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Mindfulness-Based Treatments for Co-Occurring Depression and Substance Use Disorders: What Can We Learn from the Brain?

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Abstract

Both depression and substance use disorders represent major global public health concerns and are often co-occurring. Although there are ongoing discoveries regarding the pathophysiology and treatment of each condition, common mechanisms and effective treatments for co-occurring depression and substance abuse remain elusive. Mindfulness training has recently been shown to benefit both depression and substance use disorders, suggesting that this approach may target common behavioral and neurobiological processes. However, it remains unclear whether these pathways constitute specific shared neurobiological mechanisms or more extensive components universal to the broader human experience of psychological distress or suffering. We offer a theoretical, clinical and neurobiological perspective of the overlaps between these disorders, highlight common neural pathways that play a role in depression and substance use disorders, and discuss how these commonalities may frame our conceptualization and treatment of co-occurring disorders. Finally, we discuss how advances in our understanding of potential mechanisms of mindfulness training may offer not only unique effects on depression and substance use, but also offer promise for treatment of co-occurring disorders.

Keywords

Mindfulness; Addiction; Depression; Substance Use Treatment; Functional Magnetic Resonance Imaging (fMRI); co-occurring disorders; dual diagnosis

Mindfulness training (MT) may target common underlying mechanisms of major depressive disorder (MDD) and substance use disorders (SUDs), providing an effective treatment for co-occurrence of these maladies where few currently exist. We will use “co-occurring disorder” and “dual diagnosis” to refer to the co-occurrence of MDD and an SUD in which “diagnoses of these disorders must occur simultaneously or within a one year time frame of each other” (1). As first-line treatment for substance-induced mood disorders is to treat the underlying SUD (2), substance-induced mood disorders will not be included in this discussion. Additionally, although co-occurring psychotic and anxiety disorders are common

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and warrant discussion, the majority of the current discussion will be limited to co-occurring MDD and SUDs.

(I.) MDD and SUDs: significant and growing problems

Both MDD and SUDs are major public health problems. Overall, unipolar depressive disorders were the fourth leading cause of disease burden in 2002, and are projected to be the second leading cause by 2030 (3). Further, MDD and SUDs have been found to co-occur frequently: about one third of individuals with MDD also have symptoms consistent with an SUD (4), and lifetime prevalence of a co-occurring SUD ranges from 30% to 42.8% (3,5). From 1992 to 2002, the rates of past-year major depressive episodes among people with a concurrent SUD increased from 10 to 15% (6). These data highlight the large and growing burden of co-morbid MDD and SUDs.

There are currently multiple empirically supported behavioral treatments for both MDD and SUDs as individual disorders. Well-supported behavioral treatments for depression include cognitive behavioral therapy (CBT), behavioral-activation therapy, mindfulness-based cognitive therapy and exercise (7). Similarly, substance abuse treatments include CBT, relapse prevention, motivational interviewing (MI), contingency management (CM), and 12-Step programs (8–10). Despite significant research on treating these disorders individually, few treatments have been evaluated for individuals with co-occurring MDD and SUDs (11). MI has demonstrated efficacy for many types of substance abuse, though few studies have been conducted with dual diagnosis patients (12,13). CBT has been modified for people with SUDs and depression and has shown moderate effects therein (14). CM has more recently been adopted for dually-diagnosed populations, though mood symptomatology was not measured in these studies, leaving its broader efficacy unverified (13).

(II.) Mindfulness training for co-occurring disorders: theoretical, clinical and neurobiological perspectives

Over the past two decades, the emergence of studies on treatments incorporating mindfulness training (MT) has offered promise for the treatment of MDD and SUDs independently. We offer a theoretical, behavioral and neurobiological exploration of MT for treatment of these disorders when they occur concurrently.

(a.) Theoretical perspectives

A recent consensus definition of mindfulness emphasizes two complementary elements: 1) the placement of attention on the immediate experience; and, 2) adopting an open, curious, accepting attitude toward that experience (15). It is believed that although the capacity for mindfulness is inherent, the majority of individuals move through life on “auto-pilot,” performing daily activities based on habitual behavioral patterns while their minds are elsewhere (16). Mindfulness is developed through a continual practice of “awakening” to present-moment experiences. Traditionally, this is taught through meditation practices that first focus on developing concentration capacities by repeatedly bringing attention to an object, such as the breath, then broadening the attention to include all physical and mental events that are experienced (*e.g.* bodily sensations, emotions and thoughts). Instruction for mindfulness practice can be as simple as, “when sitting, know you are sitting; when thinking, know you are thinking” (17). The intention is to bring a nonjudgmental, objective and accepting quality to this observation.

(b.) Clinical perspectives

While mindfulness practices are centuries old, they have only recently become popular in Western medicine and psychology. One of the earliest incorporations of mindfulness into medical treatment paradigms was through the mindfulness-based stress reduction (MBSR) program at the University of Massachusetts (18). MBSR showed efficacy in the treatment of chronic pain where other treatments had failed (19). After the initial success in treating chronic pain, the effectiveness of mindfulness-based therapies was investigated for treatment of other conditions including anxiety disorders (20–23), addiction (24–27), and depression (28,29), though methodological quality of these studies has been suboptimal (30). Mindfulness-based cognitive therapy (MBCT), based largely upon MBSR, has shown an absolute reduction of 44–50% in the relapse rate for individuals with three or more episodes of depression both in initial and replication studies (28,29). A study of incarcerated, substance-abusing individuals who were taught mindfulness meditation revealed significant reduction in substance use three months following release from incarceration, as well as reductions in anxiety and depression (31). Another study of individuals with alcohol and cocaine use disorders suggested that MT may be as effective as CBT in preventing relapse with specific effects on psychological and physiological stress pathways (25). A further study of a mindfulness-based treatment for substance use disorders suggested that participation in treatment was associated with greater decreases in craving and substance use as compared to a treatment as usual (32), and that the treatment may lessen the relation between depressive symptomotology and craving, thereby decreasing substance use. Taken together, these data provide a rationale for the hypothesis that MT may target shared underlying mechanisms in MDD and SUDs in a dually diagnosed population.

(c.) Neurobiological perspectives

Evidence for common underlying neural pathways in MDD and SUDs may explain some of the shared mechanisms in these disorders, offering a useful perspective on potential targets of treatment for dually-diagnosed individuals. Multiple approaches have investigated the pathophysiology of MDD and SUDs, including those based on genetics, neurotransmitters, and endocrine systems (reviewed elsewhere (33–36)). Regional brain activation studies have provided unique insight into the pathophysiology of both MDD and SUDs. Many regions have shown overlap between MDD and SUDs, suggesting possible mutual underlying pathophysiologies. For example, regions of the ventromedial prefrontal cortex (vmPFC), which is important for homeostasis, emotional regulation and decision-making, have shown dysfunction in both MDD (37–41) and SUDs (42–48). The dorsolateral PFC (dlPFC), which is involved in working memory, attention, initiation of cognitive control, and conflict-induced behavioral adjustment (49–51), the amygdala, which contributes to the formation and storage of memories associated with emotional events, memory consolidation, and reward learning and motivation (52–54), and the insula, which contributes to “sensing” of somatic states through its representation of bodily sensation (55), have all shown importance in both MDD and SUDs (37,40,56–63). While these data suggest overlapping neuroanatomical correlates for MDD and SUDs that may be reflected in common intermediary phenotypes or endophenotypes, they do not directly demonstrate functional commonalities.

The psychological and behavioral correlates of brain function in MDD and SUDs may provide insight into potential targets of effective treatments. For example, several studies suggest that rumination and stress are commonly seen in both MDD and SUDs. Rumination, described as self-focused attention on symptoms of distress without engagement in active problem solving (64), is conceived of as an automatic behavior often acquired during a first depressive episode (28). People who engage in rumination when distressed are more likely to become depressed and have longer periods of depression (64). Likewise, temporary

distraction, which may break the ruminative cycle, may lead to a decrease in dysphoria (65). Brain regions that are implicated in rumination include the amygdala and PFC (64). Ruminators have shown lower PFC activity than controls when attempting to inhibit negative distracters, as well as difficulty with cognitive shifting (66). These data are suggestive of dysfunctional cognitive control circuitry (67). Other studies suggest that rumination is associated with increased amygdalar activity during processing of emotional stimuli (68,69). A role for rumination in SUDs has been suggested by work showing that a tendency to ruminate is associated with greater inclinations to use alcohol or other substances (70). Though preliminary, these data suggest that dysfunction in specific brain regions may correlate with rumination and contribute to habitual behaviors in both MDD and SUDs.

Links between stress, depression and substance use have also been established (reviewed elsewhere (71,72)). For example, exposure to stressful life events has repeatedly been associated with MDD (33,72). Also, depressed patients often exhibit elevated plasma cortisol (the dominant circulating stress glucocorticoid hormone in humans) and abnormal cortisol suppression (73). Similarly, stress has been shown to be instrumental in SUDs: stress cross-sensitizes to both stimulant (74) and alcohol (75) use, induces craving (76), and increases self-administration of drugs such as amphetamines (77), cocaine (78), and alcohol (79). This is likely influenced by stress hormones, as in healthy volunteers, stimulants induce cortisol release, while the magnitude of the reported subjective “high” correlates with plasma cortisol concentrations (80).

The above data suggest that MDD and SUDs share several phenotypes such as stress vulnerability and rumination, pointing at possible mutual underlying neurobiological dysfunctions. Still unclear are the details of how specific this overlap may be. However, these commonalities may provide a sufficient framework from which to develop treatments targeted at shared brain and behavioral dysfunction.

(III) Mechanism of action in mindfulness training

Recent neurobiological, cognitive and behavioral data support two specific components of mindfulness, attention and acceptance, that may directly target the common intermediary phenotypes of rumination and stress, highlighting their potential utility in the treatment of MDD and SUDs. (Reviews of the general mechanisms of mindfulness can be found elsewhere (15,81–84).)

Attention

(a.) Theoretical perspectives—One primary aim of MT is to shift attention from a passive, wandering state (“default mode” –see below) to an active, intentional state. For example, during concentration meditation, when an individual’s mind strays from the object of attention or is distracted by other stimuli, the individual is instructed to intentionally “bring the attention back” to the intended focus. With practice, individuals retrain their minds to more continually “pay attention, on purpose, in the present moment” (18).

(b.) Clinical perspectives—The link between attention training and treatment of depression and addiction may not be initially apparent. It has been hypothesized that focusing and sustaining attention on present experience increases the ability to notice overlearned behavioral patterns as they arise, allowing for individualized interventions (whether cognitive or behavioral) that interrupt these patterns (15,85). For example, early in major depressive episodes, associations between mood and depressive thought patterns are established and can be reactivated in periods of dysphoria (86). In susceptible individuals, negative cognitive styles and tendencies to ruminate can interact to create the conditions for

the “perfect storm”: depression that is triggered by stressful events (87). With continued practice of mindfulness, individuals may be better able to notice these patterns, allowing for disengagement from ruminative thought patterns (*i.e.* not being caught up in the thoughts and believing them as “true”) and selection of how to relate to these experiences, rather than “automatically” reacting to them (16). Indeed, studies have suggested that decreases in distress scores following MT are mediated by a decreased tendency to ruminate (88). These findings suggest MT may be effective in targeting habitual ruminative thinking, with consequent reduction in stress and depression (28).

Stress and ruminative thought patterns have also been linked to SUDs. For example, individuals’ elevated rumination scores have been shown to predict substance abuse (70,89). And although efforts to avoid or suppress ruminative or “unwanted” thoughts are commonly used in attempts to manage cravings and relapse (90), thought suppression has been shown to lead to stronger expectancies after cue exposure (91). Interestingly, decreases in alcohol consumption following mindfulness-based treatment have been shown to be partially mediated by decreases in thought suppression indices such as avoidance (27). These findings suggest that in dually-diagnosed individuals, attentional focus on thoughts may be more effective than attempts to suppress them in decreasing their influence on behavior.

(c.) Neurobiological perspectives—It is hypothesized that specific areas of the medial PFC may be active during ruminative and/or wandering mindstates (dubbed the “default mode”)(92,93). These regions have been found to play a role in linking subjective experiences through time (94,95), holding memory of traits of the self (96,97), reflected self-knowledge (98,99), and aspirations for the future (100). Without this “narrative self reference,” or sense of identity through time, stress reactivity and rumination would not be possible (101,102).

The mechanisms by which MT influences default mode functioning are being explored. In a recent study in which participants were instructed to either elaborate on current cognitions (narrative focus, NF) or to attend to somatic sensations and merely note any cognitions without elaborating on them (experiential focus, EF), investigators found midline cortical activation during NF as compared to EF (103). After MT, midline cortical structures showed decreased activity in EF vs. NF (103). One interpretation of these data is that momentary self-experience may provide a non-self-related cortical “task” which may suppress midline cortical activity. These findings are corroborated by studies showing increased gamma-band oscillation in the brains of long-term meditators (suggesting increased neuronal synchronization (104)), and behavioral studies showing improved attentional regulation with meditation training (105–107). Together, these data suggest that present-centered attentional focus not only moves the individual away from the habitual default-mode thought process, but also manifests behaviorally. From these data, one might hypothesize that MT would benefit dually-diagnosed individuals through improved attentional focus, with consequent reduction in stress-induced ruminative thought patterns, as well as more rapid recognition of these once they have been engaged. These would likely be reflected in “lateralization” of brain activation patterns, as seen by Farb and colleagues in healthy individuals. Future studies in this population using neuroimaging attentional tasks will be informative in testing these hypotheses.

Acceptance

(a.) Theoretical perspectives—A second major component of mindfulness, acceptance, involves a non-judging/non-attached view of experiences. This perspective leads to an understanding of thoughts and sensations as “transient mental events” rather than as reality or a reflection of the self. As with attentional focus, non-attached observation, or meta-

cognition, has been hypothesized to reduce perpetuation of harmful thought patterns by shifting perspective of uncomfortable or unpleasant thoughts from “real” or “true” to viewing them as passing mental events. It should be noted that although acceptance is reported to be beneficial in MT as well as therapies that incorporate mindfulness (108,109), it is unclear whether a non-attached viewpoint fosters acceptance, acceptance fosters a non-attached viewpoint, or whether the effects are bidirectional, and to what degree these are an extension or result of insights gained from the practice of attention.

(b.) Clinical perspectives—The utility of a non-attached mode of experience in individuals with depression and/or addictions is gaining increasing support. Negative affect has been shown to predict relapse to both cigarettes and drug use (110–112). Also, higher intensity of negative affect has been correlated with longer duration of use (113), and worse distress tolerance has been associated with decreased abstinence (114). Acceptance of distressing thoughts lessens reactivity, and decreases attempts to avoid or suppress experiences, which have been linked to worsened outcomes (81,115). For example, in clinical populations, MT has been associated with increases in the ability to “let go of” (*i.e.*, disengage from) negative automatic thoughts and decreases in the tendency towards negative automatic thinking (116). Individuals with SUDs often report experiencing “urges” to use substances, and many state that the experience of an urge is increasingly tolerated and managed when working with a mindfulness approach (25,117–119). Additionally, decreases in substance use following MT have been shown to be partially mediated by decreased avoidance, but not frequency, of intrusive thoughts (27). Further, distress tolerance, drawing from Acceptance and Commitment Therapy-based approaches, has shown preliminary utility in smoking cessation (120). Finally, alcohol- and cocaine-dependent individuals have shown attenuation of self-reported anxiety and drug cravings during stress, with concomitant adaptive shifts in autonomic nervous system function, while remaining fully engaged with their experiences (25). One might expect associated normalization in plasma cortisol concentrations, as has been suggested by studies of individuals with heart disease and cancer who have undergone MT (121,122), though these studies are yet to be reported. Together, these suggest that through acceptance of both mood- and drug-related ruminative thought patterns, MT may show increased efficacy in individuals with co-morbid MDD and SUDs, where other treatments fail.

(c.) Neurobiological perspectives—Meta-cognitive skills, such as inhibition of secondary elaborative processing, may be fostered by MT, since attentional capacity is not being consumed by elaborative thinking (15,105). Supporting this, Farb and colleagues have shown a decoupling of insula-vmPFC activity and an increased coupling of the insula with dlPFC after MT (103). Further, meditation practice has been associated with thickened right insular and somatosensory cortices (123,124). These data suggest a movement away from self-referential experiences (related to midline PFC activation) towards those that are more objectively observed/felt and easily accepted. As stress has been shown to be associated with reduced dlPFC activation during particular tasks, with concomitant increased activation of the default-mode network, this lateralized brain activation pattern may also signal more adaptive responses with MT: neural resources are reallocated away from self-referential, elaborative thinking towards task-specific responses, such as more accurate assessment of internal/external situational stimuli and resultant skillful responses (125). Consistent with this hypothesis, a recent study using the Stroop color-word interference task (which may predict treatment outcomes in addicted individuals (48)), showed that MT was associated with improved cognitive flexibility (126). We would hypothesize that dually-diagnosed individuals would show similar adaptive patterns after MT with concomitant increased insular and dlPFC activation patterns, resulting in decreased perceived stress, drug use, and depression severity.

Section 8: Conclusions and future directions

Mindfulness training has shown promise in the treatment of both SUDs and MDD. Examination of the common neurobiological and behavioral dysfunction in these disorders suggests the promise of MT for dually-diagnosed individuals. MT may help those with dual diagnosis decrease avoidance, tolerate unpleasant withdrawal and emotional states (stress-related), and unlearn maladaptive behaviors (rumination). Additionally, it may lessen the interactions between these processes, thus weakening their additive effects on depression and substance use.

We can now ask: do the commonalities in regional brain dysfunction between MDD and SUDs begin to approximate potential neural correlates of human suffering? If so, is this common to other psychiatric disorders, such as anxiety disorders, that share core features with both MDD and SUDs (*e.g.* unpleasant emotional states)? Would individuals with these disorders and co-morbid SUDs be helped by MT as well? Given the burgeoning research in discerning mechanisms of mindfulness and integrating MT in the treatment of psychiatric disorders, careful studies in dually-diagnosed individuals have the potential to greatly expand our knowledge of common pathophysiology and provide effective treatments where few currently exist.

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