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## Adapting Mindfulness-Based Cognitive Therapy for Treatment-Resistant Depression: A Clinical Case Study

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### Abstract

Major depressive disorder (MDD) is currently ranked the third leading cause of disability in the world. Treatment-Resistant Depression (TRD) causes the majority of MDD's disability. Strikingly, 50% of individuals with MDD will fail to remit with two adequate trials of antidepressant medications, thus qualifying as treatment resistant. Current pharmacological and psychotherapeutic treatment strategies for TRD are limited in effectiveness so new interventions are needed. Mindfulness-Based Cognitive Therapy (MBCT) is a new psychotherapeutic treatment with established efficacy in preventing relapse of depression for individuals in complete remission. MBCT is a group-based, 8-week intervention that uses mindfulness meditation as its core therapeutic technique. It teaches people to have a different relationship to depressive thoughts and feelings. Strategies are focused on decreasing rumination, enhancing self-compassion, increasing acceptance and decreasing avoidance. This modified version of MCBT, which includes the use of metaphor and adaptations of the original intervention will be discussed through the clinical case of a woman with long-standing TRD. A brief review of the current MBCT literature and future directions for the treatment of TRD are discussed.

### Keywords

Mindfulness-Based Cognitive Therapy; Treatment-Resistant Depression; psychotherapy

### Introduction: Medication Management of Treatment Resistant Depression

Treatment-Resistant Depression (TRD) is a major public health problem and source of suffering. Persistent depression is the number one cause of disability in North America and is the third leading cause of disability worldwide (WHO, 2001). TRD is defined most commonly as failure to fully remit from depressive symptoms after two or more antidepressant medication trials (Khan, Dager, Cohen, Avery, Scherzo, & Dunner, 1991; Trivedi, Rush, Crismon, Kashner, Toprac, Carmody, Key, Biggs, Shores-Wilson, Witte, Suppes, Miller, Altshuler, & Shon, 2004). Medication combinations or switches as outlined in the STAR\*D trial, are the most commonly utilized TRD treatment strategies, but these have limited effectiveness (Rush, Trivedi, Wisniewski, Nierenberg, Stewart, Warden, Niederehe, Thase, Lavori, Lebowitz, McGrath, Rosenbaum, Sackeim, Kupfer, Luther, & Fava, 2006; Trivedi, Fava, Wisniewski, Thase, Quitkin, Warden, Ritz, Nierenberg, Lebowitz, Biggs, Luther, Shores-Wilson, & Rush, 2006). These studies indicate that 50% of patients do not fully remit after two medication trials leaving TRD as a major public health problem.

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From a psychosocial perspective, individuals with TRD tend to have certain responses that make them vulnerable to persistent depression. TRD individuals typically have more negative affect and dysfunctional cognitions than in nonresistant cases. (Beck, Rush, Shaw, & Emery, 1979; Fava, 2002). In TRD, the individual accepts the depression as part of his or her self-concept, becoming demoralized and hopeless (Moore, 2003; Wright, 2006). These individuals are often ruminative with brooding, self-critical thoughts that form an ongoing stream of consciousness (Moore, 2003). They selectively attend to the ruminations with diminished cognitive flexibility and active problem solving (Wright, 2003). The failure to respond to supposedly effective medication trials leads to a belief that the depression is part of their personality and they feel hopeless (Thase, Friedman, & Howland, 2001). This leads to reinforcement of negative beliefs about the self, the world, and the future. These beliefs in turn, lead to avoidance behaviors as the individual tries to prevent further activation of these beliefs (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996; Zettle, 2007). Avoidance behaviors diminish the chance of positive events that could counter negative beliefs and anhedonia.

Failure to respond to treatment can be due to a number of factors including incorrect diagnosis and inadequate dose or duration of therapeutic trials as potential factors relating to inadequate response. Moreover, many patients do not take antidepressant medication as prescribed (Lin, Von Korff, Katon, Bush, Simon, Walker, & Robinson, 1995), often citing issues of stigma, expense, lack of efficacy, and unpleasant side effects, including sedation, weight gain, or sexual dysfunction (Barbee, Conrad, & Jamhour, 2004; Blier & Szabo, 2005; Papakostas, 2005; Quitkin, 1999). These factors could be considered to represent pseudoresistance. In a recent multicenter European study that took the foregoing factors into account, Souery et al. (2007) (Souery, Oswald, Massat, Bailer, Bollen, Demyttenaere, Kasper, Lecrubier, Montgomery, Serretti, Zohar, & Mendlewicz, 2007) noted a number of clinical factors associated with treatment resistance including comorbid anxiety or personality disorder, suicidal risk, severity, melancholia, multiple hospitalizations, recurrent episodes, early age of initial illness onset, and nonresponse to the first lifetime antidepressant.

Although no study has identified genetic markers of TRD, it is likely that continuing work in that field may lead to the discovery of gene polymorphisms which will be predictive of nonresponse in the future (Nugent, Neumeister, Goldman, Herscovitch, Charney, & Drevets, 2008; Reiss, 2008; Wijeratne & Sachdev, 2008). Other biological markers such as specific TRD-associated changes in brain circuitry are currently being explored. For example, Mayberg and colleagues, have successfully performed deep brain stimulation in Brodmann's Area 25 of the subgenual cingulate gyrus to modulate severely refractory depression in individuals (Mayberg, Lozano, Voon, McNeely, Seminowicz, Hamani, Schwalb, & Kennedy, 2005). Hyperactivity in Brodmann's Area 25 has been associated with poor response to both antidepressants and CBT (Konarski, Kennedy, Segal, Lau, Bieling, McIntyre, & Mayberg, 2009). Converging studies suggest that relative hyperactivity in the ventral anterior cingulate cortex may be at least a marker and possibly a mediator of treatment-resistance.

There are currently no rigorous studies supporting psychotherapy as monotherapy for TRD. Cognitive Behavior Therapy (CBT) has been suggested as an augmentation to antidepressant medication for depression but a recent review of randomized clinical trials found only mixed evidence for the combination treatment (McPherson, Cairns, Carlyle, Shapiro, Richardson, & Taylor, 2005). In that review, two RCTs supported CBT's efficacy while two failed to find an effect. There is an urgent substantial need for increased research and development of innovative treatments for these complex and difficult patients.

MBCT may be well positioned to help fill this need. National self-report surveys have found Complimentary and Alternative Medicine techniques being used by 41% to 54% of people with depression, indicating substantial demand (Eisenberg DM, 1998; Kessler RC, 2001). The public is very interested in mindfulness meditation techniques as they are empowering and teach skills individuals can use on their own to control depression and other health problems (Barnes, Powell-Griner, McFann, & Nahin, 2004). Finally, MBCT is cost-effective and relatively easy to deliver to a large number of individuals at once (8 weekly 2.5 hours groups for 8 to 12 patients, delivered by 2 co-therapists). Mindfulness training can continue once formal treatment has ended through CDs and manuals patients receive during the training and treatment gains can also be facilitated with ongoing practice, alumni groups, and community practice settings.

## MBCT Studies in Relapse Prevention and Active Depression

MBCT is a recently developed group treatment integrating mindfulness meditation training with cognitive behavior therapy (CBT) and was specifically developed as a relapse prevention intervention for individuals with histories of recurrent Major Depressive Disorder (MDD) (Segal, Williams, & Teasdale, 2002). MBCT consists of 8 structured, skills-based, weekly classes that teach formal (e.g. body scan and sitting meditations) meditations mixed with informal mindfulness practices (e.g. mindfulness of everyday activities). In addition to the weekly classes, participants, do home-based practices the other six days between classes. MBCT also includes educational content about depressive illness and cognitive patterns. MBCT is designed to teach patients how to relate differently to their thoughts, feelings, and bodily sensations, (e.g., relating to thoughts and feelings as passing events in the mind, rather than identifying with them or treating them as necessarily accurate reflections of reality). In contrast with CBT's focus on changing thought content, MBCT teaches skills that allow patients to "decenter" from habitual "automatic" cognitive routines, offering a novel way for patients to disengage from automatic dysfunctional cognitive patterns (Segal, Williams, & Teasdale, 2002). This is particularly salient for people struggling with TRD as it targets depression-related thought patterns, to reduce future risk of relapse and recurrence (Teasdale, Moore, Hayhurst, Pope, Williams, & Segal, 2002).

In the original studies of MBCT, it was compared to Treatment As Usual (TAU) for individuals in remission. MBCT significantly improved relapse prevention for those who had three or more prior depressive episodes (Ma & Teasdale, 2004; Teasdale, Segal, Williams, Ridgeway, Soulsby, & Lau, 2000). The first two trials of MBCT with depressed individuals in remission, found relapse rates decreased by 42% (Teasdale, Segal, Williams, Ridgeway, Soulsby, & Lau, 2000) and 54% (Ma & Teasdale, 2004) compared to TAU at one-year follow-up. Three subsequent studies have investigated MBCT in patients with current depression. In an open trial of 11 patients with active symptoms of depression (Finucane & Mercer, 2006), Beck Depression Inventory (BDI) scores decreased from 35.7 to 17.8 after completing MBCT and Beck Anxiety Inventory (BAI) scores decreased as well. The effect size was 1.50 for depression and 0.77 for anxiety.

In another open study, Kenny and Williams studied 50 individuals with TRD with BDI scores of >10 who were allowed antidepressant changes during the course of the intervention (Kenny & Williams, 2007). They found that 43% of patients remitted with BDI mean scores decreasing from 24.3 to 13.9, with an effect size of 1.04 that did not significantly change when individuals with medication changes were excluded. Severity of initial depressive symptoms did not interfere with improvement, and suicidal patients showed no difference in their responsiveness to MBCT. MBCT therefore appeared to be a safe and effective treatment option for individuals with TRD even in the setting of suicidal ideation or severe depression. In another uncontrolled pilot study (Eisendrath, Delucchi,

Bitner, Fenimore, Smit, & McLane, 2008) of 51 depressed patients who had failed to fully recover with at least two antidepressant treatments, significant decreases in depression and anxiety were detected following an MBCT intervention. Thirty three percent of patients went into remission, and 45.1% reduced their BDI scores by 50% or more with effect sizes similar to Kenny and Williams.

The last three studies were limited by not having a control group or randomization so the effects on depressive symptoms could not be specifically attributed to MBCT. Kingston and colleagues, however, reported a controlled trial of MBCT augmentation to TAU compared with TAU alone in 19 psychiatric outpatients, and found significant decreases in both depression (effect size 1.07) and rumination scores (effect size 1.16) with MBCT (Kingston, Dooley, Bates, Lawlor, & Malone, 2007). In a randomized controlled study of MBCT, Williams and colleagues found significant reductions of interepisode depression after MBCT treatment compared to waitlist in 20 individuals with a history of unipolar depression and suicidal ideation or behavior (Williams, Alatiq, Crane, Barnhofer, Fennell, Duggan, Hepburn, & Goodwin, 2007).

### Why Applying MBCT to TRD Makes Sense

In addition to MBCT's efficacy in reducing depressive relapse and preliminary support for its treatment effects on current depression, there are theoretical considerations suggesting its utility in a TRD population more specifically. The development of MBCT was explicitly informed by a cognitive analysis of relapse vulnerability (Segal, Williams, Teasdale, & Gemar, 1996; Teasdale, Segal, & Williams, 1995), allowing for specific predictions to be made about the nature of cognitive change produced by MBCT and the association of this change with prevention of relapse. These studies have shown that for recovered depressed patients, mild dysphoria activates thinking patterns similar to those previously present in a depressive episode, whereas never depressed control subjects do not change their thinking style when tested in either euthymic or dysphoric mood (Segal, Kennedy, Gemar, Hood, Pedersen, & Buis, 2006). In remitted patients, these reactivated patterns of thinking can maintain and intensify the dysphoric state through escalating and self-perpetuating cycles of ruminative cognitive-affective processing (Teasdale, 1993).

The same cognitive processes known to make individuals prone to depression relapse are also likely active in perpetuating depression once it is established (Kenny & Williams, 2007) and appear to be some of the primary drivers of TRD, thus making MBCT a useful treatment choice for this disorder. Given its original design to prevent depression relapse in remitted patients, we have modified the original MBCT protocol to address an actively depressed, treatment-resistant population. We describe our modifications to the existing manual through a case illustration later in this paper.

MBCT emphasizes changing the relationship one has to his or her thoughts, rather than trying to explicitly target changing thought content (Segal, Williams, & Teasdale, 2002; Teasdale, Segal, & Williams, 1995; Teasdale, Segal, Williams, Ridgeway, Soulsby, & Lau, 2000). When a depressed individual thinks, "I am a bad and defective person," a CBT therapist might challenge the validity of that statement, and then help the patient to develop alternative or more balanced thoughts. In contrast, a MBCT therapist teaches patients to recognize "I am having the thought that I'm a bad and defective person", realize the thought is not necessarily a fact, and then let go of the thought. This type of "decentering," helps reduce personal identification with depressive ideas and feelings, giving the individual a wider range of possible viewpoints about his or herself (Frewen, 2008). This also allows individuals to see that their thoughts are not facts that have to be accepted as true (Segal, Williams, & Teasdale, 2002). For many depressed individuals, decentering from automatic

thoughts may be associated with a significant reduction in depressive symptoms and an increase in emotional regulation and tolerance of dysphoric states (Fresco, Segal, Buis, & Kennedy, 2007). MBCT includes four putative mediators that could positively impact TRD: mindfulness, decreased rumination, enhanced self-compassion, and increased acceptance with decreased avoidance.

Mindfulness, the core component of MBCT, has been associated with enhanced emotional regulation (Arch & Craske, 2006; Linehan, 1993). It can be defined as bringing non-evaluative awareness to one's inner and outer environment and then focusing attention on a limited range of experience (Brown, 2003). The practice of mindfulness teaches individuals to shift from going through life in "automatic pilot" mode and may allow depressed individuals relief from the continual and unintentional activation of harmful cognitive processes or "downward spirals".

In depression, rumination is usually regarded as the experience of repetitive, intrusive, negative cognitions focused on depressive symptoms and their causes, meanings, and consequences (Brosschot, Gerin, & Thayer, 2006) (Treyner, 2003). Rumination, may be an important driver of depression (Nolen-Hoeksema, 2000). Individuals with TRD tend to think such ruminations would help them escape from their dysphoric state but this response style actually appears to further deepen it. Self-perpetuating cycles may then escalate mild and transient mood disturbances into more severe and disabling depressed states (Segal, Kennedy, Gemar, Hood, Pedersen, & Buis, 2006). Several studies have noted decreased rumination as an important potential mediator of antidepressant effects (Kingston, Dooley, Bates, Lawlor, & Malone, 2007; Watkins, Scott, Wingrove, Rimes, Bathurst, Steiner, Kennell-Webb, Moulds, & Malliaris, 2007). Mindfulness meditation has been found to reduce levels of rumination in depressed patients even for those who have been previously treated with CBT (Broderick, 2005; Ramel, 2004) This suggests that mindfulness meditation can provide additional benefit above and beyond CBT.

MBCT also targets enhanced self-compassion which may be an important buffer for negative self-feelings (Leary, Tate, Adams, Allen, & Hancock, 2007). In a recent study by Kuyken et al., (Kuyken, Byford, Taylor, Watkins, Holden, White, Barrett, Byng, Evans, Mullan, & Teasdale, 2008) the researchers found that MBCT was equally effective as maintenance antidepressants in preventing relapse over a one year period in remitted patients. In a secondary analysis, self-compassion was a key mediator of MBCT's ameliorative effects on preventing depressive relapse (Kuyken, 2009). Because individuals with TRD typically have heightened self-criticisms, enhancing self-compassion may be a particularly useful attribute of MBCT in this population.

The emphasis on observation and monitoring skills in mindfulness training can increase a patient's willingness to tolerate the range of internal experiences, even negative ones (Linehan, 1993). Mindfulness practice may function as an exposure procedure in which nonjudgmental awareness of aversive depressive thoughts and feelings leads to diminished reactivity and decreased avoidance (Baer, 2003), leading in turn to decreased negative affect (Allen, Chambers, & Knight, 2006). Enhancing acceptance of depression and decreasing avoidance of unpleasant affect can help reduce overall emotional distress (Hayes, Luoma, Bond, Masuda, & Lillis, 2006). This is taught as a skill in MBCT to help individuals to engage more fully with their lives and experience increase positive reinforcement of new behaviors. This skill is critical for individuals with TRD who have often withdrawn significantly from most, if not all, life areas that could generate positive reinforcements.

## Case illustration: Jean

Jean was a 49 year-old woman referred for long-standing TRD. She described herself as having been depressed almost continuously since childhood, although with careful questioning, she was able to delineate four episodes over her lifespan with each lasting for a longer period of time than previous ones despite antidepressants and psychotherapy. Although her current episode could be related to some recent life stressors, several earlier episodes had no identifiable stressor, and seemed to start “out of the blue”.

Her current episode began one year earlier. Jean began seeing a psychiatrist at that time when her depression returned. In the past, she had tried a variety of medications and psychotherapies, including several years of psychoanalysis. In this current episode, Jean tried venlafaxine with somewhat positive results but gained forty pounds. She then changed to bupropion but did not find it helpful for her mood. Her psychiatrist also tried sertraline, as well as augmenting her antidepressants with lithium, but these steps were not effective. In addition to depressive symptoms, she also felt anxious and had difficulty sleeping with both early awakening and difficulty falling asleep, often napping for short periods during the day but never feeling well rested. She tried various sleep medications that were not very effective. Her psychiatrist suggested other medications, but Jean was not encouraged by the idea. She was referred for MBCT following the multiple failures of antidepressant medications trials.

Despite a number of successes in her professional career, Jean believed that she had been a failure in life. She had a difficult time concentrating and focusing on her work, and was unable to enjoy activities that she previously derived pleasure from, finding that completing work duties took all of her energy. She became increasingly socially isolated, withdrawing from her husband and children, and complained of depressed mood, significant insomnia, decreased appetite and libido, fatigue, anxiety in social and performance situations, and a lack of energy. She denied active suicidal thinking but hoped she would develop a fatal illness that would end her life, or that she would somehow just disappear. She had no previous suicide attempts and had never required psychiatric hospitalization.

Jean also endorsed several symptoms suggesting residual posttraumatic stress disorder related to childhood sexual abuse. She had a history of sexual trauma by a relative beginning at age 5 and ending around age 10, occasionally experiencing flashbacks and nightmares as well as periods of extreme anxiety and intrusive images. She had discussed this abuse in some of her prior psychotherapies but had not found that helpful.

Jean believed that some of her recent depressive symptoms could be accounted for by current stressors in her life, including difficulties with both her adult children. Her son was experiencing stress during his transition from college graduation to finding work, and her daughter was due to get married a few weeks from when Jean started treatment. Worries about the upcoming wedding weighed considerably on her mind. Jean was also experiencing difficulties at work where she felt betrayed by her boss in a recent planning meeting. She described herself as being passive and accepting things until they reached a critical point. She had recently contemplated going on disability due to her depression and was feeling hopeless and doubtful that any treatment could help her at this point.

## Modifications to MBCT for Jean

The MBCT intervention used to treat Jean followed the manual developed by Segal et al. (Segal, Williams, & Teasdale, 2002) with specific modifications for TRD, which aimed to promote enhanced emotional regulation through increasing nonjudgmental awareness of emotional experience in the present moment and to build skills in decentering from thoughts

and feelings, enhancing acceptance, and decreasing experiential avoidance. Modifications to the MBCT manual were necessary because the original version was designed for individuals in remission with a focus on relapse prevention. Our population consisted of actively depressed individuals, thus the following adaptations focus on current depressive symptoms specifically. For example, phrases like “when you become depressed”, were replaced with: “notice what the experience of depression is like for you right now”. In addition, we added several exercises and metaphors commonly used in Acceptance and Commitment Therapy (Luoma, 2007; Zettle, 2007) to help patients relate mindfully to their current experience.

In the first group, psychoeducation about the natural course of depression and relapse prevention in the context of acceptance was discussed. Data from published studies, including graphs and illustrations of depression as a chronic disease with relapses over the lifespan were presented (Greden, 2001) This information helped to diminish guilt about persistent symptoms and recurrent exacerbations while at the same time highlighting the importance of developing effective treatment and prevention strategies.

Also in the first group, the Chinese woven finger trap (Hayes, 1999) exercise was introduced. Participants quickly learn that trying to pull one’s fingers out of the woven trap, only produces a snigger ensnarement. The counterintuitive solution is to stop trying to pull one’s fingers out and gently move them closer together first. Getting “in close” is also a way of reducing the struggle against depression. This exercise was used as a metaphor for how acceptance and relinquishing the struggle to escape may set the path for recovery. Acceptance (e.g. stop attempting to try pull out of the trap) was contrasted with resignation. It involves seeing things as they are so an action can be skillfully chosen, not as a result of the impulse to override, or struggle to get out of the trap, in this case depression. Jean began to understand that trying to escape her depression might not be the only approach she had to take in response to it and that in fact, that tactic might be counterproductive.

In the second group session, Jean was presented with the following equation:  $SUFFERING = RESISTANCE \times PAIN$  (e.g. physical pain or emotional pain like depression) (Young, 2004). Several examples were used to illustrate this equation. If an individual has difficulty falling asleep and tries to resist that difficulty by forcing themselves to get to sleep, he or she is rarely successful. On the other hand, accepting that one is not going to get much sleep on a particular night (i.e. lowering the psychological resistance to not being able to fall asleep) may counter-intuitively allow a person to fall asleep more rapidly, or at the very least can help reduce the additional suffering that is the natural byproduct of resisting the present moment experience.

Applying this concept to depression, the MBCT group discussion elaborated that trying to avoid feeling depressed actually may contribute to the suffering of depression. Avoidance attempts may feel like they help in the short term, but not only do they fail to fix the problem long-term, they can actually make depression worse (Zettle, 2007; Zettle, 2002). Through attempts to avoid her depression, Jean buried herself in work and began to isolate herself socially, even from her family. Through MBCT exercises aimed at describing pleasant experiences, she realized she had cut herself off from things that had added pleasure to her life and began to reverse this.

Through observation of body sensations and thoughts associated with depression, Jean became more aware and mindful of both the positive and negative experiences linked to her depression. For example, noticing when she began to feel more depressed, helped Jean to activate an inventory of how she had been handling some of the interpersonal interactions in her life; this in turn put her in a position to alter those situations she felt dissatisfied with rather than being unaware of what had influenced her moods.

In the third MBCT group, a metaphor was introduced that many TRD patients have found very helpful. Winston Churchill talked about his depressive states as the “black dog” (Johnstone, 2006), and a depressed day as one in which “the black dog has returned”. This metaphor was presented in the context of an individual’s reaction to depression. There are a range of possible reactions to a large black dog, from terror to curiosity. The discussion of this metaphor invites patients to conceptualize their depression as something that they can react to in a number of different ways. This was particularly salient for Jean who began to shift her relationship to her depression, entertaining the idea that like a big black dog, depressive symptoms could be a signal about something in her life and not just a terrifying entity. In her case, Jean realized the black dog could be a signal that something was not working in her life and saw the relevancy to her relationship with her supervisor at work. She even had moments of seeing her depression not just as the enemy, but as something she could live with, and not just cower in the face of or live in fear of it returning.

Another modification made to MBCT was an exercise aimed at underscoring the mindfulness concepts of acceptance by talking about it in terms of *allowing* or *letting it be*. Jean was asked to write down something she believed had to change before she could move on with her life. She chose to change her depression. She believed that she could never lead a fulfilling life or really enjoy her life if she didn’t first get rid of her depression. Jean wrote this down on a card and put it in her pocket while the ‘donkey standoff’ metaphor was presented (Luoma, 2007). The harder one pulls on a donkey by the lead rope, the more it resists. The way to get a donkey to move is to actually move along side it and look in the direction you want to go. When this was applied to Jean’s depression, she began to see, in an experiential way, that having a full and meaningful life is not about getting rid of her depression, but rather coming alongside of it and moving with it rather than resisting and fighting it. In that way, she began to see that she could actually live her life and have depression at the same time, instead of putting her life on hold until the depression was resolved. Jean realized that despite her depression she could continue to function in her roles in her family and at work, albeit without her usual efficiency. She began to see that her functioning was not the completely negative view she originally had. She even began to assert herself in interactions with her boss, despite continuing depression, which in turn, diminished her sense of helplessness.

An important effect of MBCT for Jean was to start to see her thoughts as thoughts, and not facts. A standard MBCT exercise that resonated with her was to do a short sitting meditation focused on the breath, in which she could start to see her thoughts as they were occurring. In a modification done in the group, Jean was instructed to ask herself, “What is Jean thinking?” every few minutes. Part of what she realized through this exercise was that she could actually observe her thoughts, getting to the place where she was *having* thoughts rather than *being* what they were telling her.

Another modification was introduced towards the end of Jean’s group treatment aimed at helping her change her relationship to depression. In a group activity, self-care was discussed through the “Frankenstein exercise” which was originally observed in a mindfulness-based stress reduction class. The exercise was previewed prior to the exercise with a comment that the exercise might raise a variety of feelings that we would be discussing immediately after. In the group, Jean was paired with another group member. She took on the role of ‘victim’ and her partner assumed the role of ‘monster’. Then they reversed roles. The ‘Frankenstein monster’, as many group members spontaneously voiced could represent depression coming towards them in a threatening way. As the ‘victim’, Jean had several options. She could freeze and cower in front of the attack, she could try to sidestep it, or she could approach the monster, hold its arm and lead it in the direction she wanted to go. Each of these possibilities was acted out by the pairs of “monsters” and



“victims”. These enactments were discussed as metaphors for alternative ways to approach a difficult situation or experience and highlighted the way a mindful stance doesn't change the monster, but can make it less overwhelming and scary. The mindful, assertive response (holding the arm and leading it) allowed Jean to start to take back control of her life without necessarily needing to change or fight the depression in order for some sense of control to return. Jean then began to see that she could start trying to do more of the previously enjoyable things in her life that she had avoided despite remaining depressed. She did not have to wait for the depression to vanish before she could resume her life. This was particularly evident in her becoming increasingly more active in physical activities with her family.

The last modification to MBCT that was helpful to Jean was a discussion of expectations, and their relationship to depression and self esteem. Helping individuals with active depression set expectations at realistic levels is often critical to maintaining self-esteem. These individuals often set unrealistically high expectations and then feel critical of themselves for not achieving them. We used the following equation as a simple way of viewing the relationship between self esteem, achievement, and expectations:

$$\text{Self Esteem} = \frac{\text{Achievements}}{\text{Expectations}}$$

Adjusting expectation levels to realistic levels is much more rapidly accomplished than by increasing achievement levels. In depression, expectations are often set so high, that no matter what is achieved, an individual does not feel good. Helping Jean understand reasonable expectations for herself (a marriage, children, and a successful career) helped her begin to feel better about herself. Accepting the expectation that she might have future episodes of depression did not mean she would have to dampen her view of herself as a competent and adequate person.

## Summary Reflections

The onset of Jean's depressive episodes appeared relatively autonomous to her, which is common with recurrent depression, (Segal, Williams, & Teasdale, 2002). Her sense of hopelessness may also have rendered her less responsive to engagement in the routine clinical management of her depression. In the current episode, Jean expressed the belief that she did not expect anything would make her feel better, a belief which interfered with her treatment engagement. In addition, negative cognitions reinforced Jean's pessimistic view of further medication treatments. Her withdrawal from pleasurable activities interfered with potentially positive reinforcers in her life. All of this could have been compounded by the role of biological factors associated with depressive states, although in the clinical setting these were not measured.

Jean's history of childhood trauma may also be highly relevant to her nonresponse to medications. Nemeroff and colleagues (2003) have investigated the role of childhood trauma in affecting an individual's response to treatment for depression (Nemeroff, Heim, Thase, Klein, Rush, Schatzberg, Ninan, McCullough, Weiss, Dunner, Rothbaum, Kornstein, Keitner, & Keller, 2003). They found that individuals with a trauma abuse history typically fail to respond to a unimodal approach of either antidepressants or psychotherapy and usually required combined treatment for an optimal response. This might help explain some of the challenges that individuals like Jean represent in designing effective treatment interventions. This may also be related to both biological and psychological factors. For example, Nemeroff and colleagues have determined that these individuals may have

decreased hippocampal volume that may affect memory storage and retrieval evidently activated by trauma history (Nemeroff, Bremner, Foa, Mayberg, North, & Stein, 2006; Vythilingam, Heim, Newport, Miller, Anderson, Bronen, Brummer, Staib, Vermetten, Charney, Nemeroff, & Bremner, 2002). This may in turn affect their ability to process new information and integrate it in an effective way.

Perhaps equally relevant, Post and colleagues proposed (Post, 2007; Post & Weiss, 2004) that stressors of various types and intensity may produce brain sensitization in a manner similar to behavioral sensitization. Even in cases of only potential stress or loss, if sufficiently conditioned, an affective episode might be activated. This theory would help explain how stress-induced mood changes might become so sensitized that they could occur spontaneously. Under Post's kindling hypothesis, it would take less and less stimuli to produce an affective episode, leaving the individual vulnerable to repeated relapse that would be difficult to treat since successive episodes become more difficult to control than earlier ones. Post's research, including animal amygdala and human epileptic focus models, suggests that once a recurrent episode is induced, there may be an associated loss of medication efficacy during subsequent treatments, leading to TRD. This research underscores the importance of developing early prevention interventions and alternatives to pure medication interventions in TRD.

MBCT in Jean's case had a number of beneficial effects including some that may have been specific to the mindfulness component as discussed earlier, but also some more generic as well. In the group, she had a community of others suffering from depression that she could share her experience with and hear from others. The group offered her hope that she could develop skills that would allow her to better control her moods. She noted that other members of the group appeared "normal" despite their depression, so she reasoned that perhaps she herself may not be "so crazy". As her skills grew, she began to feel some sense of mastery which had its own antidepressant effects. After initially struggling to be able to sustain attention in the early weeks of the course, she began to notice an improvement. In fact, as the weeks progressed, Jean noted significantly improved concentration and ability to attend to her work and cognitive tasks. After completion of MBCT, her BDI score had decreased from 28 to 9 without any change in her medications having occurred.

A potential disadvantage of MBCT is that it requires motivation to attend 8 weeks of class and practice daily homework meditations. Some might reasonably question whether depressed individuals have the necessary motivation and concentration, but as Jean's participation indicated, as well as the previously mentioned open studies demonstrate, patients with TRD can indeed learn and benefit from the skills (Eisendrath, Delucchi, Bitner, Fenimore, Smit, & McLane, 2008; Finucane & Mercer, 2006; Kenny & Williams, 2007). Indeed, because of their depressive symptoms, these individuals may be highly motivated to engage in MBCT. We have also utilized free monthly alumni groups as boosters to our graduates.

## Future Directions

An upcoming, National Center for Complementary and Alternative Medicine/NIH funded, randomized controlled trial will evaluate the efficacy of MBCT as a treatment augmentation intervention to medication management in TRD. It will use an active control condition, the Health-Enhancement Program (HEP), specifically developed to serve as a credible control for mindfulness interventions (MacCoon D, 2007). HEP includes elements of nutrition, music therapy, and physical functioning. HEP will provide a rigorous control condition that a number of prior studies have not included. For example, the two original studies of MBCT for relapse prevention compared it to TAU, so it was not possible to attribute the beneficial

effects specifically to MBCT as compared to nonspecific factors. The HEP condition, which mimics many of the features of mindfulness-based stress reduction, in terms of time, attention, homework, and group support, will allow this study to have a clearer picture of what factors may be responsible for any beneficial effects. Participants will include 124 patients with MDD failing two or more adequate antidepressant trials. Treatment as usual (TAU) with medications will continue and participants will be randomly assigned to two groups: MBCT plus TAU or HEP plus TAU. All patients who enroll in the study will undergo follow-up assessments at 6 and 12 months following the 8-week group intervention. The specific aim of this study is to determine the acute augmentative efficacy of MBCT in reducing depression in adults with TRD, when compared to an active control condition. A series of secondary hypotheses and analyses will evaluate if MBCT plus TAU is more effective than HEP plus TAU in reducing disability and improving quality of life. The role of putative mediators of MBCT efficacy including enhanced mindfulness, decreased rumination, improved self-compassion, and decreased experiential avoidance will also be assessed in the RCT.

If MBCT is efficacious in this study, the next step may be to develop a larger scale effectiveness study in a broader population. In the study underway, patients are only being allowed to participate if they are in medication management in order to prevent confounding conditions, but many patients with TRD may be receiving concurrent psychotherapy and medication management. Future studies in community settings may investigate MBCT's effectiveness in patients with such concurrent treatment as it would be a highly generalizable population.

Since TRD is such a major public health problem, findings from this study will have clear significance. MBCT has the potential to be a cost-effective treatment intervention that can help reduce suffering, disability, and the medical co-morbidity often accompanying this disorder.

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## References

- Allen NB, Chambers R, Knight W. Mindfulness-based psychotherapies: a review of conceptual foundations, empirical evidence and practical considerations. *Aust N Z J Psychiatry*. 2006; 40(4): 285–294. [PubMed: 16620310]
- Arch JJ, Craske MG. Mechanisms of mindfulness: emotion regulation following a focused breathing induction. *Behav Res Ther*. 2006; 44(12):1849–1858. [PubMed: 16460668]
- Baer RA. Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clinical Psychology: Science and Practice*. 2003; 10(2):125–143.
- Barbee JG, Conrad EJ, Jamhour NJ. The effectiveness of olanzapine, risperidone, quetiapine, and ziprasidone as augmentation agents in treatment-resistant major depressive disorder. *J Clin Psychiatry*. 2004; 65(7):975–981. [PubMed: 15291687]
- Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data*. 2004; (343):1–19. [PubMed: 15188733]
- Beck, AT.; Rush, AJ.; Shaw, BF.; Emery, G. *Cognitive Therapy of Depression*. New York: Guilford; 1979.
- Blier P, Szabo ST. Potential mechanisms of action of atypical antipsychotic medications in treatment-resistant depression and anxiety. *J Clin Psychiatry*. 2005; 66 Suppl 8:30–40. [PubMed: 16336034]
- Broderick P. Mindfulness and Coping with Dysphoric Mood: Contrasts with Rumination and Distraction. *Cognitive Therapy and Research*. 2005; 29:501–510.

- Brosschot JF, Gerin W, Thayer JF. The perseverative cognition hypothesis: a review of worry, prolonged stress-related physiological activation, and health. *J Psychosom Res.* 2006; 60(2):113–124. [PubMed: 16439263]
- Brown KWR, Richard M. The benefits of being present: Mindfulness and its role in psychological well-being. *Journal of Personality and Social Psychology.* 2003; 84(4):822–848. [PubMed: 12703651]
- Eisenberg DM, Ettner SL, Appel S, Wilkey S, Van Rompay M, Kessler RC. Trends in alternative medicine use in the United States, 1990–1997: results of a follow-up national survey. *JAMA.* 1998; 280(18):1569–1575. [PubMed: 9820257]
- Eisendrath SJ, Delucchi K, Bitner R, Fenimore P, Smit M, McLane M. Mindfulness-based cognitive therapy for treatment-resistant depression: a pilot study. *Psychother Psychosom.* 2008; 77(5):319–320. [PubMed: 18600038]
- Fava M. Somatic symptoms, depression, and antidepressant treatment. *J Clin Psychiatry.* 2002; 63(4):305–307. [PubMed: 12000203]
- Finucane A, Mercer SW. An exploratory mixed methods study of the acceptability and effectiveness of Mindfulness-Based Cognitive Therapy for patients with active depression and anxiety in primary care. *BMC Psychiatry.* 2006; 6:14. [PubMed: 16603060]
- Fresco DM, Segal ZV, Buis T, Kennedy S. Relationship of posttreatment decentering and cognitive reactivity to relapse in major depression. *J Consult Clin Psychol.* 2007; 75(3):447–455. [PubMed: 17563161]
- Frewen P, Evans EM, Maraj N, Dozois DJA, Partridge K. Letting Go: Mindfulness and Negative Automatic Thinking. *Cognitive Therapy & Research.* 2008; 32:758–774.
- Greden, JF. Treatment of recurrent depression. 1st ed.. Washington, DC: American Psychiatric Pub; 2001.
- Hayes SC, Luoma JB, Bond FW, Masuda A, Lillis J. Acceptance and commitment therapy: model, processes and outcomes. *Behav Res Ther.* 2006; 44(1):1–25. [PubMed: 16300724]
- Hayes, SC.; Strosahl, KD.; Wilson, KG. Acceptance and commitment therapy: An experiential approach to behavior change. New York: Guilford Press; 1999.
- Hayes SC, Wilson KG, Gifford EV, Follette VM, Strosahl K. Experimental avoidance and behavioral disorders: a functional dimensional approach to diagnosis and treatment. *J Consult Clin Psychol.* 1996; 64(6):1152–1168. [PubMed: 8991302]
- Johnstone, M. Living with a Black Dog: His Name Is Depression. Kansas City, Mo: Andrews McMeel Publishing; 2006.
- Kenny MA, Williams JM. Treatment-resistant depressed patients show a good response to Mindfulness-based Cognitive Therapy. *Behav Res Ther.* 2007; 45(3):617–625. [PubMed: 16797486]
- Kessler SJ, Davis RB, Foster DF, Wilkey SA, Van Rompay MIMI, Eisenberg DM. The use of complementary and alternative therapies to treat anxiety and depression in the United States. *Am J Psychiatry.* 2001; 158:289–294. [PubMed: 11156813]
- Khan A, Dager SR, Cohen S, Avery DH, Scherzo B, Dunner DL. Chronicity of depressive episode in relation to antidepressant-placebo response. *Neuropsychopharmacology.* 1991; 4(2):125–130. [PubMed: 2025378]
- Kingston T, Dooley B, Bates A, Lawlor E, Malone K. Mindfulness-based cognitive therapy for residual depressive symptoms. *Psychol Psychother.* 2007; 80(Pt 2):193–203. [PubMed: 17535594]
- Konarski JZ, Kennedy SH, Segal ZV, Lau MA, Bieling PJ, McIntyre RS, et al. Predictors of nonresponse to cognitive behavioural therapy or venlafaxine using glucose metabolism in major depressive disorder. *J Psychiatry Neurosci.* 2009; 34(3):175–180. [PubMed: 19448846]
- Kuyken, W. personal communication. 2009.
- Kuyken W, Byford S, Taylor RS, Watkins E, Holden E, White K, et al. Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol.* 2008; 76(6):966–978. [PubMed: 19045965]
- Leary MR, Tate EB, Adams CE, Allen AB, Hancock J. Self-compassion and reactions to unpleasant self-relevant events: the implications of treating oneself kindly. *J Pers Soc Psychol.* 2007; 92(5):887–904. [PubMed: 17484611]

- Lin EH, Von Korff M, Katon W, Bush T, Simon GE, Walker E, et al. The role of the primary care physician in patients' adherence to antidepressant therapy. *Med Care*. 1995; 33(1):67–74. [PubMed: 7823648]
- Linehan MM. Dialectical behavior therapy for treatment of borderline personality disorder: implications for the treatment of substance abuse. *NIDA Res Monogr*. 1993; 137:201–216. [PubMed: 8289922]
- Luoma, JBH.; SC; Walsler, RD. *Learning ACT--An Acceptance and Commitment Therapy Skills-Training Manual for Therapists*. Oakland, Ca: New Harbinger Publications; 2007.
- Ma SH, Teasdale JD. Mindfulness-based cognitive therapy for depression: replication and exploration of differential relapse prevention effects. *J Consult Clin Psychol*. 2004; 72(1):31–40. [PubMed: 14756612]
- MacCoon, D.; LA; Rosenkranz, M.; Davidson, R. In *Lessons from an Active Control Condition: "McMindfulness, Shams, and the One-Fold Path*. Paper presented at the Mind Life Summer Research Institute; Garrison, New York. 2007.
- Mayberg HS, Lozano AM, Voon V, McNeely HE, Seminowicz D, Hamani C, et al. Deep brain stimulation for treatment-resistant depression. *Neuron*. 2005; 45(5):651–660. [PubMed: 15748841]
- McPherson S, Cairns P, Carlyle J, Shapiro DA, Richardson P, Taylor D. The effectiveness of psychological treatments for treatment-resistant depression: a systematic review. *Acta Psychiatr Scand*. 2005; 111(5):331–340. [PubMed: 15819726]
- Moore, RG.; Garland, A. *Cognitive Therapy for Chronic and Persistent Depression*. Chichester: John Wiley and Sons; 2003.
- Nemeroff CB, Bremner JD, Foa EB, Mayberg HS, North CS, Stein MB. Posttraumatic stress disorder: a state-of-the-science review. *J Psychiatr Res*. 2006; 40(1):1–21. [PubMed: 16242154]
- Nemeroff CB, Heim CM, Thase ME, Klein DN, Rush AJ, Schatzberg AF, et al. Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma. *Proc Natl Acad Sci U S A*. 2003; 100(24):14293–14296. [PubMed: 14615578]
- Nolen-Hoeksema S. The role of rumination in depressive disorders and mixed anxiety/depressive symptoms. *J Abnorm Psychol*. 2000; 109(3):504–511. [PubMed: 11016119]
- Nugent AC, Neumeister A, Goldman D, Herscovitch P, Charney DS, Drevets WC. Serotonin transporter genotype and depressive phenotype determination by discriminant analysis of glucose metabolism under acute tryptophan depletion. *Neuroimage*. 2008; 43(4):764–774. [PubMed: 18718871]
- Papakostas GI. Augmentation of standard antidepressants with atypical antipsychotic agents for treatment-resistant major depressive disorder. *Essent Psychopharmacol*. 2005; 6(4):209–220. [PubMed: 16041917]
- Post RM. Kindling and sensitization as models for affective episode recurrence, cyclicality, and tolerance phenomena. *Neurosci Biobehav Rev*. 2007; 31(6):858–873. [PubMed: 17555817]
- Post RM, Weiss SR. Convergences in course of illness and treatments of the epilepsies and recurrent affective disorders. *Clin EEG Neurosci*. 2004; 35(1):14–24. [PubMed: 15112460]
- Quitkin FM. Placebos, drug effects, and study design: a clinician's guide. *Am J Psychiatry*. 1999; 156(6):829–836. [PubMed: 10360119]
- Ramel W, Goldin PR, Carmona P, McQuaid JR. The Effects of Mindfulness Meditation on Cognitive Processes and Affect in Patients with Past Depression. *Cognitive Therapy and Research*. 2004; 28(4):433–455.
- Reiss D. Transmission and treatment of depression. *Am J Psychiatry*. 2008; 165(9):1083–1085. [PubMed: 18765485]
- Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR\*D report. *Am J Psychiatry*. 2006; 163(11):1905–1917. [PubMed: 17074942]
- Segal, Z.; Williams, JM.; Teasdale, J. *Mindfulness -based cognitive therapy for depression*. New York: The Guilford press; 2002.

- Segal ZV, Kennedy S, Gemar M, Hood K, Pedersen R, Buis T. Cognitive reactivity to sad mood provocation and the prediction of depressive relapse. *Arch Gen Psychiatry*. 2006; 63(7):749–755. [PubMed: 16818864]
- Segal ZV, Williams JM, Teasdale JD, Gemar M. A cognitive science perspective on kindling and episode sensitization in recurrent affective disorder. *Psychol Med*. 1996; 26(2):371–380. [PubMed: 8685293]
- Souery D, Oswald P, Massat I, Bailer U, Bollen J, Demyttenaere K, et al. Clinical factors associated with treatment resistance in major depressive disorder: results from a European multicenter study. *J Clin Psychiatry*. 2007; 68(7):1062–1070. [PubMed: 17685743]
- Teasdale, J.; Barnard, P. *Essays in cognitive psychology*. Hillsdale, NJ, England: Lawrence Erlbaum Associates, Inc.; 1993. *Affect, Cognition and Change: Re-modelling Depressive Thought*; p. 285
- Teasdale JD, Moore RG, Hayhurst H, Pope M, Williams S, Segal ZV. Metacognitive awareness and prevention of relapse in depression: empirical evidence. *J Consult Clin Psychol*. 2002; 70(2):275–287. [PubMed: 11952186]
- Teasdale JD, Segal Z, Williams JM. How does cognitive therapy prevent depressive relapse and why should attentional control (mindfulness) training help? *Behav Res Ther*. 1995; 33(1):25–39. [PubMed: 7872934]
- Teasdale JD, Segal ZV, Williams JM, Ridgeway VA, Soulsby JM, Lau MA. Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *J Consult Clin Psychol*. 2000; 68(4):615–623. [PubMed: 10965637]
- Thase ME, Friedman ES, Howland RH. Management of treatment-resistant depression: psychotherapeutic perspectives. *J Clin Psychiatry*. 2001; 62 Suppl 18:18–24.
- Treynor W, Gonzalez R, Nolen-Hoeksema S. Rumination Reconsidered: A Psychometric Analysis. *Cognitive Therapy and Research*. 2003; 27:247–259.
- Trivedi MH, Fava M, Wisniewski SR, Thase ME, Quitkin F, Warden D, et al. Medication augmentation after the failure of SSRIs for depression. *N Engl J Med*. 2006; 354(12):1243–1252. [PubMed: 16554526]
- Trivedi MH, Rush AJ, Crismon ML, Kashner TM, Toprac MG, Carmody TJ, et al. Clinical results for patients with major depressive disorder in the Texas Medication Algorithm Project. *Arch Gen Psychiatry*. 2004; 61(7):669–680. [PubMed: 15237079]
- Vythilingam M, Heim C, Newport J, Miller AH, Anderson E, Bronen R, et al. Childhood trauma associated with smaller hippocampal volume in women with major depression. *Am J Psychiatry*. 2002; 159(12):2072–2080. [PubMed: 12450959]
- Watkins E, Scott J, Wingrove J, Rimes K, Bathurst N, Steiner H, et al. Rumination-focused cognitive behaviour therapy for residual depression: a case series. *Behav Res Ther*. 2007; 45(9):2144–2154. [PubMed: 17367751]
- WHO. WHO Report 2001: Mental Health. New Hope: New Understanding; 2001. Chapter 2: Burden of Mental and Behavioral Disorders.
- Wijeratne C, Sachdev P. Treatment-resistant depression: critique of current approaches. *Aust N Z J Psychiatry*. 2008; 42(9):751–762. [PubMed: 18696279]
- Williams JM, Alatiq Y, Crane C, Barnhofer T, Fennell MJ, Duggan DS, et al. Mindfulness-based Cognitive Therapy (MBCT) in bipolar disorder: Preliminary evaluation of immediate effects on between-episode functioning. *J Affect Disord*. 2007
- Wright J. Cognitive-behavior therapy for chronic depression. *Psychiatric Annals*. 2003; 33:777–784.
- Wright, J.; Basco, MR.; Thase, ME. *Learning Cognitive -Behavior Therapy: An Illustrated Guide*. Washington, DC: American Psychiatric Publishing, Inc; 2006.
- Young, S. *Break Through Pain: A Step-by-Step Mindfulness Meditation Program for Transforming Chronic and Acute Pain*. Boulder, CO: Sounds True, Inc; 2004.
- Zettle, RD. *ACT for Depression*. Oakland: New Harbinger; 2007.
- Zettle, RDH.; SC. Brief ACT treatment of depression. In: Bond, W., editor. *Handbook of brief cognitive behaviour therapy*. Chichester, England: Wiley; 2002. p. 35-54.