Depression and reduced sensitivity to non-rewards versus rewards: Evidence from event-related potentials

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ARTICLE INFO

Article history:
Received 4 March 2008
Accepted 22 December 2008
Available online 31 December 2008

Keywords:
Feedback negativity
Depression
Reward
Dopamine
Feedback-related negativity
ERN

ABSTRACT

Depression has been characterized in recent years in terms of deficits in positive affect and an underactive approach-related motivational system. Consistent with this view, behavioral and electrocortical studies suggest that reduced sensitivity to rewards may be a fundamental feature of depression. Within the event-related potential literature, the feedback negativity (FN) has been identified as a component that is sensitive to feedback indicating non-rewards versus rewards, and has been linked to phasic changes in midbrain dopamine levels that indicate whether events are better or worse than expected; thus, the FN may be a useful marker for abnormalities in reward sensitivity associated with depression. In the current study, a simple gambling task was used to elicit an FN in participants, and the magnitude of the FN was related to levels of depressive symptoms, as well as levels of anxiety and stress. The enhancement of the FN to non-rewards relative to rewards was found to be inversely related to depression and stress reactivity; only the relationship between the FN and stress remained significant after controlling for the other psychological variables. The P3 to feedback, meanwhile, was inversely related to depression and anxiety scores regardless of feedback type. These results are discussed within the context of current models of depression and reward sensitivity.

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Depression is one of the most common, devastating, and costly forms of mental illness (Berto et al., 2000; Luppa et al., 2007). Recent approaches to depression have focused on identifying neural and information-processing abnormalities related to core symptoms of depression. For instance, a number of studies have focused on biases toward (Gotlib, 1983; Gotlib et al., 2004) and the sustained processing of (Siegle et al., 2001, 2002), negative information in clinical samples—individual differences which might relate to the type of rumination characteristic in depression. Additionally, individuals with depression, particularly those with melancholic features, are typified by anhedonia and a loss of both interest and motivation, suggesting that a core deficit in depression has to do with abnormalities of positive affect and certain forms of motivation (Clark and Watson, 1991; Watson et al., 1995a,b).

In the domains of motivation and emotion, a broad distinction is made between appetitive and aversive motivational systems (Davidson, 1992, 1998; Lang et al., 1990). In particular, an approach-related motivational system is thought to sustain goal-directed behavior and certain forms of positive affect, whereas a withdrawal-related system supports responses to aversive stimuli and forms of negative affect; there is increasing evidence that approach- and withdrawal-related motivational states relate to increased activity of the left and right prefrontal cortex, respectively (Davidson, 1998; Depue and Collins, 1999; Fowles, 1994; Gray, 1994; Harmon-Jones and Allen, 1998; Harmon-Jones and Sigelman, 2001).

Within this context, depression has been characterized in terms of a specific deficit in positive affect and approach-related motivation (Davidson, 1992, 1998; Fowles, 1994; Krings and Bachorowski, 1999; Watson et al., 1995b). In fact, EEG studies have demonstrated that individuals with current and remitted depression (Debener et al., 2000; Gotlib et al., 1998; Henriques and Davidson, 1990, 1991), as well as children of depressed mothers (Dawson et al., 1999; Field et al., 1995; Tomarken et al., 2004), show reduced resting activation of the left prefrontal cortex. One combined EEG/behavioral study found that, when anticipating the possibility of a reward, individuals with early-onset depression failed to show a frontal asymmetry that would have been consistent with activation of the approach system (Shankman et al., 2007). Along similar lines, behavioral studies have found that depressive symptoms are associated with decreased responsiveness to reward in both non-clinical (Henriques et al., 1994) and clinical (Henriques and Davidson, 2000) samples. These findings suggest that a core deficit of depression may be an underactive approach system, manifested in behavioral and electrocortical insensitivity to rewards and other pleasant stimuli.
Recent studies that measure event-related brain potentials (ERPs) in response to environmental feedback have identified a negative deflection that appears larger for negative than positive outcomes. This feedback negativity (FN) peaks approximately 250 ms following the presentation of feedback, and is larger following negative outcomes, such as errors and monetary loss (Gehring and Willoughby, 2002; Hajcak et al., 2005a, 2006; Holroyd and Coles, 2002; Holroyd et al., 2006; Milton et al., 1997; Yeung et al., 2005; Yeung and Sanfey, 2004). The FN is maximal at frontocentral electrode sites, and is thought to originate in the anterior cingulate cortex (Gehring and Willoughby, 2002; Holroyd and Coles, 2002; Luu et al., 2003; Milton et al., 1997).

Non-human animal work indicates that events that are better or worse than expected induce phasic changes in midbrain dopamine activity (for review, see Barto, 1995; Houk et al., 1995; Schultz, 2002). Linking these data on dopamine activity to human ERP studies on reward and non-reward, Holroyd and Coles (2002) proposed that the FN reflects dopaminergic disinhibition of neurons in the anterior cingulate cortex (Holroyd and Coles, 2002). In particular, increases and decreases in the FN are thought to reflect variation in dopamine when outcomes are worse or better than expected, respectively. Consistent with these predictions, findings suggest that the FN is larger for unexpected (Hajcak et al., 2007; Holroyd and Coles, 2002; Holroyd et al., 2004; Nieuwenhuis et al., 2002) and infrequent (Holroyd et al., 2003) negative feedback. Specifically, when subjects predict positive feedback but actually receive negative feedback, the FN is enhanced relative to when subjects receive predicted negative feedback (Hajcak et al., 2007).

Given that depressive symptoms have been repeatedly associated with enhanced negative expectations about future events in non-clinical samples (Ahrens and Haaga, 1993; Cane and Gotlib, 1985; Chung et al., 1996; Showers and Ruben, 1990; Strunk et al., 2006) as well as deficits in positive affect and approach motivation (Davidson, 1992, 1998; Fowles, 1994; Kring and Gotlib, 1985; Chung et al., 1996; Showers and Ruben, 1990; Strunk et al., 2006), it follows from these lines of study that the FN might be reduced in depressed individuals. If this were the case, the FN would be a useful measure for detecting abnormalities in reward sensitivity among individuals with depressive symptoms. In fact, Nestler and Carlezon (2006) have recently suggested that reward-related abnormalities of dopamine systems might be an important area for research in depression, especially with regard to the development of new antidepressant medications. Consistent with this possibility, one study found that the FN was abnormal among depressed individuals regardless of feedback type (Tucker et al., 2003); however, feedback in the Tucker et al. study was indicative of both performance (reaction time) and reward, thereby confounding these two constructs. In the current study, we sought to examine the FN elicited by outcome-based feedback that directly corresponded to rewards and non-rewards, as theoretical models (Davidson, 1992, 1998; Gray, 1994) and previous empirical studies (Henriques and Davidson, 2000; Henriques et al., 1994; Shankman et al., 2007) have repeatedly emphasized the link between depression and reward insensitivity.

To this end, the present study employed a simple gambling task in which participants could win or lose money on each trial (Dunning and Hajcak, 2007; Hajcak et al., 2005a, 2006, 2007; Holroyd et al., 2003, 2004, 2006). Consistent with earlier studies, we expected that feedback indicating monetary loss would elicit an enhanced FN relative to feedback indicating monetary reward; additionally, based on the notion that depression might be related to reduced sensitivity to rewards versus non-rewards, we predicted that the magnitude of the FN would be inversely related to levels of depression. Individual differences in the related constructs of anxiety and stress reactivity were also examined in relation to the FN. To further examine the role of expectations, we measured the P3, a positive going component maximal at parietal sites that has repeatedly been shown to be sensitive to violations of expectations (Courchesne et al., 1977; Duncan-Johnson and Donchin, 1977; Johnson and Donchin, 1980) and to be enhanced for unpredicted environmental feedback (Hajcak et al., 2005a,b, 2007). In addition, the P3 has been shown to be reduced in acutely depressed individuals, and to normalize following treatment (Blackwood, 1987).

1. Methods

1.1. Participants and measures

Eighty-eight undergraduate students participated in the current study. A total of 3 participants were excluded from analysis due to poor quality recordings, leaving 85 participants (46 male, 39 female) for the final sample. No participants discontinued their participation in the experiment once the procedures had begun. All participants received course credit and $5.00 (winnings for the gambling task) for their participation. Informed consent was obtained from participants prior to each experiment. This research was formally approved by the Stony Brook University Institutional Review Board.

The short-form version of the Depression Anxiety Stress Scale (DASS-21; Lovibond and Lovibond, 1995) was used to assess self-reported symptoms of depression, anxiety, and stress over the past week (i.e., state levels). Excellent reliability and validity of the DASS-21 in both clinical and non-clinical samples has been previously established (Antony et al., 1998; Brown et al., 1997; Clara et al., 2001; Crawford and Henry, 2003; Henry and Crawford, 2005; Lovibond and Lovibond, 1995); in the present study, the DASS-21 total, as well as the depression, anxiety, and stress subscale scores were examined with respect to the FN. The stress subscale is not a direct measure of life stressors per se, but rather a broader measure of related emotions such as restlessness, difficulty relaxing, and irritability—or reactivity to psychological stress. Moreover, this subscale appears to capture a distinct constellation of negative emotions rather than simply measuring negative affect generally or non-specific symptoms common to both depression and anxiety, as scores have been shown to be reliably stable over time but to not be uniquely predictive of future anxious or depressive symptoms (Lovibond, 1998). While the stress subscale has been less widely studied compared to the depression and anxiety subscales, it may be useful for helping to more fully single the observed interrelationships between depression and reward sensitivity.

1.2. Task and materials

The present task was administered on a Pentium D class computer, using Presentation software (Neurobehavioral Systems, Inc., Albany, California, USA) to control the presentation and timing of all stimuli. The paradigm used was identical to that described in Dunning and Hajcak (2007). During the task, participants were shown a graphic displaying two doors horizontally adjacent and were told to choose which door they wanted to open (the graphic occupied approximately 6° of the visual field vertically and 8° horizontally). Participants were told to press the left mouse button to choose the left door or the right mouse button to choose the right door. Following each choice, a feedback stimulus appeared on the screen informing the participants whether they won or lost money on that trial. A green ‘+’ indicated a correct guess and a red ‘−’ indicated an incorrect guess. Prior to each trial, a white ‘0’, ‘1’, or ‘2’ cue was presented to inform participants how many of the doors would contain a prize on the upcoming trial; therefore, ‘0’, ‘1’, or ‘2’ indicated the probability of reward on the upcoming trial was 0, 50, or 1, respectively. Only feedback following 1-cue trials were analyzed as these trials were associated with a 0.5 probability of rewards and non-rewards and therefore should elicit robust P3s. All cues and feedback were presented against a black background and occupied approximately 3° of the visual field vertically and 1° horizontally. A fixation mark (+) was presented prior to the onset of each stimulus. At the end of each trial, participants were presented with the instruction to ‘Click for the next round’. The order and timing of all stimuli were as follows: (i) cues were presented for 2000 ms, (ii) a fixation mark was presented for 500 ms, (iii) the graphic of two doors was presented indefinitely until a response was made, (iv) a fixation mark was presented for 1000 ms, and finally (v) a feedback arrow was presented for 2000 ms. The intertrial interval between feedback stimulus and the following ‘Click for the next round’ instruction was 1500 ms.

Participants were told that they would gain $0.20 each time they opened a door that hid a prize, and lose $0.10 each time they opened a door without a prize. Participants received negative feedback on exactly 50% of 1-cue trials, negative feedback on 100% of 0-cue trials, and positive feedback on 100% of 2-cue trials.

1.3. Procedure

Following a brief description of the experiment, EEG sensors were attached and participants were given detailed task instructions. To familiarize participants with the task, they were given a practice block containing five trials and told to choose
which door hid a prize. The actual experiment consisted of 100 trials (25 0-cue trials, 50 1-cue trials, and 25 2-cue trials) that were presented in random order. Every 20 trials, a running total of money earned was presented on the screen. At the end of the experiment, participants were paid their winnings (i.e., $5.00).

1.4. Psychophysiological recording, data reduction, and analysis

The continuous EEG was recorded using a custom cap (Cortech Solutions, Wilmington, NC) and the ActiveTwo BioSemi system (BioSemi, Amsterdam, Netherlands). Recordings were taken from 64 scalp electrodes based on the 10/20 system, as well as two electrodes placed on the left and right mastoids. The electrooculogram (EOG) generated from blinks and eye movements was recorded from four facial electrodes; two approximately 1 cm above and below the participant's left eye, one approximately 1 cm to the left of the left eye, and one approximately 1 cm to the right of the right eye. As per BioSemi's design, the ground electrode during acquisition was formed by the Common Mode Sense active electrode and the Driven Right Leg passive electrode.

All bioelectric signals were digitized on a laboratory microcomputer using AcqKnowledge software (Biopac). The EEG was sampled at 512 Hz. Offline analysis was performed using Brain Vision Analyzer software (Brain Products, Munich, Germany). All data were re-referenced to the average of the two mastoids and band-pass filtered with cutoffs of 1 and 30 Hz. The EEG was segmented for each trial, beginning 200 ms before feedback onset and continuing for 1000 ms. The EOG for each trial was corrected for blinks and eye movements using the method developed by Gratton et al. (1983). Specific intervals for individual channels were rejected in each trial using a semi-automated procedure, with physiological processing positive feedback, negative feedback, or both (cf., Dunning and Hajcak, 2005). This is particularly relevant in studies of the FN, insofar as non-reward trials. This latter approach was done because the absolute magnitudes of positivity that peaked at 298 ms and was most consistent with the FN; and TF3/SF1, a parietal positivity that peaked at 468 ms and was most consistent with the P3.

The FN and the P3 were scored using the peak values for their respective factors on non-reward and reward trials, as well as the difference between non-reward and reward trials. This latter approach was done because the absolute magnitudes of ERP components are not inherently meaningful—an apparent change in component magnitude can result instead from the onset of a second, opposite-going component (Luck, 2005). This is particularly relevant in studies of the FN, insofar as non-rewards and rewards are thought to elicit phasic decreases and increases in dopamine, respectively (Holroyd and Coles, 2002). By scoring the difference between loss and reward, variation in the FN may reflect abnormalities related to processing positive feedback, negative feedback, or both (cf., Dunning and Hajcak, 2007; Hajcak et al., 2007; Holroyd, 2004). All statistical analysis was performed using SPSS (14.0, SPSS Inc., Chicago, Illinois, USA).

2. Results

2.1. DASS-21

The average total score was 18.80 (SD = 19.27), with a range of 0–92. The means and standard deviations of the three subscales are presented in Table 1 for both the full sample and for low and high subgroups based on depression scores (i.e., below and above the median for depression). The three bivariate correlations between the subscales were each significant (depression and stress: $r = .64$,

| Table 1 DASS-21 subscale scores (grouped by median split on depression). |
|---------------------|---------------------|---------------------|
|                     | Full sample         | Low depression (<4) | High depression (>4) |
|                     | M  SD               | M  SD               | M  SD               |
| Depression (median = 4) | 5.32 6.84  | .72 9.8  | 13.23 7.51  |
| Anxiety             | 4.99 6.48  | 1.74 3.22  | 10.38 8.08  |
| Stress              | 8.50 8.47  | 3.13 3.52  | 17.92 7.66  |

$p < .001$; depression and anxiety: $r = .64$, $p < .001$; anxiety and stress: $r = .72$, $p < .001$.

2.2. FN

The grand average of the FN across all subjects (prior to PCA) is presented in Fig. 1. All subsequent analyses reflect values from TF3/SF1, which is presented in Fig. 2 (top). A one-sample t-test revealed the difference between non-reward and reward trials to be significantly less than zero ($M = -5.96$, SD = 6.27 μV; $t(84) = -8.76$, $p < .001$) confirming that the gambling task used in the present study reliably elicited an enhanced FN for monetary loss compared to gain.

Further analyses related the FN to psychological variables. First, a bivariate correlation was performed relating the FN (non-reward minus reward) to general distress, or the sum of anxiety, stress, and depression scores (i.e., DASS-21 total). This correlation was statistically significant ($r = .26$, $p < .05$). The FN is a negative-going ERP component, so this positive correlation indicates that higher levels of general distress were associated with a reduced difference between non-reward and reward. To assess for the specificity of this relationship, three additional bivariate correlations were performed between the FN and depression, anxiety, and stress subscale scores of the DASS-21. Similar to general distress, the FN was inversely related to depression ($r = .23$, $p < .05$) and stress ($r = .28$, $p < .01$), but not anxiety ($r = .17$, $p = .12$). Scatter-plots of the relationships with depression and stress are presented in Fig. 3. Additionally, these associations with depression and stress scores were as robust when examining individuals with a total DASS-21 score greater than zero (depression: $r = .24$, $p < .05$; stress: $r = .31$, $p < .01$; anxiety: $r = .18$, $p = .13$).

To assess for the unique contributions of depression, stress, and anxiety to the reduction of the FN, a linear regression was performed. When entering the three DASS-21 subscales as and simultaneous predictors, as well as controlling for gender, the relationship between the FN and stress remained significant ($β = .34$, $p < .05$); the regression coefficients for depression ($β = .06$) and anxiety ($β = -.11$) were non-significant (both $p’s > .50$). These results suggest that (a) there is a unique relationship between stress and the FN, where higher scores on the stress subscale were found to be inversely related to the enhancement of the FN to loss relative to reward; and (b) the association between the FN and depression might be better explained by the overlap between subscale scores.

Bivariate correlations were also performed between psychological variables and the FN on non-reward and reward trials separately. While none of these correlations reached significance, there was a trend towards the FN on reward trials being more negative in individuals with higher depression scores ($r = -.20$, $p = .07$; all other $p’s > .10$). This suggests that the significant association between depression, stress, and the FN

$1$ The primary disadvantage to scoring the FN as the difference between reward and non-reward is that it obscures potential differences in latency. Indeed, it has been proposed that outcomes, which are better than expected elicit a distinct, positive-going component resembling the P2a (Potts et al., 2006). Isolating effects of depression that are unique to either the processing of rewards or non-rewards will be an important direction for future research.

$2$ An independent samples t-test revealed that the FN did not significantly differ between men ($M = -5.35$, SD = 6.77 μV) and women ($M = -6.67$, SD = 5.61 μV; $t(83) = .967$, $p = .34$).
Fig. 1. The FN grand average across all subjects at Cz (top left). ERPs for monetary loss, gain, and the difference between the two are presented. The scalp topography (top right) represents the difference between negative and positive feedback between 250 and 350 ms following feedback onset. The FN average is also displayed for participants with depression scores below ($n = 39$) and above ($n = 26$) the median (bottom).

Fig. 2. Temporospatial factor combinations associated with the FN (top) and P3 (bottom). Waveforms are presented for Cz, where the spatial factor loadings were numerically maximal. Scalp topographies represent the difference between negative and positive feedback at peak temporal loadings of 298 and 468 ms, respectively.
associated with scores on any subscale (all reward and reward trials, however, was not significantly different between monetary losses and gains, was inversely related to depression and stress scores on the DASS-21 in the current study. That is, higher levels of depressive symptoms were associated with reduced electrocortical sensitivity to non-rewards versus rewards. These data are consistent with recent theoretical models and empirical studies that link depression to decreased positive affect (Clark and Watson, 1991; Watson et al., 1995a,b), an underactive approach system (Davidson, 1992, 1998), and reduced sensitivity to rewards (Henriques and Davidson, 2000; Henriques et al., 1994; Shankman et al., 2007), and it was found that the variance shared by depression and stress reactivity may account for this association with the FN.

The existing literature on the FN suggests that this reduction could be driven by biased expectations for negative outcomes (Hajcak et al., 2007; Holroyd and Coles, 2002; Holroyd et al., 2004; Nieuwenhuis et al., 2002), as well as abnormalities in midbrain dopamine activity elicited by unfavorable environmental feedback (Holroyd and Coles, 2002)—both of which have also been related to depression in non-clinical samples (Ahrens and Haaga, 1993; Cane and Gotlib, 1983; Chung et al., 1996; Showers and Ruben, 1990; Strunk et al., 2006) and animal models (Nestler and Carlezon, 2006). The P3 was measured in the current study to examine the possible influence of biased expectations, as numerous prior studies have demonstrated the P3 to be enhanced for stimuli that violate expectations (Courchesne et al., 1977; Duncan-Johnson and Donchin, 1977; Johnson and Donchin, 1980). While the P3 here was found to be inversely related to depression and anxiety scores on both reward and non-reward trials, the difference between non-rewards and rewards was not associated with scores on any subscale. In light of the fact that the P3 has previously been shown to be enhanced for unexpected feedback in this type of experiment (Hajcak et al., 2005a,b, 2007), these results do not provide evidence that negatively-biased expectations can explain the association between the FN and depression scores. Instead, it appears that among individuals with higher depression scores feedback was less salient in general, regardless of whether money was gained or lost on each trial. While future studies will be necessary to better examine the causal mechanism linking the FN to depression scores, it appears that the FN may be a useful direct measure of abnormal feedback sensitivity in relation to depressive symptoms.

In addition to the depression subscale of the DASS-21, the FN was also found to be inversely related to scores on the stress subscale, and unrelated to anxiety scores. The current observation that sensitivity to rewards relative to non-rewards may be related to depression and stress reactivity is not entirely surprising, however, as depression and stress reactivity themselves are also related constructs—scores on these subscales were correlated in the present study. In fact, the persistent experience of life stressors may actually relate to the onset and course of depression (Brown and Harris, 1989; Hammen, 2005; Kendler et al., 1995, 1999; Lloyd, 1980; Tennant, 2002). Although it appears that reward sensitivity, depression, and stress reactivity are all related to one another, recent work has highlighted the fact that depression and stress reactivity have conceptually distinct characteristics and can be measured separately (Crawford and Henry, 2003; Henry and Crawford, 2005; Lovibond, 1998). In support of this perspective, the relationship between the FN and depression scores was no longer significant when controlling for other DASS-21 subscale scores; in contrast, the relationship between the FN and stress scores remained intact when controlling for depression and anxiety. This preliminary finding suggests that the link between depression and sensitivity to rewards relative to non-rewards may, in fact, be better accounted for by the influence of stress reactivity.

The stress subscale of the DASS-21 measures negatively valenced experiences such as tension, irritability, difficulty relaxing, and the tendency to be easily upset or agitated (Henry and Crawford, 2005; Lovibond and Lovibond, 1995). The relationship between the FN and the stress subscale, a measure of reactivity to psychological stress, is interesting to consider in light of the results of the current study.
of previous research in non-clinical samples linking reward sensitivity to the experience of laboratory and life stressors. Acute naturalistic stressors (military training, final examinations) have been found to reduce self-reported levels of positive affect and pleasure in response to enjoyable stimuli, particularly in individuals with a family history of depression (Berenbaum and Connelly, 1993). Similarly, at least one study has found a laboratory stressor (threat of shock) to be associated with a reduction in a behavioral measure of reward sensitivity (Bogdan and Pizzagalli, 2006). There is also evidence that this link between the experience of stress and reward sensitivity may depend on the stressor being perceived as unpredictable, uncontrollable, and overwhelming (Pizzagalli et al., 2007).

The present results contrast with work by Tucker and colleagues, who found that depression was not related to the difference between good versus bad outcomes—rather, Tucker et al. (2003) found that clinical levels of depression were related to larger feedback-locked negativities overall. Additionally, they observed that control subjects exhibited an enhanced FN to both negative feedback (a grade of F, indicating monetary loss) and ambiguous feedback (a grade of C, also indicating monetary loss) relative to positive feedback (a grade of A); depressed subjects exhibited an enhanced FN to negative feedback only. An important difference between the current study and that conducted by Tucker et al., however, is that in the latter the feedback used conveyed information that conflated both performance (i.e., grades based on reaction time) and possible reward or non-reward (i.e., monetary loss); feedback in the present study was not directly self- or performance-based, instead only conveying information specific to obtained rewards and non-rewards. Thus, it is somewhat difficult to directly compare these studies, although together they suggest that performance- and reward-based feedback may be differentially altered with respect to depression. This will be an important area for future studies to clarify.

It is also worth pointing out that several previous studies have reported a relationship between both depression and anxiety and a response-locked ERP component elicited when subjects commit errors—the error-related negativity (ERN; Falkenstein et al., 1990; Gehring et al., 1993; Holroyd and Coles, 2002). The ERN has a fronto-central scalp distribution and bears a functional and topographic similarity to the FN; indeed, Holroyd and Coles propose that both the ERN and FN reflect the activity of the same action monitoring system (Holroyd and Coles, 2002). However, several studies suggest important differences between the FN and ERN. For instance, it has been observed that choices resulting in monetary loss elicit an FN even when the alternative choice would have resulted in an even greater monetary loss; that is, the FN does not simply reflect the detection of an error (Gehring and Willoughby, 2002). In addition, data from our own lab suggests that the ERN is sensitive to error value (Hajcak et al., 2005b), whereas the FN reflects the binary evaluation of good versus bad outcomes (Hajcak et al., 2006). Gehring and colleagues have also pointed out that the two components exhibit divergent scalp distributions, indicating that they cannot both be explained by a single underlying neural generator (Gehring and Willoughby, 2004). Insofar as an increased ERN has been related to both anxiety and depression in clinical (Chiu and Deldin, 2007; Gehring et al., 2000; Ladouceur et al., 2006) and non-clinical (Hajcak et al., 2003; Hajcak and Simons, 2002) samples, whereas the present study suggests a decreased FN in relation to depression and no relationship with anxiety, these data highlight another way in which the FN and ERN might differ from one another. It will be useful for future studies to examine both the FN and the ERN within the same clinical sample in order to directly compare these components.

Because the FN reflects the ERP difference between non-rewards and rewards, the relationship between the FN and self-report measures of distress could be driven by abnormalities in the processing of rewards, non-rewards, or both (Luck, 2005). However, because the association with the FN was found for the difference between non-reward and reward ERPs, the observed relationship with self-report measures does not simply reflect variation in ERP amplitudes—and rather, reflects a specific reduction in the non-reward versus reward comparison. It will be important for future studies to examine the specific relationship between depression and response to rewards versus non-rewards. Behavioral evidence suggests that symptoms of depression may specifically involve abnormal responses to rewards and not punishment or non-rewards (Henriques et al., 1994; McFarland and Klein, 2008), while at least one recent study reported that low levels of serotonin specifically altered the prediction of punishment but not reward in healthy individuals (Cools et al., 2008). Additionally, it will be important for future studies to more carefully tease apart the contribution of expectations of non-reward versus reward in depression. Even though the present analysis focused only on trials in which participants had a 50% chance of winning or losing, and data on the P3 did not indicate any systematic association between depression scores and expectations, it is possible that participants in general could have had overly optimistic or pessimistic expectations which could have subsequently influenced the magnitude of the FN. Assessing for this possibility could be done within the existing paradigm, as previously demonstrated, by inquiring about predictions of outcomes after the response on each trial but before feedback is administered (Hajcak et al., 2007).

An important limitation to the current study is the use of a non-clinical sample. While a negative linear relationship was found between depressive symptoms and FN magnitude, it remains to be demonstrated whether this relationship extends to clinically significant levels of depression, and whether the FN relates to state- or trait-like variation in depression.

In conclusion, the current results suggest that depression and stress reactivity are inversely related to the FN, and higher levels of stress reactivity may account for the relationship between depression and this reduced sensitivity to non-rewards versus rewards. These findings are consistent with research linking depression to reduced positive affect and approach behavior, as well as previously observed relationships linking stress to both reward sensitivity and depression. Additionally, in light of the potential role of midbrain dopamine in depression and reward, the FN could be a useful measure for studying abnormal processing of rewards and non-rewards, especially with regard to dopamine function, as it relates to the underlying features of depression.

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