imaging task was completed alongside neuropsychological assessments, the results of which are reported elsewhere (manuscript in preparation). Mood and estimated IQ measures were completed at screening, and participants gave a timeline of lifetime MDD episodes with specific details from the last two episodes (duration, symptoms, severity, and treatment) to ensure both episodes met DSM-IV criteria of MDD. The mood assessment was completed before each session and all other questionnaires were completed at the end of each session.

2.5. Intervention

MBCT was delivered according to the manual (Segal et al., 2013) and in adherence with the UK Network for Mindfulness-based Teachers Good Practice Guidelines (http://www.mindfulnessteachersuk.org.uk/) to a total of five groups between 2015 and 2017 each with between 7 and 15 participants. MBCT involved weekly two hour sessions with an all-day practice session around week six. Participants were encouraged to attend as many sessions as they could, but were excluded from analyses if they attended fewer than four sessions so as to ensure sufficient experience with the mindfulness-based practices. Participants were given audio practices and invited to practice in-between sessions. All MBCT groups were delivered by two mindfulness-based teachers (KW and an external teacher) who have both undergone recognised mindfulness teacher training with accredited organisations belonging to the above network.

2.6. Measures

2.6.1. Mini international neuropsychiatric interview (MINI; Sheehan et al., 1998)

The MINI is a structured experimenter-rated interview for diagnosis of axis-1 psychiatric disorders of the DSM-IV and ICD-10 classification systems, with high inter-rater reliability of above 0.75 for all diagnoses. The MINI was conducted by the lead author who was trained in its administration.

2.6.2. Self-compassion scale (SCS; Neff, 2003)

The SCS includes 26 items asking participants to rate from 1 (*almost never*) to 5 (*almost always*) how often they engage in behaviours or thoughts in difficult times (e.g., “I try to see my failings as part of the human condition”). Internal consistency in this sample was $\alpha = 0.91$ at baseline and $\alpha = 0.96$ post-MBCT.

2.6.3. *Five facet mindfulness questionnaire (FFMQ; Baer Et Al., 2006)*

The FFMQ includes 39 items asking participants to rate on a scale of 1 (*never or rarely true*) to 5 (*very often or always true*) how often they engage in behaviours or thoughts (e.g., "I find myself doing things without paying attention"). The FFMQ gives a total and five subscale scores (describing, observing, acting with awareness, non-judgemental awareness, and non-reactivity to experience). Studies have found a poor fit of the five factor model in community and clinical samples (Gu et al., 2015; Williams et al., 2014) and recommend removing 'observing', thus we have analysed the FFMQ-4 factor model (31 items) only. Internal consistency in this sample was $\alpha = 0.90$ at baseline and $\alpha = 0.96$ post-MBCT.

2.6.4. *Montgomery-Åsberg depression rating scale (MADRS)*

The MADRS is a widely used measure of depression severity. It includes 10 experimenter-rated items of depression symptoms on a scale of 0 (*absent/occasional)* to 6 (*severe/continuous*) over the last week. Internal consistency in this sample was $\alpha = 0.61$ at baseline and $\alpha = 0.71$ post-MBCT.

2.6.5. *Estimated verbal IQ: wechsler test of adult reading (WTAR; The Psychological Corporation, 2001)*

Participants read aloud 50 commonly misspelled words. The number of correctly pronounced words was converted to a standard score using age, gender, and education level, to predict verbal IQ. The scale has high internal consistency between 0.87 and 0.95.

2.6.6. *Retrospective amount of mindfulness practice*

At the start of each weekly MBCT session, participants completed a questionnaire about which formal mindfulness practices (e.g., mindfulness of breathing) and their duration were completed on each day of the previous week.

2.6.7. *Self-blame task*

This task was modified so as to focus specifically on self-blame from the value-related moral sentiment task as used in Lythe et al. (2015). The task was programmed in E-Prime Professional 2 (Psychology Software Tools, 2012) and run on a laptop projected onto a screen positioned by the participant's feet, and reflected into a mirror attached to the head coil with responses recorded using an MR-compatible button box held in their right hand. In this event-related design, participants were presented with 90 scenarios depicting negative interactions between themselves and their best friend. In 45 scenarios, the participant acted negatively towards their best friend (self > other), and vice versa in 45 scenarios (other > self; matched for content); each set of 45 scenarios included 33 negative and 12 negated-positive (i.e., does not act in a positive manner; Fig. 1) scenarios. Stimuli were selected based on mean unpleasantness ratings from Green et al. (2012). The participant's and their best friend's name (other) were entered to ensure equal familiarity with both agencies. Scenarios were presented across two 10 min runs, each with 22 fixation crosses interleaved where participants did not respond. The mean interstimulus interval (ISI) of 4000 ms was jittered in 500 ms steps from 2000 ms to 6000 ms. Each scenario was presented for up to 5 s, or until a response was given (a fixation cross would replace the scenario). Participants rated how they would feel (*extremely unpleasant* or *mildly unpleasant*) in each scenario. There were two counterbalanced versions and participants were randomised to both version order and finger assignment (index or middle finger) at each session. After scanning, participants were presented with all scenarios again and asked to rate the unpleasantness from 1 (*not unpleasant*) to 7 *(very unpleasant*) and to choose only one option for whom they would attribute blame to (*self, best friend, other/none*). If participants chose more than one option, they were asked to choose who they blamed most. Three fMRI contrasts were created: self-blame > other-blame, self-blame > fixation, and other-blame > fixation. Blame attribution proportion change over time (between baseline and post-MBCT) was analysed using a Wilcoxon signed-rank test due to non-normally distributed data. Data for scenario unpleasantness were normally distributed thus was analysed using paired sample t tests (Table 2).

2.7. *MRI data collection and analysis*

High-resolution MRI data were acquired using a 3T Philips Achieva MR scanner. Functional scans were acquired using a dual echo (12 and 35 ms) sequence and images were converted from Philips proprietary format (PARREC) to ANALYZE format using an in-house script giving functional ANALYZE images from both echoes combined. Dual echo can improve BOLD contrast in regions sensitive to susceptibility dropout (Poser et al., 2006). During the self-blame task a total of three hundred volumes were acquired, comprising 29 axial slices (4 mm thick), a TR of 2 s per volume, and voxel sizes of 4 × 4 × 4 mm. Whole brain structural data were collected using a T1-weighted MPRAGE SENSE sequence acquiring 180 slices (1.66 mm thick), TE of 3.8 ms, and a TR of 8.4 ms per volume.

2.7.1. *Spatial pre-processing*

Analyses were conducted in SPM12 (update 6225; http://www.fil.ion.ucl.ac.uk/spm) in MatLab (https://uk.mathworks.com/products/matlab.html). Images were realigned to correct for motion using a 6-

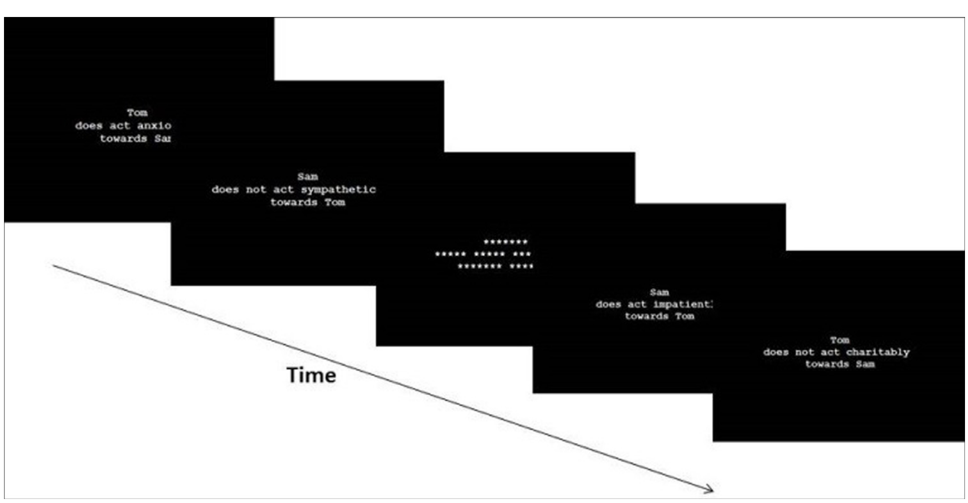

Fig. 1. Self-blame stimuli examples.

parameter rigid-body transform, registering to the first image as the reference. The T1-weighted structural and mean functional images were co-registered, followed by segmentation of the structural image into gray matter, white matter, and cerebral spinal fluid (CSF). Segmented images were normalised to SPM templates, and normalization field flow maps applied to the functional data. Finally, the normalised images were smoothed using a Gaussian kernel filter of 8 × 8 × 8 mm. To check for excess motion each participant's normalised images and realignment parameters were run through the ART SPM toolbox (http://www.nitrc.org/projects/artifact_detect/). Data were defined as unusable if >20% of functional volumes showed excessive motion of >1 mm and/or global signal changes of 3 SDs from the mean global signal. As such, data from two participants were removed giving 16 complete datasets.

2.7.2. First and second level analyses

At the first level, smoothed images were modelled for each participant with a high-pass filter of 128. Self-blame, other-blame, and fixation events were modelled, with both outlier and movement realignment parameters. At the second level, the three contrasts were created (see '2.6.7. Measures: Self-blame task'). The sgACC was defined using previously defined coordinates (−6, 22, 0) from Green et al. (2012), applying a sphere of 10 mm around the coordinates. Both baseline and change over time (subtraction: post-baseline) outcomes were analysed with one sample t tests and using peak voxel levels.

For whole brain analyses, we conducted a one sample t-test on baseline contrasts using a FWE corrected cluster-defining threshold of $p < .001$. Recent critiques of cluster-based analyses have raised concerns for an increased risk of false positives (Eklund et al., 2016, 2012). Therefore, Kessler et al. (2016) suggest applying a more conservative threshold of $pFWE < 0.001$ to all analyses, particularly with larger clusters. Significant baseline clusters were saved as a mask for small volume correction (SVC) analyses for change over time (post-baseline subtraction; both one sample t tests) to identify changes specific to those regions activated at baseline. Finally, task outcomes, mood and self-compassion questionnaire change scores, mean minutes of formal mindfulness practice during MBCT and self-report mindfulness change scores were entered as covariates to analyze correlations using a FWE corrected threshold of $p < .001$.

3. Results

Demographics are listed in Table 1. MBCT attendance was high with a mean of 7.7 (*SD* = *1.6*) sessions attended out of a possible 9 (including the all-day session at week six). During MBCT, mean time engaged in daily guided mindfulness practice was 19.6 min (*SD* = *8.4*) over a mean of 4.3 (*SD* = *1.7*) days per week. The mean time between scanning sessions was 68.9 days (*SD* = *8.5*); all participants were scanned within 14 days post-MBCT with the average time since MBCT at 5.2 days (*SD* = *3.8*).

Table 1
Demographics including baseline and post-MBCT questionnaire scores.

	Baseline	Post
Age	34.6 *(9.4)*	NA
Gender (% female)	81	NA
Estimated IQ	111.8 *(5.4)*	NA
Antidepressant medication (%)	38	NA
Previous number of episodes	6.1 *(3.3)*	NA
Age of onset	16.2 *(5.9)*	NA
Months since last MDD episode	9.8 *(6.8)*	NA
Depression symptoms (MADRS)	4.2 *(3.5)*	2.2 *(3.4)*
SCS mean total score	2.3 *(0.59)*	**3.2***** *(.82)*
SCS self-criticism subscale	3.9 *(0.85)*	**2.9***** *(.90)*
SCS self-kindness subscale	2.3 *(0.70)*	**3.2***** *(1.0)*
FFMQ-4 total score	84.13 *(14.72)*	**101.00**** *(21.71)*

Note. *N* = 16; NA = Not applicable as not repeated at post-MBCT; Values are means (*SDs*); Paired sample t tests ***$p < .001$; **$p < .01$ *$p < .05$; MADRS = Montgomery Åsberg Depression Rating Scale; SCS = Self-Compassion Scale; FFMQ-4 = Five Facet Mindfulness Questionnaire (Four Factor).

Table 2
Self-blame task results.

	Baseline	Post
Self-blame: Blame attributions		
Self > Other scenarios (34% of trials)		
Self-blame	0.84 *(0.10)*	**.74*** *(.25)*
Other-blame	0.05 *(0.05)*	0.07 *(0.08)*
No-one/other	0.11 *(0.11)*	0.19 *(0.24)*
Other > self scenarios (34% of trials)		
Self-blame	0.18 *(0.17)*	**.13*** *(.15)*
Other-blame	0.60 *(0.23)*	0.61 *(0.26)*
No-one/other	0.22 *(0.20)*	0.26 *(0.25)*
Out of scanner scenario unpleasantness		
Self-agency vs. other-agency	4.3 *(1.2)*	**3.8*ᵗ** *(1.1)*
Other-agency vs. self-agency	4.0 *(1.1)*	**3.6*** *(1.1)*

Note. *N* = 16; Values are means (*SDs*); *$p < .05$ (^{t}indicates a trend towards significance with *p* values between .05 and .09); out of scanner unpleasantness ratings are on a scale of 1 (*not unpleasant*) to 7 (*very unpleasant*); unpleasantness ratings data were normally distributed thus paired sample t tests (baseline, post-session) were used.

3.1. Behavioural results

The Wilcoxon signed rank test showed a significant decrease in self-blame attributions during self > other scenarios ($Z = -1.99$, $p = .046$; Table 2). Of interest, there was a significant decrease in self-blame attributions during other > self scenarios ($Z = -2.19$, $p = .03$; Table 2), but no significant change in the remaining scenarios. There was a significant decrease in unpleasantness in other > self ($t(15) = 2.2$, $p = .04$), but only a trend towards a significant decrease in self > other conditions ($t(15) = 2.1$, $p = .052$; Table 2).

3.2. fMRI results

3.2.1. Baseline activations

In our ROI analyses, there were no significant activations in the sgACC for any contrast. In whole brain analyses, for the self-blame > other-blame contrast, we identified one large and five moderately sized clusters extending across regions including the precentral, medial, frontal and superior temporal gyri, superior parietal lobe (SPL) and angular gyrus, dorsal anterior cingulate cortex (dACC), and into the right anterior insula (AI) and orbital inferior frontal gyrus (IFG; e.g., Supplementary Figure S1). For the self-blame > fixation contrast, we identified one large and one moderately sized cluster extending across the precentral, postcentral, medial frontal gyri and the medial and superior temporal gyri (e.g., Supplementary Figure S2). No other contrasts were significant. Full details are given in Supplementary Table S1.

3.2.2. Change over time

In our ROI analysis, there was no decrease in activation in the sgACC for any contrast. In whole brain analyses, there was decreased activation for the self-blame > other-blame (baseline > post) contrast in one midline cluster predominantly including the dACC/medial superior frontal gyrus (Fig. 2), and decreased activation for the self-blame > fixation (baseline > post) contrast in two clusters which included the left precentral and postcentral gyrus (Fig. 2). There were no significant activations for other contrasts or the post > baseline contrasts. Table 3 shows the results.

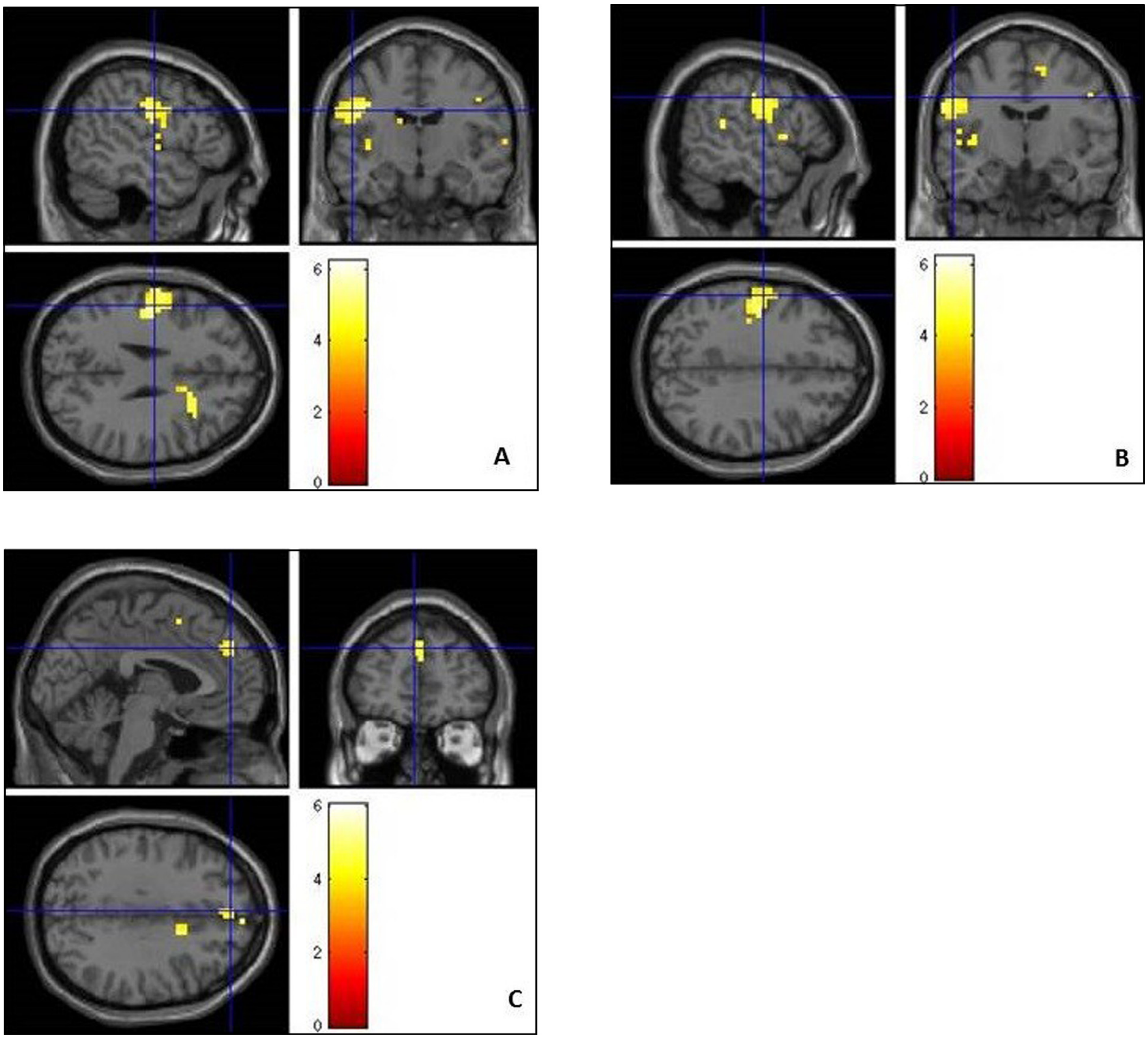

Fig. 2. Whole brain with SVC change over time in self-blame > fixation (A, B) and self-blame > other-blame (C) contrasts. A = left precentral gyrus; B = left postcentral gyrus; C = dACC/medial superior frontal; Subtractions are baseline vs. post-MBCT contrasts thus represent a reduction in BOLD activation over time.

3.3. Correlations

We did not find any significant correlations between activation changes in the self-blame > other-blame (baseline > post) contrast and self-reported changes in the SCS, or any other questionnaire measure. Further explorative analyses showed that there was a negative correlation between the self-blame > fixation (baseline > post) contrast and the SCS self-kindness subscale change (post-baseline) in one cluster ($p = .006$) including the bilateral posterior cingulate cortex (PCC) and precuneus (−6, −48, 22; Fig. 3).

4. Discussion

Our results suggest that MBCT may reduce tendencies towards self-blame in remitted depressed individuals and provide evidence for accompanying changes on a neural level. On the behavioural task, participants showed significant reductions over time in self-blame attributions in scenarios when the participant acted negatively towards their best friend, while there were no changes in other-blame attributions during scenarios where the best friend acted negatively towards the participant. This reduction in self-blame is unlikely to be solely

Table 3
Whole brain analyses. Decreases in activation for the self-blame task.

Left/Right	Region	Cluster *p*FWEc	Cluster size
Self-blame > Other-blame. Decreased activation (Baseline > Post)			
Bilateral	A small cluster predominantly in the **dACC**, extending into the **medial superior frontal gyrus**	$p = .04$	16
Self-blame > Fixation. Decreased activation (Baseline > Post)			
Left	A moderate cluster entirely within the **precentral** and **postcentral gyrus**	$p < .001$	67
Left	A small cluster entirely within the **precentral** and **postcentral gyrus**	$p = .04$	10

Note. dACC = dorsal anterior cingulate cortex.

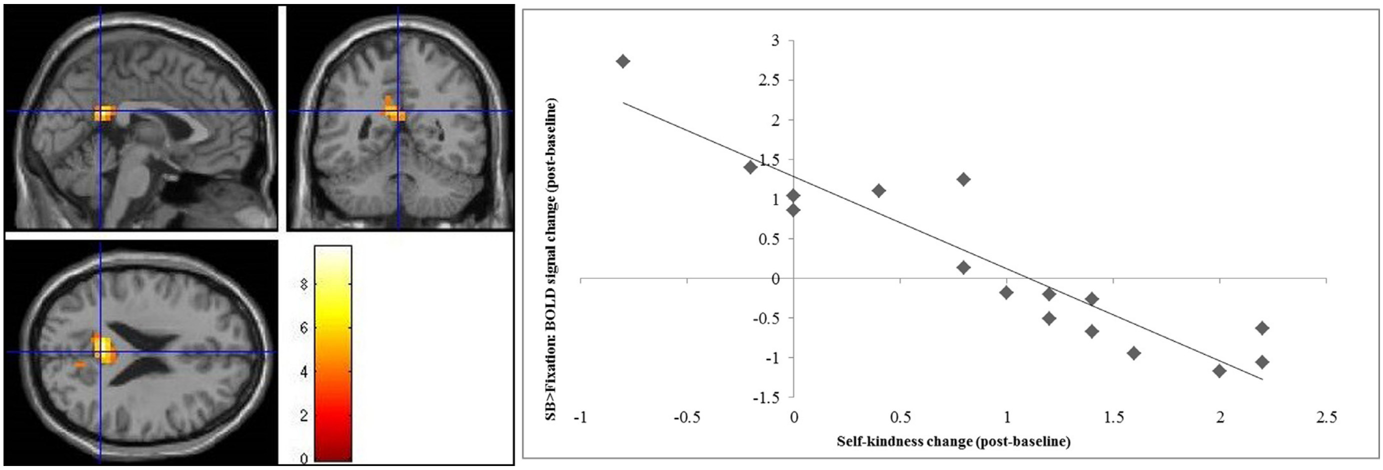

Fig. 3. Correlation between self-blame >fixation contrast BOLD signal change and self-kindness change (both post vs. baseline difference) in the bilateral PCC and precuneus.

explained by decreases in scenario unpleasantness as, although both conditions were rated less unpleasant overall, only a reduction in blame attributions was observed in the self-agency condition. Interestingly, and contributing further to evidence of a specific blame reduction, we found reductions over time in self-blame during scenarios where the best friend acted negatively towards the participant. Thus, as well as reducing the extent to which participants self-blame when they act negatively towards their best friend, MBCT may have given participants techniques to self-protect when their best friend acts negatively towards them.

In contrast to our hypothesis, self-blaming emotions were not associated with an increased sgACC activation compared to conditions in which participants blamed others, and consequently there were no significant changes in sgACC activation from before MBCT to after MBCT. This may be due to a more specific link between the sgACC and guilt-proneness as shown in previous studies (Zahn et al., 2009; Green et al., 2012) which prompted more explicit ratings of guilt, whereas our task prompted a broader definition of self-blame. However, our finding would be in line with previous studies which only identified sgACC activation when modeling for individual differences (Zahn et al., 2009; Green et al., 2012).

Further, the whole brain analysis indicated engagement of a number of other brain regions that are likely to be involved in the more general aspects of self-blaming feelings. In particular, we identified reduced activation over time in the bilateral dACC/medial superior frontal region in the self-blame > other-blame contrast. It is possible that these changes reflect changes in the saliency of self-relevant information, however previous studies using a variation of this task showed that these stimuli are highly associated with self-blaming emotions (Zahn et al., 2015). Our finding is in line with three healthy volunteer (HV) studies in which self-blame-related BOLD activations were reported in the dACC, as well as in the dorsal medial prefrontal cortex (dmPFC; Longe et al., 2010; Bruhl et al., 2014; Doerig et al., 2014). Others have reported dACC activation (extending into the medial prefrontal regions) during tasks involving rehearsal of personalised guilt experiences compared with neutral, non-guilt conditions (Fourie et al., 2014; Basile et al., 2011; Kedia et al., 2008); with guilt interpreted as part of a range of self-blaming emotions. dACC activation has also been linked with a number of negative psychological concepts in addition to self-blame, including social rejection (Kawamoto et al., 2015; Moor et al., 2012; Eisenberger et al., 2011), embarrassment (Moll et al., 2007), and during negative evaluation feedback (Dedovic et al., 2016), across healthy and clinical samples, all of which are in line with the view that the dACC is involved in the rehearsal and monitoring or salience detection of such negative experiences. Our findings suggest that MBCT in people with remitted MDD reduces engagement of neural networks associated with salient emotions when feeling self-blame. Such an explanation would be consistent with the general rationale of MBCT to help individuals respond to difficult thoughts and feelings with kindness and acceptance, in order to enable them to intentionally disengage from such thinking rather than automatically elaborate or avoid (Segal et al., 2013; van der Velden et al., 2015).

Other findings in our whole brain SVC analyses included decreases in activation over time in the left precentral and postcentral gyri in the self-blame > fixation contrast, providing further evidence for reductions in activation in areas that have previously been implicated in guilt and shame (Michl et al., 2014; Green et al., 2012; Wagner et al., 2011; Moll et al., 2007; Shin et al., 2000). Further, in a meta-analysis including 37 fMRI studies, Boccia et al. (2015) identified a network of areas which were activated during meditation tasks, which included the left precentral gyrus. However, these activations were from cross-sectional studies and therefore it remains unclear whether the decreases in activation in our study could be due to practice effects over time; a control group would have helped to elucidate this. Additionally, this change could partly be explained by motor responses during button pressing, although this would not explain the decreases in activation over time. Further, whilst there were no correlations between activation changes in the self-blame > other-blame contrast and the mindfulness questionnaire, exploratory analyses indicated a significant correlation between MBCT-induced decreases in activation in the self-blame > fixation contrast and increased self-kindness. The correlation between BOLD reductions and increased self-kindness was identified in the PCC and precuneus, regions implicated in retrieving autobiographical memories which are relevant for thinking about oneself (Cavanna and Trimble, 2006) and are part of the "default mode network" (DMN; Fransson and Marrelec, 2008). Regions overlapping with this area were previously shown to be less active in meditators compared with non-meditators (Garrison et al., 2014; Brewer et al., 2013), an observation that is also in line with the general view that mindfulness interventions serve to reduce tendencies to elaborate and engage in maladaptive patterns of thinking (van der Velden et al., 2015; Gu et al., 2015). Of note, participants were presented with a fixation cross once they had responded to each scenario therefore it could be argued that interpretation of the self-blame > fixation contrast may be confounded by participants continuing to engage with self-blaming emotions during the fixation cross. We believe this is unlikely to explain the decrease in strength of activation in this contrast over time, which would imply greater carry-over engagement with self-blame after MBCT, however this needs to be tested in an appropriately designed study.

4.1. Limitations

This study is limited by the lack of a control group and the small sample size. Therefore, our findings may partly be due to practice effects and/or task familiarity, and we cannot be certain whether our findings would be maintained with a larger sample. Thus, our results should be taken as preliminary and warrant further investigation. It should be noted that just over one third of our sample were taking antidepressants and studies have shown that antidepressants can attenuate the neural response to negative stimuli within six weeks of starting treatment (Ma, 2015). However, as participants in our study had no recent medication changes (within at least the last three months) nor changes during the course of the study, it is unlikely that antidepressant use affected our results.

There may be limitations around the self-blame task as, for example, there is evidence of reduced empathy in depression (Rütgen et al., 2019), which may affect participants' ratings towards themselves and others. However, self-blame also includes non-empathic self-blame related emotions such as shame which involves more external perceptions rather than altruistic concerns towards others (Pulcu et al., 2014). There is also evidence of increased empathic self-blaming emotions such as interpersonal guilt in people with current and remitted depression (O'Connor et al., 2002; Green et al., 2012); this may be an important consideration in further studies. Further, we cannot assume that changes arose solely from specific components of the MBCT training. MBCT is a complex intervention and changes could be driven by participation in a social group and other accompanying lifestyle changes; actively controlled studies are needed to clarify this.

5. Conclusion

To our knowledge, this is the first study to investigate the neural correlates of MBCT using fMRI, and in particular of self-blame in previously depressed participants undergoing MBCT. Our findings show reduced dACC/medial superior frontal activation to self-blame after MBCT, suggesting a change in processing self-blaming feelings at the neural level. Furthermore, neural changes in processing self-blaming feelings were associated with increases in self-kindness. Given that self-blame is detectable in over 80% of people with remitted MDD (Zahn et al., 2015), these findings are important in furthering our understanding of the neural correlates of MBCT related to preventing relapse to depression but need to be viewed as preliminary and require replication. Future studies should recruit larger, actively controlled samples and test whether changes in neural activation of self-blame predict relapse at a later point.

Contributors

KW collected and analysed the data, and prepared the initial manuscript; SM, RE, RZ, and IA guided the fMRI task design and analysis of the data; TB provided supervision of the MBCT groups; IA, TB, and RE supervised the drafting up of the manuscript, and all authors contributed to the editing and final completion of the manuscript.

Declaration of competing interest

The authors have no competing or conflicting interests to declare.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.pscychresns.2020.111152.

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