Understanding change in psychological treatments for depressive symptoms
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General introduction
Depressive symptoms may impair one’s ability to function in daily life activities. To improve functioning, psychological treatments have been developed to treat depressive symptoms. Several forms of psychological treatments, such as Cognitive Behavioral Therapy (CBT) and Mindfulness-Based Cognitive Therapy (MBCT), have been shown efficacious in reducing depressive symptoms. Yet, not all individuals may benefit sufficiently from these treatments. An important next step is therefore to investigate when and how CBT and MBCT work. In the present thesis, factors are examined that may predict whether individuals improve in Cognitive Behavioral Therapy (CBT) and Mindfulness-Based Cognitive Therapy (MBCT) for depressive symptoms.

**Depressive symptoms**
Depression is a heterogeneous term that refers to a wide range of symptom combinations with varying severity and time course (National Institute for Health and Care Excellence (NICE), 2009). The central symptoms of depression are a depressed mood and a loss of interest or pleasure (American Psychiatric Association, 1994; National Institute for Health and Care Excellence (NICE), 2009). Other depressive symptoms may include a broad range of behavioral, physical, cognitive, and emotional symptoms. For example, individuals may withdraw from social activities, become physically less active, and experience a loss of energy. Depressive symptoms may also include a decreased appetite, sleep problems, feelings of worthlessness, and even suicidal thoughts. When depressive symptoms prevail for a longer period of time, they might severely impair one’s ability to function at work or to participate in daily activities (World Health Organization, 2012).

**Diabetes and depressive symptoms**
Depressive symptoms are more common among individuals with a chronic somatic disease, such as diabetes (National Institute for Health and Care Excellence (NICE), 2009). The prevalence of depression is twice as high in people with diabetes as compared to individuals without a chronic disease (Ali, Stone, Peters, Davies, & Khunti, 2006). Diabetes mellitus is a chronic disease that prevails in about 8% of the Dutch population (Baan et al., 2009). Diabetes requires self-management by patients, including exercise, testing sugar levels, as well as adhering to a strict diet and medication regime. Depressive symptoms may negatively affect the regulation of diabetes by adversely affecting the management of the disease. Co-morbid depressive symptoms in diabetes have been associated with poorer physi-
cal functioning, poorer adherence to diet as well as medication regimens (Ciechanowski, Katon, & Russo, 2000), and poorer control over blood sugar levels (Roy & Lloyd, 2012). Therefore, effective treatment of depressive symptoms is warranted for diabetic patients.

**Psychological treatments for depressive symptoms**

Both antidepressant medications and psychological treatments are available for treating depressive symptoms in individuals with and without a chronic somatic disease. Bearing in mind that patients with diabetes need to adhere to a strict medication and diet regimen, it is not surprising that psychological treatments are preferred over antidepressant medication by patients with diabetes (Dwight-Johnson, Sherbourne, Liao, & Wells, 2000).

Cognitive Behavioral Therapy (CBT) is a regular psychological treatment for depressive symptoms. In CBT, individuals are trained to engage more in pleasurable activities and to challenge their negative thoughts about the self, others, and the future (Beck, Rush, Shaw, & Emery, 1979). CBT has proven its benefits for depression for over three decades (Butler, Chapman, Forman, & Beck, 2006; Hollon & Ponniah, 2010) and has also been shown efficacious for diabetic patients with depressive symptoms (e.g., Gonzalez et al., 2010; Penckofer et al., 2012). Yet, not everyone benefits from CBT (Cuijpers et al., 2012), indicating that CBT does not fit the needs of all individuals. Furthermore, not all individuals share the same treatment preference (Dwight-Johnson et al., 2000). It is therefore valuable to be able to offer different evidence-based psychological treatments to patients.

Mindfulness-based treatments are a popular alternative form of psychological interventions. Mindfulness-Based Cognitive Therapy (MBCT) was especially developed as a preventive treatment for recurrent depression (Segal, Williams, & Teasdale, 2002). MBCT includes mainly meditation and yoga exercises in which individuals are trained to shift their attention to present moment experiences and to acknowledge experiences in a non-judgmental way. In addition to MBCT’s merits for depressive relapse prevention (e.g., Teasdale et al., 2000), there is now sufficient evidence showing that MBCT also contributes to reducing current symptoms of depression, both in individuals without a somatic disease (Khoury et al., 2013) and with a somatic disease (Bohlmeijer, Prenger, Taal, & Cuijpers, 2010), including diabetes (van Son et al., 2013).
GENERAL INTRODUCTION

Why do we want to explain change in psychological treatments?
As has been mentioned before, not all individuals with depressive symptoms respond sufficiently to treatment. There are indications that more than half of patients do not show a clinically relevant change in depressive symptoms after receiving CBT (Cuijpers et al., 2012) or MBCT (see e.g., van Son et al., 2013). It would therefore be helpful to know which factors explain the (non) effectiveness of these treatments. Important questions are: What do therapists do during treatment that causes patients’ mood to improve? Do the skills that are trained in treatment indeed induce change in depressive mood? Which patient beliefs or behaviors predict positive treatment outcomes? More knowledge on factors that predict treatment outcomes may help improve treatments and adequate referral by taking those factors into consideration. For example, mental health care providers may be informed on patients’ perceptions that can be taken into account in treatment choice. Also, therapists might focus on those treatment strategies that are particularly likely to result in changes in depressive symptoms. The answers to the above mentioned questions might also inform depressed individuals on what they can do in daily life to improve their mental health (Kazdin & Nock, 2003). Finally, understanding how change in depressive symptoms is achieved might help identify variables that might be particularly influential in treatment outcome. Based on knowledge on mechanisms of change in psychological treatments, hypotheses can be formulated on variables that may influence the effectiveness of a treatment; i.e., for whom treatment might be more effective (Kazdin & Nock, 2003).

Assumptions on how psychological treatments work
In general, it is assumed that treatment techniques help individuals to acquire skills that enable them to cope with symptoms of depression (see e.g., Beck et al., 1979; Butler & Strupp, 1986). These treatment techniques are mostly based on empirical theories regarding the factors that cause and maintain a disorder (Butler & Strupp, 1986). For example, MBCT is partially based on the empirical finding that repetitively thinking about the causes and consequences of negative experiences (rumination) increases the risk of depression (Nolen-Hoeksema & Morrow, 1991). In MBCT, participants are trained to acknowledge present moment experiences in a non-judgmental way so that individuals learn to disengage from cognitive responses such as rumination (Segal et al., 2002). It assumed that changes in mindfulness and rumination are the mechanisms explaining the effectiveness of MBCT. Currently, it is not clear if changes in the assumed
mechanisms indeed induce changes in depressive symptoms in MBCT. Therefore, the aims of the current thesis include providing insight in how MBCT is assumed to work for depression and if changes in the assumed mechanisms underlying mindfulness-based treatments indeed induce changes in depressive mood.

In addition to treatment techniques, it is believed that common factors play a role in treatment effectiveness. Common factors are factors that are shared across all psychological treatments (DeRubeis, Brotman, & Gibbons, 2005). These include characteristics of the patient, the therapist, and their interrelationship (Butler & Strupp, 1986). Especially the therapeutic alliance between the patient and therapist has received attention in psychotherapy research. Numerous studies have shown that patients’ evaluations of the collaborative working relationship between them and the therapist predict the outcomes of psychological treatments (Horvath, Del Re, Flückiger, & Symonds, 2011; Martin, Garske, & Davis, 2000). Furthermore, patients’ perceptions of the consequences of receiving treatment are assumed to be an important common factor explaining treatment effectiveness (see e.g., Emmelkamp, 1975; Frank, 1968). The few studies that investigated this in psychological treatments for depression showed that patients’ outcomes expectations were indeed predictive of treatment outcomes (Meyer et al., 2002; Sotsky, Glass, Shea, & Pilkonis, 1991; Webb, Kertz, Bigda-Peyton, & Björgvinsson, 2013).

Several issues are not resolved yet concerning the role of the therapeutic alliance and patients’ outcome expectations in the efficacy of psychological treatments. For example, very few studies have ruled out the possibility that the therapeutic alliance is only a reflection of prior symptom gains. It is also not clear if the therapeutic alliance plays an important role in non-traditional forms of psychological treatments such as MBCT. Furthermore, there are different hypotheses on how patients’ outcome expectations affect treatment outcomes. Patients’ outcome expectations may have an immediate impact on patients’ mental state and thereby function as a ‘placebo’. Another hypothesis is that patients’ expectations affect patients’ behavioral involvement in treatment, such as the extent to which patients practice treatment techniques in daily life. The current thesis focuses on these unresolved issues and examines how and when patients’ evaluations of the therapeutic alliance and patients’ outcome expectations predict treatment outcomes.
Aim of the thesis
The general aim of the present thesis is to gain insight in factors that predict depressive symptom change in Cognitive Behavioral Therapy (CBT) and mindfulness-based treatments. An aim of the first part of the thesis is to evaluate differences and similarities in how CBT and MBCT are assumed to reduce depressive symptoms. In the first part of the thesis, we also aim to examine if changes in the assumed mechanisms of mindfulness-based treatments indeed induce changes in depressive mood. The focus of the second part of the thesis is on the role of patients’ expectations and patients’ perceptions of the therapeutic alliance in the efficacy of CBT and MBCT for depressive symptoms in patients with diabetes.

Research approach
We adopt different research designs and analytical strategies to study predictors of depressive symptom change in CBT and MBCT. A literature study is performed to gain insight in the differences and similarities between the mechanisms of change in CBT and MBCT.

A within-subject approach is used to examine if changes in the assumed mechanisms of mindfulness-based treatments indeed predict subsequent changes in depressive mood. This is a question on change processes that operate within individuals. Note that the regular between-subject approach concerns questions on whether individuals report higher levels of Y than other individuals when they have higher levels of X than other individuals. A within-subject approach concerns questions on whether individuals report higher levels of Y than before/usual when they have higher levels of X than before/usual. We are interested in the latter type of question since we aim to test if within-person increases in skills predict within-person improvements in depressive mood.

A between-subject approach was adopted in the studies examining the role of patients’ outcomes expectations and patients’ evaluations of the therapeutic alliance. A between subject approach is suitable to study, for example, whether patients benefit more from treatment than others when they hold higher outcome expectations than others. These studies were nested within a randomized controlled trial on the efficacy of CBT and MBCT for depressive symptoms in diabetic patients.

Specific outline of the thesis
The thesis is divided in two parts, based on the type of research questions, research approach, and used study populations.
Part 1: Mechanisms of change in mindfulness-based treatments

Chapter 2 ‘Why are CT and MBCT beneficial?’ includes a theoretical review on the differences and similarities between Cognitive Therapy (CT) and MBCT for depression. In this study, a comparison is provided of the theoretical foundations, treatment components, and assumed mechanisms of change of these treatments.

Chapter 3 ‘Idiographic change processes’ describes a replicated single-subject approach to studying change processes in six women with depressive symptoms receiving a mindfulness-based treatment. Possible bidirectional effects between daily mindfulness, repetitive thinking, and depressive symptoms are tested.

Chapter 4 ‘The temporal order of change’ describes an intensive longitudinal study in individuals from the general population receiving Mindfulness-Based Stress Reduction. It is investigated whether day-to-day changes in mindfulness precede or follow changes in affect and whether there are individual differences in these effects.

Part 2: The role of patients’ perceptions in CBT and MBCT for depressive symptoms in patients with diabetes

Chapter 5 ‘Design of a randomized controlled trial’ is a description of a randomized controlled trial on the efficacy of CBT and MBCT for depressive symptoms in patients with diabetes. Chapter 6 and Chapter 7 are embedded in this trial.

Chapter 6 ‘Patients’ outcome expectations’ contains a study on the role of patients’ outcome expectations in CBT and MBCT for depressive symptoms in diabetic patients. It is examined whether patients’ outcome expectations predict treatment completion, homework compliance, as well as early- and post-treatment depressive symptom improvement.

Chapter 7 ‘The therapeutic alliance’ describes the differential value of patients’ ratings of the therapeutic alliance in predicting effectiveness of CBT and MBCT for depressive symptoms in diabetic patients. Also, the possibility is examined that early symptom gains confound the association between the alliance and treatment outcomes.

Chapter 8 ‘General discussion’ includes the clinical implications and methodological considerations of the studies included in the thesis. Furthermore, the outcomes of the studies are discussed in a broader context.
Part 1

Mechanisms of change in mindfulness-based treatments