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# Craving to Quit: psychological models and neurobiological mechanisms of mindfulness training as treatment for addictions

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## Abstract

Humans suffer heavily from substance use disorders and other addictions. Despite much effort that has been put into understanding the mechanisms of the addictive process, treatment strategies have remained sub-optimal over the past several decades. Mindfulness training, which is based on ancient Buddhist models of human suffering, has recently shown preliminary efficacy in treating addictions. Interestingly, these early models show remarkable similarity to current models of the addictive process, especially in their overlap with operant conditioning (positive and negative reinforcement). Further, they may provide explanatory power for the mechanisms of mindfulness training, including its effects on core addictive elements, such as craving, and the underlying neurobiological processes that may be active therein. In this review, using smoking as an example, we will highlight similarities between ancient and modern views of the addictive process, review studies of mindfulness training for addictions and their effects on craving and other components of this process, and discuss recent neuroimaging findings that may inform our understanding of the neural mechanisms of mindfulness training.

### Keywords

Mindfulness training; craving; smoking; addiction; neuroimaging; associative learning; operant conditioning

## Introduction

Addictions are one of the costliest human conditions, having significant effects on mental, physical, and economic health. For example, the economic tolls of alcoholism typically range from 1–3% but can be as high as 6% of a country's gross domestic product (Rehm et al.). Also, cigarette smoking is the leading cause of preventable morbidity and mortality in the US, accounting for 1 in 5 deaths annually (Center for Disease Control and Prevention, 2008). Given the impact of these disorders, much convergent work has been done to identify the mechanistic underpinnings of addictions, and to develop effective treatments therein (Baler & Volkow, 2006; Goldstein et al., 2009; Kalivas & Volkow, 2005; Volkow, 2004, 2010). In this manuscript, using nicotine dependence as an example (given the large amount of research that has been done regarding its mechanistic underpinnings), we will outline current psychological models of addiction. We will also highlight how our current understanding of the addictive process relates to Buddhist psychological models of human suffering. Further, we will review studies of mindfulness training for addictions and discuss insights that they might provide with regards to targeting core components of the addictive

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process. Finally, we will relate these to recent neuroimaging studies of mindfulness training: how together, these may provide critical links between psychological models of addiction, the key components of the addictive process that mindfulness training targets, and the neurobiological mechanisms thereunder.

## The birth of an addiction

Acquisition of nicotine dependence is a complex process, developed in part from the formation of associative memories between smoking and both positive (*e.g.,* after a good meal), and negative (*e.g.,* when "stressed") affective states (see Text Box 1) (Bevins & Palmatier, 2004; Brown, Lewinsohn, Seeley, & Wagner, 1996; Kandel & Davies, 1986; Leknes & Tracey, 2008; Piasecki, Kenford, Smith, Fiore, & Baker). Subsequently, cues that are judged to be positive or negative (a process that may happen "immediately and without awareness" (Bargh & Chartrand, 1999; Curtin, McCarthy, Piper, & Baker, 2006)) can induce positive or negative affective states, which can then trigger craving to smoke (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Brandon, 1994; Carter & Tiffany, 1999; Cox, Tiffany, & Christen, 2001; Hall, Munoz, Reus, & Sees, 1993; Huston-Lyons & Kornetsky, 1992; Kassel, Stroud, & Paronis, 2003; Perkins, Karelitz, Conklin, Sayette, & Giedgowd, 2010; Shiffman & Waters, 2004; Zinser, Baker, Sherman, & Cannon, 1992). Additionally, neutral cues that have been classically conditioned may directly trigger craving (Lazev, Herzog, & Brandon, 1999). Though the centrality of craving remains controversial (Tiffany, 1990; Tiffany & Carter, 1998; Tiffany & Conklin, 2000), much evidence links craving and smoking, which, mainly through the psychophysical properties of nicotine (Imperato, Mulas, & Di Chiara, 1986), results in the maintenance or improvement of positive affective states, or reduction of negative affective states (Baker et al., 2004; Cook, Spring, McChargue, & Hedeker, 2004; Shiffman et al., 1997; Zinser et al., 1992).

### Text Box 1

Young Joe Smoker is invited to smoke a cigarette by a group of older kids who are popular at school (see #1 "positive cue" in Figure 1a). He learns to associate smoking with "being cool" – when he's outside smoking with his friends, he feels good (#2). Over time, he also learns that taking a smoke break also calms his nerves (#2–6). When Joe gets yelled at by his boss, or gets a bad grade in school (#1 "negative cue"), he feels stressed out (#2), gets a craving (#3) and goes outside for a smoke (#4). The more Joe smokes, the more he reinforces his behavior (#5–7), and the more he finds himself automatically smoking when he gets stressed out, or to ward off the unpleasantness of nicotine withdrawal. At times, he may even find himself with a half-smoked cigarette sitting between his fingers before 'waking up' to the fact that something triggered him to habitually walk outside and light up.

This process sets up positive or negative reinforcement loops respectively, by reinforcing the associative memories between these affective states and smoking (see Figure 1) (Baker et al., 2004; Bevins & Palmatier, 2004; Brandon & Baker, 1991; Carmody, Vieten, & Astin, 2007; Carter et al., 2008; Carter & Tiffany, 2001; Cook et al., 2004; Hall et al., 1993; Hyman, 2007; Rose & Levin, 1991; Warburton & Mancuso, 1998). This associative learning process may then lead to increased motivational salience of future cues (in which both positive and negative cues become more motivationally relevant) (Gross, Jarvik, & Rosenblatt, 1993; Laviolette & van der Kooy, 2004; Olausson, Jentsch, & Taylor, 2004; Robinson & Berridge, 2003; Robinson & Berridge, 1993; Robinson & Berridge, 2008; Waters et al., 2003), resulting in what, building on the work of Baker, Curtin and others (Baker et al., 2004; Curtin et al., 2006), for convenience we term the "addictive loop." Through repeated smoking, this addictive loop may become automated or habitual, leading

to cue-induced behavior that is largely outside of consciousness, let alone conscious control (Bargh & Chartrand, 1999; Curtin et al., 2006; Miller & Gold, 1994; Suhler & Churchland, 2009; Tiffany & Conklin, 2000).

There are several noteworthy aspects of this addictive loop model. First, each link in the chain is supported by convergent findings from both non-human animal and human studies, suggesting an evolutionarily conserved process. Second, as will be discussed below, it provides some explanatory power for the relative strengths and weaknesses of current treatment paradigms. Third, its self-propagating nature aligns not only with current models of operant and classical conditioning, but pre-modern psychological models of the causes of human suffering: craving and attachment.

## Why do we need new treatments for smoking? Limitations of current cessation treatments

The multitude of cues that can be associated with positive and negative affective states and smoking creates tremendous challenges for successful quit attempts. Current pharmacotherapies have focused on the reduction of background craving as well as cue-induced craving (for a review, see (Ferguson & Shiffman, 2009)). For example, nicotine patch therapy has shown benefits for nicotine withdrawal and background craving (which in contrast to cue-induced craving fluctuates slowly over time (Ferguson & Shiffman, 2009)), but not for cue-induced craving (Havermans, Debaere, Smulders, Wiers, & Jansen, 2003; Morissette, Palfai, Gulliver, Spiegel, & Barlow, 2005; Tiffany, Cox, & Elash, 2000). Further, neither nicotine gum, bupropion nor varenicline have shown benefits for prevention of cue-induced craving (Ferguson & Shiffman, 2009; Niaura et al., 2005; Shiffman et al., 2003). Only nicotine gum has been shown to provide momentary *relief* from cue-induced craving once it has been triggered (Niaura et al., 2005), but this substitution strategy (gum for cigarettes) may leave the addictive loop intact rather than extinguishing it.

Mainstay behavioral treatments for smoking cessation have focused on teaching individuals to avoid cues, foster positive affective states (*e.g.* practice relaxation or physical exercise), divert attention from cravings, substitute other activities for smoking, and develop social support mechanisms (Fiore et al., 2000; Lando, McGovern, Barrios, & Etringer, 1990). Unfortunately, these have shown only modest success, with abstinence rates for cognitively-based treatments hovering between 20–30% for the past three decades (Fiore M et al., 2008; Hernandez-Lopez, Luciano, Bricker, Roales-Nieto, & Montesinos, 2009; Law & Tang, 1995; Shiffman, 1993). This may be because triggers are omnipresent making avoidance difficult, diversion of attention requires cognitive reserves (which are often depleted after strong affective states (Muraven & Baumeister, 2000)), and effective substitutions are not always available. Further, these strategies may not actually target the core addictive loop (*e.g.* avoidance of cues decreases input into the loop, Figure 1b grey arrows), while substitute behaviors (e.g. eating carrot sticks or candy) circumvent the loop (Figure 1b blue arrows). Importantly, these strategies, at least in theory, may not diminish the loop itself (Figure 1b black arrows), instead leaving it dormant to reactivate at a later time (Bouton & Moody, 2004; Scott & Hiroi, 2010). Even cue exposure that aims to decrease the conditioned responses may not adequately disrupt the addictive loop, instead leading to different associations that are also situation-specific (Bouton, Westbrook, Corcoran, & Maren, 2006; Niaura et al., 1999). The experimental evidence for the core links of the addictive loop and the modest long-term efficacy of current treatments provide compelling evidence for the need for innovative treatments that directly dismantle this loop instead of treating “around” it (Law & Tang, 1995; Niaura & Abrams, 2002; Shiffman, 1993).

Cognitive treatments have shown that teaching skills to cope with cravings such as avoidance or distraction are strongly correlated with reductions in craving (Longabaugh & Magill, 2011). Yet, are there models of treatment that directly target the core links of the loop, such as those between negative affect and craving? Are there therapeutic interventions that aim to change the trajectory of this cycle by bringing these automated processes into the conscious realm? Remarkably, an early Buddhist model of suffering does both, and the clinical therapeutic interventions it has inspired have gained increasing support from recent studies.

## An early model of addiction

The therapeutic model offered in early Buddhist texts aims at explicating suffering, its cause, the possibility of a cure, and the interventions required to achieve that cure. Suffering is caused by many varieties of craving, or more literally translated, 'thirst'; of particular relevance here is "craving for sense pleasure". It is through the "relinquishment, release, and letting go" of craving that suffering is cured ("Dhammacakkappavattana Sutta: Setting in Motion the Wheel of Truth (SN 56.11)," 2010). Remarkably, this relinquishment of craving may be achieved through a simple psychological intervention.

Buddhist psychological models distinguish bodily, affective, cognitive, volitional, and conscious components of emotional reactions to triggers. Buddhist texts offer a detailed analysis of the causal relationships between these differentiated processes, termed 'dependent [co-]origination'. In this process, craving is said to result from a process based in automated affective reactions to perceptual stimuli. An example of this is given in the next paragraph, but briefly, when environmental cues are registered through the senses (and here thoughts are considered to be within the same category as the standard five senses, Figure 2, #1), an 'affective tone' automatically arises that is typically felt as pleasant or unpleasant (#2). The valence of this affective tone is conditioned by associative memories that were formed from previous experiences (#6 + MIND). Subsequently, a desire or craving arises (definition: "an intense, urgent, or abnormal desire or longing" ) as a psychological urge to act or perform a behavior (#3). The craving is for the continuation of pleasant, or the cessation of unpleasant feeling tones, respectively. This craving motivates action (#4) and fuels the "birth" of a self-identity around the sense object (#5), creating a link between action and outcome that gets laid down in memory (#6). Importantly, when this pleasant affective tone (or absence of an unpleasant affective tone) passes, one is left with "pain, distress and despair" of its absence, thus completing one cycle and priming the individual for the next time s/he encounters a similar sensory stimulus (#7) ("Paticca-samuppada-vibhanga Sutta: Analysis of Dependent Co-arising (SN 12.2)," 2010). In other words, an individual learns that smoking (action) decreases unpleasant feelings such as negative affect and craving, and s/he starts forming a behavior pattern related to these affective reactions, that with repetition, s/he eventually becomes identified with ("if I smoke I feel better"). To be clear, this is not a cognitive construct centered around thoughts and perceptions ("I am a smoker"); instead this birth of self is constituted by habituated reactions to affective experience. The perception of an object is influenced by previous experiences, and the formation of related memories leads to habits or dispositions – consequently 'updating' how perception will function in the future (MIND). This cycle can build on itself in another way as well: states associated with craving and aversion are themselves unpleasant, so that individuals often develop aversive reactions towards their own craving and aversion. But the iterative nature of this cycle also means that it can be disrupted at each new round.

The central point of this model is that craving and aversion arise in response to an affective tone that is associated with perceptual representations of a sensory object, rather than directly in response to the object (Grabovac, Lau, & Willett, 2011). This provides a critical

entry point for therapeutic interventions: through paying careful attention to one's own experience, the Buddhist accounts claim, one can see that perceptions and associated affective reactions (affective tone) are separate from – and indeed separable from – craving and aversion, as well as the elaborate thought processes these can motivate (Grabovac et al., 2011). As one Buddhist scholar puts it, through paying mindful attention to affective reactions, "one distinctly realizes that a pleasant feeling is not identical with lust and need not be followed by it... By doing so, he makes a definite start in cutting through the chain of dependent origination at that decisive point where feeling becomes the condition for craving... It will thus become the meditator's indubitable experience that the causal sequence of feeling and craving is not a necessary one..." (Nyanaponika, 2000). It should also be noted that even when craving has already arisen, mindful awareness can prevent further cycles of aversive reaction to the unpleasant feelings associated with this craving, and thus reduce habitual reactions that arise in an attempt to escape this unpleasantness.

Importantly, craving is the link that is targeted here in cutting through the cycle of dependent origination. Some traditional accounts take meditation practice to be aimed at the realization that there is no self. However, this interpretation has been controversial in recent secondary scholarship (Hamilton, 2000). Indeed, nowhere in the early Buddhist dialogues is the Buddha reported as claiming that there is no self; on the contrary, both the view that there is no self and the view that there is a self are said to lead to suffering ("Sabbasava Sutta: All the Fermentations (MN 2)," 2012). We postulate that mindfulness does not prevent the cognitive construction of self-identity necessary for functioning in the world, which traditional Buddhists call the relative level of self, but instead targets affective bias. Affective bias underlies emotional distortions of attention and memory (Elliot et al 2010), preventing individuals from accurately assessing what is happening in the present moment, and acting accordingly. Mindfulness functions to decouple pleasant and unpleasant experience from habitual reactions of craving and aversion, by removing the affective bias that fuels such emotional reactivity. It is the absence of emotional distortions, we suggest, that allows mindfulness practitioners to 'see things as they are'. In other words, mindfulness does not stop one from being a person, but rather from taking things personally. T

From this perspective, mindfulness allows practitioners to clearly ascertain what is driving their behavior, and whether or not it is moving them toward or away from their goals. For example, mindfulness might enable Joe to see clearly that each time that he smokes in reaction to being stressed out that he only temporizes the stress. By seeing in this way that smoking only provides a minimal amount of relief, and does not address whatever led to his stress in the first place, he can work to fix its root cause. At the same time he may also become more disenchanted with smoking by simply seeing more clearly its effects. Joe may know the health risks and financial costs of smoking but fail to give sufficient weight to these facts in his decisions about behavior. By attenuating emotional distortions in the decision-making process, mindfulness may function to enable Joe to weigh these factors more accurately.

By decoupling pleasant and unpleasant experience from habitual reactions of craving and aversion, careful attention to present moment experience can function to bring a broadening or spaciousness of awareness that allows new appraisals of life situations. A possible result of this has been a recent trend in the literature toward emphasizing the ability of mindfulness to specifically facilitate positive reappraisal. For instance, Garland et al. have given the example of mindfulness allowing individuals' reappraisal of a serious heart condition as "an opportunity to change their lifestyle and health behaviors rather than as a catastrophe portending imminent doom" (Garland, Gaylord, & Fredrickson, 2011). But traditional presentations do not support a conception of mindfulness as biasing subjects especially toward positive appraisal of life situations. Rather, as Garland and colleagues acknowledge,

mindfulness may function by "attenuating emotional distortions of stimuli perception by encouraging non-evaluative contact with phenomenological experience" (Garland, Gaylord, & Park, 2009), leading to more clearly 'seeing things as they are'. This point deserves emphasis. Explicit techniques for positive reappraisal are taught both in contemporary clinical settings and also in holistic traditional approaches to ending suffering. For example, Theravada Buddhist teachings include cultivation of loving-kindness (metta) as well as other positive or wholesome mind-states such as appreciation/sympathetic joy at the joy of others (mudita). In traditional presentations, however, these practices are clearly delineated from the practice of mindfulness (satipatthana), which involves not feeding desire *or* discontent in regard to external objects ("Satipatthana Sutta: Frames of Reference (MN 10)," 2010). Thus, the application of mindfulness in Joe Smoker's case (see Text Box 1) may not result in positive appraisal, but will allow him to clearly be aware of feelings of craving as they actually are, and what he actually gets from feeding them – a relief that is temporary, unpleasant and destructive in itself. It is through this 'seeing things as they are' that patients can counteract motivated reasoning and other unconscious strategies to seek out opportunities to appease their craving. By exposing and attenuating emotional distortions due to craving as well as those due to aversion, mindfulness practice offers an avenue for therapeutic intervention that goes beyond that which is available through positive reappraisal.

Given that one's self-identity around an object is differentiated by the formation of memories, this description of dependent origination is remarkably similar to the modern-day model of addiction that is presented above. As depicted in Figure 2, when Joe Smoker, who has learned to associate smoking with the reduction of stress and/or the temporary abatement of withdrawal states (#6), encounters a stressful situation or nicotine withdrawal symptoms such as irritability, restlessness and agitation (#1), his brain interprets these as unpleasant (#2). He wants the unpleasant feeling to go away, and consequently gets a craving to smoke (#3). When he smokes, he reinforces the habituated reaction to affective experience (e.g. "if I smoke, I will feel better"; #4–6). While Joe Smoker might take this personally, having thoughts such as 'I am smoker', and 'it's cool to be a smoker', or 'it's bad to be a smoker', it is not these particular self-related thoughts but rather the affective bias underlying the reaction of taking things personally that fuels the birth of self-identity (i.e. habituated reactions to affective experience). As the state of satisfaction from feeding the craving is short-lived, given the nature of the short half-life of nicotine and its biological effects (Imperato et al., 1986), the passing away of this mind-state inevitably ensues, leading to dissatisfaction, stress or suffering once again. Importantly, each time Joe smokes, he re-engages and reinforces this loop, resulting in a subsequent rounds of this process (#7), which is not surprisingly termed samsara, or endless wandering, as there is no obvious way out of it when propagated. He may even begin to ruminate about smoking and start planning his day around access to cigarettes, which, as we will see later, likely engages brain circuits involved in self-referential processing, thus further fueling this process. Our modern-day equivalent of this endless wandering appears remarkably similar: the addictive loop. However, the psychological terms and links employed in dependent origination will need careful refinement and empirical validation to determine their relative explanatory and predictive power in modern-day models of addiction.

## What is mindfulness training and does it work for smoking cessation and other addictions?

Derived from Buddhist practices, mindfulness training has been adapted for use in Western cultures, taking forms such as Mindfulness-based Stress Reduction, Mindfulness-based Cognitive Therapy (combined with Cognitive Therapy for depression relapse prevention), and Mindfulness-based Relapse Prevention (combined with Relapse Prevention for

addiction treatment) (Bowen et al., 2009; Kabat-Zinn, 1982; Marlatt & Gordon, 1985; Teasdale et al., 2000). Typical treatments are roughly 8 weeks in duration, though alternate lengths have been employed for targeted uses (Brewer, Mallik, et al., 2011). Common features of these treatments include the training of attention to detect and modify an individual's relationship to automatic thought patterns, among others. For a more detailed review see Holzel et al. (Hölzel et al., 2011).

Mindfulness training's effectiveness has been investigated for the treatment of pain (Kabat-Zinn, 1982; Kabat-Zinn, Lipworth, & Burney, 1985), anxiety disorders (Evans et al.; Kabat-Zinn et al., 1992; Miller, Fletcher, & Kabat-Zinn, 1995; Roemer & Orsillo, 2002), and depression (Ma & Teasdale, 2004; Teasdale et al., 2000), among other medical conditions, although the methodological quality of early studies was at times suboptimal (Ospina et al., 2008) (reviewed in (Baer, 2003; Grossman, Niemann, Schmidt, & Walach, 2004; Toneatto & Nguyen, 2007)). A recent meta-analysis reported effect sizes of .95 and .97 (Hedges's g) for patients with mood and anxiety disorders, respectively, which were maintained during follow-up intervals (mean follow-up was 27±32 weeks; median was 12 weeks) (Hofmann, Sawyer, Witt, & Oh, 2010). These data are promising, although more confirmatory studies are needed, as many of the studies were of pilot nature, small, and/or employed wait-list or other sub-optimal control conditions.

Mindfulness training has only recently been evaluated in the treatment of addictions (Bowen et al., 2009; Brewer et al., 2009; Zgierska et al., 2008), and more specifically smoking (Cropley, Ussher, & Charitou, 2007; Davis, Fleming, Bonus, & Baker, 2007). It has been operationalized to include two distinct components: 1) maintaining attention on the immediate experience; and, 2) maintaining an attitude of acceptance toward this experience (Bishop et al., 2004). These may even be viewed as 'two sides of the same coin' because when attention becomes predominant, self-referential processing (and thus judging or non-acceptance) drops away; 'bare' awareness or attention is by definition free from judgment ("Satipatthana Sutta: Frames of Reference (MN 10)," 2010). Here, for example, Joe Smoker might bring mindful awareness to the body sensations that constitute a craving, and just observe them from moment to moment. Even judgment of the craving becomes an object itself, instead of a driving force for subsequent behavior. As such, mindfulness training may specifically target the associative learning *process* with an emphasis on the critical link between affect and craving in the addictive loop ("Dhammacakkappavattana Sutta: Setting in Motion the Wheel of Truth (SN 56.11)," 2010; Gunaratana, 2002; Nyanaponika, 2000; "Paticca-samuppada-vibhanga Sutta: Analysis of Dependent Co-arising (SN 12.2)," 2010). Through changing one's relationship to craving, via non-judgmental awareness, one begins to remove the fuel from its fire, such that over time, craving and its resultant identity formations eventually burn out or die off.

Mindfulness training has been incorporated into several approaches for addiction treatment, such as Acceptance and Commitment Therapy (ACT) (Hayes, Luoma, Bond, Masuda, & Lillis, 2006) and Relapse Prevention (Mindfulness-based Relapse Prevention (Bowen et al., 2009; Brewer et al., 2009)), and has shown preliminary success therein. For example, Gifford et al. randomized 76 participants to nicotine replacement or ACT (seven individual + seven group sessions) and found 24-hour abstinence of 33% and 35% respectively after treatment and 15% and 35% at one year follow-up (Gifford et al., 2004). Because mindfulness training has the advantages of teaching just a few basic techniques (awareness) that target the addictive loop *process*, aiming both at reducing automaticity and interrupting the strengthening of the loop, it requires fewer and less specialized sessions than other treatments (*e.g.* ACT). Theoretically, this simpler, more focused approach may facilitate both conceptual and behavioral skills mastery and durability of effects in a relatively brief treatment. Studies on the efficacy of mindfulness training for addictions remain preliminary:

a recent review of trials that included mindfulness training reported only one of 22 was randomized (Zgierska et al., 2009). Importantly, a number of these studies showed no significant differences between the mindfulness and comparison conditions. However, subsequent randomized trials have shown some promise. For example, in a small pilot study of cocaine and alcohol dependence, Brewer et al. found equivalent efficacy of mindfulness training to that of CBT (which is considered a "gold-standard" treatment for addictions) during an 8-week treatment period (Brewer et al., 2009). Importantly, in this study, participants that had been randomized to mindfulness training also showed adaptive psychological and autonomic changes during a laboratory-based stress challenge that weren't observed in the CBT group at the end of treatment. Further, in a larger trial, Bowen et al. found significantly lower rates of substance use up to four months post-intervention in individuals receiving Mindfulness-Based Relapse Prevention compared to those receiving treatment as usual (Bowen et al., 2009). However, these studies should be interpreted cautiously, as MT has not yet been rigorously compared to empirically based treatments in large scale head-to-head trials, and indeed may not be more efficacious for these conditions than standard treatment (Zgierska et al., 2009).

With regards to smoking, mindfulness training has shown preliminary utility in reducing cigarette cravings and withdrawal symptoms (Cropley et al., 2007), as well as in smoking cessation (Davis et al., 2007). Bowen et al. provided college students with brief mindfulness-based instructions and found that they smoked significantly fewer cigarettes one week after the intervention compared to those that did not receive instructions (Bowen & Marlatt, 2009). Also, in an uncontrolled trial, Davis et al. found 10 of 18 patients showed abstinence six weeks post-quit after receiving Mindfulness-Based Stress Reduction (Davis et al., 2007). More recently, Brewer et al. randomized 88 subjects to receive mindfulness training or the American Lung Association's Freedom From Smoking treatment (Brewer, Mallik, et al., 2011). They found significant differences in number of cigarettes smoked as well as abstinence rates four months after treatment completion (31% vs. 6% at four months, $p = 0.01$). Interestingly, though both groups reported home practices as part of their assigned treatment, only individuals receiving mindfulness training demonstrated significant associations between home practice and smoking outcomes, suggesting a specific effect of the training rather than mere enthusiasm or interest in quitting.

Formal home practices for the MT group included 1) the 'body scan' which teaches individuals to systematically pay attention to different parts of their bodies as a way to reduce habitual mind-wandering and strengthen their momentary awareness of body sensations; 2) 'loving-kindness' meditation, which is practiced by wishing well to oneself and others, usually by repeating a phrase such as 'may I be happy,' and is theorized to help develop concentration as well as bring awareness to moments of non-acceptance such that they can be seen more clearly; and 3) 'awareness of breath' meditation in which attention is focused on the breath, which helps individuals become more aware of the present moment and refrain from habitually engaging in self-related pre-occupations concerning the future or the past. Informal home practices consisted of 1) setting daily aspirations, 2) performing daily activities mindfully, and 3) exercises for mindfully working with cravings (e.g. RAIN: Recognize, Accept, Investigate, and Note mind-states, emotions, and body sensations from moment-to-moment). Home practices for the Freedom From Smoking intervention included formal guided relaxation techniques and informal "pack tracks" in which individuals tracked their cigarette use and triggers for smoking.

Despite favorable odds ratios of MT for smoking compared to previous studies of group counseling (6.75 vs. 1.76) (Mottillo et al., 2009), this single trial is by no means definitive. Future replication studies are required as well as those that include longer follow-up periods.

Notwithstanding, these studies suggest that mindfulness training is a promising though still emerging treatment for addictions.

## How does mindfulness training work? Mindfulness training may directly target the addictive loop

Mindfulness training, in theory, has the advantage of teaching a simple concept (paying attention to, and not resisting momentary experience) that can be broadly applied to different links of the addictive loop (Grabovac et al., 2011). Effective implementation of mindfulness training may, over time, lead to the dampening and eventual dismantling of the associative learning *process* of smoking or drug use rather than just removing stimuli that might propagate it. For example, through its attentional focus, individuals learn to become more aware of habit-linked, minimally conscious affective states and bodily sensations (*e.g.* low-level craving), thus "de-automating" this largely habitual process (Brewer, Bowen, Smith, Marlatt, & Potenza, 2010; Kabat-Zinn et al., 1985; Teasdale, Segal, & Williams, 1995). In fact, a recent study showed that mindfulness training was associated with improved performance on the Stroop task, suggesting that this training may help to bring even basic, automatic reactions under more conscious, cognitive control (Moore & Malinowski, 2009). Building on this, another study found that higher trait mindfulness in alcohol-dependent individuals was related to reduced attentional bias, suggesting a reduction in incentive salience for alcohol cues (Garland, Boettiger, Gaylord, Chanon, & Howard; Robinson & Berridge, 2008).

By teaching individuals to simply observe aversive body- and mind-states (*i.e.* negative affect) rather than reacting to them, mindfulness training may foster the replacement of stress- and affect-induced, habitual reactions with more adaptive responses (*e.g.* enhanced self-control and regulation (Curtin et al., 2006)). Additionally, mindfulness training may help individuals change their relationships to negative affective or physically unpleasant states and thoughts (*i.e.* to "not take them personally" (Amaro, 2010)). To be clear, we postulate that the mechanism of action here is the attenuation of affective bias underlying the reaction of 'taking things personally', rather than a change in self-related thoughts. As noted above, it is the habituated affective bias underlying emotional reactivity that fuels further rounds of craving and habituation. Thus, with attenuation of this affective bias, no further fuel is added to the fire, ultimately leading to smoking cessation (Bowen et al., 2009; Bowen & Marlatt, 2009; Brewer et al., 2010). However, studies that directly test these hypotheses are needed.

## Is craving an important target of mindfulness training?

As stated above, mindfulness training may help individuals sit with or 'ride out' their cravings. What is meant by this, and how does it fit with mindfulness training's theoretical underpinnings? First, craving is inherently unpleasant, and so naturally drives individuals to act, whether to smoke, drink or use other drugs. The longer this craving goes unsatisfied, the more it may intensify as it becomes fueled by further reactions to the unpleasantness of the wanting itself. For example, in a study of treatment-seeking smokers, for each standard deviation increase in craving scores on the target quit date, the risk of lapsing rose by 43% on that day, and 65% on the following day (Ferguson, Shiffman, & Gwaltney, 2006). Mindfulness training teaches individuals to instead step back and take a moment to explore what cravings actually *feel* like in their bodies, however uncomfortable or unpleasant they may be. Two important insights can be learned from this process. First, individuals learn that cravings are physical sensations in their bodies rather than moral imperatives that must be acted upon. Second, they gain first-hand experience with the impermanent nature of these physical sensations. Each time they ride out a craving –experiencing its physicality without

acting on it– this reinforces their insight that cravings will subside on their own, even if not satisfied. In theory, this allows individuals to learn how to tolerate the physical sensations without acting on them. Cravings may continue to arise, but learning to sit with urges, to pause and not immediately react, may disrupt the associative learning process and the automaticity of the action ordinarily taken. In other words, the birth of an identity around an object ("This is uncomfortable for me, I'd better go smoke a cigarette") is not fostered or fed. Or put another way, the fuel has not been added to the fire, such that the fire burns out more quickly. If this is true, MT should affect the traditional observation that smoking and craving are positively correlated. In fact one might predict that it would decouple this relationship.

A recent study suggests that this decoupling may be true. In a follow up to their MT for smoking cessation trial, Brewer and colleagues examined the relationship between craving and smoking behavior during treatment (Elwafi, Witkiewitz, Mallik, Thornhill, & Brewer, under review). At the start of mindfulness training, individuals showed a strong positive correlation between average daily cigarette use and their self-reported craving for cigarettes, as measured by the Questionnaire on Smoking Urges ($r = 0.58$, $p < 0.001$, see Table 1). At the end of the 4-week treatment period, this correlation was reduced to the point of statistical non-significance ($r = 0.13$, $p = 0.49$). A positive correlation reappeared again at follow-up two weeks later ($r = 0.47$, $p < 0.02$), and grew stronger both three and four months after treatment initiation ($r = 0.79$, $p < 0.001$; $r = 0.77$, $p < 0.001$), likely due to the increased spread in the data as individuals who quit smoking reported a reduction in craving several months after quitting, while those who continued to smoke reported higher levels of craving and greater smoking (see Table 1) (Elwafi et al., under review). Importantly, individuals who quit smoking showed *no difference* in craving scores compared to those who continued to smoke at the end of treatment, but instead demonstrated a delayed reduction in reported craving, while those who did not quit reported an increase in craving concomitant with increases in smoking (see Figure 3). These results suggest that after just four weeks of mindfulness training, individuals were no longer reacting to their cravings by smoking. One interpretation of this is that mindfulness training may have decoupled the relationship between craving and smoking during treatment. In other words, mindfulness practice may help individuals stop adding fuel to the fire (craving), but the fire still continues to burn based on the fuel that is already present (i.e. individuals still crave when they first quit). Importantly, over time, without continued sustenance (smoking), the fire burns out by itself.

The possibility of craving and smoking being decoupled by MT is further supported by the amount of home practice that subjects reported. Similar to previous studies of substance use and mindfulness training (Carmody & Baer, 2008; Carroll et al., 2008), Brewer et al. initially found that increased home practice was correlated with decreased cigarette use for both formal ($r = -0.44$, $p < 0.02$) and informal practice ($r = -0.48$, $p < 0.01$) (Brewer, Mallik, et al., 2011). In fact, the amount of mindfulness practice during treatment not only predicted smoking behavior at the end of treatment (where craving no longer was able to) but moderated the relationship between craving and smoking as well: the more that individuals practiced during treatment, the less craving correlated with the number of cigarettes individuals smoked at the end of treatment (Elwafi et al., under review). One caveat here is that those individuals who engaged in more mindfulness practice may have had some predisposition to benefit from this type of training (e.g. better attentional control or increased distress tolerance which might lead to increased home practice). Future studies that tease apart these possible predisposing factors may help to individualize smoking cessation treatments in the future. For example, Libby and colleagues found that individuals who increased their parasympathetic nervous system output while meditating in a mildly stressful environment were more likely to quit smoking compared to those that demonstrated

a symphathetic predominance, regardless of whether they had or had not received prior meditation training (Libby, Worhunsky, Pilver, & Brewer, 2012).

The ability of mindfulness training to attenuate the relationship between craving and substance use has been observed in other studies as well. Witkiewitz et al. examined the relationship between depression, craving, and substance use following a randomized clinical trial of Mindfulness-Based Relapse Prevention (Witkiewitz & Bowen, 2010). They found that craving mediated the relationship between depressive symptoms and substance use in the group that received conventional treatment, but not in the group that received Mindfulness-based Relapse Prevention. Furthermore, Mindfulness-based Relapse Prevention attenuated the link between depressive symptoms and craving at a 2-month post-treatment follow-up, an effect that predicted diminished substance use at a 4-month follow-up time-point. Taken together, these results suggest that mindfulness training may indeed help individuals develop a tolerance to craving itself, thus over time acting to dismantle the addictive loop through a dis-identification with the object or dismantling of self-identity. The next logical steps will be to determine how these map onto current psychological models of change behavior. For example, do tolerance of craving and dismantling of self-identity equate to reappraisal and extinction respectively, or to other skills, or constitute unique entities unto themselves (Teasdale et al., 2002)?

## Does mindfulness training treat the causes and co-morbid conditions of addictions?

Though the topic of whether other Axis I disorders such as depression and anxiety directly lead to addictions is beyond the scope of this discussion (Robinson, Sareen, Cox, & Bolton, 2011), another theoretical benefit of mindfulness training in the treatment of addictions is that it may concurrently target co-occurring disorders, effectively ‘killing two birds with one stone’ (Brewer et al., 2010). This may be of particular importance for individuals with multiple addictions, as well as those with externalizing disorders (e.g. antisocial personality disorder) who may be more impulsive and have lower distress tolerance (Iacono, Malone, & McGue, 2008). Stress, anxiety and depression have been shown to not only be highly comorbid with substance use disorders (e.g. major depressive disorder has a lifetime prevalence of co-occurrence ranging from 30–43% (Davis et al., 2005; Lopez & Mathers, 2006)), but also often precipitate increased use or relapse. Not surprisingly, stressful life events have been associated with smoking (Balk, Lynskey, & Agrawal, 2009), while exposure to stressors increases relapse to smoking (Cohen & Lichtenstein, 1990; Swan, Denk, Parker, Carmelli, & et al., 1988), and lapses that are triggered by stress progress more quickly to relapse (Shiffman et al., 1996). Perhaps similar to what is seen with stress, depression may be perpetuated by the same type of positive and negative reinforcement learning that results from affective reactivity as that found in addictions. This is evidenced by an overabundance of rumination (Nolen-Hoeksema & Harrell, 2002). In this case, mindfulness may function to prevent the feeding of affective bias underlying the reaction of taking things personally (i.e. rumination). The high rates of comorbidity and possibly shared associative learning loops suggest that there may also be overlap in the neurobiological mechanisms of stress, affective-related and substance use disorders, and that mindfulness training may target core features that are shared among these (Brewer et al., 2010).

## Neurobiological mechanisms of mindfulness training

Brain regions that have shown overlap in a number of different maladies such as addictions and other co-morbid disorders, and importantly, have also been theoretically and functionally linked to mindfulness training may provide a logical starting point in assaying its neurobiological mechanisms (for a more detailed review of possible mechanisms, see

(Hölzel et al., 2011)). The default mode network (DMN) is a logical candidate for exploration for several reasons. First, it has been implicated in a number of disorders, ranging from addictions to Alzheimer's disease (Buckner, Andrews-Hanna, & Schacter, 2008; Walker & Jucker, 2011). Second, the DMN has been shown to be altered by mindfulness training, and third, given its prominence in mind-wandering and self-referential processing, the DMN is a biologically plausible target for mindfulness training as it teaches the inverse of these (Brewer, Worhunsky, et al., 2011; Farb et al., 2007; Mason et al., 2007; Northoff et al., 2006; Taylor et al., 2011; Weissman, Roberts, Visscher, & Woldorff, 2006). There are two primary nodes of the DMN, the medial prefrontal cortex and the posterior cingulate cortex (PCC). These have been shown to be temporally correlated with a number of peripheral nodes, and anti-correlated with brain regions involved in self-monitoring (the dorsal anterior cingulate cortex, dACC), and cognitive control (the dorsolateral prefrontal cortex, dlPFC) (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Fox et al., 2005). Though self-referential processing is a complex area of investigation in itself (Legrand & Ruby, 2009), on a first approximation, this may be where the models of the self-identity formation overlap, as memory retrieval and the 'self across time' are linked by PCC activity herein.

With regards to the effects of mindfulness training on the DMN, Farb and colleagues showed that after eight weeks of Mindfulness-Based Stress Reduction, individuals decreased DMN activity when performing a task in which they engaged in mindful awareness of adjectives that were presented visually versus determining what the words meant to them (Farb et al., 2007). Taylor and colleagues similarly found deactivation of DMN structures in meditators practicing a 'mindful state' while viewing emotionally evocative pictures (Taylor et al., 2011). Extending these, Brewer and colleagues found that in experienced meditators (> 10,000 hours of practice on average), DMN deactivation was common to three different types of meditation (concentration, loving-kindness, and choiceless awareness) (Brewer, Worhunsky, et al., 2011). These findings fit with the hypothesis that if an individual smokes due to habitually responding to triggers, be they ruminative thought patterns or negative affect and unpleasant bodily sensations from nicotine withdrawal, that MT would help them disengage from these self-identified patterns. By mindfully attending to cravings, these DMN nodes may become less active, as seen above during meditation or the viewing of evocative pictures. Over time, these circuits may even change, as the habituated sense of self around smoking fades due to lack of sustenance or fuel.

Interestingly, Brewer and colleagues found an increase in functional connectivity between the PCC, and the dACC as well as the dlPFC in experienced meditators compared to controls. This is important, because as mentioned earlier, these regions have previously been shown to be anti-correlated, and thus named the 'task-negative' (DMN) and 'task-positive' (dACC and dlPFC) networks respectively (Fox & Raichle, 2007; Fox et al., 2005). Typical anti-correlation patterns between these structures were found in controls at baseline, which decreased during meditation, suggesting a state-dependent connectivity pattern in untrained individuals. However, the observed *increased* connectivity patterns seen in experienced meditators were present *both* at baseline and during meditation, suggesting that a 'new' default mode had been established. These findings should be interpreted with caution, as this study was cross-sectional, and could be influenced by self-selection bias.

As conflict monitoring (the dACC) and cognitive control regions (the dlPFC) have been shown to be important in self-control, addictions and treatment outcomes (Brewer, Worhunsky, Carroll, Rounsaville, & Potenza, 2008; Hare, Camerer, & Rangel, 2009; Kober et al., 2010), these findings suggest that MT may fundamentally alter brain activity and connectivity patterns in networks that are important for perpetuation of addictive behaviors. In theory, the more Joe Smoker develops his capacity to pay attention to his internal and

external environment, the less he would fuel his habitual 'coping' strategies of smoking to deal with stress and withdrawal states, leading to the cooling off of his habituated affective self-identity and its eventual dying out.

However, prospective studies of individuals receiving MT for addictions that measure changes in brain activity and connectivity over time are needed to test such hypotheses. Also, it is unclear what the time course of these psychological and neural changes might be, as decoupling of craving and smoking was seen within 4 weeks in one study, but measured at different time points in other studies (Brewer, Mallik, et al., 2011; Witkiewitz & Bowen, 2010). Additionally, as structural changes have been seen with just 8 weeks of MT, it will be important to establish the relationship between the necessary duration of this training and brain changes (whether functional or structural) as they relate to outcomes, and if persistent practice is required to maintain such gains (Holzel et al., 2011). Finally, as we focused mainly on the DMN in this review, studies assessing other possible brain regions that may emerge as prominent players in the neural mechanisms of mindfulness will be important.

## Conclusions and future directions

Over the past century, much has been discovered about the addictive process and its underlying neurobiology (Goldstein et al., 2009; Kalivas & Volkow, 2005). From these findings, psychological models have been put forward that have been instrumental in the development of novel treatments that directly target core components of this process. These models show remarkable similarities to ancient models aimed at describing the causes of human suffering. Modern treatments, such as MT that are based on these Buddhist models are beginning to show preliminary efficacy in the treatment of addictions, and may be doing so through changing one's relationship to core addictive elements such as craving. Recent neuroimaging studies are converging with these concepts, suggesting that basic processes, such as DMN activation patterns, can be fundamentally altered with MT. These may manifest behaviorally, in that individuals may develop new habits such as monitoring for unskillful thought processes and automatic behaviors, and objectively observing them rather than being 'sucked in' by them and smoking, using other drugs, or engaging in other unhealthy behaviors. And the more individuals are able to decouple craving from behavior through practicing mindfulness, the less they foster the addictive loop, leading to the later dying away or cessation of craving itself. Ultimately, with practice, this may lead to more adaptive choices with concomitant decreases in stress and suffering.

The field of MT for the treatment of addictions is a young one. As highlighted in this review, current work is promising but preliminary, and models developed therefrom are only useful if they provide tangible and testable hypotheses and more importantly, inform and improve the delivery of treatment. MT may, at least in theory, confer advantages over other approaches for addictions, especially in cases of co-morbid disorders, and when individuals are particularly stuck in negative (or positive) reinforcement loops. Going forward basic caveats, such as the use of active comparison conditions for randomization, therapist training, and safety issues that uniquely relate to these populations (e.g. trauma history) will continue to need attention (Lustyk, Chawla, Nolan, & Marlatt, 2009). For example, further studies are needed to rigorously compare MT to "gold-standard" treatments to determine if it provides any additional benefit with regards to abstinence rates.

With working models of addiction in place, several questions can now be addressed by researchers in the field to both test and improve the models, and to inform treatment: 1) As most studies of addiction thus far have been conducted using different treatment protocols, is there a single, manualized delivery of MT that can be agreed upon that can be vetted and used for standardized comparison across sites? Can this be developed with input from

clinicians who are “in the trenches” to ensure that MT can be readily and feasibly disseminated, as current standards (e.g. 8-week linear frameworks) may be sub-optimal from a patient retention and clinical delivery standpoint (Brewer et al., 2009)? This will allow for a vastly accelerated and iterative process for establishing an evidence base, optimizing delivery and maximizing clinical effect. 2) Is it time to separate MT from other cognitive and behavioral frameworks (e.g. disentangle Mindfulness from Relapse Prevention), such that we are better able to measure components that are MT-specific? 3) Are there accepted laboratory and/or other behavioral measures that can be uniformly employed across different sites and substances? For example, measuring cue reactivity using dot-probe and/or substance-specific Stroop tasks pre- and post-treatment and the relationship of these tasks to subjective craving and substance use may test their hypothesized relationship in proposed models. Also, measuring resting-state functional connectivity or specific relationships between regions of the brain that are implicated in self-identity (PCC) and self-monitoring (dACC) and their relationship to MT (and home practice), may test whether these networks are indeed changed with training, as hypothesized by these models (Frewen, Dozois, & Lanius, 2008). Given the theoretical promise of MT, its early supporting evidence, and the convergence of modern behavioral and brain probes, we hope to see hypothesis-driven and collaborative efforts emerge to rigorously test this “new” treatment over the next few years that will show tangible improvements in the lives of those who suffer from addictions.

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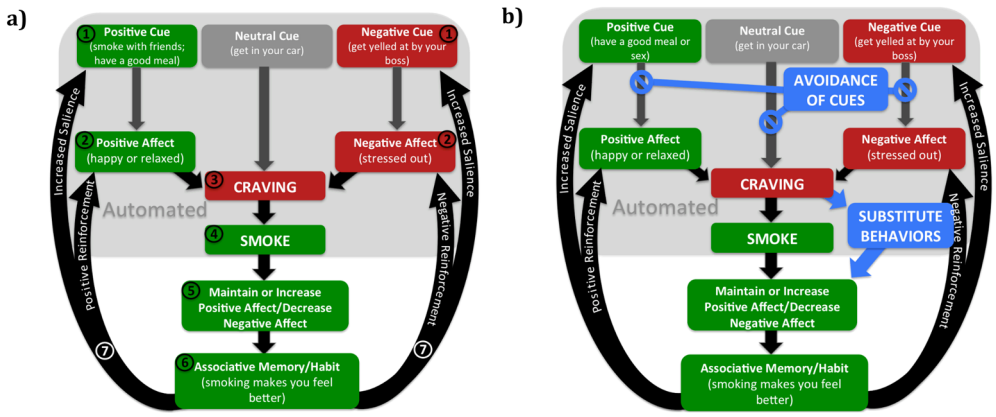


**Figure 1. Associative learning "addictive loop" for nicotine dependence**

a) Smoking becomes associated with positive (green) and negative (red) affect through positive and negative reinforcement. Cues that trigger these states (gray arrows) lead to cue-induced craving, furthering this process, which through repetition becomes automated over time. Strategies that teach avoidance of cues or substitute behaviors do not directly dismantle the core addictive loop (black arrows), leaving individuals vulnerable to relapse to smoking. b) Limitation of current treatment paradigms in dismantling the addictive loop: avoidance of cues dampens input into the addictive loop (black arrows). While substitute behaviors, such as eating candy or engaging in an activity that distracts and individual such as going for a walk (blue arrows) circumvent the targeted addictive behavior. However, neither of these strategies dismantles the addictive loop at its core. Copyright 2011 Judson Brewer. Reprinted with permission of author.

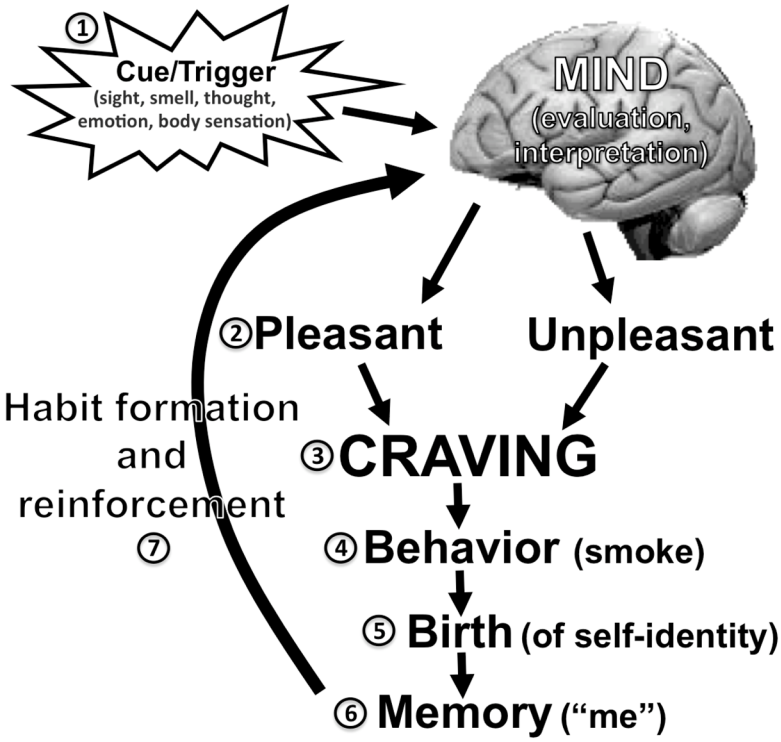


**Figure 2. Early models of addiction: dependent origination**

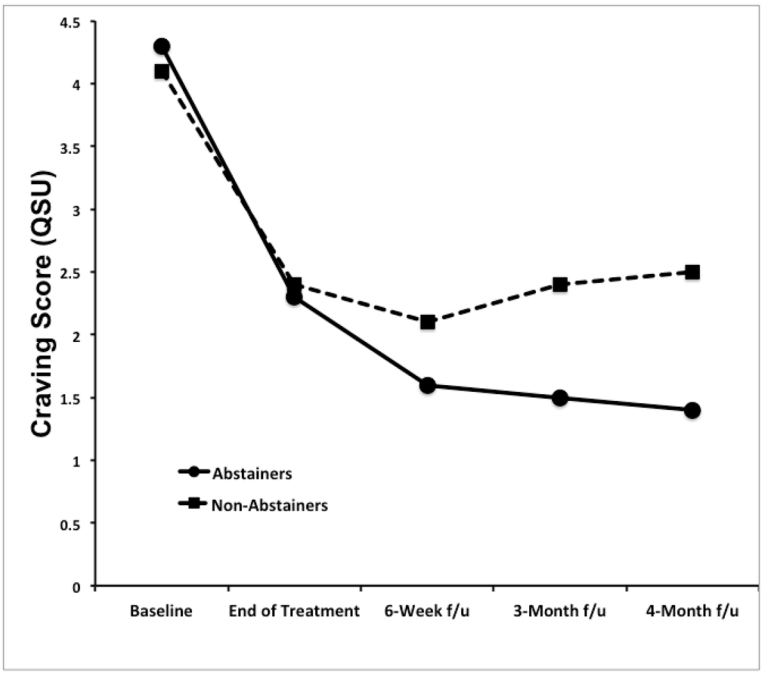


**Figure 3. Reduction in craving lags behind smoking abstinence**

Individuals who maintained smoking abstinence at 4-Months (solid lines) reported similar craving levels to those who did not achieve abstinence (dashed line) at the end of treatment. Craving continued to drop for abstainers, but increased concomitant with smoking for non-abstainers. Adapted from Elwafi et. al. (2012, under review).

**Table 1**

Correlations between craving and cigarette use, in relation to home practice with mindfulness training

| Variable | Baseline (week 0) | End of Treatment (week 4) | 6-week follow-up | 3-month follow-up | 4-month follow-up |
|---|---|---|---|---|---|
| Craving by Cigarette | r = 0.582 | r = 0.126 | r = 0.474 | r = 0.788 | r = 0.768 |
| Use | p < 0.001 | p = .491 | p < 0.020 | p < 0.001 | p < 0.001 |
| Formal Practice | N/A | 4.6 days/wk | 4.1 days/wk | 3.3 days/wk | 2.6 days/wk |
| Informal Practice | N/A | 5.1 days/wk | 3.6 days/wk | 3.6 days/wk | 2.7 days/wk |

Craving was measured by the Questionnaire on Smoking Urges (QSU). Formal home practice included 'body scan,' loving-kindness, and awareness of breath meditations. Informal home practice included the four modes of walking, mindfulness of daily activities, and RAIN (Recognize, Accept, Investigate, Note). Adapted from Elwafi et. al. (2012, under review).