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TREATMENT FOR ANHEDONIA: A NEUROSCIENCE DRIVEN APPROACH

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Anhedonia, or loss of interest or pleasure in usual activities, is characteristic of depression, some types of anxiety, as well as substance abuse and schizophrenia. Anhedonia is a predictor of poor long-term outcomes, including suicide, and poor treatment response. Because extant psychological and pharmacological treatments are relatively ineffective for anhedonia, there is an unmet therapeutic need for this high-risk symptom. Current psychological and drug treatments for anxiety and depression focus largely on reducing excesses in negative affect rather than improving deficits in positive affect. Recent advances in affective neuroscience posit that anhedonia is associated with deficits in the appetitive reward system, specifically the anticipation, consumption, and learning of reward. In this paper, we review the evidence for positive affect as a symptom cluster, and its neural underpinnings, and introduce a novel psychological treatment for anxiety and depression that targets appetitive responding. First, we review anhedonia in relation to positive and negative valence systems and current treatment approaches. Second, we discuss the evidence linking anhedonia to biological, experiential, and behavioral deficits in the reward subsystems. Third, we describe the therapeutic approach for Positive Affect Treatment (PAT), an intervention designed to specifically target deficits in reward sensitivity. Depression and Anxiety 33:927–938, 2016. *© 2016 Wiley Periodicals, Inc.*

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INTRODUCTION

A number of psychological treatments have shown to be effective for anxiety and unipolar depression, including cognitive behavioral therapy, behavioral activation therapy, interpersonal therapy, problem solving therapy, and, more recently, mindfulness-based approaches and acceptance and commitment therapy.[1–5] However, these treatments remain only partially effective. For example, within the anxiety disorders, rates of "clinically significant" improvement for cognitive and behavioral therapies hover around 50%.[6] Similar rates have been observed in the treatment of unipolar depression.[4] Thus, there is a strong need for newer treatment models that improve treatment outcomes.

Traditionally, psychological treatments for anxiety and unipolar depression aimed to reduce negative affect and associated impairment in functioning, albeit via differing therapeutic strategies and purported mediators. The focus upon negative affect (such as anxiety, fear, guilt, shame, sadness), however, ignores the deficits in positive affect that also characterize anxiety and depression. It has long been recognized that at least two core systems regulate thoughts, behaviors, and actions.[7–9] The first is the approach or appetitive system, which motivates actions toward goals and rewards, and produces positive emotions such as enthusiasm and pride. The second is the withdrawal or defensive system

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that motivates avoidance of aversive outcomes or punishments, and is linked with negative emotions such as anxiety and depression. Theorists have varied in terminology and the extent to which additional systems are postulated, although all include at least two basic dimensions describing this dichotomy.[10] Gray (1990)[11] describes a Behavioral Activation System that motivates approach, a behavioral inhibition system that motivates withdrawal, and an additional fight-flight system that energizes responses to unconditioned threat stimuli. Others like Davidson (2003)[12] do not conceptualize separate defensive systems supporting withdrawal and fight-or-flight. Despite the fundamental role played by both appetitive and defensive systems in unipolar depression and anxiety or fear, treatment to date has focused largely upon decreasing defensive responding rather than increasing appetitive Responding.

In this paper, we outline a new model of psychological treatment for anxiety and depression that targets appetitive responding (or the positive valence system). Our proposed approach is relevant to unipolar depression, but does not currently extend to bipolar depression. As such, the term "transdiagnostic" only applies to the unipolar depression and anxiety spectrum, but not the full mood spectrum. The adaptability to bipolar disorder awaits careful testing, given the unique challenges in the reward system dysregulation in this disorder.[13,14] Before discussing the treatment per se, we first review the relationship between the construct of positive affect and symptoms of anxiety and depression as well as its neural underpinnings.

NEGATIVE AFFECT AND POSITIVE AFFECT

Investigations of the structure of symptoms of anxiety and depression has reliably identified two factors, one representing negative affect and the other representing positive affect. For example, the original "tripartite model" of fear, anxiety, and depression[7] identified a negative affect (or general distress) factor that was comprised of symptoms that were shared across anxiety and depression. Symptoms of anhedonia, or the absence of positive affect, were viewed as being specific to depression whereas symptoms of physiological hyperarousal were specific to "anxiety" (it was later recognized that hyperarousal may be specific to panic disorder[9]). More recent models recognize more complex and hierarchical structures for symptoms of anxiety and depression, but continue to identify separable factors associated with negative affect and with positive affect.[9,15]

Structural models of symptoms of anxiety and depression, and the elucidation of factors of negative affect and positive affect, served as one of the cornerstones for the NIMH Research Domain Criteria (RDoC) Initiative.[16,17] For research purposes, the RDoC initiative proposes a set of dimensional constructs for studying psychopathology: negative valence systems, positive valence systems, cognitive systems, systems for social processes, and arousal or regulatory systems. Furthermore, the RDoC drives a units-of-analysis approach to the study of psychopathology, at the center of which is behavioral neuroscience, extending upward to clinically relevant variation and downward to genetic and molecular or cellular factors. Table 1 lists each of the RDoC five domains with their description, which can be analyzed on at least seven levels (*units of analysis)*, including genes, molecules, cells, circuits, physiology, behavior, self-reports, and paradigms, although most studies will likely only include a subset of the suggested units. The paradigmatic shift offered by the RDoC initiative was influenced by by Engel's seminal conceptualization of the biopsychosocial model[18] and more recently fueled by major advances in affective neuroscience that have begun to elucidate the mechanisms underlying negative and positive valence systems.

ANHEDONIA, DEPRESSION, AND ANXIETY

Symptomatic deficits in positive affect are referred to as anhedonia, and involve loss of enjoyment in pleasurable activities or loss of desire to engage in pleasurable activities.[19,20] Within major depression, anhedonia is more strongly associated with the core disturbances of depression (e.g. lassitude) than with the nonspecific symptoms that are shared with other emotional disorders (e.g. insomnia).[21] Approximately one third of depressed individuals have clinically significant anhedonia symptoms, at least as defined by cutoffs on scales that measure enjoyment of social and physical pleasure.[22] Anhedonia extends beyond major depression to anxiety. Low levels of positive emotion have been consistently linked to symptoms and diagnoses of social anxiety disorder, although with a smaller magnitude of effect than depression.[9,23] Anhedonia is associated with symptoms of generalized anxiety disorder.[15] Furthermore, in experimental paradigms (described further below), hedonic impairments have been observed in social anxiety disorder,[24] posttraumatic stress disorder,[25,26] and generalized anxiety disorder[27] including youth samples.[28] Finally, anhedonia is also relevant to schizophrenia[21] and substance use disorder[29] and as such represents a dimension of psychopathology that crosses diagnostic boundaries.

Anhedonia is not only a correlate but is also a risk marker of psychopathology. For example, self-reported anhedonia (lower levels of positive emotion) is a robust predictor of poorer longitudinal course of symptoms of major depression across a number of prospective studies.[30] In addition, anhedonia within major depression is a substantial predictor of suicide[31] as well as suicidal ideation, where the predictive effects persist even when controlling for other cognitive and affective symptoms of depression.[32] Moreover, the trait variance component of low positive affect prospectively predicted the onset of not only major depression but also social anxiety disorder and generalized anxiety disorder, although the effects were indirect and accounted for by neuroticism.[33]

TABLE 1. NIMH research domain criteria (rdoc) project-positive valence systems: workshop proceedings

Construct	Construct definition
1. Approach motivation	A multifaceted construct involving mechanisms/processes that regulate the direction and maintenance of approach behavior influenced by preexisting tendencies, learning, memory, stimulus characteristics, and deprivation states. Approach behavior can be directed toward innate or acquired cues (i.e. unconditioned vs. learned stimuli), implicit, or explicit goals; it can consist of goal-directed or Pavlovian-conditioned responses. Component processes include reward valuation, effort valuation/willingness to work, expectancy/reward prediction error, and action selection/decision making.
1a. Reward valuation	Processes by which the probability and benefits of a prospective outcome are computed and calibrated by reference to external information, social context (e.g. group input, counterfactual comparisons), and/or prior experience. This calibration is influenced by preexisting biases, learning, memory, stimulus characteristics, and deprivation states. Reward valuation may involve the assignment of incentive salience to stimuli.
1b. Effort valuation/willingness to work	Processes by which the cost(s) of obtaining an outcome is computed; tendency to overcome response costs to obtain a reinforcer.
1c. Expectancy/reward prediction error	A state triggered by exposure to internal or external stimuli, experiences or contexts that predict the possibility of reward. Reward expectation can alter the experience of an outcome and can influence the use of resources (e.g. cognitive resources).
1d. Action selection/preference-based decision making	Processes involving an evaluation of costs/benefits and occurring in the context of multiple potential choices being available for decision-making.
2. Initial responsiveness to reward attainment	Mechanisms/processes associated with hedonic responses—as reflected in subjective experiences, behavioral responses, and/or engagement of the neural systems to a positive reinforcer—and culmination of reward seeking.
3. Sustained/longer term responsiveness to reward attainment	Mechanisms/processes associated with the termination of reward seeking, e.g. satisfaction, satiation, regulation of consummatory behavior.
4. Reward learning	A process by which organisms acquire information about stimuli, actions, and contexts that predict positive outcomes, and by which behavior is modified when a novel reward occurs or outcomes are better than expected. Reward learning is a type of reinforcement learning, and similar processes may be involved in learning related to negative reinforcement.
5. Habit	Sequential, repetitive, motor, or cognitive behaviors elicited by external or internal triggers that, once initiated, can go to completion without constant conscious oversight. Habits can be adaptive by virtue of freeing up cognitive resources. Habit formation is a frequent consequence of reward learning, but its expression can become resistant to changes in outcome value. Related behaviors could be pathological expression of a process that under normal circumstances subserves adaptive goals.

Source: https://www.nimh.nih.gov/research-priorities/rdoc/development-and-definitions-of-the-rdoc-domains-and-constructs.shtml.

Furthermore, anhedonia predicts poorer response to pharmacological treatments for depression.[34,35] We were unable to locate published studies of anhedonia as a predictor of psychological treatments. However, using data from our recent trial of cognitive and behavioral therapies for social anxiety disorder ($n = 75$),[36] we found that low positive affect at baseline was a significant predictor of poorer outcomes ($b = -.70$, $B = -.25$, $P = .045$).

Existing psychological and pharmacological treatments are relatively ineffective for treating anhedonia. Specifically, standard medication treatments have little effect and may even worsen anhedonic symptoms.[37–39] In fact, anhedonia was one of the most prevalent residual disturbances following fluoxetine treatment.[40] This has led to interest in newer treatments such as ketamine that improve anhedonia, at least in the short-term.[41] In terms of psychological treatments, behavioral activation therapy is designed to increase response contingent positive reinforcement.[42] However, very few studies have reported the effects of behavioral activation upon positive affect. An iteration of Lejuez and Hopkos' version of behavioral activation therapy (which gives less emphasis to response contingent positive reinforcement than other versions) failed to improve self-rated trait anhedonia in one small-scale study[43] and failed to improve self-rated state anhedonia in another study with a larger sample, albeit with a briefer version of behavioral activation.[44] In a reanalysis of a large randomized controlled trial by DeRubeis et al. (2005),[45] cognitive therapy and antidepressant medication normalized elevations in negative affect but had limited effect on positive affect. Specifically, relative to general adult population norms,[46] percentile scores on the Negative Affect subscale of the Positive and Negative Affect Schedule (PANAS) changed from 88 to 59% for cognitive therapy and from 87 to 49% for medication treatment.[47] In contrast, end-of-treatment levels on the Positive Affect scale remained lower than typical for the general adult population; percentile scores changed from 9 to 28% for cognitive therapy and from 5 to 31% for medication. We were unable to locate reports of the

effects of interpersonal therapy, another evidence-based psychological treatment for depression, upon positive affect.

It is possible that further investigation of behavioral activation with strong emphasis upon response-contingent positive reinforcement would yield beneficial effects upon positive affect. Nonetheless, the limited effect to date is not surprising in light of the fact that little attention has been given to how behavioral activation is best conducted in order to maximize positive emotional experience.[48] Treatment strategies that specifically target the mechanisms underlying anhedonia are needed to improve treatment effects.

ANHEDONIA: BRAIN TO BEHAVIOR

Anhedonia can be viewed as a symptom of an underlying dysregulated pleasure system. Based on the pleasure cycle model, reward engagement serves a survival function, following a cyclical time course with rewards acting as motivational magnets to initiate, sustain, and switch states. Classically, reward processing has been linked to appetitive, consummatory, and satiety cycle phases[49] and are supported by multiple brain networks associated with liking, wanting, and learning.[50] While wanting processes dominate the appetitive phase and liking processes dominate the consummatory phase, learning is thought to be strongest during the satiety phase, but can also occur throughout the pleasure cycle. The reward system affects the ability to anticipate or predict expected rewards; associate relative values and costs with rewards; determine the effort required to obtain rewards; integrate this information to decide whether it is worthwhile to obtain rewards; and become motivated to perform the necessary actions to obtain rewards.[51] While researchers may emphasize different parts of the reward system, there is some convergence upon three main components: (1) anticipation of reward, (2) consumption of reward, and (3) learning of reward.[29,51] In this approach, the anticipatory component refers to the motivation for rewarding stimuli, such as planning and looking forward to a vacation, and is related to the effort expended to receive reward. It is dominated by "wanting." The consummatory component refers to the pleasure or hedonic impact of rewarding stimuli, such as the pleasure while on vacation, and is dominated by "liking." The learning component typically involves Pavlovian or instrumental associations and predictions about future rewards based on past experiences, such as the decision to take another vacation given the rewards of the last vacation.

Individuals who are depressed show deficits in the anticipation and learning of reward across multiple indices, and in the consumption of reward on certain indices.[52,53] More importantly, there is compelling evidence that reward hyposensitivity in depression reflects anhedonia.[29,54–57] In the following sections, we summarize the neural to behavioral correlates of reward responding and their relationships to anhedonia, using the three-component approach. We recognize that that others may emphasize different distinctions and constructs of relevance to the reward system (such as satiety and goal-directed versus habitual responding).

Anticipation/Wanting/Motivation. While it is difficult to fully disentangle reward anticipation and reward consumption from reward learning (since motivational factors inherent to the anticipation of reward and the hedonic impact inherent to the consumption of reward likely influence reward learning[51]), there is good evidence for distinctive neural substrates for the anticipation versus consumption components of the reward system. Specifically, dopaminergic signaling is related to the anticipation but not to the consumption of reward.[58–60] In humans, neural regions most strongly linked to the anticipation of reward include the ventral tegmental area, amygdala, and ventral striatum.[51,61] Beyond a neural signature, the anticipation of reward is associated with self-report, behavioral, and psychophysiological markers (or "units of analysis"). Specifically, reward anticipation is indexed through self-report of expectancies of outcomes and the amount of effort expenditure for reward and the extent to which signals that cue reward enhance the rate of responding in order to receive reward (Pavlovian instrumental transfer paradigms).[29] Psychophysiological indices include heart rate increases in relation to anticipation of rewards or to gain incentives (as in monetary incentive paradigms).[62–66] Within Gray's motivational theory of pathophysiology, Fowles (1988)[67] identified heart rate as the key psychophysiological variable indexing the behavioral approach or appetitive motivational system. Sympathetic excitation appears as the major driver of heart rate responses to incentives,[66] presumably in preparation for elevated metabolic demand that arises while executing the necessary activities to obtain rewards. Cardiovascular mobilization in the context of incentive task performance can therefore be interpreted as indexing the strength of anticipatory/motivational reward system activity, although levels of actual physical activity that naturally increase metabolic demand need to be controlled.[68]

There is good evidence for symptoms of anhedonia to be associated with deficits in the anticipation of reward across several units of analysis. At the level of neural activation, depressed individuals show reduced activation in reward circuitries in anticipation of reward.[69–75] Importantly, there is evidence for reduced ventral striatum responsivity to anticipation of reward to be particularly related to anhedonic symptoms.[76,77] Also, dysphoric individuals expect to feel less positive emotions in future positive events[78,79] and self-report less positive emotion in anticipation of a monetary reward[57] compared to healthy controls, although the evidence is not entirely robust.[80] At the behavioral level, trait anhedonia among healthy individuals correlates with choosing easy tasks for a small reward over harder tasks for larger rewards, indicative of less expenditure of effort to gain reward.[81] Also, depressed individuals make fewer high

reward/high effort choices than healthy controls,[82] and importantly, the effort they expend to obtain rewards correlates negatively with anhedonia.[82,83] In terms of psychophysiology, dysphoric individuals show less reliable acceleration of heart rate than healthy controls when performing memory or mental arithmetic tasks that are linked to monetary rewards.[84–86]

Consumption/Liking. The consumption of reward appears to be related to opioid and endocannabinoid pathways.[87] Neural regions most strongly linked with liking of reward include the ventral striatum (representing overlap with the anticipation of reward) and orbitofrontal cortex.[51,61] Self-report of liking of reward typically involves ratings of pleasure or preference in relation to primary and secondary rewarding stimuli.[88,89] Cognitive measures include the amount of time that attention is directed to positive stimuli using paradigms such as dot probe tasks.[90–92] Psychophysiological indices include electromyographic measurements of facial muscle activation,[88,89] eye blink startle reflexes, and heart rate acceleration while viewing pleasant or exciting pictorial stimuli.[93–96]

At the level of neural activation, there is good evidence for ventral striatum hypoactivity to positive stimuli to be associated with depression and particularly with symptoms of anhedonia.[69,97–99] Furthermore, Wacker et al. (2009)[99] established that the effects were specific to anhedonia above and beyond negative symptoms of anxiety or depression. The evidence for lower self-rated liking of reward as a function of depression is mixed, as some studies fail to show deficits in liking of reward[100–102] and others report blunted self-reported positive emotion to the sweet taste task, a basic consumption task.[103] However, the discrepancies may be partially due to anhedonia, since lower levels of self-reported positive emotions to positive stimuli are more strongly related to anhedonia than depression.[100,104] In terms of cognitive functioning, depressed individuals show less attention to positive stimuli than controls as measured via response latency times in dot probe tasks and eye tracking.[90–92] Moreover, attention to positive information is associated with positive affect.[105] Psychophysiological indices show that depressed individuals have reduced facial expressions and less contraction of zygomatic muscles to positive stimuli.[106] A number of studies have found reduced attenuation of the startle blink reflex to positive stimuli in depressed individuals[107–110] although some failures to replicate exist.[111] Deficits of pleasure-attenuation of the startle reflex have also been observed in animal models of depression.[112] Furthermore, attenuation of startle blink reflex modulation has been linked to anhedonia in depressed patients in one study Kaviani et al. (2004),[113] although another study found no association with anhedonia[107] and a third study found similar levels of startle potentiation to positive picture in patients with anhedonia and anxious arousal.[109] Thus, the findings regarding startle blink reflex and anhedonia are mixed. Finally, anhedonia is associated with reduced cardiac acceleration while viewing pleasant pictorial stimuli[94] or during imagery of pleasant emotional scripts.[114]

Learning. As with the anticipation of reward, learning of reward appears to be associated with dopaminergic signaling.[58–60] Various areas of the prefrontal cortex have been implicated in decision making and reward learning, and animal research highlights areas such as the ACC, orbitofrontal cortex (representing overlap with consumption of reward), vmPFC and dorsal lateral PFC.[51] There are no self-report measures of learning reward, although behavioral measures of reward learning include reward probabilistic tasks.[115] The distinction between anticipation of reward and reward learning is not as strong as the distinction between liking and anticipation. Nonetheless, some evidence for distinction exists. For example, dopamine enhancement increases neural activation in response to signals of incentive salience (i.e. liking) but does not increase neural activation to signals of prediction (i.e. learning)[116] and wanting of a cue can be motivated by changes in motivational state without changing prior learned associations.[117]

At the neural level, depressed individuals show reduced activation in reward circuitries during reward learning[118] and poor reversal learning after unexpected reward delivery in depressed individuals is associated with deficits in the ventral striatum.[119] The monetary incentive delay task also reveals lower activation in the dorsal caudate (an area connected with feedback driven contingency learning) in depressed individuals.[69] There is some evidence for blunted ventral striatal responses to Pavlovian[118] and instrumental conditioning tasks[120] in depression with neural responses correlating with self-reported anhedonia.[120] In terms of behavioral indices, the propensity to develop a response bias to stimuli that are more frequently rewarded is less likely to develop over time as a function of higher depressive symptoms.[115,121] Importantly, impairments in response bias formation among clinically depressed individuals correlate with self-reported anhedonia.[56,115,121] Furthermore, reduced reward learning predicted elevated anhedonia symptoms one month later[115] and depressed adults with poor, as compared to those with relatively intact reward learning, were almost eight times more likely to remain symptomatic at the end of SSRI or psychotherapy.[121]

TARGETED TREATMENT FOR DEFICITS IN THE APPETITIVE REWARD SYSTEM

The linkages between symptoms of anhedonia on the one hand, and neural, psychophysiological, behavioral, cognitive, and self-report measures of different facets of reward processing on the other hand, are clearly correlational in nature. Thus, it cannot be assumed that deficits in reward processing cause anhedonia. Yet, an extensive body of research on instrumental conditioning demonstrates a causal link between positive reinforcement for a behavior and its frequency of occurrence.[122] Also, appetitive Pavlovian conditioning

imbues neural stimuli with positive valence.[123] Furthermore, many studies have demonstrated that primary reinforcers enhance positive affect in healthy controls, as reviewed in prior sections (e.g. the sweet taste task). Together, these data raise the possibility that a treatment that specifically targets reward processing may be particularly potent for anhedonia. As reviewed above, affective neuroscience has advanced our understanding of reward processing through distinguishing the neural substrates of different components of reward processing. We have focused on the components of (1) reward anticipation/wanting/motivation, (2) reward consumption/liking and (3) reward learning (although as indicated, additional conceptualizations of reward systems, such as satiety and devaluation, exist). The distinction amongst these three components provides a format around which behavioral interventions can be structured. Furthermore, such reward-targeted treatments may influence neural systems of reward in the same way that threat-targeted treatments influence neural indices of threat responding.[124] Drawing from affective neuroscience research and experimental psychopathology research, we have developed a treatment that specifically targets three cardinal subdomains within the RDoC Positive Valence Systems: anticipation, consumption, and learning of reward. We are currently investigating the effects of this treatment in anxious or depressed individuals. Our treatment manipulates cognitive and behavioral manifestations of purported underlying neural systems (e.g. ventral striatum and orbitrofrontal cortex) with cognitive and behavioral strategies. However, future neuroimaging will be needed to demonstrate actual effects upon neurobiology of reward.

The treatment, coined Positive Affect Treatment, is comprised of three modules (see Table 2). We selected therapeutic techniques that directly target positive affect or have been shown to improve positive affect. Furthermore, we selected techniques that directly targeted one or more of the reward system components (anticipation, consumption, and learning). Given the limited mechanistic research on anhedonia, we chose a range of techniques to maximize improvements in positive affect. Dismantling studies will be necessary to isolate which techniques are essential. Furthermore, techniques aimed at reducing negative affect, such as monitoring and challenging of negative thoughts, or strategies for decreasing arousal, or exposure to feared or avoided activities, were purposefully excluded.

The first module is modified pleasant events scheduling, which combines planning for engagement in pleasurable activities (reward anticipation) and reinforcement of the positive mood inducing effects of those activities (reward learning) with "in-the-moment" recounting designed to savor pleasurable moments and enhance hedonic impact (reward consumption). Pleasant events scheduling (PES) as a treatment approach is rooted in Lewinsohn's conceptualization of etiology and maintenance of depression.[125] This view holds that depression is preceded by and correlates with low levels of reinforcement, and alleviated by treatment-induced increases in positive reinforcement. Notably, individuals with depression not only engage in less rewarding activities but experience these activities as less rewarding. Unlike cognitive theories of depression, disruption of automatic behavioral patterns (i.e. regular daily activities) is thought to be caused by environmental stressors rather than negative cognitions. The goal is thus to reactivate adaptive behaviors. Activation of adaptive behaviors within the context of Behavioral Activation, and extension from PES, has been shown to be effective for depression as a sole treatment component[126] and superior to cognitive therapy.[127] However, our treatment approach is more closely aligned with PES in that, unlike Behavioral Activation, we do not focus on depressed thinking, rumination, or active disengagement in activities that maintain negative mood.[42]

Specifically, clients engage in daily activities that are inherently pleasurable or provide a sense of accomplishment, mastery, or are consistent with valued actions. PES is closely monitored through recording daily activities and changes in mood before and after the activity, and labeling of the positive emotion experienced during the activities. We extend beyond traditional PES via in-session recounting of the activity, in which therapists guide clients as they imagine and recall their activities in the present tense. In so doing, we are training clients in how to optimize positive emotions in relation to the conduct of their activities, as recommended by Dunn (2012).[48] Clients are repeatedly guided to attend to the physical sensations, thoughts, behaviors, and positive mood associated with particular moments of the activity in order to deepen and savor positive aspects of the experience. The recounting aspect was guided by evidence for attentional control (shifting attention from one aspect of a situation to another) as a form of emotion regulation[128] and for the effects of training attention to positive aspects of experience.[129] Specifically, there is evidence showing that attentional bias to positive stimuli (using visual stimuli) can be trained and lead to subsequent preferences for positive stimuli, albeit in nonclinical samples.[130] Wadlinger and Isaacowitz (2011)[129] offer several possible mechanisms for such effects, including the possibility that attentional training to positive information increases preference for positive material which in turn decreases interest in negative information.[129] Furthermore, training positive attentional preferences may enhance attentional vigilance for and orienting toward positive information that eventually shifts more elaborate attention mechanisms toward positive meanings and facilitates encoding of positive information in daily experiences. Consequently, training attention to positive features of experience is likely to increase positive affect, perhaps via attentional processes that reinforce positive affect, and is posited to increase tendencies to approach rewards in the environment.[129] Finally, the modified PES module identifies barriers to carrying out activities and solution strategies (e.g. breaking down the activities into small, achievable tasks).

TABLE 2. Positive affect treatment overview: 15 weekly sessions

Modules	How is target engaged
Pleasant events scheduling (7 sessions)	
Design activities Targeted mediator: anticipation	Goal setting and anticipation of reward by generating and scheduling activities that (1) currently find enjoyable, once found enjoyable, or believe could be enjoyable, (2) bring value to life, or (3) produce feelings of mastery (or other positive emotions)
Conduct activities Targeted mediator: Consumption + learning	Train to savor reward and learn activity-mood instrumental associations by recording primary positive emotions prior to, during, or following the activity
Recount activities Targeted mediator: consumption	Train to savor reward through therapist-guided in-the-moment recounting of positive aspects of activities and associated emotions, sensations, and thoughts
Theoretical and empirical support[48,126,129]	
Attending to the positive (3 sessions)	
Finding the silver lining Targeted mediator: anticipation	Train attention to positive stimuli by repeated practice identifying positive features of daily situations
Taking ownership Targeted mediator:Consumption + learning	Learn to recognize behavior-mood associations and to savor positive emotions and events by repeated practice identifying behavioral contributions to positive outcomes
Imagining the positive Targeted mediator: anticipation	Train to imagine positive outcomes from imagined future events
Theoretical and empirical support[129,132–134,153]	
Cultivating the positive (4 sessions)	
Loving-kindness Generosity Appreciative joy Gratitude Targeted mediator: Consumption	Cultivate positive feelings toward self and others by daily practices of (1) mental act of giving (i.e. mentally sending happiness, health, peace, and freedom from suffering); (2) physical act of giving (i.e. engaging in an act of generosity at least once daily (without expecting return); (3) mental act of wishing good to self and others (i.e. wishing happiness and good, joy, and fortune), (4) generating sense of gratefulness. Practices are accompanied by savoring positive emotions and are supported by audio-scripts
Theoretical and empirical support.[135–137,144,154]	

Session 15 is relapse prevention.

The second module comprises a set of cognitive training exercises. Unlike cognitive therapy for depression, which aims to challenge negative cognitions, our cognitive techniques aim to identify positive aspects of experience (reward anticipation and consumption), take responsibility for positive outcomes (reward learning), and imagine and appreciate future positive events (reward anticipation). The first technique, titled *Silver Lining*, trains clients to recognize and appreciate the positive features in everyday situations, even situations with an overall negative valence. As with recounting following PES, the repeated practice of identifying multiple positive elements in everyday situations draws from evidence for training attention to positive information.[129] The second technique, called *Taking Ownership*, involves repeated practice identifying behavioral contributions to positive outcomes in daily lives (reward learning) and to savor positive emotions of pride, mastery, and excitement (reward consumption). Accomplishments can be read out loud in front of a mirror to deepen the experience of receipt of reward. Taking ownership counters the depressive attributional bias to attribute positive outcomes to external factors and is consistent with experimental evidence for training a positive attributional bias, albeit in nonclinical samples.[131] The third technique is called *Imagining the Positive*, which is based on evidence for positive mood effects of repeated practice imagining positive events.[132–134] Clients repeatedly imagine as many positive aspects as possible about an upcoming event (reward anticipation), including positive emotions such as excitement, joy, and curiosity (reward consumption).

The third module is a set of experiential exercises designed to cultivate and savor positive experiences (reward consumption).[135–137] These include daily practices of the mental act of giving (*Loving-Kindness*: mentally sending happiness, health, peace, and freedom from suffering) and the physical act of giving (*Generosity*: engaging in an act of generosity at least once daily without expecting return). They also involve daily practices of the mental act of wishing good to self and others (*Appreciative Joy*: wishing happiness and good, joy, and fortune) and of generating sense of gratefulness *(Gratitude)*. Practices are accompanied by savoring positive emotions and are supported by audio-scripts. Much of the content of these practices were adapted from loving kindness, generosity, appreciative joy, and gratitude meditations developed at the UCLA Mindful Awareness Research Center (MARC). We modified these techniques so that the exercises focused only on positive aspects.

Loving-Kindness Meditation emphasizes in-the-moment nonjudgmental, curious awareness of sensory experiences, affective states, and cognitions)[138,139] as unconditional kindness is cultivated by mentally sending specific wishes to others and oneself. Loving-Kindness Meditation is thought to be particularly

helpful for alleviating strong negative emotions such as hostility, anger, self-criticism, and shame through increases in empathy and positive mood. Practices in the exercise, even brief ones,[140] have shown to lead to increases in positivity toward self and others, improvements in positive affect and personal resources (e.g. personal relationship with others, physical health, self-acceptance, satisfaction).[141] Preliminary evidence from proof-of-concept clinical trials in individuals with schizophrenia,[142] posttraumatic stress disorder,[143] and more recently in dysthymia[144] show increases in positive emotions, anhedonia, and an improved sense of self and others. In our treatment, clients are given an audio-guide to generate an image of the recipient (self, another person, a pet), gently sending loving kindness ("may you be healthy," "may you have peace," "may you be free from suffering") while mindfully observing how "wishing well" influences their emotions in the moment. Practices proceed from recipients with which the client already has positive feelings to practices with recipients toward which the client has felt resentful, hurtful, or hostile.

Cultivating gratitude (by gratitude lists, gratitude contemplation, or the behavioral expression of gratitude) leads to state changes in positive mood, greater resourcefulness, and general well-being,[137,145–147] albeit in nonclinical samples. It is speculated that gratitude leads to increased value of help from others[137,148], which leads to seeking more social support and strengthening social bonds.[149] This "broaden and build" approach[150] is thought to add to resiliency.[151] In our treatment, clients engage in daily gratitude exercises that entail daily listing of five to ten things to be grateful for, writing a gratitude journal, or carrying of a gratitude rock that acts as a reminder, with ongoing recording of physical feelings, emotions, and thoughts.

CONCLUSION

We have outlined a novel treatment for anhedonia and its rationale based on neurobiological evidence for reward system dysfunctions. The treatment is being evaluated among anxious or unipolar depressed individuals but has the potential to contribute to the treatment of other disorders that have anhedonic features, such as substance abuse and schizophrenia. Initial findings are promising, with significant reductions in symptoms of anxiety and depression, significant improvements in positive affect, and evidence for superior outcomes in those with lower levels of positive affect at baseline.[152] Levels of clinically significant anhedonia, optimal timing of the intervention, dismantling of the intervention, and moderation and disorder-specific considerations will need to be established by future research. As treatment research moves toward targeting neurobiological systems as advocated by the NIMH RDoC initiative, the interaction of dysfunctions in the positive valence (reward) systems with those in other systems, such as negative valence and cognitive systems, will require full attention of both basic research and treatment development research. Although our knowledge of neurobiological systems is still evolving, designing and testing novel treatments can effectively probe and refine our conceptualizations of these systems. The continuous cross-fertilization between basic neurobiological research and applied research into novel treatment applications will accelerate scientific progress in this area and offer the potential for large benefit for affected individuals.

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