Mindfulness-Based Cognitive Therapy in the Treatment of Bipolar Disorders

Exploring the merit of applying a program developed for unipolar recurrent depression for bipolar disorders

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Dissertation

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Abstract

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Title: Mindfulness-based Cognitive Therapy in the Treatment of Bipolar Disorders

Supervisor: Bergljot Gjelsvik ; Co-supervisor: Catherine Crane

Bipolar disorders (BPDs) are highly recurrent and debilitating disorders characterised by large fluctuations in mood, complex comorbidity and significantly elevated risk of suicidal behaviour and subsequent death from suicide. Despite substantial efforts in clinical research to develop effective treatments for BPDs, and important contributions from pharmacotherapy and psychosocial interventions, BPDs remain notoriously difficult to treat. This is particularly the case for depressive aspects of BPDs. One possible reason for lack of progress in developing effective treatments may be that the cognitive mechanisms maintaining ongoing risk for depressive relapse in BPDs may not be sufficiently understood. Indeed, there is limited evidence as to the cognitive mechanisms underlying ongoing risk for depressive relapse in patients suffering from BPD.

It has been suggested that BPDs and unipolar depression share important dimensions, e.g. that highly RMD is as remittent as depression in BPDs and that there are several similarities in the depressive clinical picture. On that view, is there merit in applying treatments for unipolar depression that have a robust evidence base in preventing depressive relapse? I will discuss this by critically examining the potential relevance of Mindfulness-based Cognitive Therapy (MBCT) as an intervention for BPDs. MBCT is a programme developed to prevent recurrence in recurrent major depression (RMD), included in the National Institute of Clinical Excellence's (NICE) guidelines for preventing RMD in the United Kingdom. I will critically review its evidence base for preventing depressive relapse, and then go on to scrutinise potential mechanisms through which the programme might exert its protective effect. I will then review how these mechanisms might apply to BPDs, and examine the preliminary evidence for the feasibility and efficacy of MBCT in BPDs. I conclude that MBCT shows promise in the treatment of BPDs, and that the preliminary evidence strongly indicates the need for comprehensive randomized controlled trials (RCTs) in the future. The extent to which the protective mechanisms at play are similar to the ones identified in unipolar depression awaits further scrutiny.

Sammendrag

Forfatter: Caroline Ranem Mohn

Tittel: Mindfulness-basert Kognitiv Terapi i behandling av bipolare lidelser

Veileder: Bergljot Gjelsvik; Bi-veileder: Catherine Crane

Bipolare lidelser (BPL) er lidelser som kjennetegnes av perioder med forhøyet og depressivt stemningsleie. Det er også høy risiko for tilbakefall av sykdomsperioder og det er signifikant høyere risiko for selvmordsatferd og død forårsaket av selvmord. Til tross for betydelig innsats i klinisk forskning, og viktige bidrag i behandling fra både medikamentelle og psykoterapeutiske intervensjoner, forblir disse lidelsene notorisk vanskelig å behandle. Behandlingsutfordringene er spesielt knyttet til depressive aspekter ved lidelsene. En mulig årsak til mangel på framgang i utviklingen av effektive behandlinger kan være at de kognitive mekanismene som ligger til grunn for sårbarheten for depressive tilbakefall i BPL er noe som ikke er godt nok forstått. Følgelig er det også begrenset evidensgrunnlag knyttet til kognitive mekanismer som ligger til grunn for risiko for depressivt tilbakefall hos pasienter med BPL.

Det har blitt foreslått at BPL og unipolar depresjon deler viktige kjennetegn, for eksempel at tilbakevennende alvorlig depresjon (TAD) er like hyppig som bipolar depresjon og at det er flere likheter knyttet til klinisk bilde. Med utgangspunkt i dette er det interessant å spørre seg: er det grunnlag for å benytte en behandling for TAD som på robust empirisk grunnlag har vist seg å forebygge depressive tilbakefall? Dette diskuteres i denne oppgaven gjennom å kritisk undersøke den potensielle relevansen av Mindfulness-basert Kognitiv Terapi (MBKT) som en behandlings-intervensjon for BPL. MBKT er et behandlingsprogram utviklet for å forebygge tilbakefall i i TAD, og har blitt innlemmet i National Institute of Clinical Excellence (NICE) sine retningslinjer for forebygging av tilbakevendende depresjon i Storbritannia. For å undersøke relevansen av MBKT for BPL vil evidensgrunnlaget for forebygging av depressive tilbakefall vurderes kritisk. Dette inkluderer en gjennomgang av potensielle kognitive mekanismer som bidrar til risiko for tilbakefall i TAD og BPL , og hvordan disse endres gjennom MBKT, dvs. hvordan MBKT beskytter mot depressive tilbakefall. Deretter følger en gjennomgang av den foreløpige evidensen for MBKT i behandling av BPL. Jeg konkluderer med at MBKT er et lovende alternativ i behandlingen av BPL, og at den foreløpige evidensen sterkt indikerer behov for ytterligere forskning. Hvorvidt mekanismene som er sentrale i TAD har samme eller lignende funksjon for BPL er et empirisk spørsmål som krever ytterligere forskning.

Preface

I would like to thank the Department of Psychology at the University of Oslo, and the Oxford Mindfulness Centre, at Oxford University, for the exchange opportunity granted me. I would also like to thank the Research Council of Norway for their support through scholarship, and Evalill Karevold, Anne-Kari Torgdalsbøen and Vera Østensen for their support and encouragement in the application and planning process. Without the exchange, this dissertation would not have been written, and I am very grateful to have had the opportunity to study and learn at one of the world's most prestigious universities. I would also like to thank everybody at the Oxford Mindfulness Centre for welcoming me so warmly and encouraging me in my working process. Especially, I would like to thank Tanya Smith, who made my stay so much easier and more enjoyable through her dedication in making sure I had everything I needed and helping me whenever I needed it.

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A final special thanks to my soon to be husband, Torbjørn Haugen. This is for you.

Oslo, April 21st, 2015
Caroline Ranem Mohn

Table of content

1 Aims

Bipolar disorders (BPDs) are affective disorders that affect as much as 5% of the population at any time (Akiskal et al., 2000). BPDs are highly recurrent, alternating between episodes of depression and mania or hypomania, and are thus extremely debilitating both in terms of occupational functioning, social and familial functioning and perceived quality of life. Those who suffer from a BPD often struggle with the effects of comorbid diagnoses as well, such as anxiety and substance abuse disorders. Also, the prevalence of suicidal behaviour and suicide is considerably elevated in this patient group compared to other disorders, e.g. schizophrenia (Inskip, Harris, & Barraclough, 1998). Despite considerable efforts to develop treatments for BPDs, relapse rates are high (Forand, DeRubies, & Amsterdam, 2013). This raises questions as to whether existing approaches to BPDs target the mechanisms keeping people at risk.

The aim of this dissertation is to discuss the theoretical merit of and evidence base for Mindfulness-Based Cognitive Therapy (MBCT) (Segal, Williams, & Teasdale, 2013) in light of emerging evidence for cognitive mechanisms involved in maintaining and increasing risk of relapse in BPDs. Here, I will use the term "bipolar disorders" as a reference mainly to Bipolar Types I and II, as a significant amount of the research on treatment is performed including these diagnostic groups. In addition, other diagnostic categories in the bipolar spectrum, e.g. rapid cycling, may represent different clinical challenges. However, in cases where studies include other diagnostic subgroups than type I and II this will be made clear.

According to Malt (2012) it is the treatment of acute depressive episodes and maintenance treatments, that aim at preventing relapse and improving function, that are the most challenging. Further, Geddes and Miklowitz (2013) point out that despite considerable efforts, there has been little progress in this field and, perhaps due to BPDs' complexity, it turns out to be notoriously difficult to treat. Treatment is intimately connected with an understanding of what keeps people at risk. One reason why the evidence base is so limited might be that too little is known about what Geddes and Miklowitz (2013) call "basic disease mechanisms" that can be targeted by medication. Likewise, although there has been more progress in the research of psychosocial mechanisms related to risk of relapse, it may be that targeting these mechanisms has not been properly implemented in treatments. I will argue that since depressive relapse, as shown above, has been one of the most difficult aspects to treat, that it is worthwhile looking to research into unipolar recurrent major depression

(RMD) which may have relevance for understanding depressive relapse in BPDs. I will then go on to discuss clinical implications of these risk mechanisms. Research focusing on genetic and neurological aspects of BPDs is beyond the scope of this paper.

As to selection of relevant literature and research, my starting point has been the most recent meta-analyses of psychotherapeutic and mindfulness-based interventions such as Vieta and colleagues (2009), Piet and Hougaard (2011), van der Velden and colleagues (2015) and Geddes and Miklowitz (2013), as well as the most recent handbooks on treatment of BPDs, such as Goodwin and Jamison (2007) and Malt (2012). Databases included Google Scholar, PsycInfo and Web of Science.

The outline of the dissertation is as follows: First, I will outline core features of BPDs. As will be detailed below, the prevalence, high recurrence, complex comorbidity and elevated suicide risk in this patient group are all factors that have – understandably – motivated considerable efforts to develop effective treatments for this group. The next step will therefore be to discuss the evidence base for key psychotherapy approaches as adjunct to the treatment of BPDs and its challenges. As will be elaborated in the following, BPDs are challenging to treat across various psychotherapies. This is particularly the case for preventing recurrence of depressive episodes. Thus, I will then examine whether one approach that have been successful in preventing depressive recurrence in RMD, Mindfulness-Based Cognitive Therapy (MBCT), might be relevant in the treatment of BPDs. In order to review the potential of MBCT for BPDs, I will give a brief outline of mindfulness and the design of the MBCT programme, as well as its evidence base in preventing depressive relapse in RMD. I will then present and discuss three cognitive processes that are related to RMD, and which are hypothesized to underlie change through MBCT. Finally, I will discuss the preliminary evidence for MBCT in the treatment of BPDs, and critically examine methodological aspects of this research, followed by concluding remarks.

2 What are Bipolar Disorders?

BPDs have been described in medical literature since ancient Greece, but it has taken us almost as long to start understanding their nature. Today it is established that BPDs are affective disorders that can be conceptualized as systemic, meaning that they affect the body as a whole, and that have important hereditary and neurological components. Yet it is the psychological and behavioural symptoms that dominate clinical presentation (Malt, 2012). BPDs are highly recurrent, even chronic, and cause both functional and social impairment, disrupting social, work and family life (Angst et al., 2003). These disorders are also related to a high rate of comorbidity with substance abuse (Bowden, 2003) and of people who suffer from a BPD, estimates show that between 10 and 15 % die by suicide (Hawton, Sutton, Haw, Sinclair, & Harriss, 2005).

The World Health Organization (WHO) has ranked BPDs among the top 10 disabling disorders in both developed and developing countries (Goodwin & Jamison, 2007). According to Mykletun, Knudsen, and Mathiesen (2009), the prevalence of mental illness in Norway is similar to other countries in the western world. Kringlen, Torgersen, and Cramer (2014) performed a psychiatric epidemiological study in Norway, and found a lifetime prevalence for bipolar I of 1,6 % and 12-month prevalence of 0,9%. According to Mykletun and colleagues (2009), these numbers are comparable to the prevalence found in other countries, e.g. in the Netherlands Mental Health and Incidence Study (NEMESIS) performed by ten Have, Vollebergh, Bijl, and Nolen (2002).

American epidemiological studies, however, have found higher prevalence, with a lifetime prevalence of 3,3% and 12-month prevalence of 2,0% (Mykletun et al., 2009). Similar numbers were reported by Fajutrao, Locklear, Priaulx, and Heyes (2009), who claim that the prevalence of BPDs in Europe is underestimated. They point to initial misdiagnosis as a major problem, something that leads to an underestimation of costs involved. The estimated UK national costs related to BPDs are mainly due to hospitalizations, estimated at £4,59 billion. However, Fajutrao and colleagues (2009) also argue that indirect costs related to consequences such as un- or underemployment are major contributors to the overall economic burden that BPDs represent, but is something that is not always recognized in studies. In addition to being an economic burden for society, such direct and indirect costs are also a major cost for the individual affected.

2.1 Depressive, Hypomanic and Manic Aspects of BPDs

Bipolar depressions have many similarities with unipolar depressions, but are more often characterized by somatic syndrome, or melancholia (Malt, 2012). This means that there is a variation in mood during the day; sleep disturbances in the form of hypersomnia (hyposomnia is more common in unipolar depression), and also reduced emotional reactivity, loss of weight and reduced psychomotoric reactivity. According to Malt (2012), there is also often a feeling of diffuse yet deeply disturbing existential anxiety, and the person's initiative and ability to make decisions is strongly compromised. Moreover, thinking is often dominated by negative ideas about the self and one's own worthlessness and failure as a human being. So-called mixed episodes, in which symptoms of depression and mania co-occur, complicate diagnosis and treatment further. These episodes can be conceived as transitional states from one phase to another or as independent clinical states combining various mixes of mood, thought and activity components (Goodwin & Jamison, 2007).

Characteristic of BPDs is that depressive episodes fluctuate with episodes of heightened mood, referred to as hypomania or mania. Hypomania is characterized by increased activity, productivity and a feeling of happiness and well-being, and rarely leads to contact with health services (Malt, 2012). Hypomania can also be hard to confirm in diagnostic interviews in relation to treating depressive episodes, because the patient might not remember or might not have experienced the hypomania as something abnormal. Mania, on the other hand, is characterized by the same symptoms as hypomania, but magnified to a degree where it becomes maladaptive. Mania is accompanied by lack of critical judgement and irritability is quite common. There can also be delusional ideas about one's abilities and it can be characterized by flighty thoughts and impulsive, risky behaviour, both economically and sexually.

While people who are hypomanic often are perceived as extremely well functioning and productive by those around them and are also able to fulfil their roles in the family, socially and in the workplace, mania results in poor overall function due to erratic and impulsive behaviour and, consequently, a lack of ability to function normally. However, it is important to keep in mind that people with BPDs are a heterogeneous group, and that there will be considerable variation between patients, if lesser variation of the episodes' expression for a single patient (Goodwin & Jamison, 2007).

2.2 Classification of BPDs

Based on differences in how BPDs present, they have been divided into several types. Bipolar Type I includes episodes of depression and mania, Bipolar Type II includes episodes of depression and hypomania, and cyclothymic disorders, which are bipolar mood swings with abrupt and labile shifts, are the diagnoses that are recognized in both the DSM V and ICD-10. However, there is recent evidence to suggest that BPDs are under-diagnosed both due to lack of diagnostic precision (Angst et al., 2011) , and also due to the fact that that the phenotypic spectrum is broader than what is normally recognised clinically as bipolar (Akiskal et al., 2000). Goodwin and Jamison (2007) advise caution in making the definition of BPDs too broad. However, they also point to evidence showing that more highly RMD appears to be quite similar to bipolar depression in some important respects such as being equally recurrent. Still, the extent of such similarity is still unclear due to lack of evidence.

Both DSM-IV and DSM-V give precedence to polarity over cyclicity, or recurrence, as a criterion for a BPD diagnosis. However, cyclicity might be just as important to crucial aspects of treatment of BPDs as polarity, for example recognizing psychosocial mechanisms related to relapse and long-term management. By this I mean that even though BPDs differ from unipolar depression in that they involve both manic and depressed mood, those who suffer from a BPD diagnosis spend disproportionately more time depressed than hypomanic or manic. As such, BPDs are also characterized by recurrent depression. RMD, which is regarded as a variant of unipolar depression, is *as* recurrent as depression in BPDs when there has been three or more episodes (Goodwin & Jamison, 2007).

This overlap with RMD raises questions as to whether treatments that have shown promise in highly RMD but have not yet been widely used in treatment of BPDs, such as MBCT, might be relevant. Still, it is important to keep in mind that there are important differences between the two illnesses that may have clinical implications worth considering. For example, once an episode of depression has occurred, the chance of relapse is approximately 50% (Burcusa & Iacono, 2007), while for BPDs a relapse is almost certain, emphasising the chronic aspects of this group of disorders. However, it is likely that psychosocial risk factors related to vulnerability to relapse are similar for both patient groups, and that highly RMD. (three or more episodes) is more similar to BPDs than less severe RMD.

2.3 Trajectory

2.3.1 Age of onset.

Although patients with BPDs constitute a highly heterogeneous group, findings relating to the trajectory and outcome of the disorder are more consistent. People who are diagnosed with a BPD usually have their first episode in adolescence or as young adults, with a mean age of 22.2 years (Goodwin & Jamison, 2007). However, as these authors point out, the age when symptoms first appear is lower than the age at which these symptoms meet diagnostic criteria. Many patients report not having received clinical attention until 6-8 years after their first symptoms (Meeks, 1999; Suppes et al., 2001). Thus, age of first treatment is not a good indicator of onset. However, the reliability of retrospective self-reports can also be questioned. The most accurate measure, according to ICD-10 and DSM-IV, appears to be "first episode", as long as it is established using standardized criteria. Even though most patients with a BPD experience their first episode in adolescence or as young adults, there has been research into the differences between those who have earlier versus later onset.

According to Goodwin and Jamison (2007) it is not yet firmly established to what extent early- and late onset groups differ from each other on factors such as course of the illness, whether there are differences in manifestation of psychopathology or treatment response. However, the most consistent evidence seems to indicate that those with early onset, before age 18 or 19 depending on which study is sited, have significantly worse outcomes on a variety of measures such as more psychosis and mixed episodes, comorbid anxiety disorders, suicidal behaviour and treatment resistance (Carlson, Bromet, Driessens, Mojtabai, & Schwartz, 2002; Schulze et al., 2002). Similar effects of early onset have also been observed in patients with unipolar depression (Korten, Comijs, Lamers, & Penninx, 2012). It is possible that early onset is a factor of BPDs related to other factors such as heredity, or a different genotype than late onset BPDs (e.g. Bellivier et al., 2002), and it also leads to greater total illness duration. Moreover, it is not only the disorder in itself that is devastating to those who become sick - early onset occurs in a period of life where important developmental processes occur, in the transition from childhood to adulthood. This may be one reason why earlier age of onset leads to worse outcomes.

2.3.2 Recurrence.

A core feature of BPDs is recurrence. Keller, Lavori, Coryell, Endicott, and Mueller (1993) observed that relapse into a new episode of illness happened to 81-91% of the patients included in their follow-up study. To recognize the pattern of recurrence is essential in

treatment, as there is evidence to show that periods of remission become shorter until they stabilize after about five episodes (Malt, 2012) and that treatment becomes more difficult as the illness progresses (e.g. Scott et al., 2006). Moreover, there is speculation as to the role of external events in triggering episodes of illness, and whether external events play a lesser role, none at all, or differ in their effect on episodes of depression versus mania, or in the onset of later episodes (Johnson, 2005). Together, these features strongly suggest that setting a correct diagnosis as early as possible is vital, as to ensure that the patients are given the best available treatment with the goal of preventing relapse, or maintaining remission.

Recurrence has implications for treatment. Perlis and colleagues (2006) examined prospective data from a cohort of patients participating in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) over a period of 24 months. This was an effort to map the clinical features related to risk of recurrence in BPDs in patient groups receiving treatment according to contemporary guidelines. They found that recurrence was frequent, and that residual affective symptoms were associated with risk of recurrence. Following their findings they suggest that targeting residual symptoms in maintenance treatment may represent an opportunity to reduce risk of recurrence. When seen in light of the evidence provided by Judd and colleagues (2002), the targeting of residual symptoms in treatment seems particularly important.

The objective of their study was to "document the long-term symptomatic structure of this disorder based on aggregate measures of weekly affective symptom status" (Judd et al., 2002, p. 534). Their study shows that patients with bipolar I were symptomatically ill almost half the time during their follow up of 12,8 years (mean). 29,9% of weeks ill were dominated by subsyndromal, minor depressive, and hypomanic symptoms, nearly three times as frequent as major depressive and manic symptoms that made up 11,2% of the weeks with symptoms. Also, depressive symptoms dominated 31,9% of the total follow-up weeks, in contrast to manic and hypomanic symptoms making up 8,9%, and mixed episodes making up 5,9%. In other words, it is crucial that subsyndromal and minor affective symptoms are specifically targeted or attended to in some way in treatment of BPDs if the goal is to prevent relapse.

2.4 Psychiatric and somatic comorbidity

Psychiatric comorbidity provides yet another significant factor that can affect adherence rates and the course, treatment and outcome of BPDs. Between 80% and 90% of patients with a BPD have some form of psychiatric comorbidity, with anxiety-disorders and

substance abuse disorders, including alcohol abuse, being the most common (Malt, 2012). In addition, patients with a BPD are more vulnerable to a variety of somatic illnesses than the non-clinical population, such as cardiovascular and gastrointestinal diseases. Such comorbidity is the result of BPDs consequences for lifestyle and side effects of medical treatment. As Goodwin and Jamison (2007) point out, although diagnosing comorbid psychiatric disorder is crucial for the effect of treatment, it is often not done comprehensively in clinical settings, e.g. due to a focus on primary morbidity. Not treating comorbid disorders can lead to the patient being left with considerable symptoms and disability, despite recovering from the primary diagnosis, e.g. depression.

Comorbid psychiatric disorders pose great challenges for the setting of a correct diagnosis. Differentiating symptoms caused by a primary psychiatric disorder from those caused by secondary problems (e.g., substance abuse) can be difficult. There is also the question of whether some comorbid problems (e.g., anxiety) are an inherent part of how the disorder manifests, or whether it is a separate disorder. According to Goodwin and Jamison (2007) most studies have found that alcohol abuse disorder is much more prevalent in patients with BPDs than any other affective disorder. The same is the case for other types of drug abuse (e.g. marihuana), but these associations are more uncertain due to the fact that the drugs in question are illegal and therefore difficult to monitor. According to The Epidemioloigcal Catchment Area (ECA) data (Regier et al., 1990), lifetime prevalence of alcohol abuse is 46% for bipolar I, and 39% for bipolar II. Drug abuse has a prevalence of 41% for bipolar I and 21% for bipolar II. In unipolar depression the numbers are 17% for alcohol abuse and 18% for drug abuse and in the general population 13,5% for alcohol abuse and 6,2% for drug abuse.

There are several theories related to the relationship between BPDs and alcohol and drug abuse. According to Malt (2012) interview-based research reveals that most patients report that they use alcohol and/or drugs to alleviate their symptoms, like anxiety, racing thoughts and irritability. Somewhat surprising, a summary of six studies done by Zisook and Schuckit (1987) shows that those bipolar patients who increase their alcohol consumption during periods of illness do so during manic phases. If a self-medication hypothesis is to be taken into consideration, alcohol does provide some relief of symptoms such as irritability, restlessness and agitation, which is associated with mania, as well as mixed episodes. On another note, one can conceive that the increased impulsiveness and poor judgement during manic phases could also lead to increased alcohol and/or drug abuse. There may also be

important differences between those who develop substance abuse before the emergence of a BPD, and those who develop substance abuse after.

Anxiety disorders are also a very common comorbid diagnosis when there is a primary BPD, with a lifetime prevalence of 42% (Sasson, Chopra, Harrari, Amitai, & Zohar, 2003). An analysis of a cross-sectional sample of the STEP-BD project performed by Otto and colleagues (2006) found that the presence of comorbid anxiety disorder was associated with earlier age of onset, decreased likelihood of recovery, poorer role functioning, and lower quality of life. It is clear that BPDs require a treatment that does more than target symptoms or specific maladaptive beliefs alone. Given the complicated clinical picture often presented to clinicians treating patients with a BPD, it is clear that a treatment is needed that teaches transdiagnostic skills and skills of distress tolerance –at least as an adjunct to more focused therapy. MBCT stands out as an interesting possibility in this regard.

2.5 Functional impairment

Due to BPDs' fluctuating nature, people with a BPD have episodically impaired functioning. MacQueen, Young, and Joffe (2001) point out that there has been considerable research into predictors of some outcomes, such as mortality. Much less research has been aimed at inter-episode functioning, based on an idea that people with BPDs generally function quite normally between episodes in important arenas in life such as work and family. In their review article, MacQueen and colleagues (2001) included studies from the previous 25 years focusing on psychosocial functioning in BPDs. They found that, in aggregate, 30-60% of patients experienced some form of psychosocial impairment, and although there was considerable variation in these estimates, the numbers indicate disability that was surprisingly severe, enduring and pervasive. However, exactly what factors are associated with functional outcome varied between studies and have thus far been difficult to establish. What was quite clear is that premorbid functioning is among the best predictors of psychosocial recovery. Several studies cited in this review yield mixed results regarding the predictive role of past episodes or previous hospitalizations, other than that number of previous episodes seem to contribute to poorer cognitive functioning during euthymic periods, and may thus present barriers to both social and occupational recovery.

At the point when this review was published, the link between depression in BPDs and its consequences for functioning in euthymic periods had not been systematically examined, according to MacQueen and colleagues (2001). Since then, more recent and

thorough examinations of the link between symptom severity and functional disability has been performed by Judd and colleagues (2005) and Marangell and colleagues (2009). Judd and colleagues (2005) found, like MacQueen and colleagues (2001), that symptom severity and psychosocial disability fluctuate together, but also that subsyndromal depressive symptoms are associated with significant impairment for patients with both bipolar I and bipolar II diagnoses. Even when asymptomatic, the psychosocial functioning of patients with bipolar types I or II is not as good as that of healthy controls. The latest review of the research on functional impairment related to bipolar diagnoses was performed by Marangell and colleagues (2009), who investigated the functional impact of subsyndromal depressive symptoms in BPDs using data from the STEP-BD.

Marangell and colleagues (2009) conclude that those who experience subsyndromal depressive symptoms essentially bear the same burden of functional impairment as those experiencing a full episode of depression. In particular, they found that impairment was correlated with symptoms of sadness, anhedonia and lassitude. Moreover, it was found that there were more similarities between the depressed and subsyndromal groups than between the subsyndromal and recovered group. The recovered group had a shorter duration of the disorder, fewer episodes in total, and showed less evidence of comorbidity and symptoms of rapid cycling. It is important to be aware of the fact that using different methods of measurement when it comes to research on functional outcome for patients with BPDs also yield differerent results. This is pointed out by MacQueen and colleagues (2001) who refer to studies that report relatively low rates of impairment, but also define outcome by employment or independent living only. In contrast, in studies in which patients and their families have been asked about the burden of illness, reports of impairment are very high. In sum, these three reviews all present strong arguments in favour of treatments that aim specifically at aspects of BPDs, e.g. subsyndromal symptoms in euthymic periods, that can improve psychosocial functioning.

2.6 Suicidal behaviour and suicide

BPDs are associated with a significantly elevated risk of suicide and suicidal behaviour. Between 10 and 15% of patients diagnosed with a BPD die by suicide (Hawton et al., 2005). Hawton and colleagues (2005) also estimated that a further 20 to 56% attempt suicide or engage in deliberate self-harm (DSH). In contrast to the general population, they found that the relative suicide potential in women is comparable to that of men, and that there

is no association between suicide and marital or employment status, or negative life events (e.g., early loss or social isolation). Hawton and colleagues (2005) argue that the evidence suggests a higher risk of suicide in patients with bipolar II compared to bipolar I, and that the lack of association between risk of suicide and characteristics of the disorders, such as mania, rapid cycling or psychotic symptoms, may be due to the small number of studies.

The strongest factor associated with risk of suicide was found to be previous suicide attempts, and hopelessness. Investigating the risk factors associated with DSH in BPDs has yielded a greater number of factors than for suicide and suicidal behaviour, something Hawton and collleagues (2005) suggest in part mirrors the higher number of patients who self harm in comparison to how many who subsequently die by suicide. One study included in the review by Hawton and colleagues (2005) linked attempted suicide in patients with BPDs to a history of both physical and sexual abuse. There is also a clear link between attempted suicide in patients with BPDs and disorder characteristics, including rapid cycling, mixed episode, early onset, severity of depressive symptoms and comorbid substance or alcohol abuse or anxiety comorbidity (Hawton et al., 2005).

In sum, the prevalence, high risk of recurrence, complex comorbidity and elevated risk of suicidal behaviour, including death by suicide, are factors that have motivated significant efforts to develop effective treatments of BPDs. It is to this body of work that I now turn.

3 Treating Bipolar Disorders: What is the Current Evidence Base?

BPDs pose considerable challenges and costs for both those affected, for their families, and for society at large. It is therefore understandable that considerable effort has been put into developing effective treatments for these disorders. However, Geddes and Miklowitz (2013) somewhat provocatively point out that remarkably little progress has been made in developing effective treatments. The purpose of this section is to critically examine the evidence base for psychotherapeutic interventions for BPDs, and to discuss the challenges related to developing effective treatments for these complex disorders. This section will not provide a comprehensive review of all existing treatment approaches, but rather review key interventions highlighted in recent reviews and treatment guidelines.

The ways in which a disorder is understood is intrinsically linked with how it is treated (Kazdin & Kagan, 1994; Rutter & Sroufe, 2000; Teasdale, Segal, & Williams, 2003). The focus in clinical research on genetic and neuropsychological aspects of BPDs, have led to pharmacotherapy as a dominant treatment approach. This is understandable: It has been established that biological factors are a crucial part of the causal basis for developing a BPDs: bipolar types I and II have a heritability of 80%, with first-degree relatives having a 20-25 % chance of developing a BPD or unipolar depression (Malt, 2012). Moreover, there is a high rate of concordance between twins (McGuffin et al., 2003). Despite the genetic contribution having been recognised for a long time, little is known about the genes involved or the mechanisms behind its heritable transmission.

However, the high rates relapse and recurrence suggest that there might be psychological mechanisms at play that are not being sufficiently addressed through existing treatment approaches (Perlis et al., 2006). Indeed, recent reviews (e.g. Beynon, Soares-Weiser, Woolacott, Duffy, & Geddes, 2008; Vieta et al., 2009) have argued that pharmacological interventions are insufficient as prophylaxis treatment alone. Due in part to limitations of pharmacotherapy in treatment of BPDs (e.g. inability to successfully prevent relapse, non-adherence rates, and its lack of comprehensiveness in treating complex disorders), recent years have seen an increasing interest in psychological and sociocultural factors (e.g. negative life events, expressed emotion) involved in persistent vulnerability to depressive relapse in BPD, as well as the interplay between biological and psychological

factors as determinants of course and outcome. Psychotherapeutic interventions include psychoeducation (Colom et al., 2003; Colom et al., 2009), Cognitive Behavioural Therapy (CBT) (Scott et al., 2006), Interpersonal Social Rhythm Therapy (IPSRT) (Frank et al., 2005) and Family-Focused Therapy (FFT) (Miklowitz, George, Richards, Simoneau, & Suddath, 2003). Currently, the recommended treatment for BPDs, according to Forand and colleagues (2013), is a combination of psychopharmacological treatment and psychotherapeutic intervention, with a particular emphasis on psychoeducation, CBT and FFT. In the following, I will review psychoeducational and CBT interventions in the treatment of BPDs. I will not include FFT in this review because it is not directly comparable to either CBT or psychoeducation, as it is aimed not only at the patient, but includes the family and support system surrounding the patient as a central component.

3.1 Psychoeducation as a Treatment for BPDs

In 2009, Colom and colleagues published the results of an RCT (N=120) whose aim was to investigate the long-term efficacy of psychoeducation for bipolar types I and II. Their trial included a group-psychoeducation intervention and a non-structured group intervention followed up over a period of 5 years. Main outcome measures were time to recurrence of any polarity, number of recurrences, and total number of days spent ill, as well as frequency and length of hospitalizations. The 5-year follow up data shows that, over time, the psychoeducation group spent significantly less time actually ill (154 vs. 586 days) and fewer days hospitalized (30 vs. 45 days), and the number of illness episodes were much lower in the psychoeducation group than in the control group (3,86 vs. 8.37). This was true for both depression and mania, but stronger for mania. The researchers attribute this finding to the fact that changes relating to management of mania, such as regularity of habits and early detection, may be more noticeable in the long term.

Colom and colleagues (2009) claim that psychoeducation should be considered disease-management training as it goes far beyond mere delivery of information. In addition to regularity of habits, they propose that another potential active ingredient of psychoeducation may be the improvement of comorbidities, and also improved understanding of the disorder and increased awareness of individual relapse signatures. Empowerment in decision-making, for example being able to take preventive measures such as increasing medication on one's own, or a decreased burden on caregivers and family through coping with stigma, can both be results of more knowledge about the disorder. These are important

ways through which psychoeducation works. The authors recognize that these mechanisms may be somewhat speculative, but that they are clearly related to the content of the psychoeducational programme provided for the participants. As such, they argue that further research should look at the specific mechanisms by which psychoeducation reduces the different types of episodes.

Despite promising results, this trial has some limitations. Firstly, its generalizability is limited as individuals with severe comorbidities and substance misuse were excluded. Moreover, the outcome measures did not include sub-threshold symptoms of depression, which are known to have a strong and adverse impact on psychosocial functioning. On the other hand, as seen by the large response rate at follow-up, it is evident that the psychoeducation programme in question was well received by the participants. In spite of its limitations, this trial presents compelling evidence for the inclusion of psychoeducation in any form of psychotherapeutic intervention for patients with BPDs. An aspect of treatment of BPDs that this trial does not explicitly deal with is adherence to medication, even if the researchers do point out its importance. Miklowitz and colleagues (2003) randomised participants (N=120) to either a treatment condition, including psychoeducation and standard pharmacological treatment, or a non-intervention condition, including an unstructured intervention and standard pharmacological treatment. At a two-year follow up, they found that the psychoeducation intervention increased time to relapse and was effective in preventing all types of bipolar episodes. There was also a clear effect on adherence to medication, but even patients who did not have problems with adherence clearly benefited from being included in the psychoeducation group.

In a more recent review of the evidence for psychotherapy as adjunct to standard pharmacological treatment, Vieta and colleagues (2009, p. 495) argue that psychoeducation provides patients with "a theoretical and practical approach to understanding and coping with the consequences of their illness, which thus allows them to change their attitudes toward and beliefs about the illness, and provides specific coping strategies". Following this argument, psychoeducation should be implemented only with patients who are reasonably stable as the cognitive dysfunctions and behavioural symptoms that appear in and following an illness episode can make group functioning difficult and make it hard for participants to follow the treatment. As a concluding point in this account of psychoeducation in the treatment of BPDs, it is worth mentioning that Scott and colleagues (2009) explored cost-effectiveness following a psychoeducation intervention for patients with BPDs. Their results showed that in the short term, patients receiving psychoeducation had twice as many planned outpatient

appointments, and thus used more mental health resources without clear additional health gain compared to a group receiving unstructured group support. However, when viewed in the long term, the estimated mean cost of emergency consultations for this group was significantly lower compared to a control intervention. In conclusion, group psychoeducation was less costly and more effective in the long term.

3.2 CBT in Treatment of BPDs and its Evidence

Early pilot research (e.g. Lam et al., 2000; Scott, Garland & Moorhead, 2001) provided preliminary evidence for the merit of CBT for patients with BPDs. In addition to targeting maladaptive behaviour and cognitive patterns, these studies adapted CBT to be more tailored to BPDs. Thus, these interventions were not only aimed to change maladaptive cognitive styles, but also included a psychoeducational element stressing the importance of sleep and regularity of habits and coping with stress. These preliminary studies indicated that six months of CBT led to greater improvements in symptoms and higher levels of overall functioning, as well as fewer episodes of relapse during an 18-month follow-up period. The study performed by Scott and colleagues (2001) showed a 60% reduction in relapse rates in the 18 months following CBT compared to before commencing CBT, and the authors viewed these preliminary results as encouraging. However, they also emphasize that even though the pilot data were encouraging, and seeing as CBT has proven effective in treating unipolar depression, BPDs are inherently more complex than unipolar depression, and as such may require some special consideration, e.g. a high level of treatment expertise.

In spite of these results being based on small, non-representative samples, there was an understandable enthusiasm in CBT and the possibility that this treatment could be particularly useful for treating and preventing depressive episodes in particular. As has already been pointed out, treatments traditionally offered patients with BPDs – pharmacotherapy and some form of psychotherapy focusing on illness-management (e.g. establishing and keeping up a stable pattern of activity and sleep and adherence to medication) – do not prevent relapse of affective episodes in the long term. Scott and colleagues (2006) performed an RCT (N=253) of patients with a DSM-IV based diagnosis of a BPD. The participants were randomly assigned to either a treatment-as-usual (TAU) condition, which included medication and contact with mental health professionals or TAU with additional 22 sessions of CBT. Patients were assessed every eight weeks for 18 months.

Analysing the data from their study, Scott and colleagues (2006) found no between-group difference in the rate of recurrence for both depressive and manic episodes, with a relapse rate of about 30% at 6 months and about 60% at 18 months. Also, they found no differences in duration of illness episodes or in ratings of symptom severity and no effect of CBT on adherence to medication. These results were disappointing, and in their article, Scott and colleagues (2006) consider different explanations for the difference between the results in the pilot studies, compared to their RCT. They point out that studies targeting treatment for patients with BPDs often exclude patients who are harder to treat, be it because of how their illness presents (e.g. rapid cycling) or because of comorbid diagnoses (e.g. substance abuse). When excluding patients who are harder to treat, studies may frequently overestimate the efficacy of interventions targeted at patients with BPDs. It is also important to keep in mind that the different pilot studies show effects for different outcomes. Some find an effect on manic relapse, others a reduction in number of hospitalizations, and yet others on longer survival time.

In their study, Scott and colleagues (2006) recruited a more heterogenic sample than previous studies, including comorbid current substance abuse or dependence disorders, rapid cycling/cyclothymic, other Axis I comorbid disorders, as well as those currently experiencing an acute episode at the time of randomisation. They argue that this sample is more representative of the bipolar patient population than that included in previous RCTs, and the results may imply that patient characteristics and the therapeutic model used are equally predictive of the outcome of treatment. Further analysis of the results of this RCT, led the researchers to discover that CBT may be less effective with patients that experience frequent recurrence and who have experienced more than twelve episodes of illness. Based on these results, they suggest that the use of brief CBT to prevent future recurrence may be better viewed as an early option, and not as a treatment targeting those who appear more difficult to treat and have experienced a more chronic illness.

3.3 The Efficacy of Psychotherapeutic Interventions in the Treatment of BPDs

Even though evidence related to long-term effects of psychotherapy as adjunct to pharmacotherapy are mixed, there are promising results that encourage further examination. In the review by Vieta and colleagues (2009) it is argued that a number of well-designed studies, like those mentioned above, are strong indicators that adjunct psychotherapy can

enhance overall effectiveness of treatment by providing further protection from recurrence. However, there are a number of issues that may limit the usefulness of the different approaches in clinical practice. In particular, Vieta and colleagues (2009) argue that it is important to identify the core ingredients of treatments related to their relative impact on specific phase and polarity of the BPD. They also argue that selection of patients with BPDs who join clinical trials should be more representative of the heterogenic population they represent and, based on findings indicating increased severity in course for BPD, treatment should be initiated as early as possible.

The review by Vieta and colleagues (2009) is the most up to date critical evaluation of psychotherapies as adjunct to pharmacotherapy in BPDs. Geddes and Miklowitz (2013) argue that ”a more deeply characterized picture of the core clinical phenotype is urgently needed” (p. 1679), and although substantial progress has been made in the past decade in understanding the role of psychotherapy for this patient group, what ingredients that lead to the most clinical change is still not understood. In other words, there is a need for studies that systematically assess the mediators of treatment changes on the course of BPDs. As a matter of fact, a couple of years predating this article Miklowitz, Goodwin, Bauer, and Geddes (2008) published a paper in which they analyzed 14 RCTs of psychotherapeutic interventions for BPDs. They had 31 therapists who had participated in these trials fill out a questionnaire to map the use of treatment strategies in active versus TAU conditions. They found that active treatment modalities included more focus on problem solving and interventions to help the patients cope with the stigma of having a BPD. However, across the different approaches, the specific methods differed. For CBT, for example, the use of cognitive restructuring and mood charts were frequently used, while regulating sleep and daily routines were important ingredients in psychoeducative interventions. As such, these psychotherapeutic interventions have certain aspects in common, but can also be distinguished from both each other and from TAU. Miklowitz and colleagues (2008) argue that identifying the common and the treatment-specific dimensions is the first step in determining which ingredients mediate the most powerful clinical changes in patients with BPDs. However, as Geddes and Miklowitz (2013) argue, there is still a lack of studies investigating these ingredients and their mediating mechanisms.

It is not as simple as identifying the therapeutic ingredients and mechanisms that mediate clinical changes. To be clinically relevant, research needs to consider both characteristic of the patient group in question, time interval of treatment and domains of outcome. Miklowitz (2008) pointed this out when he examined the evidence for adjunctive

psychotherapeutic interventions for BPDs by focusing on which treatment works at which stage of the illness, how long a treatment should last and how enduring its effects are, whether the same treatment modifies both depressive and manic symptoms, which functional domains that are enhanced, and the mechanisms of therapeutic change. He concluded that the active treatments reviewed were associated with between 30 and 40% reduction in relapse rates over periods of follow-up varying between 12 and 30 months. He also observed that more intensive and long-lasting (12 or more sessions) treatment consistently lead to better outcomes. As might be expected, no particular treatment modality was found to be superior to the others in terms of outcome. However, the results also suggest that the different treatment approaches operate through different mechanisms, which in turn should affect different outcome variables. As there were big differences between studies and because many of the studies included had inadequate sample sizes and other methodological weaknesses, Miklowitz (2008) points out that his conclusions must be viewed as tentative. As such "inferences regarding the effectiveness of specific models of psychotherapy for bipolar disorder are best viewed as promising but preliminary" (Miklowitz, 2008, p. 1416). As pointed out above, this is something that we need more well-designed and methodically sound research to understand better.

3.4 Challenges in Clinical Research on Treatment Interventions for BPDs

Psychotherapeutic interventions can enhance overall effectiveness of prophylactic treatment for BPDs by improving adherence, helping patients identify prodromal symptoms early and teaching how to cope with these symptoms. However, relapse rates are still almost 50% in the course of two years for patients who achieve remission, even when undergoing both pharmacological treatment and psychotherapeutic intervention (Perlis et al., 2006). These data point to the need to think differently about treatment, and which mechanisms are targeted in treatment. To decide whether a particular psychosocial variable is a risk factor for the onset, course, or expression of BPDs, is not straightforward. Kraemer, Stice, Kazdin, Offord, and Kupfer (2001) point out that complex disorders, such as BPDs, may not have a single cause but a causal chain, or even multiple causal chains. Consequently, the effects of a given risk factor can only be understood in the context of all the other factors. As such, studying individual risk factors is important, but accumulating risk factors through counting or scoring them "does little to increase the understanding of etiologic processes or of how

interventions might be optimally timed, constructed or delivered to prevent or treat psychiatric conditions" (Kraemer et al., 2001, p. 848). As a result, costly and time-consuming randomised clinical trials (RCTs) that manipulate risk factors often produce disappointing results.

Kraemer and colleagues (2001) have proposed three features as a basis when mapping risk factors: temporal precedence, correlation and dominance (e.g. of risk factor A and B, which is more potent, or are they more potent together). They explain that it is important to distinguish risk factors on the basis of these features in order to avoid designing interventions to be tested in RCTs that manipulate correlates that are not risk factors or risk factors that are not causal. Moreover, when there are chains of causal risk factors, addressing only some of the mediators in the chain may result in treatment effects that have minimal clinical relevance. They point out that most prevention programmes for complex psychiatric disorder are aimed at several risk factors simultaneously, but that this approach confounds effects that derive from changing causal risk factors with effects of influences that are more peripheral, or may be unresponsive to the intervention. In other words, it is important to show what manipulations of the psychosocial factor leads to changes in symptoms, function, or relapse.

Thus, it is difficult to separate the effects of the direct reduction of risk of relapse from nonspecific therapeutic factors as the mechanism underlying any therapeutic change. Alloy and colleagues (2005) argue that BPDs present specific methodological challenges due to their presentation as recurrent with significant symptomatology in remittent periods, making it difficult to assess environmental and cognitive factors as risk factors as opposed to symptoms. Consequences of a BPD – such as leading an unstable life –increases the likelihood that patients themselves contribute to the negative features of their environment through poor judgement and coping skills. Studies disentangling various psychosocial aspects of BPDs are limited by design (mostly cross-sectional or based on retrospective report), not controlling for current mood state, relying on self-report measures, and not distinguishing between depressive and hypomanic and/or manic states. The perennial tendency across studies to include small samples is a further limitation.

In an attempt to identify whether psychosocial factors contribute risk to the onset, course, or expression of BPDs and whether the psychosocial risks for BPDs are similar to those for unipolar depression, Alloy and colleagues (2005) reviewed research on the role of individual's current environmental contexts, cognitive styles, and developmental histories as risk factors in BPDs. They conclude that even though there are relatively few studies that are methodologically sound, those that are suggest that negative life events do contribute to

increasing the risk of depressive relapse, as they do with unipolar depressed patients. They also suggest that negative life events are not only associated with depressive relapse, but manic and hypomanic relapse as well. The results are the same for social support; specifically that poor social support is associated with longer time to recovery, greater likelihood of relapse and a higher degree of impairment.

In addition to negative life events and social support, Alloy and colleagues (2005) also reviewed the evidence for the effects of cognitive styles in BPDs. There is considerable evidence that patients with BPDs have maladaptive cognitive styles similar to those found in patients with unipolar depression (e.g. negative styles for inferring causes, consequences and self-worth implications, negative self-schemata and dysfunctional attitudes). However it is not clear whether distinct cognitive styles characterize depression versus mania. When seen in relation to negative life events and social support, considerable evidence can be found to support the hypothesis that cognitive styles predict the course of bipolar depression, and more mixed evidence that they predict the course of mania or hypomania. In other words, there is a need for more knowledge about what cognitive mechanisms predict the course of BPDs, and interventions that target them.

In sum, it is difficult to find effective ways to treat patients with BPDs, and to do it in a manner that captures their complexity. It should be acknowledged that there are elements of the current psychotherapeutic interventions, like psychoeducation and CBT, whose interventions are effective in stabilizing and protecting against new episodes of depression and mania (Miklowitz et al., 2008). A key question is, which mechanisms are involved in keeping people vulnerable to persistent episodes in BPDs? This will have important implications for the design of effective interventions.

As is also evident from the research cited here, most treatment trials are understandably aimed at reducing the risk of relapse of both depressive and manic episodes or as acute treatments. However, treating acute depressive symptoms and using mood charts and psychoeducation to help prevent relapse overlooks the importance of subsyndromal symptoms and the functional impairments that follow also in remission. Miklowitz (2008) point out that research on treatment for BPDs should also include a focus on different functional domains. As an example, treatment interventions like FFT does aim at improving family function, which is an important functional domain for most people and, by extension, CBT can be seen as improving cognitive abilities important in work, another important functional domain. One thing that is missing is how many patients with a BPD who are classified as “in remission” experience a range of symptoms that impairs functioning in

important areas of life, like with family, work and friends. This is something that significantly affects quality of life and which has been identified as one of the strongest risk factor for relapse. I will argue that finding ways to relieve such impairment should be a priority in clinical research on BPD.

3.3.1 Non-adherence.

Treatment of BPDs is made difficult by more than just lack of correct diagnosis or difficulties related to the patient group being heterogenic. One severe problem is that of adherence to medication, which, according to a review by Colom, Vieta, Tacchi, Sanchez-Moreno and Scott (2005), ranges from 20% to 60% across studies. Even though psychotherapeutic intervention as adjunct to pharmacotherapy is important in the treatment of patients with a BPD, it is undoubtedly vital that patients adhere to their pharmacological treatment as well. At the most severe points of mania and depression, the acute treatment of choice will be medication that can ease the burden of symptoms and subsequently enable the patient to focus on the many psychological issues related to their disorder. It is also strongly substantiated that medication is important as prophylaxis treatment to prevent relapse, in the least being able to lengthen the period of remission and make the periods of illness shorter and less severe (Malt, 2012).

Colom and colleagues (2005) point out that those patients who do not adhere to their medication pay a high price in terms of adverse effects on many primary outcomes, such as symptom reduction, quality of life, relapse rates and suicide prevention. As one can imagine, these consequences are also costly in terms of money spent on treatment and in terms of utilisation of resources in the mental health care system. There are many reasons for why patients are non-adherent. Colom and colleagues (2005) suggest lack of insight into the disorder, irrational fears regarding medication, as well as being more prone to maladaptive beliefs or prejudices, such as considering it a form of "slavery", fearing dependence and shame or viewing it as something unhealthy and unnatural, as possible causes. In contrast to what many expect, fear of side effects has not been found to be associated very strongly with non-adherence. In any case, non-adherence is something that must be specifically addressed in any and all forms of treatment of BPDs.

As I have previously pointed out, how a disorder is understood in terms of mechanisms underlying its onset and maintenance is directly linked to how it is treated (Kazdin & Kagan, 1994; Rutter & Sroufe, 2000; Teasdale et al., 2003). Despite considerable efforts to develop efficacious treatments in BPDs, the evidence-base for treatment of acute

depression and prevention of its relapse effectively in the long term, is limited (Geddes & Miklowitz, 2013; Malt, 2012). Are existing interventions targeting the cognitive mechanisms that keep patients vulnerable to relapse – or is something important being missed?

I have argued that the limited evidence-base for treatment of depressive relapse in BPDs might reflect that mechanisms underlying this outcome may not have been properly understood. However, highly RMD has several aspects in common with BPDs. Indeed, it has been argued that it may be appropriate to conceptualize RMD as dimensionally related to BPDs (Goodwin & Jamison, 2007). Potential dimensional similarities in cognitive mechanisms related to risk of relapse in RMD and bipolar depression raise an interesting question: Is there merit in considering MBCT as an intervention for BPDs? I shall examine this question in the following.

4 Mindfulness-Based Cognitive Therapy

In order to provide a background for a discussion of the potential merit of MBCT for BPDs, I will first outline what mindfulness and MBCT is, and then go on to review the evidence for its efficacy in preventing depressive relapse and recurrence in RMD. In the following chapter I will go on to discuss through which cognitive mechanisms MBCTs might have its effect as preventive of depressive relapse, and then discuss the relevance of these mechanisms for BPDs.

4.1 What is Mindfulness?

MBCT for RMD is a programme that, as the name suggests, combines cognitive science models of RMD with ancient Buddhist mindfulness practices (Fennell & Segal, 2011; Segal et al., 2013). In order to understand what this means, it is necessary to first examine the concept of mindfulness. What is it? Mindfulness is a central aspect of a 2500 year-old tradition of Buddhist psychology (Siegel, Germer, & Olendzki, 2009). Siegel and colleagues (2009) argue that to truly understand mindfulness, one has to experience it, as cultivating mindfulness is a deeply personal journey of discovery. Thus, they suggest that mindfulness is not something one can understand solely be learning *about* it; the learning has to be experiential too. Kabat-Zinn (2003) defines mindfulness as "the awareness that emerges through paying attention on purpose, in the present moment, and non-judgementally to the unfolding of experience moment by moment". However, there was long a lack of an operationalized definition of mindfulness, which made research into the applications of mindfulness difficult. Thus, Bishop and colleagues (2004) proposed a two-component model of mindfulness. The first component is self-regulation of attention maintained in the present moment allowing for recognition of current mental events, and the second is adopting an orientation towards one's experiences in the present moment characterized by curiosity, acceptance and openness.

In a clinical context, awareness is highlighted as a way of regulating affect which implies redirecting attention (i.e., rather than trying to control or suppress powerful emotion). Siegel and colleagues (2009) point out that awareness conceptualized from a mindfulness perspective is not a passive state of mind, but a way of "actively working with states of mind

in order to abide peacefully in the midst of whatever happens" (p. 18). Central qualities of mindfulness, including non-judgement, acceptance and compassion can be considered a core attribute of any effective psychological treatment (Binder, Gjelsvik, Halland, & Vøllestad, 2014).

Moreover, Siegel and colleagues (2009) argue that the pervasiveness of everyday mindlessness is particularly striking if asked about what matters to us in life, because people generally find that it is the moments in which they were fully present that they value the most. To realize how much of our lives are spent being mindless, lost in memories of the past or fantasies of the future, while operating on automatic pilot with our minds in one place and our bodies in another, can be scary. Mindful meditation is a practice in noticing the contents of the mind and should therefore lead to a more vivid experience of our emotions. It is also about not clinging to either our pleasant or aversive experiences, but allowing them to arise and pass. Escaping pain, be it psychological or physical, is not the goal of mindful meditation. The goal is to increase our capacity to tolerate it and not react to it with avoidance or rumination, which they point out, is linked to additional suffering and pain.

Hölzel and colleagues (2011) argue that there is an array of distinct but interacting mechanisms that are at play in producing the benefits following practice of mindful meditation. They suggest that attention regulation, body awareness, emotion regulation and change in the perspective on the self all interact closely and constitute a process that leads to enhanced self-regulation. In the process of developing meditation expertise, the different mechanisms might play different roles, and the different mechanisms may also play different roles when it comes to treatment of different psychiatric disorders. The authors argue that it is possible that an improvement in attentional control is the first to evolve. Attentional control might be the skill that helps facilitate the other three processes, changing how processing of information about the self develops later in the process, following an increased awareness of the body and improved emotion regulation skills. As an extension of this reasoning, it seems that regulation of emotion and change of self-perspective is particularly important in the treatment of affective disorders, and both these processes are targeted in MBCT.

4.2 What is MBCT?

MBCT is part of a larger group of therapies, the so-called 'third wave' within the cognitive-behavioural tradition, developed over the last 20 years (Hayes, Follette, & Linehan, 2004). These therapies are characterised by incorporating mindfulness practices to a varying

degree, and by an emphasis on metacognitive awareness and compassion (Hayes et al., 2004). One of the most known mindfulness-based interventions is perhaps Kabat-Zinn's (1990) Mindfulness-based Stress-Reduction (MBSR) protocol, which has been found the be effective in alleviating the distress experienced by patients with chronic pain (Veehof, Oskam, Schreurs, & Bohlmeijer, 2011). There are components of mindfulness in Gilbert's (2009) integration of evolutionary psychology and compassion in psychotherapy, and in Dialectical-Behaviour Therapy (DBT) (Linehan et al., 1999). Moreover, Acceptance and Commitment Therapy, developed by Hayes, Strosahl, and Wilson (1999), teaches patients to observe the self and view their thoughts, emotions and sensations as separate from themselves, but not through training in meditation.

MBCT is a manualised 8-week skills-training group program developed by Segal, Williams and Teasdale in 2002 (second edition 2013) to specifically target the processes that cognitive science models hypothesise to be involved in depressive relapse – the individual's relapse signature and reacting to symptoms and aversive experiences with avoidance and rumination. This model - the Differential Activation Hypothesis (Lau, Segal, & Williams, 2004; Teasdale, 1988) - proposes that RMD is due to individual differences in the reactivation of depressive content *and* certain cognitive biases (e.g., overgeneral memory) and maladaptive information processing styles (e.g., rumination, suppression). MBCT targets these processes of vulnerability and aims to teach patients to become aware of and relate differently to their experiences through mindfulness practice in a way characterized by openness, curiosity and acceptance. In contrast with CBT, MBCT does not aim to change the content of thoughts, but to teach patients to take a different perspective on thinking and awareness itself (Barnhofer & Crane, 2009). Teasdale and colleagues (2000) emphasize that MBCT has been designed for remittent patients and not as an acute treatment of depression, although there is increasing evidence that it can be used with currently depressed patients (e.g. Barnhofer et al., 2009).

MBCT is based on the tenet that how one pays attention to symptoms – the 'mode of mind' (Williams, 2008) with which one approaches symptoms - has significant implications for whether or not symptoms are maintained, and thus for one's wellbeing. Williams (2008) points out that that a typical response to symptoms of depression, is to try to problem-solve and change the experience. This mode is characterised by trying to reduce the gap between how things are experienced in the moment and how one wants them to be, and is therefore referred to as discrepancy-based processing. Ability to solve problems efficiently is a necessary capacity, but our instincts and automatic reactions that lead to attempts to avoid or

control our emotional experiences can have unintended consequences, such as making individuals with a history of depression vulnerable to depressive relapse. Moreover, it is characterised by a harsh "inner commentary" regarding oneself. This way of thinking about self-relevant information has both been shown to be a common factor across psychiatric disorders, as well as a risk factor for developing depression and anxiety (Gilbert, 2009; Raes, 2010).

A core aim of the MBCT programme is to teach vulnerable individuals to deliberately adopt a *different* and more skilful way of relating to symptoms – and thereby short-circuiting these risk processes. Segal and colleagues (2013) describe being mindful as the "being mode" of the mind, characterised by our attentional resources being completely dedicated to experiencing the present moment. The "being mode" of the mind is contrasted with what they call the "doing mode" of the mind. This "doing mode" of the mind, according to Segal and colleagues (2013), is where people operate most of the time. It is an action-oriented mode of mind that plays an important role when working towards goals and solving problems in our daily lives. However, as pointed out above, it can also lead to a sense of being absent-minded, running on 'automatic pilot' (Segal et al., 2013) and not being aware of the reactions to one's own thoughts and interpretations of different situations.

Thus, MBCT can be seen as endeavouring to facilitate patients' ability to deliberately disengage the "doing-mode" of the mind and attend to present experiences (including depressive symptoms) with the "being-mode". This is practiced through a variety of meditation exercises, first as a way of improving abilities of attentional control and increasing awareness and recognition of the "doing mode", and later as training in recognizing and disengaging from negative emotions, cognitions and moods. A central component is the focus on being with aversive experiences in a more skilful way with an attitude of acceptance and compassion rather than avoidance. Also essential in this 8-week programme is the practice of mindfulness exercises in everyday life, given as homework each week. Barnhofer and Crane (2009) describe the course as more of an experience-based process rather than a didactic one. As such, the role of the instructor is to facilitate this process and act as a role model, inviting the participants to inquire into their meditative experiences with curiosity, openness and compassion.

MBCT (Segal et al., 2013) consists of classes delivered once a week over 8 weeks. Before the first class, participants are invited to a pre-class interview, where the purpose is to prepare the participant on the amount of homework, identify potential obstacles and clarify any questions the participant might have. In the first four sessions, the focus is learning to

pay attention, on purpose, in each moment, with a non-judgemental attitude. Through practices, participants are made aware of how little attention that is usually paid to everyday activities and how fast and automatic shifts in attention happen. Having been guided to notice this, the training focuses on how to bring back attention to a single focus, like a part of the body or to the breath. Following this, the participants learn how the "doing mode" of the mind with its automatic and habitual reactions to experiences, can lead to an increase of negative thoughts and feeling, what can be called a second layer of suffering. The authors argue that this basis is essential if the participant is to use MBCT to be able to experience their mood shifts and handle them by responding skilfully instead of reacting automatically.

Sessions five through eight are designed to teach participants skills. Whenever a negative thought or emotion arises during meditation exercises, participants are invited to allow it to simply be there, and, having acknowledged it, move their attention to their breathing for a minute and then expand the attention to the body as a whole. A key feature of the programme is its suggestion that in this way, the automatic reaction one would usually have is interrupted, giving the participant an opportunity to choose how to respond. This can be done either by dealing with the experience directly and seeing it as a passing event, or by noticing which part of the body is affected and then use breathing to "open and soften to the sensation rather than tighten and brace around it" (Segal et al., 2013, p. 87). Pausing to acknowledge what is going on in the moment, focusing on the breath as a way of gathering oneself before expanding the focus of attention to see the wider perspective of the moment is seen as an important first step. Towards the end of the course, participants are increasingly encouraged to notice their personal signatures of reaction and warning signs that precede depression and to formulate specific action plans in preparation of when this might occur.

There are a range of meditative practices throughout the course (e.g., body scan, moving meditation, walking meditation and a shorter sitting meditation). The practices may vary but share the same fundamental purpose; to cultivate sustained attention and attending to the present moment with openness, curiosity and compassion. In MBCT, an entire day of silent meditation practice is included between sessions six and seven, in which participants are invited to take part in different practices in silence. Following each session all participants are given handouts with a synopsis of the session and an outline of the homework for the next week, including a CD with instructions for that week's meditation practice. Participants are strongly encouraged to spend 40-45 minutes at least six out of seven days practicing meditation, and recent research suggests that amount of practice is strongly associated with staying well (Crane et al., 2014). Whilst MBCT has been applied for other mental disorders,

the evidence base for RMD is most relevant in the context of its possible merit as a relapse-prevention treatment for BPDs. It is to this evidence base that I now turn.

4.3 Efficacy of MBCT in the Treatment of RMD

A meta- analysis of six RCTs investigating the effect of MBCT in preventing depressive relapse in RMD concluded that MBCT reduces the relative risk of depressive relapse by 34%, and by 43% in patients having experienced three or more episodes, thus rendering it comparable to maintenance antidepressant medication (TAU) in prevention of relapse (Piet & Hougaard, 2011). There is also evidence to support that MBCT is more effective than antidepressants in reducing residual depressive symptoms and improving quality of life (Kuyken et al., 2008; Williams et al., 2014). The evidence for the efficacy of MBCT in reducing relapse rates in RMD has lead to MBCT being a recommended treatment for prevention of RMD in the National Institute for Clinical Excellence (NICE) guidelines (NICE, 2009).

Aiming a little wider than MBCT for RMD alone, Chiesa and Serretti (2011) reviewed controlled studies of MBCT on a broader range of psychiatric disorders, including major depression, BPDs and anxiety disorders. They focused on the relative usefulness of MBCT for these disorders and, similar to Piet and Hougaard (2011), found that MBCT reduced risk of relapse in patients with RMD. They further conclude that current studies also suggest that MBCT could be useful in the treatment of residual depressive symptoms and for reducing anxiety symptoms in euthymic bipolar patients. Moreover, a reanalysis of two main trials of MBCT for RMD by Williams, Russell, and Russell (2008) found that MBCT reduces the percentage of participants who relapse within one year from 70% to 39%, increases the average time to relapse by at least 18 weeks and decreases scores on Beck's Depression Inventory (1961) after treatment by nearly 5 points. All these findings were significant at the 0,01% level.They conclude that the reanalysis of these two trials has overall strengthened the original findings for MBCT for RMD.

Even using RCTs there is the important question of what kind of condition the control group is to receive, a question that demands both ethical and practical consideration, In a complex treatment intervention, such as MBCT, there are many interlinked components that are not easy to separate, and it will be difficult to know whether the effects in the treatment condition are a result of non-specific or specific factors. The effect of such non-specific effects (e.g. group identification or the normalisation of experience through hearing other

people's similar experiences) can be hard to disentangle from the mindfulness-components of treatment: what is it that leads to change? To establish this, a dismantling design is needed – where the control group shares all the non-specific factors with the treatment group, but not the component of treatment that is hypothesized to lead to change.

An example from MBCT is the homework practice, which is hypothesized to mediate change through repeated practice of attending to the present moment and whatever thoughts or feelings are present with compassion. The homework would have to make as much sense to the control group as the MBCT group, and at the same time not involve procedures that are likely to have an effect on depression. Choice of control group condition is usually decided by the state of the evidence, and MBCT has often been compared to TAU, because it has been important to establish how MBCT compares to TAU on different measures of outcome. Following results that have shown that MBCT does indeed have a comparable or significantly better effect than TAU on relapse rates with patients who have suffered multiple episodes of major depression, more recent research has been directed at investigating the specific effects of MBCT and also the merit of using MBCT in treatment of other patient groups, such as with patients with BPDs.

In the most recent systematic review of the mechanisms of change in MBCT for RMD, van der Velden and colleagues (2015) found several mechanisms that predicted or mediated change. These were mindfulness, rumination, worry, compassion and meta-awareness. Also, preliminary studies they reviewed indicated that changes in attention, memory specificity, self-discrepancy, and momentary positive and negative affect might play a role in the clinical effect of MBCT. According to the authors, these mechanisms fit quite well with the theoretical rationale behind the MBCT programme for RMD, which is the cognitive reactivity model of Segal and colleagues (2013). It is possible that these mechanisms may also predict or mediate change in BPDs, but this has yet to be investigated further.

5 Cognitive Processes Related to Risk of Depressive Relapse

As pointed out initially, the depressive episodes in BPDs are one of the most difficult aspects to treat, and subsyndromal depressive symptoms are also prevalent in euthymic periods. Moreover, it has been established that such symptoms are the strongest predictor for relapse. Despite the impact of psychotherapeutic interventions as adjuncts to TAU on several variables, the picture emerging of the efficacy of psychotherapeutic interventions for important factors such as between-episode functioning and relapse is wanting. This knowledge situation raises interesting questions: Has the huge effort put into treatment of BPDs not targeted the underlying mechanisms that keep people at risk for depressive, manic – or mixed - relapse?

Given the evidence that unipolar and bipolar depression may indeed be similar – and considering that RMD and BPDs may be dimensionally related (Goodwin & Jamison, 2007) - I will examine whether there might be merit in looking to mechanisms having been found to be involved in maintaining vulnerability to unipolar depressive relapse as a point of departure for development of treatments for depressive relapse in BPDs. How may these mechanisms, which have been found to keep patients vulnerable to depressive relapse, map onto BPDs? Basing the argument on both theoretical and empirical analysis, I will first investigate toxic self-discrepancies, then lack of self-compassion, and finally, meta-awareness. In the following chapter, I will review the evidence of MBCT for BPDs, considering its current evidence base including effects on depressogenic cognitive mechanisms outline below.

5.1 Toxic Self-Discrepancies

According to Crane and colleagues (2008), whose research focused on individuals who had recovered from depression and had a history of depression and suicidality, long-term vulnerability to depressive relapse is related to the perceived discrepancy between actual self and ideal-self. Individuals suffering from RMD tend to believe that they do not measure up to their own, or others', expectations. It is important to understand that the perceived self-discrepancies are extremely negative in nature. They can entail perception of the actual self as worthless, which is contrasted with the wish to be like one's perceived ideal self, a person of worth and value. This is, clearly, a very negative interpretation of the self, and is not

something that can be dealt with like a discrepancy of the sort where the wish is to be fitter, healthier or more conscientious with schoolwork. Of course, attending to these perceived discrepancies through problem-solving (e.g., hungry – eat) and goal-setting (wanting to go to work – be able to get there) are critical for daily functioning when there are problems that require practical solutions (e.g., I am hungry, therefore I eat) or goals that one wants to obtain. However, discrepancies relating to the self cannot easily be fixed in the same way – indeed, attempts to reduce such discrepancies have been shown in experimental studies to be highly maladaptive.

One influential theory of multifaceted self-conception is Higgins (1987) self-discrepancy theory. This theory proposes that people have two separate systems for self-regulation, termed promotion and prevention, which are concerned with the pursuit of different types of goals. The ideal self is a representation of characteristics that a person wishes or hopes to possess and is part of a promotion system of self-regulation. The second system is the ought self, the prevention system, which is concerned with the fulfilment of ones' duties and obligations. Higgins' theory poses that all humans strive to align our actual selves with our ideal and ought selves, and which is more salient to us is dependent on a range of psychological and social factors, as well as the immediate context.

According to Crane and colleagues (2008), different types of self discrepancies have different implications for affective response. Research using Higgins' conceptualizations of ideal-, ought- and actual self has shown that depression is related to perceived discrepancy between actual and ideal self (Carver, Lawrence, & Scheier, 1999) and that perceived discrepancy between actual and ought self is linked with anxiety and agitation (Scott & O'Hara, 1993). Interestingly, research by Baskerville (1999) has shown that discrepancies between actual and ideal self is more easily primed in laboratory settings with people who have experienced depression compared to people who have never been depressed before.

This suggests an acquired susceptibility and vulnerability for these cognitive processes once they have been activated. Segal and colleagues (2013) proposed a theory that a key mechanisms through which people remain at risk for depressive relapse is the extent to which small shifts in mood provoke discrepant self-processing. On a similar note, Papadakis, Prince, Jones, and Strauman (2006) did a study on adolescent girls in which they found that discrepancies in processing of actual and ideal self is mediated by an individual's tendency to ruminate and that this predicts the level of depressed mood. Of those who suffer from a BPD a large portion of patients struggle with subsyndromal depressive symptoms even in

remission, something that leaves them vulnerable to relapse. As depressive symptoms are often characterized by rumination, a picture of a depressive spiral is not far-fetched.

There is evidence that views of the self vary considerably between depressive, remittent and hypomanic or manic episodes, and that perceived discrepancies between actual and ideal or ought selves, and consequently self-esteem, can be a factor in mediating risk of recurrence of depression in BPDs (Pavlickova, Turnbull, & Bentall, 2014). As a consequence, self-referential thinking processes are important targets in psychological interventions, such as CBT (Scott & Pope, 2003). According to Strauman and colleagues (2001) self-discrepancies, how information related to our self-concept and self-esteem is processed is also one of the key psychological processes in maintenance of depression that has been found to uniquely change with psychotherapy but not with pharmacotherapy.

Self-discrepancies are highly accessible to us, and if one is to respond to such discrepancies with rumination in an attempt to reduce negative evaluations of the self, then the discrepancies perceived may become even more easily accessible, which in turn will lead to intensified negative affect (Papadakis et al., 2006; Segal et al., 2013). In other words, self-discrepancy is linked to depressed mood, and is also somewhat mood-dependent (Baskerville, 1999). Like unipolar patients, bipolar patients show evidence of toxic self-discrepancies and other aberrations in self-referent processes. Although more research is required to explore the processes underlying the effects of discrepant self-processing on depressive relapse, especially for BPDs, there is a basis here for optimism regarding treatments that target self-discrepancy, such as MBCT.

Platman, Plutchik, Fieve, and Lawlor (1969) investigated differences between BPD patients' self-reported emotions in both depressive and manic episodes compared to that of observers. The Emotion Profile Index, designed to assess eight primary emotions, was administered to 11 bipolar patients weekly both when hospitalized, and they were followed up after discharge when in remission. At least two staff members rated each patient when either depressed or manic. In addition, 12 staff members were asked to provide descriptions of their conception of depression and mania, and then this collective profile was compared with the profiles the patients had produced while either depressed or manic. The results showed that staff and patients conceptualized depression similarly on all dimensions, characterised by decreased sociability, interest in new experiences and feelings of acceptance and an increase in feelings of deprivation, aggression and rejection of others. Interestingly, mania was perceived very differently by staff and patients currently experiencing a manic

episode. In addition, patients had different perceptions of self as manic when experiencing an episode, and when in remission following a manic episode.

While manic, patients perceived themselves as sociable, trusting, moderately impulsive and cautious, but not at all stubborn or aggressive. On the contrary, staff members described manic patients as being moderately sociable, somewhat distrustful, extremely impulsive and aggressive, rejecting of others and completely incautious and unafraid. When in remission, patients recalled depressive episodes as similar to those given while experiencing a depressive episode. On the other hand, when recalling manic episodes the correlation between their own conception of self and the staff's conception of them were significantly higher than with their own conception during manic episodes. Goodwin and Jamison (2007) ask whether this discrepancy in self-perception is a result of deliberate misrepresentation of feelings during manic episodes or a lack of ability to discriminate feelings and behaviours as perceived by others.

These findings are in keeping with studies suggesting that patients with BPDs are characterized by unstable self-esteem across episodes of illness, with high self-esteem during manic-episodes, and low self-esteem during depressive episodes. Pavlickova and colleagues (2013) identify several studies that have observed abnormalities in self-referential processing in patients with BPDs, with marked similarities to unipolar depression. These processes include increased rumination, an implicit pessimistic attributional style, low self-esteem and dysfunctional attitudes towards the self. Van der Gucht, Morriss, Lancaster, Kinderman, and Bentall (2009) found that these styles of processing were most evident during depressive episodes, but also in euthymic periods, even when statistically controlling current symptoms.

In their analysis of self-esteem and its relationship to symptoms of depression and mania, Pavlickova and colleagues (2014) found that depression was associated with high negative self-esteem, dysfunctional attitudes, and low positive self-esteem, attributing negative events to self and positive events to others and low consistency between the perceptions actual and ideal self, thus supporting several previous findings. The relation between self-referential cognitive processes and mania were weaker, but high self-esteem and dysfunctional attitudes related to achievement became associated with mania after controlling for current levels of depression. Mania was also negatively associated with attributing negative events to self and positively associated with attributing negative events to others and there was also a weak positive correlation between mania and actual- and ideal-self consistency. These findings support the notion that bipolar depression is similar to unipolar depression at a psychological level. In other words, depression is related to toxic self-

discrepancies in spite of whether it is unipolar or bipolar. Toxic self-discrepancies were related to current symptom severity. The only exception was self-esteem, which seemed to not be only related to affective state, but serving as a longitudinal predictor of depression. Based on this evidence, a relevant hypothesis for treatment of BPDs is that reducing toxic self-discrepancies may affect acute depressive symptoms and contribute to reducing the risk of depressive relapse.

5.2 Lack of Self-Compassion

Another key mechanisms involved in persistent risk for RMD is lack of self-compassion. Indeed, lack of self-compassion is a core feature of RMD, reflected in depressive patients' feelings of guilt, shame and self-judgement. Self-compassion has been defined by Neff (2003a; 2003b) as being touched by and open to one's own suffering, not avoiding or disconnecting from it, generating the desire to alleviate one's suffering and to heal oneself with kindness. Neff (2003a; 2003b) has also described self-compassion as made up of three components. The first is being kind and understanding to oneself when in pain or experiencing failure instead of being self-critical. The second is to perceive one's experiences as something all people can identify with rather than seeing them as isolating, and the third is to hold painful thoughts and feelings mindfully in awareness rather than over-identifying with them.

Similarly, Feldman and Kuyken (2011, p. 144) have described compassion as a "multi-textured response to pain, sorrow and anguish". Feldman and Kuyken (2011) argue that compassion, above all, is the capacity to open to the reality of suffering and to aspire to its healing. In addition, compassion and self-compassion have also been conceptualized as more of a "hardwired" and evolutionary based capacity, in more general terms. This idea is also reflected in Compassion-Based Therapy which is based on, among others, the work of Gilbert (2009) and Gilbert and Irons (2004) where it has been observed that self-criticism, shame and a feeling of powerlessness plays an integral role in maintaining depression.

Krieger, Altenstein, Baettig, Doerig, and Holtforth (2013) aimed to investigate whether depressed people differed from never depressed people on measures of self-compassion, how self-compassion was related to cognitive behavioural processes in depression such as avoidance and rumination, and to investigate rumination and avoidance as mediators in the relationship between self-compassion and depressive symptoms. Their results show that depressed outpatients differed significantly from never depressed subjects

on all measures of self-compassion. Even if the effect size is small when controlling for depressive symptoms, the results are important considering previous research showing that individuals with higher levels of self-compassion are more resilient following stress exposure and better able to adopt a helpful perspective on negative situations compared to individuals with lower levels of self-compassion (Leary, Tate, Adams, Batts Allen, & Hancock, 2007; Neff, Kirkpatrick, & Rude, 2007). Krieger and colleagues (2013) also found that self-compassion was significantly negatively correlated with measures of both rumination and avoidance, and conclude that this supports the hypothesis that less self-compassionate people tend to be more avoidant and thus more likely to experience depressive symptoms.

In keeping with the above, MacBeth and Gumley (2012) found that higher levels of compassion were associated with lower levels of mental health problems. The argument for the role of self-compassion in treatment of psychological pain, such as depression and anxiety, is based on the observation that the instinctive, human response to pain is to recoil and avoid, become anxious and ruminate. These responses to aversive events and affect again lead to what can be conceptualized as a second layer of suffering, including feelings of blame, aversion, self-judgement and painful agitation. Feldman and Kuyken (2011) argue that the effect of this layer of reaction is a magnification of pain and stress, as well as playing a crucial role in triggering further emotional distress, such as despair, depression and helplessness. Again, this can become a circle of repetition that ruins the possibility to respond in a way that leads to less suffering.

Feldman and Kuyken (2011) point out that even if psychological theory and research into self-compassion in relation to recovery from psychopathology is at a very early stage, most studies that have examined the relationship between psychological constructs and compassion have suggested that compassion is positively associated with well-being and negatively associated with distress (Fredrickson, Cohn, Coffey, Pek, & Finkel, 2008; Fredrickson & Losada, 2005; Gilbert & Irons, 2004; Goetz, Keltner, & Simon-Thomas, 2010; Kelly, Zuroff, & Shapira, 2009; Lutz, Brefczynski-Lewis, Johnstone, & Davidson, 2008; Neff, 2003a, 2003b). On this view, self-compassion ought to be an integral part of any treatment of BPDs. Not only is it positively associated with reduced distress, but can also help a patient group with a chronic, recurrent and debilitating illness handle the stigma and burden of the disorder. I will later go on to discuss therapeutic implications of the pivotal role self-compassion may have in ameliorating bipolar trajectories.

5.3 Limited Metacognitive Awareness

A third mechanism related to risk of relapse in RMD, with potential relevance for the understanding of how vulnerability to relapse in BPDs is maintained, is limited metacognitive awareness. In affective disorders, what Williams (2010) refers to as mental model building can be an important factor. Mental model building, also called symbolic processing, is the process through which human beings pursue tasks, solve problems and meet new situations in an efficient manner throughout our daily lives. Mental models are based on recall of previous experiences and being able to maintain relevant information and related affect in the given situation, as well as responding to current contingencies. In other words, our experience of reality becomes what it is conceptualized it to be, based on rapid reactions that typically label experiences as good, bad, or neutral and as either pleasant or unpleasant (Brown & Cordon, 2009).

For this to be an efficient strategy, Williams (2010) points out that mental models must be automatically activated and be perceived as representing reality, must be based on conceptual associative structures in memory, use anticipation of future events and memories of past events in problem solving, and include the present goal when making decisions. Segal and colleagues (2013) describe how low meta-awareness is characterized by an inability to separate the self from the content of negative thoughts and emotions, which is a central feature of discrepancy-based processing. An integral part of mental models are emotions, automatic reactions to situations in which it is possible to perceive threat and feel fear, perceive loss and feel sadness, be thwarted in the pursuit of goals and feel anger, be exposed to unpleasant substances and feel disgust or experience successful achievement of goals and feel happiness.

Negative emotions are assumed by Oatley and Johnson-Laird (1987) to have a signaling function that changes how information related to self and others is perceived and processed. For emotions to be of value they must be sensitive to the external world. That means turning on when the situation demands it, and turning off when the situation changes. Williams (2010) points out that it is when our *simulations* of reality are treated by our primitive and automatic affective response system to be dealt with as real threats and losses, that problems arise. He argues that mental model building can be seen as a maintaining factor in affective disorders, something that prevents extinction of maladaptive responses. For example, experiencing something unpleasant (e.g. not getting a job), can in turn lead to rumination about how there is no hope for the future (e.g. 'I will never be able to cope'). The

rumination and depressive and anxious emotions that might follow, can lead to more rumination and attempts at avoidance, because the notion that there is no hope for the future is taken as a truth, rather than a passing mental event. However, understandable as this reaction might seem, this way of processing information can tragically backfire (Williams, 2010).

When used to avoid or ruminate on emotional expression, his way of processing information – the 'doing-mode" of the mind - can lead to a reduction in attentional capacity and control which in turn "increases the emotional disturbance and helplessness it was intended to fix" (Williams, 2010, p. 2). It is here, he argues, that training in mindfulness plays a key role, not as a way of ridding oneself of these processes, but as a way to become aware of the difference between natural, automatic reactions and the suffering that is added through simulating, elaborating and avoiding. Hargus, Crane, Barnhofer, and Williams (2010) investigated the emotional dysregulation that occurs when a person suffering from RMD adopts such discrepancy-based processing rather than a meta-aware processing mode to reflect on their illness experiences. Negative ideas about the self are taken to represent reality, discrepancies between perceived actual and ideal self leads to both striving towards the ideal self and avoidance of negative outcomes, and rumination and avoidance are used in an attempt to solve emotional and self-related problems and perceived discrepancies. They argue that such a mode of processing is likely to be both most evident and most toxic when it is used to process extremely negative and personally relevant information. As such, there is need for an intervention that targets these processes.

If this prediction were true, one would expect reductions in discrepancy-based processing, and an increased ability to see symptoms as symptoms or a thought as a thought, not to be equaled to e.g. self-worth, to be linked with increased well-being. The idea that increased meta-awareness is important for course and outcome in BPDs has already been addressed in psychoeducational interventions (Colom et al., 2009) that aim at enabling patients to recognize their relapse signatures so that preventive measures can be taken. It has also been demonstrated that lack of metacognitive awareness is an issue in regard to distorted perceptions of own mood (Platman et al., 1969), and insight into own behavior when manic (Malt, 2012). Whether increased metacognitive awareness can be a preventive measure in BPD in itself is an empirical question that awaits further scrutiny.

6 MBCT in the Treatment of Bipolar Disorders

Chiesa and Serretti (2011) argue that MBCT as an adjunct to standard treatment could optimize standard care and enhance treatment outcomes for other diagnostic groups than RMD. Not only has MBCT been found to reduce residual symptoms and prevent depressive relapse in RMD, it is also a group-based intervention that allows for greater accessibility and cost-efficiency for health services facing this challenge (Chiesa & Serretti, 2011; Kuyken et al, 2008). In the previous chapter I have reviewed research pointing to toxic self-discrepancies, lack of self-compassion and limited metacognitive awareness (i.e., the ability to adopt a decentered stance at experience; in the context of psychopathology; the ability to see toxic thoughts as mental events) as risk mechanisms involved in the maintenance of ongoing vulnerability to depressive relapse in RMD. However, research into MBCT for BPDs is still in its infancy. In the following chapter I will first review how these mechanisms – toxic-self-discrepancies, lack of self-compassion and limited meta-cognitive awareness – might change through MBCT and thus lead to changes in course and outcome for BPDs. Lastly, what existing studies suggest about the merit of MBCT for BPDs will be reviewed.

6.1 Effects of MBCT on Risk Mechanisms

One argument of interventions like MBCT for depressive relapse in BPDs is that bringing attention and compassion to feelings, thoughts and behaviours, as is extended to others' experience of suffering, is a patients' first step towards recognizing their typical patterns of reactivity and being able to recognise and relate differently to these habitual patterns. Feldman and Kuyken (2011) point out that self-compassion is developed through sustained and dedicated practice. Mindful self-compassion is an undoing of habits of aversion through attending to the present moment with kindness. One does not have a choice in whether or not pain will be experienced, but it is possible to learn to respond differently, in a way that will provide protection from another layer of pain. Through practicing mindful attending to breath, bodily sensations, thoughts and feelings, and being encouraged to meet any experience with kindness, patience and acceptance, the idea is that self-compassion will be cultivated.

Through becoming aware of the impact of our reactions to bodily sensations, thoughts and emotions, and their consequences on our perceived suffering, and developing the ability to disengage from these and respond in a kinder and more self-compassionate way, a second layer of suffering is not added to our experience. It is not only important to focus on our reactions to suffering and pain, but also to reframe the personal narrative in the sense that depression, anxiety or other difficulties are not seen as personal failures but as suffering that is as worthy of compassion as that which is extended to others. In that way, through self-compassion, self-discrepancies are also addressed in MBCT. Feldman and Kuyken (2011) argue that there are three cognitive changes that occur as skills of mindfulness are developed. The first is the cultivation of mindfulness, where through repetitive training one learns to respond to depressive thinking and attitudes with kindness instead of blame and self-judgment. The second, they argue, is the development of the capacity to see a thought as merely a thought, or an emotion as an emotion, and that such afflictions can be tolerated and befriended rather than feared. The third is a growing awareness of how human suffering and affliction is universal. These three cognitive changes are similar to Neff's (2003a; 2003b) three dimensions of self-compassion.

Laboratory studies performed by Lau and colleagues (2004) have shown that people who have recovered from depression and who are exposed to a sad mood induction revert to a depressive style of information processing in comparison to never depressed patients. Moreover, greater activation of dysfunctional thinking styles is associated with higher risk of depressive relapse. This is obviously also an important factor for depressive relapse in BPDs, as research has shown that subsyndromal depressive symptoms, that are pervasive in remittent periods for many bipolar patients, are the strongest predictor of relapse (Perlis et al., 2006). The hypothesis is that by reducing cognitive reactivity, psychological interventions will improve the outcome of treatment because they target mechanisms that are central in affective disorders that are not altered by medication. MBCT may change patterns of cognitive reactivity through teaching not to give authority to self-judgement and blame, instead teaching how to respond to such experiences with compassion. Developing the ability to do just that is suggested as a way out of maladaptive habitual patterns of reacting to aversive sensations that only leads to more suffering. In other words, MBCT seeks to cultivate meta-awareness in its practitioners.

Kuyken and colleagues (2010) investigated whether mindfulness skills and self-compassion mediated better outcome for recurrently depressed patients and whether it, in comparison with pharmacotherapy, decreased the effect of reactivation of dysfunctional

thinking on later outcome. Consistent with the theoretical basis outlined above, they found that mindfulness-skills and self-compassion mediated the effect of MBCT on depressive symptoms at 15-month follow-up. Also, following MBCT, they found no evidence that dysfunctional thinking affected outcome negatively, and an indication that increased self-compassion may act as a buffer in the relationship that usually exists between cognitive reactivity and affective relapse. The patients still experienced the same symptoms, but these symptoms no longer increased risk of relapse. This finding is interesting, as previous research on CBT in treatment of RMD showed a decrease in reactivity of dysfunctional patterns of thinking (Segal et al., 2006), but following MBCT in this study these patterns had actually increased. Still, their relationship with outcome had been eliminated, suggesting that it was the patients' response to the dysfunctional thoughts that alter its relationship with outcome at follow-up. This suggests that CBT and MBCT differ in how they bring about change, and raises interesting questions for example related to differences in long-term effect. As CBT has been shown to have an effect on relapse in BPDs, but only in the short term, this research brings up an intriguing possibility in the treatment of BPDs that may reduce relapse and thereby improve the course of the disorder in the long term.

As shown above, theoretical explanations of depression assume that discrepancy-based processing is involved in maintaining risk of depressive relapse. If that is true – what is the evidence for its change through MBCT? Hargus and colleagues (2010) investigated just this - whether training in mindfulness is able to bring about a change in processing mode, especially in relation to negative mental content. Their analysis is based on a small RCT of MBCT for patients with a history of RMD and suicidal behaviour. The participants were asked to describe what symptoms they remembered experiencing in the period leading up to a prior suicidal crisis, both before and after the MBCT intervention. They operationalized discrepancy-based processing both as the extent to which people described their experiences in an overgeneral way and the extent to which there was evidence for a lack of meta-awareness in these descriptions. This is based on previous research showing that rumination and overgeneral memory appear to be mutually reinforcing (Raes et al., 2006; Williams et al., 2007) and findings that show that previously depressed patients exhibit higher levels of overgeneral memory when exposed to self-relevant material than never depressed patients (Crane, Barnhofer & Williams, 2007; Spinhoven, Bockting, Kremers, Schene, & Williams, 2007).

One study has found that increasing awareness of idiosyncratic prodromal symptoms reduced the risk of relapse in BPDs (Lam & Wong, 2005). Similarly, low meta-awareness is

associated with reduced ability to recognize symptoms of depression as symptoms and passing events instead of as truths about the self. However, are patients at risk of relapse able to change how they approach their aversive experiences through training in mindfulness? Indeed, Hargus and colleagues (2010) found that MBCT improved RMD patients' ability to delineate the prodromal symptoms related to previously experienced suicidal crisis. Specifically, those who received MBCT described their relapse signatures with an equal level of specificity both before and after treatment, while the control group, assigned to a waitlist condition, reported their relapse signature in a more overgeneralized manner than at baseline. The authors suggest that this effect can be due to the MBCT group reflecting more on details of their prior suicidal crises, thus promoting greater maintenance of details, and that the control group in contrast may have continued trying to suppress these aversive memories, thus leading to poorer retrieval of details.

Moreover, they found that relapse signature specificity was affected by change in depressive symptoms, but only slightly, and meta-awareness was found to be unrelated to change in depressive symptoms. This suggests that specificity of recall and meta-awareness are cognitive phenomena that are not simply linked to changes in symptom severity, but changes as a result of treatment. As both overgeneralized specificity of recall and low meta-awareness has been found to predict either persistence of residual symptoms or subsequent recurrence of depression (Brittlebank, Scott, Williams & Ferrier, 1993; Peeters, Wessel, Merckelbach & Boon-Bermeeren, 2002; Teasdale et al., 2002) this makes a strong case for the application of treatment that target these cognitive phenomena, such as MBCT, in both RMD and BPDs.

Hargus and colleagues (2010) argue that memories of a suicidal crisis, and by extension I would argue also for manic or depressive crisis in patients with a BPD, can trigger the same mode of processing that was involved in the escalation of said crisis. As with suicidal patients, patients with BPDs are also faced with the challenge of having to learn from very painful past experiences that are experienced as very aversive. And they must do so without entering, yet again, into the mode of processing that has lead to maladaptive behavior in the past. In this regard, MBCT can be particularly useful as its goal is to help patients adopt a different style of processing, in which they become able to experience painful memories and events while retaining a decentered, or meta-aware, perspective on their experience. This keeps them from being drawn into the habitual, automatic and maladaptive modes of processing that would previously have contributed to relapse. Adopting a mindful and compassionate stance to experience might indirectly serve as a form of psychoeducation,

through which the individual learns to recognize the pattern of their own reactions to affect and events, and to respond to these in a way that may protect them against affective relapse.

6.2 MBCT for BPDs: Empirical Evidence

A number of MBCT trials have included patients with BPDs. Chadwick, Kaur, Swelam, Ross, and Ellett (2011) examined how patients with a BPD experienced practicing mindfulness and how it was related to living with and managing the disorder. Through thematic analysis of semi-structured interviews, the authors argue to have gained more insight into the processes of change that follow mindfulness practice. All participants reported experiencing benefits and challenges related to the mindfulness practice. They described being more focused on the present moment, something that helped them not get caught up in negative thoughts. Participants also described increased awareness of thoughts, emotions and feelings something that allowed for them to notice mood swings faster. They also reported being more accepting to the changes in mood they experienced, and experiencing different challenges related to different moods. Information gained from these interviews can be helpful in informing how MBCT programmes tailored to BPDs should be structured. The participants reported that they perceived more active practice to be beneficial when depressed, whilst focusing on breath was perceived as helpful in slowing down and decentring when experiencing heightened mood. The participants also reported that mindfulness not only helped them manage the disorder, but that they also experienced less negative affect, particularly anxiety, worry, guilt and shame. These are all elements that are implicated in depressive states and that increase risk of relapse.

The participants also reported feeling less distressed by negative thoughts, and more able to let them go, indicating higher levels of metacognitive awareness. Other clinical implications that Chadwick and colleagues (2011) derive from their analysis is that homework in MBCT courses for bipolar patients might need to be more flexible in regards to form of meditative practice. Mindfulness practice was found to be especially challenging in depressive states, something that suggest that additional support or adaptation may be required if patients with a BPD are to achieve similar benefits of mindfulness as has been observed with other groups. This is particularly important when considering the subsyndromal depressive symptoms prevalent in euthymic periods as well as depressive episodes.

Participants also reported experiencing mindfulness as helpful in preventing episodes of heightened mood. People with a BPD may find euthymic periods comparably boring to

hypomania or mania, but following mindfulness practice the participants in this study reported being more appreciative of life in euthymic periods. Another important finding is that participants reported increased acceptance, supported by being more self-compassionate and non-judgemental, of their actions when manic, something that helped ease the guilt and shame that often follow episodes of mania. This is something that might be of clinical importance as shame and guilt following an episode is related to heightened risk of relapse. The themes suggest several benefits as well as some key challenges of mindfulness practice for bipolar patients. The present study, however, cannot provide any data on clinical outcome for bipolar patients.

MBCT has also been explored in a range of feasibility and pilot trials. Across trials, MBCT has been found to be an acceptable and feasible alternative in treatment of BPDs. Three studies that aimed at exploring feasibility and potential benefits of MBCT for patients with a BPD is Williams and colleagues (2008), Miklowitz and colleagues (2009) , and Weber and colleagues (2010). Williams and colleagues (2008) hypothesized that MBCT would improve between-episode symptoms of depression and anxiety. Treatment was delivered in mixed groups of participants with both unipolar and bipolar diagnoses, and followed the standard MBCT manual. Post-treatment measures revealed a significant decrease in depressive symptoms for both unipolar and bipolar participants receiving MBCT. Interestingly, they also found a significant decrease in anxiety symptoms specific for participants with a BPD, and also an increase in anxiety symptoms in the waitlist group. No difference was found in anxiety symptoms across groups for unipolar participants. This is a potentially important finding given that comorbid anxiety disorders are associated with poor outcome and increased risk of suicide in bipolar patients (Otto et al., 2006). They authors argue that anxiety can be counted as an important indicator of treatment outcome, but one that has often been neglected.

Miklowitz and colleagues (2009) hypothesised that MBCT would lead to a reduction in symptoms of depression and suicidal ideation in patients currently in-between episodes, and predicted no increase in symptoms of mania or anxiety, as well as high treatment completion rates. Participants experienced subsyndromal symptoms in spite of being clinically considered euthymic. Miklowitz and colleagues (2009) provided their participants with a somewhat modified MBCT manual more specifically aimed at education about mood change and what factors that can provoke it (e.g., interpersonal conflicts and circadian rhythms). The participants were randomly assigned to either MBCT or a waitlist condition. Post-treatment assessment showed a decrease in scores of depression, no worsening of

symptoms of mania, as well as a modest decrease in anxiety symptoms. The third trial in question, of Weber and colleagues (2010), included only participants with a bipolar diagnosis and explored the effects of MBCT delivered in smaller groups than prescribed in the standard MBCT manual. In keeping with Miklowitz and colleagues (2009), this trial also included elements particularly aimed at managing BPDs. In addition to exploring feasibility and possible benefits of MBCT, they also wanted to assess the effect of MBCT on depressive and hypomanic symptoms. Moreover, the study also included a self-developed questionnaire to assess participants' motivation and expectation before the course, how useful they perceived the course to have been directly following completion of the course, and perceived benefit and frequency of mindfulness practice both directly following completion and at the three month follow-up.

Weber and colleagues (2010) did not replicate symptom improvement from earlier studies. However, pre-course assessment showed that participants reporting a moderate to strong expectations and confidence in that the programme might help them. Following the course 82% reported having moderately to very much benefited from the program. About 50% felt that mindfulness helped them cope with obtrusive emotions, structuring their day and keeping thoughts at a distance, a figure that increased to 67% in the 3-month follow-up. At the 3-month follow up the number of participants reported having moderately to very much benefited from the course had decreased to 67%. This is not to say that expectations predict outcome, but Weber and colleagues (2010) argue that it would be reasonable to expect positive effects of MBCT for BPD patients in general and that this diagnosis should no longer be an exclusion criterion in trials.

These results are somewhat mixed, and the trials all have similar limitations - they utilise small sample sizes and lack a control group. As such it is not possible to rule out that treatment effects are due to non-specific group factors, such as producing changes in lifestyle that encourage greater regularity. However, Williams and colleagues (2008) argue that their main goal was to explore feasibility and acceptability, and that there is reason to expect that MBCT can provide specific effects as a result of providing a strategy of mood regulation in its own right. To demonstrate differences between patients with a unipolar versus a bipolar diagnosis, or changes in symptom levels, would require a larger sample size and inclusion of measures of mania and hypomania. In the same vein, Miklowitz and colleagues (2009) argue that pilot studies such as these are essential in gauging the likelihood of success in RCTs with larger samples. They conclude that MBCT is both acceptable and feasible as an adjunctive psychotherapeutic intervention for BPDs. It is associated with short-term improvements that

need to be addressed in larger RCT's with longitudinal follow-up, and it may also have considerable pragmatic and cost advantages. Weber and colleagues (2010) point out that future studies need to include measurements that document changes in facets related to mindfulness and how it is related to clinical outcome, as well as control group and bigger sample.

The two most recent trials investigating MBCT in the treatment of BPDs have addressed some of these limitations. Deckersbach and colleagues (2011) focused on between-episode functioning, and their MBCT programme was modified both in terms of duration and content. Their MBCT included 12 sessions over a period of three months, as well as elements of CBT and psychoeducation, such as mood monitoring, problem solving and the formation of emergency plans in order to manage mood symptoms. In order to adapt to possible difficulties in executive function (e.g. sustaining attention), due to subsyndromal depressive symptoms, the body scan was shortened and the use of gentle yoga exercises as found in MBSR was used in order to facilitate sustained attention. Length of meditation exercises increased as the course progressed, and the participants get the same amount of homework as in the original manual. Results from Deckersbach and colleagues' (2011) trial showed an increase in ability to observe, be non-judgemental and being less reactive to thoughts and feelings. Also found was a decrease on measures of depressive, hypomanic and manic symptoms post-treatment. Decrease of rumination, worry and attentional deficit showed medium to large effect sizes, as did increased emotion-regulation abilities, well-being and positive affect at the end of treatment. However, these gains were generally not fully maintained, something the authors interpret as suggestive of possible positive effects of booster sessions. Also, even if this study aimed at investigating the changes in facets related to mindfulness and how this change is related to clinical outcome, the results are limited by small sample size and lack of control group. A finding supporting previous indications that MBCT is acceptable to patients with a BPD is that participant attendance was high, something Deckersbach and colleagues (2011) argue is encouraging given relatively low attendance rates in other trials.

In the RCT performed by Perich, Manicavasagar, Mithcell, Ball, and Hadzi-Pavlovic (2013) the aim was to compare the efficacy of MBCT and TAU versus TAU alone in patients with a BPD followed-up for one year post-treatment. The trial of Perich and colleagues (2013) is also limited by a small sample size, but it did include a control group. They found that MBCT did not appear to delay time to recurrence for bipolar patients, as well as no significant changes in manic, hypomanic or depressive symptoms. However, they did find

significant reduction in scores on measures of anxiety compared to the control group and also evidence for a trend of lower self-reported stress. A further analysis of the results performed by Perich, Manicavasagar, Mitchell, and Ball (2013) tested the assumption that more time spent in meditation practice is associated with greater improvements in symptoms and that there is a minimum threshold of meditation practice required for improvement. They found that those who meditated for 3 days a week or more had lower anxiety scores post-treatment, as well as lower depression scores at 12-month follow up. This resonates well with findings discussed previously that show that amount of homework predicts clinical change. Deckersbach and colleagues (2011) suggest that that the unique contribution of mindfulness skills may lie in its effects on rumination and emotion regulation that may again be beneficial in terms of manic relapse prevention. Additionally, continued practice may improve attentional and cognitive functioning, as further analysis of these data by Stange and colleagues (2011) support, and the emphasis on self-compassion and mindfulness may provide an additional buffer against the recurrence of depressive symptoms in BPDs.

In sum, the current trials investigating MBCT in the treatment of BPDs have yielded mixed results. The most robust finding seems to be the effect of MBCT on comorbid anxiety, with some indications of an effect on depression, particularly if mindfulness is practiced regularly. All the aforementioned trials indicate that MBCT is acceptable to patients with a BPD, and suggest benefits that should be explored in bigger RCTs. The above studies are promising but seeing as the results are preliminary, Perich and colleagues (2013) counsel caution as to the perceived benefit of MBCT in treatment of BPDs. There are several important factors that are particularly associated with BPDs that have not yet been investigated in RCTs of MBCT, including lack of long-term follow-up studies, limited examination of relapse rates or adequate assessment episodes of hypomania or mania and depression. This must be taken into consideration when extrapolating effects of MBCT for BPDs from its evidence base for unipolar populations. It is also important that MBCT targets other aspects of BPDs that are likely to affect outcome when the goal is to prevent relapse. Examples of such aspects are non-adherence and regularity of routine. As in the trial by Deckersbach and colleagues (2011), these aspects were taken into consideration and the MBCT manual subsequently lengthened and explicit focus was given to educating about BPDs, focusing on the importance of regularity of routine and adherence. Such measures should be taken into consideration also in future trials due to its evident importance in long-term management of BPDs (Colom et al., 2009).

7 Concluding remarks

Considerable resources have been put into clinical research on treatment interventions for BPDs. Despite important contributions from maintenance pharmacotherapy and psychotherapeutic interventions (e.g. psychoeducation and CBT), preventing relapse in the long-term remains challenging. As I have pointed out, clinical research into treatment of BPDs entails specific methodological challenges due to the recurrent nature, destructive subsyndromal depressive symptoms in remittent periods and comorbidities seen in BPDs (Alloy et al., 2005).

The evidence for MBCT for BPDs is in its early days. There is preliminary evidence suggesting a positive effect of MBCT on some aspect of BPDs, with strongest empirical support for effects on anxiety and depressive symptoms. This is promising. However, methodological limitations (e.g., lack of appropriate control groups) makes it difficult to separate the effects of the manipulation of mechanisms related to vulnerability for relapse from nonspecific therapeutic factors as the cause of change with any certainty.

One potential way ahead is to gain a better understanding of the mechanisms involved in maintaining vulnerability for relapse in BPDs. Moreover, the relevance of the knowledge base for cognitive mechanisms shown to be critically involved in vulnerability to RMD should be investigated further. I have highlighted three cognitive mechanisms – toxic self-discrepancies, lack of self-compassion and limited metacognitive awareness – involved in the ongoing risk of depressive relapse in unipolar depression, and reviewed the relevance of these mechanisms for BPDs. As pointed out, there are both similarities and differences in how depression in unipolar and BPDs present, such as somatic syndrome being more prevalent in bipolar depression. There is also a strong genetic component in BPDs, and a larger risk of recurrence following an initial episode than in unipolar depression. MBCT is based on the tenet that risk of depressive recurrence in RMD is due in part to the, over time, relatively effortless reactivation of maladaptive cognitions. However, in RMD, as more episodes of depression are experienced, minor events gain the capacity to trigger depressive episodes. Thus, onset becomes increasingly disassociated from major life events, as may also be the case in BPDs.

Despite differences that cannot be directly observed (e.g. genetics), it has been observed that unipolar and bipolar depressions share important clinical features. As such, shared cognitive mechanisms related to risk of relapse and sustained vulnerability to

depressive relapse are a reasonable possibility. Seeing as most of the treatment interventions for BPDs are not effective in preventing depressive relapse in the long run, MBCT, which incorporates aspects of both CBT and psychoeducation, as well as targeting lack of self-compassion, toxic self-discrepancies and low metacognitive awareness, presents a promising approach to preventing depressive relapse in BPDs. further research into treatment options for BPDs. Future well-designed studies are required, including use of a sufficiently large sample sizes, adequate control groups, and long-term follow-up. This includes the use of dismantling designs, which enables a test of hypothesised key mechanisms by keeping non-specific factors identical across the treatment and control group (e.g., Williams et al., 2014).

Importantly, Teasdale and colleagues (2000) have pointed out that MBCT is designed for patients with RMD who are in remittance. Thus, since patients with BPDs may suffer from the same cognitive difficulties and intense negative thinking when depressed as those with RMD, it should be considered whether MBCT should only be offered to patients with a BPD when euthymic. There are also other inclusion/exclusion criteria that need to be carefully considered. One especially important criterion is how heterogeneous the sample should be in terms of for example comorbid anxiety or abuse disorders. As Scott and colleagues (2006) observed, including a more heterogeneous sample may be one of the reasons why their treatment intervention led to no significant change. On the one hand it is important to consider the generalizability of results, suggesting the sample should be as representative as possible. On the other, it is possible that subgroups of BPDs require specific and tailored interventions, and that a bigger RCT may benefit from investigating how common aspects shared by BPD subgroups (e.g. anxiety comorbidity) mediate outcomes following MBCT.

In contrast to CBT, the aim of MBCT is not to change the content of thoughts, but to teach different and more adaptive ways to relate to mental events, such as thoughts and emotions, and in this way break the relationship between reactivated depressive cognitions and relapse into clinical depression. The evidence reviewed here supports the notion that MBCT, through targeting subsyndromal depressive symptoms, enhancing attentional capacities through mindful meditation practice and bringing compassion, openness and a meta-perspective to one's internal and external experiences, may well improve the course and outcome of BPDs in significant ways. Other outcomes may include medication adherence and improved social and occupational functioning. The extent to which the mechanisms found to be involved in on-going risk of relapse in unipolar depression apply to BPDs await further scrutiny.

References

Akiskal, H. S., Bourgeois, M. L., Angst, J., Post, R., Möller, H., & Hirschfeld, R. (2000). Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *Journal of affective disorders, 59*, 5-30. doi: 10.1016/S0165-0327(00)00203-2

Alloy, L. B., Abramson, L. Y., Urosevic, S., Walshaw, P. D., Nusslock, R., & Neeren, A. M. (2005). The psychosocial context of bipolar disorder: Environmental, cognitive, and developmental risk factors. *Clinical Psychology Review, 25*, 1043-1075. doi: 10.1016/j.cpr.2005.06.006

Angst, J., Azorin, J.-M., Bowden, C. L., Perugi, G., Vieta, E., Gamma, A., & Young, A. H. (2011). Prevalence and Characteristics of Undiagnosed Bipolar Disorders in Patients With a Major Depressive Episode. The BRIDGE Study.'. *Archives of General Psychiatry, 68*, 791-799. doi: 10.1001/archgenpsychiatry.2011.87

Angst, J., Gamma, A., Benazzi, F., Ajdacic, V., Eich, D., & Rössler, W. (2003). Diagnostic issues in bipolar disorder. *European Neuropsychopharmacology, 13*, 43-50. doi: 10.1016/S0924-977X(03)00077-4

Barnhofer, T., & Crane, C. (2009). Mindfulness-Based Cognitive Therapy for Depression and Suicidality. In F. Didonna (Ed.), *Clinical Handbook of Mindfulness*. New York: Springer.

Barnhofer, T., Crane, C., Hargus, E., Amarasinghe, M., Winder, R., & Williams, J. M. G. (2009) Mindfulness-based cognitive therapy as a treatment for chronic depression: A preliminary study. *Behaviour Research and Therapy, 47,* 366-373. doi: 10.1016%2Fj.brat.2009.01.019

Baskerville, S. L. (1999). *Self-discrepancies, depression proneness, and current mood state: a test of Higgins' and Ogilvie's theories* (Ph.D. Thesis, University of Saskathewan). Retrieved from: http://ecommons.usask.ca/bitstream/handle/10388/etd-10212004-000903/NQ37871.pdf?sequence=1

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. K. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*, 561-571. Retrieved from: http://counsellingresource.com/lib/wp-content/managed-media/Beck_AT_1961.pdf

Bellivier, F., Leroux, M., Henry, C., Rayah, F., Rouillon, F., Laplanche, J.-L., & Leboyer, M. (2002). Serotonin transporter gene polymorphism influences age at onset in patients

with bipolar affective disorder. *Neuroscience letters, 334*, 17-20. doi: 10.1016/S0304-3940(02)01029-7

Beynon, S., Soares-Weiser, K., Woolacott, N., Duffy, S., & Geddes, J. R. (2008). Psychosocial interventions for the prevention of relapse in bipolar disorder: systematic review of controlled trials. *The British Journal of Psychiatry, 192*, 5-11. doi: 10.1192/bjp.bp.107.037887

Binder, P., Gjelsvik, B., Halland, E., & Vøllestad, J. (2014). *Mindfulness i psykologisk behandling*. Oslo: Universitetsforlaget.

Bishop, S. R., Lau, M., Shapiro, S., Carlson, L., Anderson, N. D., Carmody, J., . . . Velting, D. (2004). Mindfulness: A proposed operational definition. *Clinical Psychology: Science and Practice, 11*, 230-241. doi: 10.1093/clipsy.bph077

Bowden, C. L. (2003). A different depression: clinical distinctions between bipolar and unipolar depression. *Journal of affective disorders, 84*, 117-125. doi: 10.1016/S0165-0327(03)00194-0

Brittlebank, A. D., Scott, J., Williams, J. M., & Ferrier, I. N. (1993). Autobiographical memory in depression: state or trait marker? *The British Journal of Psychiatry, 162*, 118-121. doi: 10.1192/bjp.162.1.118

Brown, K. W., & Cordon, S. (2009). Toward a phenomenology of mindfulness: Subjective experience and emotional correlates. In Fabrizio, D. (Ed.) *Clinical handbook of mindfulness* (pp. 59-81): New York: Springer.

Burcusa, S. L., & Iacono, W. G. (2007). Risk for recurrence in depression. *Clinical Psychology Review, 27*, 959-985. doi: 10.1016/j.cpr.2007.02.005

Carlson, G. A., Bromet, E. J., Driessens, C., Mojtabai, R., & Schwartz, J. E. (2002). Age at onset, childhood psychopathology, and 2-year outcome in psychotic bipolar disorder. *The American Journal of Psychiatry, 159*, 307-309. doi: 10.1176/appi.ajp.159.2.307

Carver, C. S., Lawrence, J. W., & Scheier, M. F. (1999). Self-discrepancies and affect: Incorporating the role of feared selves. *Personality and social psychology Bulletin, 25*, 783-792. doi: 10.1177/0146167299025007002

Chadwick, P., Kaur, H., Swelam, M., Ross, S., & Ellett, L. (2011). Experience of Mindfulness in people with bipolar disorder: A qualitative study. *Psychotherapy Research, 21*, 277-285. doi: 10.1080/10503307.2011.565487

Chiesa, A., & Serretti, A. (2011). Mindfulness based cognitive therapy for psychiatric disorders: a systematic review and meta-analysis. *Psychiatry Research, 187*, 441-453. doi: 10.1016/j.psychres.2010.08.011

Colom, F., Vieta, E., Reinares, M., Martínez-Arán, A., Torrent, C., Goikolea, J. M., & Gastó, C. (2003). Psychoeducation efficacy in bipolar disorders: beyond compliance enhancement. *The Journal of clinical psychiatry, 64*, 1101-1105. doi: 10.4088/JCP.v64n0917

Colom, F., Vieta, E., Sanchez-Moreno, J., Palomino-Otiniano, R., Reinares, M., Goikolea, J. M., . . . Martinez-Aran, A. (2009). Group psychoeducation for stabilised bipolar disorders: 5-year outcome of a randomised clinical trial. *The British Journal of Psychiatry, 194*, 260-265. doi: 10.1192/bjp.bp.107.040485

Colom, F., Vieta, E., Tacchi, M. J., Sanchez-Moreno, J., & Scott, J. (2005). Identifying and improving non-adherence in bipolar disorder. *Bipolar disorders, 7*, 24-31. doi: 10.1111/j.1399-5618.2005.00248.x

Crane, C., Barnhofer, T., Duggan, D. S., Hepburn, S., Fennell, M. J. V., & Williams, J. M. G. (2008). Mindfulness-Based Cognitive Therapy and Self-Discrepancy in Recovered Depressed Patients with a History of Depression and Suicidality. *Cognitive Therapy and Research, 32*, 775-787. doi: 10.1007/s10608-008-9193-y

Crane, C., Barnhofer, T., & Williams, J. M. G. (2007). Cue self-relevance affects autobiographical memory specificity in individuals with a history of major depression. *Memory, 15*, 312-323. doi: 10.1080/09658210701256530

Crane, C., Crane, R. S., Eames, C., Fennell, M. J. V., Silverton, S., Williams, J. M. G., & Barnhofer, T. (2014). The effects of amount of home meditation practice in Mindfulness Based Cognitive Therapy on hazard of relapse to depression in the Staying Well after Depression Trial. *Behaviour Research and Therapy, 63*, 17-24. doi: 10.1016/j.brat.2014.08.015

Deckersbach, T., Hölzel, B. K., Eisner, L. R., Stange, J. P., Peckham, A. D., Dougherty, D. D., . . . Nierenberg, A. A. (2011). Mindfulness-Based Cognitive Therapy for Nonremittent Patients with Bipolar Disorder. *CNS Neurosciences and Therapeutics, 18*, 133-141. doi: 10.1111/j.1755-5949.2011.00236.x

Fajutrao, L., Locklear, J., Priaulx, J., & Heyes, A. (2009). A systematic review of the evidence of the burden of bipolar disorder in Europe. *Clinical Practice and Epidemiology in Mental Health, 5*. doi: 10.1186/1745-0179-5-3

Feldman, C., & Kuyken, W. (2011). Compassion in the landscape of suffering. *Contemporary Buddhism, 12*, 143-155. doi: 10.1080/14639947.2011.564831

Fennell, M., & Segal, Z. (2011). Mindfulness-based cognitive therapy: culture clash or creative fusion? *Contemporary Buddhism, 12*, 125-142. doi: 10.1080/14639947.2011.564828

Forand, N. R., DeRubies, R. J., & Amsterdam, J. D. (2013). Combining Medication and Psychotherapy in the Treatment of Major Mental Disorders. In M. J. Lambert (Ed.), *Handbook of Psychotherapy and Behaviour Change* (6th ed.). New Jersey: John Wiley & Sons.

Frank, E., Kupfer, D. J., Thase, M. E., Mallinger, A. G., Swartz, H. A., Fagiolini, A. M., . . . Thompson, W. (2005). Two-year outcomes for interpersonal and social rhythm therapy in individuals with bipolar I disorder. *Archives of General Psychiatry, 62*, 996-1004. doi: 10.1001/archpsyc.62.9.996

Fredrickson, B. L., Cohn, M. A., Coffey, K. A., Pek, J., & Finkel, S. M. (2008). Open hearts build lives: positive emotions, induced through loving-kindness meditation, build consequential personal resources. *Journal of personality and social psychology, 95,* 1045-1062. doi: 10.1037/a0013262

Fredrickson, B. L., & Losada, M. F. (2005). Positive affect and the complex dynamics of human flourishing. *American Psychologist, 60*, 678-686. doi: 10.1037/0003-066X.60.7.678

Geddes, J. R., & Miklowitz, D. J. (2013). Treatment of bipolar disorder. *The Lancet, 381*, 1672-1682. doi: 10.1016/S0140-6736(13)60857-0

Gilbert, P. (2009). Introducing compassion-focused therapy. *Advances in psychiatric treatment, 15*, 199-208. doi: 10.1192/apt.bp.107.005264

Gilbert, P., & Irons, C. (2004). A pilot exploration of the use of compassionate images in a group of self-critical people. *Memory, 12*, 507-516. doi:10.1080/09658210444000115

Goetz, J. L., Keltner, D., & Simon-Thomas, E. (2010). Compassion: an evolutionary analysis and empirical review. *Psychological bulletin, 136*, 351-374. doi:10.1037/a0018807

Goodwin, F. K., & Jamison, K. R. (2007). *Manic-Depressive Illness. Bipolar Disorders and Recurrent Depression* (2nd ed.). Oxford: Oxford University Press.

Hargus, E., Crane, C., Barnhofer, T., & Williams, J. M. G. (2010). Effects of Mindfulness on Meta-Awareness and Specificity of Describing Prodromal Symptoms in Suicidal Depression. *Emotion, 10*, 34-42. doi: 10.1037/a0016825

Hawton, K., Sutton, L., Haw, C., Sinclair, J., & Harriss, L. (2005). Suicide and Attempted Suicide in Bipolar Disorders: A systematic Review of Risk Factors. *Journal of Clinical Psychiatry, 66*, 693-704. doi: 10.4088/JCP.v66n0604

Hayes, S. C., Follette, V. M., & Linehan, M. (2004). *Mindfulness and acceptance: Expanding the cognitive-behavioral tradition*: New York: Guilford Press.

Hayes, S. C., Strosahl, K. D., & Wilson, K. G. (1999). *Acceptance and commitment therapy: An experiential approach to behavior change*. New York: Guilford Press.

Higgins, E. T. (1987). Self-discrepancy: a theory relating self and affect. *Psychological review, 94*, 319-340. doi: 10.1037/0033-295X.94.3.319

Hölzel, B. K., Lazar, S. W., Gard, T., Schuman-Olivier, Z., Vago, D. R., & Ott, U. (2011). How Does Mindfulness Meditation Work? Proposing Mechanisms of Action From a Conceptual and Neural Perspective. *Perspectives on Psychological Science, 6*, 537-559. doi: 10.1177/1745691611419671

Inskip, H. M., Harris, E. C., & Barraclough, B. (1998). Lifetime risk of suicide for affective disorder, alcoholism and schizophrenia. *The British Journal of Psychiatry, 172*, 35-37. doi: 10.1192/bjp.172.1.35

Johnson, S. L. (2005). Life events in bipolar disorder: towards more specific models. *Clinical Psychology Review, 25*, 1008-1027. doi: 10.1016/j.cpr.2005.06.004

Judd, L. L., Akiskal, H. S., Schettler, P. J., Endicott, J., Leon, A. C., Solomon, D. A., . . . Keller, M. B. (2005). Psychosocial disability in the course of bipolar I and II disorders: a prospective, comparative, longitudinal study. *Archives of General Psychiatry, 62*, 1322-1330. doi: 10.1001/archpsyc.62.12.1322

Judd, L. L., Akiskal, H. S., Schettler, P. J., Endicott, J., Maser, J., Solomon, D. A., . . . Keller, M. B. (2002). The Long-term Natural History of the Weekly Symptomatic Status of Bipolar I Disorder. *Archives of General Psychiatry, 59,* 530-537. doi: 10.1001/archpsyc.59.6.530

Kabat-Zinn, J. (1990). *Full Catastrophe Living: Using the Wisdom of Your Body and Mind to Face Stress, Pain and Illness*. New York: Delacorte.

Kabat-Zinn, J. (2003). Mindfulness-based interventions in context: past, present, and future. *Clinical Psychology: Science and Practice, 10*, 144-156. doi: 10.1093/clipsy.bpg016

Kazdin, A. E., & Kagan, J. (1994). Models of dysfunction in developmental psychopathology. *Clinical Psychology: Science and Practice, 1*, 35-52. doi: 10.1111/j.1468-2850.1994.tb00005.x

Keller, M. B., Lavori, P. W., Coryell, W., Endicott, J., & Mueller, T. I. (1993). Bipolar I: a five-year prospective follow-up. *The Journal of nervous and mental disease, 181*, 238-245.

Kelly, A. C., Zuroff, D. C., & Shapira, L. B. (2009). Soothing oneself and resisting self-attacks: The treatment of two intrapersonal deficits in depression vulnerability. *Cognitive Therapy and Research, 33*, 301-313. doi: 10.1007/s10608-008-9202-1

Korten, N. C. M., Comijs, H. C., Lamers, F., & Penninx, B. W. J. H. (2012). Early and late onset depression in young and middle aged adults: differential symptomatology, characteristics and risk factors? *Journal of affective disorders, 138*, 259-267. doi: 10.1016/j.jad.2012.01.042

Kraemer, H. C., Stice, E., Kazdin, A., Offord, D., & Kupfer, D. (2001). How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. *The American Journal of Psychiatry, 158*, 848-856. doi: 10.1176/appi.ajp.158.6.848

Krieger, T., Altenstein, D., Baettig, I., Doerig, N., & Holtforth, M. G. (2013). Self-compassion in Depression: Associations With Depressive Symptoms, Rumination, and Avoidance in Depressed Outpatients. *Behaviour Therapy, 44*, 501-513. doi: http://dx.doi.org/10.1016/j.beth.2013.04.004

Kringlen, E., Torgersen, S., & Cramer, V. (2014). A Norwegian psychiatric epidemiological study. *The American Journal of Psychiatry, 158*, 1091-1098. doi: 10.1176/appi.ajp.158.7.1091

Kuyken, W., Byford, S., Taylor, R. S., Watkins, E., Holden, E., White, K., . . . Mullan, E. (2008). Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *Journal of Consulting and Clinical Psychology, 76*, 966-978. doi: 10.1037/a0013786

Kuyken, W., Watkins, E., Holden, E., White, K., Taylor, R. S., Byford, S., . . . Dalgleish, T. (2010). How does Mindfulness-based cognitive therapy work? *Behaviour Research and Therapy, 48*, 1105-1112. doi: 10.1016/j.brat.2010.08.003

Lam, D., & Wong, G. (2005). Prodromes, coping strategies and psychological interventions in bipolar disorders. *Clinical Psychology Review, 25*, 1028-1042. doi: 10.1016/j.cpr.2005.06.005

Lam, D. H., Bright, J., Jones, S., Hayward, P., Schuck, N., Chisholm, D., & Sham, P. (2000). Cognitive therapy for bipolar illness - a pilot study of relapse prevention. *Cognitive Therapy and Research, 24*, 503-520. doi: 10.1023/A:1005557911051

Lau, M. A., Segal, Z. V., & Williams, J. M. G. (2004). Teasdale's differential activation hypothesis: implications for mechanisms of depressive relapse and suicidal behaviour. *Behaviour Research and Therapy, 42*, 1001-1017. doi: 10.1016/j.brat.2004.03.003

Leary, M. R., Tate, E. B., Adams, C. E., Batts Allen, A., & Hancock, J. (2007). Self-compassion and reactions to unpleasant self-relevant events: the implications of treating oneself kindly. *Journal of personality and social psychology, 92*, 887-904. doi: 10.1037/0022-3514.92.5.887

Linehan, M. M., Schmidt, H., Dimeff, L. A., Craft, J. C., Kanter, J., & Comtois, K. A. (1999). Dialectical Behavior Therapy for Patients with Borderline Personality Disorder and Drug-Dependence. *The American journal on addictions, 8*, 279-292. doi: 10.1080/105504999305686

Lutz, A., Brefczynski-Lewis, J., Johnstone, T., & Davidson, R. J. (2008). Regulation of the neural circuitry of emotion by compassion meditation: effects of meditative expertise. *PloS one, 3*, e1897. doi: 10.1371/journal.pone.0001897

MacBeth, A., & Gumley, A. (2012). Exploring compassion: A meta-analysis of the association between-self-compassion and psychopathology. *Clinical Psychology Review, 32*, 545-552. doi: 10.1016/j.cpr.2012.06.003

MacQueen, G. M., Young, L. T., & Joffe, R. T. (2001). A review of psychosocial outcome in patients with bipolar disorder. *Acta Psychiatrica Scandinavica, 103*, 163-170. doi: 10.1034/j.1600-0447.2001.00059.x

Malt, U. (2012). Bipolare affektive lidelser. In U. Malt (Ed.), *Lærebok i psykiatri*. Oslo: Gyldendal Akademiske.

Marangell, L. B., Dennehy, E. B., Miyahara, S., Wisniewski, S. R., Bauer, M. S., Rapaport, M. H., & Allen, M. H. (2009). The functional impact of subsyndromal depressive symptoms in bipolar disorder: data from STEP-BD. *Journal of affective disorders, 114*, 58-67. doi: 10.1016/j.jad.2008.07.006

McGuffin, P., Rijsdijk, F., Andrew, M., Sham, P., Katz, R., & Cardno, A. (2003). The heritability of bipolar affective disorder and the genetic relationship to unipolar depression. *Archives of General Psychiatry, 60*, 497-502. doi: 10.1001/archpsyc.60.5.497

Meeks, S. (1999). Bipolar disorder in the latter half of life: symptom presentation, global functioning and age of onset. *Journal of affective disorders, 52*, 161-167. doi: http://dx.doi.org/10.1016/S0165-0327(98)00069-X

Miklowitz, D. (2008). Adjunctive psychotherapy for bipolar disorder: state of the evidence. *American Journal of Psychiatry, 165*, 1408-1419. doi: 10.1176/appi.ajp.2008.08040488

Miklowitz, D. J., Alatiq, Y., Goodwin, G. M., Geddes, J. R., Fennell, M. J. V., Dimidjian, S., . . . Williams, J. M. G. (2009). A pilot study of mindfulness-based cognitive therapy for bipolar disorder. *International Journal of Cognitive Therapy, 2*, 373-382. doi: 10.1521/ijct.2009.2.4.373

Miklowitz, D. J., George, E. L., Richards, J. A., Simoneau, T. L., & Suddath, R. L. (2003). A randomized study of family-focused psychoeducation and pharmacotherapy in the outpatient management of bipolar disorder. *Archives of General Psychiatry, 60*, 904-912. doi: 10.1001/archpsyc.60.9.904

Miklowitz, D. J., Goodwin, G. M., Bauer, M. S., & Geddes, J. R. (2008). Common and specific elements of psychosocial treatments for bipolar disorder: a survey of clinicians participating in randomized trials. *Journal of psychiatric practice, 14*, 77-85. doi: 10.1097%2F01.pra.0000314314.94791.c9

Mykletun, A., Knudsen, A. K., & Mathiesen, K. S. (2009). *Psykisk helse i Norge: Et folkehelseperspektiv*. Nasjonalt Folkehelseinstitutt.

Neff, K. D. (2003a). The development and validation of a scale to measure self-compassion. *Self and identity, 2*, 223-250. doi: 10.1080/15298860309027

Neff, K. D. (2003b). Self-compassion: An alternative conceptualization of a healthy attitude toward oneself. *Self and identity, 2*, 85-101. doi: 10.1080/15298860309032

Neff, K. D., Kirkpatrick, K. L., & Rude, S. S. (2007). Self-compassion and adaptive psychological functioning. *Journal of research in personality, 41*, 139-154. doi: 10.1016/j.jrp.2006.03.004

NICE. (2009). *Depression in adults: The treatment and management of depression in adults*. National Institute for Clinical Excellence Retrieved from http://www.nice.org.uk/guidance/cg90/chapter/1-recommendations.

Oatley, K., & Johnson-Laird, P. N. (1987). Towards a cognitive theory of emotions. *Cognition and emotion*, *1*, 29-50. doi: 10.1080/02699938708408362

Otto, M. W., Simon, N. M., Wisniewski, S. R., Miklowitz, D. J., Kogan, J. N., Reilly-Harrington, N. A., . . . Sagduyu, K. (2006). Prospective 12-month course of bipolar disorder in out-patients with and without comorbid anxiety disorders. *The British Journal of Psychiatry, 189*, 20-25. doi: 10.1192/bjp.bp.104.007773

Papadakis, A. A., Prince, R. P., Jones, N. P., & Strauman, T. J. (2006). Self-regulation, rumination, and vulnerability to depression in adolescent girls. *Development and psychopathology, 18*, 815-829. doi: 10.1017/S0954579406060408

Pavlickova, H., Varese, F., Turnbull, O., Scott, J., Morriss, R., Kinderman, P., . . . Bentall, R. P. (2013). Symptom-specific self-referential cognitive processes in bipolar disorder: A longitudinal analysis. *Psychological Medicine, 43*, 1895-1907. doi: 10.1017/S0033291712002711

Pavlickova, H., Turnbull, O. H., & Bentall, R. P. (2014). Discrepancies between explicit and implicit self-esteem and their relationship to symptoms of depression and mania. *Psychology and Psychotherapy: Theory, Research and Practice*, *87*, 311-323. doi: 10.1111/papt.12015

Peeters, F., Wessel, I., Merckelbach, H., & Boon-Vermeeren, M. (2002). Autobiographical memory specificity and the course of major depressive disorder. *Comprehensive Psychiatry, 43*, 344-350. doi: 10.1053/comp.2002.34635

Perich, T., Manicavasagar, V., Mitchell, P. B., & Ball, J. R. (2013). The association between meditation practice and treatment outcome in Mindfulness-based Cognitive Therapy for bipolar disorder. *Behaviour Research and Therapy, 51*, 338-343. doi: 10.1016/j.brat.2013.03.006

Perich, T., Manicavasagar, V., Mitchell, P. B., Ball, J. R., & Hadzi-Pavlovic, D. (2013). A randomized controlled trial of mindfulness-based cognitive therapy for bipolar disorder. *Acta Psychiatrica Scandinavica, 127*, 333-343. doi: 10.1111/acps.12033

Perlis, R. H., Ostacher, M. J., Patel, J. K., Marangell, L. B., Zhang, H., Wisniewski, S. R., . . . Gyulai, L. (2006). Predictors of recurrence in bipolar disorder: primary outcomes from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *American Journal of Psychiatry, 163*, 217-224. doi: 10.1176/appi.ajp.163.2.217

Piet, J., & Hougaard, E. (2011). The effect of mindfulness-based cognitive therapy for prevention of relapse in recurrent major depressive disorder: A systematic review and meta-analysis. *Clinical Psychology Review, 31*, 1032-1040. doi: 10.1016/j.cpr.2011.05.002

Platman, S. R., Plutchik, R., Fieve, R. R., & Lawlor, W. G. (1969). Emotion profiles associated with mania and depression. *Archives of General Psychiatry, 20*, 210-214. doi: 10.1001/archpsyc.1969.01740140082010

Raes, F. (2010). Rumination and worry as mediators of the relationship between self-compassion and depression and anxiety. *Personality and Individual Differences, 48*, 757-761. doi: 10.1016/j.paid.2010.01.023

Raes, F., Hermans, D., Williams, J. M. G., Beyers, W., Eelen, P., & Brunfaut, E. (2006). Reduced autobiographical memory specificity and rumination in predicting the course of depression. *Journal of Abnormal Psychology, 115*, 699-704. doi: 10.1037/0021-843X.115.4.699

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., & Goodwin, F. K. (1990). Comorbidity of mental disorders with alcohol and other drug abuse: Results from the Epidemiologic Catchment Area (ECA) study. *Jama, 264*, 2511-2518. doi: 10.1001/jama.1990.03450190043026

Rutter, M., & Sroufe, L. (2000). Developmental psychopathology: Concepts and challenges. *Development and psychopathology, 12*, 265-296. Retrieved from: http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=55119&fileId=S0954579400003023

Sasson, Y., Chopra, M., Harrari, E., Amitai, K., & Zohar, J. (2003). Bipolar comorbidity: from diagnostic dilemmas to therapeutic challenge. *The International Journal of Neuropsychopharmacology, 6*, 139-144. doi: 10.1017/S1461145703003432

Schulze, T. G., Müller, D. J., Krauss, H., Gross, M., Fangerau-Lefèvre, H., Ill, F., . . . Propping, P. (2002). Further evidence for age of onset being an indicator for severity in bipolar disorder. *Journal of affective disorders, 68*, 343-345. doi: 10.1016/S0165-0327(01)00306-8

Scott, J., Colom, F., Popova, E., Benabarre, A., Cruz, N., Valenti, M., . . . Vieta, E. (2009). Long-term mental health resource utilization and cost of care following group psychoeducation or unstructured group support for bipolar disorders: a cost-benefit analysis. *The Journal of clinical psychiatry, 70*(3), 378-386.

Scott, J., Garland, A., & Moorhead, S. (2001). A pilot study of cognitive therapy in bipolar disorders. *Psychological Medicine, 31*, 459-467. doi: 10.1017/S0033291701003373

Scott, J., Paykel, E., Morriss, R., Bentall, R., Kinderman, P., Johnson, T., . . . Hayhurst, H. (2006). Cognitive–behavioural therapy for severe and recurrent bipolar disorders Randomised controlled trial. *The British Journal of Psychiatry, 188*, 313-320. doi: 10.1192/bjp.188.4.313

Scott, J., & Pope, M. (2003). Cognitive styles in individuals with bipolar disorders. *Psychological Medicine, 33*, 1081-1088. doi: 10.1017/S0033291703007876

Scott, L., & O'Hara, M. W. (1993). Self-discrepancies in clinically anxious and depressed university students. *Journal of abnormal psychology, 102*, 282-287. doi: 10.1037/0021-843X.102.2.282

Segal, Z. V., Kennedy, S., Gemar, M., Hood, K., Pedersen, R., & Buis, T. (2006). Cognitive reactivity to sad mood provocation and the prediction of depressive relapse. *Archives of general psychiatry, 63*, 749-755. doi: 10.1001/archpsyc.63.7.749

Segal, Z. V., Williams, J. M. G., & Teasdale, J. D. (2013). *Mindfulness-based cognitive therapy for depression*: New York: Guilford Press.

Siegel, R. D., Germer, C. K., & Olendzki, A. (2009). Mindfulness: What is it? Where did it come from? In F. Didonna (Ed.), *Clinical Handbook of Mindfulness*. New York: Springer.

Spinhoven, P., Bockting, C. L. H., Kremers, I. P., Schene, A. H., & Williams, J. M. G. (2007). The endorsement of dysfunctional attitudes is associated with an impaired retrieval of specific autobiographical memories in response to matching cues. *Memory, 15*, 324-338. doi: 10.1080/09658210701256555

Stange, J. P., Eisner, L. R., Hölzel, B. K., Peckham, A. D., Dougherty, D. D., Rauch, S. L., . . . Deckersbach, T. (2011). Mindfulness-Based Cognitive Therapy for Bipolar Disorder, Effects on Cognitive functioning. *Journal of psychiatric practice, 17*, 410-419. doi: 10.1097%2F01.pra.0000407964.34604.03

Strauman, T. J., Kolden, G. G., Stromquist, V., Davis, N., Kwapil, L., Heerey, E., & Schneider, K. (2001). The effects of treatments for depression on perceived failure in self-regulation. *Cognitive Therapy and Research, 25*, 693-712. doi: 10.1023/A:1012915205800

Suppes, T., Leverich, G. S., Keck, P. E., Nolen, W. A., Denicoff, K. D., Altshuler, L. L., . . . Frye, M. A. (2001). The Stanley Foundation Bipolar Treatment Outcome Network: II. demographics and illness characteristics of the first 261 patients. *Journal of affective disorders, 67*, 45-59. doi: 10.1016/S0165-0327(01)00432-3

Teasdale, J. D. (1988). Cognitive vulnerability to persistent depression. *Cognition & Emotion, 2*, 247-274. doi: 10.1080/02699938808410927

Teasdale, J. D., Moore, R. G., Hayhurst, H., Pope, M., Williams, S., & Segal, Z. V. (2002). Metacognitive awareness and prevention of relapse in depression: empirical evidence. *Journal of Consulting and Clinical Psychology, 70*, 275-287. doi: 10.1037/0022-006X.70.2.275

Teasdale, J. D., Segal, Z. V., & Williams, J. M. G. (2003). Mindfulness training and problem formulation. *Clinical Psychology: Science and Practice, 10*, 157-160. doi: 0.1093/clipsy.bpg017

Teasdale, J. D., Segal, Z. V., Williams, J. M. G., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of consulting and clinical psychology, 68*, 615-623. doi: 10.1037/0022-006X.68.4.615

ten Have, M., Vollebergh, W., Bijl, R., & Nolen, W. A. (2002). Bipolar disorder in the general population in The Netherlands (prevalence, consequences and care utilisation): results from The Netherlands Mental Health Survey and Incidence Study (NEMESIS). *Journal of affective disorders, 68*, 203-213. doi: 10.1016/S0165-0327(00)00310-4

Van der Gucht, E., Morriss, R., Lancaster, G., Kinderman, P., & Bentall, R. P. (2009). Psychological processes in bipolar affective disorder: Negative cognitive style and reward processing. *The British Journal of Psychiatry, 194*, 146-151. doi: 10.1192/bjp.bp.107.047894

van der Velden, A. M., Kuyken, W., Wattar, U., Crane, C., Pallesen, K. J., Dahlgaard, J., . . . Piet, J. (2015). A systematic review of mechanisms of change in mindfulness-based cognitive therapy in the treatment of recurrent major depressive disorder. *Clinical Psychology Review, 37*, 26-39. doi: 10.1016/j.cpr.2015.02.001

Veehof, M. M., Oskam, M.-J., Schreurs, K. M. G., & Bohlmeijer, E. T. (2011). Acceptance-based interventions for the treatment of chronic pain: a systematic review and meta-analysis. *Pain®, 152*, 533-542. doi: 10.1016/j.pain.2010.11.002

Vieta, E., Pacchiarotti, I., Valenti, M., Berk, M., Scott, J., & Colom, F. (2009). A Critical Update on Psychological Interventions for Bipolar Disorders. *Current Psychiatry Reports, 11*, 494-502. doi: 10.1007/s11920-009-0090-1

Weber, B., Jermann, F., Gex-Fabry, M., Nallet, A., Bondolfi, G., & Aubry, J. M. (2010). Mindfulness-based cognitive therapy for bipolar disorder: a feasibility trial. *European Psychiatry, 25*, 334-337. doi: 10.1016/j.eurpsy.2010.03.007

Williams, J. M. G. (2008). Mindfulness, Depression, and Modes of Mind. *Cognitive Therapy and Research, 32,* 721-733. doi: 10.1007/s10608-008-9204-z

Williams, J. M. G. (2010). Mindfulness and Psychological Process. *Emotion, 10*, 1-7. doi: 10.1037/a0018360

Williams, M., Alatiq, Y., Crane, C., Barnhofer, T., Fennell, M. J. V., Duggan, D. S., . . . Goodwin, G. M. (2008). Mindfulness-based cognitive therapy (MBCT) in bipolar disorder: Preliminary evaluation of immediate effects on between-episode

functioning. *Journal of affective disorders, 107*, 275-279. doi: 10.1016/j.jad.2007.08.022

Williams, J. M. G., Barnhofer, T., Crane, C., Herman, D., Raes, F., Watkins, E., & Dalgleish, T. (2007). Autobiographical memory specificity and emotional disorder. *Psychological bulletin, 133*, 122-148. doi: 10.1037/0033-2909.133.1.122

Williams, J. M. G., Crane, C., Barnhofer, T., Brennan, K., Duggan, D. S., Fennell, M. J. V., . . . Von Rohr, I. R. (2014). Mindfulness-based cognitive therapy for preventing relapse in recurrent depression: A randomized dismantling trial. *Journal of Consulting and Clinical Psychology, 82*, 275-286. doi: 10.1037/a0035036

Williams, J. M. G, Russell, I., & Russell D. (2008) Mindfulness-based Cognitive Therapy: Further Issues in Current Evidence and Future Research. *Journal of Consulting and Clinical Psychology, 76*, 524-529. doi: 10.1037/0022-006X.76.3.524

Zisook, S., & Schuckit, M. A. (1987). Male primary alcoholics with and without family histories of affective disorder. *Journal of Studies on Alcohol and Drugs, 48*(4), 337-344.