Anhedonia in Depression and Bipolar Disorder

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Contents

Abstract Anhedonia is a hallmark feature of depression and is highly prevalent among individuals with mood disorders. The history and neurobiology of anhedonia has been most extensively studied in the context of unipolar Major Depressive Disorder (MDD), with converging lines of evidence indicating that marked anhedonia heralds a more chronic and treatment-refractory illness course. Furthermore, findings from neuroimaging studies suggest that anhedonia in MDD is associated with aberrant reward-related activation in key brain reward regions, particularly blunted reward anticipation-related activation in the ventral striatum. However, the ongoing clinical challenge of treating anhedonia in the context of Bipolar Disorder (BD) also highlights important gaps in our understanding of anhedonia's prevalence,

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Curr Topics Behav Neurosci (2022) 58: 111–128
https://doi.org/10.1007/7854_2022_323
Published Online: 10 April 2022

severity, and pathophysiology along the entire mood disorder spectrum. In addition, although current theoretical models posit a key role for reward hyposensitivity in BD depression, unlike studies in MDD, studies in BD do not clearly show evidence for reduced reward-related activation in striatal or other brain regions. Although further research is needed, the evidence to date hints at a divergent pathophysiology for anhedonia in unipolar and bipolar mood disorders, which, if better understood, could lead to significant improvements in the diagnosis and treatment of MDD and BD.

Keywords Anhedonia · Bipolar disorder · Epidemiology · Major depressive disorder · Neuroimaging · Phenomenology · Reward processing

1 Introduction

Although anhedonia is present across many psychiatric conditions, depression is perhaps its most paradigmatic disorder. This chapter provides a historical overview of the role of anhedonia in depression and its prevalence across Major Depressive Disorder (MDD) and Bipolar Disorder (BD). Complementing these epidemiological studies, we highlight qualitative studies describing the phenomenology of anhedonia, focusing on how the subjective experience of anhedonia in individuals with mood disorders extends beyond the loss of pleasure described in current diagnostic classification systems. Drawing upon these separate lines of evidence, we also highlight quantitative and qualitative differences in anhedonia in unipolar and bipolar mood disorders. Next, we provide a critical review of studies outlining the clinical significance of anhedonia, focusing on whether anhedonia and markers of its underlying neural circuitry hold utility for predicting mood disorder trajectory and treatment response. Finally, we briefly outline the current understanding of the neurobiological underpinnings of anhedonia in the context of mood disorders, focusing on how functioning in neural reward pathways goes awry in MDD and BD. Importantly, we comment on the degree to which a shared or distinct pathophysiology may underpin anhedonia in unipolar relative to bipolar mood disorders. Taken together, this overview will provide the reader with a broad knowledge of where the field stands in terms of our ability to better understand, identify, and treat anhedonia in the context of mood disorders.

2 History, Epidemiology, and Phenomenology of Anhedonia in Mood Disorders

2.1 Anhedonia as a Diagnostic Criterion for Depression

Descriptions of anhedonia have featured prominently in clinical texts on depression (or "melancholia"), dating back to the nineteenth century. In 1889, English physiologist William Bevan Lewis published *A Text-Book of Mental Diseases* (Lewis 1889), which included an analysis of 4,000 cases of mental illness treated at the West Riding Asylum, where he worked as Medical Director. In describing states of depression, he noted that "The patient exhibits a growing indifference to his former pursuits and pleasures: the ordinary duties of life and business become irksome and devoid of interest." (pp. 143–144). Around this time, the term anhedonia was formally defined by French psychologist Théodule-Armand Ribot as the "inability to experience pleasure," and proposed as a state antithetical to analgesia (i.e., the absence of pain; Ribot 1896). The marked impact of anhedonia on patients' quality of life is also evident in these early texts. In 1934, prominent psychiatrist Aubrey J. Lewis published a detailed analysis of 61 cases of mental illness treated at the Maudsley Hospital in London, where he was an Assistant Medical Officer. He observed how frequently depressed patients who had traveled from picturesque regions across Europe "...mention this failure to enjoy the sight of their fields, the sky and the trees and the flowers as one of the most distressing of their symptoms, a deprivation most keenly felt." (Lewis 1934 p. 331).

Although anhedonia was common in accounts of depression, several prominent clinicians noted the marked variability in how anhedonia manifested from patient to patient. In the early twentieth century, there was a growing interest in describing "subtypes" of depression that were more homogeneous in their clinical presentation. In *The Varieties of Religious Experience,* American psychologist William James described a particular form of depression characterized by a "passive joylessness" and "loss of appetite for all life's values." (James 1902). The notion of depressive subtypes was later formalized by American psychiatrist Donald F. Klein, who proposed the existence of "endogenomorphic depression," a unique type of depression characterized by a "sharp, unreactive, pervasive impairment of the capacity to experience pleasure or to respond effectively to the anticipation of pleasure" (Klein 1974, p. 449).

Despite descriptions of anhedonia featuring prominently in early psychiatric texts, it was not until Klein's work on endogenomorphic depression that anhedonia was included in the formal diagnostic criteria for depression. The symptom first appeared in the DSM-III (APA 1980), where it was listed among the diagnostic criteria for melancholia. With the release of the DSM-IV (APA 1994), a specifier was added to denote a subtype of depression "With Melancholic Features," which described individuals with a "near-complete absence of the capacity for pleasure, not entirely diminution." In the current DSM-5 (APA 2013) the melancholic specifier has been retained, with the intended purpose of identifying a more homogeneous

subgroup of depressed individuals who experience marked impairments in hedonic capacity. However, the degree to which this specifier serves its intended purpose remains a topic of debate. Using criteria from the DSM-5, Fried et al. (2020) calculated 10,377 unique symptom combinations that could yield a diagnosis of MDD. However, they found that there were as many as 341,737 different symptom combinations that could yield a diagnosis of MDD with Melancholic Features, challenging the notion that the melancholic specifier identifies a more homogeneous subgroup of depressed individuals.

In contrast to the rich descriptions of anhedonia documented in accounts of individuals with unipolar MDD, much less is known about the history of anhedonia in the context of BD. This may in part reflect an emphasis on the unique qualities of BD mania, as well as an assumption that depressive episodes across unipolar and bipolar mood disorders are of the same nature and kind. However, research into the neurobiology of mood disorders highlights several important points of divergence between unipolar and bipolar mood pathology. Accordingly, although the DSM criteria for a Major Depressive Episode is identical across MDD and BD, more thorough descriptive accounts of BD depression may yield important insights into the degree to which hedonic disturbances overlap and diverge across the mood disorder spectrum.

2.2 Epidemiology of Anhedonia in Mood Disorders

2.2.1 Prevalence of Anhedonia in Mood Disorders

Anhedonia is highly prevalent among individuals with mood disorders. When defined using the cut-off for clinical anhedonia on the Snaith-Hamilton Pleasure Scale ($\geq$3), anhedonia prevalence is approximately 70% in individuals with MDD (Cao et al. 2019) and 52% in individuals with BD depression (Mazza et al. 2009). Anhedonic symptoms often persist when other symptoms remit, contributing to increased inter-episode functional impairment. For example, in a study comparing the prevalence of anhedonia in euthymic individuals with BD, individuals in remission from MDD, and healthy controls, Di Nicola et al. (2013) found that one fifth of individuals with BD and one quarter of individuals with MDD had clinically significant anhedonia, despite scoring in the non-clinical range on measures of depression and mania. Although current diagnostic criteria conceptualize anhedonia as a state-like feature of a Major Depressive Episode, evidence of significant inter-episode anhedonia in individuals with mood disorders suggests that it may have a more enduring, trait-like quality.

2.2.2 Severity of Anhedonia Across Distinct Mood Disorder Diagnoses

To date, the findings from studies comparing self-reported or clinician-assessed anhedonia severity in MDD and BD samples have been mixed. Some studies report equivalent levels of anhedonia in individuals with BD and MDD in either depressed (Mula et al. 2010; Perlis et al. 2006) or euthymic (Di Nicola et al. 2013) states. In contrast, others have reported more severe anhedonia in adults with MDD than in adults with BD (Souery et al. 2012), whereas others report more severe anhedonia in youth with BD than in youth with MDD (Diler et al. 2017). The findings from studies comparing different forms of anhedonia across BD and MDD samples are also inconsistent, with some showing differences in anticipatory pleasure (Mitchell 2001), and others showing differences in consummatory pleasure (Zou et al. 2020) between the two disorders.

An important factor that likely underpins these discrepant findings is that MDD and BD samples are rarely matched on overall illness severity. Studies demonstrating more severe anhedonia in youth with BD compared to youth with MDD may reflect the fact that younger-onset BD tends to be a more severe form of the illness (Perlis et al. 2004). Similarly, evidence of more severe anhedonia in BD type II compared to BD type I (e.g., Dimick et al. 2021) may reflect the more pervasive depressive symptomatology observed in BD type II (Karanti et al. 2020). Studies using MDD and BD samples that are matched in terms of illness severity are needed to better understand differences in anhedonia severity between the two conditions.

2.3 Anhedonia Phenomenology

In the DSM-5, anhedonia is defined as a "Markedly diminished interest or pleasure in all, or almost all, activities" (APA 2013). Although this definition has changed very little since the term was first introduced by Ribot (1896), findings from phenomenological studies suggest that the actual experience of anhedonia likely encompasses a broader array of hedonic impairments, as well as their sequelae. Phenomenological studies focus on the lived experience of individuals with mental illness and provide rich insights into the features of psychiatric disorders that are most salient and/or disabling. In addition to loss of pleasure, phenomenological studies highlight the important role of loss of drive, connection, and purpose in the subjective experience of anhedonia. Watson et al. (2020) recently highlighted four key themes related to anhedonia, which emerged from a series of interviews with depressed adolescents. Two primary themes centered on the loss of joy and flattening of emotions, and difficulty with motivation and active engagement. Specifically, participants described feelings of boredom, monotony, and indifference to events happening around them. Two secondary themes also emerged: losing a sense of connection and belonging, and questioning sense of self and purpose. In particular, participants noted feeling disconnected from their social world and losing their sense

of what was important in life. Similar themes were described in a recent qualitative study in depressed adults, where "...inertia, the lack of motivation, the lack of meaning in life..." was identified as one of the most distressing aspects of living with depression (Chevance et al. 2020).

Findings from phenomenological studies are interesting for several reasons. First, they illustrate the breadth of anhedonic experiences that may need to be addressed in the clinical management of mood disorders. In particular, they demonstrate that reductions in motivational drive are a salient feature of depression that have marked impacts on daily functioning. Whether reductions in motivational drive are a consequence of reduced capacity for pleasure or reflect a primary disturbance distinct from other aspects of hedonic functioning remains an important unanswered question. Furthermore, themes emerging from phenomenological research highlight important links between loss of pleasure and other aspects of depression that, despite having a significant impact on quality of life, do not feature prominently in the modern discourse on mood disorders. One such example is depersonalization, a common feature of depression characterized by a sense of detachment from oneself and the world. Individuals experiencing depersonalization often describe themselves as functioning on autopilot without purpose, and as if the world and those around them have taken on an unfamiliar quality. Watson et al.'s (2020) findings hint at the important links between anhedonia and an individual's feelings of connection to their physical and social world, and the impact this may have on their sense of meaning and purpose in life. Gaining a better understanding of these links may help to shed light on the processes that underpin some of depression's more complex and nebulous features.

3 Clinical Significance of Anhedonia in Mood Disorders

3.1 Association with Illness Course

Converging lines of evidence suggest that anhedonia is associated with a more severe and recurrent illness course in the context of mood disorders. Cross-sectional studies show that increasing levels of anhedonia in adolescents with MDD are associated with a greater number of prior depressive episodes, longer depressive episode duration, and greater overall illness severity (Gabbay et al. 2015). Similarly, longitudinal studies in adults with MDD indicate that more severe levels of anhedonia predict a greater likelihood of depression still being present 12 months later (Spijker et al. 2001). These effects are not limited to unipolar MDD. For example, in youth with BD, severe lifetime anhedonia has been found to predict more severe lifetime mania (Dimick et al. 2021). These studies indicate that the presence of marked anhedonia may herald a more severe illness course across the mood disorder spectrum.

Anhedonia has also been linked to greater risk for suicidality, rendering it a potential indicator of patients who may require more intensive treatment and

monitoring. Heightened levels of anhedonia have been found to be associated with increased suicidal ideation cross-sectionally (Ballard et al. 2017; Ducasse et al. 2018) and longitudinally in mood disordered samples (Ducasse et al. 2021), with some studies showing that associations also extend to increased risk for suicide attempts (Fawcett et al. 1990; Sagud et al., 2021). Importantly, these associations remain significant when controlling for overall depression severity, suggesting that anhedonia may be a risk factor of suicidality independent from depression more generally.

3.2 Association with Treatment Response

Studies examining anhedonia's links with treatment response typically focus on one of two questions: (1) Does pre-treatment anhedonia severity predict treatment responsiveness? (2) Does treatment improve anhedonic symptoms? Here we review studies addressing the first of these questions, while the second is addressed in detail in Part V "Treatments".

Several studies have shown that in individuals with MDD, greater levels of anhedonia at the outset of treatment predict poorer responsiveness to a range of interventions, including antidepressant pharmacotherapy (Dunlop et al. 2020; Uher et al. 2012), cognitive behavioral therapy (Craske et al. 2016), and repetitive transcranial magnetic stimulation (Downar et al. 2014). The most consistent findings have emerged for selective serotonin reuptake inhibitors (SSRIs), where pre-treatment anhedonia predicts longer time to remission and fewer depression-free days following SSRI treatment (McMakin et al. 2012). These findings are corroborated by studies showing that behavioral and neural indices of reward processing predict treatment response in individuals with MDD. For example, studies using behavioral reward learning tasks have found that poorer pre-treatment reward learning or reward sensitivity is associated with poorer response to psychotherapy and/or pharmacotherapy (Ang et al. 2020; Vrieze et al. 2013; Whitton et al. 2020). Similarly, studies examining patterns of reward-related brain activation either using electroencephalography or fMRI have observed associations between blunted pre-treatment neural reward responsiveness and poorer response to psychotherapy (Webb et al. 2021) and pharmacotherapy (Whitton et al. 2020). Similar patterns have been observed for studies examining functional connectivity of corticostriatal circuits (An et al. 2019; Downar et al. 2014; Walsh et al. 2017). An important caveat is that few studies have included multiple active treatment arms, making it difficult to determine whether pre-treatment anhedonia/reward processing predicts response to a specific treatment or the persistence of depressive symptoms more generally. One of the few studies that has used multiple comparator treatments provides initial evidence that anhedonia/reward processing measures may predict responsiveness to dopaminergic pharmacotherapy (e.g., Ang et al. 2020), consistent with the critical role that dopaminergic abnormalities are thought to play in reward processing. Specifically, this study showed that more

normative pre-treatment reward learning and resting state corticostriatal functional connectivity predicted better response to the atypical antidepressant bupropion after failing 8 weeks of SSRI treatment (Ang et al. 2020).

In contrast, little is known about the relationship between pre-treatment anhedonia and response to BD-specific psychotherapy or pharmacotherapy (e.g., interpersonal and social rhythm therapy or mood stabilizers). The majority of the studies examining anhedonia as a predictor of treatment response have focused solely on samples with unipolar MDD, or mixed MDD and BD depression samples (e.g., Downar et al. 2014), and comprehensive studies of treatment response indicators in BD have not examined anhedonia and/or reward processing as separate predictors (e.g., Hui et al. 2019; Kleindienst et al. 2005). To date, the literature in BD has focused more closely on other clinical features, such as increased emotional reactivity and lability, as being predictive of treatment outcomes. For example, in a recent multisite study examining predictors of response to lithium in individuals with BD, Lin et al. (2021) found that treatment responsiveness was most closely related to pre-treatment anxiety and the presence of mixed episodes (i.e., mood episodes characterized by both depression and (hypo)manic symptoms). It is possible that distinct aspects of affective dysfunction relate to treatment outcome in MDD and BD, with anhedonia playing a prominent role in MDD and mood lability being more relevant in the case of BD. However, given the paucity of studies examining anhedonia as a predictor of treatment response in BD, future studies comparing distinct predictors in the same cohort are required to confirm this.

4 Neurobiology of Anhedonia in Mood Disorders

Research into the neurobiology of anhedonia in mood disorders has focused most closely on dysfunction in the domains of reward anticipation, reward consumption, and reward learning. Reward anticipation describes the ability to represent future incentives, while reward consumption captures the ability to compute the value of a reward as a function of its magnitude, predictability, time to expected delivery, and the effort required to obtain it. Reward learning integrates anticipatory and consummatory processes and encompasses mechanisms involved in learning about reward-predictive cues and how outcomes shape subsequent behavior.

Each of these processes maps onto overlapping yet partially distinct neural circuitry (for reviews, see Der-Avakian and Markou 2012; Husain and Roiser 2018). Although a comprehensive review of the neural circuitry implicated in various reward subdomains is beyond the scope of this chapter (for reviews, see Borsini et al. 2020; Haber and Knutson 2010; Höflich et al. 2019; Russo and Nestler 2013), it is important to emphasize the key role of the dopaminergic mesolimbic pathway. This pathway originates in the ventral tegmental area (VTA) and projects to the ventral (e.g., nucleus accumbens) and dorsal (e.g., caudate, putamen) striatum, and subsequently the prefrontal cortex (PFC), including the medial PFC and anterior cingulate cortex (ACC), among other regions. Relevant to our discussion, ventral

striatal regions have been found to be critically implicated in incentive motivation and reward prediction errors (RPEs; i.e., evaluating that an outcome is different than expected), whereas dorsal striatal regions have been involved in stimulus-response-reward learning (i.e., linking incentives to actions); medial PFC and orbitofrontal cortex (OFC) regions have been implicated in stimulus-reinforcement representations, including updating such representations to guide behavior; finally, the dorsal ACC has been involved in integrating reward probabilities over time.

4.1 Neural Correlates of Reward Processing in MDD

4.1.1 Blunted Anticipation-Related Activation in the Ventral Striatum as a Trait-Like Feature of MDD

Reduced striatal activation during reward anticipation is one of the most common findings in neuroimaging studies of reward processing in MDD. Meta-analyses show that compared to healthy controls, individuals with MDD exhibit blunted activation in the ventral striatum during anticipation of reward (Keren et al. 2018). Similar findings have been observed in asymptomatic individuals who are at increased familial risk for MDD (Olino et al. 2014), suggesting that blunted anticipation-related striatal activation may be a trait-like vulnerability marker for MDD. In adolescents, blunted anticipation-related ventral striatum activation has also been found to predict increases in depressive symptom severity over 2 years (Morgan et al. 2013), as well as new depression onset and concurrent anhedonia longitudinally (Stringaris et al. 2015), suggesting that this marker is associated with depressive illness course. Finally, changes in anticipation-related ventral striatal activation during SSRI treatment have been found to be associated with changes in depressive symptom severity (Takamura et al. 2017), suggesting that normalizing aberrant anticipation-related activation in the ventral striatum may be important for the clinical effectiveness of antidepressant treatments.

4.1.2 Disrupted Corticostriatal Activation to Reward Outcome (Consumption) in MDD

Reduced activation in ventral (nucleus accumbens) and dorsal (caudate, putamen) striatum, ACC, and OFC, as well as potentiated activation in various PFC regions (medial PFC, ventromedial PFC, and dorsolateral PFC) has emerged in tasks probing consummatory anhedonia (Borsini et al. 2020; O'Callaghan and Stringaris 2019; Zhang et al. 2016), with PFC over-recruitment thought to reflect over-compensation for reduced striatal activation (Forbes et al. 2009; O'Callaghan and Stringaris 2019; Pan et al. 2017). Blunted reward consumption-related ventral striatal activation has also been dimensionally linked to anhedonia severity (Epstein et al. 2006). Functional connectivity between reward hubs (nucleus accumbens,

VTA, OFC) and the ventromedial PFC while listening to pleasant music correlated negatively with anhedonia (Young et al. 2016). Finally, although striatal responses to rewards normalize after depression remission (Geugies et al. 2019), other abnormalities persist, including blunted OFC activation to reward receipt (Dichter et al. 2012) and reduced maintenance of ventral striatal responses to positive cues (Admon and Pizzagalli 2015).

4.1.3 Disrupted Reward Prediction Errors in MDD

Studies using computational modeling to quantify expected value and RPEs in MDD have generally reported reduced RPE in the ventral and dorsal striatum (Gradin et al. 2011; Kumar et al. 2008, 2018), ACC (Rupprechter et al. 2020; Ubl et al. 2015) and medial OFC (Rothkirch et al. 2017), although null findings have emerged (Rutledge et al. 2017). In a study using an instrumental reinforcement learning task, MDD was characterized by reduced medial OFC and ventral striatal RPE, which correlated with anhedonia severity (Rothkirch et al. 2017). Of note, larger ventral striatum RPE has also been found to predict reductions in anhedonia 6 months later (Eckstrand et al. 2019). In addition, although individuals in remission from MDD show normative ventral striatum RPE, VTA RPE remained upregulated, indicating that some reward-related abnormalities persist after remission (Geugies et al. 2019). Collectively, these findings suggest that blunted valuation of expected rewards and reward learning might represent MDD-related vulnerabilities.

4.2 Neurobiology of Reward Processing in BD

Theoretical models of BD posit that mania and depression are underpinned by excessive activation and deactivation of brain reward responsiveness, respectively (Bart et al. 2021). Such models have considerable face validity in terms of explaining the hyper-hedonic symptoms of mania (e.g., spending sprees, excessive sociability) and anhedonic symptoms of BD depression. However, findings from neuroimaging studies are far from conclusive, and few have examined neural correlates of anhedonia in the context of BD.

4.2.1 Heightened Reward-Related Activation in the Lateral OFC Characterizes BD

One of the most consistent findings in fMRI studies in BD is increased left lateral OFC (particularly left ventrolateral PFC) activation during reward anticipation. This has been observed across all mood states, including depression (Chase et al. 2013), mania (Bermpohl et al. 2010) as well as during inter-episode periods of euthymia (Nusslock et al. 2012), and in both BD type I (Bermpohl et al. 2010; Chase et al.

2013; Nusslock et al. 2012) and BD type II (Caseras et al. 2013). Similar patterns of activation have also been observed in unaffected first-degree relatives (Cattarinussi et al. 2019), suggesting that abnormal reward-related left lateral OFC activation may be a trait-like vulnerability marker for BD. Some studies have found that this aberrant activation extends to consummatory processes, with heightened consumption-related lateral OFC activation being found in individuals with subthreshold hypomanic symptoms (O'Sullivan et al. 2011), euthymic BD (Linke et al. 2012; Mason et al. 2014), and in unaffected first-degree relatives (Linke et al. 2012). The left ventrolateral PFC has been implicated in evaluating cues denoting the probability of immediate future reward (Coffman et al. 2021), hence, aberrant left ventrolateral PFC function might underpin sensation seeking and impulsivity in BD.

4.2.2 Mixed Pattern of Striatal Activation in Response to Reward in BD

Unlike studies in unipolar MDD, studies in individuals with BD depression do not consistently demonstrate blunted striatal responses to rewards. For example, some studies have shown decreased striatal responses during reward consumption in individuals with BD depression relative to both healthy controls and individuals with MDD (Redlich et al. 2015). Other studies have found no differences in striatal activation (Chase et al. 2013; Satterthwaite et al. 2015) or even increased striatal activation to reward when under stress (Berghorst et al. 2016) in depressed individuals with BD relative to controls. Studies of reward learning in BD have also yielded mixed findings. Studies using behavioral probabilistic reward learning tasks have reported evidence of poorer reward learning in euthymic or mildly depressed individuals with BD relative to controls (Pizzagalli et al. 2008). However, studies using this same task have produced mixed findings depending on whether the BD sample was treatment-seeking (e.g., Whitton et al. 2021) or had psychotic features (Lewandowski et al. 2016). One of the few studies to examine striatal RPE signals during a reinforcement learning task also found no differences between healthy controls or individuals with BD (Whitton et al. 2021). The variability in these findings compared to those in MDD may be attributable to greater use of medicated samples in BD research and different patterns of comorbidity. For example, studies examining striatal responses to reward in BD have used samples where nearly all individuals were taking psychotropic medication, whereas meta-analyses of neural reward responsiveness in individuals with MDD indicate that more than 80% of participants were unmedicated (Keren et al. 2018). However, an alternate possibility is that the hedonic deficits observed in BD depression may be fundamentally different from those in unipolar MDD. If true, this would prompt a revision of theoretical models of BD depression and the role reward hyposensitivity may play in this aspect of the illness. For example, rather than showing blunted responses to reward, individuals with BD depression may show increased sensitivity to reward loss, or a greater sensitivity to differences between expected and actual outcomes regardless of the valence of the outcome. Given that these processes are thought to be underpinned by partially distinct neural pathways, further clarity on these issues could highlight novel treatment targets for BD depression.

4.3 Differences in Reward-Related Brain Activation Between MDD and BD

Given the overlap in clinical presentation between MDD and BD during the depressive phase of the illness and the fact that recollection of prior (hypo)manic episodes in individuals with BD is not always clear, neural markers capable of distinguishing between these two conditions may aid in improving diagnostic precision. Toward this end, Chase et al. (2013) found that depressed individuals with BD showed increased anticipation-related activation in the left ventrolateral PFC compared to those with MDD, despite comparable disease severity. A recent study that included BD individuals in a variety of mood states also found evidence for decreased reward anticipation-related ventral striatal activation in individuals with BD relative to those with MDD (Schwarz et al. 2020). Similar findings were observed by Redlich et al. (2015) in terms of consumption-related activation, where those with BD depression showed decreased reward consumption-related activation in the striatum, thalamus, insula, and PFC relative to individuals with MDD. These studies highlight quantitative differences in neural reward processing in MDD and BD depression, suggesting that hedonic disturbances in these conditions may partly diverge in terms of their underlying causes.

5 Summary

Findings from epidemiological, phenomenological, and neuroimaging studies summarized in this chapter emphasize the clinical significance of anhedonia in mood disorders, and the critical role that anhedonia treatments will play in reducing the global burden of these disorders. Although vulnerability markers and treatment targets for anhedonia are emerging in the context of unipolar MDD, our understanding of anhedonia's causes in BD remain limited, contributing to the clinical challenges inherent in treating BD depression. Finally, despite overlapping in their clinical features, studies highlight potential divergence in anhedonia pathophysiology in MDD and BD. Future research is needed to better understand these points of divergence, as they hold significant clinical utility for improving the early diagnosis and treatment of mood disorders.

Acknowledgements and Disclosures Dr. Pizzagalli was partially supported by R37 MH068376 and P50 MH119467. Over the past 3 years, Dr. Pizzagalli has received consulting fees from Albright Stonebridge Group, Neumora Therapeutics (former BlackThorn Therapeutics), Boehringer Ingelheim, Compass Pathways, Concert Pharmaceuticals, Engrail Therapeutics, Neurocrine Biosciences, Neuroscience Software, Otsuka Pharmaceuticals, and Takeda Pharmaceuticals; honoraria from Springer (for editorial work) and Alkermes, and research funding from NIMH, Dana Foundation, Brain and Behavior Research Foundation, and

Millennium Pharmaceuticals. In addition, he has received stock options from Neumora Therapeutics (former BlackThorn Therapeutics), Compass Pathways, and Neuroscience Software. Dr. Whitton has no financial disclosures, and there are no conflicts of interest with the work conducted in this study. All views expressed are solely those of the authors.

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