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4 **A biobehavioural approach to understand how mindfulness-based cognitive**
5 **therapy reduces dispositional negative self-bias in recurrent depression**

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Abstract

Negative self-bias is a detrimental vulnerability factor of recurrent depression.

Here we examine the potential of mindfulness-based cognitive therapy (MBCT) to reduce this bias by assessing self-report and psychophysiological responses to a previously validated self-compassion exercise in individuals with recurrent depression.

One group (n= 25) received eight sessions of MBCT between two assessments (2.5 – 3 months apart). The second group was an untreated control group (n = 25) tested at similar intervals.

Our results indicate that, when the MBCT group engaged in the self-compassion exercise after MBCT, they showed reduced physiological arousal and enhanced parasympathetic activity whereas no changes were observed in the control group. Interestingly, self-reported state self-compassion after the exercise increased in both groups at both timepoints, but only in the MBCT group the overall levels of state and dispositional self-compassion were increased significantly. This suggests that MBCT reduces both strategic (self-report) and automatic (psychophysiological) negative self-bias.

Keywords: Negative Self-bias, Depression, MBCT, Self-Compassion, Psychophysiology

1 **Introduction**

2 Worldwide, approximately 350 million people suffer from major depressive disorder
3 (MDD), the most prevalent, chronic mental disorder (Kessler et al., 2009) that is a
4 leading cause of disability (WHO, 2008). With relapse rates of 50-90%, individuals
5 with depression remain highly vulnerable even after symptom reduction (Kessing et al.,
6 2004). Consequently, it is pivotal to study mechanisms driving this vulnerability and to
7 evaluate treatment approaches in their potential to address it effectively.

8 One of the most pervasive and detrimental vulnerability factors of depressive
9 relapse is negative self-bias; i.e. the habitual, highly internalized self-criticism that
10 manifests as self-deprecating thoughts and feelings of worthlessness (American
11 Psychiatric Association, 2013; Williams, Healy, Teasdale, White, & Paykel, 1990). It
12 is characterised by hard to inhibit access to negative information and difficult to retrieve
13 positive information about the self. Although pharmacological and psychological
14 treatments can reduce negative self-bias (Hilimire et al., 2015; Yoshimura et al., 2017;
15 Yoshimura et al., 2014), it persists at automatic, habitual level beyond symptom
16 reduction and can therefore be easily reactivated (Hedlund & Rude, 1995; Rude,
17 Wenzlaff, Gibbs, Vane, & Whitney, 2002; Segal, Williams, & Teasdale, 2013). This
18 habitual negative self predicts depressive relapse (Disner, Shumake, & Beevers, 2017;
19 LeMoult, Kircanski, Prasad, & Gotlib, 2017) and appears difficult to treat (Shestiyuk &
20 Deldin, 2010) making it a particularly hard to address key vulnerability factor for
21 depressive relapse (Beck, 2008; Gotlib & Joormann, 2010; Mathews & MacLeod,
22 2005).

23 A relatively novel treatment, Mindfulness Based Cognitive Therapy (MBCT),
24 was designed to help people to recognise and decentre from negative self-bias. MBCT
25 is an eight-week psychosocial program that teaches meditation to cultivate attitudes of

1 acceptance and non-judgment in order to recognise and disengage from unhelpful
2 depressive thinking patterns (Segal et al., 2013). MBCT forms an affordable alternative
3 to long term anti-depressant medication in preventing depressive relapse (Kuyken et
4 al., 2015; Kuyken et al., 2016; Piet & Hougaard, 2011) and has therefore been widely
5 implemented in UK mental health care services (NICE, 2010; Tickell et al., 2019).

6 Studies directly evaluating MBCT's benefits and mechanisms in reducing
7 negative self-bias in recurrent depression are lacking. Support for a possible role of
8 mindfulness in reducing negative self-bias comes from neuroscience research
9 predominantly conducted in healthy samples and experienced meditators. It suggests
10 that regular practice of moment-to-moment, non-judgemental awareness leads to
11 functional and structural plastic changes in brain circuitries (i.e., insula, medial
12 prefrontal cortex) involved in self-referential processing (Farb et al., 2007; Tang,
13 Holzel, & Posner, 2015). Interestingly, these brain circuitries have been altered in
14 depression and are implicated in negative self-bias (Lemogne et al., 2009; Lemogne et
15 al., 2010).

16 Additionally, intervention research showed that MBCT, although not explicitly
17 targeting it in the intervention, increases dispositional self-compassion (Holzel et al.,
18 2011; Kuyken et al., 2010); i.e., the ability to meet adversity through self-soothing
19 (Gilbert, 2009; Neff, 2003b). MBCT-related cultivation of self-compassion also
20 facilitated effective recovery from experimentally induced negative mood in
21 individuals with recurrent depression (Kuyken et al., 2010). Additionally, levels of
22 dispositional self-compassion are associated with more adaptive emotion regulation
23 and more effective repair of negative mood in individuals with current (Diedrich, Grant,
24 Hofmann, Hiller, & Berking, 2014) and remitted depression (Karl, Williams, Cardy,

1 Kuyken, & Crane, 2018). Hence, cultivating self-compassion could be a key
2 mechanism of change via which MBCT is addressing negative self-bias.

3 Despite growing evidence for self-compassion's beneficial effects in depression
4 (MacBeth & Gumley, 2012), self-soothing can be difficult for people who suffer from
5 recurrent depression (Gilbert, McEwan, Catarino, Baiao, & Palmeira, 2014). Whereas
6 in healthy populations self-compassion inductions typically lead to an increase in
7 positive self-views (Arch et al., 2014; Kirschner et al., 2019), individuals prone to self-
8 criticism struggle to disengage from negative self and to access self-soothing (Gilbert
9 et al., 2014; Gilbert, McEwan, Matos, & Ravis, 2010). This renders compassion
10 induction exercises useful for assessing individual differences in negative self-bias.
11 Critically, because most self-compassion studies heavily rely on self-report, it is vital
12 to identify mechanisms and indicators more suitable for accessing and targeting the
13 automatic, habitual nature of negative self-bias in order to effectively address
14 depressive relapse.

15 When we asked healthy individuals to engage in a specially developed self-
16 compassion meditation that invites them to direct kind and self-affirming thoughts first
17 to a significant other and then, for several minutes, to themselves (Kirschner et al.,
18 2019), we found that increased state self-compassion was accompanied by increased
19 parasympathetic activity (indicated by increased heart rate variability, a physiological
20 marker of adaptive emotion regulation, (Thayer & Lane, 2000)) and decreased
21 physiological arousal (indicated by decreased heart rate and skin conductance levels).
22 In contrast, a self-critical rumination control condition was accompanied by the
23 opposite physiological response pattern indicating a threat response (Kirschner et al.,
24 2019). In addition, Gilbert et al. (Rockliff, Gilbert, McEwan, Lightman, & Glover,
25 2008) demonstrated that individuals with high dispositional self-criticism are unable to

1 increase heart rate variability and to reduce the biological stress response when
2 practicing compassion. This threat response pattern could hence be regarded as a
3 physiological marker for negative self-bias. Based on these findings and because
4 physiological responses underlie far less explicit strategic control, they can be
5 hypothesised to be a proxy for the more automatic, habitually accessible positive or
6 negative self that appears to drive depressive relapse thus potentially allowing us to
7 differentiate healthy from depressive individuals.

8 It has not been investigated how individuals currently remitted from depression respond
9 to our one-off self-compassion meditation; i.e. if they show evidence for increased self-
10 report (strategic) and physiological (automatic) positive self, similarly to healthy
11 individuals, or if they show residual automatic negative self-bias accompanied by threat
12 patterns described above. In addition, it has not been experimentally studied if MBCT
13 helps individuals with recurrent depression to reduce negative self-bias and increase
14 positive self-views which could indicate that the latent vulnerability for depressive
15 relapse was effectively addressed. We therefore first, investigate if prior to MBCT
16 remitted patients with recurrent MDD will show a significant reduction in self-reported
17 state self-criticism and increase in state self-compassion when listening to the
18 induction, thus testing the assumption that absence of current clinical symptoms is
19 accompanied by absence of explicit negative self-bias (Hypothesis 1). Second, we will
20 examine if the self-report findings are accompanied by a reduction in physiological
21 arousal and increase in parasympathetic activation when listening to the self-
22 compassion induction as a proxy for a more automatic, habitually accessible positive
23 self (Hypothesis 2). Third, our study will investigate if self-report and physiological
24 responses to the brief self-compassion induction improve from pre-to post MBCT thus
25 investigating if MBCT further reduces negative self-bias and increases positive self

(Hypothesis 3). Fourth, our study will investigate if MBCT-related reductions in physiological arousal and increase in parasympathetic activation are associated with changes in dispositional self and depressive symptoms (Hypothesis 4).

Methods

Design and Participants

Using a mixed experimental design, we assessed within-subjects (pre- vs. post-treatment) and between-subjects (MBCT vs. control) effects on self-reported self-compassion, self-criticism, depressive symptoms and psychophysiological responses to a self-compassion exercise.

Fifty individuals who met criteria for recurrent major depressive disorder in full or partial remission according to the DSM-IV (First, Spitzer, Gibbon, & Williams, 1995) were recruited (see Supplemental Figure 1 for the participant flow chart). Two groups of individuals were included a) those who underwent an eight-week MBCT program (remitted depressed MBCT group; $N = 25$) and b) individuals recruited from the waiting list for an MBCT program (remitted depressed control group; $N = 25$). The MBCT course was delivered by trained MBCT therapist who taught > 10 courses. The MBCT course strictly followed the manualized program in length and content (Segal et al., 2013). No changes have been made to the standard MBCT program to explicitly address compassion or self-compassion. Participants were eligible when 18 years or older, right-handed and English native speakers. They were excluded if currently depressed; previously attended MBCT or currently received other psychological therapy¹. All participants gave written informed consent and the study was approved

¹ In addition, we screened out participants who: a) had visual or hearing difficulties which were not corrected for by contact lenses, glasses or a hearing aid b) had very sensitive skin or a diagnosed skin

1 by The South West Cornwall and Plymouth NHS Research Ethics Committee (ref.
2 13/SW/0099). Sample characteristics and group comparisons at baseline are in Table
3 1.

4

5 **Table 1**

6 Means, Standard Deviations, and Significance Tests for the sample characteristics at baseline
7 of the different groups.

Characteristic	Baseline		Test	p
	remitted depressed MBC T	remitted depressed Control		
N	25	25		
Gender				
Male/female: n	10/15	5/20	$\chi^2(1, N = 50) = 2.38$	.123
Female: %	60	80		
Age in Years $M(SD)$	49.92 (9.68)	47.16 (11.89)	$t(48) = .90$	.373
Marital status: n (%)				
Single	6 (24)	10 (40)		
Married or as living with someone as if married	12 (48)	12 (48)		
Separated, divorced, or widowed	7 (28)	3 (12)		
Level of education: n (%)				
No educational qualification	0	0		
Some school qualification	0	1 (4)		
High school and/ or vocational qualification	1 (4)	1 (4)		
University degree/ professional qualification	24 (96)	23 (92)		
Number of depressive Episodes: $M(SD)$	5.36 (4.06)	5.56 (5.15)	$t(48) = .15$	.879
Age of onset first depressive Episode: $M(SD)$	27.12 (8.27)	23.96 (8.09)	$t(48) = 1.37$	.178
Medication				
Yes/No	16/9	17/8	$\chi^2(1, N = 50) = .09$	.765
Medicated: %	64	68		
Self Compassion Scale				
Total: $M(SD)$	14.58 (3.75)	15.91 (4.34)	$t(47) = 1.15$	.257
FSCRS				
Reassure Self: $M(SD)$	16.21 (3.90)	18.29 (5.62)	$t(46) = 1.49$	.143
Inadequate Self: $M(SD)$	20.58 (8.62)	15.33 (8.61)	$t(46) = 2.11$	.040
Hated Self: $M(SD)$	4.70 (3.35)	3.13 (3.72)	$t(46) = 1.55$	.129
BDI: $M(SD)$	16.08 (10.21)	11.21 (10.07)	$t(48) = 1.68$	.100

8

9 *Note.* Trait self-compassion has been assessed via the SCS (Neff, 2003). The possible range of this scale
10 is 0 – 30, with higher scores indicating higher trait levels of self-compassion. The Forms of Self-
11 Criticising/Attacking & Self-Reassuring Scale (FSCRS; Gilbert et al., 2004) was used to assess trait level
12 of self-criticism. The scale measures two forms of self-criticalness; inadequate self (possible range 0 –
13 33), and hated self (possible range 0 – 20), and one form of self-reassure, reassure self (possible range 0
14 –32). BDI = Beck Depression Inventory.

15

condition c) had a history of brain surgery d) suffered from high blood pressure e) had a change in
medication within the last 3 months) had a pacemaker fitted f) suffered from epilepsy.

1 **Experimental Induction**

2 We used a previously validated, eleven-and-a-half-minute Loving-Kindness
3 Meditation for the self (LKM-S) (Kirschner et al., 2019). The self-compassion
4 manipulation was developed and recorded together with an experienced MBCT
5 therapist from the ACCEPT clinic, an NHS commissioned depression service that is
6 part of the University of Exeter Mood Disorders Centre. The guided mediation was
7 11.5 minutes long. The basis of the manipulation was a Loving Kindness Mediation
8 (LKM; see Salzberg, 1995) that was tailored to specifically cultivate state self-
9 compassion and incorporating the clinical experiences of the therapist. During the
10 manipulation participants were guided to direct loving/friendly feelings towards a close
11 person. They were then asked to direct the same feelings towards themselves.

12
13 **Measures**

14 ***Diagnostic Assessment***

15 We assessed current and past depression through the Structured Clinical Interview for
16 DSM–IV (SCID-IV) (First et al., 1995).

17 ***Self-Report Measures***

18 To assess change processes in MBCT (Feldman & Kuyken, 2011), trait levels of self-
19 compassion (Self-Compassion Scale (SCS); (Neff, 2003a)); self-criticism (Forms of
20 Self-Criticising/Attacking & Self-Reassuring Scale (FSCRS); (Gilbert, Clarke,
21 Hempel, Miles, & Irons, 2004)) and depressive symptom scores (Beck Depression
22 Inventory, Second Edition (BDI-II); (Beck, Steer, & Brown, 1996)) were administered
23 pre and post treatment. To assess the effectiveness of the self-compassion manipulation
24 on participants' state self-compassion and self-criticism, a series of Visual Analogue
25 Scales (VAS, ranging from 0 to 100) were used throughout the experimental sessions.

1 See Supplemental Materials for more information about the self-report measures used
2 in this study.

3 *Physiological Measurements*

4 Physiological responses were recorded using a BIOPAC™ MP150 system and the
5 software AcqKnowledge 4.2 (BIOPAC Systems; Goleta, CA). Skin conductance level
6 (SCL) as a measure of sympathetic activation and physiological defense response
7 (Sokolov, 1963) was continuously recorded using a BIOPAC SCL100C amplifier and
8 a skin-resistant transducer (TSD203) from the middle phalanx of the first and ring
9 fingers of the participant's nondominant hand at a sampling rate of 500 Hz with a low
10 pass filter of 1.0 Hz. Mean SCL, maximum SCL values, and minimum SCL values
11 were extracted for 1-minute segments from baseline to minute 11 of the exercise. A
12 range correction (Lykken, Rose, Luther, & Maley, 1966) was applied for each
13 participant to give a mean SCL corrected for individual differences. Heart rate (HR) as
14 an indicator of physiological arousal, was determined from raw electrocardiogram
15 (ECG) in beats per min on the basis of a semiautomatic R-wave detection algorithm
16 using AcqKnowledge. Raw ECG was acquired using a BIOPAC ECG100C amplifier
17 at a sampling rate of 1 kHz and filtered using a band pass of 0.5–35 Hz. Artifact
18 detection (i.e., noisy, missing, or ectopic beats) and removal was performed using a
19 template correlation and interpolation from the adjacent R-peaks based on established
20 procedures in less than 5% of the ECG data (Berntson et al., 1997). Mean HR in beats
21 per min was then extracted from the R-waves for the same time windows. High-
22 frequency heart-rate variability (HF-HRV) as indicator of parasympathetic activation
23 and adaptive physiological regulation capacity (Thayer & Lane, 2000) was determined
24 from the artefact-free ECG by submitting a time series of the R-peaks to a fast Fourier
25 transformation that calculated the power spectrum of the R-R interval variation for the

1 frequency range between 0.15 Hz and 0.4 Hz in a given time window (Berntson et al.,
2 1997). Mean HF HRV were then extracted for each data section similar to the HR. HRV
3 values were transformed using a percent deviation from the mean (Ellis, Sollers Iii,
4 Edelstein, & Thayer, 2008). To obtain SCL, HR and HRV response throughout the
5 audio exercise and in order to control for individual differences, we calculated each
6 participants' change values for each minute of the experimental condition by
7 subtracting the averaged baseline values from the scores during each minute of the
8 audio exercise.

9

10 **Procedure**

11 After screening for eligibility, interested participants were invited for a diagnostic
12 assessment where they provided informed consent before we assessed demographic
13 information, history of depression and current depression status through the SCID (First
14 et al., 1995). Participants were then scheduled for the physiology sessions
15 approximately 2 – 2.5 months apart. The MBCT group was tested immediately before
16 and after the intervention. The control group was tested at similar intervals. The
17 experimental procedure of the physiological sessions is shown in Figure 1A. At the end
18 of each session, participants completed the questionnaire pack.

19

20 **Statistical Analyses**

21 *Prior Intervention Effects*

22 Psychophysiological changes in response to the self-compassion exercise were
23 analyzed using paired sample t-tests across groups.

24 *Treatment Related Effects*

Treatment related changes in depression and dispositional self-compassion and self-criticism were analyzed using paired sample t-tests for each experimental group. To test whether MBCT changes psychophysiological responses to the self-compassion exercise we applied mixed ANOVA's with time (pre and post MBCT) as the within subject factor and group as the between subject factor. To analyze the physiological response trajectories, we computed an average change score for heart rate, heart rate variability and skin conductance change depending on the focus during the LKM-S (others (min 1 -5) vs. self (min 6 -11)) for the first and second assessment. For these analyses, focus (others vs. self) was added as an additional within subject factor to the ANOVAs.

Associations

In order to study the associations between treatment-related physiological change, change in dispositional self (trait self-compassion and self-criticism) and symptom reduction (changes in BDI-scores), we calculated zero order correlations. Residualized gain scores, as a validated index of pre-post treatment changes that controls for variance in initial pre-scores, were calculated for each person and change parameter by regression with postscore as outcome (Mintz, Luborsky, & Christoph, 1979; Williams, Zimmerman, Rich, & Steed, 1984). To account for multiple testing, we adjusted the p value for number of tests.

Sensitivity, Specificity And Accuracy

In order to investigate if the change in physiological responses to the LKM-S correctly classifies MBCT-patients from untreated we determined sensitivity, specificity and accuracy.

Sample Size Determination

1 Sample size was determinate using a priori sample size calculations (Faul et al., 2007).
 2 The sample size was determined for a 2 (group) x 2 (time) mixed ANOVA, assuming
 3 a statistical power of .80, $\alpha = .05$ and a medium effect size ($f = .25$). Based on this
 4 calculation it was found that a minimum of 50 participants were required for this study
 5 to detect an effect of group on the outcome variables.

6

7 **Results**

8 **Pre-Intervention Effects (Hypothesis 1 & 2)**

9 For the pre-intervention analyses, data were collapsed across intervention groups (see
 10 Figure 1B-F for visualisation of the data). We found a medium effect size for enhanced
 11 self-reported self-compassion after the LKM-S ($t(49) = 3.50, p = .001, 95\% \text{ CI } [2.77,$
 12 $9.99], d = .50$), but only a small non-significant effect size for reduced self-reported
 13 self-criticism, $t(49) = 1.54, p = .129, 95\% \text{ CI } [-9.89, 1.29], d = .22$.

14 For the physiological responses to the LKM-S, we found a reduction in SCL
 15 during the LKM-S when focusing on a loved one ($t(45) = -3.92, p < .001, 95\% \text{ CI } [-$
 16 $.17, -.06], d = .57$) and the self, $t(45) = -7.15, p < .001, 95\% \text{ CI } [-.30, -.17], d = 1.04$
 17 suggesting the absence of a defence response. While focusing on others, HR did not
 18 change, ($t(45) = -.88, p > .384, 95\% \text{ CI } [-.72, .28], d = .13$), but interestingly
 19 significantly increased when the focus changed to the self, $t(45) = 2.22, p = .031, 95\%$
 20 $\text{CI } [.06, 1.22], d = .33$, suggesting an increase in physiological arousal. Analyses on
 21 HRV changes revealed a trend for decreased HRV for the focus on others ($t(45) = -$
 22 $1.95, p = .057, 95\% \text{ CI } [-18.02, .28], d = .28$) while there was a significant medium-
 23 size decrease in HRV when focusing on the self, $t(45) = -2.80, p = .007, 95\% \text{ CI } [-$
 24 $24.29, -3.97], d = .41$ suggesting a decrease in parasympathetic activation.

Figure 1. Panel A. Experimental procedure in sequential order and accompanied by approximate timings. *Note.* The data of the cognitive task and from the EEG recordings are not presented in this paper. Panels B-F. LKM-S related changes in self-report and physiological responses across groups pre-intervention. Error bars = $\pm$ 1SE. Shades represent $\pm$ 1SE. The grey shaded area marks the time when participants focused on the self.

Treatment Related Changes

Treatment-Related Changes In Depression Symptoms And Dispositional Self-Compassion And Self-Criticism (Manipulation Checks)

MBCT was accompanied by significant reductions in symptoms of depression and dispositional self-compassion and self-criticism whereas no such changes were observed in the control group (see Figure 2 and supplementary results a detailed description of these statistics).

Figure 2. MBCT related changes in depression symptoms and dispositional self-compassion and self-criticism. Error bars = ± 1 SE. Note: * = $p < .05$; ** = $p < .01$; *** = $p < .001$ for t-tests comparing changes within each group.

Treatment-Related Changes In State Self-Compassion And Self-Criticism (Hypothesis 3a)

Both groups demonstrated a significant increase in self-compassion after the LKM-S at both testing sessions. In contrast, we did not find reductions in self-criticism. Reflecting the dispositional changes in self-compassion and self-criticism reported above, we observed increased state self-compassion and reduced state self-criticism baseline scores in the MBCT group post treatment (see supplementary Figure S3 and supplementary results for a detailed description of these statistics).

Treatment-Related Changes In Physiological Arousal And Parasympathetic Activation (Hypothesis 3b)

A detailed description of the results of the focus (others vs. self) x Time (first vs. second assessment) x group ANOVA can be found in the supplementary materials. In the following we report results from the difference waves as indicator of MBCT-related change in physiological responses (e.g. post change score – pre-change score as depicted in Figure 3).

SCL Effects. The focus x group analyses revealed a main effect of group, $F(1,42) = 7.86, p = .008, \eta^2_p = .158$, indicating that relative to the control group, the MBCT group demonstrated decreased SCL in responses to the LKM-S post treatment as compared to pre-treatment. No other effects reached significance.

HR Effects. Analyses revealed a significant group effect, $F(1,43) = 10.66, p = .002, \eta^2_p = .199$, suggesting an MBCT-related decrease in HR in response to the LKM-S. There were no effects for focus and no group x focus interaction.

HRV Effects. The Focus X Group ANOVA revealed a significant effect of focus, $F(1,43) = 5.41, p = .025, \eta^2_p = .112$, and group, $F(1,43) = 14.89, p < .001, \eta^2_p = .257$. These effects indicate higher HRV in response to the LKM-S when focusing on the self and generally higher MBCT-related HRV. In the first three minutes of self-

1 focus, only the MBCT group showed medium-size treatment related elevation of HRV
2 when changing the focus from others to the self (MBCT: $t(20) = 2.20$, $p = .040$, 95 %
3 CI [1.29, 48.21], $d = .48$; Control: $t(23) = .44$, $p = .667$, 95 % CI [-7.81, 11.99], $d =$
4 .09). This was supported by a trend for a focus x group interaction using this time
5 window, $F(1,43) = 3.76$, $p = .059$, $\eta^2_p = .080$.

6

7

8 **Figure 3.** MBCT-related changes in physiological arousal and parasympathetic activation.

9 *Note:* Shades represent ± 1 SE. The grey shaded area marks the time when participants focused
10 on the self.

11

**1 Associations Between Psychophysiological Change, Change In Dispositional Self
2 And Symptom Reduction**

3 Reductions in depression symptoms (BDI) were significantly positively correlated with
4 reductions in self-criticism (FSCRS -inadequate self and hated self) with large
5 correlation coefficients of $r = .60$ (see supplementary material for full table).
6 Conversely, they were associated with increases in self-compassion (SCS) and
7 reassured self (FSCRS), effects ranging from medium ($r = -.34$) to large ($r = -.52$).
8 Treatment-related reduction in skin conductance when directing compassion for others
9 and for self were significantly correlated with BDI symptom reduction with medium
10 correlation coefficients ranging from $r = .41$ to $r = .44$. Similarly, BDI reduction was also
11 significantly associated with treatment-related reduction in heart rate when directing
12 compassion to the self.

13 Reductions in self-criticism (FSCRS -inadequate self) were significantly
14 correlated with reductions in the heart rate and increases in the heart rate variability
15 with absolute medium effects ranging from $r = .34$ to $r = .38$. Increases in self-reassurance
16 (FSCRS) were significantly correlated with reductions in skin conductance and heart
17 rate with medium effects ranging from $r = -.31$ to $r = -.32$.

18 In addition, we found that change in HRV when directing compassion to the
19 self correctly classified 76% of participants as MBCT participants with a sensitivity of
20 69.2 and a specificity of 84.2 suggesting that 7 out of 10 MBCT participants but only 2
21 out of 10 non-MBCT patients showed an increase in HRV at their second assessment
22 when they direct compassion to themselves.

23

24 Discussion

By concomitantly assessing self-report and physiological responses to a self-compassion meditation, this study provides novel insights into positive self-referential processing as a potential marker and treatment target for recurrent depression. In our self-compassion meditation, individuals directed kind and self-affirming thoughts first to a significant other and then, for several minutes, to themselves (Kirschner et al., 2019). We studied self-report and physiological responses to both phases of the self-compassion meditation as proxies for strategic or automatic self-referential processing respectively in currently remitted individuals with a history of three or more depressive episodes before and after they completed either an eight-week MBCT course or a waiting phase. Post-MBCT, we found evidence for higher meditation-induced strategic and automatic positive self and reduced negative self, whereas prior to treatment these changes were only partially observed.

Our results not only replicated previous reports identifying self-reported changes in self-compassion and self-criticism through MBCT (Feldman & Kuyken, 2011; Kuyken et al., 2010; van der Velden et al., 2015), but also extend this research in several ways.

First, by showing reduced self-criticism and physiological arousal and increased self-compassion and increased heart rate variability to a self-compassion meditation after MBCT, we indicate that this intervention has the potential to reduce negative self-bias and to increase access to a habitual positive self. This conclusion is supported by two observations. MBCT normalized physiological responses to the self-compassion exercise in individuals with recurrent depression towards a response pattern previously seen in healthy individuals (Kirschner et al., 2019; Rockliff et al., 2008) and associated with adaptive responses to distress (Arch et al., 2014) and psychological and physiological health (Thayer & Lane, 2000; Thayer & Lane, 2007). Additionally, our

finding that the pre-to-post HRV increases when individuals direct compassion to themselves correctly classified individuals as having undergone MBCT with an accuracy of nearly 80% may suggest this as a potential biomarker to target in future research not only for improvements in emotion regulation (Thayer & Lane, 2000) following MBCT but specifically of an improved positive self (Kirschner et al., 2019). These results contribute to existing evidence that negative self-bias in depression can be changed through therapies (Hilimire et al., 2015; Yoshimura et al., 2017; Yoshimura et al., 2014) but critically extend this research by suggesting that MBCT may be uniquely placed to facilitate a more habitual, embodied positive self (Feldman & Kuyken, 2011) by its focus on practicing awareness and non-reactivity thus enabling patients to consciously choose thoughts, emotions and sensations (Chambers, Gullone, & Allen, 2009) with an orientation of acceptance. MBCT is therefore not only a cost-effective treatment alternative (Kuyken et al., 2015) but effectively addressing a key vulnerability for depression (Beck, 2008; Gotlib & Joormann, 2010; Mathews & MacLeod, 2005). This conclusion is also supported by emerging neural data (Farb et al., 2007) showing how mindfulness meditation is associated with experience-dependent plasticity in brain circuitries underlying self-referential processing (Lin, Callahan, & Moser, 2018).

Second, our findings shed light on the debate about strategic versus automatic negative self-bias in depression. The prior-to-the-intervention-phase transiently increased self-compassion at the end of the self-compassion meditation, can be seen as partial support for a temporarily increased positive self in remitted depressed patients. However, there was no reduction in state self-criticism suggesting persistence of negative self-bias beyond symptom reduction. In addition, the self-reported increase in self-compassion was not accompanied by the pattern of reduced physiological arousal

and increased parasympathetic activation that we previously identified in healthy individuals (Kirschner et al., 2019). On the contrary, in those currently remitted but still at risk for depressive relapse we found a significant increase in HR and decrease in HRV when participants focused on the self during the self-compassion meditation. This discrepancy may suggest that when remitted, individuals may be able to access less negative and more positive self at strategic but not automatic, habitual levels, thus leaving individuals vulnerable for relapse. This has been previously suggested by Shestyk and Deldin (Shestyk & Deldin, 2010) who identified a latent neural vulnerability by studying early and late brain potentials to positive or negative self-referential adjectives. Individuals after CBT-induced remission from major depression showed brain electrical responses suggestive of a successfully reduced strategic but not automatic negative self-bias. Our finding of discrepant automatic and strategic self-referential processing prior to MBCT adds to the growing evidence that it is the habitual negative self-bias uniquely contributing to depressive relapse (LeMoult et al., 2017).

Third, our data suggest that without MBCT, automatic negative self-bias persists in people vulnerable to depression. This was evidenced by the absence of changes in dispositional self-compassion and self-criticism in the untreated remitted depressed patients. Moreover, this group did not only *not* show a normalisation of their physiological response pattern but upon the second exposure to the self-compassion meditation, they appeared to experience a more adverse reaction as indicated by significantly increased skin conductance responses from pre-to-post intervention phase. These findings support that directing compassion to the self is challenging for individuals with depression (Gilbert et al., 2014; Rockliff et al., 2008) and support our conclusion that aberrant psychophysiological responses to a self-compassion

1 meditation are indicators of a persistent negative self-bias and reduced automatic
2 positive self-representation.

3

4 **Implications**

5 Our results have important theoretical and clinical implications. Differential
6 psychophysiological responses to a self-compassion meditation in line with MBCT-
7 treatment status and the ability to tap into automatic self-referential processing suggest
8 that our paradigm may lend itself for studying biomarkers of vulnerabilities for
9 recurrent depression and successful treatment response. If replicated in future research,
10 our paradigm may provide an-easy-to administer and cost-effective alternative to other
11 more expensive or labour-intensive neuroscience approaches. Our paradigm may also
12 help understand the time course of functional changes associated with symptom
13 reduction and treatment. Whereas a one-off-self-compassion meditation appeared to
14 transiently induce a more positive self at strategic, top-down control level but no
15 significant reduction in negative self at both self-report and physiological arousal level,
16 our MBCT-related changes in comparison to a no-treatment control suggest an
17 emerging transition towards a more automatic, habitual positive self-referential
18 processing. Of interest was that we found the MBCT-related physiological changes to
19 be associated with change in dispositional self and depressive symptom reduction.
20 Positioning our findings within suggested brain plasticity processes associated with
21 mindfulness meditation (Tang et al., 2015), our effects may represent short-to-medium
22 term plasticity where bottom up habitual processing start to emerge in a more stable
23 pattern that now needs to be maintained by regular practice which should activate these
24 networks and thus lead to long-term functional plasticity (Bullmore & Sporns, 2009)
25 as observed in long-term meditators (Tang et al., 2015).

1

2 **Limitations and future directions**

3 Our study has some limitations. First, although our experimental results were
 4 significantly associated with changes in validated psychometric instruments to assess
 5 dispositional self-compassion and self-criticism, we have not yet cross-validated our
 6 paradigm with other typically applied measures for assessing negative self-bias such as
 7 self-referential tasks (Markus, 1977) or neural network analyses (Bullmore & Sporns,
 8 2009). Future studies should therefore use an array of different measures and paradigms
 9 that have been shown to tap into automatic and strategic self-referential processing. In
 10 particular, to support our suggestion that we have identified a potential biomarker for a
 11 latent vulnerability in recurrent depression, it would be helpful to study the underlying
 12 neural correlates of our paradigm. This would allow us to compare them with the so-
 13 far identified neuro-signatures of self-referential processing associated with depression
 14 and its treatment and confirm if our markers lend themselves as an easy-to-administer
 15 proxy for brain plasticity.

16 Second, this study was conducted in a real-world clinical setting, making our
 17 findings susceptible to sampling bias. It should be noted that our sample was
 18 descriptively unbalanced on depressive symptoms and the inadequate self subscale of
 19 the FSCRS at baseline. When controlling for these confounds, the main treatment
 20 related effects remain qualitatively unchanged (see supplementary results). Moreover,
 21 the core focus of this study was not to establish the effectiveness of MBCT, but to
 22 explore potential mechanisms of MBCT-related changes.

23 Third, the study did not use an active treatment control group preventing us
 24 from directly testing our claim that MBCT may be uniquely addressing automatic,
 25 habitual self-referential processing in depression. Future research might address this by

1 using an active control group like CBT or more MBCT-specific comparisons such as
2 relaxation training or pseudo-meditations (Noone & Hogan, 2018).

3 Fourth, this study did not include follow-up data which would have allowed to
4 examine whether changes in strategic and automatic self-bias as identified in our study
5 predict reduced relapse rates and wellbeing at one- or two-year follow- up. Future
6 studies should therefore include follow-ups for a better understanding of long-term,
7 adaptive functional and structural plasticity associated with successful relapse
8 prevention for depression and with the study of treatment-related effects.

9

10 **Conclusion**

11 Taken together, our study suggests that MBCT might lend itself particularly well to
12 address automatic self-biases (as indicated by psychophysiological responses to a self-
13 compassion meditation) and confirms recent theoretical consideration whereby changes
14 in self-compassion might be a mechanism of change within MBCT (Holzel et al., 2011).
15 This is an important finding in addressing latent vulnerabilities for depression and
16 finding suitable biomarkers for successful treatment. Future research should investigate
17 if these physiological changes persist and if they predict lower relapse rates.

18

1 **Data Transparency and Availability**

2 The data of this study can be downloaded on the Open Science Framework at [URL to
3 be inserted after acceptance]. All materials, processing and analysis scripts are available
4 from the authors upon reasonable request.

5

6 **Disclosures**

7 W.K. is the director of the Oxford Mindfulness Centre. W.K. receives payment for
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15

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1 **Supplementary Materials**

2 A biobehavioural approach to understand how mindfulness-based cognitive therapy

3 reduces dispositional negative self-bias

4 Kirschner et. al

5

Supplementary Methods

Participant Flow

Supplementary Figure S1. Participant flow diagram. *Note:* Reasons for exclusion of physiological dataset were poor data quality. In addition, one questionnaire pack was missing from participant of the control group.

Measures

Visual Prompts For The Visual Analogue Scales Used In The Manipulation Checks

1

2 **Supplementary Figure S2.** Figure S2 depicts the visual analogue prompts used to
 3 assess the effectiveness of the self-compassion manipulation on participants' state self-
 4 compassion and self-criticism.

5

6 **Supplementary Results**

7 **MBCT Related Changes In Depression Symptoms And Dispositional Self- 8 Compassion And Self-Criticism**

9 Changes in self-compassion, self-criticism and self-reported depression scores are
 10 depicted in main Figure 2 A (remitted depressed MBCT) and main Figure 2 B (remitted
 11 depressed control). A significant increase in self-compassion could be found post
 12 MBCT, $t(24) = 2.35, p = .028, 95\% \text{ CI } [.21, 3.33], d = .47$. In line with these findings,
 13 there was a significant increase on the reassuring self subscale of the FSCRS post
 14 MBCT, $t(23) = 4.21, p < .001, 95\% \text{ CI } [2.43, 7.14], d = .86$. Moreover, MBCT led to

1 a significant decrease in self-criticism. This was quantified by significant reductions on
2 the inadequate self, $t(23) = 4.54, p < .001, 95\% \text{ CI } [-9.88, -3.69], d = .93$, and on the
3 hated self, $t(23) = 2.55, p = .018, 95\% \text{ CI } [-4.08, -.42], d = .52$, subscales of the FSCRS.
4 Finally, there was a significant decrease self-reported depressive system scores post
5 MBCT, $t(24) = 5.55, p < .001, 95\% \text{ CI } [-11.41, -5.23], d = 1.11$. In contrast, no changes
6 in self-compassion, self-criticism, or self-reported depression scores have been found
7 for the remitted depressed control group between the first and second assessment, all p
8 $> .05$.

9

10 **MBCT-Related Changes In Self-Reported State Self-Compassion And Self-** 11 **Criticism In Response To LKM-S**

12 *Changes In Self-Compassion*

13 The scores for the state self-compassion ratings are depicted in Figure S3 A&B. There
14 was a significant Treatment X Group interaction, $F(1, 48) = 7.63, p = .008, \eta^2_p = .14$.
15 Follow up analyses revealed, that both groups demonstrated significant increases in
16 state self-compassion following the self-compassion induction at the first and second
17 assessment (*MBCT Group* T1: $F(1,24) = 6.76, p = .016, \eta^2_p = .22; 95\% \text{ CI } [1.38, 12.05];$
18 T2: $F(1,24) = 7.16, p = .013, \eta^2_p = .23; 95\% \text{ CI } [.93, 7.23];$ *Control Group* T1: $F(1,24)$
19 $= 5.60, p = .026, \eta^2_p = .19, 95\% \text{ CI } [.77, 11.31];$ T2: $F(1,24) = 15.96, p = .001, \eta^2_p =$
20 $.39; 95\% \text{ CI } [5.09, 15.98]$). Interestingly, between subject follow-up analyses showed
21 that there was no difference between the groups in their state levels of self-compassion
22 before the self-compassion manipulation at the first assessment ($F(1,48) = .38, p = .541,$
23 $\eta^2_p > .01; 95\% \text{ CI } [-15.36, 8.17]$). However, a significant difference in state levels of
24 self-compassion before the self-compassion manipulation was found at the second
25 assessment, with higher scores in the remitted depressed MBCT group ($F(1,48) = 5.29,$

1 $p = .026$, $\eta^2_p = .10$; 95% CI [1.69, 25.07]). This result indicates that post-treatment, the
 2 MBCT group showed an elevation in self-reported state self-compassion before the
 3 self-compassion induction.

4

5

6 **Supplementary Figure S3.** MBCT-related changes in self-reported state self-
 7 compassion and self-criticism. Error bars = $\pm 1SE$

8

Changes In State Self-Criticism

Figure S3 C&D shows the state self-criticism ratings for both groups. The Time (pre/post induction) X Treatment (pre/ post MBCT) X Group (remitted depressed MBCT, remitted depressed control) ANOVA revealed a main of treatment with lower self-criticism scores post Treatment, $F(1, 48) = 6.98, p = .011, \eta^2_p = .13$. In addition, there was a trend for a Treatment X Group interaction, $F(1, 48) = 3.62, p = .063, \eta^2_p = .07$. Follow up analyses revealed that post MBCT the MBCT group showed decreased self-criticism scores before the self-compassion induction as compared to pre MBCT, $F(1, 24) = 5.11, p = .033, \eta^2_p = .18, 95\% \text{ CI } [-25.33, -1.15]$. No other significant effects emerged for self-reported state self-criticism change (all $p = .05$).

Changes In Physiological Arousal And Parasympathetic Activation

Skin Conductance Level Effects

The first panel of main Figure 4 shows the pattern of change in skin conductance level for the two groups. The focus (others vs. self) x Time (first vs. second assessment) x group ANOVA revealed a significant Time x Group interaction, $F(1,42) = 10.33, p = .003, \eta^2_p = .20$. Follow-up analyses revealed that the remitted depressed control group demonstrated significantly higher SCL in response to the self-compassion exercise at the second as compared to the first testing session, $F(1, 21) = 6.25, p = .021, \eta^2_p = .23, 95\% \text{ CI } [.02, .19]$. In contrast, there was a decrease in SCL in response to the self-compassion intervention after the MBCT course as compared to before, $F(1, 21) = 5.15, p = .034, \eta^2_p = .19, 95\% \text{ CI } [-.29, -.013]$. An examination of the between-subject follow-up effects revealed no group differences at the first assessment $F(1, 43) = 1.10, p = .300, \eta^2_p = .04, 95\% \text{ CI } [-.058, .18]$. However, there was a group differences at the second assessment, $F(1, 45) = 4.99, p = .030, \eta^2_p = .09, 95\% \text{ CI } [-.30, -.01]$, with lower

1 SCL in response to the self-compassion manipulation in the MBCT group. In addition,
2 there was a main effect of focus, $F(1,42) = 55.77, p < .001, \eta^2_p = .57$, indicating general
3 lower SCL levels when focusing on the self during the exercise. No other effects
4 reached significance.

5 ***Heart Rate Effects.***

6 Pattern of change in heart rate for the two groups at the first and second assessment are
7 depicted in the second panel of main Figure 4. The three-way ANOVA indicated a
8 significant Time X Group interaction, $F(1,43) = 9.35, p = .004, \eta^2_p = .179$. The heart
9 rate results suggest that the remitted depressed MBCT group had a decrease in heart
10 rate throughout the self-compassion manipulation *post-treatment* as compared to *pre-*
11 *treatment* ($F(1,20) = 9.24, p = .006, \eta^2_p = .32, 95\% \text{ CI } [-2.59, -.48]$), whereas the
12 remitted depressed control group demonstrated no change in their heart rate responses
13 to the self-compassion manipulation, $F(1,23) < 1, p = .413, \eta^2_p = .02, 95\% \text{ CI } [-.43,$
14 $1.00]$. When examining the between subject follow up effects, no differences emerged
15 at the first assessment, $F(1,44) = 2.35, p = .132, \eta^2_p = .05, 95\% \text{ CI } [-.23, 1.72]$,
16 indicating that there was no group differences in heart rate responses to the self-
17 compassion manipulation before the treatment. After MBCT, relative to the remitted
18 depressed control group, the remitted depressed MBCT group demonstrated a tendency
19 towards a decreased in heart rate in response to the self-compassion manipulation,
20 $F(1,43) = 2.99, p = .091, \eta^2_p = .07, 95\% \text{ CI } [-2.41, .18]$. No other main effects reached
21 significance.

22 ***Heart Rate Variability Effects***

23 The three-way ANOVA yielded a significant Time X Group interaction, $F(1,43) =$
24 $12.23, p = .001, \eta^2_p = .22$. Follow-up analyses revealed that the remitted depressed
25 MBCT group on average demonstrated higher heart rate variability in response to the

self-compassion manipulation after they completed the MBCT course as compared to their responses before the course, $F(1,20) = 12.11$, $p = .002$, $\eta^2_p = .38$, 95% CI [11.58, 46.25] (see main Figure 4 C). In contrast, no differences in heart rate variability responses to the self-compassion induction between the first and second assessment was found for the remitted depressed control group, $F(1,23) = 1.34$, $p = .251$, $\eta^2_p = .06$, 95% CI [-20.17, 5.53] (see main Figure 5 C). Critically, further exploration showed that the two groups did not differ in their heart rate variability responses to the self-compassion manipulation at the first testing session, $F(1, 44) = 1.86$, $p = .180$, $\eta^2_p = .04$, 95% CI [-5.58, 28.88], but at the second testing session, $F(1, 44) = 47.84$, $p < .001$, $\eta^2_p = .53$, 95% CI [33.41, 60.91], with higher heart rate variability demonstrated by the MBCT group.

Associations Between Psychophysiological Change, Change In Dispositional Self And Symptom Reduction.

Associations between treatment-related physiological change, change in dispositional self (e.g. changes in trait self-compassion and self-criticism) and symptom reduction (e.g. changes in BDI-scores) are depicted in table S1.

1 Supplementary Table S1.

2 *Zero order correlations*

Variables	1	2	3	4	5	6	7	8	9	10	11	12
1. MBCT	1											
2. BDI	-.468**	1										
3. SCS	.103	-.341*	1									
4. FSCRS - IS	-.452**	.606**	-.542**	1								
5. FSCRS - HS	-.310*	.604**	-.476**	.709**	1							
6. FSCRS - RS	.398**	-.525**	.629**	-.582**	-.613**	1						
7. dSCL - other	-.326*	.414**	-.152	.247	.065	-.323*	1					
8. dSCL - self	-.430**	.437**	-.08	.233	.145	-.320*	.865**	1				
9. dHR - other	-.443**	.150	-.171	.241	.11	-.306*	.174	.270	1			
10. dHR - self	-.472**	.309*	-.099	.379*	.313*	-.194	-.008	.244	.716**	1		
11. dHRV - other	.401**	.016	.088	-.343*	-.024	.138	.020	.032	-.400**	-.248	1	
12. dHRV - self	.541**	-.149	.186	-.347*	-.201	.268	-.134	-.154	-.209	-.362*	.589**	1

4 *Note.* ** Correlation is significant at the .01 level (2-tailed); * Correlation is significant at the
5 .05 level (2-tailed); residualized gain scores were used as quantification of treatment related
6 changes for the questionnaire data; difference waves as indicator of MBCT-related change in
7 physiological responses (e.g. post change score – pre-change score) were used as quantification
8 of physiological changes in response to the self-compassion exercise. BDI = Beck Depression
9 Inventory; SCS = Self-Compassion Scale; FSCRS = Forms of Self-Criticizing/Attacking &
10 Self-Reassuring Scale; IS = Inadequate Self; HS = Hated Self; RS = Reassuring Self; dSCL –
11 other / self = treatment related changes in skin conductance level (SCL) during other- / self-
12 focus; dHR – other / self = treatment related changes in heart rate (HR) during other- / self-
13 focus; dHRV – other / self = treatment related changes in heart rate variability (HRV) during
14 other- / self-focus

16 **Reanalysis Of Main Treatment Related Group Effects While Controlling for**
17 **Baseline Differences in Depressive Symptoms and Inadequate Self (FSCRS)**

18 To control for a potential sampling bias, we included depressive symptoms (BDI) and
19 the inadequate self subscale of the FSCRS at baseline as continuous covariates in the
20 ANOVA's investigating treatment related group effects. Here, the MBCT specific
21 elevation in self-reported state self-compassion before the self-compassion induction
22 remained significant ($F(1, 47) = 11.84, p = .001$). Similar, all group effects related to
23 changes in physiological arousal and parasympathetic activation remained significant

PSYCHOPHYSIOLOGY OF REDUCED NEGATIVE SELF-BIAS

- 1 (SCL: $F(1, 41) = 6.8, p = .013$; HR: $F(1, 43) = 7.16, p = .011$; HRV: $F(1, 43) = 12.95,$
- 2 $p > .001$; HRV focus on the self: $F(1, 47) = 13.09, p > .001$).