Reward Processing Following
Mindfulness-Based Cognitive Therapy and Cognitive-Behavioral Therapy for Wellbeing

by

Lê-Anh Laurence Dinh-Williams

A thesis submitted in conformity with the requirements for the degree of Master of Arts, Clinical Psychology

Graduate Department of Psychological Clinical Science

University of Toronto

Toronto, Canada

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REWARD PROCESSING AND RELAPSE IN MBCT CBT

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2016

Abstract

The aim of this study was to examine: (a) treatment-related changes in the reward system following two interventions designed to prevent the recurrence of depression, Mindfulness-Based Cognitive Therapy (MBCT) and Cognitive Behavioral Therapy with Wellbeing focus (CBT-WB); (b) changes following treatment that relate to relapse status at a two-year follow-up. Previously depressed patients were randomly assigned to 8-week MBCT (N=43) or CBT-WB (N=34) and scanned using fMRI while completing a card gambling task before and after treatment. Whole-brain analyses found that an increased neural sensitivity in the reward system following treatment to winning trials (outcome phase) and reduced sensitivity to the anticipation of a win were associated with relapse status. Differences between interventions were found for the anticipatory phases of winning. Overall, these findings suggest that maintenance interventions may derive their therapeutic effects from preserving baseline responses, rather than heightening reward sensitivity to outcome.
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1 Reward Processing Following Mindfulness-Based Cognitive Therapy and Cognitive-Behavioral Therapy with Wellbeing focus

1.1 Depression is a Recurrent Disorder

Major Depressive Disorder (MDD) is a prevalent clinical disorder affecting 3 to 13% of adults worldwide (Gelenberg, 2010; Richards, 2011), marked by significantly depressed mood and/or anhedonic symptoms (American Psychological Association, 2000). Although reducing these symptoms during the acute phase of the disorder tends to be the primary goal of treatment, it is increasingly being recognized that efforts to maintain this state of wellness following remission are also necessary in the management of MDD (Mueller et al., 1999). At least 50% of those who recover from a first episode of depression will experience one or more additional episodes in their lifetime, and approximately 80% of those with a history of two will have another recurrence (APA, 2000; Kupfer, Frank, & Wamhoff, 1996; Post, 1992). It is estimated that the risk of recurrence increases by 16% with each additional episode, such that individuals with three or more episodes are likely to experience the chronic, lifelong nature of MDD (Solomon et al., 2000). These rates are a major concern in the care of MDD patients and highlight the need to better understand the causes of this recurrent pattern, as well as how best to prevent the return of depressive symptoms.

1.2 Relapse Prevention in Major Depressive Disorder

The current standard of care for preventing depressive relapse is to continue with antidepressant treatment despite symptom remission (APA, 2000). The issue however is that nonadherence rates can reach up to 40% (Bockting et al., 2008), illustrating the need for alternatives to this pharmacological approach. Mindfulness-based cognitive therapy (MBCT;
Segal, Williams, & Teasdale, 2002) (Segal, Teasdale, Williams, & Gemar, 2002) and Cognitive-Behavioral Therapy with Wellbeing Focus (CBT-WB; Fava, Rafanelli, Cazzaro, Conti, & Grandi, 1998) were both designed within this framework and aim to help people vulnerable to repeated episodes of depression stay well in the long term.

**Mindfulness-Based Cognitive Therapy (MBCT).** Mindfulness-Based Cognitive Therapy helps reduce the risk of depression by combining elements of cognitive therapy with the cultivation of mindfulness. MBCT is based on a model of cognitive vulnerability to depressive relapse and recurrence (Segal et al., 2002), whereby patients who have experienced several episodes of MDD have an increased association between mood and thoughts (Irving & Segal, 2013; Kuyken, Crane, & Dalgleish, 2012). Low or depressed mood tends to trigger negative thinking similar to the thought patterns that were active during previous episodes of depression (Segal et al., 2002). Chronic reactivation of these patterns of thinking, and the feelings/sensations associated, make one vulnerable to further episodes of depression (Segal et al., 2002). MBCT was developed to target this cognitive vulnerability, and reduce the likelihood of a depressive episode to become re-established.

MBCT offers participants a systematic training in mindfulness meditation combined with elements from cognitive behavioral therapy (CBT). Through the practice of mindfulness exercises, such as the body scan, simple yoga exercises, and prolonged periods of sitting meditation, patients are taught to become aware of, turn towards and relate non-judgmentally to the change and flux of thoughts, feelings and bodily sensations, including depressed mood and emotional discomfort. Mindfulness applied can help patients develop a decentered perspective to negative thoughts, emotions, and sensations, and counteract habitual reactive patterns of thinking that promote the
cycle of depression. In addition, MBCT includes psychoeducation on cognition in depression, aimed at further examining the interrelatedness of thoughts, emotions, and behavior in inducing and maintaining depressive symptoms.

Research to date on MBCT indicate that it is effective in reducing the risk of relapse (Williams & Kuyken, 2012). In the PREVENT study by Kuyken et al. (2015), 212 patients were randomly assigned to MBCT and 212 to maintenance antidepressants. The time to relapse or recurrence of depression did not differ between MBCT and maintenance antidepressants over 24 months, nor did the number of serious adverse events. These results suggest that MBCT is as effective as the current gold standard in relapse prevention, a finding that has been replicated in previous research (Kuyken et al., 2008; Segal et al., 2010). Similarly, research examining the effectiveness of MBCT as compared to psychotherapeutic interventions has found that it is equally or more effective than other approaches in the prevention of relapse. In a randomized controlled trials (RCT) comparing MBCT + depression relapse active monitoring (DRAM) to DRAM alone, the authors found that fewer MBCT participants (3 or more previous episodes) had relapsed during the course of a two-year follow-up (Meadows et al., 2014). In a dismantling study by Williams et al. (2014), 255 participants were randomly assigned to receive either MBCT plus treatment-as-usual (TAU), cognitive psycho-education plus TAU, or TAU alone. Results indicated no group differences in time to relapse over a 12-month follow-up. However, MBCT provided additional protection against relapse for participants with increased vulnerability to relapse due to a history of childhood trauma. In a study by Shallcross et al. (2015), MBCT was compared to the Health Enhancement Program (HEP), structurally equivalent and validated intervention designed to address relapse via physical activity, functional movement, music therapy, and nutrition. Ninety-two participants in remission from MDD with residual depressive symptoms were randomized to
receive either an 8-week MBCT or HEP and relapse rates were measured over a 60-week follow-up. Both groups experienced significant and equal reductions in depressive symptoms and improvements in life satisfaction, however, the effects of HEP were more immediate. The HEP group experienced immediate symptom reduction post-intervention and then a gradual increase over the 60-week follow-up, while the MBCT group experienced a gradual linear symptom reduction. In all, there is strong evidence to suggest that MBCT is effective in reducing the risk of relapse in a population vulnerable to recurrent depression.

Although it was originally developed for these purposes, new research is emerging demonstrating a host of additional therapeutic effects, including heightened positive affect (Garland, Farb, Goldin, & Fredrickson, 2015; Geschwind, Nicolson, et al., 2011). In a study by Geschwind et al. (2011), participants with a history of one or more previous depressive episodes, currently in remission with residual depressive symptoms, were randomly assigned to receive MBCT (N=64) and treatment-as-usual (TAU) or TAU (N=66) in a parallel, open-label, randomized controlled trial. Experience Sampling Method (ESM) was used to assess momentary positive emotions as well as appraisal of pleasant activities in daily life during the six days before and after the intervention. Overall, the results of this study suggest that MBCT has the potential to promote change in positive affect following treatment. Participants reported more overall PA, increased appraisal of activities as pleasant, and an enhanced PA response (appreciation, intensity) to these positive events as a result of MBCT training. These findings were not due to decreases in depressive symptoms as these effects remained after controlling for variance in depressive symptoms. Similarly, Batink et al. (2013) reported changes in positive affect during the course of MBCT, with increases in momentary positive affect mediating the effects of MBCT on post-treatment residual symptoms of depression.
Cognitive-Behavioral Therapy with Wellbeing Focus (CBT-WB). CBT-WB is an adaptation of cognitive-behavioral therapy (CBT) designed to treat residual symptoms of affective disorders and promote lasting wellbeing (Fava et al., 1998). Traditional techniques of CBT are employed but adapted to help nurture positive affect. For instance, the first sessions help patients identify the situations and settings that trigger positive mood, followed by working on detecting automatic thoughts or beliefs that lead to the premature interruption of wellbeing. In one of the final sessions, participants learn about the factors promoting psychological wellbeing (e.g., purpose in life, self-acceptance, autonomy, environmental mastery) and discuss how to develop these strengths (Ryff, 1989). The hypothesized basis of therapeutic change is addressing the key cognitive processes and behaviors that are detrimental to wellbeing and reduce the likelihood of positive affect. In addition, working towards personal growth and connecting with the resources necessary for psychological wellbeing are likely to become additional sources of positive affect and to help build the strengths necessary to ward off the return of depression (Huta & Hawley, 2010).

Still, very few studies have examined the prophylactic effects of this intervention. In a study by Fava et al. (1998), 40 patients with a history of MDD (3 or more previous episodes) were randomly assigned to CBT-WB or clinical management. In both groups, antidepressant drugs were tapered and discontinued. Participants were monitored during a 6-year follow-up in which no antidepressant drugs were used unless a relapse ensued. At post-treatment, CBT-WB training was associated with significant reductions in residual depressive symptoms and increases in psychological wellbeing, personal growth and contentment. At a 2-year follow-up, CBT-WB was significantly more successful in reducing the risk of relapse than clinical management (25% vs. 80% of participants relapsed). This rate was maintained over an additional 4 years with the
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respective relapse rates increasing to 40% in CBT-WB and 90% in the clinical management condition (Fava et al., 2004). Overall, these results suggest that CBT-WB is effective in reducing the recurrence of depression and is associated with improvements in wellbeing.

1.3 Positive Affect and Relapse Prevention in MDD

Traditional approaches to helping MDD patients maintain wellbeing have emphasized the importance of lingering depressive symptoms or negative mood-related factors in promoting the return of symptoms. In general, this approach assumes that it is the presence of aberrant negative cognitive and affective features, rather than the absence of positive, that is predictive of recurrent depression. Research on anhedonia however suggests that positive affective experiences also play a role in the maintenance and development of depression over time. In general, lingering deficits in PA predict a negative prognosis for depression, while improvements in PA protect from the return of symptoms.

**Reduced positive affect and depression prognosis.** The absence of positive experiences seemingly creates conditions of vulnerability to future adversities that contribute to the enduring presence of MDD (Ryff & Singer, 1996). Low levels of wellbeing predict 10-year depression levels (Wood & Joseph, 2010), reductions in positive emotional experiences can partially account for depression time course (Morris, Bylsma, & Rottenberg, 2009; Peeters, Berkhof, Rottenberg, & Nicolson, 2010; Rottenberg, Kasch, Gross, & Gotlib, 2002), and self-reported anhedonia has been associated with depression symptoms over a 20-year period (Shankman, Nelson, Harrow, & Faull, 2010). As such, patients may continue to experience a paucity of PA following treatment that facilitates the presence of depressive symptoms.
Increased positive affect and resilience. On the other hand, the presence of positive affect is a substantial source of resilience for vulnerable populations. Early improvements in positive emotion have been found to predict remission from depression in response to medication, over and above any changes in negative mood (Geschwind, Nicolson, et al., 2011). Similarly, Wichers et al. (2010) found that increases in reported rewarding experiences (using Experience Sampling Method) during the course of treatment discriminated between patients who responded and those who did not, over and above changes in negative affect (Wichers, Geschwind, van Os, & Peeters, 2010b). In a recent meta-analysis, including 51 studies with both depressed and nondepressed participants, they found that interventions that specifically target positive affect in treatment (e.g., positive psychotherapy) are effective in ameliorating depressive symptoms, as well as enhancing positive functioning overall (Sin & Lyubomirsky, 2009a). Overall, it seems that increasing positive affective experiences during the course of treating an acute mood disorder is related to a successful recovery.

Increased PA within the context of relapse prevention is likely to be clinically valuable. For instance, participants with a lifetime history of depression, scoring one standard deviation higher on the ability to generate PA from pleasant daily life events, are three times less likely to experience a future episode (Wichers et al., 2010). Similarly, high levels of reward experience have been shown to protect against the development of affective symptoms (Geschwind et al., 2010). There is also emerging evidence that the ability to experience positive emotions can reduce the risk of depression in those that are genetically vulnerable to the disorder (Wichers et al., 2007). These studies help illustrate the protective effects of PA on the return of depressive symptoms. No study to date however has examined the mechanisms by which changes in PA may help reduce...
the risk of relapse, particularly in those with a history of recurrent depression and most vulnerable to the chronic nature of MDD.

1.4 The Neurobiology of Positive Affect

Neuroimaging has emerged as a valuable research tool to characterize the mechanisms underlying PA that may not be adequately captured using self-report or physiological measures and can be utilized as a sensitive and complex measure of PA.

Ultimately, neuroimaging studies implicate the *reward system* of the brain as a generalized system responsible for the amalgam of positive affective experiences. This system includes cortical regions (e.g. orbitofrontal) as well as sub-cortical structures (e.g., nucleus accumbens) that are consistently activated across positive/pleasurable events, regardless of the otherwise unique character of various PA experience. For instance, the reward system is activated while thinking of a loved one (Acevedo, Aron, Fisher, & Brown, 2012), while eating (Small et al., 2001), or winning a game (Rademacher et al., 2010). Overall, this overlapping system is responsible for evaluating the attractive and motivational properties of any stimulus/event and producing the appetitive and consummatory responses that characterize the experience of pleasure or PA. This response has been further decomposed in a set of distinct reward processes that are responsible for: (a) evaluating the hedonic value of an event and initiating the motivational processes necessary to obtain the reward (*reward wanting*); (b) experiencing the hedonic impact of pleasure itself (*reward liking*); and (c) reward-related learning aimed at maximizing reward outcome (*reward learning*). Dissociating these phases is important because they reflect different psychological states (Berridge & Robinson, 1998). For instance, anticipation is characterized by goal-directed behavior, whereas consummation involves a pleasure response (Gard, Gard, Kring, & John, 2006). In depression,
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deficits in one or the other would result in seemingly different profiles. Deficits in anticipation are likely to resemble difficulties initiating activities or performing regular duties. Deficits in consummation are more likely to result in a loss of pleasure when engaged in typically pleasurable event. A substantial amount of research has been devoted to clarifying the neurobiology underlying the “liking”, “wanting” and “learning” features of reward, and generally highlight regions within the salience network, dorsal striatum (DS), medial temporal lobe (MTL), frontal and parietal areas as key to these reward processes.

**Salience Network.** The Salience Network (SN) is an intrinsically connected large-scale network anchored primarily in the anterior insula (AI) and the dorsal anterior cingulate cortex (dACC). This network also includes additional subcortical structures, such as the amygdala, ventral striatum (VS) and the substantia nigra/ventral tegmental area (VTA). Within the context of reward, the SN, together with its interconnected brain networks, works as a dynamic hub for the detection and selection of salient stimuli based on their perceptual features (Peters, Iyer, Itti, & Koch, 2005) and for mediating interactions with other neurocognitive systems (Menon, 2015). Activity in these regions help enhance responses to stimuli that are infrequent in space or time or are of learned or intrinsic biological importance, including pleasurable or emotionally engaging events (Knudsen, 2007). Differences in activity within these regions is typically interpreted as differences in the salience or value attributed to a stimuli. An event may be salient for one group of individuals, while it may be of limited value for another. For example, exposure to drug paraphernalia is particularly more salient to individuals with a drug addiction, while less relevant for nonusers. Differences in SN activity helps capture this distinction (Menon, 2015). Nonetheless, the main cortical and subcortical nodes of the SN serve distinct functions in salience detection by virtue of their differential inputs and outputs.
Amygdala, ventral tegmental area and ventral striatum. The most characterized reward circuit in the brain comprises the dopaminergic neurons in the ventral tegmental area (VTA) that project to the nucleus accumbens (NAcc) in the ventral striatum (VS). This VTA–NAcc circuit is crucial for the early detection of rewards in the environment and for initiating their consumption (Haber & Knutson, 2010). VTA dopaminergic neurons also innervate several interconnected regions including the prefrontal cortex (PFC), amygdala and hippocampus that contribute additional motivational information via bottom-up (amygdala) or top-down processes (PFC, hippocampus). In general, these structures in addition to the ventral pallidium provide reward and motivational signals (Pessoa, 2014). They are often described as the hedonic hotspots of the reward system because of their role in generating a “liking” response. Greater activity in these regions help amplify the subjective experience of pleasure itself.

Anterior Cingulate Cortex (ACC). A wide range of functional imaging studies and theoretical models have suggested that the dorsal ACC and subgenual ACC play distinct roles in the processing of reward. The dorsal ACC is involved in the performance of actions needed to gain a reward, while the subgenual ACC is likely a reflection of the autonomic features of hedonic experiences.

The dorsal ACC has direct connections to the spinal cord and subcortical oculomotor areas (Fries, 1984), giving the dorsal ACC direct control over motor responses (Menon, 2015). In addition, activity in the dorsal ACC is engaged during a variety of complex mental operations, including attention-for-action/target selection (Frith, Friston, Liddle, & Frackowiak, 1991; Posner, Petersen, Fox, & Raichle, 1988), error detection/performance monitoring (Gehring & Knight, 2000; Luu, Flaisch, & Tucker, 2000), competition monitoring (Carter et al., 1998), anticipation
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(Murtha, Chertkw, Beauregard, Dixon, & Evans, 1996), working memory (Petit, Courtney, Ungerleider, & Haxby, 1998), novelty detection (Clark, Fannon, Lai, Benson, & Bauer, 2000), and performance monitoring. As such, the dorsal ACC is well equipped to monitor and initiate the behaviors needed to achieve a desired outcome. Within the context of reward processing, it is believed to play a role in initiating action selection, monitoring reward predictions and signaling prediction errors (Averbeck & Seo, 2008; Jessup & O’Doherty, 2010; Rushworth & Behrens, 2008; Silvetti, Seurinck, van Bochove, & Verguts, 2013; B. A. Vogt & Pandya, 1987). Increased activity in this region is believed to reflect a greater “wanting” response during reward processing.

On the other hand, the subgenual ACC is believed to play a more visceral role, particularly during the anticipation rather than receipt of a rewarding event. Lesions in this region significantly impair the ability to sustain autonomic arousal during the anticipation of rewards as measured by pupillary dilation in monkeys (Bush et al., 2002; Rudebeck et al., 2014). However, lesions did not affect autonomic arousal to unsignaled rewards or pupillary responses to light. The authors argued that the subgenual ACC is necessary for sustaining elevated autonomic arousal in anticipation of rewards, and implicate this area in the regulation of a “wanting” response.

**Insula.** The insula, particularly the anterior insula (AI), receives convergent input from multiple sensory modalities including the auditory and visual systems (Augustine, 1996; Bamiou, Musiek, & Luxon, 2003; Butti & Hof, 2010; Mesulam & Mufson, 1982; Nieuwenhuys, Savelsbergh, & Oudejans, 2012), and from the sub-cortical nodes of the SN (e.g., amygdala, VS, VTA) that are involved in the subjective experience of pleasure. In addition, the insula is also sensitive to internal bodily signals associated with autonomic processes (Garfinkel & Critchley, 2013; Singer, Critchley, & Preuschoff, 2009) and is crucial in interoceptive awareness. Together,
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these connections provide the AI with access to multimodal sensory information concerning perception, emotion, and the visceral bodily responses that are elicited by an emotional event, suggesting a major role in the integration of sensory information, sensory awareness and monitoring of salient events. Within the context of reward, activity in the AI is likely to reflect an enhanced sensory awareness of a pleasurable/rewarding event and the subjective feeling state of reward.

**Frontal Cortices.** Research with humans and evolutionarily similar nonhuman animals has provided important insight into the role of prefrontal regions in reward processing. The reward sub-cortical circuits for mediating core affective reactions (e.g., VS, amygdala) are largely similar across all mammals. As such, the complexity of a reward response observed in humans is often attributed to the massive expansion of the neocortex, including prefrontal regions, in humans compared to animals. Psychologically, these prefrontal regions can act as top-down regulators of affective reactions, utilizing higher-order processes such as attention and decision making to monitor behavior and outcome, as well as transform the initial lower-order reaction to a rewarding event in primarily sub-cortical (Izard, 2007; Panksepp, 2007; Smith et al., 2010). Lateral regions are involved in the motor planning, organization and regulation of reward-related reactions, while medial regions are involved in the sensory monitoring and evaluation of the value of a rewarding events.

**Lateral prefrontal cortices (LPFC).** The LPFC is typically associated with executive functioning and performance of the cognitive skills needed for complex mental activity. These skills involve working memory, cognitive flexibility, planning, inhibition, and abstract reasoning (Miller & Cummings, 2007).
The DLPFC in particular is well situated to orchestrate motivated behavior because of its role in planning and goal maintenance, as well as its top-down influence on sub-cortical structures. For instance, the DLPFC is believed to maintain goal-relevant information in working memory (Levy & Goldman-Rakic, 2000; Owen, McMillan, Laird, & Bullmore, 2005; Wager & Smith, 2003) to update this information as goals dynamically change during task switching (Crone, Donohue, Honomichl, Wendelken, & Bunge, 2006; MacDonald, Cohen, Stenger, & Carter, 2000; Sakai, 2008; Savine & Braver, 2010), and to arbitrate between conflicting goals during decision-making (Boettiger et al., 2007; Hare, Camerer, & Rangel, 2009; McClure et al., 2004; Ridderinkhof, van den Wildenberg, Segalowitz, & Carter, 2004).

The DLPFC is capable of modulating activity in the striatum during instructed reward-learning (Doll, Jacobs, Sanfey, & Frank, 2009; Li, Delgado, & Phelps, 2011) and influences activity in the VTA and NAcc during the anticipation of a rewarding event (Ballard et al., 2011). Together, these findings suggest that the DLPFC is involved in the representation of goals and reward information in working memory, and can act to integrate this activity to modify behavior or one’s “liking” response (Miller & Cohen, 2001; Sakagami & Watanabe, 2007; Wagner, Maril, Bjork, & Schacter, 2001). It works to represent reward-value information in relation to cognitive information (e.g., task rules and predicted motivational outcomes), and helps provide “context” to inform action selection and hedonic processing occurring in other regions (Dixon & Christoff, 2014).

**Dorsomedial prefrontal cortices (DMPFC).** Numerous fMRI studies have observed increases in activity in the dorsomedial prefrontal cortices (as well as ventrolateral, dorsolateral prefrontal cortices) when participants are instructed to deploy cognitive strategies that reduce
negative emotional experience (Ochsner & Gross, 2005). More recently, the DMPFC has been implicated as involved in the regulation of emotions, regardless of valence (Seo et al., 2014). The DMPFC is often observed during reward-seeking behaviors in combination with sub-cortical structures and is thought to enhance excitation of the hedonic hotspots of the brain (Hjelmstad, 2004; Horvitz, 2002; Kiyatkin & Rebec, 1996; Nicola, Hopf, & Hjelmstad, 2004; Nicola, Surmeier, & Malenka, 2000). In rats, inactivation of the DMPFC (via bilateral GABA agonist injections) significantly reduces firing rates in the NAcc in response to a conditioned reward cue, concomitant with a loss of reward-seeking behavioral responses (Ishikawa, Ambroggi, Nicola, & Fields, 2008). A similar pattern was observed in depressed patients whereby patients were less able to sustain activity in the NAcc (as well as the insula, temporal gyrus and right thalamus) when instructed to up-regulate their emotional response to positive images (using cognitive reappraisal). These effects were mediated by decreased connectivity between these regions and the DMPFC (Heller et al., 2009). Overall, the DMPFC during reward is believed to reflect reappraisal processes that involve reinterpreting the meaning of affective stimuli in ways that alter their emotional impact and the regulation of sub-cortical regions towards these effects (Beauregard, Lévesque, & Bourgouin, 2001; Eippert et al., 2007; Goldin, McRae, Ramel, & Gross, 2008; Kalisch et al., 2005; S. H. Kim & Hamann, 2007; Ochsner et al., 2004; Phan et al., 2005; Urry et al., 2006; van Reekum et al., 2007).

**Ventromedial prefrontal cortex (VMPFC).** During reward, activity in the VMPFC, including segments of the orbitofrontal cortex and neighboring sgACC, is believed to reflect processes involved in the evaluation of the incentive value of an outcome, rather than a pleasure response (Vassena, Krebs, Silvetti, Fias, & Verguts, 2014). For instance, Vassena et al. (2014) found that activity in the VMPFC during the receipt of a reward was not dependent on the degree
to which the reward was expected nor the extent to which the outcome was dependent on the participant’s actions during a gambling task. Instead, VMPFC appears sensitive to its incentive value. This focus on the value of an outcome in absence of intentional action (i.e. choice) is in line with what has been proposed as a specialized encoding for stimulus-based value coding in the VMPFC, as opposed to performance-based value coding (Camille, Tsuchida, & Fellows, 2011; Rudebeck et al., 2008; Rushworth, Behrens, Rudebeck, & Walton, 2007). In addition, the VMPFC and OFC are modulated by the degree to which the outcome is valued as personally or emotionally significant (Bartra, McGuire, & Kable, 2013; Chib, Rangel, Shimojo, & O’Doherty, 2009; Grabenhorst & Rolls, 2011; Sescousse, Caldú, Segura, & Dreher, 2013). Activity in the VMPFC has been shown to correlate with the subjective value attached to the stimulus by the agent (Hare et al., 2009; Padoa-Schioppa & Assad, 2008; Plassmann, O’Doherty, & Rangel, 2007) and to reflect the perceived value of a chosen option (Boorman, Rushworth, & Behrens, 2013; Grabenhorst & Rolls, 2011; Kennerley & Walton, 2011). As such, greater activity in the VMPFC during the reception of a reward is likely to reflect monitoring of the value placed on that event and a “liking” response.

Medial Temporal Lobe. The medial temporal lobe (MTL), including the hippocampus and surrounding hippocampal regions, is traditionally known for its role in memory. Within the context of reward, activity in the hippocampus is thought to reflect increased memory encoding based on the valence of the reward (Dillon, 2015). Events that are positive or negative in nature are more likely to be stored in long-term memory. Emerging evidence suggests a broader role of the MTL during reward, including the ability for future thinking. Future thinking refers to imagining future events and hypothetical outcomes. Considering the “future” during reward-based decisions can be adaptive because it allows for the consideration of potential consequences prior
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to a decision. Awareness of a future but *hypothetical outcome* can come to override goals that are immediately rewarding, but less meaningful or valuable (Boyer, 2008). The MTL activity is necessary for future thinking and related to more adaptive action selection. Participants with lesions in the MTL were impaired at pre-experiencing future events, and were more likely to select immediate rewards with smaller gain than delayed rewards with larger gains (Palombo, Keane, & Verfaellie, 2015). According to the authors, future thinking helps experience the subjective value of a decision before its time and may facilitate long-term goal achievement in the face of competing rewards (Kurth-Nelson, Bickel, & Redish, 2012; Palombo et al., 2015). Activity in this region during reward is likely to influence “liking”, “wanting” and “learning” processes.

**Dorsal Striatum.** The dorsal striatum is extensively connected to associative, motor, and limbic circuits, thereby being in an ideal anatomical position to combine both motor and affective information (Haber and Knutson, 2010). The caudate nucleus and putamen form the basis of the dorsal striatum, and are involved in learning about actions and their reward consequences (O’Doherty et al., 2004; Tricomi, Delgado, & Fiez, 2004), as opposed to more passive forms of appetitive learning found to depend on the ventral striatum (O’Doherty, 2004). However, the putamen and caudate nucleus are embedded in distinct cortico-striatal loop circuits, predominantly connected to motor-related cerebral cortical areas and frontal association areas, respectively. This difference in their cortical connections suggests that the putamen and caudate nucleus are engaged in different functional aspects of stimulus-action-reward association learning.

The caudate is believed to be involved in the monitoring of reward prediction errors and reinforcement-based learning. It interacts with medial, orbitomedial, premotor, and anterior cingulate cortices to create actions that are flexible or goal directed, temporally sensitive to the
fluctuating values of goals and to the contingencies between selected behavior and subsequent reward (Haruno & Kawato, 2006; Richard Levy & Dubois, 2006). It integrates this live performance feedback to influence subsequent reward-seeking behavior (Haruno & Kawato, 2006). In addition, caudate activity may be specific to the monitoring of the success or failure of one’s actions during reward processing, rather than the monitoring of reward based on its value. For instance, both animal and human studies have consistently indicated that striatal reward responses are contingent on the rewards if actions were performed to acquire them (Delgado, 2007). Monkey caudate neurons fire more frequently during motor actions that lead to expected rewards than during non-rewarded actions (Kawagoe, Takikawa, & Hikosaka, 1998; Schultz & Dickinson, 2000). In humans, dorsal caudate responds differentially to rewards and punishments only when they are perceived to be contingent on the participants' button presses (Tricomi et al., 2004). Patients afflicted with Parkinson’s disease are impaired in their learning of probabilistic stimuli when action contingencies are present (Poldrack et al., 2001), but are unimpaired when no contingency between action and outcome exists (Shohamy, Myers, Grossman, et al., 2004).

The putamen is similarly involved in reward learning but involves actions that are stimulus bound, relatively automatic or habitual, rather than planned (Jog, Kubota, Connolly, Hillegaart, & Graybiel, 1999; Poldrack et al., 2001). For example, Tanaka, Balleine, and O’Doherty (2008) reported increased activation of the caudate nucleus in subjects performing on a high (goal-directed) action–outcome contingency schedule compared with subjects performing a low action–outcome contingency schedule that promotes habitual responding (Tanaka et al., 2008). By contrast, the caudal putamen was preferentially activated during an outcome devaluation test when subjects’ behavioural responses were habitual (E. Tricomi, Balleine, & O’Doherty, 2009).

Similarly, lesion studies in monkeys demonstrate that the putamen plays a vital role in choices
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based on reward history, rather than immediate reward contingencies. Inactivation of the putamen caused impairments in utilizing reward-related contingencies from previous trials to guide decision making, while choices guided by a simple strategy of lose-shift and win-stay trial-to-trial format remained intact (Muranishi et al., 2011).

In all, what distinguishes the human dorsal striatum from the rest is its involvement in action-contingent reward learning (Delgado, Miller, Inati, & Phelps, 2005; Haruno et al., 2004; Knutson, Fong, Adams, Varner, & Hommer, 2001; O’Doherty, 2004; Tricomi et al., 2004). The dorsal striatum helps choose appropriately between distinct courses of action based on a history of reward-related contingencies (or habitual responding), and/or estimating the causal relationship between an action and its consequences, or outcome, with the value, or utility, of the outcome, rather than relying solely on cognition. These regions link prefrontal, premotor, sensorimotor cortices with the striatum to inform decision making (Chang, Chen, Luo, Shi, & Woodward, 2002; Lauwereyns, Watanabe, Coe, & Hikosaka, 2002; Tanaka et al., 2006).

**Summary.** As such, liking reactions result from activity in identifiable brain systems that paint hedonic value on a sensation (e.g., VMPFC, OFC, VTA, NAcc). Similarly, wanting includes incentive salience and motivational processes within reward that influence hedonic liking (e.g., insula, MTL, subgenual ACC), turn stimuli into motivationally attractive incentives, and promote the behaviors necessary to acquire or maintain the reward (e.g., dACC, DLPFC). Finally, learning includes a wide range of processes linked to implicit knowledge as well as associative conditioning (e.g., dorsal striatum) (Kringelbach & Berridge, 2012).
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1.5 Reward System in Depression

The reduced pleasure and frail motivational features of MDD are conceived as arising from a breakdown in the pleasure cycle, whereby the wanting, liking and learning phases of reward respond irregularly to opportunities (Rømer Thomsen, Whybrow, & Kringelbach, 2015). To examine appetitive-motivational functioning in MDD, studies have typically measured participants’ neural reactivity to ordinarily pleasurable events, such as gambling, listening to music, engaging in altruistic behavior, viewing the faces of close others, eating, drinking and more (Rømer Thomsen, Whybrow, & Kringelbach, 2015). The response of MDD patients to these various sources of pleasure is likely to generalize to their experience with real-world pleasant events.

Dysfunctions in ventral (i.e., nucleus accumbens) and dorsal (i.e., caudate, putamen) striatal regions as well as orbitofrontal cortex (OFC) during the processing of these rewarding experiences are among the most replicated findings, with important implications for understanding the nature of MDD (Pizzagalli, 2014). For example, Steele et al. (2007) found that the behavior of depressed patients failed to be reinforced by rewarding feedback during a card gambling task and that this decreased sensitivity to reward was associated to poorer responses in the ventral striatum (VS) and anterior cingulate cortex (ACC) while “winning” (compared to controls). This line of research has helped clarify which aspects of reward processing might be dysfunctional in depression and account for the clinical presentation of reduced PA. Decreased activity in these structures is believed to reduce the ability of MDD patients to register incoming rewarding events as such, and the potency of experienced PA (Epstein et al., 2006; Pizzagalli et al., 2009). Emerging evidence suggest that this pattern is also evident in populations at risk for the onset or recurrence depression.
Population at risk of depression. McCabe, Woffindale, Harmer, & Cowen (2012) examined whether young people, at increased risk of MDD (with familial precedence) but with no personal history of a mood disorder, demonstrate a pattern of neural reactivity to hedonic stimuli that differs from controls (with no family history of MDD). They found that participants (aged 16-21) with depressed biological parents showed diminished response in the orbitofrontal cortex (OFC) and a blunted neural response in the ACC to hedonic stimuli (pictures of chocolate and consumption of a chocolate-related product). Another study found that adolescents at familial risk for MDD exhibit demonstrated reduced activation in the dorsal striatum (putamen) and insula when anticipating rewards during a monetary incentive delay task, adapted for children, whereby an appropriate response to a set of given cues (e.g., quick response to a circle) is rewarded with points towards a selected prize (Gotlib & Joormann, 2010). These patterns suggest that there are latent abnormalities in the processing of positive stimuli that may promote an increased vulnerability to the onset of depression. The insula is a particularly driving force in reward; its activation during reward processing is associated to the urge to consume, while damage is associated to anergia and disruptions in reward seeking behavior (Naqvi & Bechara, 2010). The ACC, dorsal striatum and OFC are also highly implicated in the process of experiencing a reward and are linked to the use of affective information to guide and perform adaptive behavior (Bechara, Damasio, & Damasio, 2000; Pizzagalli et al., 2009b; Santesso et al., 2009; Treadway & Zald, 2011). Results from fMRI studies on reward processing suggest that healthy subjects recruit these areas more effectively than individuals at risk of depression and may represent a mechanism by which their ability to benefit from positive events is reduced.

Population with a history of repeated depression. Functional abnormalities in regions associated with reward processing are also apparent in people with previous episodes of
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depression. McCabe, Cowen, & Harmer (2009) examined the brain reactivity of participants, currently in remission with at least one previous episode of depression, compared to controls, while experiencing a hedonic event (e.g., eating chocolate, pictures of chocolate, strawberries). Despite no differences between the groups in stimulus ratings, patients showed decreased neural responses to the hedonic stimuli in the ventral striatum, caudate, and subgenual ACC. Furthermore, patients had a diminished neural supralinearity response (the potentiation produced by simultaneous presentation of the sight and flavor of the stimuli) in the VMPFC/medial OFC. This suggests that patients recovered from depression continue to demonstrate abnormal neural responses in regions that promote the affective value and subjective experience of a hedonic event. This reactivity may be a biomarker for continued vulnerability to depression.

Indeed, Hall, Milne, and MacQueen (2014) compared the neural response of controls, patients early in the course of depression (first lifetime episode), and remitted patients with a history of at least three previous episodes, during a reward reversal learning task with potentially small or large gains. When contrasting large vs. small gains, they found that both current and remitted depressive patients exhibited decreased reactivity in NAcc, LPFC, ACC compared to controls, but more so in remitted depressive patients with a history of chronic depression. As such, the reward system is activated greatest by controls during reward processing, less by patients early in the course of illness and least by patients with highly recurrent illness. The authors proposed that these areas may be sensitive to the impact of disease burden and may be exacerbated with repeated episodes of illness. Since each additional episode of MDD is marked by an increased risk of symptoms returning, this pattern during reward processing may be a marker of increased vulnerability to recurrent depression. These findings however have not been consistently reported (Dichter, Kozink, McClernon, & Smoski, 2012)
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Despite some inconsistencies in the sources of alterations, it is clear that across studies, dysregulation of structures involved in reward processing is a critical component of MDD; a pattern of processing that may underlie persistent difficulties with positive affect and a continued vulnerability to the disorder despite remission.

1.6 Treatment Effects on the Reward System in Depression

Recent investigations have attempted to delineate the interaction of these neural differences with various forms of treatment. One important question is whether the neural differences between MDD patients and non-depressed controls persist after treatment, or whether successful treatment eliminates or reduces such differences. The vast majority of studies addressing this question have used pharmacological antidepressant treatments and report normalization of pre-treatment activity (during the processing of negative events) in both cortical regions, including DMPFC/dorsal ACC and VMPFC/sub-genual ACC (Fitzgerald, Laird, Maller, & Daskalakis, 2008). It is likely however that different interventions exert their effects through different mechanisms of change (Ritchey, Dolcos, Eddington, Strauman, & Cabeza, 2011). For instance, Cognitive Behavioral Therapy (CBT) is an approach that emphasizes challenging and restructuring depressed patients’ cognitions (Hollon et al., 2002). Compared to pharmacological antidepressants or MBCT, this form of therapy may reflect a more “top-down” approach to managing problematic cognitions, patterns of responding and resolving depressive symptoms (Goldapple et al., 2004). Still, very few fMRI studies have examined whether problematic neural patterns during rewarding events can be rectified with effective treatment (Mayberg, 1997; Mayberg et al., 1999) and whether interventions differ in their effects on reward processing.
Cognitive-behavioral interventions. One study on CBT examined changes in the processing of emotional material (including positive) following treatment and report a pattern consistent with the hypothesis that interventions may normalize abnormal neural responses. Pretreatment activity in insula, MPFC, and DMPFC significantly decreased while viewing angry (vs happy face) from pre to post treatment, to a level similar to healthy controls (Klumpp, Fitzgerald, & Phan, 2013). These results may be interpreted as reflecting CBT’s effects on normalizing neural responses, reducing the differences between a “normal” and “depressed” brain’s response to an emotional event (Klumpp et al., 2013). To our knowledge, only one study has examined the effects of CBT on reward processing (Straub et al., 2015). In a sample of 22 medication naïve adolescents with MDD, the authors found that five sessions of cognitive behavioral group therapy (CBT-G) resulted in decreases in the left amygdala, left hippocampus, and right sgACC during the processing of win (vs. loss) trials. No change in ventral striatum activity was observed. This reduced pattern of activity in the sgACC was associated with decreases in depressive symptoms. This reduced, rather than increased, pattern of reward processing is contrary to what would be expected based on models of MDD and the alleviation of symptoms. An increased ability to react to rewarding events is arguably the “healthy” way of responding. The correlation between decreased activity and symptom improvement however suggest otherwise. Nonetheless, research thus far suggest that CBT-oriented intervention produce neurobiological changes that are relevant to treatment success. No study to date however has examined whether neurobiological changes are observed following interventions designed to reduce the risk of relapse, rather than the reduction of depressive symptoms during an acute MDD episode.

Mindfulness-based interventions. Neuroimaging studies on mindfulness support the hypothesis that the neural circuitry of reward is sensitive to mindfulness training (Garland et al.,
Nonpsychiatric populations show neural alterations in reward processing following mindfulness interventions, ranging from brief to long-term mindfulness practices. In a study by (Desbordes et al., 2012), participants received 8-weeks (2h sessions/week) of mindfulness-based training [Mindful Attention Training (MAT)] or an active control intervention consisting of a health discussion group (CTRL). In the MRI, participants were required to view and simply react naturally to a series of positive, negative and neutral pictures. This study found decreased activity in the right amygdala during the processing of positive, negative and neutral images in individuals that received mindfulness training compared to controls. These results suggest that training may reduce the habitual and automatic evaluation of whether stimuli is relevant, meaningful or threatening (Adolphs et al., 1999; Sander, Grafman, & Zalla, 2003). This is consistent with recent work using a cross-sectional design demonstrating that long-term mindfulness practice dampens habitual patterns of responding to reward (Kirk, Brown, & Downar, 2015a). This study found that meditators compared to matched controls demonstrated an improved ability to regulate anticipatory responses towards monetary gains or losses in a financial incentive task by dampening the dorsal striatum (caudate nucleus) during reward anticipation, and the VMPFC during reward receipt. Similarly, Kirk et al (2015b) found increased dorsal striatum (putamen) activity when anticipating a delayed hedonic event (i.e., fruit juice) in controls, while no such reactivity was observed in meditators.

Decreased activity in these regions during the anticipation and receipt of a pleasant event is consistent with the hypothesis that meditation training results in enduring changes in habitual responses, such as the monitoring and evaluation of whether an event is valuable, relevant to the self or more (Shapiro, Carlson, Astin, & Freedman, 2006). The central practice of mindfulness has been operationalized as cultivating an intentional, nonjudgmental form of attention focused on
experience as it unfolds in the present moment (Kabat-Zinn, 1994). Through continued focus on momentary physical sensation and viewing thoughts and reactions as mental events, mindful attention is thought to extinguish the flooding of elaborative cognitive, emotional, and behavioral responses that typically result from environmental or internal triggers. As such, it is expected that mindful individuals will be less reactive to external stimuli (Ortner, Kilner, & Zelazo, 2007), even when rewarding or positive in nature (Teper & Inzlicht, 2014).

In parallel, this shift from evaluative processing to non-judgmental awareness has been described in neuroimaging research as an increased integration of sensory information (Farb et al., 2007; Kilpatrick et al., 2011). Research on reward processing supports this view, such that a number of studies report increased recruitment of the insula and thalamus during the anticipation and receipt of reward. Elevated bilateral insula activation during monetary reward anticipation was observed in advanced meditators, compared to controls (Kirk et al., 2015a), as well as during value computation of a primary reward (fruit juice) in healthy participants following 8-weeks of mindfulness training (Kirk, Gu, Harvey, Fonagy, & Montague, 2014). More specifically, participants that received 8-weeks mindfulness training decoupled activity in the VMPFC during value computation (reflected by suppression of the VMPFC), and instead, recruited value signals that correlated with preference in the left mid/anterior insula. Similarly, Kirk et al. (2014) also reported increased insula and thalamus activity in meditators during the receipt and anticipation of a hedonic event (fruit juice) compared to controls. A similar pattern of responding is observed in patients following mindfulness training during the processing of negative emotional events (Farb et al., 2010; Farb, Anderson, Bloch, & Segal, 2011; Farb, Anderson, & Segal, 2012), characterized by a disengagement from elaborative cognitive processing (decreased MPFC) combined with increased somatosensory processing of that negative emotional event (insula). It is possible then
that mindfulness training is marked by a generalized pattern of letting both the “good” and the “bad” in, while reducing the need to evaluate and complicate these events. In the context of PA, pleasant events and emotions are usually less enduring, intense, and attention grabbing for individuals biased towards depressive cognitions (Baumeister, Bratslavsky, Finkenauer, & Vohs, 2001). This training may help these individuals vulnerable to depression reduce their tendency to overthink pleasant events and improve awareness of the rewarding nature of an event through the senses (Schroevers & Brandsma, 2010). These processes, and underlying neurobiological mechanisms, may be responsible for the improvements in PA following MBCT observed in previous research. Still, no study to date has examined the specific effects of MBCT on reward processing.

To our knowledge, no study to date has examined the effects of maintenance psychotherapy on the reward system and whether these changes predict their prophylactic effects. The influence of MBCT and CBT-WB on reward-related experiences, such as increased PA and reports of contentment, do however suggest that these interventions may affect reward processes in the brain.

1.7 Objectives of the Study

There is significant evidence suggesting that maintenance interventions help reduce the risk of recurrent depression. Yet, little is known regarding their effects on the reward system despite its relevance to depression. Moreover, no study to date has examined whether neurobiological changes in this system following maintenance psychotherapy have prophylactic effects. Therefore, this study aimed to extend findings by examining the neural correlates of reward processing that may signal change in recovered depressed patients and whether this pattern of reward processing has lasting prophylactic effects. In addition, this study will examine whether
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Activation during reward is associated to positive and negative functioning in depression. More specifically, this study will examine whether:

1) Interventions designed to prevent the recurrence of depression alter activity in the reward system during the anticipation and consummation of a rewarding event.

2) Changes in reward processing following MBCT and CBT-WB predict relapse status during a two-year follow-up period.

3) MBCT and CBT-WB demonstrate unique patterns of change on the reward system.

4) Differences in reward processing are related to measures of depression and positive functioning following treatment.

1.8 Specific hypotheses

1) Maintenance interventions will promote increased recruitment of regions involved in the reward-related deficits observed in MDD (i.e., OFC, ACC, DS, insula, VS, caudate, VMPFC, IFG) during the processing of a rewarding event (i.e., anticipation to win, win trials).

2) Decreased recruitment or a pattern of no change following MBCT and/or CBT-WB will be predictive of relapse status during the two-year follow-up.

3) The neurobiological changes observed in reward processing following treatment will differ between MBCT and CBT-WB:

   a) CBT-WB training will result in increased recruitment of prefrontal, DS, NAcc, and ACC activity; a pattern reflective of the normalizing effects of treatment on the brain.

   b) MBCT will result in increased activity in regions involved in interoceptive awareness and somatosensory processing (e.g., insula, somatosensory cortex, thalamus), as well as decreased elaborative processing of reward-related events (e.g., decreased PFC).
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1. Increases in reward processing following treatment will be associated with increased positive functioning and decreased depression-related features, as measured using self-report.

2  Method

2.1 Participants

Patients were recruited for neuroimaging from a larger clinical study titled the Mood Balance Project (MBP) through the Centre for Addiction and Mental Health in Toronto, Canada (N=97). Participants who were enrolled in the MBP had previously experienced at least one episode of MDD. Individuals were excluded if they were experiencing a full episode of major depression at the time of study, or met diagnostic criteria for schizophrenia or current psychosis; organic mental disorder or pervasive developmental disorder; current substance dependence; imminent suicide or homicide risk; an Axis I or II disorder that required primary treatment; or started or changed antidepressant medication within the eight weeks leading up to intervention. Participants on a pharmacological maintenance regimen were asked to keep medication doses stable for the 4 weeks preceding randomization. Additional exclusion criteria included the following: (a) electroconvulsive therapy (ECT) or repetitive transcranial magnetic stimulation (rTMS) within the past 6 months; (b) unwilling to be randomly assigned to either group treatment; (c) current contemplative practice (e.g. meditation, yoga); (d) had surgery or have condition (e.g. claustrophobia) that prevents participant from undergoing fMRI scanning.

2.2 Procedures

All study procedures were approved by the Centre for Addiction and Mental Health and the University of Toronto. Ninety-eight participants were recruited through clinical referrals, physician outreach and from media announcements that describe the study and clinic. All participants provided written consent prior to any research activity and after the procedures were
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fully explained. Prior to scanning, all subjects met with a licensed psychologist to determine MDD remission status based on the Structured Clinical Interview for DSM Disorders (SCID: First; et al., 2002) and Hamilton Rating Scale for Depression (Hamilton, 1980). After baseline assessment, participants were randomized to either Mindfulness-based Cognitive Therapy (N= 55) or group Cognitive Behavioral Therapy adapted for maintaining wellbeing following remission (N= 43). Patients were assigned to MBCT or CBT-WB via block randomization, utilizing a block size of 8 using computer generated quasi-random numbers. Participants completed a fMRI scan within the two weeks prior to treatment and within two weeks following the 8th (final) session of treatment. Once in the scanner, anatomical and functional scans were collected. Participants engaged in three 6-8 min runs of a card gambling task during functional scan acquisition. Participants were compensated for their time, regardless of their performance on the task. Participants also completed a battery of questionnaires before and after treatment, and were assessed for the return of depressive symptoms at follow-up sessions bi-monthly over a 24-month period. Following an intention-to-treat analysis approach, participants were not excluded based on the number of sessions attended and were analyzed according to the randomization scheme of this study.

Therapists

Research therapists were recruited from the Cognitive Behaviour Clinic at CAMH. Eligible therapists were mental health practitioners possessing a minimum of five years of experience with the administration of either CBT or MBCT for preventing depressive relapse. Twelve therapists (six per psychological treatment condition) were recruited and assigned to the intervention matching their therapeutic orientation. All therapy sessions were audio recorded and used for treatment adherence rating at a later date.
2.3 Treatment Conditions

**Mindfulness Based Cognitive Therapy.** MBCT was provided in group format for a total of eight weekly two-hour sessions according to the protocol outlined by (Segal et al., 2002). Each group had an average of twelve participants as recommended. Mindfulness was taught through eating, sitting, lying, and walking meditations, gentle yoga practices, and group discussions facilitated by MBCT therapists. The program included 45 minutes of daily homework with CD-guided and self-guided mindfulness practices. These practices are designed to train moment-by-moment nonjudgmental awareness of bodily sensations, thoughts, and feelings, together with the application of awareness skills in daily life. One of the objectives of MBCT is to help participants become more aware of the different modes of the mind (e.g., automatic pilot) and develop a metacognitive stance to their thoughts, feelings, and sensations when they arise.

**Cognitive Behavior Therapy for Wellbeing.** CBT-WB was provided in group format for a total of eight weekly two-hour sessions according to the protocol outlined by (Fava, Rafanelli, Cazzaro, Conti, & Grandi, 1998). In-group sessions had an average of eight participants per group. Strategies and techniques were used to help participants: (a) increase routines of self-care, sleep, level of activity and engagement in pleasurable activities; (b) identify cognitive distortions that undermine the impact of positive daily events, (c) respond to negative thinking and underlying dysfunctional beliefs; and (d) learn about the factors promoting psychological wellbeing (e.g., purpose in life, self-acceptance, autonomy, environmental mastery) and discuss how to develop these strengths. Participants completed daily homework and thought records to assess their cognitions and behaviours relating to wellbeing. The focus is on promoting positive prognostic factors in addition to reducing the negative in the management of MDD.
2.4 Measures

Demographics. The SCID Overview and Demographics Information form were used to collect demographic (e.g., gender, age, education) and clinical information (e.g., age of onset of first MDE) from the participant.

Depression. Three behavioral measures to index the severity of depressive symptoms, dysphoric or self-critical mood, and dysfunctional beliefs related to MDD, were included in analyses to provide a more sensitive index of depressive features than the bivariate outcome of relapse status. These include the: (a) Hamilton Rating Scale for Depression (HRSD; Hamilton, 1980), as a measure of depression severity; (b) Depressed States Checklist (DSC; Teasdale & Cox, 2001b); and (c) the Dysfunctional Attitude Scale (DAS; Weissman & Beck, 1978) as a measure of dysfunctional attitudes about the self (see Appendix A for description).

Positive functioning. Three measures of hedonic and eudaimonic functioning were employed to determine changes in positive functioning. These measures were of particular interest in this study given the focus on modelling reward-related activity as a reflection of the mechanisms underlying positive affect. Measures included in the analysis included the positive affect subscale of the Positive Affect and Negative Affect Scale (PANAS; Watson, Clark, & Carey, 1988), the Satisfaction with Life Scale (SWLS; Diener, Emmons, Larsen, & Griffin, 1985) and the Wellbeing Scale (Ryff, 1989b) as measures of hedonic functioning, satisfaction with life, and eudaimonic functioning respectively (see Appendix A). These measures are independent from measures of depression and used to quantify hedonic and eudaimonic functioning (Ryff, 2014; Huta & Hawley, 2010).
2.5 Relapse Criteria

Relapse status was monitored during a two-year follow-up and determined based on the 16-item Quick Inventory of Depressive Symptomatology (QIDS) (Rush et al., 2003). The QUIDS assesses all the criterion symptom domains designated by the DSM-IV (APA 1994) to diagnose a major depressive episode. It is employed to screen for depression and as a measure of symptom severity. It demonstrates adequate criterion validity, with scores comparable to those obtained by the HRSD and BDI ($r=0.95$ and $r=0.88$ respectively). Patients were judged to have an episode of major depression if they had a score of 12 or higher at any point during the two-year follow-up. This cut-off score is indicative of a moderate level of depression severity and is considered a lenient threshold for establishing relapse status.

2.6 FMRI card gambling task

This study used a modified event-related version of a card-guessing/reward task developed by Delgado and colleagues (2003; 2000). In this task, a series of 75 trials were used, divided into three runs of 25 trials each. Each trial lasted approximately 14-16 seconds.

At the beginning of the fMRI task, participants were reminded of the instructions for the card game and to maximize the number of “wins”. Each trial began with two visually displayed card projected onto a screen. The cards had unknown values ranging from 1 to 10, and subjects were asked to guess which card (from the left or right deck) had the greatest value. There were no learning component to this task and no monetary rewards as an incentive for correct guesses. Participants had two seconds to select a deck with the greatest value (exactly 2s), via pressing one of two buttons fiber optically coupled to a data acquisition computer outside of the magnet room, which recorded the selected deck and value of the card. Following a waiting period (1.5-2.0s), the card from the left deck was then flipped over to display its value (3.5-5.0s). During this time, it is
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assumed that participants are “anticipating win” or “anticipating loss” based on the value of the presented card. The closer the value of the card is to 10, the lower the anticipation to win. The card from the right deck is then flipped and presented (3.5-5.0). At this stage, subjects can establish whether this trial consisted of a win or a loss. This is followed by an insight period whereby participants are asked to indicate whether they have won or lost this trial (1.5s). There was an 1-2 second delay before the onset of the next trial, during which time a fixation cross was shown. Thus each trial ranged between 13-17.5 seconds in duration, allowing for a distribution of timings between the anticipation (first card shown) and result (second card shown) phases of the trial; the random jitter, varying the timing of the presentation of the stimuli, allows for a mean hemodynamic response to be calculated at the end. Before MRI scanning, all participants completed a short practice session.

Regressors. For the purposes of this study, analyses concentrated on modeling reward-relevant events and excluded loss trials. This study modeled participants’ response during Anticipation to Win (when the first card is flipped over) and during Outcome Win (when the second card is flipped, and value of the card selected by the participant is greater).

The condition Anticipation to Win will be coded as a continuous variable, reflecting the probability of winning using the following equation, whereby X is the value of the first card presented during each trial.

If X was not selected by the participant:

\[ a_0 = \text{Anticipation to win} = 11 - X \]

If X was the card selected by the participant:

\[ a_0 = \text{Anticipation to win} = X \]
The condition Outcome Win was similarly coded as a continuous variable. However, the degree of felt win in this task was not dependent on monetary incentive which is typically employed in fMRI reward-related research. Rather, the degree to which the outcome was rewarding (felt win) was modeled as a product of performance-related variables.

Research has shown that successful performance during a task is intrinsically rewarding and activates the reward system (Hoeft, Watson, Kesler, Bettinger, & Reiss, 2008; Klasen, Weber, Kircher, Mathiak, & Mathiak, 2012; Koepp et al., 1998; Ravaja, Saari, Salminen, Laarni, & Kallinen, 2006). Features of performance, such as the degree to which expectations were violated (i.e., violation of expectations) and the degree to which the outcome was better than predicted (i.e., prediction error), are known to modulate the mesocorticolimbic system of reward (Reynolds & Berridge, 2002; Seymour et al., 2005; Tobler, O’doherty, Dolan, & Schultz, 2006; Yacubian et al., 2006). As such, the outcome win trials were modelled to capture the intrinsically rewarding effects of successful performance, as well as the degree of felt win, as a product of expectancy violation and prediction error (Appendix A). Degree of felt win as a parametric modulator was calculated using the initial probability of winning based on the value of expectation to win (violation of expectation) and the value by which they won (prediction error).

\[ x = \text{Winning card value} \]

\[ a_0 = \text{Anticipation to win} \]

\[ P(a_0) = \text{Probability of winning with given anticipation} = \frac{(a_0 - 1)}{9} \]

\[ f(x) = \frac{1}{P(a_0)} + \left| x - \frac{a_0 - 1}{2} \right| \]
2.7 Imaging Data

**Setup.** Imaging data were collected with a Siemens Trio 3.0-Tesla scanner (Siemens Medical Solutions, Erlangen, Germany). The event-related design experiment was designed and implemented using the Visual Basic programming language (version Visual Studio 2005; Microsoft, Redmond, Washington). Before scanning, participants were provided with instructions and an opportunity to practice the fMRI task.

**Structural imaging.** For each participant, a three-dimensional magnetization prepared rapid gradient echo pulse sequence was employed to obtain a high-resolution T1-weighted structural volume. Functional Imaging. For each subject, a T2*-weighted gradient-echo echo-planar image (EPI) pulse sequence was prescribed and higher order shimmed for the functional trials.

**Preprocessing.** Functional activation was determined from the BOLD signal using the software Statistical Parametric Mapping (SPM12, University College London, United Kingdom; http://www.fil.ion.ucl.ac.uk/spm/software/spm12). Following image reconstruction (SPM12 DICOM import utility), the time series data for each participant were motion-corrected and coregistered with their T1-weighted structural image. The T1 image was bias-corrected and segmented using template (International Consortium for Brain Mapping) tissue probability maps for gray and white matter and cerebrospinal fluid. Warping parameters were obtained from the tissue segmentation procedure and subsequently applied to the time-series data (resampling to 3mm³ voxels). The time-series data were spatially smoothed to a 6 mm³ full-width half maximum Gaussian kernel. Lastly, a voxel level detrending procedure was applied to remove time-series components correlated with global fluctuations in the BOLD signal (15).
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**First-level statistical models.** Participants who did not complete the second fMRI were excluded from analyses. Trials were excluded if participants provided no response during the card selection or insight period. Only runs with 16 or more trials (2 SD) were included in the final analyses. A total of 20 participants were excluded on account of missing data at post-treatment or task performance (N=77).

Single subject time series data were submitted to first-level general linear statistical models. Two conditions were modelled for each trial: (1) anticipation to win, and (2) outcome win. Anticipation to win was modeled by a parametric regressor modulated by the reward expectancy. Win trials for each participant were modeled by a parametric regressor modulated by violation of expectation and the degree of prediction error. Six motion parameters were included as regressors of no interest. Using the SPM12 design specification, all regressors were convolved with a standard canonical hemodynamic response function. Each model included high-pass filtering to remove low frequency signal drift (period = 128 s), and the AR1 method of estimating temporal autocorrelation.

**Second-level random effects analyses.** Whole-brain analyses corrected for multiple comparisons were performed for our contrasts of interest (i.e., anticipation to win, outcome win). Participant reactivity maps from the first-level of analysis were subjected to a three-way mixed ANOVA to examine the main and interaction effects of Relapse (norelapse vs. relapse), Treatment (MBCT vs. CBT), and within-group factor of Time (T1 vs. T2). Activity surviving a threshold of $P < 0.005$, with a cluster ($k$) $\geq 19$ was considered significant for all analyses, corrected at cluster threshold. This threshold had an overall significance level of $p < .05$ corrected for multiple comparisons across the whole-brain established via a Monte-Carlo simulation using 3dClustSim module of the Analysis of Functional Neuroimages software (Cox, 1996). Median signal value,
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collapsed across multiple voxels, was extracted from clusters showing interaction or main effects
during whole-brain analyses using REX package (Duff, Cunnington, & Egan, 2007). BOLD signal
response time courses were extracted from each subject's region of interest (ROI) and median
retained across subjects. Follow-up t-tests were conducted on these functional regions of interest
(ROIs) derived from the group analysis.

Validity check. To verify whether the paradigm had activated reward associated brain
regions, individual contrast images of the parameter estimates for all participants were submitted
to one-sample t-tests, in which whole-brain comparisons were computed to identify anticipation
to win and outcome win responses that should match brain regions as established in previous
studies (Pizzagalli et al., 2009; Smoski, Rittenberg, & Dichter, 2011).

Explanatory variable analysis. To relate neural reactivity to clinical measures, reward-
related median signal values extracted from significant clusters were tested for correlations with
measures of positive functioning and depression. All correlations were computed as rank order
(raw) correlations.

Clinical and Neural predictors of relapse. We applied a logistic regression model using
the bivariate outcome variable of relapse status to examine the relative contribution of fMRI and
clinical predictors on relapse classification. First, a forward step regression was performed with
self-report measures to produce a predictive model of relapse dependent on clinical status
following treatment. Second, a forward step regression using median signal values extracted from
significant ROIs was performed to establish a list of neural predictors. Next, forced entry block
analyses helped examine the relative contribution of clinical measures and neural measures to
predictions of relapse.
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Exploratory analysis. To examine whether these regions were consistent markers of relapse status, a second fMRI model (Model 2) for our task was created using a more stringent relapse criteria based on Module A ratings of the SCID. Participants were considered to have relapsed if they reported depression, anhedonia, or a number of additional depressive symptoms on the SCID. However, these participants did not formally meet full criteria for a diagnosis of MDD according to the DSM-IV-TR (APA, 1994), reporting less symptoms than required to meet criterion A (less than 5 depressive symptoms), and/or symptoms were not present for more than two weeks. Ratings were determined by a research assistant trained in the SCID, Module A, and verified by a research psychiatrist (with an inter-rated reliability, Cohen’s K, of 0.85). This model yielded a total of 60 norelapse participants and 17 relapse participants. General linear mixed models were applied to examine whether activity in relapse ROIs remained significant predictors of relapse in Model 2.

3 Results

3.1 Patient Characteristics and Clinical Outcome

Demographics. MBCT and CBT groups did not differ on demographic indicators of gender, age, and ethnicity (Table 1). Significant differences in education were noted, whereby CBT was composed of a greater number of participant with 12-13 years of education or less (completed high school). However, the number of participants in the MBCT condition with this level of education (N=2) was below the threshold recommended for Chi-Square analyses. The differences noted in education may not reflect a truly significant result (p=.049). Furthermore, chi-square analyses were performed to examine whether current pharmacotherapy would confound differences observed in reward responses. No differences were found in both relapse and norelapse
(χ²(1) = .733, p=.39), as well as MBCT and CBT-WB (χ²(1)=2.51, p=.113), in the number of participants on medication at baseline.

Clinical outcome. Overall, there were no significant group differences in outcome, but both groups experienced significant growth in positive functioning following treatment. Multivariate repeated-measures ANOVA comparing treatment conditions found no significant group differences in clinical measures at baseline or post-treatment, F(1,75)=1.39, p=.695 (Table 2). There was a significant main effect for time [F(1, 75)=3.52, p=.001], with post-hoc analyses suggesting significantly large effects of treatment on measures of positive functioning (Table 2). No significant differences between relapse and norelapse participants were noted [F(1, 75)=1.2, p=.3] nor any Time x Relapse interactions [F(1, 75)=.45, p=.94]. Exploratory t-tests established a priori and corrected for multiple comparison using Bonferroni correction (p=.007) were performed on measures of positive functioning to help clarify fMRI reward-related results. At post-treatment, relapse participants reported significantly less satisfaction with life and WBS eudaimonic functioning (see Table 1, Appendix C).

Patient relapse. A total of 30 participants in the fMRI study relapsed. Of these, 27 were included in analyses and consisted of 14 MBCT and 13 CBT participants. Chi-square analysis suggested equivalent relapse rates between groups (χ² =.269; p=0.6). There are no significant differences between treatment groups in the number of participants who relapsed [t(75) = -.513, p=.61], and days until relapse [t(75) = .66, p = .51]. Patients relapsed, on average, 15 months (SD= 9.5) into the 24-month follow-up period in MBCT and 13.55 (SD= 9.5) months in CBT.

Clinical predictors of relapse. To identify features of the clinical presentation that might be predictive of relapse, correlational analyses examined the relationship between demographics
and clinical measures (baseline, post-treatment, and change scores) with relapse outcome (Table 3). There were no significant correlations between age \(r(75)=-.11, p=.222\), number of previous episodes \(r(75)=.141, p=.222\), and gender \(r(75)=.09, p=.442\) with relapse status. Clinical measures at post-treatment were particularly related to relapse status. Only dysphoric mood at baseline was significantly associated with relapse. No changes from pre-treatment to post-treatment were significantly predictive of relapse.

**Logistic regression.** A forward LR binomial logistic regression was performed to ascertain the effects of clinical outcome (at post-treatment) on the likelihood that participants will relapse. Of the 12 clinical predictor variables, our overall best model consisted of one predictor, WBS environmental mastery. This final model was statistically significant, \(\chi^2(1) = 10.12, p=.001\) and Hosmer and Lemeshow test suggests goodness of fit, \(\chi^2(7) = 2.15, p=.95\). The model explained 17% (Nagelkerke \(R^2\)) of the variance in relapse and correctly classified 71.4% of cases (vs. 64.9%, predictions based on assuming that all participants did not relapse). Sensitivity was 37%, specificity was 90%, suggesting that the model is particularly effective at predicting norelapse (vs. relapse). Of all cases that were predicted to have relapsed, 37% of them were correctly identified (positive predictive value), while 72.6% were correctly identified for norelapse. For each unit reduction in WBS environmental mastery (ranging from 7 to 42), the odds of relapsing increased by 11%, \(B(1)=-.14, p=.005, 95\%\ CI [.789, .958]\).

### 3.2 Imaging Results

Data analysis was divided into the anticipation and outcome periods to examine the potentially different importance of expectancy vs. feedback effects in characterizing treatment effects and relapse vulnerability. For each period, we performed whole brain analyses of the effects of Time x Group x Relapse on the estimates of anticipation/feedback parametric response.
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3.3 Anticipation to win

**Main effect of task.** Anticipation to win collapsed across all groups and across time revealed a neural pattern consistent with previous neuroimaging studies on reward expectancy, such as the striatum, medial OFC and thalamus, (Table 2, Appendix C).

**Main effect of Relapse.** Relapse status during anticipation to win was associated with significant activity in a cluster including the medial OFC, VMPFC and rostral ACC, $F(1, 146)=13.52, p=0.0003$ (Table 4, Figure 1A). Follow-up t-tests revealed that relapse was associated with a weaker coupling between medial OFC/VMPFC activation and the degree of anticipation.

This pattern was stable across time: the reduced activity associated with relapse was apparent both at baseline [$t(75)=2.77, p=0.007$] and following treatment [$t(75)=2.87, p=0.005$], and there was no interaction between relapse status and time.

**Interaction effect – Treatment x Time.** Differences between MBCT and CBT-WB conditions during anticipation to win were observed in the hippocampus [$F(1, 146)=13.52, p=0.0003$] and precuneus [$F(1, 146)=13.52, p=0.0003$] and several structures in the parietal region (Table 4, Figure 1B). Follow-up t-tests demonstrated that this interaction effect resulted from increases specific to MBCT.

For the hippocampus, MBCT participants demonstrated significant gain in hippocampal activity from pre to post-treatment [$t(42)=-2.61, p=0.012$], compared to no significant change following CBT-WB [$t(33)=1.75, p=0.089$]. There was significantly more activity in the hippocampus [$t(75)=3.58, p=0.001$] at post-treatment in MBCT (vs. CBT). Similarly for the precuneus, activity increased following MBCT [$t(42)= 2.08, p=0.044$], while significantly decreased was observed following CBT [$t(33)= 2.44, p=0.02$]. There was significantly more
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activity in the precuneus in MBCT participants at post-treatment, than CBT participants \[t(73)=2.82, p=0.006\]. There were no Treatment x Time effects in any additional ROIs.

**Other.** Whole-brain analysis indicated no significant three-way interaction, Treatment x Relapse interaction, or Time x Relapse interaction effects. In addition, there were no main effects for Time or for Group.

**Psychometric correlations.** Spearman correlations were performed to examine the relationship between treatment outcome and neural responses to anticipating a win at post-treatment (see Table 1, Appendix D). Rostral ACC/VMPFC cluster activity at post-treatment was linked to lower depression symptoms (Table 1, Appendix D). Greater reactivity in the hippocampus at post-treatment was negatively correlated with measures of dysfunctional attitude and depression severity. Correlation analyses were also conducted separately within the MBCT and CBT groups, but no group-specific differences were detected.

### 3.4 Outcome win

Outcome win collapsed across all groups (treatment and relapse) and across time revealed a neural pattern consistent with previous neuroimaging studies on reward processing, including the pallidium, insula, LPFC, and MPFC (Table 3, Appendix C). Results from the whole-brain analysis yielded a significant interaction for Treatment x Relapse and Time x Relapse.

**Interaction effect - Treatment x Relapse.** A general pattern emerged whereby there were significant differences between norelapse and relapse participants in MBCT at post-treatment (but not at baseline), and at pre-treatment in CBT (but not at post-treatment). This effect was primarily located in parieto-temporal regions (Table 4, Figure 2).

In MBCT, post-hoc analyses demonstrated greater recruitment of the precuneus \[t(41)=-2.57, p=0.014\], middle temporal \[t(41)=-2.84, p=.007\], mid-cingulum/PCC \[t(41)=-2.27, p=.028\]
and superior temporal \([t(41)=-2.27, \ p=.028]\) with the degree of “felt win” in MBCT-relapse participants (vs. MBCT-norelapse) at post-treatment during. No significant differences in these regions were noted at baseline, suggesting that this pattern of increased reactivity results from the effects of treatment (or time) on this population.

In CBT-WB, relapse participants (vs. norelapse) demonstrated significantly lower activity in the precuneus \([t(32)=4.1, \ p<.001]\), middle temporal \([t(32)=3.23, \ p=.003]\), mid-cingulum/PCC \([t(32)=4.19, \ p<.001]\), and superior temporal \([t(32)=3.58, \ p=.001]\) at baseline. Differences between relapse conditions were no longer significant at post-treatment in any parieto-temporal region (e.g., precuneus \([t(32)=.55, \ p=.59]\)). CBT-relapse participants demonstrated a pattern consistent with the normalization of brain activity following treatment, whereby baseline hypoactivity significantly increased from pre- to post-treatment - in the precuneus \([F(1, 32)=6.74, \ p=.01]\) and the mid-cingulum \([F(1, 32)=4.06, \ p=.05]\) – to resemble that of a less vulnerable population (CBT-norelapse).

**Interaction effect – Time x Relapse.** Differences between relapse and norelapse conditions during anticipation to win were observed in dorsal striatal, insular, frontal, and temporo-parietal regions (Table 5, Figure 3). Follow-up t-tests demonstrated that this interaction effect resulted from increases specific to relapse participants.

Overall, relapse participants demonstrated an increased reactivity to winning in the caudate \([t(26)=-3.63, \ p=.001]\), putamen \([t(26)=-3.12, \ p=.004]\), MPFC \([t(26)=-3.36, \ p=.002]\), superior temporal \([t(26)=-3.8, \ p=.001]\), precuneus \([t(26)=-3.72, \ p=.001]\), insula \([t(26)=-2.43, \ p=.02]\) and DMPFC \([t(26)=-3.04, \ p=.005]\). The degree of activity in these regions at post-treatment was significantly greater in relapse compared to norelapse \([F(1,75)=2.36, \ p=.02]\).
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**Other.** Whole-brain analysis indicated no significant three-way interaction, or Treatment x Time interaction.

**Psychometric correlations.** Spearman correlations were performed to examine the relationship between treatment outcome and neural responses to winning at post-treatment (Table 2-4, Appendix D).

**Treatment x Relapse.** Overall, increased recruitment of the superior and middle temporal following treatment correlated with more dysphoric mood (Table 2, Appendix D). Exploratory analyses were also conducted separately for MBCT and CBT groups and subjected to Fisher z transformations to examine whether within group correlations significantly differed between groups (Table 3, Appendix D). Of interest, the change observed from pre- to post-treatment was associated with lower depressive symptoms and greater WBS sense of environmental mastery in MBCT, while this same increase was negatively related with clinical outcome in CBT (at trend-level). These correlations were significantly different according to Fisher’s z transformations in the mid-cingulum (z=2.67, \( p=.007 \)) and middle temporal (z=2.57, \( p=.01 \)) for HRSD depression and precuneus for WBS environmental mastery (z=2.26, \( p=.02 \)). These findings suggest that increased reactivity to the experience of a win, in these regions, is not consistently related to negative clinical outcomes depending on treatment.

**Time x Relapse.** Correlations between clinical measures and Treatment x Relapse interactions are summarized in Table 4 (Appendix D). Overall, increased activity in these regions was predictive of negative prognostic factors. In particular, greater DMPFC activity during a win was associated with greater dysfunctional attitudes (DAS), negative views of the self (DSC Self-Concept), dysphoric mood (DSC mood), and lower SLS satisfaction with life at post-treatment. Increases in dorsal striatal activity however related to greater reports of positive affect in one’s
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daily life (PANAS positive) at post-treatment. This discrepancy alludes to the presence of mood-related inconsistencies associated with neural responses unique to relapse. Exploratory correlation analyses were also conducted separately within relapse and noRelapse groups, but no group-specific differences were found.

3.5 Predictors of Relapse

A forward LR binomial logistic regression was performed to examine whether changes in reward processing were predictive of relapse. In addition, a forced entry binomial logistic regression was performed to ascertain the incremental contribution of neural outcome to predictions based on clinical and demographic variables.

Neural predictors of relapse. First, correlations between relapse status and median signal values extracted from functional ROIs (baseline, post-treatment, change scores) were performed to examine the relationship between potential predictors and relapse status. Overall, changes from pre- to post-treatment were particularly related to relapse (Table 6)

A forward LR binomial logistic regression was performed to ascertain the effects of post-treatment neural responses on the likelihood that participants will relapse. Post-treatment neural responses were selected as predictors (rather than change scores) to examine the relative contribution of brain and clinical responses at a similar time point. Of the 12 fMRI predictor variables, our overall best model consisted of three predictors (Table 5A, Appendix D). Activity in the rostral ACC/VMPFC, DMPFC, and putamen were significant predictors of relapse, $\chi^2(3) = 31.18, p<.001$ and Hosmer and Lemeshow test suggests goodness of fit, $\chi^2(8) = 8.46, p=.39$. The model explained 45.8% (Nagelkerke $R^2$) of the variance in relapse and correctly classified 80.5% of cases (vs. 64.9%, predictions based on assuming that all participants did not relapse). Sensitivity was 59.3%, specificity was 92%, suggesting that the model is particularly effective at predicting
norelapse (vs. relapse). Of all cases that were predicted to have relapsed, 80% of them were correctly identified (positive predictive value), while 80.7% were correctly identified for norelapse. Increases in VMPFC are associated with decreases in the risk of relapse, $B(1)=-11.11$, $p=.003$. Increases in MPFC [$B(1)=3.05$, $p=.034$] and putamen activity [$B(1)=4.49$, $p=.007$] are associated with an increased risk of relapse.

**Neural and clinical predictors of relapse.** A block-wise regression was performed to examine the relative contributions of demographic, clinical and neural predictors to relapse (Table 5B, Appendix D). Demographics were entered in the first step of the model and included previously reported predictors of relapse (Burcusa & Iacono, 2007). This included age (at the time of treatment), gender, and included clinical features, such as age of first depressive episode and number of previous episodes. WBS environmental mastery at post-treatment was entered at the second step, followed by the neural predictors in the third final step.

Demographics were not significant predictors of relapse, $\chi^2(4) = 8.46$, $p=.342$, over and above predictions based on probability alone (predictions based on assuming that all participants did not relapse). WBS environmental mastery significantly improved predictions, $\chi^2(1)=11.5$, $p=.001$, correctly classifying 68.9% of cases (vs. 66.2% of cases using demographics as predictors). Decreased activity in the VMPFC (during anticipation) combined with increased activity in the MPFC and putamen (during win) significantly improved the overall model, $\chi^2(3)=27.82$, $p<.001$, correctly classifying 86.5% of cases (vs. 68.9% of cases using demographics and clinical as predictors). Overall, this final model accounted for 61.5% of the variance in relapse (vs. 26.8% using clinical and demographics as predictors). These findings suggest that both clinical and fMRI variables provide unique contributions to the prediction of relapse.
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Linearity of the continuous variables with respect to the logit of the dependent variable was assessed via the Box-Tidwell (1962) procedure. Based on this assessment, all continuous independent variables were found to be linearly related to the logit of the dependent variable. Correlations and linear regressions were performed testing for collinearity. No significant correlations between predictors were found. In addition, non-significant variance inflation factors and low tolerance indicators suggest minimal multi-collinearity for each predictor. However, wide confidence intervals for the regression coefficients of MPFC and putamen are indicative of unstable predictors (Table 5B, Appendix D)

Supplementary imaging analysis. A second fMRI model (Model 2) was created using a more stringent relapse criteria based on a subthreshold diagnosis of MDD using the SCID. In total, 16 participants relapsed (MBCT N=9; CBT N=7). The small sample size of relapse participants limited whole-brain analyses. The model was not sufficiently powered to reproduce relapse-related interaction effects and to determine the likelihood of true effects. Exploratory analyses using an ROI approach was performed to examine whether regions identified in Model 1 remained predictive of relapse in Model 2. In SPSS, a priori tests using the extracted median values from the coordinates of relapse-related ROIs in Model 1 were evaluated for the main and interaction effects of relapse based on stringent relapse status (Model 2). These results are summarized in Table 6 in Appendix D. Overall, the rostral ACC/VMPFC during anticipation to win remained significantly different between relapse and norelapse. A Time x Relapse interaction was significant for the DMPFC, MPFC, and putamen, however post-hoc tests did not yield significant differences at post-treatment between relapse and norelapse likely as a result of sample size. The middle temporal (Treatment x Relapse) during win, remained a significant indicators of relapse status in
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Model 2. Together, these exploratory findings suggest that these regions may be sensitive to the degree of relapse risk.

4 Discussion

The objective of the present study was to elucidate treatment and relapse-related changes in brain function during reward processing in previously depressed patients and their relationship with clinical outcome. Overall, this study found that both interventions resulted in clinical improvements in positive functioning. However, contrary to our initial hypotheses, changes in reward processing following maintenance treatment related to an increased risk of relapse, rather than the prophylactic effects of these interventions.

4.1 Clinical Outcome Following MBCT and CBT-WB

Depression. MBCT and CBT did not result in significant changes over time in measures of depression. However, changes in depression were not expected given remission status at baseline. The objective of maintenance interventions is to prevent the recurrence of depression, rather than further alleviate depressive symptoms. As such, the absence of significant change on depression-related measures is clinically meaningful and suggests that remission was maintained.

Positive functioning. Changes in measures of positive functioning however were present. Both MBCT and CBT-WB resulted in increases in autonomy and self-acceptance as measured using the WBS. Increases in autonomy reflect the degree to which participants viewed themselves to be living in accord with their own personal convictions (Ryff, 2014). Increases in self-acceptance reflect the knowledge and acceptance they have of themselves, including awareness of personal limitations (Ryff, 2014). These indicators are believed to reflect an eudaimonic approach to wellbeing, marked by growth, self-realization, and meaning as primary sources of positive affect, rather than a hedonic approach focused on feeling good, happy, positive, or satisfied with
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life (Ryff, 2014). Change in these domains are expected within the context of CBT-WB which was developed using an eudaimonic approach to relapse prevention and maintained wellness (Fava et al., 1998). This is the first study however to report changes in eudaimonic functioning following MBCT.

Despite not explicitly addressing themes of self-realization and human virtue, training in mindfulness meditation in combination with CBT seemingly helps previously depressed patients promote change in these domains. This is consistent with theories on mindfulness training within the context of clinical care. In the mindfulness-to-meaning theory, Garland, Farb, Goldin, and Fredrickson (2015) argue that mindfulness training helps promote positive reappraisals of the self and world to enhance eudaimonic wellbeing. By fostering nonjudgmental attention, reducing mind wandering, and improving perceptual processing, mindfulness practices may help foster a metacognitive state that transforms how one attends to experiences. In turn, this defusion from the self is argued to facilitate objective appraisals, perspective taking, and self-inquiry that facilitate eudaimonic affect and adaptive behavior (Dahl, Lutz, & Davidson, 2015). Although speculative, results of this study suggest that mindfulness training within the context of MBCT may help broaden the scope of appraisal to appreciate the value of self, including one’s limitations, as a vehicle for personal growth and action.

Clinical outcome and relapse. This study found that within group variance in measures of eudaimonic functioning was particularly relevant for predictions of relapse. Elevations in (a) autonomy, (b) self-acceptance, (c) living with meaning, purpose, and direction (purpose in life), (d) using one’s personal talents (personal growth), and (e) ability to manage one’s life situations (environmental mastery) at post-treatment were negatively related to relapse. This suggests that greater eudaimonic functioning is associated with a decreased risk of relapse. Environmental
mastery in particular was a strong predictor of relapse, accounting for 17% of the variance in relapse, and correctly classifying relapse status in 71.4% of cases. This rate was significantly greater than a model based on probability alone, assuming that none of the participants had relapsed. In addition, for each unit decrease in WBS environmental mastery, the risk of relapse increases by 11%, highlighting the value of promoting eudaimonic features for the prevention of relapse. Moreover, this study found that the level of dysphoric features (mood, views of the self) and overall satisfaction with life were related to relapse status. A finding consistent with previous research (Lewinsohn, Allen, Seeley, & Gotlib, 1999).

Overall, the findings of this study highlight the potential value of promoting eudaimonic features in relapse prevention efforts, and the effects of MBCT and CBT-WB towards these effects.

### 4.2 Treatment Effects on the Reward System in MDD Relapse Prevention

Given the evidence of aberrant anticipatory and consummatory processes in MDD, primary hypotheses concerned treatment-related changes in the reward system during the anticipation of a pleasant event (anticipation of win) and while experiencing a pleasant event (outcome win).

**MBCT effects on anticipatory processes.** In this study, anticipation to win was modeled by a parametric regressor modulated by the degree of reward expectancy. Increased reactivity during anticipation to win was hypothesized to reflect the sensitivity of a region to incremental increases in the expectation of a positive outcome. Indeed, whole brain analysis of the main response to anticipation found significant activity in regions associated with an anticipatory response, including the ACC, MPFC, and supplementary motor area (Dean, Horndasch, Giannopoulos, & McCabe, 2016; Jia et al., 2016; Vassena et al., 2014b). This response is argued to reflect real-world anticipatory processes that are critical for future-oriented emotional processes.
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that support motivated behavior (wanting) and preparation for the potential consequences of forthcoming events.

This study initially hypothesized that mindfulness training would reduce anticipatory processes given previous research on reward-related changes following mindfulness training (e.g., Kirk et al., 2015a). More specifically, decreased activity in the reward system or increased somatosensory processing was expected following MBCT (consistent with theories on mindfulness training), while increases were expected for CBT-WB (consistent with normalization). However, no such effects were found. Instead, participants following MBCT were marked by significant increases in the hippocampus and a cluster including the precuneus and PCC/mid-cingulum. On the other hand, CBT was marked by significant decreases in these regions. To examine whether this diverging pattern of treatment change was similarly therapeutic, such that decreases in CBT and increases in MBCT both correlate with positive outcome, correlational analyses examined groups separately. Increased activity in these regions while anticipating a win was found to be associated with improvements in clinical outcome, regardless of the intervention. More specifically, greater hippocampal activity following treatment was associated with a reduction in dysfunctional attitudes and overall depression severity, indicating that the increases observed following MBCT may be therapeutic. While this study was not designed to measure memory, involvement of the hippocampus during reward processing suggests a role for MBCT in addressing the memory-related difficulties in depression (Williams et al., 2007).

**Biased memory recall and MBCT.** Research has shown that MBCT can help reduce overgenerality in autobiographical memory in previously depressed patients (Williams, Teasdale, Segal, & Soulsby, 2000). Overgenerality refers to the inability to retrieve specific memories from one’s autobiographical memory. Instead, general memories are recalled, such as repeated events
or events occurring over broad periods (e.g., “I felt really stupid when I got to my meeting without my briefcase yesterday” vs. “I’m always so stupid at meetings”). A consistent finding in research is that MDD populations are marked by overgeneralized memory (Williams et al., 2007b), particularly biased towards difficulties recalling positive events (Köhler et al., 2015). For instance, when participants are asked to come up with a specific memory in response to a cued word, MDD patients are less specific and/or more overgeneral in their memory retrieval than controls, particularly during positive word trials (Dalgleish, Hill, Golden, Morant, & Dunn, 2011; Lemogne, Piolino, Jouvent, Allilaire, & Fossati, 2006; Williams et al., 2007a). Individuals with a past history of depression when asked to recall positive autobiographical memories, report events that are less detailed, vivid (Werner-Seidler & Moulds, 2011) and less emotionally intense (Werner-Seidler & Moulds, 2012) than never-depressed controls. When asked to build individual timelines, dividing their autobiographical past into chapters (e.g., “time at school”, “life after marriage”), and recall positive and negative information for each “life chapter”, MDD participants display a bias towards recalling fewer positive events for each individual chapter, while the opposite pattern is found in never-depressed samples (Dalgleish et al., 2011). Overall, the understanding is that MDD populations are less likely to recall specific details of events, particularly when positive.

A number of theories have been proposed to account for the specific deficits in episodic memory evident in depressed patients (Williams et al., 2007a). A neurobiological account suggests that hypoactivity in regions key to memory encoding and retrieval would impoverish the quality of memory formation and contribute to limited access to episodic memories. As such, we would argue that increased recruitment of the hippocampus, regarded as the seat of episodic memory (Dillon, 2015), following MBCT may reflect improvements in positive episodic memory at the stage of memory formation (e.g., encoding, consolidation).
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Indeed, there is strong evidence to suggest that increased activity during anticipation predicts the quality of memory encoding/consolidation (Dillon, 2015). For instance, in a study by Wittmann et al., (2005) participants were presented with images from two categories, only one of which reliably predicted a chance to win money. Exposure to these cues mimics the anticipatory phase of reward whereby they signal the likelihood of receiving something pleasant. Three weeks later, the authors examined whether memory for these reward-related cues (images) were influenced by hippocampal activity. Increased hippocampal activity during cue presentation (anticipation to win) predicted better memory for these reward-predicting pictures compared with forgotten pictures. In a study by Dillon et al. (2014), healthy controls and unmedicated, depressed adults were scanned as they viewed drawings followed by reward and zero (non-reward tokens). A source memory tests administered directly after encoding revealed better memory for rewarded versus non-rewarded drawings in the controls (vs. depressed patients) mediated by increased activity in the hippocampal region (and VTA/substantia nigra).

Overall, increased recruitment of the hippocampus during encoding/consolidation predicts the quality of subsequent memory retrieval, while reduced hippocampal activation predicts poorer memory formation (Kim, 2011; Spaniol et al., 2009). Although this study did not include a memory task, we hypothesize that increased recruitment of the hippocampus following MBCT during anticipation to win may reflect improvements in the encoding and consolidation of positive events. Research to date help reinforce this suggestion, such that mindfulness practices have been shown to result in better positive memory recall in healthy controls while mindfulness training more generally can improve positive memory recall (Roberts-Wolfe, Sacchet, Hastings, Roth, & Britton, 2012) and hippocampal growth (Hölzel et al., 2011).
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Future research however is needed to examine whether hippocampal activity following MBCT specifically relates to memory processes. In addition, the reasons for increased hippocampal activity following MBCT (vs CBT-WB) are unknown. While speculative, we hypothesize that the incremental increases observed in MBCT (vs. CBT) in the hippocampus may reflect the cultivation of curiosity towards experiences, a feature unique to MBCT. Research has shown that hippocampal-dependent memory is particularly robust under conditions of cue-association uncertainty (Pearce & Hall, 1980; Strange, Duggins, Penny, Dolan, & Friston, 2005; Vanni-Mercier, Mauguière, Isnard, & Dreher, 2009), novelty detection (Kaplan, Horner, Bandettini, Doeller, & Burgess, 2014), motivation (Dillon, 2015; Tracy, Jarrard, & Davidson, 2001), and curiosity (Gruber, Gelman, & Ranganath, 2014). It is possible that the increased hippocampal activity during anticipation, observed in this study, reflects varying degrees of motivation and interest in the task. Future research is needed to examine whether these psychological states are associated with hippocampal activity following MBCT (vs. CBT-WB).

Discrepancy between study findings and hypotheses. We initially hypothesized that MBCT would result in decreased activity during anticipatory processes (wanting). Research thus far suggest that decreased neural responses characterize the effects of mindfulness training on reward wanting and reflect enduring changes in habitual responses involving the evaluation of whether stimuli is relevant (Kirk et al., 2015b, 2014). While this study did not observe significant decreases in these regions during anticipation, it is possible that group differences in these regions would have been present with a different control condition (e.g., treatment-as-usual). Still, increased MTL and precuneus/PCC activity during anticipation may also reflect a change from reactive habitual responding whereby the top-down regulation of anticipatory processes are reinforced.
Although there is no clear consensus on the role of the precuneus/PCC (Leech, Braga, & Sharp, 2012; Robert Leech & Sharp, 2014), activity in this region during reward may reflect its effects on the regulation of attention (R. Leech & Sharp, 2014). More specifically, the PCC is argued to be involved in maintaining a vigilant attentional state (Gilbert, Dumontheil, Simons, Frith, & Burgess, 2007; Hahn, Ross, & Stein, 2007; Shulman et al., 1997) and signaling relevant changes in the environment (Pearson et al., 2011). For instance, levels of PCC metabolism (and functional connectivity with the dACC) correlate with the degree of state arousal and awareness (Boly et al., 2012; Laureys et al., 2004; Brent A. Vogt & Laureys, 2005). Within the context of reward, PCC activity has been shown to increase during attentional biases towards highly motivating stimuli (Mohanty, Gitelman, Small, & Mesulam, 2008), similarly to the hippocampus (Murty & Adcock, 2014; Wolosin, Zeithamova, & Preston, 2012). As such, we hypothesize that greater recruitment of the PCC/precuneus and hippocampus following MBCT (vs. CBT-WB) are likely to reflect more careful attentional processing during the anticipation phase of reward and, in theory, better memory of the event. These changes are warranted in the care of previously depressed patients who continue to demonstrate difficulties being engaged by future-oriented emotional processes (Dichter, Kozink, et al., 2012; Kerestes et al., 2012; Rømer Thomsen, Whybrow, & Kringelbach, 2015; Ubl et al., 2015).

In sum, MBCT training effects on the hippocampus and precuneus/PCC regions suggest a role for this intervention in addressing attention and memory difficulties related to depression. However, this remains speculative until further research examines whether MBCT training results in more detailed attention at the level of encoding, and subsequent improvements in the ability to retrieve memory of the event. Future research would also benefit by further examining the
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mechanisms by which MBCT may exert its effects on overgeneralization in previously depressed patients.

Differences between CBT-WB and MBCT. Overall, there were no significant therapeutic effects of CBT-WB observed during the anticipation and outcome phases of this study. Both relapse and norelapse participants demonstrated a pattern of decreased activity in the hippocampus and precuneus/PCC regions during anticipation to win that related to increases in depressive features. As such, these deactivations during anticipation may not reflect the therapeutic benefits of CBT-WB. The absence of a non-active treatment condition (e.g., treatment-as-usual) interferes with the power to determine whether these changes are an effect of the intervention or time. For instance, it is possible that CBT-WB training results in disengagement from “trivial” reward tasks (vs. meaningful sources of wellbeing). Hypoactivity in these regions at second scan may also reflect reduced mental participation as a result of familiarity with the task (decreased novelty). Regardless, this study did not find any significant changes in reward responses that were associated with improvements in positive functioning or decreases in depressive features. This is inconsistent with research demonstrating improvements in reward processing following CBT-related interventions (DeRubeis, Siegle, & Hollon, 2008; Dichter et al., 2009a; Mori et al., 2016; Pizzagalli, 2011) (DeRubeis et al., 2008; Dichter et al., 2009a; Mori et al., 2016; Pizzagalli, 2011). However, these studies examined the effects of treating acute depressive symptoms. This is the first study to examine changes in reward processing following maintenance psychotherapy in previously depressed patients.

The absence of significant CBT-WB specific effects suggests that the task employed in this study may not be appropriate for capturing the treatment effects of this intervention on reward processes. More research is needed to examine the mechanisms by which CBT-WB may exert its
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effects on the reward system. It is possible that tasks that target more meaningful sources of positive affect will capture the Eudaimonia-related training involved in this maintenance intervention.

4.3 Relapse Effects on the Reward System in MDD Relapse Prevention

To our knowledge, no study to date had examined whether reward-related processes in remitted patients predict the likelihood of relapse within a two-year follow-up. We initially hypothesized that reward-related biomarkers for MDD vulnerability observed at different stages of the disorder (e.g., at risk of first episode, during MDD episode, after remission) may be associated with the recurrence of depression. We hypothesized that increased activity in regions underlying the deficits observed in wanting (e.g., ACC, middle frontal, hippocampus, amygdala, superior frontal) and liking (e.g., nucleus accumbens, dorsal striatum, ACC, insula, VMPFC/medial OFC, LPFC, thalamus) responses characteristic of MDD would predict lasting wellness at follow-up. On the contrary however, greater was not better within the context of MDD relapse prevention.

Relapse and reward sensitivity. Previous research has relied primarily on monetary incentives or exposure to positive stimuli (e.g., pictures, positive words, appetitive food) to examine responses in the reward system during the reception of a pleasant event (liking). In this study, we hypothesized that the degree of felt win during a card game would recruit activity in a similar system of brain regions. Overall, responses to a winning outcome involved activity in the frontal, parietal, and sub-cortical regions, including the insula, OFC, and pallidium, suggesting that this task elicited a hedonic response across our sample (Ballard et al., 2011; Kawagoe et al.,
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1998; Muranishi et al., 2011; Vassena et al., 2014b). As such, differences during this task are believed to reflect varying degrees of hedonic/reward responses to a positive outcome.

A consistent finding in this study was that relapse status was associated with increased reactivity to winning following treatment. Relapse participants demonstrated increased activity in the dorsal striatum (i.e., caudate, putamen), DMPFC, precuneus/PCC, insula and TPJ following MBCT and CBT-WB, compared to norelapse. Typically, an increased response would be interpreted as reward-related progress in a population vulnerable to hypoactivity in this system (Dichter et al., 2009a; Dichter, Sikich, Song, Voyvodic, & Bodfish, 2012) (Dichter et al., 2009a; Dichter, Sikich, et al., 2012) . However, norelapse participants did not exhibit this response. Instead, a stable pattern of reward reactivity from pre- to post-treatment was characteristic of participants who did not relapse during the two-year follow-up. It is possible that an elevated reward response in relapse participants reflects compensatory mechanisms that help those most vulnerable to the disorder maintain motivational balance. Increased activity however was negatively correlated with features of depression and predictive of relapse status, suggesting that this response reflects a harmful rather than helpful response to winning. In fact, increased reward responses to winning was a significant predictor of relapse status at follow-up, over and above predictions from clinical outcome, accounting for 45.8% of the variance in relapse, and correctly classifying relapse status in 80.5% of cases. Overall, our fMRI results indicate that increased reactivity to winning is associated with an elevated risk of relapse.

These results are seemingly inconsistent with models of MDD vulnerability and the prevailing view that nurturing responses to reward are clinically beneficial. Research on anhedonia proposes that MDD populations are marked by difficulties being motivated by the prospect of
reward, adapting behavior in the pursuit of reward, and enjoying rewards (Pizzagalli, 2014; Treadway & Zald, 2011). These deficits have been shown to persist after remission (Pechtel, Dutra, Goetz, & Pizzagalli, 2013; Whitton et al., 2016) or continue to differ from healthy controls (Dichter et al., 2009b; Ubl et al., 2015), highlighting the persistent vulnerability of this system in previously depressed patients. To counter this feature of the disorder, a number of authors propose that strengthening reward-related responses are necessary in the management of MDD (Berridge & Kringelbach, 2011; Garland et al., 2010b; Geschwind, Peeters, et al., 2011; Sin & Lyubomirsky, 2009b; Treadway & Zald, 2011). In other words, increasing reactivity to reward-related events, such as anticipation and reception, would predict a better prognosis. These effects have been found in the context of treating an acute episode of MDD (Dean et al., 2016; Dichter et al., 2009a; Mori et al., 2016). However, no study to date had explicitly examined the relationship between reward/positive affective responses to treatment and the subsequent risk of relapse, nor the effects of maintenance interventions on the reward system. The results of this study suggest a diverging view whereby increased reactivity to positive outcomes, within the context of MDD relapse prevention, is potentially not recommended.

**Neural sensitivity to outcome vs. anticipation.** In this study, the pattern of brain activity observed at post-treatment suggests that a greater preoccupation with outcome may be the reward-related feature most relevant to relapse. On the other hand, increased reactivity to the anticipation of a positive outcome, rather than its reception, is an indicator of better prognosis.

**Relapse and win.** Relapse participants demonstrated increased reactivity in a set of regions associated with: (a) the attribution of salience to an event and sensory awareness (insula); (b) sensory monitoring and emotional regulation of reward (DMPFC); (c) monitoring of reward
prediction errors and reward-seeking performance (caudate); (d) automatic, habitual reinforcement learning (putamen); (e) awareness and attention (precuneus/PCC); and (f) the representation of prediction-outcome comparisons (temporo-parietal junction). Greater recruitment of these regions is likely to reflect the level of engagement in the task, active monitoring of performance, and a striving response towards winning (see neurobiology of positive affect in the introduction). As such, our findings suggest that this orientation during a pleasant outcome is characteristic of those that subsequently relapse.

Of interest, this greater “preoccupation-with-winning” was associated with both negative and positive clinical outcomes. For instance, correlational analyses between activity in these regions and treatment outcome found that elevated DMPFC responses to win was associated with more dysfunctional attitudes, poorer self-concept, dysphoric mood, and lower satisfaction with life. On the other hand, increased activity in the precuneus/PCC area correlated with reduced depressive symptoms in the MBCT relapse sample. Greater activity in the dorsal striatum was associated with more positive affect at post-treatment, as assessed using the PANAS positive subscale. While speculative, we would argue that this dual-relationship with both positive and negative clinical outcomes in combination with the neural preoccupation-with-winning is likely to reflect a more hedonic orientation towards activities in relapse participants. For instance, the increased engagement, monitoring, and striving response of relapse participants during win is consistent with descriptions of a hedonic mindset, focused on the wellbeing obtained at the end of a pursuit rather than the quality of the activity itself (Fowers et al. 2009). More importantly, research suggests that a hedonic orientation, geared towards the pursuit of pleasure and comfort, only offers short-term benefits (Huta & Ryan, 2010). In a sample of undergraduate students, a 10-day hedonic intervention resulted in immediate benefits following (e.g., increased reports of
positive affect, decreased negative affect, more satisfaction with life), but by a three-month follow-up, these changes had faded. Within the context of relapse prevention, it is possible that an increased hedonic approach to experiences following MBCT or CBT-WB is gratifying in the short-term, but is not sustainable in the face of adversity. For instance, in a study by Telzer, Fuligni, Lieberman, and Galvan (2014), the authors found that greater striatal sensitivity to hedonic rewards were maladaptive and associated with increases in depressive symptoms over a one-year follow-up in a sample of adolescents. Interestingly, the authors found that greater reactivity to eudaimonic rewards instead predicted greater declines in depressive symptoms over time. These findings indicate that increased reward responses are not inherently maladaptive, but rather the context in which they arise is most predictive of outcome. Our findings suggest a similar story concerning reactivity to outcome vs. anticipation.

Relapse and anticipation. Participants who did not relapse demonstrated consistently greater activity in a cluster including the rostral ACC and VMPFC during the anticipation to win. Most importantly, out of a host of relapse-related neural responses, differences in this region were particularly predictive of relapse and provided the most stable predictor of outcome. No changes with time were observed in this region suggesting that this region reflects a vulnerability to relapse independent of treatment.

This region has been proposed to signal outcome expectancies, such as the hypothesized characteristics and value of an outcome (Metereau & Dreher, 2015; Rushworth & Behrens, 2008). For example, expectation of a pleasant taste (juice) or money produced activation in the VMPFC, while this region did not show increased activity during anticipation of aversive juice or monetary losses (Kim et al., 2011). Rather than reflecting a preference for positive compared to negative outcomes, the VMPFC and surrounding regions are argued to be particularly sensitive to the
incentive value of an outcome (Metereau & Dreher, 2015). Lesions in this region are associated with significant apathy towards experiences, whether they are punishing or rewarding, and a reduced propensity to perform goal-directed behaviors in day-to-day life (Hogeveen, Hauner, Chau, Krueger, & Grafman, 2016). Extended to our findings, this line of research suggests that increased activity in the VMPFC is likely to reflect greater incentive-sensitivity in norelapse participants, and a tendency to be driven by the pursuit of goals. In other words, goal-oriented approaches to activities is likely to reduce the risk of relapse. It is unclear why these differences between relapse and norelapse were apparent at pre- and post-treatment, however this region appears to be quite sensitive to the effects of treatment during the acute phase of the disorder (Dean et al., 2016; Downar et al., 2014). Baseline group differences may reflect differences in treatment response at previous stages of care.

In sum, these findings suggest that elevated reward responses are not inherently maladaptive, but rather dependent on the context. Reward responses dependent on outcome/performance seemingly confer an increased vulnerability to depression. However, increased neural response to the processes leading to reward are associated with lasting wellness. This study suggests that promoting anticipatory processes in treatment may benefit relapse prevention efforts. More research is needed however to help qualify the nature of relapse-related reward responses, and identify the context in which enhanced reward sensitivity is maladaptive for the recurrence of depression. In addition, few studies have explored the distinction between hedonic and eudaimonic pursuits in reward processing. More research is needed to broaden the view of positive affect in mental health.
5 Conclusion and Limitations

This study set out to examine the potential effects of maintenance interventions on reward processes and their relationship with relapse. Surprisingly, this study noted that maintenance interventions may derive their therapeutic effects from preserving baseline responses, rather than heightening reward sensitivity. More specifically, participants that relapsed during the course of the study demonstrated an elevated reward response during rewarding outcomes. Conversely, participants that stayed well during the follow-up displayed stability in their responses to rewarding outcomes. These findings underline a problematic reaction to treatment (or time) that eventually results in the return of depressive symptoms. Following training designed to build mindfulness, cognitive, and/or wellbeing skills, a minority of participants may adopt an increased orientation towards winning or gaining in an effort to prevent the recurrence of depression. Our results indicate however that this focus may peril their chances of staying well. Instead, this study found that increased responses to the anticipatory phases of reward may be clinically adaptive. Elevated responses in regions involved in attention and memory while anticipating a win was specific to MBCT and related to reductions in depressive symptoms. Together, these findings stress the value of a goal-oriented vs. outcome-oriented approach to rewarding experiences that may significantly direct the risk of relapse.

An additional objective of this study was to explore differences between MBCT and CBT-WB, anticipating that they would respectively reflect patterns consistent with mindfulness training and cognitive restructuring. Rather, our findings imply that these maintenance interventions did not significantly differ with the exception of MBCT-related changes in anticipatory processes. MBCT resulted in significantly greater activity in regions involved in memory and attention,
indicating that mindfulness training may help previously depressed patients cultivate their level of engagement with goal-directed stages of reward processing, and potentially, reinforcing their memory of positive events.

Although this study helped isolate a pattern of reward-related vulnerability, treatment-related effects were difficult to capture. In particular, this study did not yield any CBT-WB specific effects on reward processing that related with positive outcomes. It is possible that the task used in this study is inadequate for capturing CBT-WB related variability in reward. Although it was sufficient to elicit a reward response during anticipation and outcome phases, the trivial pursuit of winning in combination with the absence of extrinsic incentives may have reduced the opportunity to elicit a variety of reward responses. Future research would benefit from the inclusion of rewards tasks that are extrinsically motivating, such as tasks using monetary incentives or appetitive stimuli. In addition, given the nature of CBT-WB, additional research should include more ecologically valid reward tasks that include meaningful rewards. For instance, future research could examine responses to eudaimonic vs. hedonic experiences following maintenance interventions to determine whether training affects different forms of reward. Furthermore, the inclusion of a subjective indicator of reward during the task (e.g., “how curious are you to know the result?”, “how satisfying was this outcome”) would help qualify the nature of the neural responses observed.

Indeed, there were a number of additional limitations to this study that may limit the interpretations of our results. For one, relapse status was based on a lenient relapse criteria that may be a reflection of normal mood-reactivity rather than relapse status. Participants were considered to have relapsed if they reported moderate levels of depression at any point during the
follow-up. Arguably, depressed mood experienced once during a period of two-years is to be expected in a normal population. However, few participants had relapsed during the course of this study. Analyses using a more stringent relapse criteria were not sufficiently powered to detect relapse-related effects. As such, this study employed the lenient relapse criteria to explore potential neural predictors of relapse. This significantly limits the generalizability of our findings to clinical populations. Second, given the exploratory nature of this study, ROI analyses were not conducted, which could have facilitated the detection of regions hypothesized as biomarkers for relapse vulnerability. Third, binomial regressions using neural predictors of relapse derived from significant fMRI relapse-related effects are likely to result in an over-fitted model that inflates its actual predictive power. This in turn will produce a model with limited predictions outside of this sample. A cross-validation approach would have been best for examining the true predictive power of neural vs. clinical outcome. However, following forward regressions, only three neural predictors were included in the model which helps reduce the risk of multi-collinearity and over-fitting the data. Furthermore, this model serves as an indicator of the relationship between these regions and relapse, rather than a model designed for predictions. Future research however should examine whether these regions continue to be significantly predictive of relapse using a cross-validation approach. Finally, measures of competence and adherence to treatment were not available to help support inferences that treatment-related effects result from the interventions rather than the effects of time. It is unknown whether participants receiving MCBT or CBT-WB received treatment according to guidelines.

Nevertheless, this study contributed additional insight on the mechanisms of change of these maintenance interventions and highlighted a relapse-related response that may have important implications for treatment. Differences between relapse and norelapse participants
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suggest that clients may react to these interventions in differing ways or misapply the skills in such a way that maintained wellness relies on gains, rather than goal-directed striving. This orientation in turn may provide immediate benefits, but is maladaptive in the long run. It would be valuable for clinicians to monitor for these patterns and potentially adapt current guidelines to integrate discussions on this distinction. Furthermore, fMRI results exposed a characteristic response to relapse participants to reward that may have potential predictive utility in clinical practice. With further research, increased reactivity to reward, as measured with fMRI or other physiological indicators, could be employed to make decisions about further treatment recommendations. Moreover, from a theoretical point of view, these results add complexity to our understanding of reward-related deficits in depression, and suggest that more is better is a simplistic approach in the management of depressive features.
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### Tables

#### Table 1

*Patient characteristics at baseline*

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<thead>
<tr>
<th></th>
<th>MBCT (%)</th>
<th>CBT-WB (%)</th>
<th>( \chi^2 )</th>
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<tbody>
<tr>
<td><strong>Gender</strong></td>
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<td></td>
<td>0.39</td>
</tr>
<tr>
<td>Male</td>
<td>28.6</td>
<td>35.3</td>
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</tr>
<tr>
<td>Female</td>
<td>71.4</td>
<td>64.7</td>
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<tr>
<td><strong>Education</strong></td>
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<tr>
<td>Did not complete high school</td>
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<td>-</td>
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<tr>
<td>Completed high school</td>
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</tr>
<tr>
<td>College / University</td>
<td>79.0</td>
<td>61.8</td>
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</tr>
<tr>
<td>Graduate / Professional school</td>
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<td>14.7</td>
<td></td>
</tr>
<tr>
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<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
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</tr>
<tr>
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<td>81.8</td>
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</tr>
<tr>
<td>Afro-Canadian</td>
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<td>-</td>
<td></td>
</tr>
<tr>
<td>Asian (includes East Asian)</td>
<td>4.7</td>
<td>12.1</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.3</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4.7</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>Unknown/Undisclosed</td>
<td>-</td>
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<table>
<thead>
<tr>
<th><strong>Years</strong></th>
<th><strong>t-statistic</strong></th>
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<tbody>
<tr>
<td>Age</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>38.6 (11.6)</td>
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Note. Significant group differences are highlighted in bold.
## Table 2

Clinical characteristics and treatment outcome differences between MCBT and CBT

<table>
<thead>
<tr>
<th>Measures</th>
<th>MCBT</th>
<th>CBT-WB</th>
<th>Main effect Time</th>
<th>Partial eta squared</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>F</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS</td>
<td>48.72 (13.4)</td>
<td>48.97 (13.5)</td>
<td>56.32 (21.3)</td>
<td>52.78 (21.2)</td>
</tr>
<tr>
<td>DSC Self-Concept</td>
<td>12.26 (12.7)</td>
<td>11.61 (11.2)</td>
<td>10.82 (11.1)</td>
<td>10.68 (11.3)</td>
</tr>
<tr>
<td>DSC Mood</td>
<td>17.77 (13.4)</td>
<td>17.71 (11.9)</td>
<td>(11.93)</td>
<td>16.30 (11.4)</td>
</tr>
<tr>
<td>DSC Total</td>
<td>30.02 (25.1)</td>
<td>29.36 (22.3)</td>
<td>(22.04)</td>
<td>27.00 (21.8)</td>
</tr>
<tr>
<td>HRSD</td>
<td>1.81 (2.5)</td>
<td>2.05 (2.7)</td>
<td>2.44 (2.18)</td>
<td>3.23 (3.8)</td>
</tr>
<tr>
<td>PANAS Positive</td>
<td>31.07 (6.12)</td>
<td>31.48 (6.3)</td>
<td>29.18 (7.70)</td>
<td>27.75 (9.4)</td>
</tr>
<tr>
<td>SLS</td>
<td>20.77 (7.9)</td>
<td>21.10 (8.0)</td>
<td>17.82 (8.1)</td>
<td>19.75 (7.7)</td>
</tr>
<tr>
<td>WBS Autonomy</td>
<td>30.79 (3.8)</td>
<td>31.08 (3.5)</td>
<td>29.68 (4.9)</td>
<td>31.42 (5.3)</td>
</tr>
<tr>
<td>WBS Personal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Growth</td>
<td>38.58 (6.2)</td>
<td>38.64 (5.3)</td>
<td>37.47 (6.0)</td>
<td>37.11 (5.0)</td>
</tr>
<tr>
<td>WBS Purpose</td>
<td>34.05 (4.9)</td>
<td>33.93 (5.4)</td>
<td>31.88 (7.4)</td>
<td>32.33 (6.2)</td>
</tr>
<tr>
<td>WBS Self-acceptance</td>
<td>30.61 (6.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.85 (7)</td>
<td>27.65 (7.7)</td>
<td>30.64 (7.3)</td>
<td><strong>8.54</strong></td>
</tr>
<tr>
<td>WBS Mastery</td>
<td>31.40 (6.6)</td>
<td>30.74 (6.2)</td>
<td>29.94 (6.6)</td>
<td>29.69 (6.5)</td>
</tr>
</tbody>
</table>

Note. T₁ = baseline scores; T₂ = post-treatment scores; T₂-T₁ = clinical change from pre- to post-treatment. DAS = dysfunctional attitude scale; DSC = depressive symptoms checklist; HRSD = Hamilton rating of depression; PANAS = positive and negative affect scale; SLS = satisfaction with life; WBS = wellbeing scale.

** Significant effects are at the 0.005 level (2-tailed).
REWARD PROCESSING AND RELAPSE IN MBCT CBT

Table 3

Correlations between clinical measures and relapse status

<table>
<thead>
<tr>
<th>Measures</th>
<th>T1</th>
<th>T2</th>
<th>T2-T1</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS</td>
<td>0.165</td>
<td>0.221</td>
<td>0.08</td>
</tr>
<tr>
<td>DSC self-Concept</td>
<td>0.222</td>
<td>.315**</td>
<td>0.138</td>
</tr>
<tr>
<td>DSC mood</td>
<td>.231*</td>
<td>.310**</td>
<td>0.064</td>
</tr>
<tr>
<td>DSC total</td>
<td>0.219</td>
<td>.324**</td>
<td>0.111</td>
</tr>
<tr>
<td>HRSD</td>
<td>0.173</td>
<td>0.167</td>
<td>0.015</td>
</tr>
<tr>
<td>PANAS positive</td>
<td>-0.029</td>
<td>-0.139</td>
<td>-0.102</td>
</tr>
<tr>
<td>SLS</td>
<td>-0.195</td>
<td>-.270*</td>
<td>-0.099</td>
</tr>
<tr>
<td>WBS autonomy</td>
<td>-0.176</td>
<td>-.293**</td>
<td>-0.099</td>
</tr>
<tr>
<td>WBS growth</td>
<td>-0.082</td>
<td>-.302**</td>
<td>-0.21</td>
</tr>
<tr>
<td>WBS purpose</td>
<td>-0.164</td>
<td>-.288*</td>
<td>-0.126</td>
</tr>
<tr>
<td>WBS self-accept</td>
<td>-0.208</td>
<td>-.320**</td>
<td>-0.16</td>
</tr>
<tr>
<td>WBS mastery</td>
<td>-0.21</td>
<td>-.346**</td>
<td>-0.136</td>
</tr>
</tbody>
</table>

Note. T1 = baseline scores; T2= post-treatment scores; T2-T1= clinical change from pre- to post-treatment. DAS= dysfunctional attitude scale; DSC= depressive symptoms checklist; HRSD= Hamilton rating of depression; PANAS=positive and negative affect scale; SLS= satisfaction with life; WBS= wellbeing scale.

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).
### Table 4

*Regional brain activity during anticipation to win (modulated by degree of expectation)*

<table>
<thead>
<tr>
<th>Anatomic region</th>
<th>Cluster</th>
<th>Co-ordinates (mm)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BA</td>
<td>Side</td>
<td>Size</td>
<td>Peak Z</td>
<td>x</td>
</tr>
<tr>
<td><strong>Main effect of Relapse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rostral ACC/medial OFC</td>
<td>11</td>
<td>L</td>
<td>45</td>
<td>3.41</td>
<td>0</td>
</tr>
<tr>
<td><strong>Interaction Time by Group</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hippocampus</td>
<td>27</td>
<td>R</td>
<td>23</td>
<td>4.17</td>
<td>18</td>
</tr>
<tr>
<td>Cerebellum</td>
<td></td>
<td>L</td>
<td>62</td>
<td>3.61</td>
<td>-33</td>
</tr>
<tr>
<td>Precuneus</td>
<td>23</td>
<td>L</td>
<td>40</td>
<td>3.46</td>
<td>-12</td>
</tr>
<tr>
<td>Lingual</td>
<td>18</td>
<td>L</td>
<td>35</td>
<td>3.30</td>
<td>-9</td>
</tr>
<tr>
<td>Calcarine</td>
<td>17</td>
<td>R</td>
<td>20</td>
<td>3.15</td>
<td>12</td>
</tr>
</tbody>
</table>

*Note.* Co-ordinates are in MNI. Only regions $p<.001$ and $k>19$ were included in the table. BA= brodman area; B = bilateral, L= left, R= right; ACC= anterior cingulate cortex; OFC= orbitofrontal cortex.
## Table 5

Regional brain activity during Outcome Win (modulated by degree of win)

| Anatomic region          | Cluster | Co-ordinates (mm) | | |
|--------------------------|---------|------------------|---|---|---|
|                          | BA      | Side  | Size  | Peak Z | x   | y   | z   |
| **Interaction Relapse by Time** |         |       |       |        |     |     |     |
| Caudate                  | L       | 32    |       | 4.47   | -18 | 8   | 14  |
| Putamen                  | R       | 38    |       | 4.05   | 21  | 20  | 5   |
| Superior frontal         | L       | 32    | 21    | 4.01   | -18 | 38  | 41  |
| Superior temporal        | R       | 42    | 57    | 3.95   | 60  | -40 | 20  |
| Precuneus                | L       | 23    | 73    | 3.72   | -12 | -52 | 29  |
|                          | R       | 37    | 45    | 3.69   | 39  | -64 | 5   |
| Superior occipital       | R       | 19    | 34    | 3.26   | -39 | -1  | 5   |
| Rolandic oper/Insula     | L       | 48    | 28    | 3.69   | 39  | -64 | 5   |
| Cerebellum               | R       | 31    | 34    | 3.69   | 39  | -64 | 5   |
| Motor/DMPFC              | L       | 23    | 21    | 3.56   | -21 | 14  | 44  |
| Occipital                | R       | 34    | 34    | 3.51   | 24  | -67 | 8   |
| Calcarine                | R       | 29    | 27    | 3.23   | 27  | -55 | -19 |
| Fusiform                 | R       | 44    | 31    | 3.22   | 27  | -70 | -31 |
| Cerebellum               | R       | 45    | 44    | 3.37   | 21  | -58 | 29  |
| **Interaction Relapse by Group** |         |       |       |        |     |     |     |
| Precuneus                | L       | 45    | 31    | 3.83   | -9  | -46 | 35  |
| Mid-cingulum / PCC       | L       | 100   | 21    | 3.55   | -45 | -52 | 11  |
| Precuneus                | L       | 76    | 31    | 3.58   | -15 | -64 | 26  |
| Parieto-occipital        | L       | 30    | 21    | 3.55   | -45 | -52 | 11  |
| Middle temporal          | L       | 23    | 21    | 3.55   | -45 | -52 | 11  |
| Superior temporal        | R       | 44    | 39    | 3.17   | 51  | -58 | 26  |

Note. Co-ordinates are in MNI. Only regions p<.001 and k >19 were included in the table. BA= brodmann area; B = bilateral, L= left, R= right; ACC= anterior cingulate cortex; OFC= orbitofrontal cortex.
Table 6

Correlations between ROI median signal value and relapse status

<table>
<thead>
<tr>
<th></th>
<th>T1</th>
<th>T2</th>
<th>T2-T1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticipation to Win</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment x Time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Precuneus</em></td>
<td>-0.068</td>
<td>-0.164</td>
<td>0.03</td>
</tr>
<tr>
<td><em>Hippocampus</em></td>
<td>-0.045</td>
<td>-0.062</td>
<td>-0.023</td>
</tr>
<tr>
<td><em>Mid-cingulum/PCC</em></td>
<td>-0.068</td>
<td>-0.164</td>
<td>0.03</td>
</tr>
<tr>
<td>Main effect Relapse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>VMPFC</em></td>
<td>-0.202</td>
<td>-.338**</td>
<td>-0.034</td>
</tr>
<tr>
<td><strong>Outcome Win</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment x Relapse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Superior temporal</em></td>
<td>-0.15</td>
<td>-0.143</td>
<td>0.174</td>
</tr>
<tr>
<td><em>Mid-cingulum/PCC</em></td>
<td>-0.066</td>
<td>-0.058</td>
<td>.268*</td>
</tr>
<tr>
<td><em>Precuneus</em></td>
<td>-0.166</td>
<td>-0.052</td>
<td>.334**</td>
</tr>
<tr>
<td><em>Middle temporal</em></td>
<td>-0.118</td>
<td>0.112</td>
<td>.249*</td>
</tr>
<tr>
<td>Time x Relapse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>DMPFC</em></td>
<td>-0.176</td>
<td>0.18</td>
<td>.400**</td>
</tr>
<tr>
<td><em>MPFC</em></td>
<td>-0.079</td>
<td>0.223</td>
<td>.405**</td>
</tr>
<tr>
<td><em>Precuneus</em></td>
<td>-0.154</td>
<td>0.013</td>
<td>.417**</td>
</tr>
<tr>
<td><em>Superior temporal</em></td>
<td>-0.099</td>
<td>0.049</td>
<td>.429**</td>
</tr>
<tr>
<td><em>Caudate</em></td>
<td>-0.137</td>
<td>0.073</td>
<td>.470**</td>
</tr>
<tr>
<td><em>Insula</em></td>
<td>-.226*</td>
<td>0.168</td>
<td>.422**</td>
</tr>
<tr>
<td><em>Putamen</em></td>
<td>-.256*</td>
<td>0.104</td>
<td>.503**</td>
</tr>
</tbody>
</table>

* Note. T1 = baseline; T2 = post-treatment.

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).
Figures

**Figure 1.** Significant main and interactions effects during anticipation to win, contrasts opened using functional ROIs at $p=0.05$. (A) Medial OFC/VMPFC activation during anticipation is consistently greater in norelapse vs. relapse participants. (B) Increased hippocampal activity was observed following MBCT, while a trend towards deactivation was visible in CBT.
Figure 2. Treatment x Relapse interaction effect in the mid-cingulum/PCC during winning. HRSD = Hamilton rating scale for depression; T1 = baseline, T2 = post-treatment. (A) Activity in the mid-cingulum during win, contrasts opened at .005, cluster size > 19. (B) Relationship between changes in depression (HRSD) and mid-cingulum activity from pre- to post-treatment. (C) Average mid-cingulum activity per sub-group across time.
Figure 3. Time x Relapse interaction effect during winning. Contrasts opened at .005, cluster size > 19. (A) Activity in the dorsomedial prefrontal cortex (B) Activity in the insula (C) Activity in the dorsal striatum (caudate) (D) Activity in the precuneus/PCC cluster. T1 = Time 1; T2 = Time 2.
Appendix A

Clinical Measures

**Depressed States Checklist (DSC; Teasdale & Cox. 2001).** The DSC is a 28-item checklist of 14 adjectives describing common affective (e.g., depressed, despondent, gloomy) and 14 self-evaluative (abandoned, incompetent, useless) components of dysphoria. Respondents were given the following instructions: “Please describe how you have felt when your mood started to go down in the last month”. and made ratings on a scale from 0 = not at all to 3 = very or extremely (range of scores 0–84). The DSC possesses adequate reliability and validity (Teasdale & Cox. 2001).

**Dysfunctional Attitudes Scale (DAS; Weissman and Beck. 1978).** The DAS is 17-item item scale measuring dysfunctional attitudes about the self, using statements such as “It is difficult to be happy unless one is good looking, intelligent, rich and creative”. These statements are associated with an increased vulnerability to depression. The DAS-17 items are rated on a 7-point Likert scale, and total DAS-17 scores range from 17 to 119, with increases in total score representing an increase in number and severity of dysfunctional attitudes. Confirmatory analyses indicated the DAS consisted of two subscales, one measuring perfectionism and performance evaluation (PPE) and the other measuring dependency (DE; de Graaf, Roelofs, & Huibers, 2009). Total score PPE and DE were moderately correlated with depression severity (Pearson r = .61, .51, and .6 respectively), were able to significantly distinguish between depressed and non-depressed participants (p < .001), and accounted for 25% of total variance in depression scores. Both subscales correlated moderately with one another and a one-factor model was also found to be sufficient to explain the factor loadings in confirmatory factor analyses (supported by Moore,
Fresco, Segal, and Brown. 2014), suggesting that the use of a total DAS score is an acceptable measure of overall dysfunctional thinking.

**Hamilton Rating Scale for Depression (HRSD; Hamilton. 1980).** The HRSD is a clinician rated scale aimed at assessing depression severity among patients. The 17-item version of the HAM-D (reproduced in the appendix to this chapter) has become the standard for clinical trials and the most widely used scale for controlled clinical trials in depression. It is a multidimensional scale, and this implies that the score of a specific item cannot be considered a good predictor of the total score. It also means that identical total scores from two different patients may have different clinical meanings (i.e., a very high rating on few items can yield the same score as a moderate rating on many items). In a recent review of the psychometric properties of the HRSD, the authors showed that the majority of HAM-D items have adequate reliability (Bagby, Ryder, Schuller, & Marshall, 2004), with an inter-rater reliability ranging from 0.8 to 0.98. It is agreed by most clinicians that scores between 0 and 6 do not indicate the presence of depression, scores between 7 and 17 indicate mild depression, scores between 18 and 24 indicate moderate depression, and scores over 24 indicate severe depression. A total HAM-D score of 7 or less after treatment is a typical indicator of remission (Frank, Prien, Jarrett, et al. 1991). A decrease of 50% or more from baseline during the course of the treatment is considered indicator of a clinically significant change.

**Positive Affect and Negative Affect Scale (PANAS; Watson et al.. 1988).** This questionnaire consists of two 10-item mood scales and was developed to provide brief measures of positive and negative affect. Positive affect (PA) reflects the extent to which a person feels enthusiastic, active, and alert. High scores indicate a state of high energy, full concentration, and pleasurable engagement, whereas low PA is characterized by sadness and lethargy. In contrast.
negative affect (NA) is a general dimension of subjective distress and unpleasurable engagement that subsumes a variety of aversive mood states, including anger, contempt, disgust, guilt, fear, and nervousness, with low NA being a state of calmness and security. These two factors represent affective state dimensions. This scale consists of 20 items describing different feelings and emotions in terms of 10 positive and 10 negative affective descriptors. Participants were instructed to rate the degree to which they had experienced these feelings and emotions in the last week on a five-point scale (ranging from “very slightly or not at all” to “extremely”). Scores on PA and NA are provided, with higher scores indicating the degree of PA or NA during the past week. The PANAS is a reliable and valid measure of the constructs it was intended to assess and exhibits measurement invariance across demographic subgroups (Crawford & Henry, 2004).

Satisfaction with Life Scale (SWLS; Diener, Emmons, Larsen, & Griffin. 1985). The SWLS is a short 5-item instrument designed to measure global cognitive judgments of satisfaction with one's life using a seven-point scale. The scale usually requires only about one minute of a respondent's time. Total score ranges from 5 (extremely dissatisfied) to 35 (highly satisfied). The SWLS is shown to have favorable psychometric properties, including high internal consistency and high temporal reliability (Diener et al., 1985). Scores on the SWLS correlate moderately to highly with other measures of subjective well-being, and correlate predictably with specific personality characteristics.

Ryff Wellbeing Scale (WBS; Ryff. 1989). The Ryff inventory consists of 42 questions (medium form), developed to examine psychological wellbeing conceptualized as distinct from the pursuit of pleasure. This measure was developed to capture the six areas of eudaimonic wellbeing including: Autonomy, environmental mastery, personal growth, positive relations with others, purpose in life, and self-acceptance. Respondents rate statements on a scale of 1 to 6, with
1 indicating strong disagreement and 6 indicating strong agreement. There are 7 items per scale (range 0-42). WBS is reliable measure of eudaimonic wellbeing, with a 6-week test-retest reliability for the six scales of r=.8 (Ryff. 1989). The WBS demonstrates high stability. In one study, using the reliable-change index, the authors found that more than 95% of the sample showed no evidence of reliable increases or decreases on any of the six wellbeing scales over a 9- to 10-year period (Christensen & Mendoza. 1986). Minimal change in WBS over time is expected, however, it has been used in clinical research as a sensitive measure of wellbeing change (Fava & Rafanelli. 1998).

**AUTONOMY**

**High Scorer:** Is self-determining and independent; able to resist social pressures to think and act in certain ways; regulates behavior from within; evaluates self by personal standards.

**Low Scorer:** Is concerned about the expectations and important decisions; conforms to social pressures to think and act based on evaluations of others; relies on judgments of others.

**ENVIRONMENTAL MASTERY**

**High Scorer:** Has a sense of mastery and competence in managing the environment; controls complex array of external activities; makes effective use of surrounding opportunities; able to choose or create contexts suitable to personal needs and values.

**Low Scorer:** Has difficulty managing everyday affairs; feels unable to change or improve surrounding context; is unaware of surrounding opportunities; lacks sense of control over external world.

**PERSONAL GROWTH**

**High Scorer:** Has a feeling of continued development; sees self as growing and expanding; is open to new experiences; has sense of realizing one’s potential; sees improvement in self and behavior over time; is changing in ways that reflect more self knowledge and effectiveness.

**Low Scorer:** Has a sense of personal stagnation; lacks sense of improvement or expansion over time; feels bored and uninterested with life; feels unable to develop new attitudes or behaviors.

**POSITIVE RELATIONS WITH OTHERS**

**High Scorer:** Has warm satisfying, trusting relationships with others; is concerned about the welfare of others; capable of strong empathy, affection, and intimacy; understands give and take of human relationships.
**Low Scorer:** Has few close, trusting relationships with others; finds it difficult to be warm, open, and concerned about others; is isolated and frustrated in interpersonal relationships; not willing to make compromises to sustain important ties with others.

**PURPOSE IN LIFE**

**High Scorer:** Has goals in life and a sense of directedness; feels there is meaning to present and past life; holds beliefs that give life purpose; has aims and objectives for living.

**Low Scorer:** Lacks a sense of meaning in life; has few goals of aims; lacks sense of direction; does not see purpose of past life; has no outlook or beliefs that give life meaning.

**SELF-ACCEPTANCE**

**High Scorer:** Possesses a positive attitude toward the self; acknowledges and accepts multiple aspects of self, including good and bad qualities; feels positive about past life.

**Low Scorer:** Feels dissatisfied with self; is disappointed with what has occurred in past life; is troubled about certain personal qualities; wishes to be different than what one is.

Appendix B

Illustration of Degree of Felt Win

The degree of felt win was modelled as a function of the initial expectation to win and the violation of that expectation. For instance, a “win” under the condition of low expectation of winning was hypothesized to reflect a greater degree of “felt win” because of the element of surprise of that event. In turn, this “felt win” is considered a rewarding event. On the other hand, if the expectation to win is high and that expectation is confirmed, the win is modelled as less rewarding. The value by which one wins (difference between cards) was also modelled to influence the degree of expectancy violation. For instance, if the expectation to win is high, but the outcome almost resulted in a loss (e.g., winning with a card of 10 vs. 9), this event is hypothetically more rewarding given the level of risk and surprise of this event. In addition, the greater the win (difference between cards), the greater the degree of “felt win”. The following figures help illustrate the degree of felt win depending on the initial expectation to win and combination with violation of expectations.
Figure 1. The degree of felt win is modelled in the following figure by the degree of expectation only. Winning at low expectation is inherently more rewarding than winning at greater degrees of expectation.

Figure 2. The degree of felt win is modelled in the following figure by the degree of expectation and the value of expectancy violation. Winning at low expectation is consistently more rewarding (and rare), but winning by the maximum or minimum value increase he rewarding effects of that event.
### Appendix C

#### Table 1

*Difference at Post-Treatment Between Relapse and Norelapse*

<table>
<thead>
<tr>
<th>Measures</th>
<th>t</th>
<th>df</th>
<th>p-value</th>
<th>Mean Difference</th>
<th>Std. Error Difference</th>
<th>95% CI Lower</th>
<th>95% CI Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>PANAS positive</td>
<td>1.42</td>
<td>75</td>
<td>.161</td>
<td>2.68</td>
<td>1.89</td>
<td>-1.09</td>
<td>6.44</td>
</tr>
<tr>
<td>Satisfaction with life</td>
<td>2.44</td>
<td>75</td>
<td><strong>.017</strong></td>
<td>4.42</td>
<td>1.81</td>
<td>.81</td>
<td>8.03</td>
</tr>
<tr>
<td>WBS autonomy</td>
<td>2.56</td>
<td>75</td>
<td><strong>.012</strong></td>
<td>2.58</td>
<td>1.01</td>
<td>.57</td>
<td>4.58</td>
</tr>
<tr>
<td>WBS personal growth</td>
<td>2.68</td>
<td>75</td>
<td><strong>.009</strong></td>
<td>3.21</td>
<td>1.20</td>
<td>.82</td>
<td>5.59</td>
</tr>
<tr>
<td>WBS purpose</td>
<td>2.44</td>
<td>75</td>
<td><strong>.017</strong></td>
<td>3.26</td>
<td>1.34</td>
<td>.60</td>
<td>5.93</td>
</tr>
<tr>
<td>WBS self-acceptance</td>
<td>2.95</td>
<td>75</td>
<td><strong>.004</strong></td>
<td>4.76</td>
<td>1.61</td>
<td>1.55</td>
<td>7.97</td>
</tr>
<tr>
<td>WBS environmental mastery</td>
<td>3.17</td>
<td>75</td>
<td><strong>.002</strong></td>
<td>4.52</td>
<td>1.43</td>
<td>1.68</td>
<td>7.36</td>
</tr>
</tbody>
</table>

*Note.* Significant results are in bold. PANAS = positive and negative affective scale; WBS = wellbeing scale. Relapse N=27; Norelapse N=50.

* Correlation is significant at the .05 level (2-tailed)

** Correlation is significant at the .01 level (2-tailed)

#### Table 2

*Regional Brain Activity During Anticipation to Win (modulated by degree of expectation)*

<table>
<thead>
<tr>
<th>Anatomic region</th>
<th>Cluster</th>
<th>Co-ordinates (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BA</td>
<td>Side</td>
</tr>
<tr>
<td><strong>Main effect of Condition (increased activity)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Occipital</td>
<td>18</td>
<td>B</td>
</tr>
<tr>
<td>Paracentral lobule</td>
<td>4</td>
<td>L</td>
</tr>
<tr>
<td>/Supplementary motor area cluster</td>
<td>4</td>
<td>R</td>
</tr>
<tr>
<td>Caudate</td>
<td>48</td>
<td>B</td>
</tr>
<tr>
<td>Putamen</td>
<td>48</td>
<td>L</td>
</tr>
<tr>
<td>Precuneus</td>
<td>31</td>
<td>L</td>
</tr>
<tr>
<td>Mid-cingulum/PCC</td>
<td>23</td>
<td>R</td>
</tr>
<tr>
<td>Thalamus</td>
<td>27</td>
<td>L</td>
</tr>
<tr>
<td>ACC/medial OFC</td>
<td>10</td>
<td>L</td>
</tr>
<tr>
<td>Medial superior frontal</td>
<td>32</td>
<td>B</td>
</tr>
<tr>
<td>/Superior frontal cluster</td>
<td>9</td>
<td>R</td>
</tr>
<tr>
<td>Cerebellum crus</td>
<td></td>
<td>R</td>
</tr>
</tbody>
</table>

*Note.* Co-ordinates are in MNI. Only regions p<.001 and k>19 were included in this table. BA= brodmann area; B = bilateral. L= left. R= right; Co-ordinates are in MNI.
Table 3

Regional Brain Activity During Outcome Win (modulated by degree of felt win)

<table>
<thead>
<tr>
<th>Anatomic region</th>
<th>Cluster</th>
<th>BA</th>
<th>Side</th>
<th>Size</th>
<th>Peak Z</th>
<th>x</th>
<th>y</th>
<th>z</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Main effect of Condition (increased activity)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior frontal cluster</td>
<td></td>
<td>44</td>
<td>B</td>
<td>398</td>
<td>5.00</td>
<td>-48</td>
<td>20</td>
<td>32</td>
</tr>
<tr>
<td><em>Middle frontal</em></td>
<td></td>
<td>44</td>
<td></td>
<td></td>
<td>4.10</td>
<td>-30</td>
<td>14</td>
<td>38</td>
</tr>
<tr>
<td>Medial superior frontal cluster</td>
<td></td>
<td>9</td>
<td>B</td>
<td>131</td>
<td>3.86</td>
<td>-15</td>
<td>35</td>
<td>47</td>
</tr>
<tr>
<td><em>Mid-cingulum</em></td>
<td></td>
<td>32</td>
<td></td>
<td></td>
<td>3.60</td>
<td>6</td>
<td>35</td>
<td>38</td>
</tr>
<tr>
<td>Inferior parietal</td>
<td></td>
<td>40</td>
<td>L</td>
<td>380</td>
<td>4.71</td>
<td>-48</td>
<td>-55</td>
<td>47</td>
</tr>
<tr>
<td>Parietal cluster</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Precuneus</em></td>
<td></td>
<td></td>
<td>R</td>
<td>535</td>
<td>4.53</td>
<td>15</td>
<td>-61</td>
<td>47</td>
</tr>
<tr>
<td><em>Supramarginal</em></td>
<td></td>
<td>40</td>
<td>R</td>
<td></td>
<td>4.24</td>
<td>51</td>
<td>-43</td>
<td>44</td>
</tr>
<tr>
<td><em>Angular</em></td>
<td></td>
<td>39</td>
<td>R</td>
<td></td>
<td>4.22</td>
<td>36</td>
<td>-61</td>
<td>47</td>
</tr>
<tr>
<td>Medial/sub-cortical prefrontal cluster</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Insula</em></td>
<td></td>
<td>13</td>
<td>L</td>
<td>247</td>
<td>4.26</td>
<td>-33</td>
<td>20</td>
<td>-4</td>
</tr>
<tr>
<td><em>OFC</em></td>
<td></td>
<td>47</td>
<td>L</td>
<td></td>
<td>4.07</td>
<td>-42</td>
<td>20</td>
<td>-10</td>
</tr>
<tr>
<td><em>Pallidium</em></td>
<td></td>
<td></td>
<td>L</td>
<td></td>
<td>4.02</td>
<td>-15</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Pallidium</td>
<td></td>
<td></td>
<td>R</td>
<td>48</td>
<td>4.21</td>
<td>12</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Inferior occipital</td>
<td></td>
<td>19</td>
<td>R</td>
<td>28</td>
<td>3.20</td>
<td>33</td>
<td>-76</td>
<td>-7</td>
</tr>
<tr>
<td>Cerebellum crus</td>
<td></td>
<td></td>
<td>R</td>
<td>121</td>
<td>4.27</td>
<td>21</td>
<td>-70</td>
<td>-31</td>
</tr>
</tbody>
</table>

Note. Co-ordinates are in MNI. Only regions p<.001 and k>19 were included in this table. BA= brodmann area; B = bilateral. L= left. R= right; OFC = orbitofrontal cortex.
Appendix D

Table 1
Correlations Between Clinical Scores and Neural Responses During Anticipation to Win at Post-Treatment

<table>
<thead>
<tr>
<th>Clinical Measures</th>
<th>Treatment x Group</th>
<th>Main effect relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Precuneus</td>
<td>Hippocampus</td>
</tr>
<tr>
<td>DAS</td>
<td>-.198</td>
<td>-.242*</td>
</tr>
<tr>
<td>DSC Self-Concept</td>
<td>-.185</td>
<td>-.147</td>
</tr>
<tr>
<td>DSC Mood</td>
<td>-.138</td>
<td>-.164</td>
</tr>
<tr>
<td>DSC Total</td>
<td>-.168</td>
<td>-.176</td>
</tr>
<tr>
<td>HRSD</td>
<td>-.215</td>
<td>-.230*</td>
</tr>
<tr>
<td>PANAS positive</td>
<td>-.047</td>
<td>-.002</td>
</tr>
<tr>
<td>SLS</td>
<td>-.077</td>
<td>-.124</td>
</tr>
<tr>
<td>WBS autonomy</td>
<td>.021</td>
<td>.038</td>
</tr>
<tr>
<td>WBS personal growth</td>
<td>-.033</td>
<td>-.036</td>
</tr>
<tr>
<td>WBS purpose</td>
<td>-.129</td>
<td>-.039</td>
</tr>
<tr>
<td>WBS self-acceptance</td>
<td>.008</td>
<td>.027</td>
</tr>
<tr>
<td>WBS mastery</td>
<td>-.026</td>
<td>.022</td>
</tr>
</tbody>
</table>

Note. DAS = dysfunctional attitude scale; DSC = depressed symptom checklist; HRSD = hamilton rating scale for depression; PANAS = positive and negative affect scale; SLS = satisfaction with life; WBS = wellbeing scale. N= 77
* Correlation is significant at the .05 level (2-tailed)
** Correlation is significant at the .01 level (2-tailed)
## Table 2

*Correlations Between Changes in Clinical Scores and Neural Responses During Outcome Win*

<table>
<thead>
<tr>
<th>Contrast x Relapse</th>
<th>DAS</th>
<th>DSC Self-Concept</th>
<th>DSC Mood</th>
<th>DSC Total</th>
<th>HRSD</th>
<th>PANAS positive</th>
<th>SLS</th>
<th>WBS autonomy</th>
<th>WBS personal growth</th>
<th>WBS purpose</th>
<th>WBS self-acceptance</th>
<th>WBS mastery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superior temporal</td>
<td>0.054</td>
<td>0.095</td>
<td><strong>0.226</strong></td>
<td>0.206</td>
<td>0.072</td>
<td>-0.188</td>
<td>-0.04</td>
<td>-0.187</td>
<td>-0.081</td>
<td>-0.07</td>
<td>0.054</td>
<td>-0.012</td>
</tr>
<tr>
<td>Mid-cingulum</td>
<td>-0.044</td>
<td>-0.1</td>
<td>-0.101</td>
<td>-0.116</td>
<td>-0.126</td>
<td>0.128</td>
<td>0.036</td>
<td>-0.063</td>
<td>0.138</td>
<td>0.104</td>
<td>0.151</td>
<td>0.22</td>
</tr>
<tr>
<td>Precuneus</td>
<td>-0.098</td>
<td>-0.057</td>
<td>-0.041</td>
<td>-0.067</td>
<td>-0.109</td>
<td>0.096</td>
<td>0.069</td>
<td>-0.012</td>
<td>0.122</td>
<td>0.127</td>
<td>0.132</td>
<td>0.214</td>
</tr>
<tr>
<td>Middle temporal</td>
<td>0.098</td>
<td>0.216</td>
<td><strong>0.315</strong></td>
<td><strong>0.276</strong></td>
<td>0.044</td>
<td>-0.03</td>
<td>0.027</td>
<td>-0.066</td>
<td>0.13</td>
<td>-0.061</td>
<td>0.157</td>
<td>0.071</td>
</tr>
<tr>
<td>Time x Relapse</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPFC</td>
<td>0.108</td>
<td>0.217</td>
<td><strong>0.246</strong></td>
<td><strong>0.235</strong></td>
<td>0.049</td>
<td>0.008</td>
<td>0.01</td>
<td>0.061</td>
<td>0.047</td>
<td>-0.083</td>
<td>0.108</td>
<td>0.179</td>
</tr>
<tr>
<td>MPFC</td>
<td>0.109</td>
<td>0.071</td>
<td>0.047</td>
<td>0.045</td>
<td>0.056</td>
<td>0.066</td>
<td>-0.043</td>
<td>-0.102</td>
<td>-0.041</td>
<td>0.027</td>
<td>0.027</td>
<td>0.084</td>
</tr>
<tr>
<td>Precuneus</td>
<td>0.031</td>
<td>-0.003</td>
<td>-0.069</td>
<td>-0.051</td>
<td>-0.065</td>
<td>0.105</td>
<td>-0.071</td>
<td>-0.147</td>
<td>-0.017</td>
<td>0.019</td>
<td>-0.006</td>
<td>0.112</td>
</tr>
<tr>
<td>Superior Temporal</td>
<td>-0.032</td>
<td>-0.102</td>
<td>-0.054</td>
<td>-0.088</td>
<td>-0.016</td>
<td>0.077</td>
<td>0.009</td>
<td>-0.078</td>
<td>0.126</td>
<td>0.121</td>
<td>0.159</td>
<td><strong>0.269</strong></td>
</tr>
<tr>
<td>Caudate</td>
<td>0.035</td>
<td>0.043</td>
<td>0.08</td>
<td>0.063</td>
<td>0.065</td>
<td>0.009</td>
<td>-0.01</td>
<td>-0.099</td>
<td>-0.015</td>
<td>-0.021</td>
<td>0.101</td>
<td>0.106</td>
</tr>
<tr>
<td>Insula</td>
<td>0.087</td>
<td>0.139</td>
<td>0.217</td>
<td>0.187</td>
<td>0.142</td>
<td>-0.035</td>
<td>-0.104</td>
<td>-0.083</td>
<td>-0.052</td>
<td>0.027</td>
<td>0.066</td>
<td>-0.005</td>
</tr>
<tr>
<td>Putamen</td>
<td>0.119</td>
<td>-0.017</td>
<td>0.069</td>
<td>0.038</td>
<td>0.082</td>
<td>0.145</td>
<td>-0.106</td>
<td>-0.09</td>
<td>-0.008</td>
<td>-0.119</td>
<td>0.052</td>
<td>0.112</td>
</tr>
</tbody>
</table>

Note. DAS = dysfunctional attitude scale; DSC = depressed symptom checklist; HRSD = hamilton rating scale for depression; PANAS = positive and negative affect scale; SLS = satisfaction with life; WBS = wellbeing scale. N= 77

*Correlation is significant at the 0.05 level (2-tailed).

**Correlation is significant at the 0.01 level (2-tailed).
Table 3

Correlations Between Changes in Clinical Scores and Neural Responses in MBCT and CBT-WB (Outcome win)

<table>
<thead>
<tr>
<th></th>
<th>DAS</th>
<th>DSC Self-Concept</th>
<th>DSC Mood</th>
<th>DSC TOTAL</th>
<th>HRSD</th>
<th>PANAS positive</th>
<th>SLS</th>
<th>WBS autonomy</th>
<th>WBS personal growth</th>
<th>WBS purpose</th>
<th>WBS self-accept</th>
<th>WBS mastery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MBCT Change</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior temporal</td>
<td>0.298</td>
<td>0.125</td>
<td>0.243</td>
<td>0.213</td>
<td>-0.031</td>
<td>-0.059</td>
<td>-0.086</td>
<td>-0.21</td>
<td>-0.156</td>
<td>-0.022</td>
<td>-0.048</td>
<td>0.04</td>
</tr>
<tr>
<td>PCC</td>
<td>0.012</td>
<td>-0.157</td>
<td>-0.077</td>
<td>-0.142</td>
<td>0.360*</td>
<td>0.297</td>
<td>-0.002</td>
<td>-0.015</td>
<td>0.243</td>
<td>0.248</td>
<td>0.143</td>
<td>0.352*</td>
</tr>
<tr>
<td>Precuneus</td>
<td>0.069</td>
<td>-0.063</td>
<td>-0.03</td>
<td>-0.075</td>
<td>-0.311*</td>
<td>0.095</td>
<td>0.153</td>
<td>-0.019</td>
<td>0.173</td>
<td>0.216</td>
<td>0.132</td>
<td>0.400**</td>
</tr>
<tr>
<td>Middle temporal</td>
<td>0.310*</td>
<td>0.222</td>
<td>0.380*</td>
<td>0.312*</td>
<td>-0.254</td>
<td>0.085</td>
<td>0.128</td>
<td>-0.222</td>
<td>0.109</td>
<td>0.126</td>
<td>0.132</td>
<td>0.211</td>
</tr>
<tr>
<td><strong>CBT Change</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Superior temporal</td>
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<td>0.245</td>
<td>0.208</td>
<td>0.242</td>
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<td>-0.009</td>
<td>-0.17</td>
<td>-0.008</td>
<td>-0.14</td>
<td>0.137</td>
<td>-0.119</td>
</tr>
<tr>
<td>PCC</td>
<td>-0.106</td>
<td>-0.002</td>
<td>-0.065</td>
<td>-0.053</td>
<td>0.201</td>
<td>-0.06</td>
<td>0.069</td>
<td>-0.054</td>
<td>0.047</td>
<td>-0.086</td>
<td>0.223</td>
<td>0.053</td>
</tr>
<tr>
<td>Precuneus</td>
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<td>-0.038</td>
<td>-0.041</td>
<td>0.135</td>
<td>0.144</td>
<td>-0.017</td>
<td>-0.081</td>
<td>0.104</td>
<td>0.003</td>
<td>0.101</td>
<td>-0.117</td>
</tr>
<tr>
<td>Middle temporal</td>
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<td>0.219</td>
<td>0.231</td>
<td>0.234</td>
<td>0.299</td>
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<td>-0.108</td>
<td>0.05</td>
<td>0.135</td>
<td>-0.251</td>
<td>0.138</td>
<td>-0.129</td>
</tr>
</tbody>
</table>

Note. DAS = dysfunctional attitude scale; DSC = depressed symptom checklist; HRSD = hamilton rating scale for depression; PANAS = positive and negative affect scale; SLS = satisfaction with life; WBS = wellbeing scale. N= 77

* Correlation is significant at the 0.05 level (2-tailed).
** Correlation is significant at the 0.01 level (2-tailed).
### Table 4

**Correlations Between Clinical Scores and Neural Responses at Post-Treatment During Outcome Win**

<table>
<thead>
<tr>
<th>Contrast</th>
<th>DAS Self-Concept</th>
<th>DSC Mood</th>
<th>DSC Total</th>
<th>HRSD</th>
<th>PANAS positive</th>
<th>SLS</th>
<th>WBS autonomy</th>
<th>WBS personal growth</th>
<th>WBS purpose</th>
<th>WBS self-acceptance</th>
<th>WBS mastery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment x Relapse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior temporal</td>
<td>0.153</td>
<td>0.087</td>
<td>0.079</td>
<td>0.09</td>
<td>-0.093</td>
<td>0.052</td>
<td>-.227*</td>
<td>-0.088</td>
<td>-0.031</td>
<td>-0.047</td>
<td>-0.081</td>
</tr>
<tr>
<td>Mid-cingulum</td>
<td>0.021</td>
<td>-0.012</td>
<td>0.049</td>
<td>0.028</td>
<td>0.061</td>
<td>0.078</td>
<td>-0.111</td>
<td>-0.079</td>
<td>-0.033</td>
<td>0.083</td>
<td>0.02</td>
</tr>
<tr>
<td>Precuneus</td>
<td>0.083</td>
<td>0.069</td>
<td>0.052</td>
<td>0.054</td>
<td>0.122</td>
<td>0.1</td>
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<td>-0.172</td>
<td>-0.099</td>
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<td>0.097</td>
<td>0.143</td>
<td>0.179</td>
<td>0.168</td>
<td>0.048</td>
<td>0.057</td>
<td>-.227*</td>
<td>0.01</td>
<td>0.031</td>
<td>0.164</td>
<td>-0.005</td>
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<tr>
<td><strong>Time x Relapse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>DMPFC</td>
<td>.318**</td>
<td>.330**</td>
<td>.381**</td>
<td>.375**</td>
<td>0.125</td>
<td>0.088</td>
<td>-.272*</td>
<td>-0.09</td>
<td>-0.057</td>
<td>0.014</td>
<td>-0.214</td>
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<td>0.209</td>
<td>.249*</td>
<td>.230*</td>
<td>0.185</td>
<td>0.127</td>
<td>-0.198</td>
<td>0.123</td>
<td>0.095</td>
<td>-0.002</td>
<td>-0.063</td>
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<td>Precuneus</td>
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<td>0.074</td>
<td>0.138</td>
<td>0.115</td>
<td>0.107</td>
<td>0.124</td>
<td>-0.112</td>
<td>-0.056</td>
<td>-0.012</td>
<td>0.072</td>
<td>0.014</td>
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<td>Superior Temporal</td>
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<td>0.163</td>
<td>0.149</td>
<td>0.149</td>
<td>0.102</td>
<td>0.101</td>
<td>-0.058</td>
<td>-0.163</td>
<td>-0.05</td>
<td>0.003</td>
<td>-0.024</td>
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<tr>
<td>Caudate</td>
<td>0.09</td>
<td>-0.049</td>
<td>0.048</td>
<td>0.019</td>
<td>-0.112</td>
<td>0.272*</td>
<td>0.009</td>
<td>-0.094</td>
<td>0.039</td>
<td>0.135</td>
<td>0.057</td>
</tr>
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<td>0.221</td>
<td>.291*</td>
<td>.275*</td>
<td>0.174</td>
<td>0.03</td>
<td>-0.094</td>
<td>-0.189</td>
<td>-0.125</td>
<td>0.044</td>
<td>-0.052</td>
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<td>Putamen</td>
<td>0.082</td>
<td>-0.068</td>
<td>0.03</td>
<td>-0.004</td>
<td>-0.078</td>
<td>.230*</td>
<td>-0.013</td>
<td>-0.042</td>
<td>0.021</td>
<td>0.025</td>
<td>0.094</td>
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</tbody>
</table>

Note. DAS = dysfunctional attitude scale; DSC = depressed symptom checklist; HRSD = hamilton rating scale for depression; PANAS = positive and negative affect scale; SLS = satisfaction with life; WBS = wellbeing scale. N= 77

a log transformation of average frequency of time spent in formal practice

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).
Table 5
Binomial Logistic Regression for Predictions of Relapse Status

<table>
<thead>
<tr>
<th>Variables in the Equation</th>
<th>B</th>
<th>SE</th>
<th>Wald</th>
<th>df</th>
<th>p-value</th>
<th>Exp(B)</th>
<th>95% CI for Exp(B)</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A) Neural model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>VMPFC.ew</td>
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<td>3.76</td>
<td>8.75</td>
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<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>.02</td>
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<tr>
<td>MPFC.w</td>
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<td>1.44</td>
<td>4.51</td>
<td>1</td>
<td>.03</td>
<td>21.08</td>
<td>1.27</td>
<td>35.88</td>
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</tr>
<tr>
<td>Putamen.w</td>
<td>4.92</td>
<td>1.81</td>
<td>7.39</td>
<td>1</td>
<td>.01</td>
<td>136.57</td>
<td>3.94</td>
<td>4733.18</td>
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</tr>
<tr>
<td><strong>B) Clinical and Neural model</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>-.07</td>
<td>.04</td>
<td>2.91</td>
<td>1</td>
<td>.09</td>
<td>.93</td>
<td>.86</td>
<td>1.01</td>
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<tr>
<td>Age 1st episode</td>
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<td>.07</td>
<td>3.09</td>
<td>1</td>
<td>.08</td>
<td>1.13</td>
<td>.99</td>
<td>1.30</td>
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<tr>
<td>Prior episodes</td>
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<td>.17</td>
<td>1.08</td>
<td>1</td>
<td>.30</td>
<td>1.19</td>
<td>.86</td>
<td>1.64</td>
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<tr>
<td>Gender</td>
<td>.96</td>
<td>.83</td>
<td>1.35</td>
<td>1</td>
<td>.25</td>
<td>2.61</td>
<td>.52</td>
<td>13.15</td>
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</tr>
<tr>
<td>WBS mastery</td>
<td>-.23</td>
<td>.08</td>
<td>7.97</td>
<td>1</td>
<td>.01</td>
<td>.80</td>
<td>.68</td>
<td>.93</td>
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<td>VMPFC.ew</td>
<td>-1.68</td>
<td>4.26</td>
<td>6.28</td>
<td>1</td>
<td>.01</td>
<td>.00</td>
<td>.00</td>
<td>.10</td>
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<tr>
<td>MPFC.w</td>
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<td>5.26</td>
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<td>.02</td>
<td>72.16</td>
<td>1.86</td>
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<td>Putamen.w</td>
<td>4.94</td>
<td>2.09</td>
<td>5.58</td>
<td>1</td>
<td>.02</td>
<td>14.26</td>
<td>2.32</td>
<td>848.60</td>
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</tr>
</tbody>
</table>

Note. Significant neural responses to anticipation to win are identified with .ew and .w for outcome win. SE= standard error; Exp(B) = odds ratio; VMPFC= ventromedial prefrontal cortex; MPFC= medial prefrontal cortex; WBS = wellbeing scale.

PANAS = positive and negative affect scale; SLS = satisfaction with life; WBS = wellbeing scale. N= 77
\[ a \] log transformation of average frequency of time spent in formal practice

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).
Table 6
Relationship Between Time, Relapse, and Treatment in Model 2

<table>
<thead>
<tr>
<th>Contrast</th>
<th>F</th>
<th>Sig.</th>
<th>Partial eta squared</th>
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</thead>
<tbody>
<tr>
<td><strong>Anticipation to Win</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Main effect relapse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VMPFC</td>
<td>14.6</td>
<td>0**</td>
<td>0.088</td>
</tr>
<tr>
<td>Outcome win</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Time x Relapse</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DMPFC</td>
<td>4.07</td>
<td>.047*</td>
<td>0.051</td>
</tr>
<tr>
<td>MPFC</td>
<td>4.25</td>
<td>.043*</td>
<td>0.054</td>
</tr>
<tr>
<td>Precuneus</td>
<td>1.56</td>
<td>.216</td>
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</tr>
<tr>
<td>Superior temporal</td>
<td>2.07</td>
<td>.155</td>
<td>0.027</td>
</tr>
<tr>
<td>Caudate</td>
<td>3.88</td>
<td>.052</td>
<td>0.049</td>
</tr>
<tr>
<td>Insula</td>
<td>2.96</td>
<td>.089</td>
<td>0.038</td>
</tr>
<tr>
<td>Putamen</td>
<td>7.08</td>
<td>.01*</td>
<td>0.086</td>
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<tr>
<td><strong>Group x Relapse</strong></td>
<td></td>
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<tr>
<td>Superior temporal</td>
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<td>.121</td>
<td>0.028</td>
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<td>Mid-cingulum/PCC</td>
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<td>.085</td>
<td>0.026</td>
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<tr>
<td>Precuneus</td>
<td>2.76</td>
<td>.098</td>
<td>0.025</td>
</tr>
<tr>
<td>Middle temporal</td>
<td>9.59</td>
<td>.002**</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Note. Significant effects are highlighted in bold. VMPFC = ventromedial prefrontal cortex; DMPFC = dorsomedial prefrontal cortex; MPFC = medial prefrontal cortex; PCC = posterior cingulate cortex.

** Correlation is significant at the 0.01 level (2-tailed).

* Correlation is significant at the 0.05 level (2-tailed).