

Chapter 2

Understanding Anhedonia: The Role of Perceived Control

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Abstract Perceived control appears to play an important role in the manifestation of anhedonic symptoms, as it is integrally related to underlying neurobiological reward systems and motivated behaviors. Perceived control refers to the conscious process by which an event is determined to be manageable, or more simply put, it can be thought of as the extent to which an individual/organism believes that he/she has the resources and capability to manage an event. Consequentially, perceived control has a rich history in the depression literature (e.g., learned helplessness) and appears to be an important determinant in the manifestation of anhedonia. However, to this date, the link between perceived control and anhedonia remains unclear. In order to further elucidate this relationship, this chapter provides a model that seeks to explain perceived control's role in determining our psychological and behavioral responses to stress. To do so, we will discuss shared neurobiological mechanisms (i.e., the mesocorticolimbic system) in relation to how they pertain to perceived control and approach-avoidance motivation. Additionally, clinical implications will be discussed through the framework of perceived control's impact on specific coping strategies.

Keywords Perceived control • Emotion regulation • Positive affect • Negative affect • Mesocorticolimbic system • Individual differences • Anhedonia

Abbreviations

fMRI Functional magnetic resonance imaging
HPA axis Hypothalamic-pituitary-adrenal axis

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NAc	Nucleus accumbens
PFC	Prefrontal cortex
RN	Raphe nuclei

2.1 Introduction

Anhedonia can be defined as a profound diminished interest and/or loss of pleasure in activities, and while it is most notably found within depression and schizophrenia, it manifests in several other neuropsychiatric disorders. Perceived control appears to play an important role in the manifestation of anhedonic symptoms, as it is integrally related to underlying neurobiological systems that are involved in approach-avoidance motivation. Specifically, low perceived control appears to decrease approach-oriented behaviors and to increase behavioral avoidance. *Perceived control* refers to the conscious process by which an event is determined to be manageable, or more simply put, it can be thought of as the extent to which an individual/organism believes that they have the resources and capability to manage an event. From a neurological perspective, basic research suggests that motivated behaviors are significantly influenced by the controllability of the event through fluctuations of dopamine levels within the mesocorticolimbic system. These biological mechanisms are also associated with affective traits, in which positive affect is believed to facilitate approach behaviors while negative affect appears to promote behavioral avoidance, possibly through modulating levels of dopamine within the mesolimbic systems [1]. In order to elucidate the relationship between perceived control and anhedonia, this chapter provides a model that seeks to explain perceived control's role in determining our psychological and behavioral responses to stress. To do so, we first provide a brief history of perceived control, followed by a discussion of approach-avoidance motivation. Next, the mesocorticolimbic system functions are discussed in detail in order to provide a framework for our model. These findings are then integrated to highlight how individual differences in affective traits and approach-avoidance motivation impact perceptions of controllability. Subsequently, the relationship between mesocorticolimbic functioning and perceived control in relation to specific behavioral correlates that are endemic of anhedonia are discussed. To conclude, clinical implications are discussed through the framework of perceived control's influence on the use of specific coping strategies and approach-avoidance motivation.

This chapter has taken an interdisciplinary approach to examining the relationship between perceived control and anhedonia. In doing so, a broad amount of terminology for similar yet distinct phenomena was found across the different branches of psychology. Additionally, it is important to forewarn that some of the theory constructs discussed in this chapter, particularly in regards to emotional processing and motivational systems, overlap with one another and are not without controversy. Given these factors, for the sake of simplicity and coherency, we have attempted to organize these potentially confusing concepts into an integrated coherent model.

2.2 Perceived Control

Perceived control has a rich history in the depression literature, and as we will later discuss appears to play an important role in the manifestation of anhedonia. There is an overwhelming amount of interdisciplinary evidence that suggests that the extent to which an organism believes that their behavior is able to exert control over a stressor, has profound effects on their neuropsychological and physiological responses to stress. Early research, using animal paradigms, found that the process of learning (i.e., *expectancy*) that outcomes were uncontrollable via repeated exposure to non-contingent aversive stressors resulted in motivational (e.g., failure to escape), cognitive (e.g., failure to learn new contingency relationship), and emotional (e.g., aberrant physiological arousal) performance deficits (for reviews, see [2, 3]). This led to the *learned helplessness hypothesis*, which posits that when organisms learn and come to expect that their behavior is independent of the stressor outcome (i.e., future expectancy of response-reinforcement independence), it produces aberrant motivational, cognitive, and emotional reactions [for review of the infrahuman literature, see 2]. While some initial support was found for the learned helplessness model in humans [4, 5], the original model could not account for *facilitation effects* (i.e., performance improvements that occurred following exposure to the uncontrollable condition) or individual differences in perceptions of controllability [6]. Thus, since that time the construct has evolved to acknowledge that the learned helplessness outcome is interdependent with global perception of events and individuals' causal attributions of lack of control (e.g., if participants believe that they have failed due to their general incompetence as opposed to non-personal aspects of the task itself will influence whether the behavioral correlates of learned helplessness occur) (for reviews, see [6, 7]).

Several factors appear to moderate whether an individual experiences “learned helplessness” in response to an uncontrollable stressor. Similar to animal models, in humans, the duration of the exposure (acute vs. chronic) and expectancies of personal control (i.e., organisms' expectations regarding their capability of controlling outcomes generally or in a particular instance) moderate the relationship between learned helplessness and controllability. Furthermore, the salience of the threat to self, meaning of the event, and attributions of causality moderate reactions to uncontrollable stressors [6, 7]. Within most, if not all, learned helplessness models, a necessary factor appears to be whether the non-contingency relationship of uncontrollability is learned. However, as we will discuss, recent developments in neuroscience have begun to challenge the notion that learning the non-contingency relationship is the basis of learned helplessness [8].

2.3 Motivation and Goal-Directed Behaviors

Motivation to perform goal-directed behaviors is integral to hedonic experience in that reduced motivation can manifest as reduced effort to obtain the goals one used to enjoy (i.e., no longer “wanting” to do a pleasurable activity). According to

Maslow, “man is a perpetually wanting animal” [9]. Maslow’s theory of motivation stressed the importance of recognizing that “wanting” is influenced by prior situations and “prepotent needs” [9]. These prepotent needs or “goals” that predominate our motivational drives are pursued hierarchically. Basic needs (e.g., gratification of bodily needs) are the system’s foundation. The next level entails the goal of safety from physical or psychological threat (which also entails cognitive components such as familiarity and manageability). Above this level, are goals that we can define as psychological needs or desires (e.g., love, affection, and acceptance), which is followed by the goal of self-esteem (e.g., self-confidence and the belief in one’s capabilities). The pinnacle of the system’s hierarchy is self-actualization (e.g., self-fulfillment, creative expression, and the fulfillment of one’s potential and use of one’s capacities). A critical component to this theory is that an individual’s current level of need impacts his/her motivational goals. In this regard, individual differences that influence levels of need would be expected to substantially influence motivational goals. Using this model, we will later describe how individual differences in affective traits and approach-avoidance motivation can influence an individual’s motivational goals (via level of need) through impacting perceptions of controllability.

Central to motivational theories of goal-directed behaviors are the concepts of approach and avoidance. Earlier “approach-withdrawal” motivation theories, operationally defined motivation by observable behaviors of an organism moving either towards (approach) or away from (withdrawal) a stimulus; however, such theories had important limitations and were unable to adequately address the complexity of human motivation systems [10]. Important to the understanding of human motivation is the concept of affective valence. *Affective valence* refers to the notion that stimuli have attractive (positive valence) and repellant (negative valence) properties that are connected with behavioral action tendencies to either approach or avoid the stimuli [10]. Other theories have built on this concept of affective valence to suggest that positively or negatively valenced stimuli may gain motivational properties (i.e., incentive motivation) through three processes that will be a focus of this chapter: (1) “liking” a stimulus triggers the positive affective state of pleasure or aversion to a stimulus triggers a negative affective state (e.g., fear or disgust), (2) associative learning processes connect the stimulus to its motivational properties, and (3) guided by associative learning processes, attributions regarding a stimulus’ motivational value (its saliency and valence) are encoded through engagement of dopamine systems (i.e., “wanting”) [11]. Central to this chapter is the knowledge that in the absence of this third process – the stimulus’ motivational value attributions – associative learning processes and activation of hedonic systems do not appear to have the capacity to alone motivate goal-directed behavior in response to stimuli; rather, they only appear to be able to activate affective states [11]. In this regard, positive and negative affective stimuli are salient forces that attract or repulse individuals due to their positive or negative reinforcing properties, and through the three-step process described above are able to gain *affective value* that serves to motivate approach and/or avoidant behaviors.

Elliot posited that in approach motivation, behavior is guided by perceptions that a positive/desirable event may occur, whereas in avoidance motivation, behavior is guided by perceptions that a negative/undesirable event may occur [12]. Consistent with this view, there are several theories that, while not synonymous with each other, share the assumption that (1) the motivated behaviors of approach and avoidance are a function of valence, and which further specify that (2) there are specific underlying biological mechanisms that are the basis of approach and avoidant motivational processes [13–17]. Here, the distinction between *drive* as compared to approach-avoidance motivation theories is important to make: the original drive theories suggested that behaviors are largely driven by negative reinforcement in order for the organism to return to homeostasis (e.g., the action of obtaining food removes the negative emotional state of hunger) [18]. In contrast, approach-avoidance theories suggest that behavioral motivation is an adaptive process that, through affective value, is able to guide and shape future behaviors through positive reinforcement. For example, the experience of having a pleasant meal at a restaurant provides motivation to make plans to return to that restaurant for another meal. In this definition of motivation, the experience of enjoying the meal (“liking” it) has gained affective value, which will serve to motivate future behaviors (I “want” it again). It is important to note that these theories are not mutually exclusive in that basic needs or drives such as hunger can influence affective value (e.g., whether or not an individual is satiated will also impact the affective value of a meal).

The ability to take goal-directed action requires not only a coordinated motor response but also requires the ability to perceive the outcome of the event. Basic research has well established that the ability to perform complex goal-directed actions frequently involves associative learning processes [19, 20]. Two important ways by which associations are learned are the principles of contiguity and contingency. *Contiguity* refers to learning that events co-occur with each other and is determined by the temporal space between events (i.e., events that frequently occur in close proximity of one another will become associated with one another). *Contingency* refers to learning that an event occurs only if a specific condition(s) is met (e.g., a reward that only occurs if a tone is presented). According to Elsner and Hommel [21], it is through these associative learning processes that goal-directed behaviors become automatically primed by perceptions of previous event outcomes. Take for example, a student’s study behaviors (i.e., the action) in relationship to whether they receive “good” or “bad” grades (i.e., the affective stimulus which is related to perceived outcomes). If the student consistently receives good grades on tests after the process of studying, and receives bad grades on tests when they do not the study, both the contiguity and contingency association between the process of studying and type of grade will be made (i.e., the type of grade received on a test depends on the study behavior). Furthermore, we can expect that the student will make distinct attributions about the outcome (success or failure) of receiving a good as compared to a bad grade on the test (“e.g., I succeeded because I studied”). In this example, studying behavior has acquired an affective value due to attributions made about the outcome; in turn, perceptions of this outcome will significantly influence subsequent events in that actions are controlled by the anticipation of their effects (i.e., “There will be a positive

outcome if I study”). Conversely, we can imagine if a student exerts effort towards a test (“studied hard”) and still fails the test, then the relationship between action (studying behavior) and outcome will not be learned (i.e., approach-oriented behaviors are not related to a positive outcome). In this case, over time we would expect that perceptions of failure despite exerted effort would decrease approach motivation towards studying behaviors through priming memories of failure.

Altogether, motivated behaviors appear to be substantially shaped by an organism’s knowledge about their environment and the likelihood of the possible effects of performing that action in a given situation. This acquired knowledge guides future behaviors in efforts to achieve future goals through allowing an individual to select a suitable/appropriate behavior-action repertoire that will serve to meet the desired goal (e.g., obtaining a reward or avoiding an aversive experience). Of additional importance, and in accord with Maslow’s hierarchy, a stimulus’ affective value is not static, and appears to fluctuate with an organism’s needs. Thus, factors that have the capacity to influence perceptions of a stimulus’ affective value would be able to impact motivational goals and the development of approach-avoidance behavioral repertoires.

This chapter acknowledges that there are differences in the various theories used to describe the distinction between approach and avoidant behaviors [10]. However, given the broad amount of terminology utilized in the field of motivation, for the sake of simplicity and coherency we will follow Elliot and Covington’s [10] lead in using the label “approach–avoidance motivation” to describe the distinction between approach and avoidant behaviors within this chapter. Additionally, while there are also subtle differences behind the labels that are used to describe a stimulus’ ability to motivate approach and avoidant behaviors (e.g., motivational value, incentive value, and affective value), in an effort to reduce the amount of terminology, we will heretofore refer to this stimulus property as *affective value*.

Given the importance of approach-avoidance motivation to adaptive human behavior, the following sections will highlight the role of the mesocorticolimbic dopaminergic system in connecting hedonic experience to the stimulus’ affective value, and discuss the interdependency of reward processing functions and how fluctuations in dopamine release within this system influence approach-avoidance motivation. To do so, we will build on animal models that illustrate how individual differences in dopamine functioning may impact perceptions of stressor controllability and influence approach-avoidance motivation.

2.4 Approach-Avoidance Motivation and the Mesocorticolimbic Dopamine Pathway

Dopamine within the mesocorticolimbic system plays a large role in motivated behaviors and learning reinforcing properties (e.g., encoding the affective value); specifically, a role of the mesocorticolimbic systems appears to be to connect hedonic experience to the affective value, which serves to produce adaptive

behaviors (goal-directed actions) [22, 23]. The mesocorticolimbic dopamine pathway is often discussed in terms of two separate pathways, the mesolimbic and mesocortical pathways, which have feedback connections to each other. While both pathways originate in the ventral tegmental area (VTA) of the midbrain, the mesolimbic pathway dopaminergic neurons project to the limbic system (amygdala, nucleus accumbens [NAc], and hippocampus) while the mesocortical pathway dopaminergic neurons project to the prefrontal cortex (PFC) [24, 25]. Dopamine within the mesocorticolimbic pathway serves a number of functions. To begin, dopamine systems appear necessary for “wanting” the stimulus, which entails ascribing the affective value to the stimulus [for review, see 11]. A general modulatory role for phasic (i.e., bursts of neuronal activity) dopamine release in updating reward predictions in response to changing contingencies (i.e., the difference between expected and actual reward) has been found in both humans and animals [26]. Moreover, it is generally accepted that phasic dopamine release supports associative learning and is responsible for encoding reward value (i.e., affective value of the stimulus) [11]. For example, phasic dopamine is released in situations in which an unexpected or underestimated reward is received (for review, see [27]). Conversely, when an expected reward’s value is overestimated or not received, there is a significant decrease in dopamine firing. Dopamine functioning within the NAc also appears to be necessary in order to sustain effort to obtain rewards. For instance, administration of dopamine antagonists in the NAc of rats decreases responses for large rewards that require higher effort, whereas responding for small rewards that require little effort is increased [22]. VTA dopaminergic neurons that synapse on the NAc (i.e., increasing levels of mesoaccumbens dopamine) appear to substantially influence the efficacy of reward learning during exposure to novel reward experiences [28] and are also involved in responses to stress (for review, see [29]). In humans, it has been shown that as anticipation of reward increases, dopaminergic neurons in the VTA and the NAc become more active to cues of reward (e.g., in response to monetary gain) [30], in which this activity and the subsequent goal-related behaviors may be directly influenced by innervations from the dorsolateral PFC [31]. Finally, as will later expand on, Depue and Collins [16] have provided a convincing argument that variations in mesolimbic dopamine functioning, which presumably involve genetic as well as environmental influences, provide the foundation by which individual differences in approach-avoidance motivation occurs. The following sections will begin to elaborate on the individual differences in mesocorticolimbic dopamine functioning, and how these individual differences in dopamine functioning are related to perceptions of control and approach-avoidance motivation.

2.5 Perceived Control and Approach-Avoidance Motivation

Of great interest is the impact that perceptions of uncontrollable stress have on the mesocorticolimbic dopamine pathway’s functions and how this influences motivated behaviors. The motivated behaviors of approach and avoidance both appear to

be significantly influenced by fluctuations of dopamine levels within regions of the mesocorticolimbic dopamine pathway. Basic research suggests that the controllability of an event and the duration of the stressor also largely influence the functioning of dopaminergic neurons within this region. Specifically, it appears that dopamine release to stressors follows an inverted-U pattern that is influenced by both stressor duration and perceptions of controllability. Tonic NAc dopamine levels initially appear to be enhanced in response to acute controllable stress, while tonic NAc dopamine appears to be inhibited with prolonged exposure to uncontrollable stressors [for review, see 29]. These dopamine patterns in turn support behavioral changes, such that increased dopamine tone in the NAc appears to motivate active/approach-oriented coping strategies (e.g., learning necessary behaviors to escape from shock) in response to an acute controllable stressor, while decreased dopamine tone appears to support behavioral withdrawal from chronic uncontrollable stressors [29].

Importantly, evidence suggests that the ventromedial PFC is the mechanism that regulates responses to uncontrollable stressors. A series of studies by Christianson and colleagues [8] indicates that the ventromedial PFC may be the underlying mechanism that mediates the relationship between stressor controllability and subsequent anhedonic-like behaviors; more specifically, the ventromedial PFC appears to play an inhibitory role in stress response systems when behavioral control is present. These studies demonstrated that pharmacological inactivation (via the GABA_A agonist muscimol) of the ventromedial PFC appears to prevent the protective effects of the presence of control (i.e., the ability to escape to from shock) and leads to less social exploration. In light of this and other evidence [32, 33], Christianson et al. suggested that the learned helplessness outcome may not be dependent on the individual learning the non-contingency relationship of uncontrollability; rather, it appears to be a function of ventromedial PFC emotion-regulatory processes (i.e., the presence of control activates the ventromedial PFC, which results in the attenuation of stress response systems). The next section will continue to discuss the implication of these findings in the context of how emotion-regulation processes appears to be responsible for underlying individual differences in perceptions of control.

2.6 Mesocorticolimbic Involvement in Emotion Regulation Processes

Importantly, emotions appear to influence appraisals that are made about stressful events. To build on this idea, we will first need to discuss how emotions are processed. According to LeDoux's model of emotional processing [19], emotions are thought to serve the important function of coordinating the mind and body. From a neurological perspective, the amygdala is critical in processing emotional information and is believed to play an important role in controlling behavioral, autonomic, and endocrine responses [20]. LeDoux proposed that emotional stimuli have a "low road" and a "high road" to the amygdala [19]. The low road of emotional processing

refers to the direct pathway from the thalamus to the amygdala. The thalamo-amygdala pathway detects danger and allows for immediate activation of arousal systems that motivate behaviors; however, the information that is sent is only a crude representation of the stimulus. The high road of emotional processing is not as direct; however, it benefits from cortical processing and is able to differentiate between stimuli. The high road of emotional processing involves emotional stimuli entering the thalamus via sensory pathways, the thalamus then projects this information to the cortex, and the cortex subsequently sends this information to the amygdala for further processing. Importantly, the cortico-amygdala pathway is bidirectional in that the amygdala provides the cortex with internal feedback about the stimulus via chemical signals, and the cortico-amygdala pathway can override the projections from the thalamo-amygdala pathway. The benefit of having separate appraisal systems is that an emotional appraisal system allows for faster responding in the face of threat, while cognitive appraisal systems allow for more flexible responses that may be more adaptive to the situation [for review, see 20].

The animal literature has provided ample evidence that certain behavioral responses do not require learned cognitive responses and appear to be species engrained (e.g., species-specific defense reactions) [34]. These automatic behaviors are guided by emotions. For instance, negative emotions such as fear appear to reduce an organism's behavioral repertoire [19]. Specifically, the experience of fear creates a highly inflexible state that promotes avoidant behaviors such as freezing or fleeing in response to threats through activating stress response systems (e.g., the hypothalamic-pituitary-adrenal (HPA) axis and the autonomic nervous system) as well as systems that promote behavioral disengagement (i.e., the periaqueductal gray) [19]. In the short term, these emotional reactions help provide the individual with the physiological resources necessary to cope with stress. However, there is a wide body of research that suggests that chronic activation of stress response systems can potentially impede an individual's ability to adapt to their environment through altering their physiological responses to stress via continued activation of stress response systems [35–37]. In this regard, the ability to effectively regulate emotions via cognitive appraisal systems in response to stress is critical to both mental and physical health.

A large body of research suggests that the mesocorticolimbic system plays an important role in emotion regulation. *Emotion regulation* refers to the ability to monitor and control the expression of emotional states via evoked thoughts and behaviors (i.e., cognitive appraisals) [38]. Emotion regulation is a dynamic process that engages several psychobiological processes in order to cope with sources of stress. It appears that both purposively increasing or decreasing negative emotions (i.e., intentional up- and down-regulation of negative emotion) via cognitive appraisals is dependent on regions of the PFC to modulate amygdala activity [39]; in turn, both of these structures directly and indirectly communicate with other stress response systems (e.g., the HPA axis which releases the stress hormone cortisol). Specifically, research indicates that PFC projections to the amygdala exert a top-down, inhibitory influence over negative affective states [39–41]. The top-down regulation of negative affect and the subsequent dampening of HPA axis stress responses via cognitive reappraisals appears to be a function of PFC efferent

projections (presumably via the ventromedial PFC) to the amygdala [41]. Upon receiving signals from the ventromedial PFC, amygdala activity is attenuated and its projections to the hypothalamus are inhibited, thereby reducing/halting further cortisol secretion from the HPA axis. Conversely, when levels of negative affect are intentionally increased through negative cognitive appraisals (e.g., “something terrible is going to happen to me”), there is an increase in amygdala activation [39], which in turn appears to elicit cortisol release, thereby prolonging activation of stress response systems [41].

Individual differences in the ability to down-regulate negative emotions appear to be a function of underlying differences in PFC activation. Functional magnetic resonance imaging (fMRI) studies of emotion regulation in non-clinical populations have found that intentionally increasing negative emotions appears to primarily recruit left PFC systems [39, 40], whereas intentionally decreasing negative emotion bilaterally recruits PFC [39]. Additionally, there appears to be a functional dissociation between limbic and cortex activation in the down-regulation of negative emotions, such that limbic activity (in particular, the NAc and amygdala) has an inverse relationship with activation of the prefrontal cortices [40]. Conversely, greater self-reported intensity of negative affect positively associates with increased amygdala activity and decreased activation of the region of the brain responsible for conflict resolution (i.e., the dorsal anterior cingulate) [40]. Of clinical relevance, individual differences in observed fMRI patterns of neural activation in response to regulating negative affect have been found in individuals with a major depressive disorder as compared to a non-clinical control group, such that individuals with depression have been found to demonstrate greater bilateral PFC activation, while non-depressed individuals display left-lateralized PFC activation when down-regulating negative affect [42]. Furthermore, in a task designed to intentionally decrease negative emotions through reappraisal of negative emotional stimuli, non-depressed individuals demonstrated the predicted pattern of greater activation in the left ventrolateral PFC associating with decreased amygdala activity. However, this pattern of attenuated amygdala activity was not observed within depressed individuals; instead, there was positive association between ventromedial PFC and amygdala activity [42]. Further individual differences in hemispheric activation have been found in that increased avoidance motivation (as measured by a self-report, the Behavioral Inhibition System scale [43]) is associated with greater tonic electroencephalography activity in the right posterior dorsolateral PFC [44], and greater relative right to left prefrontal activation is positively associated with avoidance motivation and negative affect [45]. Conversely, greater left PFC activation is linked to increased levels of positive affect and decreased negative affect [46], as well as being associated with greater approach motivation and faster physiological recovery to negative events [15]. Altogether, there appears to be evidence of a biological basis for individual differences in the ability to regulate negative emotions that outwardly manifests in the trait characteristics of negative affect and positive affect. This is particularly important considering that failure to successfully regulate negative emotional responses is associated with increased avoidance motivation and dysregulation within the mesocorticolimbic system. Conversely, effective emotion regulation would be expected to allow the individual to more effectively use emotions to

successfully guide his or her behaviors and thoughts. In conclusion, affective traits appear to be important psychosocial factors that influence both physiological and psychological responses to stress. In this regard, as we will later discuss, differences in affective traits and their underlying proposed mechanisms, play an important role in perceived control.

2.7 Individual Differences in Approach-Avoidance Motivation

Importantly in human subjects, variability in baseline striatal dopamine functioning appears to be responsible for associative learning processes related to perceptions of reward and punishment. In this regard, individual differences in baseline dopamine functioning (e.g., having extremely high levels versus low levels of tonic dopamine) play an important role in anhedonia. Baseline dopamine functioning appears to be supported by a steady state concentration of dopamine neuron firing (i.e., tonic firing) [see 47]. Moreover, baseline striatal dopamine levels appear to be involved in the prediction error signal, which updates reward predictions in response to changing contingencies, and has been measured by performance on probabilistic reversal learning paradigms [48, 49]. In such paradigms, individuals initially learn to choose via trial and error with corrective feedback whether a highlighted stimulus leads to reward or punishment. Subsequent trials then reverse these learned stimulus-outcome associations, and participants must learn to switch (i.e., update) their responses to match the new unexpected reward or punishment contingencies. “On such tasks, those with higher baseline striatal D2 dopamine synthesis capacity showed better reversal learning performance from unexpected rewards than from unexpected punishments, whereas those with relatively lower baseline striatal D2 dopamine synthesis capacity performed better after unexpected punishments than after unexpected rewards.” However, when these same individuals were given a single dose of bromocriptine (i.e., a D2 receptor agonist that increased dopamine levels), those low in baseline striatal dopamine improved their performance whereas those high in baseline striatal dopamine now had impaired performance (an “overdose” effect) [48]. In this sense, dopamine levels and reward-based reversal learning performance follow an inverted-U pattern; tonic dopamine levels create the set point from which additional dopamine synthesis capacity enhances or impairs reward-based reversal learning among other cognitive functions (e.g., working memory) [49]. Furthermore, unmedicated individuals with major depressive disorder show impaired reward, although not punishment, reversal accuracy as well as reduced striatal response to unexpected reward [50]. The authors suggested this mechanism may underlie the *negativity bias* seen in depression, wherein individuals are more sensitive to punishing stimuli and do not adapt as quickly to rewarding stimuli. In conclusion, punishing stimuli appear to hold more weight than rewarding stimuli and internal cost-benefit calculations do not accurately represent (i.e., update) the value of rewarding situations within depressed individuals.

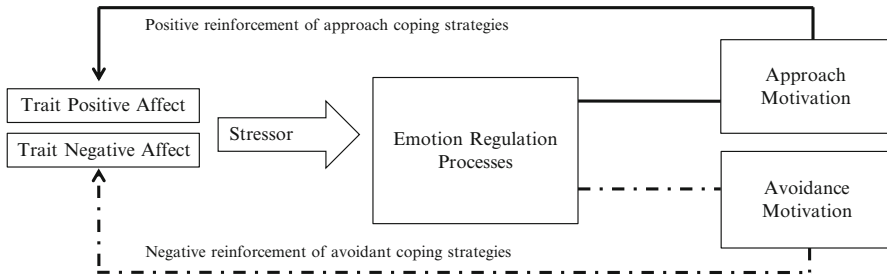


Fig. 2.1 *Bold line* represents the emotion regulation process of trait positive affect and the *dashed line* represents the process of trait negative affect

Greater self-reported approach motivation (as measured by the Achievement scale of the Multidimensional Personality Questionnaire [51]) is also correlated with higher left relative to the right hemisphere dopamine receptor availability in healthy subjects [52]. It has been proposed that genetic variation that influences the expression of dopamine D2 receptors differentially influences reward-seeking behaviors, such that individuals with the allele (A1+) associated with reduced dopamine receptor concentration may be more likely to seek out experiences that increase dopamine receptor stimulation, whereas individuals with higher levels of dopamine (A1- allele) would be more likely to avoid stimulus-seeking behaviors because of adverse effects on the brain [53]. D2 receptor availability is also associated with individual differences in hedonic experience, such that in healthy individuals, those with high D2 receptor availability find stimulating drugs to be less pleasant and experience greater negative emotional states (annoyance and distrust) than those with low D2 receptor availability [for review, see 54]. Thus, there is evidence to suggest that genetic differences in dopamine influence hedonic experience and tendencies toward approach- or avoidant-oriented behavior in ways that compensate for their relatively lower or higher dopamine levels, respectively. As we will describe in the following section, there is also evidence to suggest that dopamine plays a role in individual trait differences in the degree of approach as compared to avoidance motivation (Fig. 2.1).

2.8 Affective Traits Role in Motivated Behaviors in Response to Stress

Depue and Collins posited that individual differences in the functioning of VTA dopamine projections largely explain differences in approach motivation [16]. According to Depue and Collins, positive affective stimuli are salient forces that attract individuals due to their positive reinforcing properties. In this regard, active/approach-oriented behaviors are promoted by the anticipation of reward

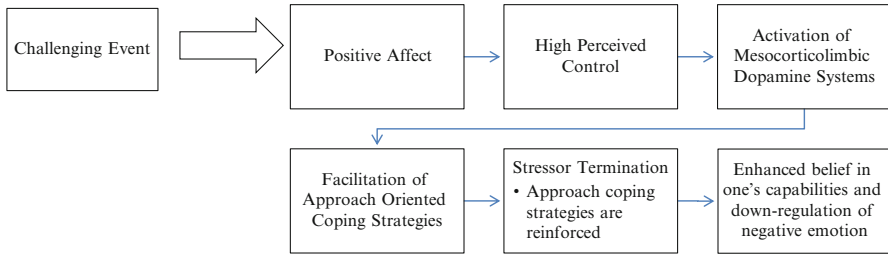


Fig. 2.2 Positive affect's role in motivated behavior

acquisition and enhanced VTA dopamine release into the NAc [16]. These dopamine-mediated differences in increased sensitivity to reward as compared to punishment are presumed to be reflected in predispositions towards the personality trait of extroversion, which is believed to be composed of several individual personality characteristics that facilitate approach behaviors (e.g., positive emotionality, sociability, and achievement) [16]. Other theorists have proposed similar underlying higher-order factors of personality traits, most notable is Watson and colleagues' [55] conceptualization of affective traits (positive and negative affect). Trait positive affect and trait negative affect are important individual difference variables that appear to play a key role in moderating individuals' response to stress. The neurobiological mechanisms of approach-avoidance motivation appear to be coupled to affective traits, such that dispositions towards positive approach emotions (e.g., interest and enthusiasm) are associated with greater activation of left frontal regions of the brain, whereas greater avoidant-related emotions (e.g., fear) are associated with selective activation of the right frontal region [14]. Affective traits also have a robust relationship with coping strategies, in which trait negative affect is associated with significantly greater use of avoidant coping strategies while positive affect is positively associated with greater use of approach oriented coping strategies [56]. Furthermore, the pattern of high negative/low positive affect has been repeatedly linked to both depression and schizophrenia [57–60]. Building on this, we provide two models (see Figs. 2.2 and 2.3) that elucidate how individual differences in affective traits and their hypothesized underlying neural mechanisms influence stressor outcomes.

Uncontrollable stress has been shown to reliably provoke large psychophysiological changes, particularly in HPA axis activity in both humans and animals (for reviews, see [35–37]). However, there are individual differences in the degree of susceptibility to it. It has been recognized that individuals often vary widely in their subjective responses to the same situations; thus, a useful indicator of experienced distress depends upon the individual's perceptions of the event and not the situation per se [37]. As we have discussed, stressor duration and perceptions of one's capability of controlling event outcomes moderate the relationship between learned helplessness and controllability. Further important factors that determine the reaction to the stressor are the salience of the threat to self, meaning of the

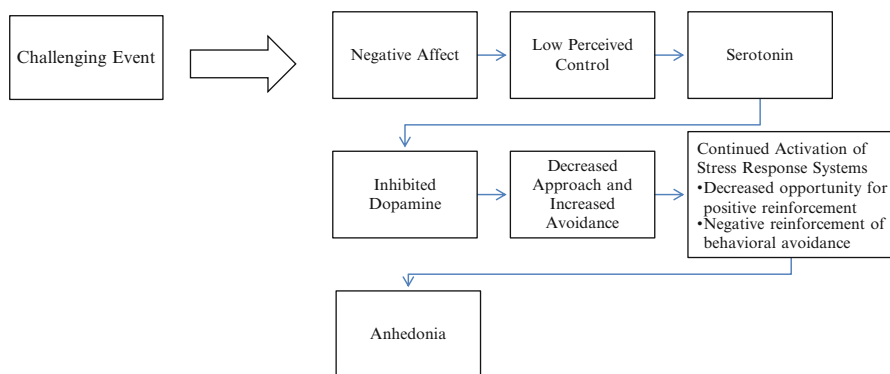


Fig. 2.3 Negative affect's role in motivated behaviors

event, and attributions of causality [6]. Of relevance, the process of learning to behaviorally control stressors appears to lead to improvements in executive functioning performance under stress, but only in individuals with a moderate level of self-reported response to stress and not in those with extreme subjective responses to stress [61]. All considered, individual differences in the ability to regulate emotional reactions to challenging events appear to be the basis of how perceived control exerts its effects. Importantly, individual differences in affective traits and their proposed underlying biological mechanisms appear to be related to differences in the ability to regulate negative emotion and approach-avoidance motivation. Because the capacity to successfully guide behaviors in the face of distress is critical to both psychological and physiological resilience, we will now build on these concepts in order to provide a model of how differences in trait positive affect as compared to trait negative affect and their respective underlying mechanisms have the capacity to alter perceptions of controllability by influencing appraisals of the stimulus' affective value.

Importantly, the experience of positive emotions appears to promote physiological states that serve to guide behavior that supports not only basic survival, but also overall states of well-being [62]. *Trait positive affect* is believed to represent the general tendency to experience positive emotional states, such as joy and enthusiasm, and is associated with the facilitation of rewarding experiences [55]. Trait positive affect is associated with greater amounts of approach behaviors, as well as lower autonomic arousal to negative stimuli [15]. Individuals who experience more positive affective states also have faster physiological recovery and generally lower cortisol output following stress [63–65]. Conversely, ecological momentary assessment ratings of low positive affect have been linked to a potential biomarker of neuroendocrine dysregulation (i.e., greater cortisol awakening response) [64].

Another potential mechanism by which the benefits of trait positive affect may occur is through the cognitive appraisals of the event. Importantly, “challenge” as compared to “threat” appraisals are dependent on the degree to which the

individual feels that they have the capacity to manage or control the event [66]. In this regard, approach motivation that is associated with trait positive affect, would also play an important role in one's personal expectancies (e.g., "It may be difficult but I can manage it"). Thus, it may be that individuals that are high in positive affect and approach motivation experience stressors as being challenging, rather than threatening, because they perceive that they are capable of managing the problem. In turn, these appraisals of challenge, as compared to threat, promote adaptive problem-solving skills that produce positive outcomes [66]. In turn, through associative learning processes, a positive cycle is created such that this acquired knowledge of successfully handling the problem by one's actions serves to guide future adaptive behaviors through priming perceptions of this successful outcome. Consistent with this notion, the experience of positive emotional states is thought to broaden individuals' behavioral repertoires, such that positive emotions appear to promote active exploration of the environment, which in turn allows individuals to accrue positive reinforcing experiences that presumably foster a sense of well-being and mastery of their environment (i.e., a sense of personal control; see Fredrickson's Broaden and Build Theory [67]). Furthermore, stressors that are appraised as being a "challenge" rather than a "threat" are characterized by the experience of positive emotions [66, 68]. Lastly, individuals high in positive affect also appear to be more effective at ascribing a positive meaning to a negative event that has occurred (e.g., "I really grew as a person from this experience") [66]. Altogether, positive affect appears to positively reinforce approach-oriented coping strategies and increase environmental interactions that serve to foster self-esteem and beliefs in one's own competencies.

According to the dopaminergic theory of positive affect, the experience of mild positive affect is accompanied by increased dopamine release primarily within the mesocorticolimbic system; more specifically, positive affect in conjunction with heightened dopamine levels within the mesocorticolimbic system appears to increase cognitive flexibility via executive attention systems [for review, see 69]. This improved cognitive flexibility is believed to be responsible for the enhancement in creative problem-solving skills.

Sustaining high levels of positive affect in the face of adversity has been proposed to be the mechanism by which resiliency to stress occurs [14, 15]. In this view, it is not that individuals high in trait positive affect do not experience adverse events along with negative emotions, but rather such individuals appear to be more effective at attenuating negative emotions, and thus recover faster both psychologically and physiologically.

As Fig. 2.2 illustrates, we suggest that individuals high in trait positive affect tend to appraise stressful events as challenges rather than as uncontrollable threats. In turn, high perceived control activates regions of the PFC that inhibit further physiological responses to stress and promotes adaptive mesocorticolimbic functioning by inhibiting stress responses and freeing cognitive resources in order to successfully cope with the demand. Approach-oriented coping strategies are facilitated by concomitant elevations in positive affect (e.g., hope) and dopamine within the mesocorticolimbic system. Through the use of approach-oriented coping

strategies (e.g., problem solving), which is mediated by frontal cortex inputs, the individual may begin to work on resolving their conflict, which will continue to attenuate the experience of distress through the down-regulation of stress response systems (e.g., dampening amygdala activity and HPA-axis responses). In this regard, approach-oriented coping strategies would be positively reinforced. The final outcome becomes somewhat of a self-fulfilling prophecy in that high perceived control leads to an enhanced belief in one's own self-efficacy that serves to guide future adaptive behaviors and personal expectancies of control. In this respect, trait positive affect promotes a cycle of behaviors that impact future motivational goals and allows the development of approach behavioral repertoires that may lend psychological resilience to stress.

Trait negative affect reflects the general tendency to experience negative emotional states (e.g., fear, shame and anger) [55]. In contrast to positive affective states, dysfunction in the mesolimbic dopamine-mediated reward system is related to increased negative affective states (e.g., anxiety and depression) [70]. Negative affective states are also associated with heightened physiological reactivity to stress and slower physiological recovery following stress [63–65]. Individuals who are high in trait negative affect appear to be prone to heightened emotional reactivity to stress and engage in greater amounts of behavioral avoidance in response to stress [71–73]. Additionally, eliciting negative emotions (anger and shame) as compared to a positive emotion (pride) has been found to differentially associate with stressor attributions, physiological reactivity, and task performance in an uncontrollable social evaluation performance task. Specifically, in contrast to those in whom a positive emotion (pride) was elicited, participants in whom a negative emotion was elicited appraised the same performance task as threatening and difficult, displayed significantly higher cardiovascular reactivity to the task, and demonstrated an impaired performance with an increased level of avoidant coping strategies [74]. Additionally, ecological momentary assessment techniques have found that individuals within a broad age range (18–89 years old) report higher negative affect on days in which they felt less in control [75]. Furthermore, negative affect is associated with an increased expectancy of uncontrollable negative events and decreased feelings of self-efficacy [76]. Lastly, as previously discussed, individuals that are high in trait negative affect appear to be less effective at down-regulating negative emotional reactions to stress. Overall, negative affect appears to have a clear relationship with heightened reactions to stress and perceptions of uncontrollability.

Of clinical relevance, the continued experience of negative emotions appears to prolong states of physiological and psychological distress through engagement of the amygdala and its connections with stress response systems. This heightened sensitivity to threat would promote the motivational goal of safety from perceived threats. In this regard, individuals who are high in negative affect developmentally may have less opportunity to accrue experiences that foster resiliency to stress, as their motivational goal of safety would be less frequently met, and thus cognitive resources would be spent on monitoring potential environmental threats. As Fig. 2.3 outlines, we suggest that this heightened sensitivity to stress in individuals high in trait negative affect decreases perceptions of

controllability. As perceptions of control decrease, avoidance motivation increases and negative emotions are up-regulated (presumably mediated by fluctuations of dopamine and activation of stress response systems). Additionally, as the next section will discuss, low perceived control appears to activate serotonergic neurons within the raphe nuclei, thereby creating a cascade of psychological and physiological effects within the mesocorticolimbic system that heralds the decreased use of approach-oriented coping strategies and increased use of avoidant coping strategies. In turn, because avoidant coping strategies can temporarily reduce exposure to the aversive situation, they have the capacity to blunt physiological responses to stress. In this regard, avoidant coping strategies are negatively reinforced due to their capacity to initially attenuate distress. In the long-term, avoidant coping strategies would impede an individual's ability to adapt to their environment through altering their physiological responses to stress and decreasing opportunities for positive reinforcement and, thus, reinforce a cycle that reduces perceptions of control and increases behavioral avoidance.

2.9 Understanding the Relationship Between Perceived Control and Anhedonia: Functional Interaction Between Serotonin and Dopamine Systems

Serotonin neurons play a large role in regulating dopamine function within the mesocorticolimbic dopamine system and appear to be particularly sensitive to stressors that are perceived to be uncontrollable [23, 77]. The raphe nuclei host serotonin-containing cell bodies that send their projections to dopaminergic cells within the mesocorticolimbic systems (namely, VTA, NAc, and PFC), as well as to the substantia nigra and its terminals in the striatum [23]. Serotonin plays both an inhibitory as well as excitatory role in dopamine functioning, and although we will not go into detail, it is important to note that serotonin serves diverse functions that appear to be mediated by the wide variety of serotonin receptor types [23]. For our purposes, it is important to note that the role serotonin plays in the mesocorticolimbic dopamine system is largely inhibitory. For example, it appears that activation of serotonin receptors via pharmacological agonists decrease VTA activation and dopamine release within the NAc, while serotonin antagonists enhance mesocorticolimbic dopamine function (for review, see [78]). Uncontrollable stressors (e.g., inescapable shock) as compared to controllable stressors have been shown to significantly increase extracellular serotonin levels [8, 79]. Moreover, activation of serotonin neurons appears to play a causal role in the observable changes in motivated behaviors and increased negative affect that are produced by uncontrollable stress: stimulation of serotonin neurons in the dorsal raphe nuclei (1) inhibits defensive behaviors (fight or flight) via projections to a region of the midbrain that induces freezing behavior (dorsal periaqueductal gray), as well as (2) sends excitatory projections to the amygdala [79]. Furthermore, differential effects of serotonin

have been found such that serotonin microinjected into the rat amygdala enhances resistance of conditioned fear to extinction, whereas serotonin antagonists in the same region appear to block conditioned responses to punishment; and serotonin microinjected into the periaqueductal gray inhibits unconditioned fear responses (i.e., biologically innate fear from a predator) [80]. Similar effects have also been found in humans via pharmacological manipulation of serotonin [for review, see 81]. In sum, serotonin has a modulatory effect on dopamine in the mesocorticolimbic system which influences stress related responses and impacts motivated behaviors.

Given serotonin's role in inhibiting dopamine within the mesocorticolimbic system and its differential role in emotional responses to uncontrollable stress, it would appear that the functional interaction between serotonin and dopamine along with perceived control's ability to elicit serotonin play a crucial role in the behavioral correlates of anhedonia. Consistent with this notion, disinhibition of the mesocorticolimbic dopamine system has been posited to be the mechanism of action within several antidepressant drugs [77]. For example, the antidepressants amitriptyline and mianserin, which have a high affinity for serotonin receptors found within the mesolimbic system, appear to enhance dopamine release in the rat NAc potentially through the blockade of these receptors [78]. Administration of amitriptyline and mianserin have also proven to be effective at reversing uncontrollable stress-induced anhedonic behaviors (i.e. decreased consumption of sucrose) in rats, and these beneficial effects were reversed when selective dopamine antagonists were administered to the rats [82]. It is also important to note that although the exact mechanisms of action remain unclear, certain atypical antipsychotics that have had some success with attenuating negative as well as positive symptoms of schizophrenia appear to act on both serotonin and dopamine systems [83]. These observed beneficial effects of atypical antipsychotics appear to be mediated by a preferential increase of dopamine release in the medial PFC [for review, see 84]. There is also evidence that individual differences in perceived control influence responses to reward. For instance, predispositions for learned helplessness in rats (i.e., congenital learned helplessness) appear to interact with uncontrollable stress to trigger reductions in consumptive behaviors to preferred liquids and decreased pleasure-attenuated startle response [85]. In humans, the degree to which participants report low perceived control over present life stressors is associated with a reduced hedonic capacity in objective laboratory measures that test reward responsiveness [86]. In conclusion, there is evidence to suggest that perceptions of uncontrollable stress induce anhedonic-like behavior in animals and humans.

Importantly, as we have outlined, perceptions of control influence reward expectancies, modulate psychophysiological responses to stress, and are involved in dysregulation of the mesocorticolimbic dopamine system. In all, the experience of uncontrollable stress appears to reduce hedonic capacity and to alter functioning of the neural circuitry involved in approach-avoidance motivation.

2.10 Mesocorticolimbic System and the Behavioral Correlates of Anhedonia

We have defined anhedonia as a profound diminished interest and/or loss of pleasure in activities; however, behavior that outwardly manifests as anhedonia has numerous independent and inter-dependent reward-related neural mechanisms that complicate theoretical explanations of this symptom. Of further complication, the term “consummatory behavior,” which is often used to describe hedonic capacity, actually reflects a number of behaviors that are not a united category of responses [e.g., 11]. More recent evidence has shown that “wanting” and “liking” neural pathways are only two potential areas of reward-related dysfunction among a milieu of other mechanisms, with separate yet inter-related neural correlates, which may each or in some combination manifest outwardly as behavior that has been considered exemplary of “anhedonia.” Along with deficits in experiential pleasure received in-the-moment for obtaining a reward or outcome (i.e., liking or consummatory pleasure), it is recognized that deficits in (1) the ability to predict or anticipate whether a reward will occur (i.e., wanting or anticipatory pleasure), (2) updating stimulus value (i.e., computing the cost vs. reward in relation to how much the stimulus was previously liked), (3) the ability to accurately calculate the amount of effort necessary to acquire reward, (4) conducting a cost-benefit analysis of potential behavioral actions (e.g., Is the amount of effort required worth it?), and (5) having sufficient motivation to perform the necessary behaviors in order to obtain reward, may be governed by different neural mechanisms and may all lead to behaviors that outwardly manifest as anhedonic symptoms [22]. However, these reward processing deficits do not necessarily reflect deficits in the ability to experience pleasure. For example, deficits in the ability to accurately predict a reward’s value (e.g., predicting how enjoyable a party will be) does not equate to one not actually enjoying the activity (e.g., having fun at the party). In this regard, “wanting to go to the party” and “liking the party” represent distinct processes with different underlying neurological mechanisms that serve them.

Numerous theories of motivation have been studied over the decades but understanding the underlying mechanisms involved in “wanting” as compared to “liking” has proven to be a formidable task. Given the multiple roles that the mesolimbic pathway plays in the processing of both rewards and stressors, determining factors that alter functioning within this region has garnered a large amount of interdisciplinary interest. The actual experience of pleasure appears to be mediated by activation of cannabinoid and opioid receptors in the NAc regions of the mesolimbic pathway. In this regard, animal research has been useful in identifying discrete biological underpinnings (e.g., cannabinoid and opioid receptors in the nucleus accumbens) that are specifically associated with hedonic capacity [22]. In some respects, better delineating these respective features of reward processing has begun to increase our understanding of the underlying mechanisms involved in

anhedonia. However, as we have discussed, the systems involved in hedonic experience are substantially influenced by mesocorticolimbic dopamine functioning. Moreover, this task is complicated in that whether these factors are reducible to their respective functions remain to be determined, as there is a significant amount of interaction between these processes. Furthermore, many of these processes (particularly, associative learning processes) appear to have the capacity to alter hedonic properties (e.g., the stimulus' affective value). Thus, while fine-grained distinctions between the various underlying neurological mechanisms and their respective functions may be made, it is important to note the interdependency of these systems in relation to how individual differences in these underlying processes impact motivation as a whole. While preclinical models of anhedonia may be useful for clarifying the discrete neural correlates for specific reward deficits, these models are limited in the generalizability to human clinical models of anhedonia due to the complex interdependence of these mechanisms as well as certain aspects of clinical anhedonia that are not easily operationalized in preclinical models (e.g., subjective ratings of perceived control and perceived benefit of executing a specific action in anticipation of pleasure). All considered, clinical anhedonia appears to reflect a sequelae of psychobiological events that alter reward processing functions.

2.11 Clinical Implications of Mesocorticolimbic Dopamine Functioning

Motivation to perform goal-directed behaviors is integral to hedonic experience. Research suggests that impairments in the ability to adjust behaviors as a function of prior reinforcements may be the basis of diminished hedonic capacity in depression [87]. Deficits in motivated behavior have also been linked to impairments in reinforcement reward learning in individuals with a major depressive disorder (MDD), in individuals high in trait anhedonia, upon stress exposure, and with pharmacological manipulation of dopamine tonicity [22, 88]. As with major depression [89], individuals with schizophrenia also do not show the same increase in effort to obtain higher rewards compared to healthy individuals [90]. Moreover, this decreased willingness to expend effort for higher rewards is correlated with higher negative symptoms in individual with schizophrenia [90]. In addition, the belief that behavioral responses and reinforcement are independent of one another appears to play an important role in situational depression [91]. All considered, alterations in dopamine functioning would be expected to play a large role in the manifestation of schizophrenia and depression. Indeed, there is evidence that dysfunction in mesolimbic dopamine functioning is involved in the pathophysiology of both of these disorders [84]. Furthermore, dysfunction within prefrontal dopamine functioning, which plays a regulatory role in mesolimbic dopamine functioning, has been linked to decreased motivation in both depression and schizophrenia [for review, see 84]. Lastly, abnormalities in mesocorticolimbic activation (i.e., heightened activation in the amygdala and decreased activation in both the dorsolateral prefrontal cortex

and anterior cingulate cortex) in response to criticism has been associated with a vulnerability towards depression [92]. Thus, in both depression and schizophrenia, mesocorticolimbic dysfunction has been related to deficits in motivation and connecting positive affective value to pleasurable events; these deficiencies appear to outwardly manifest as a reduced ability to anticipate and evaluate potentially pleasurable or rewarding events.

In schizophrenia, in addition to the posited low tonic levels of dopamine within the frontal cortex (hypoactive mesocortical pathway) and consequent mesolimbic hyperactivity, Grace posits that this imbalance leads to homeostatic compensations that dysregulate phasic dopamine release [47]. Grace suggested that mesolimbic dopamine tone appears to be mediated by prefrontal regions of the cortex and that tonic dopamine levels set the boundaries for phasic dopamine release; that is, the amount of extracellular dopamine already present affects the magnitude of the effect of phasic dopamine release [47]. Of clinical relevance, in patients with schizophrenia, normal reward processing appears to be disrupted by abnormalities in phasic dopamine release [93] which is believed to contribute to increased behavioral avoidance learning and negative symptoms [94]. Similarly, phasic levels of dopamine are associated with anhedonic-like behavioral changes in response to uncontrollable psychosocial stress in mice. Optogenetic induction of phasic activation of VTA dopamine neurons that project to the NAc (mesolimbic pathway), but not PFC projections (mesocortical pathway), have been found to mediate the relationship between anhedonic-like behaviors (social avoidance and decreased sucrose intake) and psychosocial stress to a social defeat paradigm [95]. Conversely, the authors found that optogenetic inhibition of the VTA–NAc projection induced resilience to the psychosocial stressor. Furthermore, the VTA–NAc pathway's heightened sensitivity to uncontrollable psychosocial stress has been linked to increased social avoidance in mice, which is reversible with chronic antidepressant treatment [96]. In summary, it has been recognized that consequences to dysregulation of dopamine systems result in disruptions to normal reward encoding processes that are likely due to complex compensatory mechanisms that attempt to restore the organism to homeostasis [47], and the coordination between affective stimulus value and approach motivation appears to be disrupted.

2.12 Clinical Implications, Conclusions, and Future Directions

There is a growing body of research that suggests that the clinical symptom of anhedonia observed in patients with depression and schizophrenia is associated with aberrant motivational, cognitive, and emotional reactions to stress that are related to mesocorticolimbic dopamine functioning. Of importance, ineffective emotion regulation processes, reflected in individuals coping strategies, appear to substantially mediate these effects.

Coping with stress involves both the anticipation of future stressful events and the recovery from distress [97]. In this view, coping is a dynamic process, in which individuals make adjustments (via thoughts and behaviors) in attempts to reduce the negative impact of stress. There is substantial evidence to suggest that the development of dynamic behavior-action repertoires in response to emotional distress are shaped significantly by both affective and cognitive appraisal processes. We have proposed a model in which affective traits and their proposed underlying biological mechanisms interact with emotion regulation processes to guide behavioral responses to stress. In this model, individual differences in affective traits, which are presumed to have biological underpinnings, substantially influence approach-avoidance motivation and impact perceptions of controllability. In turn, high and low perceived control differentially activate a biological cascade that helps the individual cope with the source of stress: whereas low perceived control activates systems that promote avoidant coping strategies, high perceived control activates systems that facilitate approach-oriented coping strategies.

Over time, when an individual learns that his or her behavior is an unreliable predictor of outcomes in their environment (i.e., low perceived control), approach motivation decreases and motivational goals are adjusted. This acquired knowledge guides future behaviors in efforts to achieve goals through allowing an individual to select a suitable/appropriate behavior-action repertoire that will serve to meet the desired goal (e.g., avoiding an aversive experience). In this regard, cognitive resources are directed at avoiding unpleasant experiences, rather than attempting to improve the outcome. In contrast, positive affect enhances personal expectancies of control and promotes adaptive coping strategies that are directed at managing the stressor. In this regard, trait positive affect appears to promote a cycle of behaviors that lead to psychological resilience to stress, while trait negative affect in conjunction with low perceived control decreases an individual's capacity to adapt behaviors to shape future motivational goals (through priming perceptions of past negative event outcomes). In conclusion, motivated behaviors are substantially shaped by an organism's knowledge about their environment and the likelihood of the possible effects of performing that action in a given situation (i.e., cost-benefit analysis). In this regard, the same event can have disparate affective value for different individuals that substantially effects motivated behaviors.

It is important to note that there are several relevant considerations in the relationship between anhedonia and mesocorticolimbic functioning that were outside the scope of this chapter that are important for future work. First, we believe that memory encoding processes play a large role in relationships between anhedonia and approach-avoidance motivation. For example, research suggests that anticipatory activation of this mesolimbic circuit is involved in translating motivation into memory [30] and memory encoding processes appear to be affected by uncontrollable stress (e.g., disruption of synaptic plasticity in the hippocampus [for review, see 98]). Additionally, while we focused on the interaction between dopamine and serotonin systems, several other neuromodulators and neurotransmitters play a role in "wanting" behaviors (e.g., dopamine's interaction with glutamate [99]). Moreover, while we discussed the dynamic relationship between tonic and phasic levels of

dopamine, it also bears mention that individual differences in serotonin functioning play an important role in the relationship between stress and anhedonia. Specifically, a functional polymorphism in a serotonin transporter gene (short vs. long allele) appears to moderate the relationship between depression and stress reactivity [100, 101]; furthermore, this polymorphism is associated with a decreased capacity for problem-solving strategies in the face of stress [102]. In this regard, future work should aim to clarify the precise neural mechanisms underlying specific aspects of motivated behavior as well as the forces driving the functional interactions between them. Moreover, these functional interactions should be studied longitudinally over the course of depression and schizophrenia as well as other neuropsychiatric disorders with anhedonic symptoms (e.g., Parkinson's disease, substance dependence and withdrawal) to explore the causal role that positive/negative affect and perceived control play in the development of these symptoms. Lastly, it is of great import to consider that cognitive therapy may be less efficacious in those individuals who are less effective at down-regulating negative emotional states. Indeed, research has demonstrated that behavioral activation for depression (i.e., a psychosocial therapy that focuses on behavioral changes) is as effective as therapies that incorporate cognitive restructuring (i.e., cognitive therapy) [103]. In this regard, developing empirically supported psychological interventions that incorporate active coping strategies (i.e., behavioral activation) with emotion regulation strategies may be the front line intervention for those individuals who are high in trait negative affect/low trait positive affect.

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