Mindfulness in Treatment Approaches for Addiction — Underlying Mechanisms and Future Directions

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Abstract

Purpose of Review While the treatment of addictive disorders proves to be challenging, new treatment approaches that evolved around the concepts of mindfulness and acceptance have been utilized and investigated in recent years. Our goal is to summarize the efficacy and possible underlying mechanisms of mindfulness-based interventions (MBI) in addictive disorders.

Recent Findings Various meta-analyses have suggested that MBIs show clinical efficacy in the treatment of addictive disorders. Considering the factors that impact addictive disorders, MBIs have been indicated to augment responsiveness to natural rewards in contrast to addiction-related cues as well as to increase top-down cognitive control, decrease subjective and physiological stress perception, and enhance positive affect.

Summary In summary, MBIs hold promise in treating addictive disorders while larger randomized controlled trials with longitudinal study designs are needed to confirm their utility. Newest clinical endeavors strive to enhance the clinical utility of MBIs by augmentation or personalization.

Keywords Mindfulness · Addiction · Mechanisms · Intervention · Reward · Stress

Introduction

The hallmark of substance use disorders as well as behavioral addictions is habitual or even compulsive behavior such as recurrent use of drugs or repetitive performance of activities such as gaming or gambling. Individuals continue this behavior despite the harm it inflicts on themselves and others [1]. Various mechanisms are involved in the emergence, progression, and maintenance of addictive disorders and treatment is vastly

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difficult, which is reflected by high rates of relapse [2, 3]. Traditional treatment entails, among others, patient group therapy or cognitive behavioral therapy (CBT) [4]. In addition, contextual CBTs or so-called third-wave treatments such as mindfulness-based relapse prevention (MBRP) or mindfulness-oriented recovery enhancement (MORE) have been specifically tailored to be applied in the context of addictive disorders, while acceptance and commitment therapy (ACT), which employs an acceptance and mindfulness approach that integrates values and broader behavior change strategies, has been applied in addictive disorders in the recent years [5]. To clarify, while all MBIs centrally employ mindfulness meditation practices, MBRP additionally focusses on cognitive behavioral relapse prevention treatment [6], while MORE additionally provides training in reappraisal and savoring skills [7]. These third-wave treatments share a common emphasis on the use of mindfulness techniques that might target several aspects of addiction such as the reward value of the behavior or drug of choice, conditioned automatized behavior, or the reinforcement of alternative rewards [8, 9]. Opposed to standard behavioral therapy that mainly aims to change and regulate cognition, mindfulness-based interventions (MBI) operate through the alteration of awareness and perception towards cognizance of the "present moment" without

judgement [10]. Research has suggested that MBIs are effective in treating addictive disorders in comparison to standard treatment [11–13].

Furthermore, the focus on the efficacy of MBIs as addiction interventions has been broadened to explore the underlying effects of these interventions on cognitive, affective, and neural processes that drive addictive disorders. Therefore, we aim to give a qualitative overview of efficacy studies as well as research that investigates the underlying mechanisms of substance-related and behavioral addictions that are targeted by MBIs. In addition, we summarize novel approaches to MBI such as augmentation by pharmacological interventions as well as neurostimulation.

Mindfulness

Mindfulness is a concept that is of eastern traditional origin and is linked to the practice of mindfulness-mediation [14]. It has been described as a state of consciousness in which one pays "attention in a particular way: on purpose, in the present moment, and non-judgmentally" [15]. In other words, this state is characterized by a non-critical, attentional focus on current experiences, cognitions, perceptions, and feelings. In addition, mindfulness can also be described in terms of a trait that has shown to be increased with practice of mindfulness-meditation [16].

First applied for chronic pain, Mindfulness-Based Stress Reduction (MBSR) was the first MBI that was applied in a secular medical setting. Treatment success and positive effects on mood and anxiety led to the development of MBIs utilized for psychiatric disorders and later specifically tailored to addictive disorders [17]. As of today, various MBIs for the treatment of addiction have been developed and investigated [17] [7]. In addition, mindfulness is conceptually integrated in some third-wave approaches in psychotherapy which have also been adapted for the treatment of addictions, like dialectical behavior therapy (DBT) [18]. This also applies to ACT, which is focused on psychological flexibility processes that orient to facets of mindfulness including acceptance, cognitive defusion, self-as-context, and flexible attention to the present [19].

Due to the recent interest in MBIs, their therapeutic potential for the treatment of addictive disorders has been explored through several reviews and meta-analyses. The following section aims at giving an overview of the conclusions related to the efficacy of MBIs on substance-related and behavioral addictive disorders (Table 1).

Efficacy of MBIs

A systematic review and meta-analysis by Li et al. [20] examined the results of 42 studies on the efficacy of MBIs on substance use. The authors concluded that the efficacy of MBIs was promising as indicated by generally producing larger improvements relative to control interventions such as treatment as usual (TAU) or CBT. These findings related to clinical outcome measures such as abstinence, craving, and quantity of use as well as substance-related problems, with rather variable small to large effect sizes favoring MBIs. Among MBIs, MORE produced the largest effect sizes observed in this meta-analysis. In line with that, another meta-analysis of 9 RCTs evaluating MBRP specifically concluded that in comparison with control conditions, MBRP yielded significantly better results in terms of withdrawal and craving symptoms (SMD = −.13) as well as negative consequences of substance use (−.23) [21]. Effects of MBRP on substance use frequency or relapse, however, did not differ from standardized treatment approaches including CBT and TAU [21]. Broadly reviewing the efficacy of MBIs on substance-related and behavioral addictive disorders, a review of 54 randomized controlled trials (RCT) determined MBIs to be effective, but with unclear long-term outcomes and with greater results tending to be found when MBIs were combined with TAU [13]. The authors further conclude that MBRP and MORE were the most effective intervention programs. Tying in with the systematic review by Li et al. [20], a more recent systematic review concludes MBIs to be as effective, and in some cases more effective than control interventions that were mostly comprised of standard treatment approaches [22]. MBIs in the treatment of tobacco use specifically were assessed by one meta-analysis that emphasized that the reviewed evidence was characterized by poor quality and small sample sizes [23]. Over the 10 reviewed studies, no significant improvements on tobacco use outcome measures could be detected in comparison to control treatment approaches or when aggregating effects across 6 RCTs (OR = 2.52 favoring MBIs, 95% CI = .76, 8.29) [23].

The effect of MBIs and ACT explicitly on alcohol use disorder (AUD) was concluded to be comparable to other existing treatment approaches in another meta-analysis [12]. Results furthermore indicated the utility of MBIs and ACT in the treatment of comorbid mental health conditions such as depression or other affective disorders that often occur in conjunction with addictive disorders. A meta-analysis of 10 RCTs comparing ACT to other active treatments (e.g., TAU, CBT) found significant small effect sizes favoring ACT on substance use ($g = .29 - .45$) [5]. A more recent review of 22 studies concluded that ACT alone or in combination with other treatments was effective in reducing substance use [24].

Maynard et al. [25] examined the efficacy of MBIs in the treatment of gambling disorder and included seven studies in their meta-analysis. Moderate to large effect sizes of the interventions on clinical outcome measures indicate MBIs to be effective for gambling disorder patients. Although MBIs are generally considered effective and safe in the treatment of behavioral addictions, only a small number of clinical trials have investigated them in this context [26]. In a recent RCT,

Table 1 Overview of MBI studies grouped by target mechanism

Mechanism	First author (year)	Treatment	Intervention description	N	Control	Addictive disorder	Outcomes
Restructuring of responses to drug and natural reward cues	Froeliger (2017)	MORE	10 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills; first 4 sessions psychoeducation following and sessions focused on coping mechanisms, mindful attention of the body, and relationship triggers for relapse	13	No study treatment	TUD	Measurement: participants underwent two fMRI scans pre-tx and after 8-weeks of MORE. MORE significantly reduced smoking and increased positive affect; MORE participants evidenced decreased CR-BOLD response in VS and vPFC and increased positive ER-BOLD in VS and vPFC; ER was correlated with smoking reduction and increased positive affect
	Garland (2019)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills. Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording and practicing mindful breathing before deciding to take an opioid dose	135	SG	OUD	Measurement: before and after 8 weeks all participants viewed opioid and natural reward cues while an electroencephalogram biomarker of target engagement was assessed. MORE was associated with decreased opioid cue-reactivity and enhanced capacity to regulate responses to opioid and natural reward cues; increased positive affective responses to natural reward cues were associated with decreased craving and mediated MORE's therapeutic effects on opioid misuse
	Garland (2016)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills. Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording	51	SG	OUD	Measurement: affective picture viewing task with HR and HRV measures. In MORE group increases in HRV responsivity (affective picture trials) and decreases in cue-elicited HR (drug cues) were seen. MORE led to increased responsiveness to natural reward cues relative to drug cues. The relative responsiveness predicted opioid uses at 3-month follow-up
	Garland (2015)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills. Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording	29	SG	OUD	Measurement: ERPs in response to natural reward/neutral cues. MORE decreased LPP response to natural reward relative to neutral cues. That in turn was correlated with increased positive affective responses and decreased opioid craving post-treatment
	Garland (2014)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills. Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording	49	SG	OUD	Measurement: measured before and after 8 weeks of treatment via HR and HRV responses during a dot-probe task that included opioid-, pain-related, and natural reward stimuli, as well as craving ratings. MORE group evidenced less subjective opioid cue-reactivity, greater HR decelerations, and greater increases in HRV to all cues after treatment compared to the SG; HR and HRV effects were most pronounced for natural reward cues; HR deceleration to natural reward cues was correlated with increased subjective arousal to the cues, whereas HR deceleration to opioid cues was correlated with decreased subjective arousal; effects of MORE on craving were mediated by enhanced RR
	Hanley (2020)	Study 1: NA Study 2: MORE	NA	68/39	NA	OUD	Measurement: NA Study 1: exposure to the patient's own prescribed opioid resulted in significantly greater increases in salivation and cue-elicited craving than exposure to a neutral cue

Table 1 (continued)

Mechanism	First author (year)	Treatment	Intervention description	N	Control	Addictive disorder	Outcomes
							Study 2: MORE intervention evidenced significantly greater decreases in opioid cue-reactivity than participants in an active control condition as evidenced by both reduced salivation and craving ratings
	Janes (2019)	MT	Daily app-based MT sessions over a 3-week period including 22 learning modules (5–15min/module) of daily training videos and in vivo on-demand exercises; features are designed to help users self-monitor their smoking habits, identify triggers for smoking, learn methods to become aware of cravings and use mindfulness practices to ride them out; program calculates and encourages a gradual taper based on baseline data	67	NCI	TUD	Measurement: smoking cue-induced PCC reactivity was measured using functional magnetic resonance imaging at baseline and 1 month after receiving smartphone app-based MT vs. an active control MT group demonstrated a significant correlation between reduction in PCC reactivity to smoking cues and a decline in cigarette consumption while no association was found in the control group; no effects of group alone were found in PCC or cigarette reduction; association is sex specific, particularly in women
Top-down control	Andreu (2018)	MBRP inspired MM	Four-stage cue-exposure: open a pack of cigarettes (1), place a cigarette in front of you (2), place the cigarette in your mouth (3), and bring a lighter to the cigarette without igniting the cigarette (4); afterwards participants received instructions to accept feelings, sensations, or thoughts in a mindful/non-judgmental way and were also given instructions for "urge-surfing"	50	No study treatment	TUD	Measurement: immediately after intervention a smoking Go/NoGo task was performed, while their brain activity was recorded at behavioral level, no group differences were observed; EEG analyses revealed a decrease in P3 amplitude during NoGo vs. Go trials in the mindfulness vs. control group
	Garland (2020)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording and practicing mindful breathing before deciding to take an opioid dose	95	SG	OUD	Measurement: HRV during mindfulness meditation MORE participants showed decreased opioid intake compared to SG. MORE was also related to higher HRV increase during meditation. HRV alterations partially mediated the effect of MORE on reduced opioid intake
	Garland (2019)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording	57	SG	OUD	Measurement: Emotional Go/NoGo task MORE participants showed decreased errors of commission on pain-related trials relative to neutral trials. Minutes of practicing and nonreactivity were related to improvements in emotional response inhibition which was in turn associated with in pain severity reductions at 3-month follow-up
	Garland (2017)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording and practicing mindful breathing before deciding to take an opioid dose	115	SG	OUD	Measurement: Dot probe task to assess opioid AB MORE reduced 200 ms opioid AB which was associated with reduced opioid misuse by 3-month follow-up
	Garland (2010)	MORE	10 weekly sessions involving mindfulness training and experiential exercises delivered by a mindfulness-experienced instructor	53	SG	AD	Measurement: psychophysiological cue-reactivity (stress-primed alcohol cues/HRV) and alcohol AB (dot probe task) MORE led to decreased AB to brief (200 ms) visual alcohol cues as well as improved HRV recovery after exposure to alcohol cues following stress induction. These effects were correlated to changes in thought suppression

Table 1 (continued)

Mechanism	First author (year)	Treatment	Intervention description	N	Control	Addictive disorder	Outcomes
	Hudak (2020)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills. Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by an audio recording and practicing mindful breathing before deciding to take an opioid dose	62	SG	OUD	Measurement: EEG during meditation. MORE increased alpha and theta power as well as FMT coherence. This was in turn linked to altered self-referential processing. Reduced opioid intake over time linked to endogenous theta stimulation in the prefrontal cortex
	Li (2018)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills; sessions were focused on awareness of automatic, addictive video gaming behaviors (1), coping with negative affective states (2), enhancing positive affective states (3), awareness of video game craving (4), stress reduction (5), acceptance of unwanted thoughts and distressing experiences (6), decreasing interpersonal stress (7), and developing a plan to use mindfulness skills to continue recovery (8). Homework: practicing mindful breathing and body scan meditation guided by a MP3 audio and log the amount of time they spent on mindfulness practice	30	SG	IGD	Measurement: directly before and after treatment and 3-month following treatment completion using self-report instruments. MORE participants had significantly greater reductions in number of DSM-5 IGD criteria they met, craving for video gaming, and maladaptive cognitions associated with gaming than SG participants; therapeutic benefits were maintained at 3-month follow-up
	Tang (2016)	IBMT	5 days with brief sessions involving systematic training of attention and self-control with an attitude of acceptance and openness to internal and external experiences	80	Relaxation training	TUD	Measurement: after intervention Positive and Negative Affect Schedule (PANAS) and Profile of Mood States (POMS) to measure emotion regulation, salivary cortisol for the stress response, and fMRI for brain functional and structural changes were assessed. Improved self-control abilities in emotion regulation and stress reduction were found after training and these changes were related to increased ACC/mPFC activity following training in both groups; compared with nonsmokers, smokers showed reduced ACC/mPFC activity in the self-control network before training, and these deficits were ameliorated after training
	Valls-Serrano (2016)	GMT + MM (+ TAU)	8 weekly, 160-min morning sessions involving theoretical and practical elements pursuing the development and implementation of goal-directed behavior and meditation techniques; GMT part includes inhibiting automatic behaviors and directing attention to the present, establishing/maintaining goals in mind, dividing tasks into smaller steps, monitoring behavior and making decisions, reassessing and adjusting behavior. MM part includes regulating emotional input, focusing attention on the present moment and to reducing stress through mindful attention and body scan techniques	32	TAU	PSUD	Measurement: evaluated between one and 15 days before onset of treatments and after end of treatments. GMT + MM was superior to control in improving basic measures of working memory and reflection impulsivity, along with initial thinking times during planning; GMT + MM was superior to control in improving performance in the MET-CV
Stress and negative affect	Carroll (2018)	MBRP	NA	901	NA	SUD	Measurement: meta-analysis of 9 randomized controlled trials. No statistically significant differences between MBRP and comparators on relapse, frequency of use, treatment dropout, depressive symptoms, anxiety symptoms and mindfulness found; significant differences in favor of MBRP on

Table 1 (continued)

Mechanism	First author (year)	Treatment	Intervention description	N	Control	Addictive disorder	Outcomes
	Davis (2018)	MBRP (+ TAU)	NA	79	TAU	SUD	withdrawal/craving symptoms and negative consequences of substance use found; negligible evidence of adverse events. Measurement: NA. MBRP resulted in lower substance use, craving, and stress comparing to TAU condition; reduced stress during treatment partially mediated observed outcome differences between MBRP and TAU for substance use
	Garland (2017)	MORE	8 weekly, 2-h group sessions involving mindfulness training, cognitive reappraisal, and savoring skills; intervention provided instruction in mindfulness techniques to address automatic habit behavior and foster nonreactivity to pain sensations, cognitive reappraisal skills to promote emotion regulation and restructure motivations for opioid use, and savoring pleasant events and emotions to remediate deficits in natural reward processing and boost positive affectivity. Homework: engaging in daily 15-min mindfulness, reappraisal, and savoring practice sessions at home guided by CD	55	SG	OUD	Measurement: self-report before and at the end 8-week intervention + daily EMA report. Patients in MORE reported significantly greater improvements in momentary pain and positive affect than patients in the SG; patients in MORE were significantly more likely to exhibit positive affect regulation than patients in the SG; improvements in positive affect (but not pain) over the course of intervention were associated with reduced risk of misusing opioids by post-treatment
	Garland (2019)	MORE	8 weeks of MORE treatment including 112 random EMA measures of craving, pain, and affect, as well as event-contingent craving ratings	30	TAU	OUD	Measurement: NA. EMA showed significantly greater improvements in craving, pain unpleasantness, stress, and positive affect for participants in MORE than for participants in TAU; participants in MORE reported having nearly 1.3 times greater self-control over craving than those in TAU; positive affect was associated with reduced craving, an association that was significantly stronger among participants in MORE than TAU
	Kober (2017)	MBRP inspired MT	2 weekly group sessions for 4 weeks including training in mindfulness as a two-component process: attention to present moment experience, even if it includes craving or negative emotion (1) and an accepting attitude towards this experience (2). Session 1/2: introduction to concept of cue-induced craving, as well as strategies for mindfully working with craving and practicing mindfulness meditation. Session 3: mindfully working with stress and negative emotion, and introduces loving-kindness meditation as a way to work with them through direct well-wishing. Session 4: practicing mindfulness techniques. Session 5/7: learning about possible triggers for habitual behavior and additional mindfulness practices and reinforced acceptance as a tool for working with negative emotions and changing habits. Session 8: summary	23	FFS	TUD	Measurement: self-reported smoking was assessed during treatment and at each of the follow-up sessions; primary outcome measure was average number of cigarettes per day across the 4 treatment weeks and through week 17 follow-up. Stress reactivity in several brain regions including the amygdala and anterior/mid insula was related to reductions in smoking after treatment, as well as at 3-month post-treatment follow-up across the whole sample; conjunction analysis revealed that these same regions also differentiated between treatment groups such that the MT group showed lower stress-reactivity compared to the FFS/CBT group
	Paz (2017)	PMAA	7-min audio experiential induction of PMAA subsequently exposed to a 2.5-min paced over breathing (hyperventilation) stressor designed to elicit acute anxious arousal	104	Cope-as-usual	TUD	Measurement: anxious arousal and emotion (dys)regulation was measured before, during and following the stressor via

Table 1 (continued)

Mechanism	First author (year)	Treatment	Intervention description	N	Control	Addictive disorder	Outcomes
							self-report, skin conductance levels and respiratory sinus arrhythmia PMAA reduced psycho-physiological dysregulation in response to an anxiogenic stressor, as well as moderated the anxiogenic effect of distress intolerance on psychological but not physiological responding to the stressor among smokers pre-disposed to experience distress via deprivation
	Shuai (2020)	MT	6-min audio with instructions to relax and concentrate on breath sensations, then count each outbreath, at normal pace, from one to ten, and then start again from one; after listening participants were asked how much attention they had paid to the recording on a scale ranging from 1 ("a little") to 5 ("a lot"), and how pleasant they had found to the experience on a scale ranging from 1 ("Unpleasant") to 5 ("Pleasant")	192	no study treatment	AUD	Measurement: alcohol pictorial choice and subjective mood were measured at baseline; subjective happiness and annoyance measured at post-intervention timepoint Breath counting vs. control intervention improved subjective mood relative to baseline, attenuated the worsening of subjective mood produced by stress induction, and accelerated recovery from a stress induced increase in alcohol-seeking behavior; recovery from stress induced alcohol-seeking by breath counting was weaker in more alcohol-dependent participants

vPFC, ventral prefrontal cortex; ER, emotion regulation; SG, (active) support group; CR, cue reactivity; OUD, opioid use disorder; HRV, heart rate variability; HR, heart rate; AB, attentional bias; ERPs, event-related brain potentials; LPP, late positive potential; AD, alcohol dependence; TUD, tobacco use disorder; NCI, National Cancer Institute's QuitGuide app; MBRP, mindfulness-based relapse prevention; PCC, posterior cingulate cortex; FMT, frontal midline theta; IGD, internet gaming disorder; IBMT, integrative body-mind training; MM, mindful meditation; GMT, goal management training; PSUD, poly-substance use disorder; MET-CV, Multiple Errands Test — contextualized version; SUD, substance use disorder; EMA, ecological momentary assessments; TAU, treatment as usual; RR, reward responsiveness; MT, mindfulness training; FFS, Freedom From Smoking (CBT); PMAA, present moment attention and awareness training

an MBI intervention was compared to CBT approaches in a group of patients with problem gambling [27]. The authors state that the MBI was as effective as TAU and more efficient than a manualized CBT intervention. Investigating the effect of an MBI in a sample of students with excessive smartphone use, the authors found smartphone use to be significantly reduced after treatment compared to a control group [28].

Although not classified as addictive disorders by ICD-11 or DSM-5, problematic pornography use as well as binge eating share some criteria with SUD and behavioral addictions such as lack of control over habitual or even compulsive behavioral patterns [29] [30]. Meta-analyses showed that ACT was effective in reducing pornography viewing time as well as improving measures of quality of life. Furthermore, MBIs were moderately to largely effective in the treatment of binge eating [31] [32]. Further research in behavioral addictions has been limited so far to the investigation of trait mindfulness [33] and case-reports [34].

Even though generally favorable, some meta-analyses conclude that MBIs are comparable but not superior to existing treatment approaches. In addition, Witikiewitz et al. found that, possibly due to participants' struggles with regular mindfulness practice, compliance rates are lower than those of relapse prevention [35]. Overall, these results indicate, especially in the context of behavioral addictions, the need for larger confirmatory efficacy trials with high quality methodological controls to determine the efficacy of MBIs in the treatment of addiction.

Addictive Disorders

SUD and other addictive disorders are often marked by a gradual shift from goal-directed behavior mediated by the positive reinforcing effects of the substance or behavior to an increasing loss of control over the behavior or drug intake, thus developing into habitual actions [36, 37]. Habitual actions are rather automatic and disconnected from their possibly adverse outcomes. This explains why addictive disorders are characterized by persistent relapse rates over time despite severe negative consequences [38]. Despite the conscious choice to decrease or stop the drug use or compulsive behavior, it can be almost unattainable to remain abstinent over time for many individuals [39, 40]. Habitual and compulsive behavior in the context of addiction can be triggered by cues that are associated with the substance or behavior in question as well as stressful or negative events [41]. In that context, experiential avoidance of states of negative mood or anxiety can drive individuals to cope through substance use or behavioral patterns, which can become habitual or even compulsory in the course of addiction; also, avoidance of imminent states of withdrawal could instigate relapse [42–45]. For people with addictive disorders, drug cues are imbued with incentive salience through conditioning processes and thereby become

more salient than natural rewards [46, 47]. At the same time, the responsiveness to natural rewards is blunted [48]. These processes both drive increased drug intake as a means of maintaining hedonic equilibrium. Thus, in a kind of vicious circle, the attempt to preserve a dwindling sense of well-being through increased drug use can further dysregulate reward system function and exacerbate dysphoria, drug-related cue-reactivity, and craving [49]. In addition, deficits in top-down cognitive control further augment the impact of craving on addictive behavior or substance intake [50]. This expands into impulsive choice behavior that is manifested as discounting of delayed rewards which has been associated with the severity of various addictive disorders [51].

Based on this hypothetical model of the emergence and course of addictive disorders, the following section aims at summarizing previous findings on the working mechanisms of MBIs and mindfulness in a broader context (Fig. 1).

Restructuring of Responses to Drug and Natural Reward Cues

Craving as an overwhelmingly strong urge is often evoked by exposure to addiction-related cues and can trigger averse physical and physiological responses as well as the strong desire to carry out the behavior in question [52]. It has been suggested that mindfulness can alleviate cue-induced craving in response to addiction cues. In favor of this notion, Westbrook et al. [53] found that mindful attention during the exposure to cigarette-related images reduced self-reported as well as neuronal measures of cue-induced craving in treatment-seeking smokers. In addition, reduced functional connectivity between the subgenual anterior cingulate cortex (sgACC) and other regions such as insula and ventral striatum might reflect reductions of craving-associated neurocircuitry when confronted with addiction-related cues. In line with that, a review of acceptance- and mindfulness-based approaches suggests that decoupling — reduction of the associations between different internal experiences or explicit behavior — might be a central underlying mechanism of MBIs in the treatment of addiction [54].

In a small pilot study, it was found that smokers that underwent the MORE protocol showed significantly reduced smoking as well as increased positive affect. Functional magnetic resonance imaging (fMRI) revealed decreased neuronal cue reactivity to cigarettes in the ventral striatum (VS) as well as medial prefrontal cortex (mPFC) coupled with increased responsivity within that same circuit during savoring of natural healthy rewards [55] — suggesting that MORE was restructuring reward processes in the brain. Furthermore, cue-induced posterior cingulate cortical (PCC) activation was significantly linked to decreased cigarette consumption in a group of smokers that received an app-based MBI [56].

Fig. 1 Proposed processes that drive addictive disorders. Excessive cue-reactivity and blunted natural reward responsiveness as well as stress susceptibility, negative affect, and decreased top-down control enhance habitual decision-making that in turn can lead to automatic or even compulsive substance use or behavior
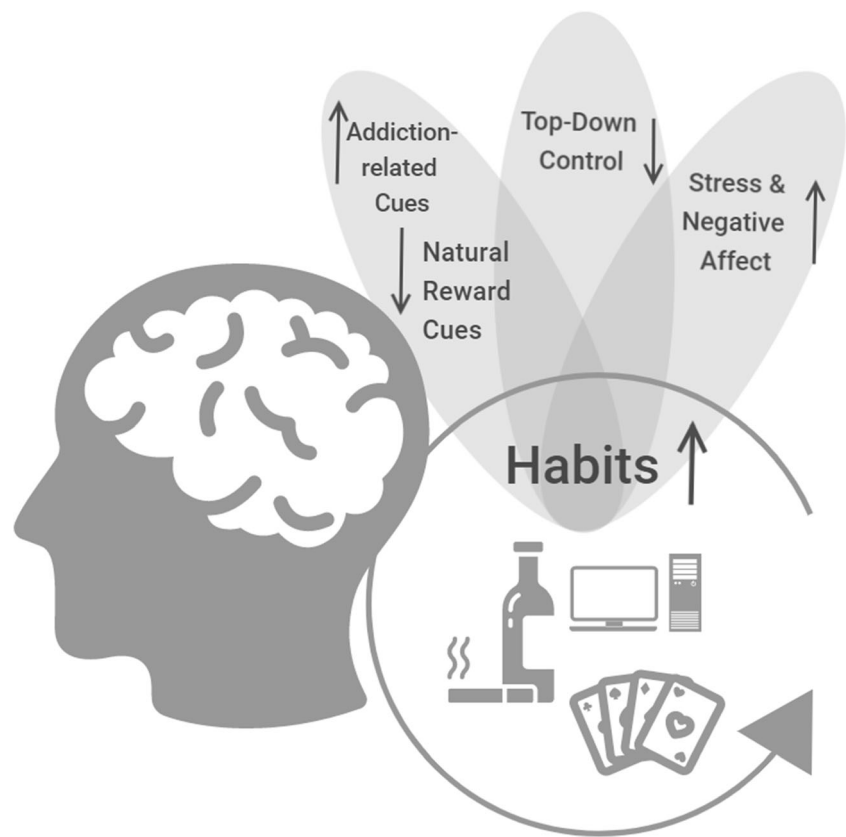
Given the risk of developing substance use disorder during chronic opioid therapy, a sample of prescription opioid users either underwent a support group control intervention or participated in 8 weeks of MORE. Next to decreased quantified opioid misuse and craving, the MBI was associated with less self-reported cue-reactivity towards opioid images, decelerated heart rate (HR), and increased heart rate variability (HRV). In addition, cardiac-autonomic reactivity to natural rewards was more pronounced in the treatment group [57, 58]. In line with these findings, another cohort of opioid users was assessed after 8 weeks of MORE and cue-reactivity was measured on a neurophysiological level via electroencephalogram (EEG) [59, 60]. MORE was associated with a decrease in late positive potential (LPP) towards opioid cues, indicating a reduction of cue-reactivity. On the other hand, responsiveness towards natural rewards was increased compared to the control group. Recently, salivation was found to be an adequate marker of cue-reactivity and the application of MORE led to reduced subjective craving as well as salivation in response to substance cues in opioid users [61]. Taken together, these data provide support for the hypothesis of restructuring reward processing, which asserts that MBIs shift valuation from drug-related rewards back to natural rewards, and in so doing, reduce craving and addictive behavior [62].

Top-Down Control

The influence of craving through cue-conditioning has even more impact on the manifestation and course of addictive disorders when paired with a decreasing capacity for behavioral inhibition [63]. Lack of top-down control might lead to a variety of maladaptive behaviors such as risk-taking, struggling with unhealthy choices, and the need for instant gratification through external rewards [50], albeit strong withdrawal symptoms can also account for the desire for reward, be it money to buy drugs or drug consumption itself [45]. Neuroscientific research has shown that decreased self-control can be associated with impairments in prefrontal neurocircuitry that has been affected by striatal neuroadaptations or even direct neurotoxic effects in the case of SUD [64, 65]. Self-control can be trained, however, as a vast amount of research suggests and mindfulness might improve executive function through e.g. emotion regulation [66, 67].

In line with this, it was found that a brief mindfulness intervention led to reduced systolic blood pressure and increased error monitoring in a flanker task [68]. Mindfulness mediation also had positive effects on behavioral inhibition, which were associated with improved conflict and response monitoring measured by neurophysiological parameters in EEG [69, 70]. Neuroimaging studies also indicate neural change in prefrontal cognitive control areas associated with mindfulness training:

Several studies found that mindfulness training increased resting state connectivity between regions of the default mode network and prefrontal cortical areas, which are associated with executive function that contribute to top-down control [71, 72]. Additionally, increases in prefrontal activation during an executive attention task, white matter volume, and increased glutamate metabolism in prefrontal regions such as the anterior cingulate cortex were associated with brief mindfulness interventions [73, 74].

Polysubstance users that received an MBI next to TAU exhibited improved working memory abilities as well as goal-directed control and increased reflected decision-making, in comparison to a control group [75]. In prescription opioid users with chronic pain conditions, treatment with MORE led to decreased errors of commission in an emotional Go/NoGo task when faced with pain-related distractors. Emotional response inhibition was furthermore correlated with the length of mindfulness practice as well as nonreactivity and reduced pain severity at follow-up [76].

In smokers, it was found that an MBI normalized activation in a self-control network comprised of the ACC and mPFC, and that those neural alterations were linked to improved emotional regulation control [77]. A brief MBI also led to enhanced response inhibition indicated by neurophysiological markers during an EEG recorded Go/NoGo task in smokers [78].

In participants with internet gaming disorder (IGD), MORE treatment led to reduced maladaptive gaming-related cognitions, and this reduction mediated decreases in craving and IGD severity [79]. The authors suggest that mindfulness strengthens metacognitive awareness of habitual internet gaming by involvement of top-down cognitive control.

Among opioid misusers, MORE has been shown to increase inhibitory control in the face of negative emotional distractors in an Emotional Go/NoGo Task [80], and to modify addiction-related attentional bias among people with alcohol use disorder [81] and those engaged in opioid misuse [82]. In addition, MORE may enhance self-regulatory strength and self-control over opioid use as indicted by increases in HRV [83] as well as enhanced endogenous theta stimulation in the prefrontal cortex during active mindfulness meditation [84]. These data indicate that MORE may increase cognitive control in the face of perturbations evoked by motivationally salient, drug-associated stimuli.

Stress and Negative Affect

In addictive disorders, reward seeking initially may occur for its positively reinforced value but over time, the behavior can shift to avoidance of negative reinforcement. This increases the relapse risk immensely as this negative affective state is most prominent in the withdrawal stage [45]. Negative affect is directly linked to enhanced reactivity in the brain's response to stressors [63].

Early studies on the effects of mindfulness meditation on distress and negative affect have shown that practicing mindfulness meditation can lead to reduced distress that is mediated by a decrease in rumination [85]. After a MBI, participants also improved in terms of bias towards negative emotional stimuli, while emotion processing in general was decreased [86]. Participants of a brief MBI also showed significant decreases in negative affect and state anxiety [87], as well as increased positive affect and a reduction of subjectively perceived stress that was linked to decreases in cortisol levels [88]. Neuroimaging studies furthermore revealed structural and functional alterations associated with mindfulness meditation training. Low-frequency amplitude changes in a region of the default mode network (DMN) were directly linked to a reduction of depression scores, indicating a positive effect of mindfulness on mood [89].

Ecological momentary assessments (EMA) have been used to examine the effect of MBIs on real-time affective experiences. In chronic pain patients with opioid use, MORE led to significant improvements in the patients' pain perception as well as positive affect. EMA confirmed that positive affect regulation was increased during treatment with MORE, and that positive affect was associated with reduced risk for opioid abuse [90]. In another EMA study, opioid use disorder patients reported increased self-control over craving as well as improvements in stress and positive affect. In addition, positive affect was associated with reduced craving in MORE participants [91]. In SUD patients, reduced stress as an outcome of MBRP also positively impacted on post-treatment substance use as a mediator [92]. In a recent study, following an ultra-brief MBI, stress-induced mood worsening as well as alcohol seeking was attenuated, while subjective mood improved in comparison to baseline. However, the reduction of stress-induced alcohol seeking was less pronounced in participants with more severe alcohol problems [93].

Another recent physiological study revealed that MBRP in SUD patients led to higher cardiac vagal control reflected by higher heart rate variability (HRV) and lower anxiogenic stress reactivity [94]. In deprived smokers that were exposed to a stressor, a brief MBI decreased the anxiogenic stress reactivity as indicated by subjective measures, but a buffering effect on physiological stress responses could not be discovered [95].

Neuroimaging also suggests that reduced stress reactivity might underlie some aspects of the efficacy of MBIs in addictive disorders. An fMRI study in smokers revealed that post-treatment reductions in smoking were linked to decreased neuronal activation in the amygdala and insula in response to stress. Moreover, these changes were greater in participants that received MBI [96].

While numerous studies have investigated how MBIs effectively target stress reactivity and negative affect, experiential avoidance has been identified as another driver of addictive disorders that might be commonly targeted by all MBIs. Substance use and other addictive behaviors (e.g., gambling, binge eating) may function as a means of avoiding aversive emotions and other internal experiences, which can lead to the initiation and maintenance of addictive disorders [44]. Commonly, MBIs aim to change how individuals respond to distress by increasing acceptance cognitive decentering, and other objective, non-judging responses while decreasing avoidance and suppression of negative emotions related to addictive behavior or substance use [17]. In the light of this, it was suggested that reducing high levels of smoking-specific experiential avoidance would decouple the urge to smoke from experience of internal distress [97]. Clinical studies support this notion. In addition to reduce cigarette use, participants of a mindfulness training intervention exhibited a decreased association between craving and smoking [98]. Furthermore, participation in an intensive meditation class was related to significant decreases in avoidance of thoughts, which partially mediated the reduction in post-treatment alcohol use in an incarcerated population [99]. Comparing an online-based ACT intervention with a widely accessed smoking cessation website, ACT participants exhibited significantly larger cessation rates that were mediated by increase of acceptance of physical, cognitive, and emotional smoking cues [100].

Altogether, the previous sections of this review show that different evidence-based mechanisms have been proposed to elucidate the pathways by which MBI and mindfulness conceptually impact the course of addictive disorders and abstinence. Consistent with current theories of addictive disorders, these proposals advocate that MBIs reduce cue-reactivity, attenuate cognitive control abilities, decrease stress-reactivity and negative affect as well as increasing acceptance of emotional states, and alleviate corresponding reactive behavior.

Augmented Mindfulness

Consistent with the growing popularity of mindfulness research, latest research has also investigated the effects of add-on or augmented interventions that aim at increasing the therapeutic efficacy of MBIs in addictive disorders. For instance, ketamine, a dissociative anesthetic, has been suggested to disrupt stimulant self-administration in cocaine users for a prolonged period and suggested to increase the efficacy of behavioral interventions [101, 102]. In a pilot study, the combination of an MBI with a single ketamine infusion led to decreases of treatment dropout as well as craving scores compared to the MBI alone [103]. However, neuromodulation with transcranial direct current stimulation (tDCS) in addition to an MBI in AUD participants has shown that, although the

MBI was effective in reducing drinking as well as cue-reactivity, the stimulation did not improve the efficacy of the treatment [35].

Study protocols indicate that further technologically advanced methods have been considered to be effective in augmenting the effect of MBIs as well. Currently undergoing research investigates the effect of virtual reality cue-exposure in addition to an MBI in methamphetamine use disorder patients [104]. Pursuant to this, real-time fMRI neurofeedback in addition to an MBI is presently examined in patients with AUD [105].

Discussion

Mindfulness practices have been growing in popularity over the last decade and simultaneously emergent research started to examine the efficacy and underlying mechanisms of MBIs in the context of mental health [106]. MBIs have also been implemented in the context of behavioral and substance-related addictive disorders, and results have been very promising [20, 21]. Two meta-analyses, however, concluded that MBIs are not of superior efficacy as already implemented treatment approaches [12, 24]. As mindfulness research is still in its infancy, more longitudinal RCTs with large sample sizes are needed to confirm the clinical use in addictive disorders. Emergent with the neurocognitive research on the causes and maintenance of addiction, several processes have been highlighted to lead to habitual or even compulsive behavior or substance use [36, 37, 63]. Taking up the literature on cue-reactivity, cognitive control as well as stress and negative affect, among others, researchers have been embedding neurocognitive tasks or stress challenges into their applied research on MBIs. In addition, brief mindfulness trainings have been investigated to elucidate the direct effect of mindfulness meditation on cognitive functioning or substance use [70, 93]. The assessment of brief mindfulness training on different cognitive and neurobiological variables is crucial, as conclusions regarding specific mechanistical effects are challenging because MBIs are characteristically composed of a variety of interventional techniques [22]. For instance, MBRP combines mindfulness meditation practices with cognitive behavioral relapse prevention treatment [6], while MORE integrates training in mindfulness with reappraisal and savoring skills [7]. In addition to the neurocognitive alterations induced by MBIs, it is also important to consider that their efficacy might depend on the target group. For instance, it was suggested that participants with lower substance use severity are more prone to profit from MBIs [93, 107]. Another crucial matter in the clinical practice of MBIs is suboptimal compliance rates that have been found to be lower than in relapse prevention alone [35, 108]. MBI participants have been seen to have problems with practicing mindfulness on a regular basis, which Witkiewitz et al. [35] hypothetically link to potential shortfalls in executive cognitive functioning in some patients

with addictive disorders. This limitation, however, might possibly be overcome through the use of app-based MBI programs, which are additionally cost-effective, accessible, and personalizable to increase compliance. In smokers, they have been shown to be effective in reducing craving-induced smoking [56, 109]. Moreover, augmented MBIs are currently under investigation and hold promise in utilizing and combining mindfulness with other auspicious treatment approaches [103].

In sum, large, robust, and controlled clinical trials are needed to draw conclusions on the efficacy as well as cognitive and neurobiological mechanisms underlying mindfulness as an interventional approach in addictive disorders. Especially research in the field of behavioral addictions is still scarce. However, in light of this review, we feel the future of MBIs in the field of addiction therapy is promising.

Declarations

Conflict of Interest The authors declare no competing interests.

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