Hypomania and Depression Associated with Distinct Neural Activity for Immediate and Future
Rewards

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Abstract

Bipolar spectrum and unipolar depressive disorders have been associated with distinct and opposite profiles of reward-related neural activity. These opposite profiles may reflect a differential preexisting vulnerability for both types of disorders. In support, recent event-related potential (ERP) studies find that following reward feedback a larger reward positivity (RewP) is associated with greater vulnerability for bipolar spectrum disorders whereas a smaller RewP is associated with greater vulnerability for depression. However, prior studies have only investigated immediate rewards and have not examined dimensions of both bipolar disorder and unipolar depression within the same sample. The present study is the first to investigate feedback-related ERP correlates of proneness to hypomania and unipolar depressive tendencies within the same sample and to expand our scope to include future rewards. Participants completed a modified time-estimation task where the same monetary reward was available immediately or at one of five different future dates. Results revealed proneness to hypomania and unipolar depressive tendencies were related to an elevated and blunted RewP, respectively, but only following immediate rewards (e.g. today). Following rewards in the distant future (e.g. eight-months), proneness to hypomania and depressive tendencies were associated with elevated and blunted amplitudes for the P3, respectively, a subsequent ERP component reflecting motivational salience during extended feedback processing. Furthermore, these opposing profiles were independent of, and significantly different from, one another. These results suggest that feedback-related ERPs following immediate and future rewards are candidate biomarkers that can physiologically separate vulnerability for bipolar spectrum from unipolar depressive disorders.
1. Introduction

Bipolar spectrum disorders are characterized by extreme emotional highs and lows while unipolar depressive disorders share only the lows. Although many studies have reported transdiagnostic deficits across both disorders in domains like threat-related processing, executive control, and working memory (see Nusslock & Alloy, 2017 for review), identifying markers of differential risk that can separate the two can improve early detection and facilitate early intervention. For example, bipolar patients typically present to clinicians when they are depressed (Hirschfeld et al., 2005), leading to a common misdiagnosis of major depressive disorder up to 66% of the time (Hirschfeld et al., 2003). A cardinal feature of bipolar spectrum disorders absent in unipolar depression are manic and hypomanic symptoms (see Urošević, et al., 2008 for review) that manifest as increased approach motivation, goal-pursuit, and elevated mood (American Psychiatric Association, 2013). These symptoms fall on a continuum of severity that extend to the general population (Angst et al., 2002) where individuals with sub-threshold symptoms may express increased vulnerability for developing bipolar or unipolar depressive disorders (Kwapil et al., 2000; Cuijpers & Smit, 2004).

1.1. Distinct Profiles of Reward Sensitivity

Prevailing theories suggest that distinct and opposite profiles of reward sensitivity constitute a preexisting risk factor for, rather than a consequence of, bipolar spectrum and unipolar depressive disorders (see Alloy et al., 2016 for review). Reward sensitivity relates to the value an individual places on rewards, the perceived expectation of reward receipt, and the mechanisms by which rewards are processed. Numerous neuroimaging studies have linked vulnerability for bipolar spectrum and unipolar depressive disorders to respective elevated and blunted profiles of reward-related neural activity (see Nusslock & Alloy, 2017). These differential profiles are driven in part by abnormal phasic dopamine signaling (see Whitton et al., 2015 for review) among frontostriatal neural pathways implicated in reward processing (Berridge et al., 2009; Haber & Knutson, 2010). Electroencephalogram (EEG) studies utilizing event-related potentials (ERPs) have linked individual differences in reward sensitivity to modulation in an ERP known as the Reward-Positivity (RewP: Holroyd et al., 2008; Lange et al., 2012; Bress & Hajcak,
The RewP is a positive ERP deflection elicited approximately 300 ms following positive (vs. negative) reward feedback and has been linked to covariation within the frontostriatal circuit, including the ventral striatum (Foti et al., 2011; Carlson et al., 2011; Becker et al., 2014). Reinforcement learning theories argue that the RewP may be associated with a phasic increase in mesencephalic dopamine signaling within the frontostriatal pathway, called a reward prediction error, that tracks violations in reward expectation between actual and predicted outcomes (Montague et al., 2004; Schultz, 2002; Holroyd & Coles 2002).

Previous research has found a blunted RewP amplitude in individuals with a family history of unipolar depression (Kujawa et al., 2014) which may prospectively predict risk for depressive disorders (Bress et al., 2013b; Bress et al., 2015). Although less research has investigated the relationship between the RewP and bipolar spectrum symptoms, two recent studies suggest proneness to hypomania may be related to an increased RewP positivity (Mason et al., 2012a; Mason et al., 2012b). However, no prior study has investigated ERP correlates of hypomanic and depressive tendencies within the same sample. While each disorder displays opposite profiles of reward-related neural activity, hypomanic and unipolar depressive symptom profiles likely represent separable, rather than opposite, psychometric dimensions (Youngstrom et al., 2013; Solomon et al., 2003; Johnson et al., 2011). In this way, the same individual can score high or low on one or both dimensions. One of the primary goals of the present study was to, within the same sample, test the hypothesis that tendencies toward unipolar depression versus hypomania are characterized by a distinct and opposite RewP amplitude.

1.2. Future Rewards

However, most prior neuroscientific research investigating reward processing has focused on immediate rewards. Real-world rewards are often delayed over long periods of time and it remains unknown whether neural activity elicited by future rewards may be related to hypomanic or depressive symptoms. Affective forecasting research has shown that as rewards approach the future, emotional reactions become less tangible and more difficult to predict (Rick & Loewenstein, 2008; Van Boven et al., 2009). As a result, experiences following rewards in the present are used as an affective reference.
point to signal the value of future rewards (Rick & Loewenstein, 2008; Gilbert & Wilson, 2007). This line of research suggests that opposite profiles of reward sensitivity in the present among individuals prone to either hypomania versus unipolar depression may facilitate opposite profiles of neural activation for future rewards as well.

Prior studies have found that future rewards recruit distinct neural regions relative to their immediate counterparts (McClure et al., 2004; Ballard & Knutson, 2009). For example, immediate rewards have been associated with the midbrain dopamine system whereas future rewards have been associated with fronto-parietal regions relevant for abstract mental representations and extended cognitive processing in (McClure et al., 2004). Therefore, for more distant future rewards, we predicted hypomanic and depressive symptoms would be associated with respective increases and decreases in two later ERP components linked to extended feedback-related processing: the P3 and late-positive potential (LPP).

First, the P3 is a positive ERP component reflecting enhanced incentive salience of the feedback stimulus (Yeung & Sanfey, 2004). Prior work has linked the P3 to motivational salience and individual differences in reward sensitivity (Van den Berg et al., 2011). Second, directly following the P3, the LPP reflects extended cognitive and attentional processing (Pornpattananangkul and Nusslock, 2015; Althaus et al., 2010; Van Meel et al., 2011; Groen et al., 2013) and has been referred to as the “emotional counterpart” of the P3 (Groen et al., 2008).

The present study is the first to investigate feedback-related ERP correlates of proneness to hypomania and unipolar depressive tendencies within the same sample and to expand our scope to include future rewards. We recruited participants from the undergraduate Northwestern community whom completed a time-estimation task where the same reward (e.g. $10) was available today or at one of five future delays (see figure 1). First, following immediate outcomes, we predicted that proneness to hypomania and depressive tendencies would be related to an elevated and blunted RewP, respectively, consistent with prior studies (Mason et al. 2012b; Proudfit, 2015). Second, a recent study reported no relationship between the P3 and vulnerability for hypomania for future rewards up to one-month in the future (Mason et al., 2012a). Prior research indicates that rewards in the near-future may not be distant
enough to require extended feedback processing (Freitas et al., 2001; Trope & Liberman, 2003; McClure et al., 2004; Rick & Loewenstein, 2008; Gilbert & Wilson, 2007). Therefore, only following feedback in the eight-month condition, we predicted proneness to hypomania would be associated with increases in the P3 and LPP while depressive tendencies would be related to reductions in both components. Finally, we did not predict that either symptom dimension would be related to ERPs in any of the intermediate delay conditions.

2. Methods

2.1. Participants

Fifty-eight right-handed, medication free, native English speakers (28 female) reported individually to a study described as an investigation of how people process words, sentences, and pictures. All participants received credit toward a course requirement for their participation but were also told they could win money based on their performance. Participants ages ranged from 18 to 22 ($M = 18.68$, $SD = .91$). Participants were excluded for excessively noisy EEG data (quantified using visual inspection, $N = 5$), excessive EEG artifact rejection (greater than 50% for any feedback condition, $N = 3$), and not looking at the screen during the time-estimation task ($N = 2$). One additional participant was excluded because they did not believe the experiment would result in real money. After these exclusions 47 participants (25 female) remained for analysis. This study was approved by the Northwestern University Internal Review Board.

2.2. Procedure

Following informed consent, participants completed self-report questionnaires assessing proneness to hypomania and unipolar depression. Next, participants completed a short behavioral task as part of a larger study whose results were not investigated in the current study. After questionnaires, participants were set-up with EEG and completed a modified time-estimation task where, on each trial, they could win the same amount of money (e.g. $10) either today or at one of five future delays (Miltner, 1997). Following this task, participants were unhooked from EEG, compensated, and debriefed.
2.3. Self-Report Measures

Individual differences in proneness to hypomania were measured using the Hypomanic Personality Scale (HPS: Eckblad & Chapman, 1986). The HPS was developed to identify individuals at risk for bipolar disorder and increased scores indicate a greater presence of hypomanic personality traits, such as elevated mood and racing thoughts. Increased hypomanic personality scores have been shown to prospectively predict bipolar disorder onset over a 10-year follow-up period (Kwapil et al., 2000) and has been linked to elevated reward-related activation in electrophysiological and neuroimaging studies (Damme et al., 2017; Peterson et al., 2008; Pornpattananangkul et al., 2015). This questionnaire includes 48 true or false questions that measure hypomanic personality traits (e.g. “I often feel excited and happy for no apparent reason” and “I frequently find that my thoughts are racing”) and is scored by adding up the number of true statements. To assess proneness to unipolar depressive symptoms, we utilized the 7-Down questionnaire from the Seven-Up Seven-Down Inventory (Youngstrom et al., 2013), a subscale used to measure trait-like depressive tendencies. Higher scores on the 7-Down indicate a greater presence of depressive symptoms, such as worthlessness and hopelessness. This 7-item questionnaire was developed from the Generalized Behavioral Inventory to psychometrically separate unipolar depressive from hypomanic symptoms (Youngstrom et al., 2013; Depue et al., 1981). Participants are instructed to answer how often they experience a list of depression symptoms on a scale from 0 (“never, or hardly ever”) to 3 (very often or almost constantly) (e.g. “Have you had periods when it seemed that the future was hopeless and things could not improve?”). Importantly, both HPS and 7-Down are trait measures of propensity to hypomanic symptoms and depressive tendencies, respectively, and represent separable psychometric dimensions (Youngstrom et al., 2013; Solomon et al., 2003; Johnson et al., 2011). Mean scores were used to quantify the totals for both questionnaires. Specifically, HPS was scored as a value from 0 to 1 where larger values indicate higher proneness to hypomania ($M = .47, SE = .14, \alpha = .76$) and 7-Down was scored as a value from 0 to 3 where larger values indicates higher presence of depressive tendencies ($M = .52, SE = .08, \alpha = .84$).

2.4. Time Estimation Task
To assess individual differences in reward-related EEG activity, participants completed a modified time-estimation task (Miltner, 1997, Damen & Brunia 1987, Kotani et al 2003; see figure 1) programmed using E-Prime while EEG was recorded. Specifically, participants were instructed to press a button exactly three-seconds following the presentation of a cue and received feedback after every trial. Each trial began with a fixation-cross presented for a jittered length of time randomly chosen between 750 ms and 1250 ms, followed by a text-cue indicating when participants could win money ("today", "two-days", "two-weeks", "one-month", "three-months", and "eight-months"). Following cue presentation, participants estimated three-seconds as closely as possible. Once the participant estimated that three seconds had elapsed, they were instructed to press a button with their right index finger on a response box. The cue remained on the screen unchanged for the duration of the time-estimation window. Once the button was pressed, the cue-text turned bold-italicized and remained on the screen for 2000 ms to ensure participants remained aware of the condition of that particular trial prior to feedback presentation (e.g. the date at which they can potentially win money). Finally, positive ("win") and negative ("fast" or "slow") feedback was presented for a total of 1000 ms.

Following prior studies (Kotani et al 2003; Ohgami et al 2006), an adaptive algorithm was used to keep gains and no-gains constant at approximately 50%. This method was chosen to limit variation in feedback probability between gains and no-gains that has been found to modulate feedback-related ERPs (Holroyd & Coles, 2002). Specifically, accurate responses were defined as button presses within a sliding time-window that adaptively shortened or lengthened by 10 ms following correct or incorrect responses, respectively. The time-window began at +/- 200 ms centered around three-seconds (e.g. 2800 ms to 3200 ms). Participants first completed a practice set of thirty trials to familiarize themselves with the task. The practice block contained five trials of each cue presented in a random order. In addition, response times from the practice block were used to tailor the appropriate time-window for accurate responses to be used at the start of the first block. Before and after practicing, participants were permitted to press a button and hear a beep sound exactly three-seconds later as many times as they desired to familiarize themselves with the duration of three-seconds. The study itself consisted of ten blocks of thirty trials each containing
five trials of each cue (e.g. 300 trials total with equal distribution of 50 trials per cue). The presentation of 
cues within each block was randomized.

Instructions indicated that gains resulted in $10 while fast or slow feedback carried no monetary 
gain or loss. A constant magnitude of $10 per trial was chosen to keep participants motivated on every 
trial. Participants were told that, following the experiment, four trials would be randomly chosen to 
determine their total earnings. If a gain trial was chosen, the participant was instructed they would receive 
$10 for that trial at the delay given on that trial, while if a no-gain trial was chosen the participant would 
not gain or lose any money. However, in the interest of fairness, all participants received exactly $20 in 
cash following the experiment and were thoroughly debriefed.

[Insert Figure 1]

2.5. Electrophysiological Recording

Continuous EEG data were recorded during the time-estimation task using Neuroscan amplifiers 
(DC to 100Hz on-line, Neuroscan Inc.) within an electro-magnetic shielded booth. Fifty-eight passive 
Ag/AgCl scalp electrodes were used (following the international 10-20 standard, Jasper 1958) with four 
additional placed above and below the left eye, and beside both eyes. A nylon cap with conductive gel 
was used. EEG data were digitized at a 500 Hz sampling rate, online referenced to the left mastoid, and 
re-referenced offline to average of both mastoids. Impedance was kept below 5 kOHM and 10 kOHM for 
the scalp and eye electrodes, respectively. Offline, all EEG processing was done using EEGLAB 
(Delorme & Makeig, 2004) and ERPLAB (Lopez-Calderon & Luck, 2014) in MatLab (Mathworks, 
2017b). Data were re-sampled at 250 Hz and high-pass filtered at .01 Hz. Large scalp artifacts were 
rejected using continuous automated artifact detection and noisy channels were identified by excessive 
kurtosis and interpolated. Next, independent components analysis was carried out to correct for 
ocular/muscular artifactual components. Once artifactual independent components were removed, data 
were low-pass filtered at 30 Hz, and 1100 ms epochs were extracted for feedback-locked activity. These 
epochs were then detrended, baseline corrected at 100 ms prior to feedback, and rejected if containing
artifacts exceeding +/- 75 uV. In addition, epochs associated with response times greater than 5000 ms or less than 1000 ms were removed to control for large outlier responses with approximately 1% (~2.5 trials) of the epochs removed per participant. After artifact rejection, the average number of trials for gains and no-gains in each delay condition were approximately equal (gains: $M = 24.8$, $SE = .21$; no-gains: $M = 24.27$, $SE = .18$).

Finally, single-trial EEG epochs were averaged separately for all twelve feedback conditions to extract time-locked ERPs. To isolate reward-related neural activity specific to gaining rewards (vs. no-gain outcomes), we utilized a difference wave approach by subtracting gains from no-gains. Difference waves are useful because they avoid ongoing neural activity that does not differentiate between gains and no-gains and may not be specific to reward-related modulation (Luck, 2014). Following prior studies, the RewP was measured as the mean activity from 250-350 ms following feedback onset at electrode site Cz, consistent with visual inspection of the grand average difference waveform (Foti et al., 2011; Threadgill & Gable, 2016). The P3 was measured as the mean activity between 400-600 ms after feedback onset at site Pz where positivity was maximal. Finally, from visual inspection, the LPP was quantified at electrode site Pz as the mean activity from 600-800 ms time-locked to feedback onset. This time window was chosen for the LPP as the end of the P3 component (i.e. 600 ms post-feedback) to the point where the difference between gains and no-gains approached baseline (i.e. 800 ms post-feedback), consistent with prior studies (Groen et al., 2013; Althaus et al., 2010). RewP difference waves were calculated by subtracting no-gains from gains while P3 and LPP difference waves were calculated by subtracting gains from no-gains.

3. Results

3.1. Behavioral Variables

Accuracy was quantified as the total number of gains divided by the total number of trials and confirmed that our adaptive algorithm kept gains and no-gains at approximately 50% ($M = 50.1\%$, $SE = .002$). Response times were calculated separately for each delay condition. First, trials with response times greater than 5000 ms or less than 1000 ms were removed to control for large outlier responses, with
an average of less than 1% of all trials (~ 2.5 trials) removed per participant. Second, all response times were calculated as the absolute value of the difference between the total response time and 3000 ms to capture how close each response was to the 3000 ms target response time. Response times for gains ($M = 99.33, SE = 4.49$) and no-gains ($M = 383.19, SE = 17.62$) were entered into a 2 (outcome) × 6 (delay) repeated measures ANOVA. Results revealed a significant main effect of outcome ($F (1, 46) = 456.78, p < .001, \eta^2 = .91$) and an outcome x delay interaction ($F (5, 230) = 2.86, p = .02, \eta^2 = .06$), but no main effect of delay ($p > .2$). Follow-up t-tests revealed that response times for gains were significantly closer to the target of 3000 ms than response times for no-gains ($ts (46) > 18.03, ps < .001$). To unpack the interaction, response times for gains were subtracted from no-gains at each delay to attain a difference score reflecting the relative improvement in response time (that is, response times closer to 3000 ms) on gain trials over no-gain trials. Follow-up t-tests on response time difference scores revealed that response times for immediate gains (vs. no-gains) were significantly more accurate than every delayed reward ($ts (46) < -2.12, ps < .034$), except non-significantly different from two-days ($p > .43$)

3.2. ERPs

We conducted a series of 2 (outcome: gain vs. no-gain) x 6 (delay: today, two-days, two-weeks, one-month, three-months, eight-months) repeated measure ANOVAs on the RewP, P3, and LPP (see table S1 and figure S1). For the RewP, results revealed a significant effect of outcome ($F (1, 46) = 53.88, p < .001, \eta^2 = .54$) with t-tests indicating that gains were significantly more positive than no-gains for all delays ($ts (46) > 3.81, ps < .001$). A main effect of delay was also significant ($F (5, 230) = 19.41, p < .001, \eta^2 = .30$) with t-tests showing that the average RewP voltage on immediate outcomes were significantly more positive than all future outcomes ($ts (46) > 5.69, ps < .001$). In addition, paired t-tests between future outcomes revealed several significant effects: First, two-days was significantly more positive than two-weeks ($t (46) = 2.02, p = .049$), one-month ($t (46) = 2.31, p = .025$), and three-months ($t (46) = 4.11, p < .001$), second, two-weeks was significantly more positive than three-months ($t (46) = 2.10, p = .041$), and, third, one-month was significantly more positive than three-months ($t (46) = 2.09, p = .042$). No other significant effects emerged for the RewP ($p > .06$).
For the P3, a significant effect of outcome emerged \((F(1, 46) = 33.08, p < .001, \eta_p^2 = .42)\) with t-tests revealing that gains were significantly less positive than no-gains for all outcomes \((ts (46) < -2.14=9, ps < .034)\). A significant effect of delay also emerged \((F(5, 230) = 9.31, p < .001, \eta_p^2 = .17)\) with t-tests showing that immediate outcomes were significantly more positive than all future outcomes \((ts (46) > 3.71, ps < .001)\). Finally, the outcome x delay interaction was also significant \((F(5, 230) = 3.10, p = .013, \eta_p^2 = .06)\). Follow-up t-tests performed on difference waves at each paired delay revealed that immediate outcomes were significantly larger than all future outcomes \((ts (46) > 2.14, ps < .038)\), although this effect only approached significance at Two-Days \((p = .066)\). No other significant effects emerged for the P3 \((ps > .06)\).

For the LPP, a significant effect of outcome was found \((F(1, 46) = 34.42, p < .001, \eta_p^2 = .43)\) with t-tests showing that gains were significantly less positive than no-gains \((ts (46) < -2.12, ps < .04)\).

In addition, a main effect of reward delay was also significant \((F(5, 230) = 6.78, p < .001, \eta_p^2 = .13)\) with t-tests showing that immediate outcomes were significantly more positive than all future outcomes \((ts (46) > 3.22, ps < .010)\). No further significant associations emerged for the LPP \((ps > .10)\).

[Insert Figure 2]

### 3.3. Associations Between ERPs, Self-Report, and Behavior

First, and in line with expectation, we confirmed that self-report scores for HPS and 7-Down were not significantly related to one another \((r = .13, p = .37)\). Next, we examined the pearson correlations between self-report measures (i.e., HPS and 7-Down) and each ERP difference wave (i.e., the RewP, P3, and LPP) at each delay (see figure 4 and table S2). The RewP following immediate outcomes showed a significant correlation with HPS \((r = .30, p = .043)\) and a significant but opposite correlation with 7-Down \((r = -.313, p = .032)\). Furthermore, the difference between both these opposite correlations was significant \((z = 2.91, p < .010)\). The P3 also significantly correlated with HPS \((r = .31, p = .037)\) and, in the opposite direction, 7-Down \((r = -.32, p = .031)\), but only for the Eight-Month delay. Again, the difference in correlation at eight-months between HPS and 7-Down for the P3 difference wave were significant \((z = 3.01, p < .010)\). However, the LPP following Eight-Months was only significantly correlated with HPS \((r = .35, p = .017)\), but not with 7-Down \((r = -.24, p = .111)\), although the
correlational difference between HPS and 7-Down was again significant ($z = 2.82, p < .010$). There were no other significant correlations between ERPs and either HPS or 7-Down ($ps > .05$), although the association between 7-Down and the RewP at the Two-Week delay approached significance ($r = .28, p = .053$; see table S2).

Finally, we investigated the relationships between HPS and 7-Down with behavioral variables. Neither self-report scale was related to accuracy ($ps > .3$); however, 7-Down was significantly associated with worse response times for no-gains, relative to gains, following eight-month cues ($r = .35, p = .017$). No other significant associations emerged ($ps > .06$).

### 3.4. Regression Analyses

To test the independence of correlations between ERP difference waves and questionnaire measures, linear regressions were performed with the inclusion of both HPS and 7-Down within the same model. In each regression, mean-centered scores for HPS and 7-Down were entered as predictors of our specific hypotheses: 1) the RewP following immediate outcomes and 2) the P3 and LPP following Eight-Month outcomes. Results revealed significant independent effects for both HPS and 7-Down in predicting the RewP (HPS: $\beta = .35, p = .014$; 7-Down: $\beta = -.36, p = .011$), P3 (HPS: $\beta = .35, p = .012$; 7-Down: $\beta = -.36, p = .010$), and LPP (HPS: $\beta = .39, p < .010$; 7-Down: $\beta = -.29, p = .040$). These results indicate that, for each ERP component, the unique associations between proneness to hypomania and depressive tendencies were independent of one another. In addition, we performed identical regression analyses for each ERP difference wave separately at every other delay. Of interest, 7-Down significantly predicted the RewP following Two-Week outcomes ($\beta = .311, p = .034$), but HPS did not ($\beta = -.20, p = .17$). No other significant effects emerged ($ps > .1$, see table S2).

### 4. Discussion
The present study is the first to investigate multiple feedback-related ERP correlates of hypomanic and depressive symptoms within the same sample and to expand our scope to include future rewards. First, our results offer novel insights into the electrophysiological correlates of reward processing and how these are modulated by future rewards. The RewP, P3, and LPP were all modulated by reward delay and displayed increased positivity for immediate over future rewards. However, only the P3 showed a significant outcome by delay interaction such that immediate rewards generated larger P3 difference waves than future rewards. Second, we found that proneness to hypomania and depressive tendencies were associated with opposite profiles of feedback-related ERPs for immediate and distant future rewards. Proneness to hypomania and depressive tendencies were related to an increased and decreased RewP difference wave, respectively, but only following immediate rewards (delivered today). In contrast, proneness to hypomania and depressive tendencies were related to an elevated and reduced P3 difference wave, respectively, but only following distant future rewards (delivered in eight-months). Importantly, proneness to hypomania and depressive tendencies were unrelated to each other and their associations with ERP components remained significant while controlling for the opposing symptom dimension, suggesting these relationships are independent of one another.

4.1. ERP Correlates of Immediate and Future Rewards

Our results shed new light on the electrophysiological correlates of reward processing following feedback for immediate and future rewards. Consistent with prior studies, the RewP and P3 displayed greater average positivity for immediate over future outcomes (Blackburn et al., 2012; Cherniawsky & Holroyd, 2013; however, see Qu et al., 2013), a pattern that we show for the first time also extended to the LPP (see figure 2). These results suggest that immediate reward feedback was evaluated as “better than expected”, elicited enhanced motivational salience, and displayed extended attentional and affective processing than their future counterparts. Interestingly, the RewP tended to display greater positivity for sooner (vs. later) rewards, while the P3 and LPP did not show any significant differences between future outcomes, suggesting positivity in the RewP time window may in part track reward delay.
In addition, all three components were modulated by feedback valence following immediate and future rewards (see figure 2): whereas the RewP was greater for gains, the P3 and LPP were greater for no-gains. These results support prior studies suggesting the LPP following reward feedback may reflect a “negativity bias” where negative feedback elicits greater extended affective and attentional processing than positive feedback (Smith et al., 2003). We show for the first time that this negativity bias extended to future rewards. In addition, although many studies have not found the P3 is sensitive to valence (Yeung and Sanfey, 2004), and some found positive feedback was more positive than negative feedback (Hajcak et al., 2007; Bellebaum & Daum, 2008; Zhou et al., 2010), other studies reported that negative (vs. positive) feedback was more positive when tasks implement feedback that contains performance information (Chase et al., 2011; Frank et al., 2005; Cohen & Ranganath, 2007). In the present study, no-gains may have generated greater P3 amplitudes than gains to motivate more accurate responding on subsequent trials and maximize upcoming rewards.

For ERP difference waves, we report for the first time that the P3 difference wave was significantly modulated by reward delay, whereas the RewP and LPP difference waves were not (see figure 2). Specifically, the P3 difference wave following immediate rewards was significantly greater than delayed outcomes later than two-days in the future. An enhanced P3 for no-gains over gains likely reflects an increased motivational signal to facilitate subsequent behavioral adjustments following no-gains to maximize upcoming rewards (Chase et al., 2011; Frank et al., 2005; Cohen & Ranganath, 2007). This finding indicates that the P3 may track differences in reward delay such that the motivational salience of no-gains (vs. gains) is reduced for future rewards in comparison to their immediate counterparts. These results are consistent with a recent electrophysiological study that suggested it is the motivational salience of immediate rewards, rather than their hedonic impact, that biases the motivational value of future rewards during delay discounting (Blackburn et al., 2012).

4.2. Distinct Profiles of RewP Amplitude

Our results also support models of reward sensitivity that posit differential profiles of reward-related neural activity may predict clinical risk for bipolar spectrum versus unipolar depressive disorders.
(see Nusslock & Alloy, 2017 for review). Despite numerous studies that separately investigated relationships between neural activity and vulnerability for hypomania and depression (see Alloy et al., 2016 for review), the present results are the first to report that hypomaniac and depressive symptoms are associated with differential profiles of feedback-related ERPs within the same sample (see figures 3 and 4) and to show that these associations are independent of, and significantly different from, one another (see figure 5). Although these measures are associated with opposite profiles of reward-related neural activity, previous research indicates that hypomaniac and depressive symptoms are independent constructs and represent separable, rather than opposing, psychometric dimensions (Youngstrom et al., 2013; Solomon et al., 2003; Johnson et al., 2011). Our results suggest that feedback-related ERPs may independently identify risk for bipolar spectrum and unipolar depressive disorders within the same individuals. These findings not only have implications for understanding the differential pathophysiology underlying bipolar spectrum and unipolar depressive disorders, but also may help identify electrocortical biomarkers that could facilitate more accurate and timely diagnoses.

As expected, depressive tendencies were related to a blunted RewP difference wave following immediate outcomes (see figures 3 and 4). This finding supports emerging research suggesting reduced RewP amplitude may constitute a potential biomarker of risk for depressive disorders (Bress et al., 2013; Bress et al., 2015; see Proudfit, 2015 for review). Surprisingly, regression analyses showed that depressive tendencies were also significantly related to a blunted RewP difference wave following two-week outcomes (although correlational results only approached significance), suggesting rewards available in the near future may also elicit blunted neural responses to feedback. In contrast, proneness to hypomania was associated with an elevated RewP difference wave following immediate outcomes, converging with a prior study that found more positive RewP amplitudes following gains and losses in hypomania-prone individuals during a reinforcement learning task (Mason et al., 2012b). These results are consistent with recent neuroimaging evidence that vulnerability for hypomania and unipolar depressive disorder are related to opposite profiles of reward prediction error (Greenberg et al., 2015; O’Sullivan et al., 2011; Kumar et al., 2008). Consistently elevated or blunted reward prediction errors in
the present may convey a teaching signal that biases the predicted value of upcoming rewards and alters their motivational salience. For example, elevated reward prediction errors among those prone to hypomania have been linked to an expectancy bias toward positive outcomes that fails to update future expectations accordingly (Mason et al., 2012b; O’Sullivan et al., 2011; Eisner et al., 2008; Johnson et al., 2005) and has prospectively predicted increases in hypomanic symptoms (Stange et al., 2012). In contrast, blunted reward predictions errors among individuals with higher levels of unipolar depressive symptoms have been linked to an inability to effectively integrate reward feedback and alter behavior to maximize future rewards (Huys et al., 2009; Chase et al., 2010; Greenberg et al., 2015). Our results suggest this blunted reward prediction error may extend to rewards available in the near future as well. Together, these results suggest that abnormal reward prediction errors in the present may index a potential biomarker of differential risk for bipolar spectrum and depressive disorders.

4.3. Distinct Profiles of P3 and LPP Amplitude

Proneness to hypomania and depressive tendencies were also associated with an elevated and blunted P3 difference wave (see figure 3 and 4), respectively, but only following the most distant possible future reward (e.g. eight-months). Importantly, these associations were independent of each other and significantly different from one another (see figure 5). These results suggest opposite profiles of reward-related neural activity associated with proneness to hypomania and depressive tendencies emerge for future rewards, but disrupt extended feedback evaluation, indexed by the P3, rather than reward prediction error, indexed by RewP. Whereas proneness to hypomania was associated with increased motivational salience for no-gains (vs. gains) following eight-month outcomes, depressive tendencies were associated with the opposite pattern. Increased motivated salience following no-gains (vs. gains) among those with elevated hypomanic symptoms may facilitate enhanced goal-pursuit for especially distant future rewards. On the other hand, depressive symptoms were associated with reduced salience of rewards eight-months in the future and may decrease motivation to pursue especially distant future rewards. In support of this perspective, increased depressive tendencies were related to less accurate response times for no-gains (relative to gains) in the present study, but only following eight-month cues.
This result suggests that depressive tendencies are related to deficits in time-estimation performance when rewards are available in the distant future, which may result from a decreased motivation to pursue them. Finally, Pearson correlations revealed that only proneness to hypomania was associated with an elevated LPP following eight-month outcomes (see table S2), although regression analyses showed a significant but opposite correlation with depressive tendencies (see figure 5). This result indicates that proneness to hypomania was associated with elevated affective and attentional processing for distant-future rewards while depressive tendencies were only associated with a reduction in motivational salience.

While no prior studies have investigated depressive symptoms and feedback-related ERPs following rewards in the future, one study investigated vulnerability for hypomania and the P3 following future rewards, but found no such relationship (Mason et al., 2012a). However, the most distant future reward in that study was one-month in the future while we found effects only for eight-months. Prior studies have found that future rewards recruit discrete neural systems that involve abstract mental representations and extended feedback processing (McClure et al., 2004; Ballard & Knutson, 2009). Importantly, these distinct neural systems may only be recruited following especially distant future rewards that are sufficiently intangible and abstract, whereas near-future rewards may not rely on extended feedback processing to properly evaluate outcomes (Trope & Liberman, 2003; Rick & Loewenstein, 2008; Gilbert & Wilson, 2007; Freitas et al., 2001). When rewards become distant enough in the future, emotional reactions become increasingly difficult to predict and, as a result, the present is used as a reference point to evaluate their significance (Rick & Loewenstein, 2008; Gilbert & Wilson, 2007). Therefore, opposing profiles of P3 amplitude between hypomanic and depressive symptoms may only emerge following feedback for rewards in the distant future while rewards in the near-future remain unaffected.

4.4. Limitations and Future Directions

The present study has some important limitations. First, our results only revealed significant associations between ERPs and symptom dimensions among immediate and eight-month outcomes with no significant effects for the four future rewards in between. It is possible our sample size may be
underpowered to detect significant effects for near-future rewards for the RewP and distant rewards closer to eight-months for the P3. Future studies should continue to probe the relationships between symptom dimensions and neural responses to immediate and varying delayed reward (including larger delays that 8 months) in larger samples. Second, depressive tendencies predicted blunted RewPs following two week-outcomes, but not two-days. This may be due to our sample population which consisted of undergraduates who were not at the extremes for hypomanic personality traits or unipolar depressive tendencies. Future studies should investigate whether individuals with clinical levels of hypomania or depression may display more robust relationships with feedback-related ERPs following immediate and future rewards. Third, due to experiment-length considerations to prevent participant fatigue, we did not include a loss or neutral condition (e.g. feedback that is not linked to monetary gains or losses), so the present results are limited to gain-specific modulation of ERPs. Future studies should investigate how future rewards affect neutral- and loss-related ERPs during feedback processing and whether these may be related to dimensions of hypomanic and depressive symptoms.

4.5. Conclusion

Together, our results provide novel insights into the neural mechanisms underlying reward dysfunction across hypomanic and depressive symptom clusters for both immediate and future rewards. Proneness to hypomania and depressive tendencies were related to elevated and blunted RewP difference waves, but only following immediate rewards. This result suggests the RewP following immediate rewards may be a good candidate biomarker of differential risk that separates both disorders. In addition, both measures displayed similar relationships with the P3 difference wave, but only following distant rewards eight-months in the future, indicating disruptions of extended feedback processing following distant-future rewards. Together, our findings reveal new avenues to investigate differential electrophysiological correlates of risk that may help physiologically bifurcate the fine line between bipolar spectrum and depressive disorders.
Citations


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Acknowledgments.

This material is based upon work supported by the National Science Foundation Graduate Research Fellowship [DGE-2016231981 to J.E.G].

Disclosure statement.

Authors have nothing to disclose and have no conflict of interests to report.
Figure Captions.

**Figure 1:** Trial structure for the modified time-estimation task. Before each trial, a fixation cross was displayed during a jittered time window. On each trial, one of six cues were presented indicating the time of reward receipt (e.g. Today, Two-Days, Two-Weeks, One-Month, Three-Months, or Eight-Months). Cues were displayed until a response was received and then became bold and italicized. After 2000 ms, reward feedback indicated a gain (“Win”) or a no-gain (“Fast” or “Slow”).

**Figure 2:** ERPs displaying immediate vs. eight-month reward feedback ERPs and their difference wave (today – future) collapsed across gains and no-gains. Top: Feedback-locked ERPs displaying the RewP at electrode site Cz. Bottom: Feedback-locked ERPs displaying the P3 and LPP at electrode site Pz.

**Figure 3:** Median split ERP no-gain-gain difference waves for hypomanic personality scores and depressive tendencies. Top: Feedback-locked ERP for immediate outcomes at electrode site Cz displaying the RewP. Bottom: Feedback-locked ERP for eight-month outcomes at electrode site Pz displaying the P3 and LPP.

**Figure 4:** Bar graphs displaying average amplitude of the RewP difference wave (gain – no-gain) following immediate outcomes (left) and the average amplitude of the P3 and LPP difference waves (no-gain – gain) following eight-month outcomes (right). Graphs are median split by proneness to hypomania (red) and depressive tendencies (blue).

**Figure 5:** Partial regression plots for the RewP difference wave (gain – no-gain) following immediate outcomes (top) and the P3 and LPP (no-gain – gain) following eight-month outcomes (middle and bottom) plotted against hypomanic personality traits (left) and depressive tendencies (right). In each regression plot, analyses controlled for the opposing symptom dimension. Both the HPS and 7-Down self-report scales are mean-centered.
Figure 1.
Figure 3.
Figure 4.

[Bar chart showing voltage levels for RewP, P3, and LPP over time for different vulnerability and depressive tendency groups.]
Figure 5.

<table>
<thead>
<tr>
<th>Hypomanic Personality Traits</th>
<th>Depressive Tendencies</th>
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<tr>
<td><strong>REW Difference: Today (nY)</strong></td>
<td><strong>REW Difference: Eight Months (nY)</strong></td>
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<td>![Graph 4](β = -.36, p = .010)</td>
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