Compassion in depression

Mindfulness-based compassionate living for recurrent depression

Rhoda Schuling

Colophon

For reasons of consistency within this thesis, some terms have been standardised throughout the text. As a consequence, the text may differ in this respect from the articles that have been published.

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Kintsugi (金継ぎ, "golden joinery") is the Japanese art of repairing broken pottery by mending the areas of breakage with lacquer dusted or mixed with powdered gold, silver, or platinum. As a philosophy, it treats breakage and repair as part of the history of an object, rather than something to disguise.

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It's a fragile thing,
this life we lead,
If I think too much,
I can get over-
whelmed by the grace,
by which we live
our lives
with death over our shoulders

Pearl Jam - Sirens

Contents

1

General introduction

Major depressive disorder

Major depressive disorder (MDD) has prevailed as a leading cause of non-fatal health loss for nearly three decades according to the World Health Organization and is predicted to be the leading cause of disability worldwide by 2030 (Vos, Abajobir et al. 2017). It is a common psychiatric disorder, affecting about 30.3 million people each year in Europe alone (Wittchen, Jacobi et al. 2011). Approximately one out of five adults will suffer from one or more depressive episodes during their lifetime.

MDD, or depression in short, is characterized by persistent symptoms, of which the main two are sad mood and decreased interest in normally enjoyable activities. Other symptoms of depression include insomnia or hypersomnia, feelings of excessive guilt or worthlessness, reduced or increased appetite or changes in weight, fatigue or loss of energy, psychomotor agitation or retardation, concentration problems, and recurrent thoughts about death or suicide. To diagnose MDD, one of the two core symptoms must be present, and a total number of five symptoms, for a period of two weeks or longer (American Psychiatric Association DSM-5 2013).

Adding to the burden, depression is also characterized by high relapse rates (Mueller, Leon et al. 1999): about 75% of all patients experience more than one episode during their lifetime (Boland, Keller et al. 2002). In a study examining up to 15 years of prospective follow-up data on the course of MDD, Hardeveld et al. (2010) found that a cumulative proportion of 85% of the 380 recovered subjects experienced a recurrence, versus only 35% in the general population. The number of depressive episodes has been shown to be a consistent predictor: the risk of recurrence rises with each new episode. Presence of subclinical residual symptoms, i.e. depressive symptoms that do not fulfil the diagnosis of major depression, appeared to be the strongest predictor however. Therefore, in addition to acute treatment, further treatment of residual symptoms is highly important (Hardeveld, Spijker et al. 2010).

Available treatment options

Currently, both psychological and pharmacological treatments are relatively well established as having at least moderate efficacy for the treatment of acute major depression (Bauer, Whybrow et al. 2002, Undurraga and Baldessarini 2012, Baldessarini, Lau et al. 2015). Examples of psychological treatments are cognitive behaviour therapy (CBT), interpersonal psychotherapy, problem-solving therapy, non-directive supportive therapy, behavioural activation therapy and Acceptance

and Commitment Therapy (ACT), which have been found more effective than treatment-as-usual or placebo in a variety of mental health disorders, including depression (Schene, Sabbe et al. 2008, A-tjak, Davis et al. 2015). The differences between different psychological treatments are small (Cuijpers, Andersson et al. 2011). An equally common course of action for moderately to severely depressed patients is a combination of psychological treatment and pharmacotherapy (Cuijpers, Noma et al. 2020). In two separate studies, Cuijpers et al. (Cuijpers, Dekker et al. 2009, Cuijpers, Van Straten et al. 2009) showed that this combination is more effective than both psychotherapy or pharmacotherapy alone.

Considering the high rates of relapse and recurrence it is recommended to continue antidepressant medication for at least 6–12 months following apparent clinical remission of acute depression, and often longer for patients who have experienced multiple recurrences (Baldessarini 2013).

Despite these therapeutic options, in their review on unipolar depression, Forte et al. (2015) found that during an average follow-up period of 12 to 13 years depressive patients reported being ill nearly 50% of the time. Taking into account the presence of substantial residual symptoms in depressive patients who have been successfully treated, there is a clear need for improving the treatment of depression and prevention of relapse. Research recommendations include further exploration of specific, improved individual and combination therapies (pharmacological and psychological), as well as identification of clinical predictors of treatment responses in MDD (Sim, Lau et al. 2016).

Mindfulness-based cognitive therapy

To address the need for new psychological interventions targeting relapse prevention, Segal, Williams and Teasdale developed Mindfulness-Based Cognitive Therapy (MBCT) (2012). MBCT is an adaptation of Mindfulness-Based Stress Reduction (MBSR; (Kabat-Zinn 1990), developed in the late 1970s for patients with chronic pain or medically unexplained symptoms. A frequently used definition of mindfulness is "paying attention in a particular way: on purpose, in the present moment, and non-judgmentally" (Kabat-Zinn 1994) (p.4). MBCT is a group-based intervention combining mindfulness meditation techniques with elements of CBT. In contrast to CBT, that is aimed at identifying and examining the content of dysfunctional automatic thoughts, MBCT aims to cultivate decentering, i.e. experiencing thoughts as an activity of the mind and focusing on the process of thinking rather than its content. Implicitly, an accepting and friendly attitude towards this process is encouraged.

Since its introduction, evidence for the effectiveness of MBCT has accumulated. Nowadays, MBCT is included in multidisciplinary guidelines as a strategy to prevent relapse in remitted depressed patients (NICE Depression 2009) (Spijker, Bockting et al. 2013). Kuyken et al. (2016) conducted the most recent meta-analysis on the effectiveness of MBCT as a relapse prevention program, re-analysing individual data of 1258 patients with three or more previous depressive episodes. He concluded that MBCT is effective in reducing risk of relapse by 31% in a period of 60 weeks and is at least as effective as antidepressant medication. In a recent face-to-face comparison between MBCT and CBT both interventions also appeared to be equally effective in relapse prevention. MBCT and CBT helped participants develop similar metacognitive skills for the regulation of distressing thoughts and emotions (Farb, Anderson et al. 2018).

In a meta-analysis of Strauss et al. (2014), MBCT appeared to also significantly reduce depressive symptoms in patients with a current depressive disorder compared with inactive control conditions. MBCT was shown to be as effective as other active treatments, including CBT. However, residual symptoms seem to remain considerable even after MBCT (Piet and Hougaard 2011). Thus, the results seem to leave room for improvement.

Sequential treatment

An alternative to lengthening an initially-effective treatment, such as is done in the case of ADM, is offering different evidence-based treatments in a sequence to maximize effectiveness. Sequential treatment designs are common in both pharmacological treatments of depression (Popova, Daly et al. 2019), as well as the combination of pharmacotherapy and psychological treatment (Cuijpers, Van Straten et al. 2009), but could equally well be applied in combining different psychological treatments. Generally, sequential treatment seems to be more effective than single treatment (Cuijpers, Dekker et al. 2009).

Targeting depressive symptoms with sequential treatments has additional advantages: it allows allocation of treatment options according to stages of development of the illness and not simply based on disease classification. The model is thus more in line with the chronicity of mood disorders compared to the standard randomized controlled trial, which is based on the acute disease model (Fava and Tomba 2010).

The offering of two different psychological interventions may be a fruitful approach, as many patients do not want to take medication (Steidtmann, Manber et al. 2012) or suffer from adverse effects of medication (Bet, Hugtenburg et al.

2013). As MBCT for recurrent depression appears to be effective but also leaves room for improvement, a worthwhile approach may be to gain insight into its working mechanisms and capitalize on operative ingredients in a second, sequential treatment.

Working mechanisms of MBCT

Reduction of rumination is one of the most established working mechanisms of MBCT. A meta-analysis by Van der Velden et al. (2015) including 23 studies on MBCT reported that alterations in rumination, worry and meta-awareness were associated with, predicted or mediated treatment outcome. Besides this, mindfulness and compassion were also found to mediate treatment outcome (Kuyken, Watkins et al. 2010). Kuyken et al. found a decoupling of the relationship between cognitive reactivity and depressive symptoms after MBCT, which was associated with the cultivation of self-compassion, i.e. normally cognitive reactivity predicts depressive relapse, but in participants who developed self-compassion this was no longer the case. Gilbert and Proctor (2006) found that one of the possible underlying mechanisms for the chronic and recurrent nature of depressive symptoms is low self-esteem or self-denigration (Gilbert and Procter 2006). These findings are in line with research by Beck (Beck 1967, 1979), indicating that recurrently depressed patients suffer from severely self-denigrating core beliefs. It may be that the relation between cognitive reactivity and relapse is connected to the triggering of such self-denigrating core beliefs, and that compassion mitigates the effect of this triggering, or even prevents it. Being able to adopt a caring attitude towards the self might then be a skill that could help reduce the undermining mechanisms of self-criticism and hence reduce the vulnerability to recurrence or persistence of depressive symptoms. As self-compassion is taught mostly implicitly in MBCT (Segal, Williams et al. 2012), explicitly cultivating self-compassion may offer a complementary contribution to reducing rumination and increasing mindfulness skills for individuals who are prone to depressive relapse or recurrence.

Improving outcome - a compassion approach?

Contemplative literature has already emphasized for a long time the importance of developing mindfulness and (self)compassion together, as the proverbial 'two wings of the same bird'. Feldman and Kuyken (2019) (p.180) emphasize that the key insight is that mindfulness reminds us to return to the actuality of the present with an attitude of befriending, to establish a body of stillness and calm where we can find the strength to meet the difficult with balance and compassion. Mindfulness is defined as awareness of the present moment, intentional and non-judgmental (Kabat-Zinn 1990). Compassion is defined as the capacity to open to the reality of suffering and to aspire to its healing, presenting a multi-textured response to pain, sorrow and anguish including kindness, empathy, generosity and acceptance (Feldman and Kuyken 2011). In line with this definition, Strauss et al. conclude in their systematic review of self- and observer-rated measures that compassion consists of five elements: recognizing suffering, understanding the universality of human suffering, feeling for the person suffering, tolerating uncomfortable feelings, and motivation to act/acting to alleviate suffering (Strauss, Taylor et al. 2016). Neff (2003), who developed the Self-Compassion Scale, describes (self)compassion as a combination of a) self-kindness, b) a sense of common humanity and c) mindfulness - holding painful thoughts and feelings in balanced awareness rather than identifying with them.

Compassion Interventions

In recent years, there has been a surge in psychological interventions developed to explicitly target the cultivation of (self)compassion. A recent meta-analysis on compassion-based interventions (k=21, 1285 participants) identified at least eight different compassion-based interventions, the most important of which are CFT, MSC and Cultivating Compassion Training (Kirby, Tellegen et al. 2017). Compassion-Focused Therapy (CFT) (Gilbert 2009) was developed for people with chronic mental health problems who experience high self-criticism and shame and who do not respond well to conventional therapies. CFT is grounded in a theoretical model about three affective systems that can be active at any given moment: threat, drive and soothing system. Enhancing the soothing system, also known as the parasympathetic rest-and-digest nervous system, may help us balance stressful thoughts and emotions that typically arise when the threat system is activated. Techniques such as (self)compassionate meditation, imagery, letter writing and dialogic role-play are part of CFT (Gilbert 2009).
Mindful Self-Compassion therapy (MSC) is an 8-week group programme similar in format to MBCT developed by Kristin Neff and Christopher Germer (2013) for the general public but also some clinical populations. MSC contains core meditations (e.g., affectionate breathing), other meditations (e.g., compassionate body scan), and informal self-compassion practices (e.g., self-compassion break).

Compassion Cultivation Training was explicitly designed as a general training program to enhance compassion in non-clinical populations and has a fairly similar format to MBCT, including eight weeks of two-hour sessions (Jazaieri, Jinpa et al. 2013). Every session contains a mix of psycho-education, group inquiry and formal meditation, whereby the latter is derived from Tibetan Buddhist contemplative practices and some of the experiential exercises from Western psychology. CCT is taught as an entirely secular approach to enhancing compassion though, just as MSC and CFT, and follows a six-step programme that focuses on compassion for self, compassion to others and compassion from others.

Although still in its infancy, the evidence base for the efficacy of compassion programmes is growing. A meta-analysis on compassion-based interventions in non-clinical populations including 21 RCTs showed moderate effect sizes for improvements of compassion, self-compassion, mindfulness skills, depression and well-being (Kirby, Tellegen et al. 2015). In 2019 however, Ferrari et al. found in their meta-analysis that (self)compassion interventions led to a significant improvement (Ferrari, Hunt et al. 2019). In the overall population, a hedge's g of 0.66 was found for depression and 0.75 for (self)compassion. In the clinical subpopulation a hedge's g of 0.82 was found for self-compassion. They also found that the results of compassion interventions were stronger for group-based than for individual delivery methods.
Despite these promising findings, it should be noted that the large diversity in intervention types leads to heterogeneity in the reviews (Ferrari, Hunt et al. 2019). Additionally, results largely stem from RCTs with small (underpowered) sample sizes in non-clinical populations RCTs (Kirby, Tellegen et al. 2017).

Mindfulness-based Compassionate Living

In 2012, Van den Brink and Koster developed Mindfulness-Based Compassionate Living (MBCL) (van den Brink and Koster 2015). In line with the conclusion mentioned above, that explicitly cultivating self-compassion may offer a complementary contribution to the treatment of recurrent depression, the developers found that the 8-week foundation course (i.e. MBCT or MBSR) is too short for many people, particularly for participants with persistent unhealthy or dysfunctional patterns (p.28). So, although it can be used in both clinical and non-clinical settings, it was developed with a clinical population in mind, who find it especially difficult to really take the kinder, gentler attitude to heart in the face of harsh self-criticism and feelings of shame and unworthiness (p.28).

MBCL is a group intervention, consisting of classes up to 12 participants. The format of the MBCL program is similar to MBSR and MBCT, including eight weekly sessions of 2.5 hours, containing a mixture of mindfulness practice, group enquiry and didactic and interactive teaching. However, the content is more actively geared towards the experience of suffering and explicitly focus on developing a kind attitude in the midst of this. Accordingly, the enquiry and didactic teaching have that same focus. The primary practice consists of mildness meditation (Van den Brink and Koster 2015) In this practice, the participant is gradually guided through several steps of developing kindness towards self and others.

Preliminary evidence for MBCL seems promising: a first, uncontrolled pilot study on MBCL in 33 patients with a variety of psychiatric disorders (Bartels-Velthuis, Schroevers et al. 2016) and who had previously attended MBSR or MBCT showed a reduction in depressive symptoms and increases in both mindfulness and self-compassion skills. In addition, Krieger et al. (Krieger, Reber et al. 2019) conducted a randomized controlled trial with a total of 122 self-referred participants with increased levels of self-criticism, who were randomly assigned to care as usual (CAU) or an intervention group (CAU + online MBCL). At post-treatment, the intervention group showed a significant reduction in depressive symptoms and increase in (self)compassion and mindfulness skills compared to the control group, with medium to large effect sizes.

MBCL as a sequential treatment to MBCT

With regards to choosing an intervention to follow MBCT in a sequential treatment regime, MBCL seems the most suitable format to use as it was specifically designed as a follow-up of MBCT and a group-based intervention, which according to the Ferrari study (Ferrari, Hunt et al. 2019) is more effective than individual delivery methods. Perhaps even more importantly, it was designed with a clinical population in mind. The advantage of offering MBCL after MBCT is that participants have already established the capacity to mindfully attend to difficult thoughts and emotions before learning to actively approach them with a (self)compassionate attitude, which may be crucial in clinical, more vulnerable populations. In line with ideas formulated by Segal et al. (2012), the developers of MBCL expected that a foundation in mindfulness is necessary for participants to be able to practice with (self)compassion explicitly. Particularly, an established mindfulness practice might be necessary to cope with the so-called 'backdraft'-effect: a potential resurfacing of overwhelming,

long-suppressed emotions due to increased exposure to them as part of the program. In addition, MBCL closely resembled the MBCT format and was developed in Dutch, making it easily applicable in our treatment centre for a population of recurrently depressed individuals.
In terms of sequential designs, two options are available. One option is to follow a pragmatic approach, offering the second treatment (MBCL) to a population that has already followed the first (MBCT), like in Daly et al. (2018). Ideally, the efficacy of sequential treatment design is tackled by a prospective study offering both treatments in sequence to a population that has received neither before (Popova, Daly et al. 2019). As little was known about MBCL efficacy in patients with recurrent depression at the start of our study, we decided to use the pragmatic approach by offering MBCL to a population that only included patients who had followed MBCT at some point in the past.

Aims and outline of this thesis

The aim of this thesis is to examine the efficacy of MBCL as a follow-up to MBCT in adults suffering from recurrent depression, in a (pragmatic) sequential treatment design. As little was known about the feasibility and acceptability of MBCL in this population, we first conducted a pilot study to co-create a suitable MBCL format and assess preliminary effectiveness in a small sample of recurrently depressed patients who had previously participated in MBCT at our own centre. Next, we conducted an RCT comparing MBCL added to treatment as usual (TAU) to TAU alone in patients with recurrent depression who had participated in MBCT in the past. We were also interested in examining longer-term consolidation of treatment effects. Lastly, we embedded a qualitative study into the RCT, exploring what additional value patients experienced of participating in MBCL after having participated in MBCT.

In sum, this dissertation addresses the following research questions:

- How can MBCL be co-created with recurrently depressed patients who previously participated in MBCT so that it is feasible and acceptable ?
- Is MBCL, as a follow-up after MBCT, efficacious in reducing (residual) depressive symptoms in recurrently depressed adults?
- What is the longer-term consolidation of MBCL's potential effect on depressive symptoms?
- What added value of MBCL after MBCT do patients experience?

This thesis is divided into seven chapters. Following this general introduction, **chapter 2** describes the results of our first study, which aimed to investigate the feasibility and acceptability of the MBCL program as a follow-up to MBCT in patients with recurrent depression. We qualitatively assessed helpful and unhelpful elements of the program, adapted it based on the outcome, and offered it again to the same group. This enabled us to co-create the most suitable format together with the target population. In addition, we examined the preliminary effectiveness of the MBCL in reducing depressive symptoms and worry, as well as in increasing self-compassion and mindfulness skills. **Chapter 3** outlines the trial design and protocol for the RCT we conducted next. In **chapter 4** we describe the results of two studies. Study 1 consisted of the RCT investigating the efficacy of MBCL to reduce depressive symptoms in patients with recurrent depression who had already participated in MBCT (N=122). In one condition, patients received MBCL in addition to TAU and in the other they received only TAU. As secondary aims we wanted to examine possible mediators and moderators of treatment outcome. Post-treatment assessments took place at four months after baseline. In study 2, we examined the consolidation of treatment outcome over a 6-months follow-up period after completion of treatment in both the patients who were initially assigned to MBCL and those randomized to TAU only, who were offered to participate in MBCL after the control period. Lastly, our aim was to gain insight into participants' experiences with MBCL, in particular whether there was additional value in participating in MBCL after having participated in MBCT. To this end, we conducted qualitative interviews with a subsample of the RCT population (n= 23), of which the results are described in **chapter 5**. A summary and general discussion of results is presented in **chapter 6**. A summary in Dutch is given in **chapter 7**.

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2

The co-creation and feasibility of a compassion training as a follow-up to Mindfulness Based Cognitive Therapy in patients with recurrent depression

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Abstract

The aim of this study was to assess the feasibility, acceptability and preliminary effectiveness of Mindfulness Based Compassionate Living (MBCL) as a follow-up intervention to Mindfulness Based Cognitive Therapy in adults with recurrent depression. We conducted an uncontrolled study in 17 patients with recurrent depression, in two successive groups. The first group contained novices to compassion training (N=14), in the second group ten of these participated again, in addition to three new participants (N=13). The overall group contained 15 females and 2 males, aged between 37 and 71. The MBCL program was qualitatively evaluated using post-intervention focus group interviews in both groups. In addition, self-report questionnaires assessing depressive symptoms, worry and both self-compassion and mindfulness skills were administered before and after MBCL. No patients dropped out of the intervention. Average attendance was 7.52 (SD 0.73) out of 8 sessions. Helpful elements were: theory on the emotion regulation systems, practicing self-compassion explicitly, and embodiment of a compassionate attitude by the teachers. Unhelpful elements were the lack of a clear structure, lack of time to practice compassion for self, and the occurrence of the so-called back draft effect. We adapted the program in accordance with the feedback of the participants. Preliminary results showed a reduction in depressive symptoms in the second group, but not in the first group, and an increase in self-compassion in both groups. Worry and overall mindfulness did not change. MBCL appears to be feasible and acceptable for patients suffering from recurrent depressive symptoms who previously participated in MBCT. Selection bias may have been a factor as only experienced and motivated participants were used; this, however, suited our intention to co-create MBCL in close collaboration with knowledgeable users. Examination of the effectiveness of MBCL in a sufficiently powered randomized controlled trial is needed.

Introduction

Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders. It is characterized by high relapse rates (Mueller et al., 1999; Solomon et al., 2000), partly due to persistence of residual symptoms after remission (Hardeveld, Spijker, De Graaf, Nolen, and Beekman, 2010). Given the increasing risk of relapse after each successive episode, prevention of relapse is as important as acute treatment (Hardeveld et al., 2010). To address the need for psychological interventions targeting relapse prevention, Segal, Williams and Teasdale developed Mindfulness-Based Cognitive Therapy (MBCT; 2000). A meta-analysis (Kuyken et al., 2016) showed that MBCT for patients with recurrent depression in remission resulted in a reduction of the risk of a relapse/recurrence of 31%. A growing number of studies indicate that MBCT may also be effective in decreasing current depression (Strauss, Cavanagh, Oliver, and Pettman, 2014). Van Aalderen et al. (2015) reported effectiveness of MBCT to be comparable in both remitted and currently depressed patients, substantiating effectiveness and acceptability of MBCT as acute treatment of depression.
Though these results are encouraging, even after MBCT room for improvement remains considerable (Piet and Hougaard, 2011) and mild levels of depression (average BDI score of 10) remain present in many patients (Van Aalderen et al., 2015). It is therefore necessary to explore ways to further improve outcomes for recurrently depressed patients. A closer look at working mechanisms of MBCT yields insight in how to proceed: Kuyken et al. (2010) showed that the effect of MBCT on relapse/recurrence was mediated by increased self-compassion and mindfulness. Both significantly predicted depression levels 13 months after treatment: patients who reported an increase in mindfulness skills or self-compassion had lower rates of depressive symptoms. It seems one of the evident options to explore in improving outcome for recurrently depressed adults is self-compassion.

Mindfulness-Based Compassionate Living (MBCL) was designed as a follow-up intervention for patients who have already attended MBCT or MBSR (Van den Brink and Koster, 2012; Van den Brink and Koster, 2015). Van den Brink and Koster (2015) identified two components of compassion: 1) Developing the willingness and courage to turn towards suffering both in oneself and others rather than turning away, and 2) Dedicating oneself to acquiring the wisdom and skills of engaging in the appropriate actions for alleviation and prevention of suffering (p. Xvii). Amongst others, MBCL is inspired by Compassion Focused Therapy (Gilbert, 2009), with its focus on use in clinical settings, and by Neff and Germer's Mindful Self Compassion program for non-clinical populations (2013).

Preliminary results of these programs indicated people may benefit from a training in self-compassion (Gilbert, 2009; Gilbert and Procter, 2006; Neff and Germer, 2013). Lack of self-Compassion was both linked to negative self-esteem and self-criticism, as well as the maintenance and recurrence of depression (Gilbert, 2009; Neff, 2003). According to Neff's (2013) trial with the Mindful Self-compassion program, significantly larger increases in self-compassion, mindfulness and wellbeing in intervention participants were found compared to a control group. In a recent meta-analysis, compassion was indicated as an important explanatory variable in understanding mental health and resilience (MacBeth and Gumley, 2012).

MBCL is a group-based intervention which consists of eight 2,5 hour sessions once every fortnight and a silent day. It uses a format similar to MBCT, combining central practices, inquiry and didactic teaching. Theory focuses on the following aspects: 1) (dis)balance of emotion regulation systems (*threat*, *hunt* and *rest and digest* system), 2) instinctive stress reactions (fight-flight-freeze) and more nourishing stress responses (tend-befriend), 3) three modes of operation (threat mode, competitive mode and compassion mode), with emphasis on the inner critic or bully as a particular manifestation of the threat mode or system, 4) the back draft effect (how compassion practice to self and others may give space for old pain to resurface, causing the participant to feel overwhelmed and, often, discouraged), 5) relational qualities of compassion, 6) processes of over-and de-identification from a compassionate perspective and finally 7) common humanity and the four life companions (kindness, compassion, joy and equanimity). Theory in each session is supported by accompanying practices which often include imagination, i.e. imagining a safe haven for oneself or imagining a compassionate companion. The Metta or befriending practice is gradually expanded over the course of the sessions: in the first four sessions, emphasis is on self-compassion, after which the compassion practice expands to include compassion for other people.

The importance of self-compassion within the MBCT program has also been underscored by Segal, Williams and Teasdale (2012), who stated: "one of the most important things people learn from an MBCT program is kindness and self-compassion. We regard this as fundamental" (p.137). However, it may be the case that particularly patients with recurrent depression need more explicit instructions and additional support to develop a compassionate attitude to both self and others, as they are often highly self-critical and plagued by feelings of shame, guilt and inferiority (Gilbert et al., 2012; Gilbert et al., 2008; Gilbert and Procter, 2006). In contrast to the more implicit teaching of compassion in MBCT, cultivating compassion is the primary focus of MBCL. Throughout the entire curriculum, the invitation is to practice kindness and compassion to self and others in the midst of suffering. This is in fact one of the main differences between MBCL and MBCT. MBCL deliberately gears towards focus on unpleasant experiences. Investigation of feasibility is therefore warranted, which in addition to this exposure to the difficult might shed light on the influence of the more varied practices offered in MBCL and the fact that many MBCL practices make use of participants' imaginative ability.

To ensure participants have had opportunity to practice observing and de-identification with thoughts and emotions, before attending to the more difficult ones, MBCL has been designed as a follow-up to MBCT. Practices such as the 'safe haven' and 'compassionate companion' are specifically designed as a further support for this. So far, the MBCL program has been evaluated in a (small) heterogeneous clinical sample (Bartels-Velthuis et al., 2016), but not in a recurrently depressed population specifically.

The aim of our study was to investigate the feasibility and acceptability of the MBCL program as a follow-up intervention after MBCT in patients with recurrent depression, by qualitatively assessing helpful and unhelpful elements of the program. Furthermore, we examined the preliminary effectiveness of MBCL to reduce depressive symptoms as well as worry, a common type of perseverative negative thinking in patients suffering from recurrent depression which often induces or maintains depressive symptoms. We also examined preliminary effectiveness on self-compassion and mindfulness skills.

Method

Participants

Regarding who should participate in co-creation of technology services, Franke et al. (2006) claimed that users who are able to co-create should have cutting edge knowledge within the area; thus, only consumers who are leading users should be involved. We therefore sought highly motivated patients with recurrent depression, who had previously participated in MBCT, who were willing to invest time and effort in attending and evaluating the MBCL program and able to offer an informed opinion. We recruited possible participants at the regular reunion meetings offered at the Radboudumc Centre for Mindfulness in Nijmegen, the Netherlands. Inclusion criteria were minimum age of 18 and diagnosis of recurrent depression according to the Diagnostic and Statistical manual of Mental disorders (4th edition) criteria (First, Gibbon, Spitzer, and Williams, 1996). Most patients had participated in previous research for which the interview data was known. For those who had not, we conducted Mini

International Neuropsychiatric Interviews (MINIs; (Sheehan et al., 1998). Patients with past (hypo) manic or psychotic episodes or recent alcohol and/or drug abuse (last twelve months) were excluded.
Fourteen patients participated in the first MBCL course. Ten of them and three additional patients participated in the second course. Average attendance rate was 7.4 (first course) and 7.6 (second course) out of 8 sessions. The majority of the participants were female (N=15, 87%) and the average age was 53.4 (SD 9.3). Attendance rate of the MBCT is known for seven out of 17 participants: this was eight sessions for all of them. For specifics of each group, see Table 1.

Table 1 Gender, age and time lapse since MBCT of both groups of participants

	Group 1 (N=14)	Group 2 (N=13)	
		Doubles (n=10)	Novices (n=3)
Female (N)	13	9	2
Age (SD)	56 (9.8)	58.7 (5.7)	57.8 (2.1)
Age range	37-71	46-66	56-60
Time lapse since MBCT (months)	32.1	47.3	54

Procedure

We set up a pilot study to develop and evaluate MBCL as a follow-up intervention to MBCT in adults with recurrent depression. After the training, we conducted a focus group interview, after which necessary adaptations were made to the MBCL program. By involving patients in the development of the program in this way, we essentially opted for co-creation of a new format. Though very little described or researched in the field of Psychology, in technology development co-creation refers to collaboration with customers for the purpose of innovation and has become a foundational premise of the service-dominant logic (Lusch, Vargo, and O'Brien, 2007). In this context, the basis for the collaboration is the experiences that a customer has gained when using a company's product or service (Vargo and Lusch, 2004), in order to ascertain the value of that product or service and unearth latent customer needs that the service should address.
We recruited participants until a first group could be formed (N=14). The MBCL was offered in accordance with the curriculum of the original developers (Van den Brink and Koster, 2012). Patients were invited to practice at home for about thirty minutes on a daily basis, supported by CDs, and to keep a record of their experiences. The intervention was taught by two teachers (HJ and RM) who both meet the advanced criteria of the Association of Mindfulness Based Teachers in

the Netherlands and Flanders (which correspond to the Good Practice Guidelines for teaching mindfulness-based courses by the UK Network for Mindfulness-Based Teacher Training Organizations). In addition, both were trained in the MBCL program by the developers (Van den Brink and Koster).
Following the last session of the first group, a focus group interview was held on facilitators and barriers, i.e. helpful and unhelpful elements of the course, led by an experienced researcher (AS) who had not been involved in the training. Also present were both teachers (HJ and RM) and a junior researcher taking notes (RS). Focus groups started with explaining confidentiality and the explorative nature of the interview. Questions were asked in an open non-directive manner, allowing participants to speak freely about their experiences. The research question addressed in the interview was: What was helpful in the training and what difficult?; and What improvements, if any, could be made? The duration of the interview was one-and-a-half hours. The interview was audio and videotaped.
Self-report questionnaires on depressive symptoms, worry, mindfulness and self-compassion skills were administered before the first session and after the last.

Measures

Depressive symptoms. The Dutch translation of the 20-item Beck Depression Inventory (BDI-II (Beck, Steer, and Brown, 1996); Dutch version: BDI-II-NL (Van der Does, 2002) was used to assess depressive symptoms. This standardised questionnaire contains 21 items, scored on a 0-3 scale. The BDI-II has been validated in psychiatric outpatients. The internal consistency varies from .84 to .91 and the retest reliability ranged from .73 to .96 (Beck, Steer, Ball, and Ranieri, 1996; Wang and Gorenstein, 2013).
Worry. The Dutch translation of the 16-item Penn State Worry Questionnaire (PSWQ (Meyer, Miller, Metzger, and Borkovec, 1990) was used to assess worry (responses are given on a 5-point scale). Possible range of scores is 16-80. The PSWQ has been demonstrated to have strong internal consistency (α of .95 at both test and retest) (Meyer et al., 1990).
Self-compassion. The Dutch translation of the Self-Compassion Scale (SCS (Raes, Pommier, Neff, and Van Gucht, 2011) was used to measure self-compassion skills of patients. The questionnaire consists of 26 items divided over 3 subscales: 1) self-kindness versus self-judgment, 2) common humanity versus isolation, and 3) mindfulness versus over-identification. On a scale of 1 to 5, participants indicate the extent to which they agree with statements such as: I try to be loving towards myself when I'm feeling emotional pain (self-kindness), When things are going badly for me, I see the difficulties as part of life that everyone goes through (common humanity) and When I'm feeling down I try to approach my

feelings with curiosity and openness (mindfulness). Internal consistencies of the different subscales vary from .75 to .81 and test-retest reliabilities vary from .80 to .93 (Raes et al., 2011). The SCS is sensitive to change in MBCT (Kuyken et al., 2010).

Mindfulness. Mindfulness skills were measured using the Five Facet Mindfulness Questionnaire (FFMQ-NL; (Baer et al., 2008), which has five subscales: observing, describing, acting with awareness, non-judging of inner experience and non-reactivity to inner experience. Internal consistencies of the different subscales vary from .72 to .93 (Baer et al., 2008). The FFMQ is sensitive to change in mindfulness-based interventions (i.e. MBSR; Carmody and Baer, 2008).

Data analyses

The focus group interview was transcribed verbatim by RS and coded independently by RS and a senior researcher (HvR). These two coding researchers were trained in mindfulness, having successfully completed the teacher training program at the Radboudumc Centre for Mindfulness, as well as qualitative analysis, in a separate, intensive course. After the focus group, the codes were compared and discussed by the two coding researchers to identify possible discrepancies between codes until reaching consensus. This led to a coding scheme, to which new codes from the second focus group could be added. After the two focus groups, RS and HvR together with HJ, RM and AS grouped the codes into subthemes, and subthemes into themes for thematic analysis (Braun and Clarke, 2006).

Emerging themes indicating suggestions for improvement from the first focus group were discussed with the original developers of MBCL (Van den Brink and Koster) and the MBCL program was adapted accordingly. Because the adaptations were major, we chose to offer the revised program for a second time to the original participants, of whom ten (71%) agreed to participate. The group was extended by three patients with recurrent depression who had not previously participated. A renewed focus group interview was conducted after the second course, also led by AS, accompanied by both teachers and RS, and lasting one-and-a-half hours. The interview was audio and videotaped, and transcribed verbatim (RS). RS and HvR coded the interview and discussed coding and thematic analysis with HJ, RM and AS. The themes emerging from the second interview were also discussed with the original developers Van den Brink and Koster and gave rise to a few additional, minor improvements of the program. The iterative process of analysis, adaptation and re-evaluation involving all parties in every step enabled the co-creation of an adapted format for MBCL.

To analyze the quantitative data we conducted repeated measures ANOVA on all (sub)scales using SPSS 20. We report the findings of the two subsequent groups separately: the first analysis containing all novices to compassion training, the second one containing three novices in addition to ten second-time participants.

Results

First focus group interview

Facilitators, i.e. elements of the program that were considered helpful by the participants, could be grouped into five themes, of which the three most salient ones are described in table 2.

Table 2 Main facilitating programme components

Facilitators	Description
Didactic teaching	Evolutionary development and universality of the three emotion regulation systems Addressing and explanation of the back draft effect as a possible occurrence
Compassion practices	The explicit focus on self-compassion development in the practices, as well as on obstacles to self-compassion (inner bully/critic)
Embodiment teacher	Consistent mild attitude/responsiveness of the teachers Practical translation of compassion in daily life

Facilitators

Didactic teaching

This theme was made up from theoretic elements in the content of the MBCL, such as theory on the evolution and universality of the human brain, theory on the three emotion regulation systems (threat, hunt and rest and digest system) and information regarding the back draft effect. Participants reported being helped by being reminded of the universality of the brain. Also, knowledge of the three systems gave them a reference point for practice.

> *The explanation, I found so illuminating. Which system you automatically step into. It starts with your brain, so enlightening. … It's applicable to every brain and that is also comforting.*

By addressing the back draft effect and its possible occurrence beforehand, participants were able to allow their emotions to be overwhelming for a while: they could accept it as a natural step in their process instead of taking it to mean something was wrong.

Compassion practices
Specific practices that were appreciated during the sessions and as homework included the safe haven and the compassionate body scan. As homework or more informal practice, writing a compassionate letter, keeping a diary, and paying specific attention to the inner bully or critic were mentioned. This last practice involved practicing mindfulness of the primarily judgmental, critical voice or thought that often pops up for patients, helping them to discover when this voice is most present (i.e. supported by recognizing which system is active: threat, hunt or soothe) and what attack it will usually go for:

> *The inner bully was addressed extensively and that was a real eye-opener for me, … very recognizable as one of the major causes of distress. And by naming it and looking at it more compassionately, it got a place for me and it is a less dominant factor in my life than before.*

Teacher embodiment of compassion to self and others
Embodiment and compassion to self and others modelling by the teacher was considered very helpful by the participants:

> *It's just that they [the teachers] also shared their own struggles with things that are difficult, so you're really investigating this together.*

Though many participants commented that the MBCL was confrontational and they suffered the back draft effect, most also indicated that going through this stage and cultivating an attitude with which the suppressed emotions could be approached instead of avoided, was what really propelled the development of compassion to self and others. The ability to approach seemed to be aided substantially by the teachers' response to what participants shared in the group:

> *It really connects with me … when you listen to what people are sharing and what reactions you as instructors have to that. That is what's helped me most of all … that translation ... in a safe group, which I found the most important, I've really experienced that.*

Peer support
Group exchanges on (home) practices and experiences was also considered helpful by most participants:

> *You're in a very democratic process of struggling together with what it is, and err yes that helps (…) especially when you're depressed a lot, you think: o help, I'm so pathetic, and here you come into this group and yes, you're in it together.*

Structure of the training
In terms of the duration of the training, most participants indicated that eight sessions was good to get fully immersed in the program, though some thought that 10-12 sessions would be even better. Because of the amount of theory to address in the program, the number of practices to get acquainted with and importantly, the complexity of the subject, coming together once every other week instead of every week was highly appreciated by the participants.

Barriers
Barriers, i.e. elements of the program that were considered unhelpful by the participants, could be grouped into two themes (see Table 3).

Table 3 Main barriers in programme components

Barriers	Description
Compassion development	Being confronted with one's lack of self-compassion as well as lack of compassion for others The resurfacing of old pain, i.e. the back draft effect
Structure of the training	Lack of structure Lack of core practice Too many practice options Unappealing course folder: language/volume

Compassion development
In general, participants commented on the MBCL being confrontational. Almost all participants reported struggling with the back draft effect during practices: being overwhelmed by old pain resurfacing now that they were allowing themselves to practice with approaching instead of avoiding hard thoughts and emotions. Also they reported being confronted by how difficult it was to be kind to themselves, and how this realization grieved them.

… to look at myself more compassionately, has (…) made me confront a whole bunch of things that (…) are hard. I've found that (…) the price of this training, that it wasn't easy for me, (…) it's something to take into account.

Though they were helped by the theory on the back draft effect and the teachers' approach of the subject, they stated they would have appreciated explanation of this phenomenon earlier in the program and also to have it addressed recurrently:

For me, it would have been easier if it had been addressed in some form in each session.

Structure of the training

Participants mentioned the program lacked a clear structure. For some participants, the main focus didn't become obvious until session 4 or 5:

Perhaps followed by a summary and a reference of what the next step was going to be, what will we do next time and why is that a logical step considering what we've done before.

You [the teacher] returned to the soothing system and I thought: ah, finally, that's what it's about; I've been waiting five sessions to hear that.

In line with participants commenting on the lack of clear structure, they also found a lack of a core practice: each session brought a new practice and practices were seldom revisited in the curriculum. Also the number of options to choose from for home practice seemed to be confusing to participants.

I do see the advantage of having a large shop in which to choose what I like, but for me I tend to walk past the shop when it's like that.

It was not clear what should be practiced from session to session and participants were insecure about what was obligatory and what was non-obligatory:

Now everyone had done something else, so you can't share so much how you've struggled with a particular practice.

It would have helped me to know which exercises are specific for this session, and then to be offered the rest as added options, in case you want to do more.

One of the participants mentioned that especially when you're depressed, your ability to make even relatively small decisions such as what to practice, is compromised:

A characteristic of depressed people is their difficulty with making decisions.

Participants also found the content of the course folder much too dense, and the language unappealing and dry:

I've really had words which I had to look up on the Internet.

It was a difficult, heavy read for me.

Some attributed their difficulties with the practice to the fact that they couldn't place the program in a mindfulness framework; they had expected more common ground between MBCT and MBCL.

Several participants mentioned having difficulty with the content of the Metta or befriending practice in MBCL. Some found it hard to feel compassion for others in general, and some would have preferred the program to attend to self-compassion longer before moving on to compassion for others:

Yes, … it's finally your turn and then you already had to transfer to someone else and then I thought, yeah but I don't feel like doing that at all, I am finally on a roll with myself so that can wait a couple of sessions. I'm not saying to take it out of the program but it's very liberating that you're allowed to just have compassion with yourself for a change.

Adaptations to the MBCL program after the first focus group interview

The possible improvements that emerged from analysis of the first interview and subsequent discussion with the developers were used to adapt the MBCL. Considering the impact of the back draft effect on the participants, we decided to address the possible occurrence of this effect earlier in the program (session 2 instead of 4) and check up on this more regularly and explicitly throughout the entire program. Allocating more time to the back draft effect meant we had to sacrifice some time to discuss the inner critic though.

Next we addressed the curriculum practicalities of MBCL: we restructured the curriculum over the sessions according to the MBCT format more explicitly. Especially session 3 and 4 were restructured to resemble MBCT's format of

addressing craving and aversion respectively. The course folder was highly simplified and the style of writing was made more personal. Given the comments on the overwhelming amount of homework options, we simplified the program by cutting down the number of exercises. An exercise on imagining a compassionate companion was removed from the program as a separate practice, though it was introduced in modified manner at the beginning of the Metta practice. The simplification of practices enabled us to introduce the Soften-Soothe-Allow exercise from Germer (2009), which guides practitioners very gently and gradually to being with an unpleasant experience, as well as providing support for the back draft effect. We slowed down the transition from self-compassion to compassion for others, essentially dividing the program into 4 sessions focusing on self-compassion and 4 sessions focusing on both self-compassion and compassion for others.

Second focus group interview

Thematic analysis of codes found in the second focus group interview largely supported the adaptations made to the program. Participants reported being very happy with the extra space allowed for the back draft effect. Also, Soften-Soothe-Allow (Germer, 2009) was indeed mentioned as particularly helpful support in dealing with this effect. Participants also indicated being much more satisfied with the number of homework options offered the second time around, though they would still like to reduce the total number. The exercises that were removed from the program did not seem to be missed. Due to the simplification of the program and reduction in practice options, participants felt that there was more room for inquiry and exchange than during the first course. Even more than in the first evaluation, they commented that the honest and often vulnerable sharing of the teachers of their own experiences was a good model of a compassionate attitude to both self and others:

> *The second time we took more time to exchange experiences in the group on what was encountered, if you were managing to practice or not, how you dealt with yourself. For me, I feel that taught me most of all, because you [the teachers] were very consistent in being mild.*

Also, the additional time for enquiry encouraged the exchange between participants. When participants couldn't work with compassion to self or others in a certain difficult experience, it was helpful to hear from others how they did just that:

> *Yes, okay, it's explained, but still.. and then someone would say something that would make it click with me, so what they [the teachers] said became clear through her [participant] story.*

In terms of practicalities, it seemed the course folder had been condensed too much: participants commented on elements they now missed, such as the background information on the inner critic or bully:

> *In the first course, the inner bully was addressed extensively and that was a huge eye-opener for me like that is so recognizable as one of the major causes of all the unrest, and by naming it and looking at it from a compassionate viewpoint, it has a less dominant role in my life than before.*

We adapted the course folder accordingly. For an overview of the entire adapted MBCL program, see Appendix I in the Supplemental Materials.

Preliminary effectiveness

The study was set up as a co-creation and feasibility study, not as a randomized controlled trial. Therefore this paragraph only contains preliminary indications of effectiveness, which must be interpreted as such. For the first course, we analysed N=13 as one of the participants failed to hand in the post-measurement. For the remaining 13 participants, no changes in outcome were found with regards to depressive symptoms or worry. With the exception of the subscale *Observe*, mindfulness skills did not change (see Table 4.1). Self-compassion overall did change (Cohen's $d = 0.56$), particularly the subscale *Common Humanity* (Cohen's $d = 0.54$).

For the second course, we analysed N=9 participants as one did not hand in the pre-measurement, and three others did not hand in the post-measurement. In group 2, a significant reduction of depressive symptoms was found (Cohen's $d = 0.66$), but no changes in worry. Except for *Non-judgment* (Cohen's $d = 0.68$), no changes in mindfulness skills were found, but overall self-compassion (Cohen's $d = 0.37$) again improved, particularly *Self-kindness* (Cohen's $d = 0.53$), *Isolation* (Cohen's $d = 0.57$) and *Overidentification* (Cohen's $d = 0.93$) (see Table 4.2, and table 5 for specifics for 'doubles' and 'novices').

Table 4.1 Quantitative results MBCL from pre to post for group 1, using a repeated measures ANOVA

GROUP 1 (N=14)						
Scale	**Subscale**	**MEAN**		**CI (diff)**	***p***	***d***
		PRE (SD)	**POST (SD)**			
BDI-II	Depression	13.14 (9.9	10.79 (7.7)	-1.90-6.61	.253	0.26
PSWQ*	Worry	43.69 (6.7)	42.15 (6.7)	-1.97 - 5.05	.359	0.23
FFMQ	Mindfulness	80.64 (8.8)	83.79 (9.1)	-8.13-1.84	.196	0.35
	Observe	15.93 (1.1)	17.00 (1.5)	-1.87- -0.27	.013*	0.81
	Describe	20.00 (4.2)	20.21 (3.8)	-1.85-1.42	.782	0.05
	Act with awareness	15.36 (2.2)	15.93 (3.1)	-2.31-1.16	.489	0.21
	Non-judgment	14.14 (2.7)	15.14 (4.0)	-2.52-0.52	.179	0.29
	Non-reactivity	15.21 (2.7)	15.50 (2.8)	-1.86-1.29	.702	0.11
SCS*	Self-compassion	23.09 (5.2)	26.25 (6.0)	-6.21- -0.11	.043*	0.56
	Self-kindness	4.03 (1.2)	4.60 (1.4)	-1.14-0.03	.059	0.44
	Self-judgment	4.33 (1.1)	4.04 (1.3)	-0.90-1.48	.606	0.24
	Common humanity	4.10 (1.3)	4.75 (1.1)	-1.28- -0.03	.041*	0.54
	Isolation	4.56 (1.1)	4.02 (1.3)	-0.80-1.87	.397	0.49
	Mindfulness	4.51 (1.0)	4.90 (0.9)	-0.80-0.02	.058	0.41
	Overidentification	4.67 (1.1)	3.94 (1.1)	-0.49-1.95	.218	0.69

*N=13, one post measurement missing

Table 4.2 Quantitative results MBCL from pre to post for group2, using a repeated measures ANOVA

GROUP 2 (N=13)*						
Scale	**Subscale**	**MEAN**		**CI (diff)**	***p***	***d***
		PRE (SD)	**POST (SD)**			
BDI-II	Depression	21.13 (12.4)	13.00 (12.1)	4.60-11.66	.001*	0.66
PSWQ**	Worry	43.14 (8.3)	45.57 (8.2)	-9.16-4.30	.411	0.29
FFMQ	Mindfulness	79.38 (17.2)	81.63 (14.5)	-8.12-3.62	.395	0.14
	Observe	15.50 (3.0)	15.86 (2.6)	-2.32-1.57	.662	0.13
	Describe	18.88 (4.9)	17.88 (4.4)	-0.84-2.84	.240	0.21
	Act with awareness	16.25 (4.4)	16.63 (3.3)	-1.92-1.17	.584	0.10
	Non-judgment	14.25 (3.0)	16.63 (3.9)	-4.32- -0.43	.023*	0.68
	Non-reactivity	15.50 (4.2)	14.63 (3.2)	-1.42-1.17	.826	0.23
SCS*	Self-compassion	22.31 (7.8)	25.26 (8.0)	-5.81- -0.09	.045*	0.37
	Self-kindness	3.81 (1.6)	4.63 (1.5)	-1.53- -0.09	.032*	0.53
	Self-judgment	4.00 (1.3)	4.41 (1.4)	-2.51-1.70	.662	0.30
	Common humanity	3.72 (1.6)	4.14 (1.7)	-1.26-0.43	.281	0.25
	Isolation	4.75 (1.7)	3.81 (1.6)	-1.76-3.63	.438	0.57
	Mindfulness	4.25 (1.4)	4.60 (1.4)	-0.70-0.01	.054	0.25
	Overidentification	4.72 (1.1)	3.70 (1.1)	-0.68-2.74	.197	0.93

*N=9, one pre and three post measurements missing (all female), **N=8

Table 5 Quantitative results MBCL from pre to post for group 2 specified for 'doubles' and 'novices', using a repeated measures ANOVA

	Doubles (N=10)* MEAN		**Novices (N=3) MEAN**	
	Pre (sd)	**Post (sd)**	**Pre (sd)**	**Post (sd)**
BDI-II	20.6 (11.9)	10.4 (11.6)	25 (9)	22 (1.4)
PSWQ	42.8 (7.8)	41.7 (7.1)	54 (2)	59 (0)
FFMQ	79.8 (15.2)	85.7 (12.8)	70 (14.4)	72.5 (17.7)
SCS	24.2 (6.5)	28.5 (7.5)	15.3 (4.5)	1.2 (1.5)

*N=6, one pre and three post measurements missing (all female)

Discussion

The results of our pilot study on the co-creation and feasibility of a compassion training for patients with recurrent depression are encouraging. The attendance rate was very high for both courses. In contrast to the first version of the course, participants reported being very satisfied with the adapted program. In accordance with this, the reduction of depressive symptoms was greater in the second course than in the first. Pre-scores on the BDI-II of the second group were on average higher than in the first group; this difference was however strongest with the novices in the second course. In both groups improvements in self-compassion were found, both overall and in several subscales, with effect sizes ranging from small to large. This may indicate that MBCL delivered what it is designed to do: improve (self)compassion skills. No reduction was found in worry, nor improvement in mindfulness skills overall. This might be explained by the fact that all participants already participated in an MBCT course before taking part in the compassion training. It is known that MBCT results in a reduction of worry and an improvement of mindfulness skills (Van Aalderen et al. (2012). However, as the study sample was small, it is obvious that these quantitative results should be interpreted with the utmost caution: especially the reduction in depressive symptoms in the second group may also have been due to the 'double dosage' of MBCL that most participants in that group had received by then. In general though, these results are congruent with the hypothesis proposed by Koster and Van den Brink (2012) that self-compassion skills can be significantly increased by explicitly training them. It seems that even for patients who previously attended MBCT explicit compassion training is of added value.

By inviting frequent attendees of reunion meetings to participate in this pilot study, our selection procedure was probably biased in favour of patients who had followed MBCT quite some time ago: they may have experienced a decline in experienced effects from MBCT and thus have been motivated for a follow-up program. This may have overestimated our results. The acceptability and effectiveness might be less pronounced in less motivated participants, or if we had recruited participants immediately after MBCT. In addition, we have very little data on the proportion and characteristics of patients who declined our offer to participate; these patients may be especially interesting in terms of barriers to the MBCL program.

However, we were also very happy to be able to work with highly motivated participants ('lead users') in order to get informed feedback on the MBCL to improve the curriculum. As we received ample feedback on how to improve the first version of the course and were able to evaluate the adapted version of the programme with almost all original attendees, we are confident we now have a program suitable for this population.

To further examine the effectiveness of MBCL, a properly powered randomized controlled trial should be conducted. This may help to answer questions about a) the possible added value of an explicit training in compassion for patients with recurrent depression who previously participated in MBCT; b) whether compassion training should be a follow-up to MBCT, or whether it might be valuable as an adapted/stand-alone intervention in this population.

In conclusion, MBCL as an intervention for patients suffering from recurrent depressive symptoms appears to be feasible and acceptable, and the preliminary results on the effectiveness of the program in terms of reducing depressive symptoms and increasing self-compassion are promising. The results of this pilot study indicate that the cultivation of self-compassion might deserve more attention in this population than it currently gets. Though this is a small and uncontrolled feasibility study and our findings are preliminary, the next step should be a properly powered, randomized-controlled trial.

Ethical approval

As per the guidelines of the Medical Ethical Committee of the region Arnhem-Nijmegen in the Netherlands, no approval was necessary for this study. For the subsequent randomized controlled trial, approval was granted under number 2013/220.

Funding

This study was funded by the Radboudumc Centre for Mindfulness.

Conflict of interest

The clinical research team declares it had no part in the original development of the MBCL program, though AS and RS made modifications to it in collaboration with the original developers in this study. The team does not gain income from the sale of books on MBCL, nor does it gain income from giving lectures or workshops about it. AS is founder and clinical director of the Radboudumc Centre for Mindfulness, where MBCL is also taught. HJ, RM, HvR, RS and AS are affiliated with the Radboudumc Centre for Mindfulness. Van den Brink and Koster gain income from the sale of their book on MBCL and by giving workshops and trainings in MBCL.

Author Contributions

RS: collaborated with the design of the study, executed the study, participated in the focus group interviews, transcribed the interviews, conducted the data

analyses, and wrote the paper. MH: collaborated with writing the study and editing of the final manuscript. HJ: taught the MBCL groups and participated in the focus group interviews. RM: taught the MBCL groups and participated in the focus group interviews. FK: collaborated with conducting data analyses. EvdB: collaborated with conducting data analyses. HvR: collaborated with writing the study and editing of the final manuscript. AS: designed the study, led the focus group interviews, collaborated in the data analyses and editing of the final manuscript.

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Supplemental Materials

APPENDIX I
Summarized description adapted MBCL

Session 1
Introduction to compassion
Practice : Compassionate body scan + inquiry
Psycho-education on the three systems, connected to stress reactions of fight/flight/freeze
Practice: Safe haven
Compassionate breathing

Session 2
Arriving
Practice: Soften-soothe-allow + inquiry
Inquiry home practice
Theoretical information on back draft effect and obstacles to self-compassion in general
Practice: Metta (only benefactor) + inquiry
Homework suggestions
Compassionate breathing space + poem

Session 3
Arriving
Practice: Compassionate movement (lying down) + inquiry
Inquiry home practice
Theoretical information on the inner bully (part 1)
Exercise with scheme therapy questionnaires to identify compensation strategies
Practice: Metta (benefactor and self) + inquiry
Homework suggestions
Compassionate breathing space

Session 4
Arriving
Practice: Soften-soothe-allow + inquiry
Inquiry home practice
Theoretical information on recognizing patterns; the inner bully (part 2)
Practice: Metta (benefactor and self) + inquiry
Homework suggestions
Compassionate breathing space with emotional pain

Session 5
Arriving
Practice: Compassionate movement exercises (standing) + inquiry
Inquiry home practice
Practice: Metta (benefactor, self and important other)
Homework suggestions
Compassionate breathing space with emotional pain

Session 6
Arriving
Practice: Metta (benefactor, self, important other and neutral person) + inquiry
Inquiry home practice
Interactive psycho-education on common humanity:
Writing a compassionate letter to yourself
Practice: Compassionate walking
Homework suggestions
Compassionate breathing space and poem

Session 7
Arrival
Practice: Soften-soothe-allow + inquiry
Inquiry home practice
Practice: Forgiveness towards others
Practice: Metta (benefactor, self, important other, neutral person and difficult other or some aspect(s) of yourself you struggle with) + inquiry
Homework suggestions
Compassionate breathing space

Session 8
Arrival
Practice: Metta (benefactor, self, important other, neutral person, difficult other or some aspect(s) of yourself you struggle with and all beings) + inquiry
Inquiry home practice
Group exchange on the future: what is your plan?
Ending the course through symbols participants were invited to bring, what do you wish for yourself and others?
Compassionate breathing space and poem

3

A parallel-group, randomized controlled trial into the effectiveness of Mindfulness-Based Compassionate Living (MBCL) compared to treatment-as-usual in recurrent depression: trial design and protocol

Schuling, R., Huijbers, M.J., Van Ravesteijn, Donders, A., H., Kuyken, W., & Speckens, A.E.M. (2016). A parallel-group, randomized controlled trial into the effectiveness of Mindfulness-Based Compassionate Living (MBCL) compared to treatment-as-usual in recurrent depression: trial design and protocol. *Contemporary Clinical Trials, 50, 77-83.*

Abstract

Background: Mindfulness based cognitive therapy (MBCT) has been shown to reduce the risk of relapse in patients with recurrent depression, but relapse rates remain high. To further improve outcome for this group of patients, follow-up interventions may be needed. Compassion training focuses explicitly on developing self-compassion, one of the putative working mechanisms of MBCT. No previous research has been done on the effectiveness of compassion training following MBCT in patients with recurrent depression.

Aims: To investigate the effectiveness of mindfulness-based compassionate living (MBCL) in reducing (residual) depressive symptoms in patients with recurrent depression who previously participated in MBCT.

Methods/design: A randomized controlled trial comparing MBCL in addition to treatment as usual (TAU) with TAU only, in patients suffering from recurrent depressive episodes who completed an MBCT course in the past. Assessments will take place at baseline, post-treatment and at six-months follow-up. After the control period, patients randomized to the TAU condition will be offered MBCL as well.

Outcome measures: Primary outcome measure is severity of depressive symptoms according to the Beck Depression Inventory-II (BDI-II) at post-treatment. Secondary outcome measures are presence or absence of DSM-IV depressive disorder, rumination, self-compassion, mindfulness skills, positive affect, quality of life, experiential avoidance and fear of self-compassion.

Discussion: Our study is the first randomized controlled trial to examine the effectiveness of compassion training following MBCT in a recurrently depressed population.

Introduction[1]

Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders. It is characterized by high relapse rates (Mueller, Leon et al. 1999, Solomon, Keller et al. 2000), partly due to persistence of residual symptoms after remission (Hardeveld, Spijker et al. 2010). Given the high psychological as well as social and economic burden associated with MDD, the prevention of relapse is extremely important. To address the need for psychological interventions targeting relapse prevention, Segal, Williams and Teasdale developed Mindfulness-Based Cognitive Therapy (MBCT; Teasdale, Segal et al. 2000). Mindfulness can be defined as paying attention in a particular way: on purpose, in the present moment, and non-judgmentally (Kabat-Zinn 1990). MBCT helps patients with recurrent depression to develop non-judgmental awareness in the face of difficult thoughts, feelings, and bodily sensations, and fosters an intentional, skilful response to these experiences instead of avoiding them or reacting 'on automatic pilot'. A meta-analysis (Piet and Hougaard 2011) showed that MBCT for patients with recurrent depression in remission resulted in a reduction of the risk of a relapse/recurrence of 34%. A growing number of studies indicate that MBCT may also be effective in decreasing residual levels of depression (Kenny and Williams 2007, Eisendrath, Delucchi et al. 2008, Barnhofer, Crane et al. 2009, Bockting, Hollon et al. 2015). An RCT conducted by our own team in 205 patients with three or more previous depressive episodes showed that patients who were currently depressed benefitted as much from MBCT as those who were in remission in terms of depressive symptoms (Van Aalderen, Donders et al. 2012). These findings were maintained during a one-year follow-up, showing a similar course of depressive symptoms in depressed and remitted patients (Aalderen, Donders et al. 2015). These results were subsequently confirmed by a meta-analysis of n=12 studies on the effectiveness of MBCT for people with a current depression, which found significant improvements of depressive symptoms following MBCT in comparison to control conditions (Hedges g=−0.39, 95% CI=−0.15 to −0.63) (Strauss, Cavanagh et al. 2014).

However, even after MBCT relapse rates remain considerable (38%; Piet and Hougaard 2011) and mild levels of depression (average BDI score of 10) remain

1 **List of abbreviations used**
AAQ-II: Acceptance and Action Questionnaire II; BDI-II: Beck Depression Inventory II; CFT: Compassion Focused Therapy; CMT: Compassionate Mind Training; CSRI: Client Service Receipt Inventory; CTQ: Childhood Trauma Questionnaire; FFMQ: Five Facet Mindfulness Questionnaire; FoCS: fear of Compassion Scale; MBCL: Mindfulness Based Compassionate Living; MBCT: Mindfulness Based Cognitive Therapy; MBI: Mindfulness Based Intervention; MSC: Mindful Self Compassion; RCT: Randomized Controlled Trial; RRS: Ruminative Response Scale; SCID-I: Structured Clinical Interview for DSM Disorders; SCS: Self-Compassion Scale; TAU: Treatment as Usual; WHO-QoL: World Health Organization Quality of Life

present (Aalderen, Donders et al. 2015). Therefore, it is important to look for ways to further improve outcomes for this group of recurrently depressed patients. Residual symptoms of depression are an important predictor of relapse (Hardeveld, Spijker et al. 2010), and may be a useful target for a follow-up intervention. A possible candidate for such a follow-up intervention is compassion training, a training that focuses explicitly on developing (self)-compassion as one of the putative working mechanisms of MBCT. Kuyken and colleagues (Kuyken, Watkins et al. 2010) showed that the effect of MBCT on relapse/recurrence was mediated by increased self-compassion and mindfulness, along with a decoupling of the relationship between reactivity to depressive thinking and poor outcome. The cultivation of self-compassion was associated with this decoupling in the intervention group.

Compassion

In 2012, Van den Brink and Koster developed a training in self-compassion as a follow-up intervention for patients who have already attended MBCT or MBSR, Mindfulness-Based Compassionate Living (MBCL; Van den Brink E. 2012, van den Brink and Koster 2015). It is based on previous work in compassion research as conducted by Neff, Germer and Gilbert amongst others (Germer 2009, Gilbert 2009, Neff 2011, Neff and Germer 2013) and is designed to be used in both clinical and non-clinical settings. In contrast to the more implicit teaching of compassion in MBCT, cultivating self-compassion is the primary focus of the training. Throughout the entire curriculum, the invitation is to practice kindness and compassion in the midst of suffering.

Considering the preliminary evidence linking lack of self-compassion to negative self-esteem and depression (Neff 2003, Gilbert 2009, MacBeth and Gumley 2012, Neff and Germer 2013), MBCT combined with a follow-up training with a more explicit focus on self-compassion may be a fruitful approach to further reduce (residual) symptoms of depression in patients with recurrent depression who previously participated in MBCT. The extent to which this, in turn, contributes to the prevention of relapse and enhancement of psychological wellbeing is the question.

To date, the effectiveness of compassion training has not been studied in a clinical population in a large, adequately powered RCT. As a first step, we investigated the feasibility, acceptability and preliminary effectiveness of the MBCL in a pilot study, showing an increase in self-compassion and mindfulness skills and a trend in reducing depressive symptoms (Schuling et al., 2017). Participants of this study (N=17) were all previous participants of an MBCT course and regular attendees of reunion meetings organised by our centre.

Aims

The aims of the present study are: 1) to examine the effectiveness of MBCL in adults with recurrent depression who are either in (partial) remission or currently depressed, and who previously participated in MBCT. Considering the effectiveness of MBCT even in patients who are currently depressed (Van Aalderen, Donders et al. 2012), we will include patients with and without current depression. For this reason, our primary outcome measure is depressive symptoms and not relapse. 2) To investigate the impact of MBCL on rumination, fear of self-compassion, experiential avoidance, type of positive affect, self-compassion, mindfulness and quality of life, and 3) to investigate the added value of MBCL to only MBCT based on participants' experiences using one-on-one, in-depth, qualitative interviews.

Methods

Design

This study is designed as a parallel-group RCT. Patients will be randomized to [a] MBCL in addition to TAU or [b] TAU only. The protocol was approved by the ethical review board CMO Arnhem-Nijmegen and registered under number 2013/220.

Study population

The study will be conducted at the Radboudumc Centre for Mindfulness, Nijmegen, the Netherlands. This centre was founded in 2007 and has a threefold purpose: 1) to provide mindfulness based interventions to patients with either mental health problems, such as recurrent depression, or somatic diseases, such as cancer; and subjects from the general population; 2) to conduct and disseminate research on the effectiveness and working mechanisms of mindfulness based interventions; and 3) to offer a teacher training program to become a mindfulness teacher. Approximately 228 patients from all over the Netherlands were taught MBCT in 2015, Mindfulness Based Stress Reduction was taught to 218 health care professionals and subjects from the general population. The centre also hosts fortnightly reunion meetings for attendees of both MBCT and MBSR courses, which were attended by a total of 310 participants in 2015.

The study population will consist of patients with recurrent depression who previously participated in an MBCT course at the Radboudumc Centre for Mindfulness in Nijmegen, the Netherlands. In order to be eligible to participate in this study, participants must meet the following criteria: 1) recurrent

depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders (fourth edition; DSM-IV) criteria, with or without a current depressive episode; and 2) having participated in an MBCT (>=4 sessions) training before (>= 1 year ago). Exclusion criteria are: 1) one or more previous (hypo)manic episodes according to the DSM-IV criteria; 2) primary psychotic disorder; 3) clinically relevant neurological or somatic conditions that could be causally related to the depression; 4) current alcohol and/or drug dependence, 5) recent electro convulsive therapy (less than 3 months ago); 6) inability to complete interviews and/or self-report questionnaires.

Interventions

Mindfulness Based Compassionate living

MBCL is set up as a follow-up intervention to MBSR or MBCT. Its main purpose is to offer those participants with persistent dysfunctional thinking or behavioural patterns a means to practice more explicitly with cultivating a kinder, gentler attitude towards themselves. These patients are often highly self-critical and are tormented by feelings of shame and guilt. As MBSR and MBCT, MBCL is a group intervention, consisting of classes up to 12 participants. The format of the MBCL programme is similar to MBSR/MBCT, including eight weekly sessions of 2.5 hours, containing a mixture of mindfulness practice, group enquiry and didactic and interactive teaching. However, the content of the practices and focus of the enquiry and didactic teaching is quite different, in the sense that they are actively geared towards the experience of suffering and explicitly focus on developing a kind attitude in the midst of this.

Participants are typically provided with a course folder containing background reading on each session, an explanation or description of practices used and helpful suggestions for practice. They are also given a set of CDs containing audio files with guided meditations. It is recommended that MBCL for patient populations is taught by health care professionals who are also qualified to teach MBCL.

The primary practice is that of Metta, a Pali word generally translated as loving kindness and which the MBCL developers translate as mildness meditation (Van den Brink and Koster 2015). In this practice, the participant is gradually guided through several steps of developing kindness towards self and others, starting with imagining a person by whom they feel unconditionally accepted and formulating intentions for their well-being, continuing with the self, a close other, a neutral person, and a difficult person. An overview of the intervention, as modified by us in the pilot study, is given in Table 1. Specifics of the original program can be found in Koster and Van den Brink (Van den Brink and Koster 2015).

Patients are invited to practice at home for about thirty minutes on a daily basis, supported by CDs, and to record their experiences on homework forms.

Delivery of MBCL

MBCL will be provided at the Radboud university medical centre for Mindfulness. Groups will be taught by one of two teachers who both have 7 years of experience with teaching MBCT (more than 50 groups) and who both meet the UK guidelines for teaching MBCT (Good Practice Guidelines for teaching mindfulness-based courses by the UK Network for Mindfulness-Based Teacher Training Organizations). In two previous trials (Huijbers, Spijker et al. 2012, Huijbers, Spinhoven et al. 2015), both teachers met level four of the Mindfulness Based Interventions Teaching Assessment Criteria (MBI-TAC; Crane, Kuyken et al. 2012). The teachers are also both trained to teach MBCL by the developers Frits Koster and Erik van den Brink: 100 hours of training in MBCL plus 80 hours of supervised teaching of MBCL. Integrity of the programme and teaching are assessed by review of two randomly selected videotapes (of each teacher) of training sessions by two experienced mindfulness teachers with the MBI:TAC (Crane, Kuyken et al. 2012) (slightly adapted to be congruent with MBCL instead of MBSR/MBCT).

Treatment as usual

TAU consists of regular medical and psychiatric or psychological treatment. Participants will be requested not to change their medication during the study, if at all possible, and to refrain from other compassion-focused interventions. Health care use of all participants (including necessary changes of medication) will be assessed at baseline, end of treatment/control period and during the six months follow-up using the Client Service Receipt Inventory (CSRI; Chisholm, Knapp et al. 2000).

Adherence

Participant compliance to the MBCL program will be assessed during the intervention period using a calendar on which participants indicate their adherence to formal and informal exercises on a daily basis.

Outcome measures

Primary outcome measure

Depressive symptoms. Primary outcome measure will be severity of depressive symptoms as measured by the Beck Depression Inventory-II (Beck, Steer et al. 1996) (Dutch version: BDI-II-NL (Van der Does 2002). This standardised questionnaire contains 21 items, scored on a 0-3 scale. The BDI-II has been

Table 1 MBCL overview per session

Theme of the session	Similarities in structure and exercises from MBSR/MBCT	Compassion practice *Session 1-4 to self* *Session 5-8 to self and others*	Psycho-education	Homework
1 – Why do we need compassion?	- Compassionate body scan - Compassionate breathing space	- The safe haven (Van den Brink and Koster 2015)	- Introduction compassion - Evolutionary development of the human brain: three emotion regulation systems: threat, drive and soothe system. Exploration of balance between these systems (Gilbert 2010)	- Safe haven - Compassionate body scan - Diary: moments of kindness and compassion
2 – Development of self-compassion	- Self compassion and dealing with obstacles - Compassionate breathing space	- experiencing acceptance from a friendly other	- Obstacles to compassion: confrontation with (old) pain - Five paths to self-compassion	- Soften-soothe-allow - Metta: unconditionally accepting other - Diary: recording moments of experiencing threat
3 – Craving and Compassion	- Compensating unpleasant feelings by chasing what we want: recognising automatic patterns - Compassionate breathing space in difficult moments	- Experiencing acceptance from a friendly other and self - Soften-soothe-allow: compassion for self (Germer 2009)	- Reflection on the inner bully: convictions and behaviour	- Compassionate floor yoga - Metta: unconditionally accepting other and self - Diary: drive system
4 – Aversion and Compassion	- Compensating unpleasant feelings by avoiding what we don't want: recognising automatic patterns - Compassionate breathing space with emotional pain	- Experiencing acceptance from a friendly other and self - Soften-soothe-allow: compassion for self	- Exploration of compassionate stance towards unhelpful automatic patterns - Exploration of guilt and shame	- Soften-soothe-allow - Metta: unconditionally accepting other and self - Diary: soothe system
5 – Compassion to others	- Responding to stress - Compassionate breathing space with emotional pain	- Experiencing acceptance from a friendly other, self and important other	- Reflection on what contributes to happiness	- Compassionate standing yoga - Metta: unconditionally accepting other, self and important other - Diary: exploring the possibility to be kind and compassionate
6 – Common humanity	- Responding to stress: forgiving self: the compassionate letter - Compassionate breathing space	- Experiencing acceptance from a friendly other, self, important other, neutral other	- Exploration of forgiving self - Exploration of common humanity	- Metta: unconditionally accepting other, self and neutral person - Compassionate walking - Diary: recording moments of kindness and compassion
7 – Compassion in action	- Responding to stress: forgiving others - Compassionate breathing space in action	- Experiencing acceptance from a friendly other, self, important other, neutral other and difficult other or difficult characteristics of yourself	- Exploration of forgiveness others: five stages of acceptance - Reflection on compassionate qualities and skills	- Metta: unconditionally accepting other, self, neutral person and difficult person or characteristics of yourself you have difficulty with - Soften-soothe-allow - Diary: acting out of compassion
8 – Resourced by compassion	- Responding to stress - Compassionate breathing space	- Experiencing acceptance from a friendly other, self, important other, neutral other and difficult other or difficult characteristics of yourself and including all beings	- Reflection of the four heart qualities: kindness, compassion, joy and equanimity	

validated in psychiatric outpatients. The internal consistency varies from .84 to .91 and the retest reliability ranged from .73 to .96 (Beck, Steer et al. 1996, Wang and Gorenstein 2013).

Secondary outcome measures

Depressive disorder. Presence, partial or full remission of depressive disorder will be assessed with the Structured Clinical Interview for DSM-IV disorders (SCID), part 1 (First, Gibbon et al. 1996). The interview (either face-to-face or, at follow-up, sometimes by telephone) will be administered at baseline, end-of-treatment/ end-of-control and six months after completion of treatment. Previous studies on inter-rater reliability of the SCID-I have reported Cronbach's alpha values between .61 and .80 (Zanarini, Skodol et al. 2000, Lobbestael, Leurgans et al. 2011). All interviews will be audio taped and a random sample of N=30 interviews will be second-rated by an independent and blind assessor to assess inter-rater reliability in the current study.

Rumination will be assessed with the Ruminative Response Scale (Dutch translation; Raes, Hermans et al. 2003), a 26-item, 4-point scale, self-report questionnaire designed to measure ruminative thought in response to (recalled) moments of feeling 'sad, down or depressed'. It consists of two subscales: reflection and brooding. Internal consistencies vary from .72 to .77 and test-retest reliabilities vary from .60 to .62 (Treynor, Gonzalez et al. 2003). Rumination seems to be sensitive to change in mindfulness-based interventions (Van Aalderen, Donders et al. 2012).

Experiential avoidance will be measured using the Dutch version of the Acceptance and Action Questionnaire (AAQ-II; Jacobs, Kleen et al. 2008), a 7-item questionnaire scored on a 7-point scale. Internal consistency is good (Cronbach's alpha of .89) and convergent validity with the BDI-II is high (Jacobs, Kleen et al. 2008). Items examples include: 'My painful experiences and memories make it difficult for me to lead a valuable life' and 'I am afraid of my emotions'.

Fear of Compassion will be measured using the Fear of compassion of self-subscale of the Fears of Compassion Scales (Gilbert, McEwan et al. 2011). This subscale is a 15-item, 5-point scale which was tested on a student and therapist population (Cronbach's alpha respectively .92 and .85; (Gilbert, McEwan et al. 2011). Subscale item examples include: 'I feel that I don't deserve to be kind and forgiving to myself', 'I fear that if I become more self-compassionate, I will become a weak person' and 'Getting on in life is about being tough rather than compassionate'. As there was no Dutch version available, the list of items was translated and back translated by the authors. Discrepancies between original and translated version of the scale were discussed among the authors upon which a shared decision was made about the best translation.

Self-compassion will be measured using the Dutch version of the Self-Compassion Scale (SCS) (Raes, Pommier et al. 2011). The questionnaire consists of 26 items divided over 3 subscales: 1) self-kindness versus self-judgment, 2) common humanity versus isolation, and 3) mindfulness versus over-identification. On a scale of 1 to 5, participants indicate the extent to which they agree with statements such as: 'I try to be loving towards myself when I'm feeling emotional pain' (self-kindness), 'When things are going badly for me, I see the difficulties as part of life that everyone goes through (common humanity) and When I'm feeling down I try to approach my feelings with curiosity and openness' (mindfulness). Internal consistencies of the different subscales vary from .75 to .81 and test-retest reliabilities vary from .80 to .93 (Raes, Pommier et al. 2011). The SCS is sensitive to change in MBCT (Kuyken, Watkins et al. 2010).

Mindfulness skills will be measured using the Five Facet Mindfulness Questionnaire (FFMQ-NL; Baer, Smith et al. 2008), which has five subscales: observing, describing, acting with awareness, non-judging of inner experience and non-reactivity to inner experience. Internal consistencies of the different subscales vary from .72 to .93 (Baer, Smith et al. 2008). The FFMQ is sensitive to change in mindfulness-based interventions (Carmody and Baer 2008).

Positive affect will be measured using the Types of Positive Affect Scale (Gilbert, McEwan et al. 2008), an 18-item, 5-point scale which measures the extent to which participants find certain descriptions of positive affect characteristic to themselves. Factor analysis showed three types of positive affect: activated, relaxed and safe. Item examples include lively, tranquil, and secure, respectively. Internal consistency was good (Cronbach's alpha .83 for activated and relaxed affect, .73 for safe affect) and test retest reliability was good (for safe and activated) to moderate (for relaxed) (Gilbert, McEwan et al. 2008). As there was no Dutch version available, the list of items was translated in Dutch and translated back in English by the authors.

Quality of Life will be measured using the 26-item self-report WHO-QoL short version (WHO-QoL-bref; The Whoqol Group 1998), which measures subjectively experienced quality of life in four domains: physical, psychological, social, and environmental. Items are scored on a 5-point scale. The internal consistency is satisfactory to good, with an alpha of .80 for the domain physical health, .74 for psychological health and .66 for social relationships (Trompenaars, Masthoff et al. 2005).

Process measures

At the beginning of each session, participants will be asked to fill out weekly questionnaires, consisting of ten items: six items with the highest factor loading for each subscale of the SCS (Raes, Pommier et al. 2011), as well as two positive

and two negative items with the highest factor loadings from the PANAS (Thompson 2007).

Sample size

Based on our pilot study of MBCL in patients with recurrent depression with or without a current depressive episode (Schuling, Huijbers et al. 2017), we estimated the change in Beck Depression Inventory (BDI-II; Beck, Steer et al. 1996) scores in the intervention group to be four, with a standard deviation of nine. Using a two-sided alpha of 0.05 and a power of 80%, we would need 162 participants in total. However, using an ANCOVA analysis controlling for baseline levels and assuming the correlation between pre- and post-treatment measures to be 0.5 (Van Aalderen, Donders et al. 2012), we could adapt the analysis with the design factor $1 - r^2$ (Borm, Fransen et al. 2007), resulting in a required number of participants of 104. Based on the absence of drop-out in the pilot study, we anticipate possible drop-out to be no higher than 15% and therefore aim to recruit N=120 patients for the study.

Recruitment procedure

Baseline assessment

Patients with recurrent depression who previously participated in an MBCT course at our centre will be informed about the study by letter and invited to take part. Those interested will be invited for a research interview by the principal investigator, including questions about socio-demographic information, medical and psychiatric treatments over the past six months, medication and the extent to which participants are still practicing mindfulness. The SCID-I will be administered to assess the DSM-IV criteria for current depression, partial or full remission, number of previous depressive episodes and age of onset. All SCID-interviews will be conducted by the principal researcher (RS) who has received SCID training and is supervised by a consultant psychiatrist (AS). A subset of SCID-interviews will be audio taped and rated by a second, independent senior researcher to establish inter-rater reliability. In addition, patients will be requested to fill out a set of questionnaires, including the Childhood Trauma Questionnaire (CTQ; Bernstein and Fink 1998), which assesses childhood trauma in terms of sexual and physical abuse, and emotional neglect.

Randomization

Those eligible for the study will be asked to sign the informed consent form and are subsequently randomized to MBCL+TAU or TAU only. Randomization will take place by a computerised programme, designed by an independent statistician. The Randomization will be in blocks of four and minimized for presence, partial

Table 2 Schedule of enrolment, interventions, and assessments

		STUDY PERIOD			
	Enrolment	Allocation	Post-allocation		
TIMEPOINT	$-t_1$	0	t_1	t_2	t_3
ENROLMENT:					
Eligibility screen	X				
Informed consent		X			
Allocation		X			
INTERVENTIONS:					
[MBCL+TAU		♦———	♦		
[TAU]		♦———	♦		
ASSESSMENTS:					
Baseline demographics		X			
CTQ		X			
BDI-II		X	X	X	X
SCID-I*		X	X	X	X
RRS		X	X	X	X
AAQ-II		X	X	X	X
FoCS		X	X	X	X
TPAS		X	X	X	X
SCS		X	X	X	X
FFMQ		X	X	X	X
WHO-QoL-BREF		X	X	X	X
Calendar (mindfulness adherence)			X	X	
CSRI (use of health care service)		X	X	X	X

t_1 end-of-treatment intervention group / end-of-control control group
t_2: follow-up intervention group / end-of treatment control group
t_3: follow-up control group
* Module depression (current and/or in the past)
CTQ: Childhood Trauma Questionnaire; BDI-II: Beck depression Inventory-II; SCID-I: Structured Clinical Interview Diagnostics part I; RRS: Ruminative Response Scale; AAQ-II: Acceptance and Action Questionnaire-II; FoCS: Fear of Compassion Scale; TPAS: Type of Positive Affect Scale; SCS: Self-compassion scale; FFMQ: Five Facet Mindfulness Questionnaire; WHO-QoL-BREF: World Health Organisation Quality of Life short form; CSRI: Client Service Receipt Inventory

or full remission of depressive disorder, age of onset, total number of previous depressive episodes (1-2; 3-4; or >5) and presence or absence of either physical or sexual abuse during childhood. After Randomization, the principal researcher will inform the participants of the condition they are allocated to.

Blinding

As in most psychological intervention studies, it will be impossible to blind the participants to the intervention they receive. As the principal investigator will be involved in the coordination of the trial, she will not be able to be blind to the assignment of participants either. However, the primary outcome measure and most of the secondary outcome measures are self-report questionnaires which do not involve an assessor at all. The training groups will consist of a mixture of patients allocated to the intervention and patients allocated to the TAU condition participating in the MBCL after completion of the control period. The MBCL teachers will be blinded to who belongs to which group.

Follow-up assessments

End-of-treatment/control assessments will place at the end of the intervention/control period. After that, those assigned to the TAU condition will be offered to participate in MBCL. After the TAU group has completed MBCL, they will also have their end-of-treatment assessment. Both those initially assigned to MBCL and those participating in MBCL after the control period will have a follow-up assessment six months after completion of treatment. At end of treatment and six months follow-up, a standardized psychiatric interview will take place (SCID; First, Gibbon et al. 1996), and health care use since last assessment will be collected for each individual patient using an adapted version of the Client Service Receipt Inventory (CSRI; Thornicroft 2001). Patients will also be asked to complete another set of self-report questionnaires online. A purposive sample of participants will be asked to participate in one-on-one, in-depth interviews about their experiences with MBCL.

Potential harms and dropout

When receiving an indication of harm by the principal investigator or MBCL teachers, contact will be made with the participant to assess the nature of the problem, after which it will be reported to the Medical Ethical Committee appointed to the study. In case of dropout from the intervention, the participants will be asked to state his/her reasons to assess whether the intervention has brought harm to the participant. Subsequently, they will be requested to nevertheless complete the follow-up assessments as the study will be analysed on an intention-to-treat basis.

Statistical analysis

All analyses will be carried out using both intention to treat (primary) and per protocol samples (secondary). We will use multiple imputation with regard to missing data, and conduct sensitivity analyses using other reasonable scenarios for imputation. Post-treatment BDI-II scores will be compared between the two groups, controlling for baseline levels. All analyses are performed using ANCOVA. A Cohen's *d* effect size will be calculated. SPSS package 20.0 will be used for analyses and graphs.
Results will be reported in accordance with CONSORT guidelines (Schulz, Altman et al. 2010). The one-on-one, in-depth interviews will be analysed using Grounded Theory (Corbin and Strauss 1990).

In addition to the effectiveness of the MBCL, we will explore possible moderators of treatment effects, such as number of previous episodes (Teasdale, Segal et al. 2000, Ma and Teasdale 2004), childhood adversity (Bernstein and Fink 1998), and early age of onset (Bockting, Hollon et al. 2015). As a 'rule of thumb', the number of moderators we will explore will not exceed one per ten participants. In terms of mediation of treatment effect, we will look at possible mediators as adherence to the program, self-compassion, rumination, experiential avoidance and mindfulness (Gu, Strauss et al. 2015, van der Velden, Kuyken et al. 2015). For the mediation analysis, we will follow the recommendations of Preachers and Hayes for multiple mediation models (Preacher and Hayes 2008), whose bootstrapping method can be used on relatively small sample sizes.

Qualitative study

Lastly, in order to gain more insight into the possible additional value of compassion training after MBCT, we will conduct a qualitative study using one-on-one, in-depth interviews with a purposive sample of the participants. We aim to interview a sample that is as diverse as possible in terms of gender, age and current depressive disorder, and aim to include both completers and non-completers of the intervention. We will analyse the interviews using the constant comparative method in order to be able to establish Grounded Theory (Corbin and Strauss 1990). In this method, it is common to include as many participants as is necessary to reach saturation on the subject of the research question, i.e. we will keep on interviewing participants until no more new information is being brought forward by them on the added value of MBCL over MBCT alone. We expect to be interviewing between fifteen and 25 people.

Data monitoring

The data will be monitored in a number of ways: a random subsample (N=30) of the SCID-interviews will be rated by an independent, senior researcher to assess inter-rater reliability. All MBCL sessions will be recorded on DVD, of which two random sessions per teacher will be reviewed by both the principal researcher and an independent experienced MBI teacher to assess therapist competency and adherence to the MBCL curriculum adherence. All statistical analyses will be reviewed by an independent statistician. No interim analyses will be performed. Lastly, all data collection and analysis will be done independently from the fund that financially supported the trial.

Discussion

To our knowledge, this is the first RCT investigating the effectiveness of compassion training in patients with recurrent depression. Therefore, we have chosen to compare the intervention with TAU. We are aware that this design does not allow us to draw any conclusions about the specificity of compassion training over and above non-specific therapeutic factors such hope, rationale, therapeutic relationship and peer support. Due to the fact that we did not want to disappoint the patients who were interested in participating in the compassion training, we have chosen to offer patients randomized to the TAU condition to participate in the training after the end-of-control assessment. In this way, we have to examine the consolidation of treatment effect in an uncontrolled rather than a controlled sample. Recruitment of the trial started July 2013 and ended December 2014. All data have been collected, the follow-up data on the last cohort of participants was collected in November 2015. Data analysis is currently in progress.

If the findings of this first study are positive, a replication RCT with an active control condition and a longer follow-up period of one year is warranted. Also, future research will be needed to look at the best implementation of compassion training, i.e. should it indeed be a follow-up to a mindfulness-based intervention (MBI) like MBCT, should it be incorporated in existing MBIs or may it even be added to the list of existing MBIs as a stand-alone intervention?

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Competing interests
The clinical research team declares it had no part in developing the MBCL program, though Dr Speckens and Ms Schuling made modifications to it in collaboration with the original developers following the pilot study (Schuling, Huijbers et al. 2017). The team does not gain income from the sale of books on MBCL, nor does it gain income from giving lectures or workshops about it. Dr Speckens is founder and clinical director of the Radboud UMC Centre for Mindfulness. Ms Schuling, Dr Van Ravesteijn and Dr Huijbers are affiliated with the Radboudumc Centre for Mindfulness. Dr Kuyken is director of the Oxford Mindfulness Centre. Dr. Donders is part of the Radboudumc Department for Health Evidence and declares no competing interests.

Author's contributions
All authors contributed to the design of the study. AS is the principal investigator of the study. RS, MH and AS drafted the paper, which was added to and modified by HR, RD and WK. RS, HR and AS were involved in recruiting participants. RD contributed specifically to the statistical analysis plan. All authors read and approved the final manuscript.

Ethics, consent and permissions
All participants signed a patient consent form, consenting to participation in the research and giving permission to obtain data during research and using it in publication after anonymization.

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4

Recovery from recurrent depression: Randomized controlled trial of the efficacy of Mindfulness-Based Compassionate Living compared with treatment-as-usual on depressive symptoms and its consolidation at longer term follow-up

Schuling, R., Huijbers, M.J., Van Ravesteijn, Donders, A., H., Cillessen, L., Kuyken, W., & Speckens, A.E.M. (2020). Recovery from recurrent depression: Randomized controlled trial of the efficacy of Mindfulness-Based Compassionate Living compared with treatment-as-usual on depressive symptoms and its consolidation at longer term follow-up. *Journal of Affective Disorders, 273, 265-273.*

Abstract

Introduction: Mindfulness-Based Cognitive Therapy (MBCT) has been shown to reduce depressive symptoms in patients with recurrent or chronic depression. However, sequential, follow-up interventions are needed to further improve outcome for this group of patients. One possibility is to cultivate mechanisms thought to support recovery from depression, such as (self-)compassion. The current study examined the efficacy of mindfulness-based compassionate living (MBCL) in recurrently depressed patients who previously received MBCT, and consolidation effects of MBCL at follow-up.

Methods: Part one is a randomized controlled trial (RCT) comparing MBCL in addition to treatment as usual (TAU) with TAU alone. The primary outcome measure was severity of depressive symptoms. Possible mediators and moderators of treatment outcome were examined. Part two is an uncontrolled study of both intervention- and control group on the consolidation of treatment effect of MBCL over the course of a 6-months follow-up period.

Results: Patients were recruited between July 2013 and December 2014 (N = 122). MBCL participants (n = 61) showed significant improvements in depressive symptoms (Cohen's d = 0.35), compared to those who only received TAU (n = 61). The results at 6-months follow-up showed a continued improvement of depressive symptoms.

Limitations: As MBCL was not compared with an active control condition, we have little information about the possible effectiveness of non-specific factors.

Conclusion: MBCL appears to be effective in reducing depressive symptoms in a population suffering from severe, prolonged, recurrent depressive symptoms. To optimise the (sequential) treatment trajectory, replication of the study in a prospective sequential trial is needed.

Registered at ClinicalTrials.gov: NCT02059200

Introduction[2]

Major depressive disorder (MDD) is characterised by persistent symptoms and high relapse rates (Mueller et al., 1999). Mindfulness-based cognitive therapy (MBCT) has been demonstrated to reduce the risk of a relapse/recurrence in patients with recurrent depression in remission in a 60-week follow-up period by 31% (Kuyken et al., 2016). Given their high psychological, social and economic burden as well as their predictive value in terms of relapse, the treatment of current depressive symptoms is also very important (Hardeveld, Spijker, De Graaf, Nolen, and Beekman, 2010). A growing number of studies indicate that MBCT may also be effective in decreasing depressive symptoms in patients with current depression (Strauss, Cavanagh, Oliver, and Pettman, 2014). However, residual symptoms seem to remain considerable even after MBCT (Piet and Hougaard 2011), leaving substantial room for further improvement.

Reduction of rumination is one of the most established working mechanisms of MBCT. A meta-analysis by Van der Velden et al. (n=23; 2015) reported that alterations in rumination, worry and meta-awareness were associated with, predicted or mediated MBCT outcome. However, not only reduction in rumination and increase in mindfulness skills were demonstrated to be mediators of treatment outcome, also compassion. Since one of the possible underlying mechanisms for the chronic and recurrent nature of MDD is low self-esteem or self-denigration (Gilbert and Procter, 2006), the finding that compassion mediates MBCT's treatment effect is interesting. Being able to adopt a caring attitude towards the self might be a skill that could help reduce the undermining mechanisms of self-criticism and hence reduce the vulnerability to recurrence or persistence of depressive symptoms. As self-compassion is taught mostly implicitly in MBCT (Segal et al., 2012), the explicit cultivating of self-compassion may pay a complementary contribution to reduction of rumination and increase in mindfulness skills in the prevention of depressive relapse or recurrence, or reduction of depressive symptoms.

To this end, Van den Brink and Koster (2015) developed mindfulness-based compassionate living (MBCL), a training to cultivate compassion in patients who previously participated in MBCT. The advantage of offering MBCL as a follow-up to MBCT is that participants have already laid the foundation of non-judgmental, present-moment awareness before exposing themselves more actively to difficult, painful experiences with a (self)compassionate attitude. A first pilot study on MBCL in patients with a variety of psychiatric disorders

2 MBCT: Mindfulness-based Cognitive Therapy; MBCL: Mindfulness-based Compassionate Living; RCT: Randomized controlled trial; TAU: Treatment-as-usual.

who previously followed mindfulness-based stress reduction (MBSR) or MBCT showed a reduction in depressive symptoms and increases in both mindfulness and self-compassion skills (Bartels-Velthuis et al., 2016). A pilot study of our own group showed that MBCL appeared to be feasible and acceptable in 17 patients with recurrent depression who previously followed MBCT, and demonstrated some preliminary improvements of depression and self-compassion (Schuling et al., 2017). The pilot was primarily focused on facilitators and barriers of MBCL, which helped us tailor it to our population by using a qualitative co-creation design.

Offering MBCL after MBCT could be conceptualised as a sequential treatment. Sequential treatment designs are more commonly known in both pharmacological treatments of depression (Popova, Daly et al. 2019) and the combination of pharmacotherapy and psychological treatment (Cuijpers, Noma et al. 2020). In contrast, MBCT and MBCL are both psychological treatments.
Targeting depressive symptoms with a double or sequential treatment has particular advantages: it allows randomization of patients to treatment alternatives according to stages of development of their illness and not simply to disease classification. The model is thus more in line with the chronicity of mood disorders compared to the standard randomized controlled trial, which is based on the acute disease model (Fava and Tomba 2010). In addition, sequential treatment seems to be more effective than single treatments (Cuijpers, Noma et al. 2020). Given the percentage of people that doesn't improve with a primary treatment, using additional treatment in a sequence seems a fruitful approach. One option is to follow a pragmatic approach, offering the second treatment to a population that has already followed the first (Daly, Singh et al. 2018). Ideally however, the efficacy is tackled by a prospective study offering both treatments in sequence to a population that has received neither before (Popova, Daly et al. 2019). As little is known about MBCL efficacy in patients with recurrent depression, we decided to use the pragmatic approach by offering MBCL to a population that had previously followed MBCT.

In this paper, two studies are reported. Study 1 is an RCT comparing MBCL and TAU in their efficacy to further reduce depressive symptoms in patients with recurrent depression who previously participated in MBCT. As secondary outcomes in the RCT we assess current depression status, rumination, self-compassion, mindfulness and quality of life. We also examine possible mediators and moderators of treatment outcome. Study 2 is an uncontrolled follow-up study of both the original MBCL condition and the patients who were offered MBCL after completion of TAU to investigate the consolidation of treatment outcome using the same outcome measures.

Method - Study I

Study design

The first study was a parallel-group RCT, in which patients who had previously participated in MBCT were randomized to MBCL combined with TAU or TAU alone. Assessments took place at baseline and after treatment (four months after baseline). The study was carried out at the Radboudumc Centre for Mindfulness in the Netherlands, from July 2013 to April 2015, with follow-up assessments continuing until November 2015. The protocol was approved by the ethical review board CMO Arnhem-Nijmegen (2013/220) and published (Schuling et al., 2016). The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Participants

The study population consisted of adults (>=18 years of age) who had been diagnosed with recurrent depressive disorder at the Radboudumc and had previously participated in an MBCT course at the same institute (>=4 sessions, at least one year prior to this study). Patients were invited to participate by letter. If interested, they were invited for a research interview, during which the in- and exclusion criteria were assessed (cf. trial design and protocol paper; Schuling et al 2016). In case of eligibility, written informed consent was obtained, after which relevant socio-demographic data were collected, including the Childhood Trauma Questionnaire (CTQ) (Bernstein and Fink, 1998), and participants were randomized. Both intervention and control group completed a post-treatment at four months after baseline.

Randomization and masking

Randomization to the two conditions was performed on a 1:1 ratio using a website-based application, developed specifically for this study by an independent statistician. The randomization took place in blocks of four minimizing for the following variables: depression status (current depression/ partial remission/full remission), age of onset (<21/ 21-30/ 31-38/ >39), number of episodes (1-2/ 3-4/ >5) and presence of childhood trauma in terms of physical or sexual abuse during childhood. Presence of trauma was operationalised as at least one item pertaining to physical or sexual abuse on the CTQ being answered positively. An example of such an item is: 'During my childhood, someone wanted me to perform sexual acts or watch sexual acts'.
Participants were informed about the condition they had been assigned to by the first author, who also conducted the post-treatment and 6-months follow-up assessments for which she consequently was not blinded.

Interventions

MBCT (prior to RCT)

Prior to participating in MBCL, all participants had followed MBCT, which was originally developed as a relapse prevention program for remitted patients (Segal et al., 2012). MBCT is an adaptation of MBSR, developed in the late 1970s for patients with chronic pain or medically unexplained symptoms (Kabat-Zinn 1990). A frequently used definition of 'mindfulness' is paying attention in a particular way: on purpose, in the present moment, and non-judgmentally (Kabat-Zinn 1994) (p.4). MBCT is a group-based intervention consisting of eight 2.5-hour sessions and one 'day of silence' in the second half of the training (Segal 2012). Additionally, participants are encouraged to practice at home for 30 to 45 minutes a day. The practices consist of formal and informal techniques such as the 'body scan', sitting meditation, gentle movement based on hatha yoga, and the 'three-minute breathing space'. The mindfulness meditation techniques are combined with elements of Cognitive Behavioural Therapy (CBT). In contrast to CBT, MBCT aims to cultivate decentering, i.e. experiencing thoughts as activity in the mind, by focusing on the process of thinking rather than the content of negative thoughts. Implicitly, a friendly attitude towards this process is encouraged. Group inquiry, which is part of the programme, is also geared towards this.

MBCL

Based on the pilot study, MBCL was delivered as a group-based intervention consisting of eight 2.5-hour sessions once every two weeks (Schuling et al., 2017). The format of the programme was similar to MBCT, containing a mixture of mindfulness practice, group inquiry and didactic and interactive teaching. Patients were invited to practice at home for about 30 minutes on a daily basis, supported by CDs. A more elaborate description of the intervention is provided in both our pilot study (Schuling et al., 2017) and published protocol (Schuling et al., 2016).

MBCL was delivered in groups of about 8-10 participants taught by one of two teachers. Both teachers met the Good Practice Guidelines for teaching mindfulness-based courses by the UK Network for Mindfulness-Based Teacher Training Organizations (Crane et al., 2013) and had been trained to teach MBCL by its developers Koster and Van den Brink. Treatment integrity and therapist competence was assessed by two experienced, independent raters as competent, based on two randomly selected videotapes of each teacher using the mindfulness-based intervention teacher assessment criteria (MBI:TAC) (Crane et al., 2013)

TAU

In our study, TAU consisted of all medical and psychological treatments received between baseline and post-treatment (four months), which were recorded using the TIC-P (Hakkaart-van Roijen, Van Straten et al. 2002).

Outcome measures

All measures are described extensively in Schuling et al. (2016). The primary outcome measure was severity of depressive symptoms, measured by the Beck Depression Inventory-II (BDI-II-NL) (Van der Does, 2002). It contains 21 items, scored on a 0-3 scale and its internal consistency was 0.90. Depression status in terms of current depression, partial or full remission was assessed with the Structured Clinical Interview for DSM-IV disorders (SCID), part 1 (First et al., 1996), by a trained assessor. All interviews were audio taped and a random sample of N=30 interviews was second-rated by an independent and blind assessor to assess inter-rater reliability. The agreement between first and second ratings was found to be moderate (kappa (κ) = 0.60, 95% CI = 0.45 to 0.76, p = .000) (McHugh 2012), the percentage of agreement was 87%. Rumination was assessed with the brooding subscale of the Ruminative Response Scale (Raes, Hermans, and Eelen, 2003). We selected the brooding subscale because over time, brooding has been related to higher levels of depression, whereas the reflection subscale has been linked to lower levels of depression (Treynor, Gonzalez et al. 2003). The internal consistency was 0.63. Self-compassion was measured using the Self-Compassion Scale (Raes, Pommier, Neff, and Van Gucht, 2011). The internal consistency was 0.93. Mindfulness skills were measured using the Five Facet Mindfulness Questionnaire (FFMQ-NL) (Bohlmeijer, Peter, Fledderus, Veehof, and Baer, 2011). The internal consistency was 0.91. Quality of life was measured using the 26-item self-report WHO-QoL short version (WHO-QoL-bref) of the WHO-QoL group (1998). Items are scored on a 5-point scale. The internal consistency was 0.92.

As described in our protocol (Schuling, Huijbers et al. 2016), all measures (including the SCID) were assessed at baseline, at post-treatment four months after baseline, and at follow-up six months after completion of the treatment.

Statistical analysis

A total of 104 participants (52 per group) was needed to demonstrate a difference of minus four on the Beck Depression Inventory, with a power of 0.80 and alpha of 0.05 (Schuling et al., 2016). Taking account of possible dropout, we aimed to recruit N=120 patients for the study.

Analysis of the efficacy of MBCL

We report intention-to-treat (ITT) analyses based on complete cases in terms of assessments. In line with the protocol, we used ANCOVA analyses to compare post-treatment scores on all measures between the two groups, controlling for baseline levels. We also entered the minimization criteria used for randomization, i.e. depression status, age of onset, number of previous episodes and presence of childhood trauma, as covariates. Additionally, a Cohen's d type effect size was calculated for each measure, by dividing the (adjusted) mean difference at post-treatment by the pooled standard deviation at pre-treatment for each measure.

We used multiple imputation modelling as a sensitivity analysis, creating ten imputed datasets based on the minimization criteria, sex, age and the primary and secondary outcome measures. We then ran an ANCOVA on the imputed datasets using the minimization criteria as covariates, analogous to our main analysis.

Mediation analysis

In line with the protocol, we conducted the mediation analyses following the recommendations of Preacher and Hayes (2008) for multiple mediation models. In all mediation analyses, severity of depressive symptoms at post-treatment was controlled for baseline levels. Standardised residualized change scores for all potential mediators (rumination, self-compassion and mindfulness) were calculated (MacKinnon, 2008). We first assessed the indirect effect of all potential mediators using a univariate model and, if shown to be a mediating factor, they were entered into a multivariate model in order to assess their possibly independent contribution. A nonparametric bootstrapping method was used to assess the indirect effect based on 5000 bootstrapped samples using bias corrected and accelerated 95% confidence intervals (BCa CI) as provided by Hayes (2017) [SPSS PROCESS macro version 3.3].

Moderation analysis

All moderation analyses were performed on severity of depressive symptoms at post-treatment, using residualized change scores. Moderation analyses were performed using univariate analyses of variance (ANOVA) for a) age, b) gender, c) diagnostic status for MDD (current depression /full remission), d) number of previous episodes (1-2/ 3-4/ 5+), e) age of onset (0-20/ 21-30/ 31-38/ 39+) and f) presence of childhood trauma (considered present when at least one item of the CTQ pertaining to physical or sexual abuse was answered positively). The analyses were performed for each moderator separately, using condition, the moderator and the interaction term condition x moderator.

Method - Study II

Design

The second study is an uncontrolled follow-up study of the combined sample of the patients in the initial MBCL group and those who received MBCL after having completed the TAU period of four months in the control condition. In this study, we used the end-of-control assessment as baseline for the participants who had been randomized to TAU only. Further assessments for this study took place after treatment and at six months after completion of treatment. All RCT outcome measures were used in this study as well.

Statistical analysis

Consolidation of treatment outcome at 6-months follow-up

Linear mixed effect models were used to analyse consolidation of treatment effects on the primary and secondary outcome measures in the combined ITT sample. We also report the within group effect size for both the pre- to post-treatment and the 6-months follow-up period. Separate models were run for each of the outcomes, in which the particular outcome measure was used as dependent variable. Time (post-treatment/follow-up) was used as within subject factor, and the baseline assessment was added as covariate, to control for baseline severity. We used the post-TAU scores of the TAU alone group as baseline assessment for the follow-up study, as these were closer in time to the start of MBCL. There were no differences between pre-and post-TAU scores in the TAU alone group. A random intercept for participants was added to account for dependency in the data due to repeated assessments. We used a restricted maximum likelihood estimation, as this estimation methods deal effectively with missing data (Newman, 2014) and we used a diagonal covariance structure.

Results - Study I

Participant flow and characteristics

A total number of 122 patients were included in the study (MBCL+TAU: n=61, TAU: n=61; cf. figure 1a for a detailed description of the patient flow). The average time elapsed since participating in MBCT was 4,1 years for the MBCL group vs. 4,5 for the TAU group (range 1-7 years). In total, 11 groups were delivered, containing an average of 5,5 MBCL + TAU participants per group. The first group only contained MBCL + TAU participants, after this groups were mixed between MBCL + TAU and TAU only participants. Therefore TAU only participants received MBCL in ten groups, averaging 6.1 participants per group.

Average attendance for the MBCL group was 6,1 sessions (SD: 2,4). Participant demographic and clinical characteristics for both the RCT and the combined follow-up sample are detailed in table 1.
No differences in percentage of patients using health care services during the intervention period were observed between the two conditions (see Table 2). However, with the exception of their general practitioner, TAU participants paid significantly more visits to all health care providers than MBCL participants.

Efficacy of MBCL

The ITT analysis based on complete cases showed that the MBCL group had less depressive symptoms after MBCL than the TAU group (d=0.35; p=.034). The results correspond with a number-needed-to-treat of 5. As we did not find any baseline differences between those who completed the post-treatment assessments and those who did not, the sensitivity analyses were conducted with the assumption that missing data (7.4%) were missing at random (MAR). Multiple imputation analysis showed a significant reduction in depressive symptoms in seven of the ten imputed datasets.
In the MBCL condition, 36,7% of the MBCL participants was depressed at baseline and 24,5% at post-treatment. In the TAU group, 29,3% was depressed at baseline and 40,7% at post-treatment. These percentages did not differ significantly between the groups (p=.074).
Table 3 shows all other secondary outcomes at post-treatment. We found a significant reduction in rumination in the MBCL compared with the TAU group (d=0.38, p=.011). In addition, MBCL was associated with significant improvements in self-compassion (d=0.41; p=.002), mindfulness skills (d=0.39; p=.004), and quality of life (d=0.63; p=.000).

Mediation of MBCL's effect

For the reduction in depressive symptoms, the univariate analyses showed a mediating role for rumination, self-compassion and mindfulness skills. In the multivariate model, only self-compassion remained a significant mediator (cf. figure 2).

Moderation of MBCL's effect

Only age and age of onset appeared to be moderators of treatment outcome, i.e. those who were younger or had an earlier age of onset benefited more from MBCL (Cohen's d=0.56, p=.004 and Cohen's d=0.40, p=.040 respectively). Presence of childhood trauma appeared not to be a moderator of treatment outcome.

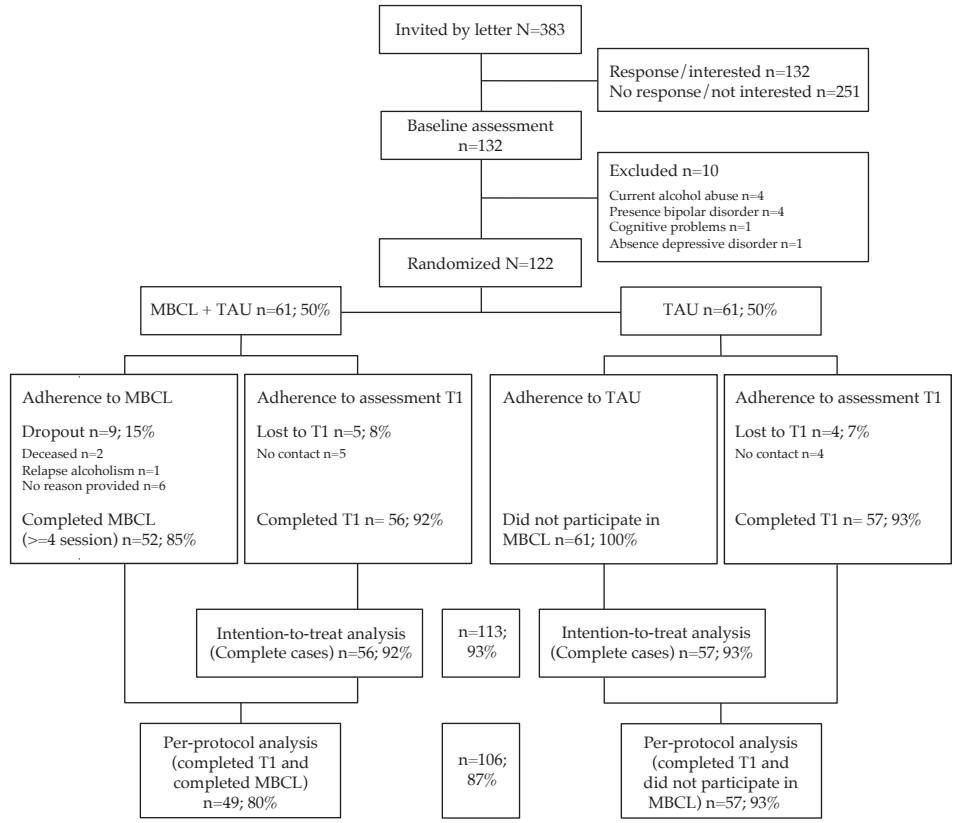

Figure 1a RCT CONSORT diagram: Flow of participants from screening to analysis, comparing MBCL+TAU to TAU alone. MBCL: Mindfulness based compassionate living; TAU, Treatment-as-usual; T1, end-of-treatment / end-of-control assessment.

Adverse events

Two patients randomized to the intervention group unfortunately died by suicide. Both were randomized into the MBCL condition. As one suicide occurred before the start of MBCL, and the other after one session only, the medical ethical committee of the region Arnhem-Nijmegen considered the events to be unrelated to the patients' participation in the study.

Table 1 Baseline demographic and clinical characteristics of participants[a] in the RCT sample (MBCL added to TAU and TAU only) and the FU sample (the joint follow-up sample).

Variable	MBCL (N=61)	TAU (N=61)	FU (N=122)
Female	47 (77%)	44 (72.1%)	91 (74.6%)
Age (years) mean ± SD	55.9±8.7	55.3±12.4	55.6±10.6
Educational level			
Low	3 (4.9%)	5 (8.2%)	8 (6.6%)
Middle	48 (78.7%)	38 (62.0%)	86 (70.5%)
High	9 (14.8%)	14 (23.0%)	23 (18.9%)
Marital status			
Married/cohabiting	38 (62.3%)	38 (62.3%)	76 (62.3)
Divorced/widowed	9 (14.8%)	6 (9.8%)	15 (12.3)
Single	13 (21.3%)	13 (21.3%)	26 (21.3%)
Employed	33 (54.1%)	30 (49.2%)	63 (51.6%)
Current ADM use	27.0 (44.3%)	30.0 (49.2%)	57 (46.7%)
Three or more previous episodes[b]	53.0 (86.9%)	53.0 (86.9%)	106 (86.0%)
Age at MDD onset[b] (years) mean ± SD	23.8±11.2	26.3±13.0	25.0±12.2
Presence of childhood trauma[c]	27.0 (44.3%)	26.0 (42.6%)	53 (43.4%)
Time since MBCT[d] (years) mean ± SD	4.1±1.9	4.5±1.8	4.3±1.9
Depressive symptoms (BDI-II) mean ± SD	17.8±10.4	15.8±11.2	16.8±10.8
Current depression (SCID-I)	20.0 (32.8%)	17.0 (27.9%)	37 (30.3%)

ADM: Anti-depressant medication; BDI-II: Beck Depression Inventory; FFMQ: Five Facet Mindfulness Questionnaire; FU: follow-up; MBCT: Mindfulness-Based Cognitive Therapy; MDD: Major depressive disorder; RCT: randomized controlled trial; RRS-brood: Ruminative Response Scale, subscale brooding; SCID-I: Structured Clinical Interview for DSM-IV Axis I disorders part I; SCS: Self-Compassion Scale; SD: Standard deviation; TAU: treatment-as-usual; WHOQOL-Bref: World Health Organization Quality of Life- abbreviated version.

[a] Other nationalities: German (3), Belgian (3), French (2), Czech (1). All were fluent in Dutch.

[b] Based on self-report.

[c] Presence of physical or sexual abuse as measured by the physical and sexual abuse subscales of the childhood trauma questionnaire (Bernstein and Fink, 1998).

[d] Five participants had attended MBCT twice in the past.

Table 2* Utilisation of usual care, other than trial intervention, in the Mindfulness-Based Compassionate Living and Treatment As Usual group from baseline measurement to post-treatment.

Type of care	MBCL N=21[a] (35%)		TAU N=30[a] (48%)			
	Users; N (%)	Mean nr of visits[b] (SD)	Users; N (%)	Mean nr of visits[b] (SD)	P_{users}	P_{visits}
General practitioner	15 (71%)	1.4 (0.9)	23 (77%)	1.9 (1.0)	.458	.710
Psychiatrist	3 (14%)	0.7 (1.7)	8 (27%)	1.6 (2.7)	.241	.001
Psychologist/psychotherapist	3 (14%)	1.1 (2.8)	7 (23%)	3.0 (5.5)	.334	.000
Other[c]	14 (67%)	5.6 (4.0)	19 (63%)	6.1 (4.7)	.523	.045
Hospitalisation[d]	1 (5%)	n.a.	0 (0%)	n.a.	.412	n.a.
General outpatient care	7 (33%)	0.9 (1.2)	16 (53%)	1.0 (0.9)	.130	.003
(m)ADM	11 (52%)	n.a.	16 (53%)	n.a.	.586	n.a.

*This table serves only to compare TAU for both arms of the study, therefore information on MBCL is excluded.

[a] Due to a technical-procedural error not all TAU was assessed during the intervention period. Data were available for 21 (35%) of participants in MBCL and for 30 (48%) in TAU.

[b] Calculated for the group of users.

[c] Including physiotherapist, acupuncturist etc.

[d] Dep. of gynaecology

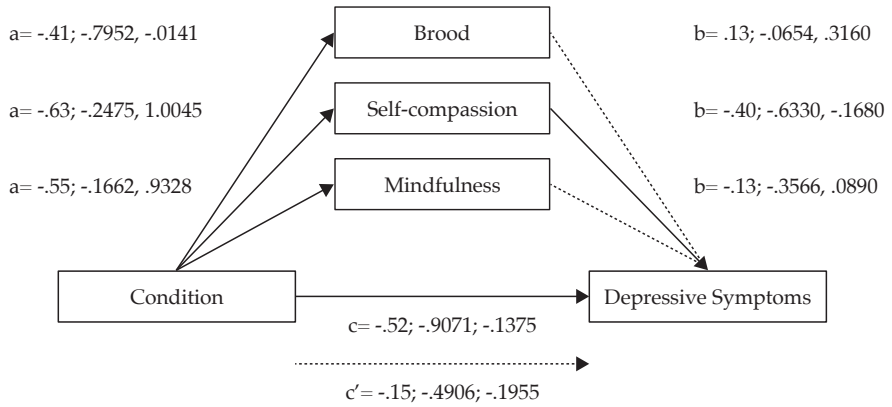

Figure 3 Multivariate mediation of treatment outcome in depressive symptoms.

Table 3 Post-treatment levels of depressive symptoms, quality of life, rumination, self-compassion skills and mindfulness skills after Mindfulness-based compassionate living (MBCL) or Treatment-as-usual(TAU), controlling for baseline levels of depression.

	Mean (SD)						
	MBCL (n=56)		TAU (n=57)		Group difference		
	Pre	Post	Pre	Post	(95% CI)[a]	p	d
Primary measure							
BDI-II	17.79 (10.42)	13.77 (10.63)	15.80 (11.18)	15.68 (11.64)	-3.75 (-7.21 to -0.29)	.034	0.35
Secondary measures							
RRS-Brood	11.61 (3.05)	10.70 (3.01)	11.90 (2.95)	11.93 (2.70)	-1.15 (-2.003 to -0.27)	.011	0.38
SCS	21.31 (6.18)	24.47 (5.84)	20.52 (5.70)	21.83 (5.67)	2.43 (0.93 to 3.93)	.002	0.41
FFMQ	122.52 (16.99)	128.31 (20.0)	119.97 (19.22)	120.65 (20.86)	7.12 (2.30 to 11.95)	.004	0.39
QoL-bref	87.12 (14.20)	93.17 (14.57)	90.05 (14.71)	87.11 (15.94)	9.05 (4.86 to 13.23)	.000	0.63

BDI-II: Beck Depression Inventory; RRS: Ruminative response Scale; SCS: Self-Compassion Scale; FFMQ: Five Facet Mindfulness Questionnaire; WHO-QOL-Bref: World Health Organization Quality of Life- abbreviated version; PP: per protocol.

[a] Corrected for baseline values

Results - Study II

Participant flow and characteristics

From the 61 patients assigned to the control group, n=57 (93%) accepted the invitation to participate in the MBCL after completion of the TAU period. So, the combined sample of both the original MBCL group and the patients who received MBCL after the TAU group was N=119. Average attendance overall was 6,2 sessions (SD: 2,4). The flow of participants from RCT to the 6-months follow-up is presented in figure 1b. The baseline characteristics of the combined group can be found in Table 1.

Change of primary and secondary outcome measures

From start-of-treatment to end-of-treatment we found no reduction in depressive symptoms in the combined sample (within-groups effect size d=0.41, p=.064). A significant difference in diagnostic status for MDD was found in the combined sample: 33,1% was depressed at baseline and 25,7% at post-treatment (p=.002). We observed improvements from pre- to post-treatment in all other outcomes except quality of life. The results are presented in Table 4.

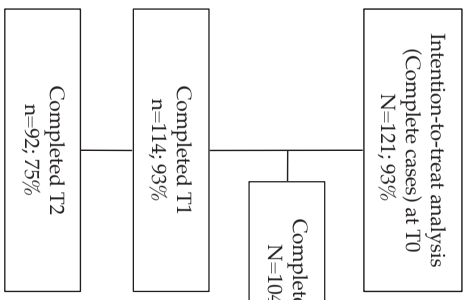

Fig.1b 6-months follow-up CONSORT diagram: MBCL, Mindfulness based compassionate living; TAU, Treatment-as-usual; T1, end-of-treatment / end-of-control assessment; T2, 6-months follow-up assessment.

Table 4 Means and standard deviations of uncontrolled follow-up data, and results of linear mixed effect models regarding consolidation effect (N=119).

	Pre-MBCL[a]	Post-MBCL	Follow-up	Pre- to post-MBCL analyses		Consolidation analyses[b]	
	M±SD	M±SD	M±SD	Cohen's *d*[c]	p	Cohen's *d*[c]	p
Depressive symptoms	16.76±10.98	14.75±11.09	11.39±11.39	0.42	.064	0.67	<.001
Brooding	11.78±2.87	11.35±2.91	10.73±2.96	0.30	.046	0.47	.137
Self-compassion	21.54±5.90	23.09±5.87	25.10±6.42	0.82	.000	0.74	<.001
Mindfulness	121.54±18.84	124.31±20.65	131.76±21.70	0.35	.026	0.79	<.001
Quality of life	87.18±14.91	90.02±15.35	93.51±17.30	0.22	.450	0.48	.011

[a] These baseline values reflect the baseline score for the MBCL group and the post-TAU score (pre-MBCL) for the TAU group.
[b] Linear mixed effect models to test the difference between post-MBCL and six-month follow-up, controlled for the baseline level before MBCL.
[c] Within groups.

Consolidation of treatment outcome at 6-months follow-up

In the combined sample, there was a significant decrease in the primary outcome, severity of depressive symptoms, from post-treatment to follow-up (p=<.001, cf. table 4). Within group effect size (Cohen's d) for the combined population from post-treatment to follow-up was 0.67 and from pre-treatment to follow-up 1.07. In diagnostic status for MDD in the combined sample we found 36,0% was depressed at follow-up, this differed significantly from the post-treatment results (p=.044). We observed improvements from post-treatment to follow-up in all other outcomes except rumination (cf. table 4).

Discussion

Summary and comparison with the literature

The present study is the first trial examining the efficacy of MBCL in patients with recurrent depression, who previously followed MBCT. Our findings indicate that MBCL, offered as a sequential intervention to MBCT, results in a significant reduction of depressive symptoms at post-treatment (d=0.34), corresponding with a number-to-treat of five. Furthermore, we found a reduction of rumination and improvements in self-compassion, mindfulness skills and quality of life in MBCL versus TAU. In the follow-up study containing the combined population, we found a comparable effect size to the RCT study from pre- to post-treatment (Cohen's d of 0.41), though the difference was not significant. For the pre-treatment to follow-up period we found a large effect size: 1.07.

As MBCT is also known to reduce depressive symptoms and rumination, and increase mindfulness skills and self-compassion (Van Aalderen et al., 2012), the improvements observed in the MBCL group are noteworthy. In a group of patients with relatively severe symptoms, the large effect size for the improvement of quality of life is particularly encouraging. This improvement was larger than in a similar population treated with MBCT (Van Aalderen, Donders et al. 2012), using the same instrument. It is possible that the more active and explicit compassionate approach to difficult experiences in MBCL, compared with the more implicit focus on compassion in MBCT, is responsible for this difference.

As previously demonstrated for MBCT (Van der Velden et al., 2015), self-compassion appeared to be a mediator of treatment outcome of MBCL, lending support to self-compassion being the hypothesized working mechanism of MBCL. It is noteworthy that no mediation for rumination was found in MBCL, as it has been consistently found to be a mediator of MBCT (Van der Velden, 2015). This

suggests the working mechanisms of MBCL might be different and possibly complementary to those of MBCT. Furthermore, the program appeared most effective for those who were younger and/or had an earlier age of onset. This is partly in accordance with previous studies which have shown treatment outcome of MBCT to be moderated by variables related to an underlying vulnerability to depressive symptoms, such as childhood trauma, baseline severity of depressive symptoms, number of previous episodes and age of onset (Williams et al., 2014). However, in contrast with previous studies of MBCT (Kuyken et al., 2016), presence of childhood trauma did not moderate treatment outcome of MBCL. Rumination was not found to be a moderator of treatment outcome either, whereas in a sample of chronically depressed, treatment-resistant patients following MBCT, it was (Cladder-Micus, Speckens et al. 2018).

In the RCT part of the study, the comparison with the control group takes account of regression towards the mean. For the uncontrolled follow-up study, this might be a problem. But given the reduction of depressive symptoms during the treatment phase of the study, one would expect this to mitigate in the follow-up phase. In contrast, we actually observed a further reduction, which supports the findings of study I (RCT). As residual symptoms are an important predictor of depressive relapse and recurrence, this finding supports the potential clinical relevance of MBCL, and its possible influence on relapse rates. Furthermore, we found small improvements in rumination, self-compassion and mindfulness skills and a moderate increase in quality of life and in MBCL versus TAU. This observation of consolidation or further improvement over the course of follow-up rather than attenuation of treatment effect has in fact been demonstrated in earlier studies of MBIs for both patients with ADHD and cancer patients (Cillessen, Schellekens et al. 2018, Janssen, Kan et al. 2019), as well as patients suffering from recurrent depressive symptoms (van Aalderen, Donders et al. 2015). This may be due to the experiential rather than cognitive nature of both MBCT and MBCL, including regular practice, therefore having the potential to structurally change habitual patterns. This change may result in continued improvements over time.

Strengths and limitations

The main strengths of the current study are its adequate sample size, randomized controlled design and innovative nature, as this is one of the first studies investigating the efficacy of MBCL for patients with recurrent depression who previously followed MBCT. Though our approach to the sequential treatment design was pragmatic, the sequencing of MBCT and MBCL is another strength, given that such designs better fit the chronic, recurrent nature of depression (Cuijpers, Noma et al. 2020). Especially for patients suffering from relatively

severe symptoms, as in our sample, a sequential approach might prove more efficacious. Furthermore, inclusion of participants went smoothly and we had low levels of attrition, signalling that MBCL is not only acceptable to this population but even seems to meet a tacit need. In addition, we were able to work with teachers with long-standing experience, who were trained by the MBCL-developers themselves. Testing mediation is also a strength of this study, as it tells us something about the specificity of the efficacy of MBCL, and the study explored possible moderating variables that may influence the reduction in depressive symptoms. Additionally, we looked at the consolidation of treatment effect in an uncontrolled sample including participants from both intervention and control group, who received MBCL after completing the TAU alone period.

The pragmatic nature of the sequential treatment design is also one of the limitations of this study: participation was offered to all former MBCT participants who met the in- and exclusion criteria, so we did not, for example, select participants who did not remit after MBCT. In addition, the time elapsed between MBCT and MBCL varied greatly. Consequently, we do not have any information about a possible selection bias of the participants in the study: we have little insight into the characteristics of those who responded versus those who did not. In the previous MBCT trial, BDI-II levels had dropped from 14.9 to 10.3 during MBCT (Van Aalderen, Donders et al. 2012). However, a 2011 systematic review showed that even after MBCT, room for improvement remains (Piet and Hougaard 2011). So our population may have consisted of patients with remaining symptoms after MBCT, for whom MBCT might have been less effective. In addition, at the start of our current study, baseline levels of depression were even higher (BDI-II: 16,8), suggesting the study attracted patients in need of another treatment, who may have been interested in using MBCL to reconnect with the practices learned in MBCT.

Though our recruitment strategy, inviting MBCT participants with and without depression and using relatively few exclusion criteria, increases generalisability to the 'normal' clinical setting, a systematic, prospective sequential trial should be conducted, assigning patients to initial MBCT followed by MBCL or to initial MBCT only. This would help to gain more information about the proportion and characteristics of those patients who might benefit from additional MBCL in comparison with MBCT alone, and enable proper investigation of potential moderators.

It is also possible (part of) the effects of the trial might be due to a double dosage of treatments rather than to the effect of MBCL specifically. Additionally, we did not compare MBCL with an active control condition. Consequently, we have little information about the specificity of the treatment effect. To investigate both

double dosage and specificity, one might need to compare MBCL to a renewed course of MBCT.
Furthermore, it is possible that participants randomized to the control group suffered demoralization, causing their symptoms to worsen (Cunningham, Kypri, and McCambridge, 2013). In addition, letting patients in the control condition start MBCL after the TAU period, means the current study did not include a follow-up for the TAU condition. We therefore cannot compare the long-term follow-up results between both conditions: consequently, it is unclear how this population fares over time without being offered MBCL. Finally, the single-centre design might have reduced the generalisability of our findings so it will be important to replicate these findings in a multi-centre context.

Clinical and research implications

With regard to the clinical implications of our study, we must first address the two suicides that occurred in the initial phase of the RCT, even though they did not seem to be related to participation in the study. Based on our experience, even though the prevention of suicide cannot be guaranteed, we conclude that in this population active monitoring of suicidal ideation should take place at each study assessment. If patients express signs of increased suicide risk, the regular procedures, i.e. direct contact with the psychiatrist on duty or emergency unit, should be put in place.
Based on the current study, MBCL seems useful to implement as an additive approach to improve depression levels and quality of life. From a clinical perspective, however, offering MBCL as an additive treatment to MBCT has the disadvantage that only patients who have already followed MBCT can participate, and MBCT is not yet widely available. An alternative approach to the sequential treatment design would be to investigate whether MBCL might work better as a first step for patients with depression, or perhaps a subsample of them. For example, those with high levels of self-criticism might benefit from a more explicit approach to self-compassion early on. Especially in terms of cost-effectiveness, this approach would be another interesting avenue for future research. Additionally, cost-effectiveness is interesting to investigate further as MBCL participants made less use of health care services during MBCL, apart from general practitioners.
To optimise the (sequential) treatment trajectory, we recommend replicating our study in a prospective sequential trial, comparing MBCT+MBCL to MBCT only, or possibly using MBCT as active control to MBCL to correct for the potential 'double dosage' effect. As an earlier age of onset and younger age seem to be associated with a better outcome, MBCL may be particularly suitable for this subset of patients. So, future trials should include these as moderating variables to test this hypothesis. More generally, it would be interesting to further explore how MBCT and MBCL fit in with current available treatments, and whether and how they could be sequenced with CBT or (m)ADM.

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5

Mindfulness Based Compassionate Living (MBCL): a Qualitative Study into the Added Value of Compassion in Recurrent Depression

Schuling, R., Huijbers, M.J., Van Ravesteijn, Kuyken, W., & Speckens, A.E.M. (2020). Mindfulness Based Compassionate Living (MBCL): a Qualitative Study into the Added Value of Compassion in Recurrent Depression. *Mindfulness, Submitted June 2020*.

Abstract

Background: Mindfulness based cognitive therapy (MBCT) has been found effective in reducing depressive symptoms in adults suffering from recurrent depression. However, sustained recovery after MBCT is modest, so additional ways to improve long term-outcomes are necessary. Basing such additions on known working mechanisms of MBCT, like increases in self-compassion, is likely to reap further benefits. Mindfulness based compassionate living (MBCL) is designed as a follow-up to MBCT and has also been shown effective in reducing depressive symptoms. It has a similar format to MBCT: it is an 8-week program consisting of weekly sessions with a teacher and home practice in between. Compared with MBCT, MBCL has a more explicit focus on cultivating (self-) compassion as a response to difficult experiences. Little is known, however, about how participants experience the potential added value of MBCL in comparison with MBCT. The current study aims to fill this gap.

Method: Thematic analysis was used to analyse in-depth, face-to-face interviews, which were held post-intervention with a purposive sample of patients who participated in a randomized controlled trial of MBCL for recurrent depression.

Results: Participants indicated that MBCL had particular added value in terms of its immediate applicability in situations of deep suffering. Four themes emerged: (1) the container of kindness; (2) exposure to the difficult; (3) empowerment, and (4) common humanity.

Conclusion: This study shows that participants experienced an added value of MBCL over and above MBCT. The thematic outcome gives insight into the processes underlying the efficacy of MBCL in reducing depressive symptoms and may help address underlying mechanisms of vulnerability in this population as well as tap into mechanisms that enhance resilience.

Introduction

Major depressive disorder (MDD) is predicted to be the leading cause of disability worldwide by 2030 (Vos, Abajobir et al. 2017). It is characterized by persistent symptoms and high relapse rates (Mueller, Leon et al. 1999). Given the high psychological, social and economic burden associated with depression, as well as the predictive value of residual symptoms in terms of relapse, the treatment of residual symptoms is very important (Hardeveld, Spijker et al. 2010). To address the need for psychological interventions targeting relapse prevention, Segal, Williams and Teasdale developed mindfulness-based cognitive therapy (MBCT) (2012). A meta-analysis (Kuyken, Warren et al. 2016) showed that MBCT for patients with recurrent depression in remission resulted in a 31% risk reduction of a relapse/recurrence in a 60-week follow-up period compared with all control conditions. A growing number of studies indicate that MBCT may also be effective in decreasing depressive symptoms in patients with current depression (Strauss, Cavanagh et al. 2014). However, residual symptoms seem to remain considerable even after MBCT (Piet and Hougaard 2011, Van Aalderen, Donders et al. 2012), showing sustained recovery after MBCT is modest. Focusing on known working mechanisms of MBCT in additional treatment may lead to further benefits, in particular as generally, sequential treatment seems to be more effective than single treatment (Cuijpers, Noma et al. 2020). One of the possible underlying mechanisms for the chronic and recurrent nature of depressive symptoms is low self-esteem or self-denigration (Gilbert and Procter 2006). Being able to adopt a caring, soothing, compassionate attitude towards the self might be a skill that could help reduce the undermining mechanisms of self-criticism and hence further reduce the vulnerability to the recurrence or persistence of depressive symptoms. Thus, targeting the development of this attitude could possibly lead to even better outcomes.

Contemplative literature also emphasizes the importance of developing mindfulness and (self)compassion simultaneously, as the proverbial 'two wings of the same bird'. In their most recent publication, Feldman and Kuyken (2019) (p.180) emphasize that the key insight is that mindfulness reminds us to return to the actuality of the present with an attitude of befriending, to establish a body of stillness and calm where we can find the strength to meet the difficult with balance and compassion. Mindfulness is defined as awareness of the present moment, intentional and non-judgmental (Kabat-Zinn 1990). Compassion is defined as the capacity to open to the reality of suffering and to aspire to its healing, presenting a multi-textured response to pain, sorrow and anguish including kindness, empathy, generosity and acceptance (Feldman and Kuyken 2011). In line with this definition, Strauss et al. conclude in their systematic

review of self- and observer-rated measures that compassion consists of five elements: recognizing suffering, understanding the universality of human suffering, feeling for the person suffering, tolerating uncomfortable feelings, and motivation to act/acting to alleviate suffering (Strauss, Taylor et al. 2016).
Although still in its infancy, the evidence base for the efficacy of compassion programmes is growing. A meta-analysis on compassion-based interventions in non-clinical populations including 21 RCTs showed moderate effect sizes for improvements of compassion, self-compassion, mindfulness skills, depression and well-being (Kirby, Tellegen et al. 2015). In 2019, Ferrari et al. found in their meta-analysis that (self)compassion interventions led to a significant improvement. In the overall population, a hedge's g of 0.66 was found for depression and 0.75 for (self)compassion. In the clinical subpopulation a hedge's g of 0.82 was found for self-compassion (Ferrari, Hunt et al. 2019).

Mindfulness based compassionate living

In 2012, Van den Brink and Koster developed Mindfulness-Based Compassionate Living (MBCL) (Van den Brink and Koster 2015), partly based on previous work in compassion research as conducted by Neff (Neff 2011, Neff and Germer 2013), Germer (2009) and Gilbert (2009). MBCL is designed as a follow-up training to MBCT or Mindfulness-Based Stress reduction (MBSR), to be used in both clinical and non-clinical settings. For a more detailed description of MBCL, we refer to Schuling et al. (2016). Recently, we conducted an RCT to assess efficacy of MBCL in a population of recurrently depressed adults (N=122) (Schuling, Huijbers et al. 2020) which showed MBCL resulted in a reduction in depressive symptoms and an increases in self-compassion, mindfulness and quality of life. The increase in self-compassion appeared to mediate the improvements of depressive symptoms. In a 6-months follow-up period, the outcome appeared to improve even further. Despite these positive findings, little is known about participants' perspectives on the experienced added value of MBCL. Although kindness and compassion are key attitudes underlying MBCT, in its pedagogy they are conveyed more implicitly. Particularly patients with recurrent depression may need more explicit instructions and additional support to develop a compassionate attitude to both self and others, as they often are highly self-critical and plagued by feelings of shame, guilt and inferiority (Gilbert and Procter 2006, Judge, Cleghorn et al. 2012).

Method

Study design

We conducted a qualitative, in-depth, face-to-face interview study with a purposive sample of 122 adults with recurrent depression participating in an RCT on the efficacy of MBCL following MBCT. The participants had all participated in MBCT at our centre, at least one year prior to the trial. We selected participants with a sampling strategy aimed at having as much diversity as possible, taking account of gender, age, current status of depression, number of previous depressive episodes, age of onset of depression, childhood trauma and satisfaction with MBCL (as perceived by the teacher). As the aim of the study was to explore the potential added value of MBCL we only contacted participants who had participated in a minimum of four sessions. The interviews were conducted within three months after the last session of MBCL. Of the 23 patients contacted by telephone, one person indicated that he did not want to participate in an interview. The remaining 22 participants were able and willing to participate. After 22 interviews, saturation was reached. All participants provided written informed consent before participation in the study. Participants' demographic and clinical characteristics are shown in Table 1.

Intervention

MBCL was developed by Frits Koster and Erik van den Brink for clinical populations as a follow-up to MBCT (Van den Brink and Koster 2019). A more comprehensive description of the intervention was provided in both our pilot study (Schuling, Huijbers et al. 2017) and study protocol of the RCT (Schuling, Huijbers et al. 2016). The MBCL courses were delivered at the Radboudumc Centre for Mindfulness, Nijmegen, the Netherlands. Groups of about 8-10 participants were taught by one of two teachers, who both met the Good Practice Guidelines for teaching mindfulness-based courses by the UK Network for Mindfulness-Based Teacher Training Organizations (https://app.ukmindfulness-network.co.uk/guidelines/) (Crane, Eames et al. 2013) and were trained to teach MBCL by its developers Frits Koster and Erik van den Brink (HJ and RM). The MBCL training consisted of 100 hours of training plus 80 hours of supervised teaching. Treatment integrity and therapist competence were assessed as competent based on two randomly selected videotapes of each teacher using the adapted mindfulness based intervention teacher assessment criteria (MBI:TAC) (Crane, Eames et al. 2013), rated by two experienced mindfulness teachers.

Data collection

We report the data collection and analysis process in accordance with the COREQ-checklist as propagated by Tong (Tong, Sainsbury et al. 2007), divided into three domains: (i) research team and reflexivity, (ii) study design and (iii) data analysis and reporting. The interviews were held with participants who consented to participate. The first eighteen interviews were audiotaped at the Radboudumc, the remaining four were held by telephone and also audiotaped. The interviews lasted between 20 and 60 minutes. In total, 37.4 hours of audio-taped interview data were collected (mean duration was 36.5 minutes per interview). No-one but the participant and interviewer were present during the interview. At the time of data collection, RS was a 37-year old female linguist, MBSR teacher and PhD student. She had practiced mindfulness for approximately eight years, had graduated from the MBSR/MBCT teacher-training program and had taught six MBSR classes. The second researcher (HR) was a 33-year-old female psychiatrist. She had practiced mindfulness for approximately eight years and had taught five MBCT courses for patients with psychiatric disorders. RS held a prior relationship with the participants, whom she had done assessments with pre and post intervention for the RCT. HR had no prior relationship with the participants.

Each interview started with the question: do you feel MBCL has had an added value over MBCT alone, and if so, what is this added value according to you? If participants responded positively on the first question, the added value was explored using additional, open-ended questions. If answered negatively, overall experiences with the MBCL were explored. The interviewers pursued unexpected areas of interest in order to collect as wide a variety in responses as possible.

Data analysis

All interviews were audio-recorded, transcribed verbatim and processed in Atlas.Ti7. Thematic analysis was used to analyse the data (Braun and Clarke 2006). Analysis started as soon as the first data were collected and continued with each additional interview. Field notes and memos were used as sources of information throughout this process. Two researchers (RS and HR) independently coded the data to minimize subjectivity.

The first phase of the thematic analysis 'familiarisation of the data' as well as the second phase 'coding' was carried out independently by the two researchers. After every second interview the codes were compared and discussed by the two researchers until they reached consensus. A new coding scheme was then developed for further use and new codes could be added. After 12 interviews, in the third phase ('searching for themes'), the two researchers together with one of the MBCL teachers (HJ) grouped the codes into subthemes, and subthemes into themes, enabling them to derive hypotheses from the data. These themes were discussed in the larger research group consisting of the two researchers and a female psychiatrist and MBSR/MBCT teacher (AS), and a female teacher-trainer of MBSR/MBCT employed by the same institute (NS). AS and NS are both also trained in another compassion intervention, namely the Mindful Self Compassion program (Germer and Neff 2013). It was then concluded that the existing themes needed more clarification and depth, so six more interviews were conducted. With the additional data collected and coded by RS and HR, the team as a whole, including HJ and RM, critically reassessed the themes again (the fourth phase). A few themes seemed not fully saturated yet, so another four interviews were held to be certain all essential information had been gathered. The transcripts of these additional interviews were again coded and themed by RS and HR, after which the last phase began, which involved 'defining and naming themes' and 'producing the report'. In these phases, a more detailed analysis of each theme was developed and compelling quotes were selected.

Ethical considerations

The qualitative study was exempt from ethical approval by the Medical Ethical Committee Arnhem/Nijmegen, the Netherlands; the RCT was approved by the same committee (2013/220). According to Dutch law, no further measures for ethical approval were required for this additional qualitative study. However, all participants were informed about the study and participation was entirely voluntary. Consent to audio-recordings of the interviews and to the use of data for research purposes was sought before the interview commenced.

Results

Participants

In table 1, an overview of demographic and clinical characteristics of the study population is given. Two of the 22 participants interviewed indicated they had not experienced additional value: one was neutral, stating the value was the same as that of MBCT and the other found that the value was less: MBCL exercises, with their focus on imagery and recalling difficult experiences, drew him into thinking instead of feeling. For all participants, MBCT had been of sufficient value to be interested in a follow-up program, though nearly all had dropped practice routine.

Table 1 Demographic and clinical characteristics of the participants (subsample of the randomized controlled trial into the efficacy of Mindfulness Based Compassionate Living added to treatment-as-usual, compared to only treatment-as-usual; N=22). *out of 18 instead of 22.

Variable[a]	**N**	%
Female	17	77
Educational level*		
Low	2	11.2
Middle	11	61.1
High	4	22.2
Missing	1	5.6
Marital status*		
Married/in relationship	16	88.9
Missing	1	5.6
Children*		
One or more children	13	72.2
Missing	1	5.6
Employed*	2	11.1
Missing	2	11.1
Childhood trauma present (CTQ)	7	32
Current depression at baseline (SCID)*	7	39
3 or more previous depressive episodes at baseline (m)	20	91
ADM use		
	Mean (range)	**SD**
Age	52.9 (33-73)	11.7
Age at onset MDD	25.6 (14-42)	7.8
Pre-treatment (baseline) depressive symptoms (BDI-II)	20.3 (1-39)	11.0
Post-treatment depressive symptoms (BDI-II)	15.8[b] (1-44)	11.2
Attendance	7.6 (6-8)	0.7

BDI-II: beck depression inventory II; CTQ: childhood trauma questionnaire; SCID: Structural Clinical interview Diagnosis (DSM-IV)

[a] No differences were found between the Added Value population and that of the whole RCT on any variables

[b] The pre-post difference of -4.5 seems comparable to the RCT sample as a whole, which was -4.02

Results from the thematic analysis

Four themes and ten subthemes emerged from the data, these were:

1. The container of kindness;
   a. coping with the 'backdraft' effect;
2. Exposure to the difficult;
   a. overcoming resistance: approaching rather than avoiding the difficult;
   b. allowing the difficult without trying to fix it;
   c. effects of feeling the difficult;
3. Empowerment;
   a. compassion for self;
   b. confidence in self and the future;
   c. self-care;
4. Common humanity;
   a. relating to others;
   b. modelling by others;
   c. compassion for others.

Each theme is described more extensively below. It is important to note that participants elaborated to different extent on the topics that came up.

THEME 1: The container of kindness. Participants mentioned that from the start, the program was infused with explicit kindness, evident in all elements: the practices, theory, guidance of the teacher and group inquiry. The container was sometimes described as a very basic quality of 'being okay' with and welcoming all that participants experienced and brought into the sessions. Participants noted that practicing within this container changed their experience of phenomena:

> *So every time when observing: can you try to be kinder? What happens then is that bit by bit the colour brightens. If you're constantly telling yourself: That's not okay and then someone very kindly says: It IS okay. It's okay in this moment. Yeah, but I feel so awful. Even then, look at it with kindness. Again and again, changing the colour of your observation. (Male, 70)*

> *In one word: allowing. Yes, that's right. Allowing, but especially allowing in so much love. (Male, 70)*

Not only the content and guidance of practices was experienced as explicitly geared towards kindness; participants also reported how the teacher, during inquiry, encouraged participants to be flexible and lenient with home practice:

Well, I simply couldn't do it, and normally I would see that as a huge failure, but because there was space for: if it doesn't work, it simply doesn't work. I didn't get that feeling of failure as much and I felt a sense of mildness come over me. (Female 37)

SUBTHEME: coping with the 'backdraft' effect. Not all participants found it easy to connect with kindness though. Some noted they were not used to being gentle with themselves, which made it hard and confronting:

That was a real shift that brought with it a lot of resistance. That I should be happy with myself and allow myself space and loving and safe thoughts. All emotions and thoughts that are distant from me, I've spent years or perhaps my whole life in a mode of self-criticism and disapproval and negative judgments. (Female, 37)

Many participants identified the resistance as a signaller of deeply painful experiences and stated that with hindsight, not giving in to the resistance, and subsequently allowing gentle exposure to what had been feared, was what propelled transformation of the pain the most.

THEME 2: Exposure to the difficult. Throughout the interviews it became evident that being able to expose oneself to a fearful or painful experience required a willingness to allow that experience. Participants reported the active approach to the difficult as an essential difference between MBCT and MBCL. Within the container of kindness and self-care as described in theme 1, participants were explicitly invited and supported in approaching fearful or painful emotions and thoughts that sometimes had been repressed for a long time.

SUBTHEME A: Overcoming resistance: approaching rather than avoiding the difficult. This active approach was reported by many participants, therefore we identified it as an important subtheme within exposure to the difficult. Participants stated that during MBCT, in contrast, they had been able to remain in more 'neutral' observing, essentially avoiding what scared them the most.

That was in soften-soothe-allow. It was very hard for me to bring the soft, the calm, that acceptance into it, because with difficult situations I'm naturally much more inclined to want to destroy instead of embrace. It feels, or felt, so foreign to me, so I felt a lot of resistance. Yeah, I really thought, oh my, this is so much harder than just looking at what is here and letting it be. (Female, 37)

Quite a few participants were able to identify tendencies of passive or active avoidance behaviours that normally prevented approaching the difficult:

I notice now it doesn't help me, talking about things. I made a very conscious choice not to do that. It can trigger me even more. Really staying aware of yourself and letting yourself feel the emotions is a lot more helpful. (Female, 61)

Participants noticed the difference between avoiding emotions by thinking about them, and actually feeling them. As one participant remarked:

It's allowed to touch you, it's okay that it hurts. Those things are really helpful when you let yourself experience it and don't suppress it. That's the difference, I feel *it, it's not just theoretical anymore. If it were just theory, you'd think: 'sure, it's okay to feel pain. Whatever.' Then you're just using tricks. So the authenticity [of the experience] is what's most important to me. (Female, 61)*

In many practices this approaching was promoted by asking participants to recall painful memories and allowing them to come to the foreground:

*I only know what it's called in German. '*Zuwendung' [turning towards]. *It's a particular mode of observing. (Female, 46)*

SUBTHEME B: allowing the difficult without trying to fix it. Several participants mentioned that aside approaching the difficult instead of avoiding it, a non-fixing attitude was required to expose themselves to deeper suffering. It seemed easier to expose themselves to pain if they let go of their desire to change it.

I guess I always hoped I would eventually be rid of my depression. That if I tried extra hard, that may be the solution. But it doesn't actually work that way. So I noticed: 'Oh! That's how I do that!' And then there's this pain all over my body from holding onto that [trying to get rid of it]. But by saying: 'I'm not doing it really well, but I am doing it' and experiencing how my body feels, that was a relief. (Female, 60)

Definitely. That's it. Surrendering to what's here. And then comes the peace. (Female, 48)

SUBTHEME C: effects of feeling the difficult. Participants reported that once pain had been approached and allowed, there was room for exposure, experiencing the felt sense of difficult emotions:

I'm not so fearful anymore. My husband says it too: You were so angry all the time. Angry and panicky. There's grief underneath and I'm no longer afraid to let the grief in now. (Female, 48)

This was mentioned as a specific aspect that MBCL addressed more than MBCT did, and it seemed to result in a diminishing of suffering:

> *For me, it was a revelation… now I dare to feel that emotion using those CDs and for the first time in my life I'm letting myself feel all that and I know: well, I'm not going to die, it's not going to end horribly. (Female, 48)*

Participants reported having a felt experience of emotion in the body especially seemed to make it accessible, as something concrete and actual that they could 'work with'.

> *So when the recording asked where is the pain? I was taken aback, because it was actually somewhere [points to chest] and I would feel my tension. That was more specific for me, much more, it was more present. (Female, 61)*

This more actually felt experience of emotions made people take their emotions more seriously:

> *I started to take my [emotional] pain much more seriously, I took it seriously before, but it would be caught up in phrases and thoughts and now it was here [points to chest], I focused on it for a while and noticed much more clearly: what is pain? (Female, 61)*

In a more general sense, participants stated that after the program compassion was 'just there in their system':

> *It seems like the sting is gone. My body was full of splinters and they've been taken out one by one. (Male, 70)*

THEME 3: Empowerment. When participants had practiced cultivating the kind container and been able to expose themselves to deeper layers of suffering, they seemed to experience a new empowerment in life.

> *I used to think I was very dysfunctional, but I notice more and more: actually, I function quite well. (Male, 50)*

> *I've always thought I couldn't do it alone. But that's no longer the case. I think: Gosh, being alone doesn't kill me. You know? And I see, more and more, how much I have inside of me. That's quite something, isn't it? (Female, 48)*

This empowerment seemed to be the result of three different developments: an increase in self-compassion, confidence in the self and the future, and self-care.

SUBTHEME A: compassion to self. Addressing the 'inner critic' is an important part of MBCL. The interview data indicate that the influence of this critical inner voice was being diminished, making room for self-compassion:

> *For me the value of compassion training is that for the first time in my life I've followed a program that is actually helpful. In the sense that I'm not so harsh on myself anymore and that's amazing. (Female, 48)*

> *I think that trust comes from lowering the bar. From not continually being so harsh on myself, allowing myself to make mistakes. 'Everything has to go well, otherwise I'm worthless.' There's much more room now. (Female, 37)*

SUBTHEME B: confidence in self and the future. As already alluded to in the last quote, for many participants, approaching and feeling the difficult within the container of kindness led to a sense of confidence. They seemed impressed by their own ability to bear difficult feelings:

> *I don't want to idealize it, but that compassion training has certainly meant so much for my life. I was just thinking, jeez I've become so much softer towards myself. It's all still very new and shaky… but the fact I can see myself this way and I'm able to bear it all. Yes. (Female, 48)*

> *And to also think about the future, to think I'm not so stupid after all, I'm able to think well... What possibilities are there in my life? What can I do? I had completely lost that, seeing possibilities. (Female, 42)*

SUBTHEME C: self-care. The patients indicated that MBCL had particular added value in terms of its applicability in acute situations of deep suffering. They used compassion often as immediate self-care, taking agency in that situation:

> *Now when I notice I feel bad, I can work with it. I can embrace it, I can try to invoke my compassionate companion. I can truly allow it. … After just the mindfulness training [MBCT, ed.] I would have still been caught up in a feeling of despair. I would have noticed it, but I wouldn't have known what to do next. (Female, 37)*

This increased trust and empowerment in turn seemed to affect self-care. A few participants decided to go for (longer) walks outside, one started decided to work fewer hours:

> *At the beginning of the year I said I wouldn't give up a second of work. And now I think, well 28 hours a week is just not doable for me. I've tried that five times and I've relapsed five times. If I want to take good care of myself, then I just have to stop that. (Female, 51)*

THEME 4: Common humanity. For quite a few participants, it was helpful to hear others struggling with the same issues and hear about their insights. Three subthemes emerged within this theme:

SUBTHEME A: relating to others. Participants seemed to gain additional insight into how suffering is part of the human condition. Naturally, this common struggling with life comes up in MBCT as well, but as participants were explicitly geared towards deeper suffering in MBCL, the commonalities seemed to gain even more weight.

> *I think it was specifically the compassion training that was good. I experienced that very differently and learned from people around me. Some seemed to be so at ease while I felt so turbulent inside, and then that turned out not to be true and I thought: 'oh right, we all have our own portion, our own share'. That gives some peace of mind like: okay, we're all soldiering on'. (Female, 66)*

SUBTHEME B: modelling by others. Other participants modelling what compassion feels or looks like when applied successfully was revealing as well. For many, compassion was such an alien concept that they really needed this modelling by others:

> *It was really helpful for me to see how others were working with it. It gave me a sort of, this sounds quite loaded, but a sort of signpost showing me where to go, what I was meant to be doing. (Female, 65)*

SUBTHEME C: compassion for others. Additionally, participants reported an increased sense of compassion for others. Though the MBCL is geared towards self-compassion solely in the first half of the program, the second half includes practices on compassion for others:

> *I was always a good listener, but now I notice thinking: 'Oh, this must be awful for you. So being able to say that first and think the other person feels understood, at least. (Female, 66)*

Discussion

This qualitative study provides insight into the experiences of patients with recurrent depression with MBCL as a follow-up to MBCT. Participants seemed able to incorporate the program and gain substantial benefits in terms of self-compassion and self-care. Specifically, MBCL seemed to enable approaching and being with difficult emotions and thoughts with kindness. The programme also seemed to cultivate skills to immediately apply kindness in difficult situations.

In MBCL, the practice is experiential and not cognitive. In other words, participants are stimulated to attend to their direct experience, be it pleasant or unpleasant, rather than think about it. We may view this as a type of exposure. MBCL shares this aspect of exposure with other evidence-based treatments like CGT and ACT, for example (Gloster, Hummel et al. 2012).
In MBCT, exposure to the difficult is also practised. When comparing the two however, some participants stated that during MBCT, they had been able to remain in more 'neutral' observing, as it lacked the active invitation to approach the difficult. This made it possible to continue not engaging with strongly-rooted avoidance patterns. This seems in congruence with a basic assumption underlying Compassion Focused Therapy, namely that the target population is not only highly self-critical, but also highly fearful of both negative and positive emotions, i.e. that resistance to working with difficult experiences is partly rooted in fear of positive emotions surfacing as well as negative ones (Gilbert 2009, Gilbert, McEwan et al. 2013). This resistance is in line with what participants describe in our qualitative study: they seemed to meet a lot of resistance in the first couple of sessions. They stated that exposure to experiences and emotions that they had suppressed for long times whilst being kind to themselves felt alien for them to do.
It seems the crucial element is the practice in self-compassion itself: through various practices, step-by-step, gentle guidance is offered through difficult experiences, creating a bedding of safety and kindness to facilitate exposure. This bedding of safety and kindness and being encouraged to set their own pace seemed to support participants in actively responding to suffering, applying that response in difficult or painful daily life situations. The wish to respond to

the suffering is in accordance with the definition of compassion, which emphasizes recognizing suffering combined with a wish to alleviate it (Strauss, Taylor et al. 2016). In this light, we might formulate the added value of MBCL as giving participants the immediate tools and bedding in safety and self-compassion to facilitate exposure to deeper levels of suffering, which then leads to desensitization to fear. In sum, there seems to be a process of a) approaching and allowing the difficult, b) a soothing and self-compassionate response, which c) leads to more trust in being able to handle suffering, which d) seems to lead to a growing experience of safety and kindness. These steps seem to mutually reinforce each other instead of forming a linear process, which fits in with Garland et al.'s mindful positive emotion regulation (Garland, Farb et al. 2015). This mutual reinforcing may account for the continued and further improvements observed over time, in particular the further improvement in quality of life (Schuling, Huijbers et al. 2020). It seems then, MBCL is a useful addition to MBCT in enhancing sustained recovery in adults suffering from recurrent depression. This may hold in particular for populations with stronger or deeper-rooted suffering in terms of trauma or core beliefs regarding shame and guilt, with accompanying passive and active avoidance behaviours. For these populations, MBCT, with its more implicit cultivation of kindness, might not be enough to encourage opening up to difficult emotions and learning to meet them with a compassionate attitude rather than self-criticism and rejection.

Strengths and limitations

This is the first study that qualitatively explores the experienced additional value of compassion training (MBCL) after MBCT in a group of recurrently depressed patients. The original developers of MBCL were involved in both the research and the teaching of the teachers, who were already highly experienced in teaching mindfulness-based interventions. We had a large population from which to draw a purposive sample and were able to continue collecting data until saturation was reached. Both the data collection and analysis were conducted by independent interviewers and coders and we were able to use a diverse team for thematization.

One of the limitations of recruiting participants from our RCT sample is that it potentially caused selection bias: it was a clinical population, suffering from relatively severe depressive symptoms, that had completed and possibly benefited from MBCT in earlier treatment. There may have been an underrepresentation of negative experiences as a result. We used purposive sampling to minimize the potential bias however, and asked about experiences with MBCT. Additionally, the primary researcher was also the interviewer, possibly resulting

in social desirability. We also didn't collect additional data such as written evaluations or teacher interviews, so no data triangulation could be done, nor did we perform member checks. Furthermore, though the teachers were highly qualified, we used only two and they were both from the same centre. As the researchers were all also employed by this centre, they may have been biased. The centre offers both MBCL and MBSR/MBCT courses however, and has no financial gain by answering the research question.
Lastly, it is difficult to differentiate the effects of MBCT and its repeated application from the effects of MBCL. This is complicated further by the overlap in the two programs.

Implications for research and clinical practice

The results lead to interesting hypotheses about possible working mechanisms of MBCL, in particular the focus on actively approaching the difficult. Future research would benefit from exploring potential mediators drawn from the interviews, such as the level of fear of self-compassion, and changes in agency, trust and self-confidence. Equally important would be studying potential predictors: are participants who suffer from trauma or who are highly self-critical indeed the ones to benefit most from MBCL? Furthermore, as our qualitative results are based on a single trial, replication of the findings in a multi-trial is warranted.
Explicit cultivation of compassion seemed crucial in this population. There may be multiple ways of explicitly cultivating compassion: this qualitative study focused on the potential of MBCL to add value to what was previously learned in MBCT in a sequential approach, i.e. offering MBCL after MBCT. Another way would be to integrate explicit compassion in MBCT. However, this may be overwhelming for this population and lead to (too much) resistance or the backdraft effect: Segal et al. expect that in clinically depressed people, practicing warmth and kindness without a foundation in mindfulness may trigger vulnerability (2012). Integration of more explicit compassion elements or offering the training as a stand-alone intervention would however, if shown effective, reduce the trajectory for patients on their way to mental resilience and higher quality of life, making it worthy of investigation. This would also bypass the need to follow MBCT first, which is not yet widely available everywhere. Lastly, given participants' experiences, offering MBCL before MBCT might be worth investigating. Answering that question requires randomized research in which also potential moderators are assessed in order to aid identifying the correct indications for participation.
A fruitful approach to examining the various options in treatment trajectories may be to list empirically supported principles of change (and prediction)

coming from the research recommendations mentioned above, instead of focusing on trademarked therapies or other treatment packages, in line with Rosen and Davison (Rosen and Davison 2003). This approach enables the creation of new, perhaps personalised trajectories by adding evidence-based components to already listed effective treatments.

Conclusion

This study shows that MBCL, in addition to being efficacious in reducing depressive symptoms and increasing quality of life in recurrently depressed adults, has an experiential added value for participants who previously followed MBCT. This might hold in particular for participants with more severe shame and guilt or trauma, who may need the more explicit safe and kind container of self-compassion to be able to allow the exposure to and exploration of deep suffering. The thematic outcome gives insight into the processes underlying the efficacy of compassion training in reducing depressive symptoms and improving quality of life, as well as the usefulness and potential of (self-)compassion cultivation in recurrently depressed adults in general. These insights may inform new perspectives on how to address underlying mechanisms of vulnerability in this population.

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6

Summary and General Discussion

Summary and General Discussion

The overall goal of the studies included in this thesis was to a) co-create a format for Mindfulness Based Compassionate Living (MBCL) suitable for patients with recurrent depression and assess its preliminary effectiveness; b) examine the efficacy of MBCL as a follow-up to Mindfulness Based Cognitive Therapy (MBCT) in a (pragmatic) sequential treatment design, in patients suffering from recurrent depression; c) examine potential mediators and moderators of treatment outcome; d) examine longer-term consolidation of MBCL's potential effect on depressive symptoms; and finally e) explore whether participants experienced additional value in attending MBCL after having participated in MBCT. This chapter summarizes and discusses the studies in relation to the existing literature. In addition, strengths and limitations are identified and directions for future research and clinical implications are given.

Summary

Chapter 2 described a mixed-methods approach, assessing the feasibility, acceptability and preliminary effectiveness of MBCL as a follow-up intervention to MBCT in patients with recurrent depression. An uncontrolled study in 17 patients with recurrent depression was conducted in two successive, partly overlapping cohorts. The results were encouraging: the attendance rate was very high for both cohorts, and, in contrast to the first version of the course, participants reported being very satisfied with the adapted, second version of the program. Depressive symptoms improved in the second cohort. Additionally, in both cohorts improvements in self-compassion were found, both overall and in several subscales, with effect sizes ranging from small to large. As we received ample feedback on how to improve the first version of the course and were able to evaluate the adapted version of the programme with almost all original participants, it seemed warranted to further test the co-created MBCL in a larger RCT.

Chapter 3 described the rationale, design and methods of the RCT comparing MBCL + treatment as usual (TAU) to TAU alone in a sample of recurrently depressed patients. All participants had participated in MBCT at least one year prior to participating in the RCT. Before and after MBCL or TAU, depressive symptoms, rumination, self-compassion, mindfulness and quality of life were assessed. In addition, presence of depressive disorder was established with a psychiatric interview. After the control period, patients randomized to the TAU condition were offered MBCL as well. The joint sample was assessed again at

6-months after completion of MBCL to investigate consolidation of treatment effects. In **chapter 4**, the findings of both the RCT and the consolidation study were presented. In total, 122 participants were included in the RCT. Our findings showed that MBCL, offered as a sequential intervention to MBCT, resulted in a significant reduction of depressive symptoms at post-treatment, with a small effect size (*d*=0.34), corresponding with a number-to-treat of five. It also resulted in a reduction of rumination and improvements in self-compassion, mindfulness skills and quality of life. Though the difference in diagnostic status was not significant, more participants in the MBCL condition no longer met diagnostic criteria of depressive disorder. Self-compassion appeared to mediate the treatment effect. Moderation was not found for any of the hypothesized moderators, except for age and age of onset. Participants who were younger or with a lower age of onset showed significantly less depressive symptoms at post-treatment when allocated to MBCL compared with TAU.

In the follow-up study, containing the combined population (n=119), we found a large effect size in the reduction of depressive symptoms (ES=1.07) for the whole trajectory from pre-treatment to follow-up period, using linear mixed modelling.

Chapter 5 described the findings of the qualitative study into participants' perspectives (n=22) on the experienced added value of MBCL in comparison to MBCT. Participants indicated that MBCL had particular added value in terms of its immediate applicability in situations of deep suffering. Four overarching themes emerged from the data: (1) the container of kindness; (2) exposure to the difficult; (3) empowerment, and (4) common humanity. Participants seemed able to incorporate the program and gain substantial benefits in terms of self-compassion and self-care. Specifically, MBCL seemed to enable approaching and being with difficult emotions and thoughts with kindness, both during practices and in difficult situations in daily life. This seemed to facilitate a corrective emotive experience (i.e. lessening of the pain/trauma).

Having this deeper layer of suffering as an explicit topic in group exchanges also made participants realise the common humanity of suffering. This resulted in a further development of compassion, allowing other, potentially even more difficult experiences. Thus, the four themes we identified in participants' experiences seem to present an upward spiral of mutually reinforcing processes rather than a linear process. This ultimately appeared to leave participants feeling empowered, in touch with their own abilities, and having more agency over their lives.

Efficacy of MBCL as a follow-up to MBCT for patients with recurrent depressive symptoms

Both our pilot study and the RCT resulted in promising findings, indicating beneficial effects of MBCL as a follow-up to MBCT in reducing depressive symptoms and rumination, and improving self-compassion, mindfulness skills and quality of life. These improvements are noteworthy, as MBCT is also known to reduce depressive symptoms and rumination, and increase mindfulness skills and self-compassion. The improvement in quality of life, which was encouraging in this group of patients with relatively severe symptoms, was larger than in a similar population treated with MBCT (Van Aalderen, Donders et al. 2012), using the same instrument.

The observation of consolidation or even further improvement over the course of follow-up rather than attenuation of treatment effect was also encouraging and has in fact been demonstrated in earlier studies of MBIs for both patients with ADHD and cancer patients (Cillessen, Schellekens et al. 2018, Janssen, Kan et al. 2019), as well as in patients suffering from recurrent depressive symptoms (Van Aalderen, Donders et al. 2015). Residual symptoms are an important predictor of depressive relapse and recurrence, therefore this finding supports the potential clinical relevance of MBCL, and its possible influence on relapse rates.

A crucial difference with the curriculum of MBCT is the more active and explicit compassionate approach to difficult experiences in MBCL, as compared to the more implicit focus on compassion in MBCT. Possibly, this explicit focus is responsible for the reduction of depressive symptoms at post-treatment and further improvement at 6-months follow-up. When assessing working mechanisms in the RCT, self-compassion indeed appeared to be a mediator of treatment outcome of MBCL. This was previously demonstrated for MBCT as well (Kuyken, Watkins et al. 2010). In contrast to MBCT, where rumination has been found to be one of the most robust mediators (van der Velden, Kuyken et al. 2015), in the current study no mediation by rumination was found in MBCL. This suggests the working mechanisms of MBCL might be different and possibly complementary to those of MBCT: the qualitative study into participants' experiences suggests that an increasing sense of both agency and common humanity may also mediate the outcome. In contrast, predictors of treatment effect seemed to be similar between MBCL and MBCT. MBCL appeared to be most effective for those who were younger and/or had an earlier age at onset. Looking at MBCT literature, age and age at onset have also been found to moderate treatment outcome (younger people having more benefit from MBCT) (Kuyken, Warren et al. 2016, ter Avest, Dusseldorp et al. 2019). Other moderators that have been suggested in the MBCT literature, such as childhood trauma, baseline severity

of depressive symptoms, and number of previous episodes (Williams, Crane et al. 2014, Kuyken, Warren et al. 2016) were not found in the current study on MBCL. Additionally, rumination was not found to be a moderator of treatment outcome, whereas in a recent individual patient data-analysis including three randomized-controlled trials comparing MBCT added to treatment-as-usual to only treatment-as-usual (N=292), it was (ter Avest, Dusseldorp et al. 2019).
The added value study suggests that practicing (self)compassion may be particularly important for those with stronger or deeper-rooted suffering in terms of trauma or core beliefs regarding shame and guilt, with accompanying passive and active avoidance behaviours. For these populations, MBCT, with its more implicit cultivation of kindness, might not be enough to encourage opening up to difficult emotions and learning to meet them with a compassionate attitude rather than self-criticism and rejection. Consequently, higher levels of emotional avoidance or aversion to (self)compassion may be predictors of treatment outcome of MBCL.

An important aspect of both MBCT and MBCL that needs to be taken into account when exploring potential working mechanisms is that they include regular practice. From the literature on adherence in MBCT, we see there are indications that more practice leads to more effect: in their meta-analysis on self-reported home practice during MBCT, Parsons et al., found that across 28 studies (N=898), there was a small but significant association between participants' self-reported home practice and intervention outcomes (Parsons, Crane et al. 2017). We do not know what this is like for MBCL, but it seems plausible the same would hold for this program. Related and potentially even more important is that the practice is experiential and not cognitive. In other words, participants are stimulated to attend to their direct experience, be it pleasant or unpleasant, rather than think about it. This experiential aspect of mindfulness-based interventions is shared with exposure-based therapies. Exposure therapy is based on the assumption that when people are fearful of something, they tend to avoid the feared objects, activities or situations. Although typically applied in clinical populations suffering from anxiety disorders, this seems relevant to patients with recurrent depression too. In fact, a basic assumption underlying Compassion Focused Therapy is that the target population is not only highly self-critical, but also highly fearful of both negative and positive emotions, i.e. that resistance to working with difficult experiences is partly rooted in fear of positive emotions surfacing as well as negative ones (Gilbert 2009, Gilbert, McEwan et al. 2013). This resistance is in line with what participants describe in our qualitative study: they seemed to meet a lot of resistance in the first couple of sessions. They stated that exposure to experiences

and emotions that they had suppressed for long times whilst being kind to themselves felt alien for them to do:

> *That was a real shift that brought with it a lot of resistance. That I should be happy with myself and allow myself space and loving and safe thoughts. All emotions and thoughts that are alien to me: I've spent years or perhaps my whole life in a mode of self-criticism and disapproval and negative judgments.*

Looking at MBCL efficacy from the perspective of increased exposure, we may begin to understand more of how it works. The process described by participants in the qualitative interviews seems similar to that of exposure therapy: after bearing or going through what was resisted and feared the most, the experience of anxiety seemed to decrease and a lessening of trauma seemed to occur. Looking back, many participants identified overcoming this resistance as the most important aspect of increased mental health and wellbeing. MBCL shares this aspect of exposure with other evidence-based treatments like CGT and ACT, for example (Gloster, Hummel et al. 2012). The effectiveness of exposure (elements) in treatments for depression isn't surprising, given the findings of Spinhoven et al. (2011), showing that 75% of those with a depressive disorder had a lifetime comorbid anxiety disorder.

In MBCT, exposure to the difficult is also practised. When comparing the two however, some participants stated that during MBCT, they had been able to remain in more 'neutral' observing, as it lacked the active invitation to approach the difficult. This made it possible to continue not engaging with strongly-rooted avoidance patterns. As one participant stated:

> *It was very hard for me to bring the soft, the calm, that acceptance into it, because with difficult situations I'm naturally much more inclined to want to destroy instead of embrace. It feels, or felt, so foreign to me, so I felt a lot of resistance. Yeah, I really thought, oh my, this is so much harder than just looking at what is here and letting it be.*

However, only turning the invitation to practice self-compassion from passive and implicit to active and explicit does not seem sufficient to propel a deepening of exposure to the difficult.
From what participants said, it seems that the crucial element is the practice in self-compassion itself: through various practices, step-by-step, gentle guidance is offered through difficult experiences, creating a bedding of safety and kindness to facilitate exposure. At any point, participants could pause if they felt overwhelmed, and practice compassion about this as well. This bedding of

safety and kindness and being encouraged to set their own pace seemed to support participants in actively responding to suffering, applying that response in difficult or painful daily life situations. This wish to respond to the suffering is in accordance with the definition of compassion, which emphasizes recognizing suffering combined with a wish to alleviate it (Strauss, Taylor et al. 2016). In this light, we might formulate the added value of MBCL as giving participants the immediate tools and bedding in safety and self-compassion to facilitate exposure to deeper levels of suffering, which then leads to desensitization to fear. In sum, there seems to be a process of a) an approaching and allowing the difficult, b) a soothing and self-compassionate response, which c) leads to more trust in being able to handle suffering, which d) seems to lead to a growing experience of safety and kindness. These steps seem to mutually reinforce each other, giving rise to increasing mental flexibility, which may account for the continued and further improvements observed over time, in particular the further improvement in quality of life.

Strengths and limitations

The current thesis investigated the possible value of MBCL in a comprehensive way, first finding the best format of delivery, co-created with the target population of recurrently depressed patients, then taking the next step of assessing efficacy, working mechanisms, prediction and consolidation in a full RCT, followed by qualitative interviews on the added value of MBCL as a follow-up to MBCT. The main strengths of the RCT are its adequate sample size, randomized controlled design and innovative nature, as this is one of the first studies investigating the efficacy of MBCL for patients with recurrent depression who previously attended MBCT. Though our approach to the sequential treatment design was pragmatic, the sequencing of MBCT and MBCL is another strength, as such designs may better fit the chronic, recurrent nature of depression (Cuijpers, Noma et al. 2020).

Population

Especially for patients suffering from relatively severe symptoms, a sequential approach might prove more efficacious. Our sample fits this profile, as almost 90% had suffered three or more episodes before start of the intervention and 44% had suffered childhood trauma. The pragmatism of our recruitment strategy, i.e. inviting MBCT participants with and without a current depressive episode and using relatively few exclusion criteria, also increased the generalisability of our findings to the 'normal' clinical setting.

However, the pragmatic nature of the sequential treatment design is also one of the limitations of this study: there is no head-to-head link between this study and one investigating MBCT in the same population. Due to the lack of such a link, we do not know which population applied for participation in the second phase (MBCL). Another limitation is the large variation in time span between MBCT and MBCL for participants (1-7 years). In short, we know little about a possible selection bias, or about the type of patients who might particularly benefit from additional MBCL in comparison with MBCT alone. They may have equally likely been patients who benefitted from MBCT and wished to deepen or further their practice or patients who did not benefit from MBCT, i.e. perhaps a more treatment-resistant population, who were looking for new ways to improve their mental well-being.

On the plus side, inclusion of participants went smoothly and we had low levels of attrition, signalling that MBCL is not only acceptable to this population but seems to meet a tacit need.

Intervention

For the MBCL, we were able to work with teachers with long-standing experience, who were trained by the MBCL-developers themselves. Assessing teacher competence was done through an instrument geared towards mindfulness teachers however (MBI:TAC), this instrument may need adaptation for assessing competence in compassion teachers.

Adherence to the sessions was high (six out of eight sessions on average). However, as an intervention that requires regular (experiential) practice and that seems to be applicable in daily life situations, we may wish to learn more about how formal and informal practice is applied by participants. In everyday life, most of us are repeatedly engaged in situations that allow for practicing compassion, for example being cut off in traffic or someone in the street asking our help. The current study did not include data collection in this regard.

Additionally, we did not compare MBCL with an active control condition, leaving us with little information about the specificity of the treatment effect. Though this is common in studies assessing initial efficacy of interventions and testing early stages of treatment, participants randomized to the control group may have suffered demoralization, causing their symptoms to worsen (Cunningham, Kypri et al. 2013). This may lead to artificial inflation of intervention effect estimates (Furukawa, Noma et al. 2014). Related to this, it is possible that the effects of MBCL are (partly) due to a double dosage of treatments rather than to the specific effects of MBCL. To investigate both specificity and double dosage, one might need to compare MBCL to a renewed course of MBCT. From our qualitative study however, we have some preliminary indications that MBCL taps into different processes than MBCT does.

Measures

Testing mediation is also a strength of this study, as it tells us something about the specificity of the efficacy of MBCL. On the other hand, we did not conduct mid-treatment or weekly assessments. The qualitative study provides insight into possible new avenues in working mechanisms. The study also explored possible moderating variables that may influence the reduction in depressive symptoms. Due to the limited sample size however, these results should be regarded as preliminary.

The perspectives gained from the mediation and moderation, but especially the qualitative study, indicate that perhaps underlying mechanisms of vulnerability in this population may be better addressed by targeting quality of life than reducing clinical symptoms. In this respect, we may need to rethink the type of measures used in the study, i.e. perhaps (improved) measures of quality of life should be primary outcome measures.

Follow-up

Having patients in the control condition start MBCL after the TAU period means the current study did not include a controlled follow-up. We therefore cannot compare the long-term follow-up results between both conditions: consequently, it is unclear how this population fares over time without being offered MBCL. Another consequence of this design is that in the uncontrolled follow-up study there may have been regression towards the mean. However, given the reduction of depressive symptoms during the treatment phase of the study, one would expect this to mitigate in the follow-up phase. In contrast, we actually observed a further reduction over time, which supports the findings of the RCT.

Qualitative study

The qualitative study was one of the first to explore the experienced additional value of compassion training (MBCL) after MBCT in a group of recurrently depressed patients. We had a large population from which to draw a purposive sample and were able to continue collecting data until saturation was reached. Both the data collection and analysis were conducted by independent interviewers and coders and we were able to use a diverse team for thematization. However, it is difficult to differentiate the effects of MBCT and its repeated application from the effects of MBCL. This is complicated further by the overlap in the two programs.

Implications for research and clinical practice

MBCL seems to offer benefits to a population of recurrently depressed individuals and therefore bears potential to be offered on a larger scale. Naturally, as this thesis contains studies conducted in a single centre, replication is needed in a multi-centre context.

To optimise the (sequential) treatment trajectory, we recommend replication of our study in a prospective sequential trial, comparing MBCT+MBCL to MBCT only. In such a trial, we would have much better insight into who is participating and be able to properly assess moderators. MBCT may also be used as active control to MBCL to preclude a potential 'double dosage' effect., i.e. we could compare MBCT+MBCL to MBCT+MBCT.

More generally, it would be interesting to further explore how MBCT and MBCL fit with currently available treatments, and whether and how they could be sequenced with Cognitive Behavioural Therapy or antidepressant medication, for example, or even EMDR (Eye Movement Desensitization and Reprocessing) or other exposure therapies.

It seems important to look beyond the working mechanisms that have been suggested in MBCT, and explore different factors that might be specific for the effects of MBCL. This may extend beyond mediators to outcome measures, possibly related to positive mental health. The results of the qualitative study lead to interesting hypotheses about possible working mechanisms of MBCL, in particular the focus on actively approaching the difficult coupled with practicing self-compassion in acute situations. Future research would benefit from exploring potential mediators drawn from the interviews, such as the level of fear of self-compassion, and changes in agency, trust and self-confidence. Equally important would be studying potential predictors: as an earlier age of onset and younger age seem to be associated with a better outcome, MBCL may be particularly suitable for this subset of patients. If so, it may be useful to investigate adaptation of the program to suit an older population. We may also want to explore whether participants who, for example, are highly self-critical or have particularly strong avoidance tendencies are the ones to benefit most from MBCL. So, future trials should include these as moderating variables to test this hypothesis. A fruitful approach to examining the various options in treatment trajectories may be to list empirically supported principles of change (and prediction) coming from such research, instead of focusing on trademarked therapies or other treatment packages, in line with Rosen and Davison (2003; Behavior modification). This approach enables the creation of new, perhaps personalised trajectories by adding evidence-based components to already listed effective treatments.

For clinical practice, offering MBCL as an additive treatment to MBCT has the disadvantage that only patients who have already followed MBCT can participate, and both MBCT and MBCL are not yet widely available. The

important question is if MBCL has to follow MBCT. Though Segal et al. suggested that in clinically depressed people, practicing warmth and kindness without a foundation in mindfulness may trigger vulnerability (Segal, Williams et al. 2012), earlier integration of explicit compassion elements or offering the training as a stand-alone intervention might significantly reduce the treatment trajectory for patients on their way to mental resilience and higher quality of life. Therefore, it seems warranted to further study this option.

As suggested above, having more insight into the evidence-based components of both MBCT and MBCL, as well as predictors of treatment outcome, may lead to personalised approaches. In these, elements of the two programmes could be integrated, or added to other treatments/treatment components.

Another option is to test effectiveness of MBCL as a stand-alone treatment. Those with high levels of self-criticism or avoidance tendencies might benefit from a more explicit approach to self-compassion early on. We may compare initial MBCT to initial MBCL or even the effect of reverse order: MBCT+MBCL to MBCL+MBCT. In both options, predictors could be assessed and weekly measures or experience sampling could be included to assess participants' process.

This approach would also be interesting in terms of cost-effectiveness, which deserves further investigation as MBCL participants made less use of health care services than those in the TAU group, except for attending the general practitioner.

Lastly, If MBCL is to be offered on a larger scale, serious attention should be given to the quality and certification of teachers, accreditation and possible adaptation of the MBI:TAC assessment criteria for teaching MBIs, to include MBCL. In short, it is vital that the quality and certification of MBCL teachers become protocolized through professional and internationally set standards, analogous to MBCT.

Conclusion

This thesis included a series of studies showing that MBCL appears to improve mental health in recurrently depressed adults, which seems to consolidate and perhaps even further improve over time, and has an added value for participants who previously attended MBCT. As residual symptoms are an important predictor of depressive relapse and recurrence, our findings support the potential clinical relevance of MBCL. For this population the more explicit safe and kind container of self-compassion may be needed to be able to mindfully expose themselves to the experience of deep suffering, which can promote increased well-being.

Further insight into the effectiveness and value of compassion practices as an add-on to mindfulness/MBCT, or other treatments, could improve by research focusing on working mechanisms and prediction in particular. The outcomes could optimise treatment trajectories for this population.

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7

Samenvatting (Summary in Dutch)

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Dit proefschrift is gebaseerd op een verzameling artikelen die voortkomt uit de Compassie studie die in 2013 is opgestart. De studie was gericht op het onderzoeken van de effectiviteit van op mindfulness gebaseerde compassietraining bij volwassenen met terugkerende depressieve klachten. Hieronder volgt de Nederlandse samenvatting van de achtergrond van het onderzoek, de methode en de resultaten ervan, alsmede een bespreking van de bevindingen vanuit een breder perspectief.

Depressie en behandeling

Depressie, of Major Depressive Disorder (MDD), is volgens de World Health Organization in de afgelopen drie decennia de belangrijkste oorzaak gebleken van niet-dodelijk verlies van gezondheid en zal naar verwachting in 2030 de belangrijkste oorzaak van invaliditeit wereldwijd zijn (Vos, Abajobir et al. 2017). Het is een veelvoorkomende psychiatrische stoornis, waarmee alleen al in Europa 30.3 miljoen mensen elk jaar te maken hebben (Wittchen, Jacobi et al. 2011). Ongeveer een op de vijf volwassenen zal één of meerdere depressieve episodes doormaken gedurende zijn leven.

Depressie wordt gekarakteriseerd door aanhoudende symptomen, waarvan de belangrijkste twee een verdrietige, neerslachtige stemming en een verminderde interesse in (gewoonlijk plezierige) activiteiten zijn. Andere symptomen zijn een verandering in eetlust of gewicht, slaapproblemen, psychomotorische geremdheid of agitatie, vermoeidheid of futloosheid, gevoelens van waardeloosheid of extreme schuldgevoelens, cognitieve problemen zoals gebrek aan concentratie of besluiteloosheid, en regelmatig terugkerende gedachten aan zelfdoding of een intentie daartoe. Om van een depressieve stoornis te spreken moeten vijf van de negen symptomen gedurende minimaal twee weken aanwezig zijn (American Psychiatric Association DSM-5 2013).

In aanvulling hierop wordt depressie ook gekarakteriseerd door hoge terugvalpercentages: ongeveer 75% van alle patiënten ervaart meer dan één episode gedurende hun leven (Boland, Keller et al. 2002). In een studie waarin tot 15 jaar aan prospectieve data over het verloop van depressie werd bekeken, vonden Mueller, Leon et al. (1999) dat een cumulatief percentage van 85% van de 380 herstelde deelnemers een terugval ervoer, tegenover slechts 35% van de algemene populatie. Eén voorspeller van terugval is het aantal depressieve episodes: met elke nieuwe episode stijgt de kans op terugval. Echter de aanwezigheid van residuele, subklinische symptomen van depressie, oftewel depressieve symptomen

die niet voldoen aan de diagnose van volledige depressie, blijkt de grootste voorspeller te zijn. De aanpak van deze residuele symptomen, naast acute behandeling, is dan ook essentieel (Hardeveld, Spijker et al. 2010).

Op dit moment zijn er zowel psychologische als farmacologische behandelingen beschikbaar voor de behandeling van acute depressie (Bauer, Whybrow et al. 2002, Undurraga and Baldessarini 2012, Baldessarini, Lau et al. 2015). Gezien de hoge terugvalpercentages wordt bij antidepressieve medicatie aanbevolen om de behandeling ten minste zes tot 12 maanden voort te zetten na herstel van de depressie, en bij terugkerende depressies nog langer (Baldessarini 2013). Het combineren van een psychotherapeutische en farmacotherapeutische behandeling wordt ook vaak ingezet (Cuijpers, Noma et al. 2020) en is effectiever gebleken dan alleen psychotherapie of farmacotherapie (Cuijpers, Dekker et al. 2009, Cuijpers, Van Straten et al. 2009).
Ondanks deze gevestigde behandelopties echter, zien Forte et al. (2015) in hun review over unipolaire depressie, dat depressieve patiënten gedurende een vervolgperiode van 12 tot 13 jaar rapporteren 50% van de tijd ziek te zijn. Het lijkt dus noodzakelijk te zoeken naar manieren om uitkomsten voor deze populatie verder te verbeteren, met inachtneming van de invloed van residuele symptomen op terugval. Aanbevelingen voor onderzoek zijn dan ook verdere exploratie van specifieke, verbeterde individuele en combinatie therapieën, en het nader identificeren van klinische voorspellers van behandelrespons in depressie (Sim, Lau et al. 2016).

Mindfulness-based cognitieve therapie

Een interventie die bij depressieve klachten kan worden ingezet, al dan niet in combinatie met medicatie, is mindfulness-based cognitieve therapie (MBCT). Deze interventie werd ontwikkeld met het oog op terugvalpreventie bij terugkerende depressies (Segal, Williams and Teasdale (2012). Een veelgebruikte definitie van mindfulness luidt: mindfulness is aandacht schenken op een bepaalde manier: bewust, in het huidige moment en zonder oordeel (Kabat-Zinn, 1994) (p.4). MBCT is een groepsinterventie die mindfulness meditatietechnieken combineert met elementen uit de cognitieve gedragstherapie (CGT). In tegenstelling tot CGT, een therapie die gericht is op het identificeren en onderzoeken van disfunctionele automatische gedachten, is MBCT gericht op het loskomen van de inhoud van de gedachten en deze met een zekere afstand te beschouwen. Dit wordt ook wel 'decentering' genoemd en richt zich op het ervaren van gedachten als activiteit van de geest, met een focus op het proces van denken in plaats van op de inhoud. Daarnaast wordt een accepterende en vriendelijke houding ten opzichte van de ervaringen, die zich van moment tot moment voordoen, aangemoedigd.

Tegenwoordig is MBCT opgenomen in multidisciplinaire richtlijnen voor strategieën om terugval bij depressieve patiënten te voorkomen (NICE Depression 2009) (Spijker, Bockting et al. 2013). Kuyken et al. (2016) voerden de recentste meta-analyse op de effectiviteit van MBCT als terugvalpreventieprogramma uit, waarbij individuele data van 1258 patiënten, die drie of meer episodes hadden ervaren, opnieuw geanalyseerd werd. In een periode van 60 weken bleek MBCT het risico op terugval met 31% te verlagen. Tevens bleek MBCT effectiever dan antidepressieve medicatie. In een recente een-op-een vergelijking tussen MBCT en CGT bleken beide interventies even effectief in het voorkomen van terugval (Farb, Anderson et al. 2018).
In een meta-analyse van Strauss et al. (2014) bleek MBCT ook effectief bij patiënten met een huidige depressie in het verminderen van depressieve symptomen, vergeleken met een inactieve controlegroep. Echter, ook na MBCT lijken residuele, subklinische symptomen aanzienlijk aanwezig te blijven (Piet and Hougaard 2011). De resultaten laten dus zien dat er ruimte is voor verbetering.

Opeenvolgende (sequentiële) behandelingen

Eén manier om residuele symptomen te verminderen is het verlengen van een effectief gebleken behandeling, zoals in het geval van antidepressieve medicatie. Een andere manier is om verschillende effectieve behandelingen opeenvolgend aan te bieden. Behandeltrajecten met een opeenvolgende farmacotherapeutische en psychologische behandeling zijn gebruikelijk (Popova, Daly et al. 2019), maar trajecten met twee opeenvolgende psychologische behandelingen worden ook gebruikt (Cuijpers, Van Straten et al. 2009). In het algemeen lijkt een traject met sequentiële behandelingen effectiever dan een enkelvoudige behandeling (Cuijpers, Dekker et al. 2009).
Een sequentieel behandeltraject heeft nog aanvullende voordelen: het zorgt ervoor dat behandelopties kunnen worden geboden op basis van stadia van ziekte in plaats van het acute ziektebeeld. Het model van een dergelijk traject komt dus meer overeen met de chroniciteit van stemmingsstoornissen in vergelijking met de standaard gerandomiseerde, gecontroleerde trial, die op een acuut ziektebeeld is gebaseerd (Fava and Tomba 2010). Daarnaast kan deze aanpak geschikt zijn voor patiënten die geen medicatie willen nemen (Steidtmann, Manber et al. 2012) of die (ernstige) bijwerkingen ervaren van medicatie (Bet, Hugtenburg et al. 2013).
Aangezien MBCT effectief is gebleken bij terugkerende depressie, maar ook ruimte voor verbetering laat zien, zou het waardevol kunnen zijn om inzichten uit studies naar werkingsmechanismen van MBCT te vertalen naar een tweede, opeenvolgende behandeling en zodoende nog meer te profiteren van de werkzame ingrediënten van MBCT.

Werkingsmechanismen van MBCT

Vermindering van rumineren is een van de best vastgestelde werkingsmechanismen van MBCT. Een meta-analyse van Van der Velden et al. (2015) gebaseerd op 23 studies liet zien dat veranderingen in rumineren, piekeren en meta-bewustzijn de behandeluitkomst voorspelden, medieerden of hieraan gerelateerd waren. Ook mindfulness en compassie medieerden behandeluitkomst (Kuyken, Watkins et al. 2010). Kuyken et al. vonden een ontkoppeling van de relatie tussen cognitieve reactiviteit en depressieve symptomen na MBCT, die geassocieerd werd met het cultiveren van zelfcompassie. Cognitieve reactiviteit is de mate waarin men gaat piekeren over een verandering in de stemming. Zelfcompassie heeft te maken met de mate waarin mensen zichzelf zorgzaam en vriendelijk bejegenen. In de meeste gevallen voorspelt de mate van cognitieve reactiviteit de mate van depressieve symptomen, maar in deelnemers die zelfcompassie hadden ontwikkeld was dit niet langer zo. Met andere woorden: bij een verandering in stemming gingen zij daar niet extra over piekeren.

Gilbert en Proctor (2006) concludeerden dat een lage eigenwaarde of zelfdenigratie een van de mogelijke onderliggende oorzaken is voor de chronische en terugkerende aard van depressieve symptomen (Gilbert and Procter 2006). Deze bevindingen komen overeen met het onderzoek van Beck (1967, 1979), dat aantoont dat terugkerende depressieve patiënten ernstige zelfdenigrerende kernovertuigingen hebben. Het zou kunnen dat de relatie tussen cognitieve reactiviteit en terugval in depressie te maken heeft met het oproepen van zulke zelfdenigrerende kernovertuigingen (als 'trigger'), en dat compassie het effect van deze trigger beperkt of zelfs voorkomt.

In staat zijn om een zorgzame houding naar zichzelf aan te nemen zou daarmee een vaardigheid kunnen zijn die het ondermijnende mechanisme van zelfkritiek vermindert, en daarmee ook de kwetsbaarheid voor terugval of het aanblijven van depressieve symptomen. Aangezien zelfcompassie voornamelijk impliciet in MBCT is verwerkt (Segal, Williams et al. 2012), zou het meer expliciet cultiveren van zelfcompassie een aanvullende bijdrage kunnen leveren aan het verminderen van rumineren en vergroten van mindfulness-vaardigheden, bij individuen die kwetsbaar zijn voor terugval.

Interventies gebaseerd op compassie

Psychologische interventies die expliciet gericht zijn op het ontwikkelen van (zelf)compassie zijn de laatste jaren in opkomst. Een recente meta-analyse van compassie-interventies bij niet-klinische doelgroepen (k=21, N=1285) beschreef ten minste acht verschillende op compassie gebaseerde interventies, waarvan de meest gebruikte zijn: Compassion-Focused Therapy (CFT), Mindful Self-Compassion (MSC) en Cultivating Compassion Training (CCT) (Kirby, Tellegen et al. 2017). Er werd een medium effect gevonden in verbeteringen in compassie, zelfcompassie, mindfulness-vaardigheden, depressie en algeheel welzijn. De meta-analyse van Ferrari et al. (2019) liet ook een significante verbetering na zelf-compassie-interventies zien, met een medium effect bij de gehele onderzochte populatie en een groot effect bij een klinische subpopulatie.

Mindfulness-based Compassievol Leven

In 2012 brachten Van den Brink en Koster het boek Mindfulness-Based Compassievol Leven uit (Van den Brink and Koster 2015). In overeenstemming met het eerder geschetste idee dat het expliciet cultiveren van zelfcompassie een aanvullende bijdrage zou kunnen leveren aan de behandeling van terugkerende depressie, merkten de ontwikkelaars dat een basistraining van acht weken (MBCT) voor veel mensen te kort is. In het bijzonder geldt dit voor deelnemers met aanhoudende ongezonde of disfunctionele patronen (p.28). Daarom, ondanks dat het programma zowel in niet-klinische als klinische setting kan worden gebruikt, is MBCL ontwikkeld met een klinische doelgroep in gedachten, die het in het bijzonder moeilijk vindt om vriendelijker en zachter te zijn wanneer harde zelfkritiek en gevoelens van schaamte en waardeloosheid op de voorgrond zijn (p.28).

MBCL is net als MBCT een groepsinterventie, met groepen tot 12 deelnemers, en qua format vergelijkbaar: er zijn acht wekelijkse bijeenkomsten van 2.5 uur waarin een mix van mindfulness-oefeningen, groepsinquiry en interactieve didactiek aan bod komt. De inhoud is echter actief gericht op het ervaren van moeilijke of negatieve gevoelens en het ontwikkelen van een vriendelijke houding tijdens zulke ervaringen. De groepsinquiry en didactiek hebben diezelfde focus.

Voorlopig onderzoek naar MBCL lijkt veelbelovend: eerste studies van Bartels-Velthuis et al. (2016; N=33) en Krieger et al. (2019; N=122) laten beiden een vermindering van klachten zien na MBCL, in respectievelijk depressie en zelf-kritiek, en een toename in mindfulness- en compassievaardigheden.

MBCL als sequentiële behandeling na MBCT

MBCL lijkt een geschikte kandidaat als sequentiële behandeling na MBCT: het is specifiek als vervolgtraining na MBCT ontwikkeld, en als groepstraining, hetgeen volgens Ferrari et al. (Ferrari, Hunt et al. 2019) effectiever is dan een individuele behandeling. Misschien essentiëler nog is dat MBCL ontwikkeld is met een klinische populatie voor ogen. Het voordeel van MBCL na MBCT aanbieden is verder dat deelnemers naar verwachting al geoefend zijn geraakt in het mindful aanwezig zijn bij moeilijke gedachten en gevoelens, voordat ze leren deze actief te benaderen met een vriendelijke, zorgzame houding. Dit zou

cruciaal kunnen zijn in klinische, kwetsbare groepen: Segal, Williams en Teasdale, de grondleggers van MBCT, hebben ook de verwachting geuit dat een fundament in mindfulness nodig is voordat deelnemers expliciet met zelfcompassie gaan oefenen (2012). In het bijzonder zou een basis in mindfulness nodig zijn om om te gaan met het zogeheten 'backdraft effect': het mogelijk aan de oppervlakte komen van overweldigende, lang-onderdrukte emoties naar aanleiding van exposure binnen MBCL.
Ook het feit dat MBCL qua format sterk op MBCT lijkt, en daarmee op herkenning stuit bij deelnemers, en in het Nederlands ontwikkeld is, maakt dat het programma makkelijk toepasbaar is.

Twee opties zijn mogelijk binnen een sequentieel design: de ene is om een pragmatische aanpak te volgen door simpelweg MBCL aan te bieden aan een groep die in een eerder stadium MBCT heeft gevolgd, in navolging van Daly et al. (2018). Idealiter echter wordt de effectiviteit van een sequentieel behandeltraject onderzocht in een prospectieve studie die beide programma's aanbiedt aan een populatie die beide nog niet gevolgd hebben (Popova, Daly et al. 2019). Aangezien nog weinig bekend was over de effectiviteit van MBCL bij de start van onze studie hebben wij voor de pragmatische aanpak gekozen, waarbij dus alleen patiënten geïncludeerd werden die MBCT op enig moment in het verleden hadden gevolgd.

Doelen en hoofdlijn van dit proefschrift

Het overkoepelende doel van de studies in dit proefschrift was om de effectiviteit van MBCL te onderzoeken als een vervolg op MBCT bij volwassenen met terugkerende depressieve klachten, in een (pragmatisch) sequentieel design. Om dit doel te bereiken zijn de volgende stappen ondernomen: a) het co-creëren van een format van MBCL dat geschikt was voor de doelgroep en de voorlopige effectiviteit van MBCL testen; b) de effectiviteit van MBCL als vervolg op MBCT onderzoeken in een gerandomiseerde, gecontroleerde trial die MBCL bovenop reguliere zorg vergeleek met alleen reguliere zorg, bij volwassenen met terugkerend depressieve klachten en die in het verleden MBCT hadden gevolgd; c) het onderzoeken van potentiële mediatoren (werkingsmechanismen) en moderatoren (voorspellers) van behandeluitkomst; d) het onderzoeken van het langere termijn verloop van depressieve klachten na MBCL; en ten slotte e) het kwalitatief exploreren van de toegevoegde waarde van compassietraining die deelnemers mogelijk ervoeren bovenop de effecten van MBCT. Dit hoofdstuk vat de studies samen en bediscussieert ze in het licht van bestaande literatuur.

Samenvatting van de resultaten

Hoofdstuk 2 beschrijft een pilotstudie die inzicht geeft in de haalbaarheid, toegankelijkheid en voorlopige effectiviteit van MBCL als een vervolgtraining van MBCT bij patiënten met terugkerend depressieve klachten (N=17). De resultaten waren bemoedigend: het aanwezigheidspercentage was hoog en de deelnemers waren tevreden met een aangepaste, tweede versie van MBCL. Depressieve symptomen verminderden en zelfcompassie nam toe. Het leek erop dat expliciete compassietraining van toegevoegde waarde zou kunnen zijn bij patiënten die eerder MBCT hebben gevolgd.
Hoofdstuk 3 beschrijft de achtergrond, het design en de methodes van een RCT die MBCL toegevoegd aan reguliere zorg vergelijkt met alleen reguliere zorg in een groep van terugkerend depressieve patiënten. Alle deelnemers hadden ten minste één jaar eerder MBCT gevolgd. Depressieve symptomen, rumineren, zelfcompassie, mindfulness en kwaliteit van leven werden bepaald voor en na MBCL/de controleperiode (T0 en T1). Ook de aanwezigheid van depressie werd vastgesteld met een psychiatrisch interview. Na de controleperiode werd MBCL aangeboden aan deelnemers die in de controlegroep waren gerandomiseerd. De gecombineerde sample, dus beide groepen samen, werd zes maanden na het volgen van MBCL (T2) nogmaals onderzocht om het verloop van depressieve klachten na MBCL op langere termijn in kaart te brengen. In **hoofdstuk 4** worden de bevindingen van zowel de RCT als de verloop-studie beschreven. In totaal waren er 122 deelnemers in de RCT. De resultaten laten zien dat MBCL ten opzichte van de controlegroep, tot een significante vermindering van depressieve klachten leidt van voor tot na de interventie, met een klein effect (d=0.34), overeenkomend met een number-needed-to-treat van vijf. Er werd tevens een vermindering in rumineren gevonden en een toename in zelfcompassie, mindfulness en kwaliteit van leven. Zelfcompassie leek het behandeleffect te mediëren. Daarnaast bleken leeftijd en leeftijd van aanvang (van de eerste episode) voorspellers van het behandeleffect: jongere deelnemers en deelnemers met een lagere leeftijd van aanvang lieten een sterkere verbetering zien dan oudere deelnemers of deelnemers met een latere aanvangsleeftijd.
In de vervolgstudie met de gecombineerde sample (n=119) werd een groot effect gevonden op vermindering van depressieve klachten gemeten van T0 tot T2. Dit lijkt op een verdere vermindering van depressieve klachten te duiden een half jaar na de training, ten opzichte van de nameting (T1).
Hoofdstuk 5 beschrijft de resultaten van een kwalitatieve studie naar de ervaringen van deelnemers, gericht op de mogelijke toegevoegde waarde van MBCL na MBCT (n=22). Deelnemers gaven aan dat MBCL in het bijzonder toegevoegde waarde had door de directe toepasbaarheid van compassievaar-

digheden op momenten dat negatieve ervaringen of gevoelens aanwezig zijn. Vier overkoepelende thema's kwamen voort uit de data: (1) het fundament van vriendelijkheid; (2) blootstelling aan het moeilijke; (3) "empowerment", en (4) gedeelde menselijkheid. Deelnemers leken in staat het programma tot zich te nemen en er substantieel baat van te ondervinden op gebied van zelfcompassie en zelfzorg. In het bijzonder leek MBCL de deelnemers in staat te stellen moeilijke gedachten en gevoelens actief op te zoeken en ermee te 'zijn' met vriendelijkheid in plaats van zelfkritiek, zowel gedurende oefensituaties als in het dagelijkse leven. Dit leek een herstellende emotionele ervaring te faciliteren, dat wil zeggen het verzachten van pijn of traumatische ervaringen. Bovendien bleken de thema's elkaar in een opwaartse spiraal te versterken.

Effectiviteit van MBCL als vervolg op MBCT bij patiënten met terugkerende depressieve symptomen

De gevonden effecten van MBCL zijn opmerkelijk, aangezien we weten dat MBCT ook depressieve klachten en rumineren vermindert en mindfulness- en compassievaardigheden vergroot. De verbetering in kwaliteit van leven, die bemoedigend was in deze groep met relatief zware symptomen, was groter dan in een vergelijkbare populatie die alleen met MBCT was behandeld (gemeten met hetzelfde meetinstrument) (Van Aalderen, Donders et al. 2012).
De bestendiging of verdere verbetering van behandeluitkomst op T2 was ook bemoedigend. Deze is eerder gevonden in studies naar mindfulness-based interventies voor zowel patiënten met ADHD en kanker (Cillessen, Schellekens et al. 2018, Janssen, Kan et al. 2019), als terugkerend depressieve patiënten (Van Aalderen, Donders et al. 2015). Residuele, subklinische symptomen zijn een belangrijke voorspeller van terugval, daarom ondersteunt deze bevinding de potentiële klinische relevantie van MBCL en zijn mogelijke invloed op terugval-percentages.

Een cruciaal verschil met MBCT is de actieve en expliciete compassionele toenadering tot moeilijke ervaringen die in MBCL gestimuleerd wordt. Het zou deze expliciete compassionele focus kunnen zijn die de vermindering in depressieve klachten en verdere verbetering bij T2 tot gevolg had. Zelfcompassie leek ook inderdaad een mediator van het gevonden effect te zijn. Hoewel dit eerder ook voor MBCT is gevonden (Kuyken, Watkins et al. 2010), is de meest robuuste mediator van MBCT, namelijk rumineren (van der Velden, Kuyken et al. 2015), niet bij MBCL gevonden. Dit suggereert dat de werkingsmechanismen van MBCL mogelijkerwijs anders zijn dan die van MBCT en deze laatste wellicht complementeren. De kwalitatieve studie laat zien dat een verhoogd gevoel van regie en gedeelde menselijkheid ook mogelijke mediatoren zijn.

Moderatoren van beide interventies lijken deels overeen te komen: MBCL leek effectiever bij deelnemers met een jongere leeftijd of een lagere leeftijd van aanvang, hetgeen ook voor MBCT is gevonden (Kuyken, Warren et al. 2016, Ter Avest, Dusseldorp et al. 2019). Andere moderatoren die in verband zijn gebracht met MBCT zoals jeugdtrauma, ernst van klachten en aantal voorgaande episodes (Williams, Crane et al. 2014, Kuyken, Warren et al. 2016) zijn echter in deze studie bij MBCL niet gevonden. Ook rumineren lijkt geen moderator van MBCL te zijn, terwijl dit in een recente individuele patiënt-data-analyse (N=292) wel het geval was bij MBCT (Ter Avest, Dusseldorp et al. 2019).
De studie naar de toegevoegde waarde van MBCL lijkt te laten zien dat het beoefenen van zelfcompassie in het bijzonder belangrijk kan zijn voor mensen met sterker of dieper geworteld lijden in termen van trauma of kernovertuigingen over schaamte en schuld, met bijbehorende passieve en actieve vermijdingsstrategieën. Voor deze populaties zou MBCT, met de meer impliciete focus op het ontwikkelen van vriendelijkheid, wellicht niet voldoende zijn om het blootstellen aan moeilijke gevoelens mogelijk te maken, en het leren deze gevoelens te benaderen met een compassievolle houding in plaats van zelfkritiek en afwijzing. In dat geval zou een hoge mate van emotionele vermijding of aversie tegen zelfcompassie een voorspeller van het behandeleffect van MBCL kunnen zijn.

Een belangrijk aspect dat zowel voor MBCT als MBCL geldt is dat de beoefening experiëntieel (ervaringsgericht) is en niet cognitief. Met andere woorden: deelnemers worden gestimuleerd om aandacht te hebben bij directe ervaring, of deze nu plezierig of onplezierig is, in plaats van over de ervaring na te denken. Dit aspect van mindfulness-based interventies komt overeen met exposure-based therapieën, die gebaseerd zijn op de aanname dat wanneer mensen iets vrezen, zij de neiging hebben deze objecten, activiteiten of situaties te vermijden. Alhoewel exposure-based therapieën vooral bij angststoornissen in klinische populaties worden toegepast, lijkt deze neiging tot vermijden ook van toepassing bij mensen met terugkerende depressieve klachten. Een van de onderliggende aannames van Compassion-Focused Therapy is zelfs dat de doelgroep niet alleen in hoge mate zelfkritisch is, maar ook in hoge mate angst heeft voor zowel negatieve als positieve emoties (Gilbert 2009, Gilbert, McEwan et al. 2013). Deze weerstand tegen het aangaan van moeilijke ervaringen lijkt ook in onze populatie in de kwalitatieve studie naar voren te komen, vooral in de eerste sessies. Deelnemers gaven onder andere aan dat zichzelf blootstellen aan ervaringen en gevoelens die ze lang onderdrukt hadden tegennatuurlijk voelde.

Wanneer we MBCL vanuit het perspectief van exposure bezien, krijgen we misschien een beter idee van hoe het werkt. Het proces dat door deelnemers in de kwalitatieve studie wordt beschreven lijkt vergelijkbaar met processen bij exposure therapieën: nadat wat het meest gevreesd werd aangegaan en verdragen is, lijkt de ervaring van spanning en angst te verminderen en een verzachten van lijden of trauma op te treden. Terugkijkend identificeerden veel MBCL-deelnemers het overwinnen van weerstand als de belangrijkste drijvende kracht achter hun toegenomen mentale gezondheid en welzijn. MBCL deelt dit aspect van exposure met andere evidence-based behandelingen zoals CGT en Acceptance and Commitment Therapy (Gloster, Hummel et al. 2012). De effectiviteit van exposure (elementen) in depressiebehandelingen is niet verrassend, aangezien 75% van mensen met een depressieve stoornis een co morbide angststoornis heeft (Spinhoven et al. (2011).

Ook in MBCT wordt blootstelling aan moeilijke ervaringen beoefend. De deelnemers gaven echter aan dat als ze de twee vergelijken, ze tijdens MBCT nog konden zorgen dat ze bij meer 'neutrale' ervaringen bleven, omdat in MBCT minder actief wordt ingezoomd op moeilijke ervaringen. Dit maakte het mogelijk om dieper gewortelde vermijdingspatronen niet aan te gaan.
Uit wat deelnemers aangaven lijkt het erop dat het cruciale element van MBCL de beoefening van zelfcompassie zelf is: in verschillende oefeningen wordt stap-voor-stap milde begeleiding geboden door de moeilijke ervaringen heen. Hierdoor wordt een fundament van veiligheid en vriendelijkheid gevormd die blootstelling vergemakkelijkt. Op elk moment konden deelnemers pauzeren als ze zich overweldigd voelden, en werden uitgenodigd ook hiervoor vriendelijkheid te beoefenen. Dit fundament van veiligheid en vriendelijkheid leek deelnemers in staat te stellen om actief te reageren op lijden. Vervolgens kon deze reactie in moeilijke of pijnlijke dagelijkse situaties toegepast worden. De behoefte om te reageren op lijden komt overeen met de definitie van compassie zoals geformuleerd door Strauss et al., die als kern het herkennen van lijden heeft, gevolgd door de behoefte deze actief te beantwoorden of te verlichten (Strauss, Taylor et al. 2016). Samenvattend lijkt er een proces gaande te zijn waarbij a) moeilijke ervaringen of gevoelens actief benaderd en toegelaten worden, b) een troostend en zelfcompassioneel antwoord komt, hetgeen tot c) meer vertrouwen in het verdragen en aangaan van lijden leidt, en tot d) een steeds sterker wordende ervaring van veiligheid en vriendelijkheid. Deze stappen lijken elkaar te versterken en tot meer mentale flexibiliteit te leiden, die mogelijk weer bijdraagt aan de verdere verbetering van klachten op den duur, in het bijzonder de kwaliteit van leven.

Sterktes en beperkingen

Een belangrijke sterkte van de RCT is de adequate sample size, het gerandomiseerde design en het innovatieve karakter van de studie: dit is een van de eerste studies die de effectiviteit van MBCL bij patiënten met terugkerende depressies onderzoekt. Hoewel onze sequentiële aanpak pragmatisch was, dat wil zeggen aangeboden aan mensen die in het verleden, buiten de RCT om, de MBCT hadden gevolgd, is deze aanpak wel een sterkte, aangezien dit type design mogelijk beter bij de chronische, terugkerende aard van depressie past (Cuijpers, Noma et al. 2020).

Populatie

Zeker voor patiënten die aan relatief zware symptomen lijden kan een sequentiële aanpak effectiever zijn. Ons sample heeft dit profiel: bijna 90% had drie of meer episodes ervaren voor aanvang van de studie en 44% leed aan jeugdtrauma. Het includeren van patiënten zowel met een huidige depressie als in remissie, en het hanteren van relatief weinig exclusiecriteria, heeft naar verwachting de generaliseerbaarheid van onze resultaten vergroot.
De pragmatische aanpak levert echter ook beperkingen op: er is geen een-op-een link tussen deze studie en een studie die MBCT in dezelfde populatie heeft onderzocht. Daardoor weten we niet welke populatie zich precies heeft aangemeld voor de tweede fase (MBCL). Ook het grote verschil in tijd tussen MBCT en MBCL bij deelnemers (1-7 jaar) is een beperking. We weten aldus weinig over een mogelijke selectiebias, noch over het type patiënt dat potentieel in het bijzonder baat heeft bij MBCL na MBCT in vergelijking met alleen MBCT. Het zouden evengoed patiënten kunnen zijn die baat ondervonden van MBCT en die dit wilden verdiepen, of patiënten die juist geen baat hadden van MBCT, bijvoorbeeld een meer behandelresistente groep, die op zoek waren naar nieuwe manieren om hun mentaal welzijn te verbeteren.
Aan de andere kant verliep de inclusie zeer soepel en hadden we een geringe mate van uitval, hetgeen aangeeft dat MBCL niet alleen acceptabel is voor deze populatie maar ook aan een stille behoefte voldoet.

Interventie

We konden voor de MBCL interventie samenwerken met trainers met zeer ruime ervaring met mindfulness-based interventies en die opgeleid waren door de MBCL-ontwikkelaars zelf. Gemiddeld waren deelnemers zes van de acht sessies aanwezig. We zouden echter meer willen weten over de toepassing van mindfulness- en compassietechnieken in het dagelijks leven, aangezien de training dit soort toepassing als doel heeft. In het dagelijks leven hebben we doorgaans regelmatig situaties waarin we compassie zouden kunnen oefenen,

zoals vastzitten in het verkeer of iemand zien struikelen. De huidige studie heeft hier geen data over verzameld.
Ook is MBCL niet met een actieve controle conditie vergeleken, zodat we weinig informatie hebben over de specificiteit van het behandeleffect. Hoewel dit gebruikelijk is bij studies die initiële effectiviteit onderzoeken, zou het kunnen dat de controlegroep gedemoraliseerd is geraakt en een verslechtering van klachten heeft ervaren (Cunningham, Kypri et al. 2013). Zo kan het effect van de interventie kunstmatig verhoogd zijn (Furukawa, Noma et al. 2014). Vanwege de sequentiële opzet zou het kunnen zijn dat de effecten van MBCL gedeeltelijk veroorzaakt zijn door de dubbele dosering van behandeling in plaats van door specifieke effecten van MBCL. Om zowel de specificiteit als de dubbele dosering te onderzoeken zou MBCL vergeleken moeten worden met een hernieuwde MBCT als actieve controleconditie. Vanuit de kwalitatieve studie zijn er echter wel indicaties dat MBCL andere processen in gang brengt dan alleen MBCT.

Metingen

Het onderzoeken van mediatie is een sterkte van de studie, aangezien dit ook inzicht in de specificiteit van de effectiviteit van MBCL geeft. Zelfcompassie bleek inderdaad een factor te zijn die de effectiviteit (mede) verklaarde. We hebben mediatie echter niet met tussentijdse metingen getest. De kwalitatieve studie geeft wel inzicht in mogelijke werkingsmechanismen.
De studie heeft ook voorspellers van het behandeleffect bekeken. Doordat voor een goede analyse van voorspellers doorgaans (veel) grotere groepen nodig zijn, moeten deze resultaten als voorlopig worden beschouwd.
De bevindingen op gebied van mediatie en moderatie, maar vooral die uit de kwalitatieve studie, wijzen erop dat het wellicht beter is de aanpak van onderliggende mechanismen van kwetsbaarheid in deze populatie te richten op verbetering van kwaliteit van leven, in plaats van op het verminderen van klinische symptomen zoals depressieve klachten. Vanuit dit perspectief zouden de nu gekozen uitkomstmaten wellicht herzien moeten worden.

Verloop-studie

Doordat de controlegroep na T1 meteen MBCL kreeg aangeboden hebben we voor de verloop-studie geen gecontroleerd vervolg. We kunnen daarom de langere termijn resultaten niet vergelijken tussen beide condities. Hierdoor is het onduidelijk hoe het deze groep zou zijn vergaan zonder MBCL. Een ander gevolg van dit ontwerp is dat er regressie naar het gemiddelde kan hebben plaatsgevonden. Echter, gezien de verlaging van depressieve symptomen gedurende MBCL (tussen T0 en T1) zou men verwachten dat dit in de vervolgfase

beperkt is gebleven. We zien hier echter juist een verdere vermindering van klachten, hetgeen de resultaten van de RCT ondersteunt.

Kwalitatieve studie

De kwalitatieve studie was een van de eerste die de mogelijke toegevoegde waarde van compassietraining (MBCL) na MBCT heeft onderzocht in een groep terugkerend depressieve patiënten. We konden de deelnemers aan de kwalitatieve studie uit een grote groep halen en konden data blijven verzamelen tot saturatie was bereikt. Zowel de dataverzameling als de analyse is door twee onafhankelijke onderzoekers gedaan en we konden van een divers team gebruik maken voor het thematiseren. Het is echter moeilijk te differentiëren tussen de effecten van MBCT en herhaalde toepassing van principes uit MBCT, en de effecten van MBCL. Dit wordt verder bemoeilijkt door de overlap tussen de twee programma's.

Implicaties voor onderzoek en de klinische praktijk

MBCL lijkt van waarde te zijn voor patiënten met terugkerende depressieve klachten en zou daardoor op grotere schaal kunnen worden ingezet. Aangezien deze studie is uitgevoerd in één centrum, is replicatie van het onderzoek in een context met meerdere deelnemende centra noodzakelijk.
Om het (sequentiële) behandeltraject te optimaliseren is het onze aanbeveling om de studie te herhalen in een prospectieve sequentiële RCT, die MBCT+MBCL met alleen MBCT vergelijkt. In een prospectieve trial zouden we meer inzicht krijgen in wie precies deelneemt en kunnen moderatoren beter onderzocht worden. MBCT zou ook als actieve controleconditie gebruikt kunnen worden om op het mogelijke dubbele doseringseffect te anticiperen, de vergelijking zou dan MBCT+MBCL vs. MBCT+MBCT zijn.
Het zou in algemenere zin interessant zijn om te onderzoeken hoe (elementen van) MBCT en MBCL ingepast zouden kunnen worden in huidige beschikbare behandelingen, en te kijken of ze ook sequentieel aangeboden kunnen worden met bijvoorbeeld CGT of antidepressieve medicatie, of zelfs EMDR (Eye Movement Desensitization and Reprocessing) of andere exposure therapieën.
Het lijkt ook goed om verder te kijken dan werkingsmechanismen die voorgesteld zijn voor MBCT en andere factoren te onderzoeken die mogelijk specifiek zijn voor de effecten van MBCL, zoals de mate van angst voor of weerstand tegen zelfcompassie, en veranderingen in (zelf)regie, vertrouwen en weerbaarheid. Dit zou ook uitgebreid kunnen worden naar mediatoren van andere uitkomstmaten die gebruikelijk zijn bij bijvoorbeeld positieve mentale gezondheid. De resultaten van de kwalitatieve studie leiden tot interessante hypotheses over mogelijke werkingsmechanismen, vooral de focus op het actief toelaten van moeilijke

ervaringen gecombineerd met de directe toepassing van zelfcompassievaardigheden. Even belangrijk zijn moderatoren: MBCL zou in het bijzonder geschikt kunnen zijn voor jongere mensen of mensen met een lagere leeftijd van aanvang. Wellicht zou het programma voor oudere populaties aanpassing behoeven. Er zou ook gekeken kunnen worden naar deelnemers met bijvoorbeeld een sterke mate van zelfkritiek of sterkere vermijdingspatronen: zijn zij degenen die meer baat hebben bij een compassietraining?
Een mooie benadering zou kunnen zijn om verschillende opties in behandeltrajecten vorm te geven door empirisch bewezen principes van mediatie en moderatie in kaart te brengen, in plaats van te focussen op vaststaande therapieën, zoals Rosen en Davison voorstellen (2003; Behavior modification). Een dergelijke aanpak maakt de totstandkoming van nieuwe, gepersonaliseerde trajecten mogelijk door evidence-based elementen te verwerken in reeds vastgestelde, effectieve behandelingen.

Voor de klinische praktijk heeft het sequentiële ontwerp het nadeel dat alleen mensen die al MBCT hebben gevolgd kunnen deelnemen aan MBCL, terwijl beide interventies nog niet overal beschikbaar zijn. De vraag is of MBCL noodzakelijkerwijs op MBCT moet volgen. Hoewel Segal et al. aangeven dat bij klinisch depressieve patiënten het beoefenen van warmte en vriendelijkheid zonder een basis in mindfulness iemands kwetsbaarheid zou kunnen vergroten (Segal, Williams et al. 2012), zou een vroegere integratie van expliciete compassie-elementen of het aanbieden van MBCL als enkelvoudige behandeling het behandeltraject aanzienlijk verkorten en ook kosten-effectiever zijn. Het lijkt daarom goed deze optie wel te onderzoeken, mede omdat in het bijzonder patiënten met een hogere mate van zelfkritiek en vermijdingspatronen baat zouden kunnen hebben bij zo'n versneld traject. In lijn met deze gedachtegang zou de sequentiële aanpak losgelaten kunnen worden om enkelvoudig MBCT met MBCL te vergelijken.

Tot slot is het belangrijk dat er aandacht wordt geschonken aan kwaliteit en certificering van trainers: deze zouden voor MBCL, net als voor MBCT, geprotocolleerd moeten worden volgens professionele en internationaal vastgestelde standaarden, hetgeen nu nog niet het geval is.

Conclusie

Dit proefschrift beschrijft een verzameling studies die aantonen dat MBCL bevorderlijk kan zijn voor de mentale gezondheid van volwassenen die aan terugkerende depressies lijden. De klachten lijken na verloop van tijd, dus vanaf de nameting, zelfs verder te verbeteren. MBCL lijkt daarmee een toegevoegde waarde te hebben na MBCT. Omdat residuele, subklinische symptomen een belangrijke voorspeller van terugval zijn, wordt de potentiële klinische relevantie van MBCL door de resultaten ondersteund. Voor deze populatie zou de meer expliciete, veilige en vriendelijke bodem van zelfcompassie nodig kunnen zijn om blootstelling aan diepere lagen van lijden mogelijk te maken, hetgeen welzijn kan bevorderen.
Meer inzicht in de effectiviteit en waarde van compassietraining als vervolg op of toevoeging aan MBCT of andere behandelingen zou verkregen kunnen worden door onderzoek dat zich richt op werkingsmechanismen en voorspellers. De uitkomsten hiervan zouden behandeltrajecten voor deze populatie kunnen optimaliseren.

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Appendix

Dankwoord (Acknowledgements)
Curriculum Vitae
List of publications

Dankwoord (Acknowledgements)

In de afgelopen acht jaar heb ik heel wat verschillende beeldspraak gehoord waarmee men het werken aan een proefschrift aanduidt. Het merendeel daarvan wijst op de monumentale omvang van de opgave. Zo beleefde ik het ook. Mij heeft het erg geholpen, eerst onbewust en later meer bewust, steeds de hoeveelheid werk die nog voor me lag, te onderschatten. Zoals Frits Koster vaak zegt: "Misschien hoef je de olifant niet in één keer op te eten. Je kunt ook kleine hapjes nemen." Nu eet ik veganistisch, dus ik zou nooit een olifant eten, maar toch.
Maar dit is slechts één van de twee bijdragen aan het succesvol afronden van mijn proefschrift. De andere is: alle mensen die erbij betrokken waren. Alsof ook maar iets ervan tot stand had kunnen komen zonder de inzet van velen! Dit laatste hoofdstuk is een dankwoord aan hen.

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In de initiële opzet en begeleiding heb je een grote kluif aan me gehad. Ik bracht dan wel essentiële dingen mee als een natuurlijke nieuwsgierigheid en de ambitie om altijd en overal de diepte in te gaan, maar ik had weinig tot geen vaardigheden op het gebied van METC-goedkeuringen, trials ontwerpen, validiteit van meetinstrumenten onderzoeken of überhaupt noemenswaardige statistische technieken. Je had geduld met me, beantwoordde mijn vragen, hielp me verder en gaf kritische feedback op iedere stap. Ook logistiek hielp je me: ik denk met warmte terug aan de drie jaar die ik van je logeerkamer gebruik mocht maken op woensdagavond, de gesprekken met je zoons aan de keukentafel en onze gezamenlijke liefde voor Engeland, muziek en Dumbledore. Dat je me die Thaise massage die ik je in Rome liet ondergaan mag vergeven… Tevens heb je me een prachtig promotieteam gegeven: Marloes en Hiske, wat was het ontzettend fijn om met jullie samen te werken. Hiske, ontzettend bedankt voor de hand die je hebt gehad in mijn ontwikkeling in kwalitatief onderzoek. Het was duidelijk dat dit een type onderzoek is waar we beiden veel affiniteit mee hebben. Ook als trainers en beoefenaars van mindfulness hebben we vaak met elkaar gezeten: allebei onderkenden we het grote belang van expliciete aandacht voor compassie.

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Hier lag dan het fundament voor de compassiestudie: een goed, exploratief plan en een mooi team. Het is heel moeilijk in woorden te vatten hoe dankbaar ik ben voor de mensen die vervolgens betrokken werden: de deelnemers van de studie. Nog groter misschien is mijn bewondering voor deze groep. Zoals herhaaldelijk in de inleidingen van mijn papers beschreven wordt, is depressie een volhardende aandoening, die keer op keer terugkomt en met enorm leed gepaard gaat. Het negatieve sociale stigma waar mensen met depressie ook vandaag de dag nog mee te kampen hebben is daarom zo onterecht: ik zie alleen maar heel dappere mensen, die in weerwil van de statistiek en hun eigen ervaring nog een keer een traject wilden aangaan met hoop op verbetering, verlichting, iets dat de ervaring van het zelf en het leven positief beïnvloedt. Dank voor jullie inzet tijdens de training en voor jullie bereidheid om wéér vragenlijsten in te vullen, ook als dat betekende dat jullie geconfronteerd werden met moeilijke gevoelens. Ook dank dat jullie openstonden voor de mogelijkheid, dat verandering of verbetering zich in een heel andere vorm aankondigde dan verwacht.
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room within the first ten seconds of the body scan, only to return after I had finished. "Now you know you can always teach from exactly where you are", you said afterwards. And you were so right.
I have also been inspired by the work of Tara Brach and especially Pema Chödrön, both of whom obviously have no idea who I am, and continue to be grateful for meeting Barry Kerzin at the Mind and Life Summer Research Institute on the Fraueninsel of the Chiemsee. If this work ever reaches you Barry, know that I feel your love and well-wishing always and it is very much reciprocated.
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Rhoda, november 2020

Curriculum Vitae

Rhoda Schuling was born in Garmerwolde (Ten Boer) on October 3, 1978. She finished her secondary education at the Praedinius Gymnasium in Groningen in 1996. After spending a year in Bangor, North Wales, to study English, Linguistics and Russian, she moved back to Groningen to study Linguistics at the University of Groningen. In 2003, she obtained her Master's degree.

In 2013, Rhoda started her PhD project at the department of Psychiatry, Radboud university medical centre. Within the Centre for Mindfulness she conducted a randomized controlled trial and a qualitative study, which led to the current dissertation. During her PhD, Rhoda spoke at several international gatherings amongst which the International Conference on Mindfulness (ICM; Rome 2016, Amsterdam 2018) and at the Omega Institute (New York, 2018). Besides her PhD project, Rhoda worked as an MBSR teacher at the Centre for Mindfulness between 2014 and 2017, and as coastal skipper and instructor at the Zeezeilers van Marken since 2018. Currently, she works as a researcher and teacher at the Hanze University of Applied Sciences in Groningen, where she lives with her two children.

List of Publications

Schuling, R., Huijbers, M. J., van Ravesteijn, H., Donders, R., Kuyken, W., & Speckens, A. E. (2016). A parallel-group, randomized controlled trial into the effectiveness of mindfulness-based compassionate living (MBCL) compared to treatment-as-usual in recurrent depression: trial design and protocol. *Contemporary clinical trials*, *50*, 77-83.

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Submitted

Schuling, R. van Ravesteijn, H., Huijbers, M., Kuyken, W. & Speckens, A. Mindfulness Based Compassionate Living (MBCL): a qualitative study into the added value of compassion in recurrent depression. *Mindfulness, 2020*.

Ter Avest, M., Schuling, R., Greven, C., Huijbers, M., Speckens, A. & Spinhoven, P. Weekly measures of Self-compassion and Affect during Mindfulness-Based Cognitive Living for Depression: A Structural Equation Modelling approach. *Behavioural research and Therapy, 2020.*