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Role of Reward Sensitivity and Processing in Major Depressive and Bipolar Spectrum Disorders

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Abstract

Since Costello's (1972) seminal *Behavior Therapy* article on loss of reinforcers or reinforcer effectiveness in depression, the role of reward sensitivity and processing in both depression and bipolar disorder has become a central area of investigation. In this article, we review the evidence for a model of reward sensitivity in mood disorders, with unipolar depression characterized by reward hyposensitivity and bipolar disorders by reward hypersensitivity. We address whether aberrant reward sensitivity and processing are correlates of, mood-independent traits of, vulnerabilities for, and/or predictors of the course of depression and bipolar spectrum disorders, covering evidence from self-report, behavioral, neurophysiological, and neural levels of analysis. We conclude that substantial evidence documents that blunted reward sensitivity and processing are involved in unipolar depression and heightened reward sensitivity and processing are characteristic of hypomania/mania. We further conclude that aberrant reward sensitivity has a trait component, but more research is needed to clearly demonstrate that reward hyposensitivity and hypersensitivity are vulnerabilities for depression and bipolar disorder, respectively. Moreover, additional research is needed to determine whether bipolar depression is similar to unipolar depression and characterized by reward hyposensitivity, or whether like bipolar hypomania/mania, it involves reward hypersensitivity.

Keywords

reward sensitivity; major depression; bipolar disorder

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Costello's Legacy: Loss of Reinforcers or Reinforcer Effectiveness in Depression

In a classic article published in *Behavior Therapy*, Costello (1972) reviewed conceptual arguments and evidence about whether unipolar depression is best characterized as resulting from behavioral extinction due to a loss of reinforcers (rewards) or to a loss of interest in the environment (anhedonia) due to a loss of the effectiveness of rewards. Costello's (1972) review ultimately concluded that anhedonia and a reduction in the effectiveness of rewards were central to an understanding of depression. In the more than 40 years since the publication of Costello's seminal article, research on low reward sensitivity and reward processing in depression has burgeoned, and reward or Behavioral Approach System (BAS; Gray, 1994) hyposensitivity is now one of the prominent models of major depression (Pizzagalli, 2014; Treadway & Zald, 2013). Similarly, the BAS or reward hypersensitivity model has become one of the leading biopsychosocial theories of the onset and course of bipolar spectrum disorders (BSDs; Alloy & Abramson, 2010; Alloy, Abramson, Urošević, Bender, & Wagner, 2009; Alloy, Nusslock, & Boland, 2015; Depue & Iacono, 1989; Johnson, 2005; Johnson, Edge, Holmes, & Carver, 2012; Urošević, Abramson, Harmon-Jones, & Alloy, 2008). Consequently, in homage to Costello's recognition of the importance of the reward system in depression, in this article, we provide a model and up-to-date review of the role of reward sensitivity and processing in the onset and course of the full range of mood disorders--both unipolar depression and BSDs.

The Reward System

The reward system, also known as the BAS (Gray, 1994) has been linked to a fronto-striatal neural circuit that responds to stimuli involving the anticipation and receipt of rewards (e.g., Depue & Collins, 1999; Haber & Knutson, 2010). This system regulates goal-directed behavior and approach motivation and is activated by internal (e.g., expectancy of a job promotion) or external (e.g., opportunity to win a prize) goal- or reward-relevant cues or events. Activation of the reward system leads to increased incentive motivation, goal-related cognitions, and motor behavior directed toward attaining rewards, as well as positive goal-striving emotions such as happiness and hope (Depue & Collins, 1999; Gray, 1994), or to anger when goal-striving is frustrated or blocked (Carver, 2004; Harmon-Jones & Sigelman, 2001). Down-regulation or deactivation of the reward system leads to decreased motivation, decreased goal-related cognitions, and increased withdrawal, as well as emotions such as sadness and anhedonia.

Both animal and human research indicate that the ventral striatum (VS) and orbitofrontal cortex (OFC), among other regions, are involved in this fronto-striatal neural circuit (Haber & Knutson, 2010; Kringelbach & Rolls, 2004; Schultz, 2002). The VS appears to play a central role in reward anticipation and is involved in processing both primary (e.g., food) and secondary (e.g., monetary) rewards. The OFC is particularly important for assessing probability of reward receipt and encoding reward value (Haber & Knutson, 2010). Higher self-reported BAS/reward sensitivity has been associated with elevated VS activity during reward anticipation (Caseras, Lawrence, Murphy, Wise, & Phillips, 2013), and individual

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differences in reward dependence are associated with connectivity between the VS and OFC (Cohen & Ranganath, 2007).

There has been extensive theorizing about adolescent brain development as it relates to changes in reward sensitivity (e.g., Forbes & Dahl, 2012; Olino, in press). Adolescents, relative to children and adults, demonstrate heightened responsivity to rewards across multiple measurement strategies including self-reports of BAS (Pagliaccio et al., in press), reward pursuit behaviors (Anokhin, Golosheykin, & Mulligan, 2015), and neural indices of reward processing (e.g., Forbes, Ryan, et al., 2010). This work has largely relied on cross-sectional studies; thus, additional longitudinal work is needed to further evaluate these trends. Although there are developmental trends in reward processes, our review finds very similar patterns of results of studies of youth and adults, such that development does not appear to be a key moderator of the relationship between reward sensitivity and either unipolar or bipolar mood disorders. However, these developmental patterns in reward sensitivity are important as these changes appear to be synchronous with emergence of mood disorders (Hankin et al., 1998; Lewinsohn, Klein, & Seeley, 1995).

Major Depression and Bipolar Disorder as Opposite Ends of a Reward Sensitivity Dimension

There is a growing recognition of the importance of identifying pathophysiological mechanisms that cut across, or are common to, multiple psychiatric disorders (Insel et al., 2010). An equally important objective, however, is to identify mechanisms and biosignatures that are unique to specific psychiatric disorders. Relevant to these goals, and as summarized here, is evidence that abnormal reward sensitivity is involved across the entire mood disorders spectrum, with blunted reward sensitivity serving as a risk factor for major depression (e.g., Pizzagalli, 2014; Treadway & Zald, 2013), whereas abnormally elevated reward sensitivity is a risk factor for BSDs (e.g., Alloy et al., 2015; Johnson, Edge, et al., 2012). Collectively, this suggests that risk for depression and BSDs are characterized by extreme and opposite profiles of reward sensitivity. For individuals with abnormal reward sensitivity, when they experience reward system deactivating or activating environmental cues or events, their reward systems become too strongly deactivated or activated, leading to depression or hypomania or mania (referred to herein as hypo/mania), respectively (see Figure 1).

There are several important implications of identifying mechanisms of differential risk for depression versus BSDs. First, it can inform our understanding of the pathophysiology of these disorders. We propose that what differentiates risk for BSDs versus depression is vulnerability to hypo/mania. As summarized here, one of the primary risk factors for hypo/mania involves a propensity to experience abnormally elevated approach motivation and reward-related affect to reward cues in the environment (see red pathway in Figure 1). Thus, reward sensitivity may be important for understanding what distinguishes depression and BSDs. Second, behavioral indices or biological markers of reward sensitivity that distinguish risk for depression versus BSDs could potentially complement self-report based diagnostic strategies to facilitate accurate assessment and differential diagnosis. This is particularly

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relevant to BSDs, where it can take 6–10 years or longer to receive an accurate diagnosis and appropriate treatment (Ghaemi, Boiman, & Goodwin, 2000; Ghaemi, Sachs, Chiou, Pandurangi, & Goodwin, 1999). Finally, identifying distinct profiles of reward sensitivity in depression and BSDs can facilitate pharmacological and psychosocial treatments to help regulate reward processing and reward-related brain function across mood disorders.

In our review, we consider whether aberrant reward sensitivity and processing are mood-independent traits of, provide vulnerability to, and influence the course of mood disorders, or whether they serve simply as correlates of these disorders. We use the term "vulnerability" to refer to reward-related factors that contribute to the initial onset of depression or BSD, whereas we use the terms "predictors of course" to mean reward-related factors that maintain or worsen mood disorders. Specifically, predictors of course may predict symptoms, functional status, relapse, recurrence of mood episodes, or progression to more severe disorders along the unipolar or bipolar mood disorder spectra. Consequently, for the sections on correlates of depression and BSD, we include cross-sectional studies because such studies cannot determine whether reward processes represent vulnerabilities, course predictors, or consequences of mood disorders. In the sections on reward sensitivity as a trait, we include studies of euthymic individuals in remission from mood episodes; these studies can determine whether aberrant reward sensitivity is an enduring characteristic independent from mood disorder symptoms, and thus, are relevant to establishing potential vulnerability markers. In the vulnerability sections, we include evidence from truly prospective longitudinal investigations; these include studies in which reward sensitivity or processes are assessed prior to the first onset of depression or BSD. We also review studies that examine reward functioning in individuals with no prior history of mood disorder, but who are known to be at risk for developing depression or BSD (e.g., offspring of parents with mood disorder or individuals with established behavioral risk markers for mood disorder). Finally, in the sections on predictors of course of mood disorders, we review evidence from longitudinal studies of individuals with depression or BSD that assess reward functioning at a time point prior to assessment of illness course (e.g., relapse, recurrence, symptom worsening, progression to more severe disorders on the spectrum).

Reward Hyposensitivity in Major Depressive Disorder: Theory and Evidence

In the following sections, we present the Reward Hyposensitivity Model of depression and evidence relevant to whether reward hyposensitivity is a correlate, mood-independent trait, vulnerability, and/or predictor of the course of depression. The evidence spans various levels of analysis including behavioral and self-report measures, personality/temperament styles, life events research, and neurophysiological and neural assessments.

Reward Hyposensitivity Model of Major Depressive Disorder

There are two chief conceptualizations of the role of reward hyposensitivity in depression. The first follows from a strict behavioral perspective on the development and maintenance of depression. From the behavioral perspective, Costello (1972) concluded that unipolar depression is a result of the emergence of anhedonia due to a loss of the effectiveness of

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rewards. Thus, this perspective emphasizes the influence of experience on attenuated responsiveness to rewards. In contrast, the second perspective emphasizes hyporesponsivity to rewards as a trait-like individual difference characteristic. In our model, in line with the second perspective, we posit that individuals vulnerable to unipolar depression have reduced reward sensitivity. Unlike individuals with BSDs, those with unipolar depression do not experience heightened reward sensitivity following positive events. However, following negative events, individuals vulnerable to depression demonstrate further attenuated anticipation of and response to rewards (see the dark blue pathway in Figure 1). This response, in turn, leads to symptoms of depression. A number of constructs have been proposed to describe reward hyposensitivity in depression, including Gray's (1994) BAS perspective and other, similar domains of function. For example, positive emotionality and extraversion (Tellegen & Waller, 2008; Watson & Clark, 1997) are two individual difference characteristics that emphasize seeking reward and positive affect, which parallel BAS constructs. Thus, we include results of studies of BAS sensitivity, extraversion, and positive emotionality here, which are all associated with being responsive to rewards or motivating an individual to pursue rewards. Individuals with reduced reward sensitivity are at risk for developing or maintaining depression because they have both a diminished capacity to seek out and react to rewards. Thus, this may be described as a two-hit model with vulnerability to depression being reflected in reduced responsivity to *and* reduced pursuit of rewards.

Is Reward Hyposensitivity a Correlate of Major Depressive Disorder?

One of the cardinal symptoms of depression is anhedonia, markedly diminished interest or pleasure in activities (American Psychiatric Association, 2013). Yet, depression may be diagnosed without the presence of anhedonia. Regardless of whether this criterion is endorsed, numerous lines of research find reward hyposensitivity, measured via a variety of methods, is associated with depression.

First, both adults and youth in a current depressive episode report reduced pleasure sensitivity and increased anhedonia than individuals without depression (Fawcett, Clark, Scheftner, & Gibbons, 1983; Kazdin, 1989; Luby, Mrakotsky, Heffelfinger, Brown, & Spitznagel, 2004). Similarly, studies have shown that individuals with depression exhibit lower self-reported BAS sensitivity than those without depression (Kasch, Rottenberg, Arnow, & Gotlib, 2002; Pinto-Meza et al., 2006). Many studies also have examined links between depression and self-reports of normative reward-relevant personality traits, with most of these studies focusing on extraversion. A recent meta-analysis of these studies indicated that individuals with depression demonstrated significantly lower levels of extraversion than those without depression, and chronic depression was particularly marked by reduced extraversion (Kotov, Gamez, Schmidt, & Watson, 2010). However, findings from the above studies have several caveats. First, the results may be contaminated by mood-state response biases that inflate differences between individuals with and without depressive disorders. Second, personality measures are global in their assessment of diminished reward seeking behaviors. Thus, more focal assessments are necessary to identify specific reward-related processes that are impacted by depression. Identification of specific reward functioning processes in individuals with depression has recently been addressed using behavioral and neuroscience methods.

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Investigators have developed several behavioral reward paradigms to assess distinct elements of reward sensitivity/processing, including reward learning (Bechara, Damasio, Damasio, & Anderson, 1994; Pizzagalli, Jahn, & O'Shea, 2005), decision-making, and pursuit (Treadway, Buckholtz, Schwartzman, Lambert, & Zald, 2009). In studies of adults (Cella, Dymond, & Cooper, 2010) and youth (Han et al., 2012), depressed individuals fail to approach higher and more valued rewards whether rewards are clearly approached (e.g., using the Iowa Gambling Task or the Effort Expenditure for Rewards Task, Cella et al., 2010; Han et al., 2012, respectively) or implicitly learned (signal detection task; Morris, Bylsma, Yaroslavsky, Kovacs, & Rottenberg, 2015; D. A. Pizzagalli, D. Iosifescu, L. A. Hallett, K. G. Ratner, & M. Fava, 2008; Pizzagalli et al., 2005).

Generally corroborating the self-report and behavioral evidence, numerous investigations of reward functioning in depression have included resting state frontal electroencephalograpy (EEG) asymmetry, evoked response potentials (ERP), and functional magnetic resonance imaging (fMRI). Early work showed that patterns of frontal asymmetry during rest were associated with the experience of positive and negative affect (Davidson, Schwartz, Saron, Bennett, & Goleman, 1979). Specifically, greater left, relative to right, asymmetry was associated with reward and approach behaviors, whereas greater right, relative to left, asymmetry was associated with withdrawal-related affect and behaviors.[1] Despite some mixed findings, results of a meta-analysis indicated that depression is characterized by heightened right, relative to left, activation (Thibodeau, Jorgensen, & Kim, 2006); this would suggest that depression is better characterized by increased withdrawal-related affect (overall $r = .26$). More recently, EEG recordings have been assessed with temporal links to experimental events. In one study, Shankman et al. (2007) assessed frontal and parietal EEG activity while participants with and without depression completed a gambling task. They did not find group differences on frontal EEG activation; however, depressed participants with early-onsets demonstrated reduced left frontal asymmetry relative to depressed participants with late-onsets and participants without depression. Thus, frontal asymmetry may be specifically associated with only a subtype of depression, and these associations may need to be probed using active experimental paradigms.

In addition to event-related EEG, ERPs also have been examined in the context of depression. ERPs are electrical potentials embedded within EEG signals that occur in preparation for or in response to discrete internal or external events. The feedback negativity (FN) is an ERP component that has garnered support as an index of reward sensitivity (Proudfit, 2014). FN amplitude is usually more negative following a bad outcome compared to a good outcome, and thus, the FN traditionally has been viewed as reflecting binary evaluation of bad vs. good outcome (Folstein & Van Petten, 2008; Hajcak, Moser, Holroyd, & Simons, 2006). Importantly, there is accumulating evidence that variation in FN amplitude is primarily driven by reward-related brain activity elicited to the good (as opposed to bad) outcome (Foti, Weinberg, Bernat, & Proudfit, 2015; Foti, Weinberg, Dien, & Hajcak, 2011),

[1]In line with the perspective that resting frontal EEG asymmetry reflects trait-like activation patterns is research indicating that approximately 60% of the variance in frontal asymmetry is due to individual differences on a temporally stable latent trait (Hagemann, Naumann, Thayer, & Bartussek, 2002). This percentage of variance accounted for by trait-related factors is comparable to other trait-related measures of individual differences (e.g., the Big Five personality traits; Roberts & DelVecchio, 2000).

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and thus, an elevated FN has been associated with elevated reward sensitivity, and a reduced or blunted FN with decreased reward sensitivity. In line with the reward hyposensitivity perspective of depression, Foti and Hajcak (2009) demonstrated that higher depression symptom severity among undergraduates is associated with blunting of the FN ERP component. Similarly, Liu et al. (2014) reported that depressed individuals demonstrated a blunted FN relative to individuals without depression, and there was some specificity for the influence of anhedonia in this association.

Whereas ERP studies provide high temporal resolution for psychophysiological signal, fMRI provides a high degree of spatial resolution for identifying which neural regions are active by indexing relative blood flow during experimental conditions. Investigators have developed a number of fMRI tasks to assess reward sensitivity (Richards, Plate, & Ernst, 2013), including simple guessing for rewards (Delgado, Nystrom, Fissell, Noll, & Fiez, 2000), behavioral performance for rewards (Knutson, Adams, Fong, & Hommer, 2001; Knutson, Fong, Adams, Varner, & Hommer, 2001), and decision making reward tasks (Ernst et al., 2004). Multiple studies have revealed that individuals with depression have reduced VS response to rewards (Chantiluke et al., 2012; Forbes et al., 2009; Pizzagalli et al., 2009; Remijnse et al., 2009; Smoski et al., 2009; Smoski, Rittenberg, & Dichter, 2011), although there are some exceptions (Knutson, Bhanji, Cooney, Atlas, & Gotlib, 2008). Recently, a meta-analysis of this literature reported that individuals with depression demonstrate significantly reduced VS response to monetary and other positive stimuli (e.g., positive IAPS pictures, positive words) for both anticipation and receipt of rewards (Zhang, Chang, Guo, Zhang, & Wang, 2013).

In sum, this work provides strong evidence that reduced reward responsivity and related constructs are correlates of depressive disorders. Generally, these findings come from studies that either study individuals without medication or report their results after controlling for the influence of medication. However, these studies do not address whether hyposensitivity to rewards is a trait independent of current depressive mood or relevant for the development and/or maintenance of the disorder.

Is Reward Hyposensitivity a Mood-Independent Trait of Major Depressive Disorder?

At the broadest level, individuals with remitted depression tend to report lower levels of extraversion and BAS sensitivity relative to those without depression (e.g., Pinto-Meza et al., 2006). However, conflicting results have been reported as well (Kasch et al., 2002). Studies relying on behavioral measures of reward sensitivity have generally supported mood dependent effects on reward seeking behaviors, with no differences found between never depressed controls and individuals with remitted depression (Westheide et al., 2007; Yang et al., 2014). Studies also have reported medication effects on these domains of functioning, such that interventions increase levels of reward sensitivity (e.g., Harkness, Bagby, Joffe, & Levitt, 2002). The most consistent evidence for mood-independent influences on reward functioning in depression come from fMRI studies that find reduced responsiveness to rewards is present when depressive episodes remit (Dichter, Kozink, McClernon, & Smoski, 2012; Schiller, Minkel, Smoski, & Dichter, 2013; Takahashi et al., 2009). Thus, although

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there are mixed findings, consistent evidence supporting mood-independent reward hyposensitivity is most prominent from studies relying on fMRI methods.

Is Reward Hyposensitivity a Vulnerability for Major Depressive Disorder?

In this section, we address whether reward hyposensitivity is a vulnerability marker for depression by focusing on two study designs. First, given that offspring of depressed parents are at heightened risk for depression themselves (Goodman et al., 2011), there is an emerging literature examining whether these high-risk offspring exhibit alterations in reward sensitivity, despite not having yet developed depressive symptoms. Second, several prospective studies have examined whether reduced reward responsivity predicts later development of depressive symptoms and/or disorders, both in those with and without familial risk. Here, we review studies of never depressed, medication naïve individuals.

Many studies have examined reward-related differences between offspring of parents with and without depression to identify vulnerability markers for depression. Further, many investigations have studied preschoolers, school-age children, and early adolescents who have not entered the peak age of risk for depression. Thus, these studies have greater temporal separation between assessing vulnerability and psychopathology, and thus, they reduce potential confounding of assessments of reward-related processes and depression. However, with these younger samples, few studies have examined self-reported differences in reward-related traits among offspring with versus without depressed parents. In one of the few studies that did utilize self-reports, Olino et al. (2014) did not find differences in positive affect between adolescent offspring of depressed and non-depressed parents in an ecological momentary assessment study.

Studies relying on behavioral measures, including both observations and performance, provide additional insights into reward hyposensitivity as a vulnerability for depression. Studies find that positive affect behaviors are reduced in offspring of depressed parents compared to offspring of healthy parents (Durbin, Klein, Hayden, Buckley, & Moerk, 2005; Olino, Klein, Dyson, Rose, & Durbin, 2010). However, there are mixed findings in the literature that may be due to different subtypes of parental depression. In a later study, Olino et al. (2011) found that low positive affect in youth was associated with parental depression, but only when including just those parents who had onsets in childhood (i.e., earlier than age 13), often with a chronic course, highlighting the role of chronic/recurrent depression.

Studies examining reward-related behavioral performance among youth at familial risk for depression also demonstrate alterations in reward sensitivity. For example, in a study examining reward-related decision making in a gambling task, Mannie et al. (2015) reported that youth at risk for depression made more conservative wagers than youth not at risk across all task conditions. These findings suggest that at-risk youth did not modulate their behavior in light of more favorable chances of winning, as did their low-risk peers. However, not all studies agree. In a study examining reward learning in youth using a probabilistic learning task, Morris et al. (2015) found that youth at risk for depression demonstrated similar biases towards rewards as those not at risk.

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Studies of reward sensitivity using EEG methods in offspring of depressed parents have yielded mixed results. Consistent with cross-sectional comparisons of depressed and healthy individuals, offspring of depressed parents demonstrate greater right, relative to left, frontal activation in infant samples (Thibodeau et al., 2006). This similar pattern of increased right relative EEG asymmetry predicted depression scores at a one-year follow-up (Blackhart, Minnix, & Kline, 2006), and the development of a first onset depressive episode over the course of a three-year follow-up (Nusslock et al., 2011). Only one study examined individual differences in the FN ERP between youth with and without a family history of depression: Kujawa, Proudfit, and Klein (2014) discovered that 9-year old children of mothers with depression, but not mothers with both depression and anxiety, demonstrated a reduced FN (i.e., blunted reward-related neural activity) compared to offspring of mothers without depression.

There has been recent interest in examining offspring of depressed and non-depressed parents on their reward function using fMRI (Gotlib et al., 2010; McCabe, Woffindale, Harmer, & Cowen, 2012; Monk et al., 2008; Olino et al., 2014; Olino, Silk, Osterritter, & Forbes, 2015; Sharp et al., 2014). These studies differed based on the reward modalities, although most focused on monetary incentives, and specific offspring developmental periods, ranging from late childhood through early adulthood. Regardless of task differences, they provide consistent evidence of reduced neural reward responses in youth at-risk for depression.

In addition to examining reward sensitivity as a vulnerability in high-risk offspring designs, studies find that reward sensitivity prospectively predicts depression. Caspi et al. (1996) found that behavioral observations of inhibition at age three during routine doctor visits predicted depressive, but not anxiety, disorders at age 21. Although an important finding, there are some concerns about specificity, as the inhibition construct included both fearful wariness and low approach characteristics. However, shorter-term longitudinal studies have provided converging support for reward hyposensitivity as a predictor of depression. Dougherty et al. (2010) showed that both behavioral observations of low positive emotionality and parent reports of child low positive emotionality at age 3 predicted depressive symptoms at age 10, even after controlling for depressive symptoms at age 7 and internalizing problems at age 3. Rawal, Collishaw, Thapar, and Rice (2013) examined the progression of risk-taking behavior using a wagering task in a sample of youth who were all offspring of depressed parents. These authors found that low reward seeking, based on reduced wagering in the task, was predictive of new depression onsets in the offspring.

Other prospective studies using self-report measures of temperament have recently emphasized the interplay between reward-related dimensions and negative affect in understanding the emergence of depression. For example, Wetter and Hankin (2009) found that low levels of positive emotionality prospectively predicted anhedonic depressive symptoms. However, the association was stronger when individuals also demonstrated high levels of negative emotionality. Further, Wetter and Hankin also found the relationship between positive emotionality and anhedonic symptoms was moderated by *and* mediated through supportive relationships. Thus, there are multiple influences on the magnitude of the prospective association between reward sensitivity and depressive symptoms.

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Few studies of neural response to reward have attempted to predict depressive symptoms or disorder onsets. Bress et al. (2013) observed that a reduced FN predicted depression onset among adolescent girls over a one-year follow-up. And, Morgan et al. (2013) found that for boys reduced VS activation during anticipation of rewards predicted increases in depressive symptoms over a two-year follow-up.

In summary, across multiple levels of analysis and study design, there are mixed findings on whether reward hyposensitivity is a marker of risk. However, based on the available data, prospective studies provide good support for the reward hyposensitivity model of unipolar depression. Additional research is needed to identify for whom attenuated reward responsivity is associated with vulnerability to unipolar depression.

Does Reward Hyposensitivity Affect the Course of Major Depressive Disorder?

Several studies have examined whether reward hyposensitivity is associated with the naturalistic course or treatment outcome of depression. Morris, Bylsma, and Rottenberg (2009) reviewed the literature on positive emotions and concluded that greater reward sensitivity, including BAS functioning, extraversion, and positive affect measures, is associated with more positive naturalistic course and treatment outcome for depression. Since their review, additional data have emerged that expand the literature on reward function and course of unipolar depression. Shankman et al. (2010) examined the influence of anhedonia on the course of depression over 20 years among former psychiatric inpatients. These authors found that anhedonia was associated with fluctuations in depression over time, and functional outcomes were more strongly predicted by anhedonia than by depressive symptoms. Likewise, other research has demonstrated that higher anhedonia predicted poorer treatment outcome for both adolescents (McMakin et al., 2012) and adults (Uher et al., 2012). Similar results have been seen in studies of reward learning. Vrieze et al. (2009) showed that weaker reward learning biases at pretreatment were associated with greater probability of having a depression diagnosis at 8-week follow-up among individuals admitted to a psychiatric hospital.

Only a few studies have investigated neurophysiological or neural indices of reward function and course of depression among individuals with the disorder. Such investigations consistently find that EEG indices of reward function predict treatment response, but not typically using frontal EEG alpha asymmetry. Rather, EEG signal from other waves (e.g., theta wave activity) have been associated with treatment response (Bares et al., 2008; Iosifescu et al., 2009; Pizzagalli et al., 2001). In an exception, Bruder et al. (2001) demonstrated that frontal EEG asymmetry (greater right, relative to left, activation) was associated with poorer recovery from depression. To our knowledge, there have been no studies examining whether variability in the FN (an ERP index of reward sensitivity) predicts course of depression among individuals with the disorder.

Finally, limited research has examined whether reward function assessed using fMRI is associated with course of treatment among individuals with depression. Forbes et al. (2010) found that reduced VS response during reward anticipation was associated with slower rate of change of anxiety, but not depressive, symptoms during open cognitive behavior therapy with or without SSRI treatment. Using a paradigm that called for participants to modulate

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their expression of positive affect, Light et al. (2011) showed that greater ventral lateral PFC activation during suppression of positive affect (relative to maintaining positive affect) was associated with smaller changes in anhedonic depression symptoms. The authors suggested that this phenomenon may be related to over-regulation of reward seeking in individuals with depression.

Reward-relevant life events also are related to the course of depression. According to the reward hyposensitivity model of major depression (discussed above), life events that deactivate the reward system should precipitate depressive symptoms and episodes (see Figure 1). Multiple conceptual frameworks similarly emphasize the role of life events in depression (Hammen, 2005; Monroe & Harkness, 2005), and empirical studies agree that stressful life events predict depression onset in early childhood (Bufferd et al., 2014), adolescence (Monroe, Rohde, Seeley, & Lewinsohn, 1999), and adulthood (Kendler, Hettema, Butera, Gardner, & Prescott, 2003). Consistent with the reward hyposensitivity model, reward-deactivating events involving irreconcilable failures and losses have been shown to predict first onset and recurrences of depression (see Alloy, Abramson, Walshaw, & Neeren, 2006 for a review).

The role of life stress on the development of depression is hypothesized to emerge in adolescence. Davey, Yucel, and Allen (2008) argue that prefrontal cortex processes are developing during adolescence that support mentalizing of newly emerging and complex distal goals, including expanding social networks, initiating romantic relationships, and working towards long-term goals (e.g., college admissions). At the same time, adolescents demonstrate increases in reward motivation for immediate rewards (Steinberg et al., 2009). However, as important rewards are not immediately achieved, adolescents' goal striving may be frustrated and they may not experience incremental advancements toward their goals as rewarding. Instead, these non-rewarding experiences toward goals may dampen reward pursuit.

There are critical links between experience of stress and reward function. Animal models demonstrate that experience of stress reduces reward related behavior (reviewed in Pizzagalli, 2014), and there is an emerging literature on the experience of stress and reward function in humans. Both acute threat (Bogdan & Pizzagalli, 2006) and history of peer victimization were associated with reward sensitivity.

In summary, across an array of research contexts, including naturalistic and intervention studies, and relying on multiple assessment strategies, there is consistent evidence that attenuated response to reward and motivation to seek out rewards is indicative of poorer prognosis among individuals with depression. However, many of these studies have relied on self-report and behavioral measures of reward functioning. Thus, further work examining neural response to reward as a predictor of depression course is also needed.

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Reward Hypersensitivity in Bipolar Spectrum Disorders: Theory and Evidence

Whereas unipolar depression involves blunted reward system activation and processing, hypersensitivity to reward is hypothesized to characterize BSDs. Below, we present the Reward Hypersensitivity Model of BSDs and evidence relevant to whether reward hypersensitivity is a correlate, mood-independent trait, vulnerability, and/or predictor of the course of BSDs. We present evidence from behavioral and self-report measures, prodromes of BSDs, reward-relevant life events, and neurophysiological and neural paradigms.

Reward Hypersensitivity Model of Bipolar Spectrum Disorders

Depue and Iacono (1989) originally proposed the BAS or reward hypersensitivity theory of BSD, and Alloy and colleagues (Alloy & Abramson, 2010; Alloy, Abramson, Urošević, et al., 2009; Alloy et al., 2015; Urošević et al., 2008) and Johnson and colleagues (Johnson, 2005; Johnson, Edge, et al., 2012) further expanded this model. According to this theory, vulnerability to BSDs is the result of a reward system that is overly sensitive and reactive to goal- and reward-relevant stimuli. In response to life events involving goal-striving and attainment of rewards, reward hypersensitivity leads to excessive approach-related affect and reward motivation, which, in turn, leads to hypo/manic symptoms (see red pathway in Figure 1)—in particular, to a cluster of psychomotor activation symptoms (elevated energy and confidence, increased goal-directed activity, decreased need for sleep, and irritability if goal-pursuit is frustrated; Alloy et al., 2015). On the other hand, in response to nonattainment of rewards or goals (e.g., irreconcilable failures or losses), this hypersensitivity leads to excessive deactivation or downregulation in approach motivation and affect, which, in turn, leads to depressive symptoms (see the light blue pathway in Figure 1), particularly low motivation, psychomotor retardation, anhedonia, fatigue, and hopelessness. Thus, the reward hypersensitivity theory postulates that excessive reward system activation leads to hypo/manic symptoms, whereas excessive deactivation gives rise to depressive symptoms. It is important to distinguish between trait hypersensitivity of the reward system to reward-relevant cues (the vulnerability) and state levels of activation or deactivation of the system, which are the more proximal precursors of hypo/manic versus depressive symptoms or episodes. In addition, the transactional component of the expanded reward hypersensitivity theory (Alloy, Abramson, Urošević, et al., 2009; Alloy et al., 2015; Urošević et al., 2008) suggests that individuals who are hypersensitive to reward may engage in behaviors that lead them to be exposed to goal- or reward-relevant events more frequently via “stress generation” processes (Hammen, 1991), as well as responding more strongly to these events when they occur. Thus, the theory includes a “two-hit” model in which vulnerable, reward-hypersensitive people have greater exposure to the very goal- and reward-relevant events that trigger excessive responses from their reward systems.

Is Reward Hypersensitivity a Correlate of Bipolar Spectrum Disorders?

Consistent with reward hypersensitivity as a correlate of BSDs, findings from self-report measures of BAS sensitivity[2] and personality characteristics related to high reward drive and incentive motivation support an association between reward hypersensitivity and BSDs.

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Controlling for bipolar mood symptoms, individuals all along the bipolar spectrum report higher self-reported BAS sensitivity (e.g., Alloy et al., 2008; B. Meyer, Johnson, & Winters, 2001; Salavert et al., 2007; but see Hayden et al., 2008 for contrary findings) and higher achievement motivation and more ambitious goal-striving (particularly for popular fame and financial success; Johnson, Edge, et al., 2012; Johnson, Eisner, & Carver, 2009; Lozano & Johnson, 2001) compared to controls. Moreover, following unexpectedly high progress toward a goal, BSD individuals are less likely to "coast" or lessen their goal-striving efforts than controls, suggesting that they have difficulty curbing their ambitious goal-striving (Fulford, Johnson, Llabre, & Carver, 2010). Self-reported high BAS sensitivity also distinguishes BSD patients from those with unipolar depression (Quilty, Mackew, & Bagby, 2014). Similarly, Gruber et al. (2013) found that parents' reports of their adolescent offspring's BAS sensitivity were associated with both manic and depressive symptoms of those offspring. Thus, BSDs are associated with elevated self-reported reward sensitivity and reward-relevant personality traits.

Corroborating the self-report evidence, individuals with BSDs show elevated cognitive, emotional, behavioral, and neural responsiveness to rewards on behavioral tasks, as well as greater relative left-frontal neurophysiological activation at rest. For example, Johnson et al. (2005) reported that current hypomanic symptoms were associated with greater positive affect and success expectancies following success feedback and monetary rewards on a button-pressing task. And, compared to healthy controls, bipolar I patients exhibited an inability to delay responding for rewards on a behavioral task (Swann, Lijffijt, Lane, Steinberg, & Moeller, 2009). Also consistent with the reward hypersensitivity theory of BSD, fMRI studies that employ established reward-related tasks indicate that BSD is associated with elevated fronto-striatal reward circuit neural activation to rewards and approach-related stimuli (see Alloy et al., 2015; Nusslock, Young, & Damme, 2014; Phillips & Swartz, 2014 for reviews). Moreover, neurophysiological evidence indicates that BSD individuals in a hypomanic or manic episode display elevated relative left-frontal EEG activity at rest compared to euthymic and depressed BSD individuals (Kano, Nakamura, Matsuoka, Iida, & Nakajima, 1992; Nusslock, Harmon-Jones, et al., 2012). In sum, individuals with BSDs exhibit increased responsiveness to rewards at multiple levels of analysis.

Finally, consistent with the role of reward hypersensitivity in BSDs, the most common prodromal signs of impending mania include increased goal-setting, goal-directed activity, and success expectancies (Lam & Wong, 1997; Lam, Wong, & Sham, 2001), whereas decreased goal-setting and motivation, anhedonia, and low self-confidence are among the most common prodromal signs of bipolar depression (e.g., Bauer et al., 2006; Molnar, Feeney, & Fava, 1988). In addition, during manic prodromes, if individuals with BSD employ cognitive-behavioral deactivation strategies such as engaging in calming activities, restraining themselves, and modifying high success expectations, they are less likely to

[2]The investigation of self-reported reward sensitivity in bipolar disorder has been aided by the development of the BAS scale of the Behavioral Inhibition System/Behavioral Activation System (BIS/BAS) scales by Carver and White (1994). The BAS scale has strong psychometric properties (see Carver & White, 1994 for review) and we reported reliability (Cronbach's alpha) of .80 for the BAS-Total scale in a sample of 9,991 adolescents ages 14–19 (Alloy, Bender, et al., 2012).

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experience a manic relapse (Lam et al., 2001), whereas engaging in behavioral activation during a depressive prodrome reduces the likelihood of full-blown depression. Consistent with this, individuals with bipolar I disorder report avoiding rewarding activities in an effort to try to prevent onset of mania (Edge, Johnson, Ng, & Carver, 2013).

Is Reward Hypersensitivity a Mood-Independent Trait of Bipolar Spectrum Disorders?

Although studies of individuals with BSDs in a euthymic state who are currently in remission from hypo/manic and depressive episodes cannot determine whether reward processes are concomitants, vulnerabilities, or consequences of bipolar disorder, they can address whether reward hypersensitivity is a trait independent of mood symptoms. Consistent with trait status for hypersensitive reward system functioning in bipolar disorder, individuals with BSDs exhibit higher self-reported BAS sensitivity than controls even when euthymic (Alloy et al., 2008; Salavert et al., 2007). Euthymic BSD individuals also display increased behavioral and neurophysiological responsiveness to rewards on various reward-relevant tasks. For example, on a card sorting task, Hayden et al. (2008) found that euthymic bipolar I patients were more behaviorally responsive to small monetary rewards than controls. Similarly, in their meta-analysis of Iowa Gambling Task performance, Edge et al. (2013) found that euthymic bipolar I patients make more risky choices for rewards on this task than do controls. Additionally, on a probabilistic learning task, Duek and colleagues (2014) found that euthymic bipolar patients did well in the reward learning and punishment learning conditions, but had more difficulty alternating between these conditions than matched controls. Moreover, Harmon-Jones et al. (2008) reported that euthymic BSD individuals exhibited elevated relative left-frontal EEG activity during a reward-related anagrams task compared to healthy controls, suggesting that frontal EEG asymmetry may be sensitive to bipolar trait status. Finally, during a Roulette task involving monetary wins and losses, Mason, Trumillo-Barreto, Bentall, and El-Deredy (in press) found that euthymic BSD participants exhibited elevated reward-related neural activity, as indexed by ERP, relative to matched controls, indicating that an early attentional bias for reward may be a bipolar trait.

Also consistent with trait status for reward hypersensitivity in BSDs, individuals with euthymic bipolar I (Nusslock, Almeida, et al., 2012) and bipolar II (Caseras et al., 2013) disorders displayed greater VS, medial OFC (Brodmann area [BA] 10), and left lateral OFC (BA 47) activation during anticipation of monetary rewards compared to healthy controls, and elevated VS activation in euthymic bipolar I individuals extends to social rewards as well (Dutra, Cunningham, Kober, & Gruber, 2015). Moreover, Trost et al. (2014) found that euthymic bipolar I patients exhibited decreased suppression of reward-related activation in the reward circuit when they had to reject immediate reward in favor of a long-term goal on the “desire-reason dilemma” task (Diekhof & Gruber, 2010) compared to healthy controls. Such findings indicating that euthymic BSD individuals exhibit elevated reward-related neural activation relative to controls suggest that fronto-striatal hyperactivity may be a trait-like profile of BSD.

In accordance with this possibility, individuals with bipolar I disorder also display elevated lateral OFC activation during reward anticipation both in hypo/manic (Bermpohl et al.,

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2010) and depressed (Chase et al., 2013) episodes, suggesting that elevated reward-related neural activation may not be mood-state dependent. However, inconsistent with this trait hypothesis, unmedicated individuals with bipolar II or bipolar disorder not otherwise specified (NOS) exhibited decreased dorsal, but not ventral, striatal activity during reward anticipation compared to matched healthy controls (Yip, Worhunsky, Rogers, & Goodwin, 2015), and increased depression severity across both bipolar and unipolar depressed adults was associated with reduced VS activation for reward compared to loss trials (Satterthwaite et al., 2015). On the other hand, Satterthwaite et al. found that resting-state connectivity was higher in bipolar than unipolar depressed adults at multiple reward circuit nodes. These findings suggest that bipolar depression may have a state effect that suppresses trait vulnerability for elevated reward processing in the VS, whereas elevated cortical (lateral OFC) reward processing is maintained even during bipolar depression. Further research is needed to clarify whether depression in the context of BSD is associated with elevated cortical (lateral OFC) processing of rewards even in the absence of elevated striatal responses to rewards.

In sum, most, although not all, studies of euthymic individuals in remission from bipolar mood episodes employing multiple levels of analysis suggest that reward hypersensitivity may be a mood-independent trait of BSDs. As such, these data suggest that overly sensitive reward functioning could serve as a vulnerability for BSDs, an issue we turn to next.

Is Reward Hypersensitivity a Vulnerability for Bipolar Spectrum Disorders?

Prospective studies that examine reward-related predictors of first onset of BSD provide the strongest evidence that reward hypersensitivity provides vulnerability to BSDs. However, studies that examine reward-related constructs in individuals at genetic or behavioral risk for BSD are also relevant to establishing reward hypersensitivity as a vulnerability for BSD.

Given that individuals with no history of bipolar disorder who score highly on the Hypomanic Personality Scale (HPS; Eckblad & Chapman, 1986) have been found to be more likely to develop a BSD prospectively (Kwapil et al., 2000), high HPS scores have been considered a behavioral indicator of risk for BSD. However, the HPS has some content overlap with hypomanic symptoms themselves, which makes it less than an ideal risk marker. Likewise, as described later in this section, individuals with high self-reported BAS sensitivity have been found to be at increased risk for developing a first onset of BSD, and the self-report measures of BAS sensitivity have some advantage in that they do not have content overlap with hypomanic symptoms. Thus, consistent with the vulnerability hypothesis of the reward hypersensitivity theory of BSD, compared to controls, individuals with high HPS scores exhibit greater positive generalization and cognitive reactivity to success on a behavioral task (Carver & Johnson, 2009; Eisner, Johnson, & Carver, 2008; Johnson, Ruggero, & Carver, 2005). Ambitious goal setting and high achievement-related cognitions also have been reported in individuals with no history of BSD but who are considered at risk for BSD based on either high HPS scores (Carver & Johnson, 2009; Finucane, Jordan, & Meyer, 2013; Johnson, 2005; Johnson & Carver, 2006; T. D. Meyer & Krumm-Merabet, 2003) or high self-reported BAS sensitivity (Stange et al., 2013). Adolescents at risk for BSD based on high self-reported BAS sensitivity, but with no history

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of bipolar disorder, also exhibit greater tendencies to overgeneralize from positive outcomes compared to low-risk adolescents with moderate BAS sensitivity (Stange et al., 2013). Moreover, controlling for baseline hypomanic symptoms, self-reported high BAS sensitivity interacted with this positive overgeneralization style to predict increases in hypomanic symptoms prospectively in adolescents with no prior history of BSD (Stange et al., 2012).

In genetic high-risk samples, Nurnberger et al. (1988) observed greater self-reported sensation-seeking and Chang et al. (2003) reported a greater tendency to approach novel, rewarding situations on a temperament scale in offspring of bipolar parents without mood disorders themselves compared to the offspring of control parents. However, Jones et al. (2006) did not observe differential self-reported BAS sensitivity in the adolescent offspring of bipolar parents, even those with mood symptoms themselves, compared to offspring of control parents.

As shown in Figure 1, and discussed above, the reward hypersensitivity theory also makes predictions about specific types of life events that should precipitate bipolar mood episodes. Specifically, reward system-activation events, involving goal striving, goal attainment, or goal obstacles evoking anger and irritability, should trigger hypo/manic episodes, whereas reward system-deactivation events, involving definite failures or losses that cannot be remediated, should trigger depressive episodes. Although no prospective study to date has examined goal- or reward-relevant life events specifically as predictors of first onset of BSD, evidence for reward-relevant stress generation in individuals at risk for BSDs may have relevance to whether reward-related events provide vulnerability to BSD. Consistent with the concept of reward-related event generation, adolescents with no prior history of BSD, but at risk based on high self-reported BAS sensitivity, experienced higher levels of reward system-activation and deactivation life events over follow-up than did moderate BAS sensitivity adolescents (Boland et al., in press). Thus, through their characteristics and behaviors, individuals with high reward sensitivity may be exposed to higher rates of the very environmental cues that overly activate or deactivate their reward systems, which could contribute to bipolar mood episodes.

Just as there are no prospective studies of reward-related life events as predictors of first onset of BSD to date, no prospective studies have examined neurophysiological or neural measures of reward sensitivity as predictors of first onset of BSD. However, there is some evidence of elevated neurobiological indices of approach motivation and reward sensitivity in individuals at genetic or behavioral risk for BSD. With regard to neurophysiological evidence, individuals without BSDs, but at risk for mania based on exhibiting high HPS scores, displayed greater reward responsiveness, as indexed by ERP, compared to individuals with low or moderate HPS scores (Mason, O'Sullivan, Bentall, & El-Deredy, 2012).

At the neural level, individuals at genetic risk for BSD, but without yet exhibiting the illness, have reduced gray matter volume in the VS and anterior cingulate cortex (another region implicated in the fronto-striatal circuit; Haber & Knutson, 2010). In addition, genetic high-risk fMRI studies using established reward paradigms support reward hypersensitivity as a potential vulnerability for BSD. Singh and colleagues (2014) reported that compared to low-risk children, the healthy children (ages 8–15) of bipolar parents displayed greater left OFC

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activation during receipt of rewards. In high-risk children, impulsivity also was associated with increased striatal and insula activation during reward receipt. Further, using a probabilistic reversal learning task, Linke et al. (2012) found that compared to controls, unaffected first-degree relatives of patients with bipolar I disorder displayed increased right medial OFC and amygdala activation in response to rewards and increased right medial OFC activation in response to reward reversal contingencies. Further, individuals with a hypomanic temperament who had not yet developed BSD (Harada et al., 2013) also exhibited elevated VS and left-lateral OFC activation during reward processing. Collectively, these findings suggest that abnormalities in neural reward circuitry may reflect preexisting vulnerabilities for BSD, rather than consequences of bipolar disorder.

In a retrospective behavioral high-risk design, Alloy and colleagues (2006) found that late adolescents (ages 18–24) selected to have high levels of self-reported reward sensitivity (on two different self-report BAS questionnaires) but not currently in a mood episode were six times more likely to meet diagnostic criteria for a lifetime BSD (50%) than were those with moderate levels of reward sensitivity (8.3%). Although these findings are consistent with reward hypersensitivity as a vulnerability for BSD, the directionality of the association is unclear in this retrospective design. Subsequently, in a truly prospective study, Alloy, Bender, et al. (2012) studied younger adolescents (ages 14–19) with no prior lifetime history of BSD or hypomania, who were selected to be in the top 15% (high BAS group) or middle 40–60% (moderate BAS group) of a large screening sample on two different self-report measures of reward sensitivity, and followed them prospectively for over a year. At baseline, the participants also completed a measure of ambitious goal-setting and a behavioral task assessing responsiveness to monetary rewards. Controlling for baseline mood symptoms and family history of BSD, the high BAS group was significantly more likely than the moderate BAS group to develop first onset of a BSD (12.3% versus 4.2%) and had a shorter time to onset of BSD. After controlling for BAS risk group status, as well as baseline mood symptoms and family history of BSD, greater ambitious goal-setting and reward responsiveness on the behavioral task also predicted a higher likelihood and shorter time to onset of BSD. Thus, this prospective study demonstrates reward-related psychological vulnerabilities that predict first lifetime onset of BSD.

In summary, only one truly prospective study of reward hypersensitivity as a predictor of initial onset of BSD has been conducted to date. This study demonstrated that high self-reported reward sensitivity, ambitious goal-setting, and behavioral reward responsiveness do, in fact, predict first lifetime onset of BSD; this study thus provides direct support for the vulnerability hypothesis. However, additional self-report, behavioral, and neural evidence from studies of individuals with no history of bipolar disorder who were at behavioral or genetic risk for BSD also is suggestive that reward hypersensitivity may provide vulnerability to bipolar disorder.

Does Reward Hypersensitivity Affect the Course of Bipolar Spectrum Disorders?

Longitudinal studies of individuals with BSDs are required to determine whether reward hypersensitivity predicts subsequent indicators of the course of bipolar disorder. Several longitudinal studies have examined self-reported reward sensitivity as a course predictor. For

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example, Alloy et al. (2008) reported that higher baseline BAS sensitivity predicted a shorter time to relapse of hypo/manic episodes and higher baseline BAS reward responsiveness (a subscale of the BAS questionnaire) predicted a shorter time to depressive episode relapse over a three year follow-up in individuals with BSDs, the vast majority of whom were unmedicated. This was true even when controlling for initial hypomanic and depressive symptoms. Further, high self-reported reward sensitivity also predicted progression to more severe disorders along the bipolar spectrum. Alloy, Urošević et al. (2012) found that high Time 1 BAS sensitivity (and particularly the fun-seeking subscale) predicted a greater likelihood of progression to bipolar II disorder (onset of a major depressive episode) over follow-up among individuals with cyclothymia or bipolar NOS, and a greater likelihood of progression to bipolar I disorder (onset of a manic episode) among individuals with bipolar II, cyclothymia, or bipolar NOS, controlling for family history of BSD, medication and psychotherapy, and baseline hypomanic and depressive symptoms. Further, high BAS sensitivity (and particularly the fun-seeking subscale) predicted increased substance use problems over follow-up in this same sample (Alloy, Bender, et al., 2009). Meyer and colleagues (2001) reported that BAS sensitivity levels at post-mood-episode recovery predicted greater manic symptoms over follow-up in a bipolar I patient sample. Likewise, Salavert et al. (2007) found that higher baseline BAS sensitivity predicted hypo/manic episode relapse among medicated bipolar I patients followed for 18 months. In addition, lower baseline BAS sensitivity predicted depressive episode relapse; this latter finding runs contrary to the reward hypersensitivity model of BSD, which proposes that high, rather than low, BAS sensitivity should predict bipolar depressive relapse.

Reward-relevant personality and neurophysiological characteristics also have been found to predict the course of BSDs. In bipolar I samples, ambitious goal-setting for popular fame and financial success predicted increases in manic symptoms over a three-month follow-up (Johnson, Carver, & Gotlib, 2012); and both high achievement motivation (Lozano & Johnson, 2001) and personal goals rated as objectively more ambitious (Tharp, Johnson, Sinclair, & Kumar, in press) predicted increases in manic symptoms over a six-month follow-up. Moreover, Nusslock, Harmon-Jones, et al. (2012) found that elevated relative left frontal EEG activity at rest prospectively predicted a greater likelihood of progression from bipolar II or cyclothymic disorder to bipolar I disorder over a 4.7 year follow-up, controlling for baseline mood symptoms and medication status. Thus, this study identified a reward-related neurophysiological marker that predicts conversion to bipolar I disorder.

Finally, studies of the role of reward-relevant life events in the course of BSD have been consistent with the reward hypersensitivity theory. Johnson et al. (2008; 2000) found that goal-attainment life events, but not general positive events, predicted increases in manic, but not depressive, symptoms over follow-up among patients with bipolar I disorder. Likewise, Nusslock et al. (2007) reported that independent of treatment and medication status, undergraduate students with BSDs were more likely to develop a new hypomanic episode, but not depression, during goal-striving life events (studying for and taking final exams) than were other, nonstudent BSD individuals who did not experience the goal-striving events (43% vs. 4%). Additionally, events involving anger-provocation, theorized to also activate the reward system, have been shown to predict hypomanic symptoms (e.g., Carver, 2004; Harmon-Jones et al., 2002). On the other hand, evidence suggests that life events theorized

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to deactivate the reward system (e.g., failures or losses) may precipitate depressive episodes (see Alloy et al., 2005; Alloy, Abramson, Walshaw, et al., 2009 for a review).

Thus, among individuals with BSDs, reward hypersensitivity assessed primarily via self-report measures and reward-relevant life events predict subsequent bipolar and substance use symptoms, recurrences of bipolar mood episodes, and progression to more severe bipolar diagnoses. One study corroborated these self-report findings with a neurophysiological indicator of reward hypersensitivity, with results indicating that increased relative left frontal cortical activation on EEG at rest predicted progression to bipolar I disorder among BSD individuals. Overall, these findings suggest that reward hypersensitivity maintains and exacerbates bipolar symptoms.

Bipolar Depression: Reward Hyposensitivity or Hypersensitivity?

As shown in Figure 1, we suggest that unipolar depression is characterized by reward hyposensitivity and that reward hypersensitivity typifies BSDs. This raises the obvious and important question of what type of reward mechanisms are involved in bipolar depression. In its original conceptualization, the reward hypersensitivity model of BSDs proposed that reward hypersensitivity underlies risk for both hypo/manic and bipolar depression symptoms (e.g., Depue & Collins, 1999). The logic of this original conceptualization was that reward hypersensitivity should make individuals hyperreactive to both cues signaling the possible attainment and loss of rewards, and that in the face of loss, individuals with reward hypersensitivity should be at increased risk for depression given the high value they place on rewards (see light blue pathway in Figure 1). From this perspective, reward hypersensitivity is viewed as a risk for excessive lability in approach motivation, with excessive increases in approach motivation (i.e., hypo/mania) occurring in the context of reward attainment and excessive decreases in approach motivation (i.e., depression) occurring in the context of reward loss. To date, however, there is some, but limited, support for this lability perspective (Alloy & Abramson, 2010; Johnson, 2005; Johnson, Edge, et al., 2012), as the data indicate that reward hypersensitivity is more strongly related to risk for hypo/manic symptoms than bipolar depression symptoms. This suggests two possibilities. The first is that there is a relationship between reward hypersensitivity and bipolar depression that researchers have yet to fully identify. For example, by considering bipolar depression as a homogenous or unitary construct, researchers may have missed or masked the relationship between reward hypersensitivity and specific depressive symptoms among BSD individuals. The second possibility, however, is that reward hypersensitivity is less related to bipolar depression and that different etiological mechanisms (e.g., elevated threat processing) may underlie bipolar depression. Future research is needed to test these competing hypotheses.

Conclusions and Future Directions

Since Costello's (1972) seminal article, the role of reward sensitivity and processing in mood disorders has become an important topic of investigation. As discussed herein, abnormal reward system functioning appears to be centrally involved in both unipolar depression and bipolar disorders, with blunted reward sensitivity and processing characteristic of unipolar depression and heightened reward sensitivity and processing

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characteristic of hypo/mania. Collectively, this suggests that unipolar depression and bipolar disorder are characterized by distinct and opposite profiles of reward processing and reward-related neural activation. As yet, it remains unclear whether bipolar depression involves hypo- or hyper-sensitivity to rewards. In addition, the existing evidence is supportive of a trait component to reward hypersensitivity in BSD independent of current bipolar symptoms, and a possible trait component for reward hyposensitivity in unipolar depression based most consistently on fMRI studies of neural reward function. Moreover, although the number of studies relevant to testing vulnerability or course predictor status for aberrant reward functioning are sparse, the extant literature suggests that reward hypo- and hyper-sensitivity may provide vulnerability to onset and a worse course of unipolar depression and BSDs, respectively.

Further research is needed to 1) more definitively determine whether abnormal reward system functioning provides vulnerability for onset of depression and BSD, and 2) whether these abnormalities impact the course of these mood disorders. For example, only a handful of truly prospective studies have examined reward hyposensitivity assessed via self-report, behavioral task, neurophysiology, or fMRI as a predictor of initial onset of depression. And, only one study exists demonstrating that reward-relevant mechanisms (self-reported BAS sensitivity, ambitious goal striving, and high behavioral reward responsiveness) are vulnerabilities to BSD and predict first lifetime onset of BSD. Therefore, future research must examine multiple indices of reward hyposensitivity and hypersensitivity, as well as the occurrence of reward deactivation and activation events, as vulnerabilities for first onset of depression and BSD, respectively. Evidence is also needed to test explicitly the hypothesized link between reward-activation and deactivation events and actual activation and deactivation of the reward system, as well as the link between reward system activation and deactivation and specific symptom profiles. Finally, further research is needed to determine whether bipolar depression is similar to unipolar depression and characterized by reward hyposensitivity, or whether it is distinct from unipolar depression and mediated by reward hypersensitivity. Given the highly promising body of research to date that implicates dysfunctional reward processing in depression and BSD reviewed in this article, we anticipate that further research testing the reward models of mood disorders should yield enhanced understanding of the pathophysiological mechanisms underlying mood disorders, and, in turn, generate more targeted reward-relevant interventions for these illnesses.

It will be important for future research on reward sensitivity in mood disorders to take into consideration medication-related issues, given that many medications for both depression and bipolar disorder directly target dopamine transmission in the fronto-striatal reward circuit (Abler, Erk, & Walter, 2007; Vieta et al., 2005). These analyses can: 1) examine the relationship between reward indices and medication load, which takes into consideration the type, number, and dosage of medication an individual is taking (see Nusslock, Almeida, et al., 2012); 2) include medication load as a covariate in analyses; and/or 3) exclude participants from analyses who are on dopaminergic agonists/antagonists. It is important to emphasize, however, that dopamine-blocking antipsychotics frequently used for treating hypo/manic states reduce reward-related neural activation in the VS (Abler et al., 2007), whereas antidepressants of diverse mechanisms increase dopamine reward-related behaviors (D'Aquila, Collu, Gessa, & Serra, 2000). This suggests that the findings reviewed above

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supporting the reward hyposensitivity and hypersensitivity models of MDD and BSD respectively are likely not an artifact of medication-related mechanisms, and, if anything, medication may be attenuating the strength of the reported findings. Future research is needed to more fully examine this possibility.

Finally, we argue that it will be important for future research to move beyond examining depression and bipolar disorder as unitary constructs or homogenous disorders, and instead, to examine the relationship between reward sensitivity and specific symptom clusters. Drawing on existing theory and research, we propose that reward hyposensitivity will be most strongly associated with anhedonia, a diminished interest or pleasure in response to rewarding stimuli. In line with this perspective is growing evidence that decreased reward sensitivity, as assessed by self-report (see Treadway & Zald, 2011 for a review), behavioral (Pizzagalli et al., 2005), neurophysiological (Shankman et al., 2010), and neural (Epstein et al., 2006; Keedwell, Andrew, Williams, Brammer, & Phillips, 2005; Wacker, Dillon, & Pizzagalli, 2009) indices, is particularly related to anhedonia, as opposed to depression severity more generally. By contrast, we propose that reward hypersensitivity will be most strongly associated with a cluster of hypo/manic symptoms characterized by excessive reward- and approach-related motivation (i.e., elevated energy, increased goal-directed activity, decreased need for sleep, and irritability when goal-pursuit is thwarted). We base this prediction on evidence that both reward sensitivity and the fronto-striatal neural circuit underlying reward processing is most directly involved in generating incentive motivation and goal-pursuit emotions, rather than positive/hedonic moods or cognitive processes (Berridge, Robinson, & Aldridge, 2009; Haber & Knutson, 2010; Kringelbach & Rolls, 2004). Examining the relationship between reward processing and specific symptoms will enhance our understanding of the pathophysiology of mood disorders, and, ideally, increase the precision with which we can assess and treat mood disorder symptoms.

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References

Abler B, Erk S, Walter H. Human reward system activation is modulated by a single dose of olanzapine in healthy subjects in an event-related, double-blind, placebo-controlled fMRI study. Psychopharmacology. 2007; 191(3):823–833. [PubMed: 17265148]

Alloy LB, Abramson LY. The role of the Behavioral Approach System (BAS) in bipolar spectrum disorders. Current Directions in Psychological Science. 2010; 19(3):189–194. [PubMed: 20606725]

Alloy LB, Abramson LY, Urošević S, Bender RE, Wagner CA. Longitudinal predictors of bipolar spectrum disorders: A behavioral approach system (BAS) perspective. Clinical Psychology. 2009; 16(2):206–226. [PubMed: 20161008]

Alloy LB, Abramson LY, Urošević S, Walshaw PD, Nusslock R, Neeren AM. The psychosocial context of bipolar disorder: environmental, cognitive, and developmental risk factors. Clinical Psychology Review. 2005; 25(8):1043–1075. [PubMed: 16140445]

Alloy LB, Abramson LY, Walshaw PD, Cogswell A, Grandin LD, Hughes ME, Hogan ME. Behavioral Approach System and Behavioral Inhibition System sensitivities and bipolar spectrum disorders: Prospective prediction of bipolar mood episodes. Bipolar Disorders. 2008; 10(2):310–322. [PubMed: 18271911]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Alloy LB, Abramson LY, Walshaw PD, Cogswell A, Smith JM, Neeren AM, Nusslock R. Behavioral approach system (BAS) sensitivity and bipolar spectrum disorders: A retrospective and concurrent behavioral high-risk design. Motivation and Emotion. 2006; 30(2):143–155.

Alloy LB, Abramson LY, Walshaw PD, Gerstein RK, Keyser JD, Whitehouse WG, Harmon-Jones E. Behavioral approach system (BAS)-relevant cognitive styles and bipolar spectrum disorders: Concurrent and prospective associations. Journal of Abnormal Psychology. 2009; 118(3):459–471. [PubMed: 19685944]

Alloy LB, Abramson LY, Walshaw PD, Neeren AM. Cognitive vulnerability to unipolar and bipolar mood disorders. Journal of Social and Clinical Psychology. 2006; 25(7):726–754.

Alloy LB, Bender RE, Wagner CA, Whitehouse WG, Abramson LY, Hogan ME, Harmon-Jones E. Bipolar spectrum-substance use co-occurrence: Behavioral approach system (BAS) sensitivity and impulsiveness as shared personality vulnerabilities. Journal of Personality and Social Psychology. 2009; 97(3):549–565. [PubMed: 19686007]

Alloy LB, Bender RE, Whitehouse WG, Wagner CA, Liu RT, Grant DA, Abramson LY. High Behavioral Approach System (BAS) sensitivity, reward responsiveness, and goal-striving predict first onset of bipolar spectrum disorders: A prospective behavioral high-risk design. Journal of Abnormal Psychology. 2012; 121(2):339–351. [PubMed: 22004113]

Alloy LB, Nusslock R, Boland EM. The development and course of bipolar spectrum disorders: An integrated reward and circadian rhythm dysregulation model. Annual Review of Clinical Psychology. 2015; 11:213–250.

Alloy LB, Urošević S, Abramson LY, Jager-Hyman S, Nusslock R, Whitehouse WG, Hogan M. Progression along the bipolar spectrum: A longitudinal study of predictors of conversion from bipolar spectrum conditions to bipolar I and II disorders. Journal of Abnormal Psychology. 2012; 121(1):16–27. [PubMed: 21668080]

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth. Arlington, VA: Author; 2013.

Anokhin AP, Golosheykin S, Mulligan RC. Long-term test-retest reliability of delayed reward discounting in adolescents. Behavioural Processes. 2015; 111:55–59. [PubMed: 25447508]

Bares M, Brunovsky M, Kopecek M, Novak T, Stopkova P, Kozeny J, Höschl C. Early reduction in prefrontal theta QEEG cordance value predicts response to venlafaxine treatment in patients with resistant depressive disorder. European Psychiatry. 2008; 23(5):350–355. [PubMed: 18450430]

Bauer M, Grof P, Rasgon N, Bschor T, Glenn T, Whybrow PC. Temporal relation between sleep and mood in patients with bipolar disorder. Bipolar Disorders. 2006; 8(2):160–167. [PubMed: 16542186]

Bechara A, Damasio AR, Damasio H, Anderson SW. Insensitivity to future consequences following damage to human prefrontal cortex. Cognition. 1994; 50(1):7–15. [PubMed: 8039375]

Bermpohl F, Kahnt T, Dalanay U, Hagele C, Sajonz B, Wegner T, Heinz A. Altered representation of expected value in the orbitofrontal cortex in mania. Human Brain Mapping. 2010; 31(7):958–969. [PubMed: 19950195]

Berridge KC, Robinson TE, Aldridge JW. Dissecting components of reward: 'liking', 'wanting', and learning. Current Opinion in Pharmacology. 2009; 9(1):65–73. [PubMed: 19162544]

Blackhart GC, Minnix JA, Kline JP. Can EEG asymmetry patterns predict future development of anxiety and depression? A preliminary study. Biological Psychology. 2006; 72(1):46–50. [PubMed: 16223557]

Bogdan R, Pizzagalli DA. Acute stress reduces reward responsiveness: Implications for depression. Biological Psychiatry. 2006; 60(10):1147–1154. [PubMed: 16806107]

Boland EM, Stange JP, LaBelle DR, Shapero BG, Weiss RB, Abramson LY, Alloy A. Affective disruption from social rhythm and behaviorral approach system (BAS) sensitivities: A test of the integration of the social zeitgeber and reward theories of bipolar disorder. Clinical Psychological Science. (in press).

Bress JN, Foti D, Kotov R, Klein DN, Hajcak G. Blunted neural response to rewards prospectively predicts depression in adolescent girls. Psychophysiology. 2013; 50(1):74–81. [PubMed: 23252717]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Bruder GE, Stewart JW, Tenke CE, McGrath PJ, Leite P, Bhattacharya N, Quitkin FM. Electroencephalographic and perceptual asymmetry differences between responders and nonresponders to an SSRI antidepressant. Biological Psychiatry. 2001; 49(5):416–425. [PubMed: 11274653]

Bufferd SJ, Dougherty LR, Olino TM, Dyson MW, Laptook RS, Carlson GA, Klein DN. Predictors of the onset of depression in young children: a multi-method, multi-informant longitudinal study from ages 3 to 6. Journal of Child Psychology and Psychiatry. 2014; 55(11):1279–1287. [PubMed: 24828086]

Carver CS. Negative affects deriving from the behavioral approach system. Emotion. 2004; 4(1):3–22. [PubMed: 15053723]

Carver CS, Johnson SL. Tendencies toward mania and tendencies toward depression have distinct motivational, affective, and cognitive correlates. Cognitive Therapy and Research. 2009; 33(6): 552–569. [PubMed: 20376291]

Carver CS, White TL. Behavioral-Inhibition, Behavioral Activation, and Affective Responses to Impending Reward and Punishment - the BIS BAS Scales. Journal of Personality and Social Psychology. 1994; 67(2):319–333.

Caseras X, Lawrence NS, Murphy K, Wise RG, Phillips ML. Ventral striatum activity in response to reward: differences between bipolar I and II disorders. American Journal of Psychiatry. 2013; 170(5):533–541. [PubMed: 23558337]

Caspi A, Moffitt TE, Newman DL, Silva PA. Behavioral observations at age 3 years predict adult psychiatric disorders: Longitudinal evidence from a birth cohort. Archives of General Psychiatry. 1996; 53(11):1033–1039. [PubMed: 8911226]

Cella M, Dymond S, Cooper A. Impaired flexible decision-making in major depressive disorder. Journal of Affective Disorders. 2010; 124(1):207–210. [PubMed: 20004023]

Chang KD, Blasey CM, Ketter TA, Steiner H. Temperament characteristics of child and adolescent bipolar offspring. Journal of Affective Disorders. 2003; 77(1):11–19. [PubMed: 14550931]

Chantiluke K, Halari R, Simic M, Pariante CM, Papadopoulos A, Giampietro V, Rubia K. Fronto-Striato-Cerebellar Dysregulation in Adolescents with Depression During Motivated Attention. Biological Psychiatry. 2012; 71(1):59–67. [PubMed: 22015111]

Chase HW, Nusslock R, Almeida JR, Forbes EE, LaBarbara EJ, Phillips ML. Dissociable patterns of abnormal frontal cortical activation during anticipation of an uncertain reward or loss in bipolar versus major depression. Bipolar Disorders. 2013; 15(8):839–854. [PubMed: 24148027]

Cohen MX, Ranganath C. Reinforcement learning signals predict future decisions. The Journal of Neuroscience. 2007; 27(2):371–378. [PubMed: 17215398]

Costello CG. Depression: Loss of reinforcers of loss of reinforcer effectiveness? Behavior Therapy. 1972; 3(2):240–247.

D'Aquila PS, Collu M, Gessa GL, Serra G. The role of dopamine in the mechanism of action of antidepressant drugs. European Journal of Pharmacology. 2000; 405(1–3):365–373. [PubMed: 11033341]

Davey CG, Yucel M, Allen NB. The emergence of depression in adolescence: Development of the prefrontal cortex and the representation of reward. Neuroscience & Biobehavioral Reviews. 2008; 32(1):1–19. [PubMed: 17570526]

Davidson RJ, Schwartz GE, Saron C, Bennett J, Goleman DJ. Frontal versus parietal EEG asymmetry during positive and negative affect. Psychophysiology. 1979; 16:202–203.

Delgado MR, Nystrom LE, Fissell C, Noll DC, Fiez JA. Tracking the hemodynamic responses to reward and punishment in the striatum. Journal of Neurophysiology. 2000; 84(6):3072–3077. [PubMed: 11110834]

Depue RA, Collins PF. Neurobiology of the structure of personality: dopamine, facilitation of incentive motivation, and extraversion. Behavioral and Brain Sciences. 1999; 22(3):491–517. discussion 518-469. [PubMed: 11301519]

Depue RA, Iacono WG. Neurobehavioral aspects of affective disorders. Annual Review Psychology. 1989; 40:457–492.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Dichter GS, Kozink RV, McClernon FJ, Smoski MJ. Remitted major depression is characterized by reward network hyperactivation during reward anticipation and hypoactivation during reward outcomes. Journal of Affective Disorders. 2012; 136(3):1126–1134. [PubMed: 22036801]

Diekhof EK, Gruber O. When desire collides with reason: Functional interactions between anteroventral prefrontal cortex and nucleus accumbens underlie the human ability to resist impulsive desires. The Journal of Neuroscience. 2010; 30(4):1488–1493. [PubMed: 20107076]

Dougherty LR, Klein DN, Durbin CE, Hayden EP, Olino TM. Temperamental positive and negative emotionality and children's depressive symptoms: A longitudinal prospective study from age three to age ten. Journal of Social and Clinical Psychology. 2010; 29:462–488.

Duek O, Osher Y, Belmaker RH, Bersudsky Y, Kofman O. Reward sensitivity and anger in euthymic bipolar disorder. Psychiatry Research. 2014; 215(1):95–100. [PubMed: 24230992]

Durbin CE, Klein DN, Hayden EP, Buckley ME, Moerk KC. Temperamental emotionality in preschoolers and parental mood disorders. Journal of Abnormal Psychology. 2005; 114(1):28–37. [PubMed: 15709809]

Dutra SJ, Cunningham WA, Kober H, Gruber J. Elevated striatal reactivity across monetary and social rewards in bipolar I disorder. Journal of Abnormal Psychology. 2015; 124(4):890–904. [PubMed: 26390194]

Eckblad M, Chapman LJ. Development and validation of a scale for hypomanic personality. Journal of Abnormal Psychology. 1986; 95(3):214–222. [PubMed: 3745642]

Edge MD, Johnson SL, Ng T, Carver CS. Iowa Gambling Task performance in euthymic bipolar I disorder: A meta-analysis and empirical study. Journal of Affective Disorders. 2013; 150(1):115–122. [PubMed: 23219060]

Eisner LR, Johnson SL, Carver CS. Cognitive responses to failure and success relate uniquely to bipolar depression versus mania. Journal of Abnormal Psychology. 2008; 117(1):154–163. [PubMed: 18266493]

Epstein J, Pan H, Kocsis JH, Yang Y, Butler T, Chusid J, Silbersweig DA. Lack of ventral striatal response to positive stimuli in depressed versus normal subjects. American Journal of Psychiatry. 2006; 163(10):1784–1790. [PubMed: 17012690]

Ernst M, Nelson EE, McClure EB, Monk CS, Munson S, Eshel N, Towbin K. Choice selection and reward anticipation: An fMRI study. Neuropsychologia. 2004; 42(12):1585–1597. [PubMed: 15327927]

Fawcett J, Clark DC, Scheftner WA, Gibbons RD. Assessing anhedonia in psychiatric patients: The Pleasure Scale. Archives of General Psychiatry. 1983; 40(1):79. [PubMed: 6849623]

Finucane L, Jordan G, Meyer TD. Risk for mania and its relationship to implicit and explicit achievement motivation. Journal of Individual Differences. 2013; 34(4):214–221.

Folstein JR, Van Petten C. Influence of cognitive control and mismatch on the N2 component of the ERP: a review. Psychophysiology. 2008; 45(1):152–170. [PubMed: 17850238]

Forbes EE, Dahl RE. Research Review: altered reward function in adolescent depression: what, when and how? Journal of Child Psychology and Psychiatry. 2012; 53(1):3–15. [PubMed: 22117893]

Forbes EE, Hariri AR, Martin SL, Silk JS, Moyles DL, Fisher PM, Dahl RE. Altered striatal activation predicting real-world positive affect in adolescent major depressive disorder. American Journal of Psychiatry. 2009; 166(1):64–73. [PubMed: 19047324]

Forbes EE, Olino TM, Ryan ND, Birmaher B, Axelson D, Moyles DL, Dahl RE. Reward-related brain function as a predictor of treatment response in adolescents with major depressive disorder. Cognitive Affective & Behavioral Neuroscience. 2010; 10(1):107–118.

Forbes EE, Ryan ND, Phillips ML, Manuck SB, Worthman CM, Moyles DL, Dahl RE. Healthy adolescents' neural response to reward: associations with puberty, positive affect, and depressive symptoms. Journal of the American Academy of Child and Adolescent Psychiatry. 2010; 49(2): 162–172. e161–e165. [PubMed: 20215938]

Foti D, Hajcak G. Depression and reduced sensitivity to non-rewards versus rewards: Evidence from event-related potentials. Biological Psychology. 2009; 81(1):1–8. [PubMed: 19162124]

Foti D, Weinberg A, Bernat EM, Proudfit GH. Anterior cingulate activity to monetary loss and basal ganglia activity to monetary gain uniquely contribute to the feedback negativity. Clinical Neurophysiology. 2015; 126(7):1338–1347. [PubMed: 25454338]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Foti D, Weinberg A, Dien J, Hajcak G. Event-related potential activity in the basal ganglia differentiates rewards from nonrewards: temporospatial principal components analysis and source localization of the feedback negativity. Human Brain Mapping. 2011; 32(12):2207–2216. [PubMed: 21305664]

Fulford D, Johnson SL, Llabre MM, Carver CS. Pushing and coasting in dynamic goal pursuit: Coasting is attenuated in bipolar disorder. Psychological Science. 2010; 21(7):1021–1027. [PubMed: 20519486]

Ghaemi SN, Boiman EE, Goodwin FK. Diagnosing bipolar disorder and the effect of antidepressants: A naturalistic study. Journal of Clinical Psychiatry. 2000; 61(10):804–808. quiz 809. [PubMed: 11078046]

Ghaemi SN, Sachs GS, Chiou AM, Pandurangi AK, Goodwin K. Is bipolar disorder still underdiagnosed? Are antidepressants overutilized? Journal of Affective Disorders. 1999; 52(1–3): 135–144. [PubMed: 10357026]

Goodman SH, Rouse MH, Connell AM, Broth MR, Hall CM, Heyward D. Maternal depression and child psychopathology: A meta-analytic review. Clinical Child and Family Psychology Review. 2011; 14(1):1–27. [PubMed: 21052833]

Gotlib IH, Hamilton JP, Cooney RE, Singh MK, Henry ML, Joormann J. Neural processing of reward and loss in girls at risk for major depression. Archives of General Psychiatry. 2010; 67:380–387. [PubMed: 20368513]

Gray, JA. Framework for a taxonomy of psychiatric disorder. Hove: Lawrence Erlbaum; 1994.

Gruber J, Gilbert KE, Youngstrom E, Youngstrom JK, Feeny NC, Findling RL. Reward dysregulation and mood symptoms in an adolescent outpatient sample. Journal of Abnormal Child Psychology. 2013; 41(7):1053–1065. [PubMed: 23783771]

Haber SN, Knutson B. The reward circuit: Linking primate anatomy and human imaging. Neuropsychopharmacology. 2010; 35(1):4–26. [PubMed: 19812543]

Hagemann D, Naumann E, Thayer JF, Bartussek D. Does resting electroencephalograph asymmetry reflect a trait? an application of latent state-trait theory. Journal of Personality and Social Psychology. 2002; 82(4):619–641. [PubMed: 11999928]

Hajcak G, Moser JS, Holroyd CB, Simons RF. The feedback-related negativity reflects the binary evaluation of good versus bad outcomes. Biological Psychology. 2006; 71(2):148–154. [PubMed: 16005561]

Hammen C. Generation of stress in the course of unipolar depression. Journal of Abnormal Psychology. 1991; 100(4):555–561. [PubMed: 1757669]

Hammen C. Stress and depression. Annual Review of Clinical Psychology. 2005; 1:293–319.

Han G, Klimes-Dougan B, Jepsen S, Ballard K, Nelson M, Houri A, Cullen K. Selective neurocognitive impairments in adolescents with major depressive disorder. Journal of Adolescence. 2012; 35(1):11–20. [PubMed: 21782233]

Hankin BL, Abramson LY, Moffitt TE, Silva PA, McGee R, Angell KE. Development of depression from preadolescence to young adulthood: Emerging gender differences in a 10-year longitudinal study. Journal of Abnormal Psychology. 1998; 107:128–140. [PubMed: 9505045]

Harada M, Hoaki N, Terao T, Hatano K, Kohno K, Araki Y, Kochiyama T. Hyperthymic temperament and brightness judgment in healthy subjects: involvement of left inferior orbitofrontal cortex. Journal of Affective Disorders. 2013; 151(1):143–148. [PubMed: 23778201]

Harkness KL, Bagby RM, Joffe RT, Levitt A. Major depression, chronic minor depression, and the five-factor model of personality. European Journal of Personality. 2002; 16(4):271–281.

Harmon-Jones E, Abramson LY, Nusslock R, Sigelman JD, Urosevic S, Turonie LD, Fearn M. Effect of bipolar disorder on left frontal cortical responses to goals differing in valence and task difficulty. Biological Psychiatry. 2008; 63(7):693–698. [PubMed: 17919457]

Harmon-Jones E, Abramson LY, Sigelman J, Bohlig A, Hogan ME, Harmon-Jones C. Proneness to hypomania/mania symptoms or depression symptoms and asymmetrical frontal cortical responses to an anger-evoking event. Journal of Personality and Social Psychology. 2002; 82(4):610–618. [PubMed: 11999927]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Harmon-Jones E, Sigelman J. State anger and prefrontal brain activity: evidence that insult-related relative left-prefrontal activation is associated with experienced anger and aggression. Journal of Personality and Social Psychology. 2001; 80(5):797–803. [PubMed: 11374750]

Hayden EP, Bodkins M, Brenner C, Shekhar A, Nurnberger JI Jr, O'Donnell BF, Hetrick WP. A multimethod investigation of the behavioral activation system in bipolar disorder. Journal of Abnormal Psychology. 2008; 117(1):164–170. [PubMed: 18266494]

Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Wang P. Research domain criteria (RDoC): Toward a new classification framework for research on mental disorders. American Journal of Psychiatry. 2010; 167(7):748–751. [PubMed: 20595427]

Iosifescu DV, Greenwald S, Devlin P, Mischoulon D, Denninger JW, Alpert JE, Fava M. Frontal EEG predictors of treatment outcome in major depressive disorder. European Neuropsychopharmacology. 2009; 19(11):772–777. [PubMed: 19574030]

Johnson SL. Mania and dysregulation in goal pursuit: A review. Clinical Psychology Review. 2005; 25(2):241–262. [PubMed: 15642648]

Johnson SL, Carver CS. Extreme goal setting and vulnerability to mania among undiagnosed young adults. Cognitive Therapy and Research. 2006; 30(3):377–395. [PubMed: 20198117]

Johnson SL, Carver CS, Gotlib IH. Elevated ambitions for fame among persons diagnosed with bipolar I disorder. Journal of Abnormal Psychology. 2012; 121(3):602–609. [PubMed: 22103804]

Johnson SL, Cuellar AK, Ruggero C, Winett-Perlman C, Goodnick P, White R, Miller I. Life events as predictors of mania and depression in bipolar I disorder. Journal of Abnormal Psychology. 2008; 117(2):268–277. [PubMed: 18489203]

Johnson SL, Edge MD, Holmes MK, Carver CS. The behavioral activation system and mania. Annual Review of Clinical Psychology. 2012; 8:243–267.

Johnson SL, Eisner LR, Carver CS. Elevated expectancies among persons diagnosed with bipolar disorder. British Journal of Clinical Psychology. 2009; 48(Pt 2):217–222. [PubMed: 19254445]

Johnson SL, Ruggero CJ, Carver CS. Cognitive, behavioral, and affective responses to reward: Links with hypomanic symptoms. Journal of Social and Clinical Psychology. 2005; 24(6):894–906.

Johnson SL, Sandrow D, Meyer B, Winters R, Miller I, Solomon D, Keitner G. Increases in manic symptoms after life events involving goal attainment. Journal of Abnormal Psychology. 2000; 109(4):721–727. [PubMed: 11195996]

Jones SH, Tai S, Evershed K, Knowles R, Bentall R. Early detection of bipolar disorder: A pilot familial high-risk study of parents with bipolar disorder and their adolescent children. Bipolar Disorders. 2006; 8(4):362–372. [PubMed: 16879137]

Kano K, Nakamura M, Matsuoka T, Iida H, Nakajima T. The topographical features of EEGs in patients with affective disorders. Electroencephalography and Clinical Neurophysiology. 1992; 83(2):124–129. [PubMed: 1378377]

Kasch KL, Rottenberg J, Arnow BA, Gotlib IH. Behavioral activation and inhibition systems and the severity and course of depression. Journal of Abnormal Psychology. 2002; 111(4):589–597. [PubMed: 12428772]

Kazdin AE. Evaluation of the pleasure scale in the assessment of anhedonia in children. Journal of American Academy of Child & Adolescent Psychiatry. 1989; 28(3):364–372.

Keedwell PA, Andrew C, Williams SC, Brammer MJ, Phillips ML. The neural correlates of anhedonia in major depressive disorder. Biological Psychology. 2005; 58(11):843–853.

Kendler KS, Hettema JM, Butera F, Gardner CO, Prescott CA. Life event dimensions of loss, humiliation, entrapment, and danger in the prediction of onsets of major depression and generalized anxiety. Archives of General Psychiatry. 2003; 60(8):789–796. [PubMed: 12912762]

Knutson B, Adams CM, Fong GW, Hommer D. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. The Journal of Neuroscience. 2001; 21(16):RC159. [PubMed: 11459880]

Knutson B, Bhanji JP, Cooney RE, Atlas LY, Gotlib IH. Neural responses to monetary incentives in major depression. Biological Psychiatry. 2008; 63(7):686–692. [PubMed: 17916330]

Knutson B, Fong GW, Adams CM, Varner JL, Hommer D. Dissociation of reward anticipation and outcome with event-related fMRI. NeuroReport: For Rapid Communication of Neuroscience Research. 2001; 12(17):3683–3687.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Kotov R, Gamez W, Schmidt F, Watson D. Linking “big” personality traits to anxiety, depressive, and substance use disorders: A meta-analysis. Psychological Bulletin. 2010; 136(5):768–821. [PubMed: 20804236]

Kringelbach ML, Rolls ET. The functional neuroanatomy of the human orbitofrontal cortex: Evidence from neuroimaging and neuropsychology. Progress in Neurobiology. 2004; 72(5):341–372. [PubMed: 15157726]

Kujawa A, Proudfit GH, Klein DN. Neural reactivity to rewards and losses in offspring of mothers and fathers with histories of depressive and anxiety disorders. Journal of Abnormal Psychology. 2014; 123(2):287–297. [PubMed: 24886003]

Kwapil TR, Miller MB, Zinser MC, Chapman LJ, Chapman J, Eckblad M. A longitudinal study of high scorers on the hypomanic personality scale. Journal of Abnormal Psychology. 2000; 109(2): 222–226. [PubMed: 10895560]

Lam D, Wong G. Prodromes, coping strategies, insight and social functioning in bipolar affective disorders. Psychological Medicine. 1997; 27(5):1091–1100. [PubMed: 9300514]

Lam D, Wong G, Sham P. Prodromes, coping strategies and course of illness in bipolar affective disorder--A naturalistic study. Psychological Medicine. 2001; 31(8):1397–1402. [PubMed: 11722154]

Lewinsohn PM, Klein DN, Seeley JR. Bipolar disorders in a community sample of older adolescents: Prevalence, phenomenology, comorbidity, and course. Journal of the American Academy of Child & Adolescent Psychiatry. 1995; 34(4):454–463. [PubMed: 7751259]

Light SN, Heller AS, Johnstone T, Kolden GG, Peterson MJ, Kalin NH, Davidson RJ. Reduced right ventrolateral prefrontal cortex activity while inhibiting positive affect is associated with improvement in hedonic capacity after 8 weeks of antidepressant treatment in major depressive disorder. Biological Psychiatry. 2011; 70(10):962–968. [PubMed: 21867991]

Linke J, King AV, Rietschel M, Strohmaier J, Hennerici M, Gass A, Wessa M. Increased medial orbitofrontal and amygdala activation: evidence for a systems-level endophenotype of bipolar I disorder. American Journal of Psychiatry. 2012; 169(3):316–325. [PubMed: 22267184]

Liu WH, Wang LZ, Shang HR, Shen Y, Li Z, Cheung EF, Chan RC. The influence of anhedonia on feedback negativity in major depressive disorder. Neuropsychologia. 2014; 53:213–220. [PubMed: 24316199]

Lozano BE, Johnson SL. Can personality traits predict increases in manic and depressive symptoms? Journal of Affective Disorders. 2001; 63(1–3):103–111. [PubMed: 11246086]

Luby JL, Mrakotsky C, Heffelfinger A, Brown K, Spitznagel E. Characteristics of depressed preschoolers with and without anhedonia: evidence for a melancholic depressive subtype in young children. American Journal of Psychiatry. 2004; 161(11):1998–2004. [PubMed: 15514399]

Mannie Z, Williams C, Browning M, Cowen P. Decision making in young people at familial risk of depression. Psychological Medicine. 2015; 45(02):375–380. [PubMed: 25066689]

Mason L, O'Sullivan N, Bentall RP, El-Deredy W. Better than I thought: positive evaluation bias in hypomania. PLoS One. 2012; 7(10):e47754. [PubMed: 23082210]

Mason L, Trujillo-Barreto NJ, Bentall RP, El-Deredy W. Attentional bias predicts increased reward salience and risk taking in bipolar disorder. Biological Psychiatry. (in press).

McCabe C, Woffindale C, Harmer CJ, Cowen PJ. Neural processing of reward and punishment in young people at increased familial risk of depression. Biological Psychiatry. 2012; 72(7):588–594. [PubMed: 22704059]

McMakin DL, Olino TM, Porta G, Dietz LJ, Emslie G, Clarke G, Birmaher B. Anhedonia predicts poorer recovery among youth with selective serotonin reuptake inhibitor treatment–resistant depression. Journal of the American Academy of Child and Adolescent Psychiatry. 2012; 51(4): 404–411. [PubMed: 22449646]

Meyer B, Johnson SL, Carver CS. Exploring behavioral activation and inhibition sensitivities among college students at risk for bipolar spectrum symptomatology. Journal of Psychopathology and Behavioral Assessment. 1999; 21(4):275–292. [PubMed: 21765591]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Meyer B, Johnson SL, Winters R. Responsiveness to threat and incentive in bipolar disorder: Relations of the BIS/BAS scales with symptoms. Journal of Psychopathology and Behavioral Assessment. 2001; 23(3):133–143. [PubMed: 21765592]

Meyer TD, Krumm-Merabet C. Academic performance and expectations for the future in relation to a vulnerability marker for bipolar disorders: The hypomanic temperament. Personality and Individual Differences. 2003; 35(4):785–796.

Molnar G, Feeney MG, Fava GA. Duration and symptoms of bipolar prodromes. American Journal of Psychiatry. 1988; 145(12):1576–1578. [PubMed: 3195679]

Monk CS, Klein RG, Telzer EH, Schroth EA, Mannuzza S, Moulton Iii JL, Fromm S. Amygdala and nucleus accumbens activation to emotional facial expressions in children and adolescents at risk for major depression. American Journal of Psychiatry. 2008; 165(1):90. [PubMed: 17986682]

Monroe SM, Harkness KL. Life stress, the "kindling" hypothesis, and the recurrence of depression: considerations from a life stress perspective. Psychological Review. 2005; 112(2):417–445. [PubMed: 15783292]

Monroe SM, Rohde P, Seeley JR, Lewinsohn PM. Life events and depression in adolescence: Relationship loss as a prospective risk factor for first onset of major depressive disorder. Journal of Abnormal Psychology. 1999; 108(4):606–614. [PubMed: 10609425]

Morgan JK, Olino TM, McMakin DL, Ryan ND, Forbes EE. Neural response to reward as a predictor of rise in depressive symptoms in adolescence. Neurobiology of Disease. 2013; 52:66–74. [PubMed: 22521464]

Morris BH, Bylsma LM, Rottenberg J. Does emotion predict the course of major depressive disorder? A review of prospective studies. British Journal of Clinical Psychology. 2009; 48(3):255–273. [PubMed: 19187578]

Morris BH, Bylsma LM, Yaroslavsky I, Kovacs M, Rottenberg J. Reward learning in pediatric depression and anxiety: Preliminary findings in a high-risk sample. Depression and Anxiety. 2015; 32:373–381. [PubMed: 25826304]

Nurnberger J Jr, Guroff JJ, Hamovit J, Berrettini W, Gershon E. A family study of rapid-cycling bipolar illness. Journal of Affective Disorders. 1988; 15(1):87–91. [PubMed: 2970497]

Nusslock R, Abramson LY, Harmon-Jones E, Alloy LB, Hogan ME. A goal-striving life event and the onset of hypomanic and depressive episodes and symptoms: Perspective from the behavioral approach system (BAS) dysregulation theory. Journal of Abnormal Psychology. 2007; 116(1): 105–115. [PubMed: 17324021]

Nusslock R, Almeida JR, Forbes EE, Versace A, Frank E, Labarbara EJ, Phillips ML. Waiting to win: Elevated striatal and orbitofrontal cortical activity during reward anticipation in euthymic bipolar disorder adults. Bipolar Disorders. 2012; 14(3):249–260. [PubMed: 22548898]

Nusslock R, Harmon-Jones E, Alloy LB, Urosevic S, Goldstein K, Abramson LY. Elevated left mid-frontal cortical activity prospectively predicts conversion to bipolar I disorder. Journal of Abnormal Psychology. 2012; 121(3):592–601. [PubMed: 22775582]

Nusslock R, Shackman AJ, Harmon-Jones E, Alloy LB, Coan JA, Abramson LY. Cognitive vulnerability and frontal brain asymmetry: Common predictors of first prospective depressive episode. Journal of Abnormal Psychology. 2011; 120(2):497–503. [PubMed: 21381804]

Nusslock R, Young CB, Damme KS. Elevated reward-related neural activation as a unique biological marker of bipolar disorder: Assessment and treatment implications. Behaviour Research and Therapy. 2014; 62:74–87. [PubMed: 25241675]

Olino TM. Future research directions in the Positive Valence Systems: Measurement, development, and implications for youth unipolar depression. Journal of Clinical Child and Adolescent Psychology. (in press).

Olino TM, Klein DN, Dyson MW, Rose SA, Durbin CE. Temperamental emotionality in preschool-aged children and depressive disorders in parents: Associations in a large community sample. Journal of Abnormal Psychology. 2010; 119(3):468–478. [PubMed: 20677836]

Olino TM, Lopez-Duran NL, Kovacs M, George CJ, Gentzler A, Shaw DS. Individual differences in positive and negative affect over time: Associations with maternal history of psychopathology. Journal of Child Psychology and Psychiatry. 2011; 52:792–799. [PubMed: 21039488]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Olino TM, McMakin DL, Morgan JK, Silk JS, Birmaher B, Axelson DA, Forbes EE. Reduced reward anticipation in youth at high-risk for unipolar depression: A preliminary study. Developmental Cognitive Neuroscience. 2014; 8:55–64. [PubMed: 24369885]

Olino TM, Silk JS, Osterritter C, Forbes EE. Social Reward in Youth at Risk for Depression: A Preliminary Investigation of Subjective and Neural Differences. Journal of Child and Adolescent Psychopharmacology. 2015; 25(9):711–721. [PubMed: 26469133]

Pagliaccio D, Luking KR, Anokhin AP, Gotlib IH, Hayden EP, Olino TM, Barch DM. Revising the BIS/BAS to study development: Metric Invariance and normative effects of age and sex from childhood through adulthood. Psychological Assessment. (in press).

Phillips ML, Swartz HA. A critical appraisal of neuroimaging studies of bipolar disorder: Toward a new conceptualization of underlying neural circuitry and a road map for future research. American Journal of Psychiatry. 2014; 171(8):829–843. [PubMed: 24626773]

Pinto-Meza A, Caseras X, Soler J, Puigdemont D, Perez V, Torrubia R. Behavioural Inhibition and Behavioural Activation Systems in current and recovered major depression participants. Personality and Individual Differences. 2006; 40(2):215–226.

Pizzagalli DA. Depression, stress, and anhedonia: toward a synthesis and integrated model. Annual Review Clinical Psychology. 2014; 10:393–423.

Pizzagalli DA, Holmes AJ, Dillon DG, Goetz EL, Birk JL, Bogdan R, Fava M. Reduced caudate and nucleus accumbens response to rewards in unmedicated individuals with major depressive disorder. American Journal of Psychiatry. 2009; 166(6):702–710. [PubMed: 19411368]

Pizzagalli DA, Iosifescu D, Hallett LA, Ratner KG, Fava M. Reduced hedonic capacity in major depressive disorder: Evidence from a probabilistic reward task. Journal of Psychiatric Research. 2008; 43(1):76–87. [PubMed: 18433774]

Pizzagalli DA, Iosifescu DV, Hallett LA, Ratner KG, Fava M. Reduced hedonic capacity in major depressive disorder: Evidence from a probabilistic reward task. Journal of Psychiatric Research. 2008; 43(1):76–87. [PubMed: 18433774]

Pizzagalli DA, Jahn AL, O'Shea JP. Toward an objective characterization of an anhedonic phenotype: A signal-detection approach. Biological Psychiatry. 2005; 57(4):319–327. [PubMed: 15705346]

Pizzagalli DA, Pascual-Marqui RD, Nitschke JB, Oakes TR, Larson CL, Abercrombie HC, Davidson RJ. Anterior cingulate activity as a predictor of degree of treatment response in major depression: Evidence from brain electrical tomography analysis. American Journal of Psychiatry. 2001; 158(3):405–415. [PubMed: 11229981]

Proudfit GH. The reward positivity: From basic research on reward to a biomarker for depression. Psychophysiology. 2014; 52(4):449–459. [PubMed: 25327938]

Quilty LC, Mackew L, Bagby RM. Distinct profiles of behavioral inhibition and activation system sensitivity in unipolar vs. bipolar mood disorders. Psychiatry Research. 2014; 219(1):228–231. [PubMed: 24857564]

Rawal A, Collishaw S, Thapar A, Rice F. 'The risks of playing it safe': a prospective longitudinal study of response to reward in the adolescent offspring of depressed parents. Psychological Medicine. 2013; 43(01):27–38. [PubMed: 22617461]

Remijnse PL, Nielen MMA, van Balkom A, Hendriks GJ, Hoogendijk WJ, Uylings HBM, Veltman DJ. Differential frontal-striatal and paralimbic activity during reversal learning in major depressive disorder and obsessive-compulsive disorder. Psychological Medicine. 2009; 39(9): 1503–1518. [PubMed: 19171077]

Richards JM, Plate RC, Ernst M. A systematic review of fMRI reward paradigms used in studies of adolescents vs. adults: The impact of task design and implications for understanding neurodevelopment. Neuroscience & Biobehavioral Reviews. 2013; 37(5):976–991. [PubMed: 23518270]

Roberts BW, DelVecchio WF. The rank-order consistency of personality traits from childhood to old age: a quantitative review of longitudinal studies. Psychological Bulletin. 2000; 126(1):3–25. [PubMed: 10668348]

Salavert J, Caseras X, Torrubia R, Furest S, Arranz B, Duenas R, San L. The functioning of the Behavioral Activation and Inhibition Systems in bipolar I euthymic patients and its influence in

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subsequent episodes over an eighteen-month period. Personality and Individual Differences. 2007; 42(7):1323–1331.

Satterthwaite TD, Kable JW, Vandekar L, Katchmar N, Bassett DS, Baldassano CF, Wolf DH. Common and dissociable dysfunction of the reward system in bipolar and unipolar depression. Neuropsychopharmacology. 2015; 40(9):2258–2568. [PubMed: 25767910]

Schiller CE, Minkel J, Smoski MJ, Dichter GS. Remitted major depression is characterized by reduced prefrontal cortex reactivity to reward loss. Journal of Affective Disorders. 2013; 151(2):756–762. [PubMed: 23835103]

Schultz W. Getting formal with dopamine and reward. Neuron. 2002; 36(2):241–263. [PubMed: 12383780]

Shankman SA, Klein DN, Tenke CE, Bruder GE. Reward sensitivity in depression: A biobehavioral study. Journal of Abnormal Psychology. 2007; 116(1):95–104. [PubMed: 17324020]

Shankman SA, Nelson BD, Harrow M, Faull R. Does physical anhedonia play a role in depression? A 20-year longitudinal study. Journal of Affective Disorders. 2010; 120:170–176. [PubMed: 19467713]

Sharp CR, Kim S, Herman L, Pane H, Reuter T, Strathearn L. Major depression in mothers predicts reduced ventral striatum activation in adolescent female offspring with and without depression. Journal of Abnormal Psychology. 2014; 123(2):298–309. [PubMed: 24886004]

Singh MK, Kelley RG, Howe ME, Reiss AL, Gotlib IH, Chang KD. Reward processing in healthy offspring of parents with bipolar disorder. JAMA Psychiatry. 2014; 71(10):1148–1156. [PubMed: 25142103]

Smoski MJ, Felder J, Bizzell J, Green SR, Ernst M, Lynch TR, Dichter GS. fMRI of alterations in reward selection, anticipation, and feedback in major depressive disorder. Journal of Affective Disorders. 2009; 118(1–3):69–78. [PubMed: 19261334]

Smoski MJ, Rittenberg A, Dichter GS. Major depressive disorder is characterized by greater reward network activation to monetary than pleasant image rewards. Psychiatry Research-Neuroimaging. 2011; 194(3):263–270.

Stange JP, Molz AR, Black CL, Shapero BG, Bacelli JM, Abramson LY, Alloy LB. Positive overgeneralization and Behavioral Approach System (BAS) sensitivity interact to predict prospective increases in hypomanic symptoms: A behavioral high-risk design. Behaviour Research and Therapy. 2012; 50(4):231–239. [PubMed: 22342167]

Stange JP, Shapero BG, Jager-Hyman S, Grant DA, Abramson LY, Alloy LB. Behavioral Approach System (BAS)-relevant cognitive styles in individuals with high vs. moderate BAS sensitivity: A behavioral high-risk design. Cognitive Therapy and Research. 2013; 37(1):139–149. [PubMed: 23459574]

Steinberg L, Graham S, O'Brien L, Woolard J, Cauffman E, Banich M. Age differences in future orientation and delay discounting. Child Development. 2009; 80(1):28–44. [PubMed: 19236391]

Swann AC, Lijffijt M, Lane SD, Steinberg JL, Moeller FG. Severity of bipolar disorder is associated with impairment of response inhibition. Journal of Affective Disorders. 2009; 116(1–2):30–36. [PubMed: 19038460]

Takahashi T, Yucel M, Lorenzetti V, Nakamura K, Whittle S, Walterfang M, Allen NB. Midline brain structures in patients with current and remitted major depression. Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2009; 33(6):1058–1063. [PubMed: 19505522]

Tellegen, A.; Waller, NG. Exploring personality through test construction: Development of the Multidimensional Personality Questionnaire. In: Boyle, GJ.; Matthews, G.; Saklofske, DH., editors. The SAGE handbook of personality theory and assessment, Vol 2: Personality measurement and testing). Thousand Oaks, CA: Sage Publications, Inc; US; 2008. p. 261-292.

Tharp J, Johnson S, Sinclair S, Kumar S. Goals in bipolar I disorder: Big dreams predict more mania. Motivation and Emotion. (in press).

Thibodeau R, Jorgensen RS, Kim S. Depression, anxiety, and resting frontal EEG asymmetry: A meta-analytic review. Journal of Abnormal Psychology. 2006; 115(4):715–729. [PubMed: 17100529]

Treadway MT, Bossaller NA, Shelton RC, Zald DH. Effort-based decision-making in major depressive disorder: A translational model of motivational anhedonia. Journal of Abnormal Psychology. 2012; 121(3):553–558. [PubMed: 22775583]

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Treadway MT, Buckholtz JW, Schwartzman AN, Lambert WE, Zald DH. Worth the 'EEfRT'? The effort expenditure for rewards task as an objective measure of motivation and anhedonia. PLoS One. 2009; 4(8):e6598. [PubMed: 19672310]

Treadway MT, Zald DH. Reconsidering anhedonia in depression: lessons from translational neuroscience. Neuroscience & Biobehavioral Reviews. 2011; 35(3):537–555. [PubMed: 20603146]

Treadway MT, Zald DH. Parsing anhedonia: Translational models of reward-processing deficits in psychopathology. Current Directions in Psychological Science. 2013; 22(3):244–249. [PubMed: 24748727]

Trost S, Diekhof EK, Zvonik K, Lewandowski M, Usher J, Keil M, Gruber O. Disturbed anterior prefrontal control of the mesolimbic reward system and increased impulsivity in bipolar disorder. Neuropsychopharmacology. 2014; 39(8):1914–1923. [PubMed: 24535101]

Uher R, Perlis R, Henigsberg N, Zobel A, Rietschel M, Mors O, Bajs M. Depression symptom dimensions as predictors of antidepressant treatment outcome: replicable evidence for interest-activity symptoms. Psychological Medicine. 2012; 42(5):967–980. [PubMed: 21929846]

Urošević S, Abramson LY, Harmon-Jones E, Alloy LB. Dysregulation of the behavioral approach system (BAS) in bipolar spectrum disorders: Review of theory and evidence. Clinical Psychology Review. 2008; 28(7):1188–1205. [PubMed: 18565633]

Vieta E, Ros S, Goikolea JM, Benabarre A, Popova E, Comes M, Sanchez-Moreno J. An open-label study of amisulpride in the treatment of mania. Journal of Clinical Psychiatry. 2005; 66(5):575–578. [PubMed: 15889942]

Vrieze E, Claes SJ. Anhedonia and increased stress sensitivity: Two promising endophenotypes for major depression. Current Psychiatry Reviews. 2009; 5(3):143–152.

Wacker J, Dillon DG, Pizzagalli DA. The role of the nucleus accumbens and rostral anterior cingulate cortex in anhedonia: integration of resting EEG, fMRI, and volumetric techniques. Neuroimage. 2009; 46(1):327–337. [PubMed: 19457367]

Watson, D.; Clark, LA. Extraversion and its positive emotional core Handbook of personality psychology. San Diego, CA: Academic Press; 1997. p. 767-793.

Westheide J, Wagner M, Quednow BB, Hoppe C, Cooper-Mahkorn D, Strater B, Kuhn KU. Neuropsychological performance in partly remitted unipolar depressive patients: focus on executive functioning. European Archives of Psychiatry and Clinical Neuroscience. 2007; 257(7): 389–395. [PubMed: 17629730]

Wetter EK, Hankin BL. Mediational pathways through which positive and negative emotionality contribute to anhedonic symptoms of depression: A prospective study of adolescents. Journal of Abnormal Child Psychology. 2009; 37(4):507–520. [PubMed: 19184402]

Yang X, Huang J, Zhu C, Wang Y, Cheung EFC, Chan RC, Xie G. Motivational deficits in effort-based decision making in individuals with subsyndromal depression, first-episode and remitted depression patients. Psychiatry Research. 2014; 220(3):874–882. [PubMed: 25262638]

Yip SW, Worhunsky PD, Rogers RD, Goodwin GM. Hypoactivation of the ventral and dorsal striatum during reward and loss anticipation in antipsychotic and mood stabilizer-naive bipolar disorder. Neuropsychopharmacology. 2015; 40(3):658–666. [PubMed: 25139065]

Zhang W, Chang SP, Guo L, Zhang K, Wang J. The neural correlates of reward-related processing in major depressive disorder: A meta-analysis of functional magnetic resonance imaging studies. Journal of Affective Disorders. 2013; 151(2):531–539. [PubMed: 23856280]

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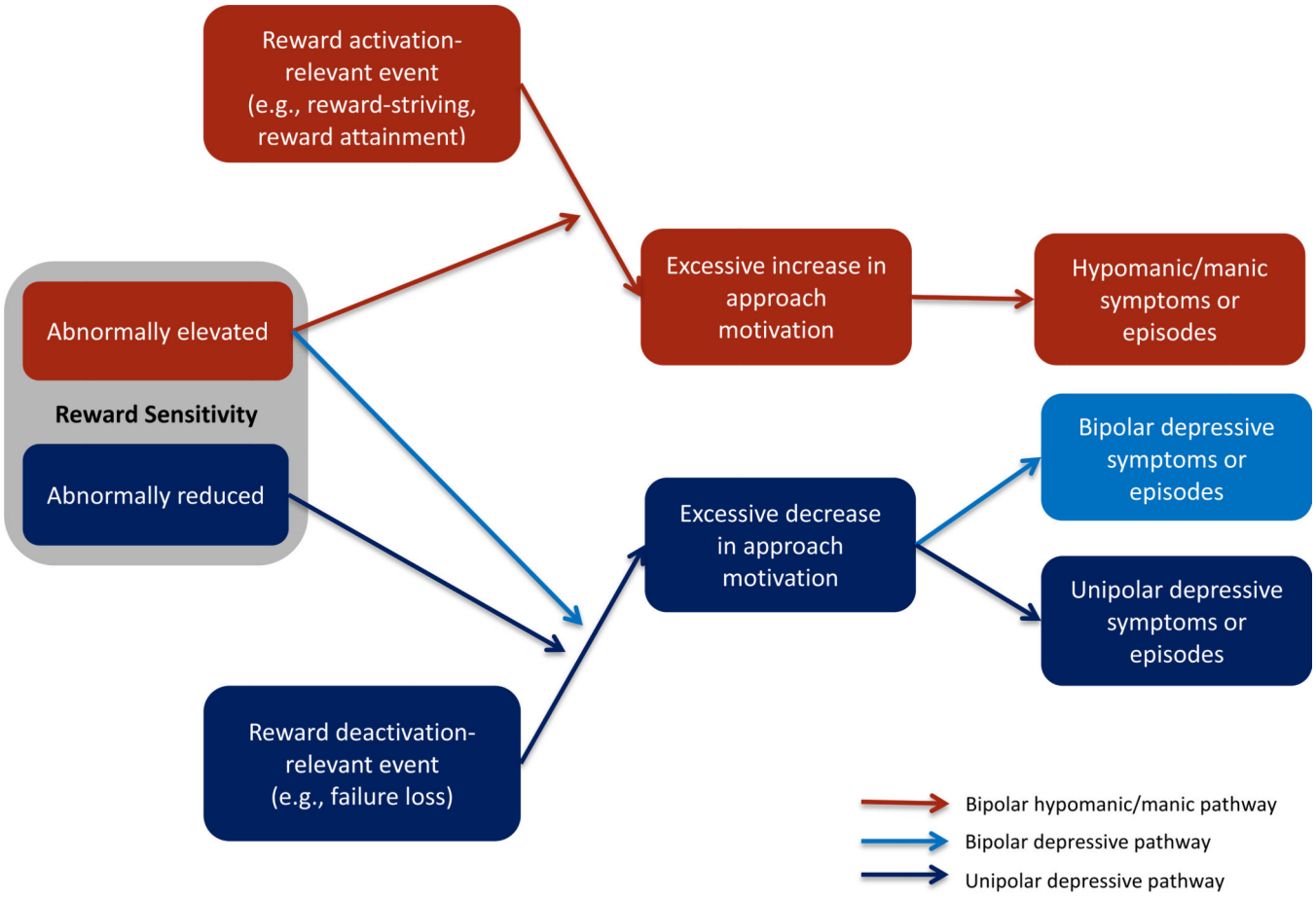

Figure 1.