The influence of anhedonia on feedback negativity in major depressive disorder

Wen-hua Liu,a,b,c Ling-zhi Wang,c He-rui Shang,a Yue Shen,a Zhi Li,a Eric F.C. Cheung,d Raymond C.K. Chanb,e

Abstract

Anhedonia is associated with reward-processing deficits of the dopamine system, which may increase the risk of depression. Nevertheless, few previous studies have examined the influence of hedonic tone on event-related potential (ERP) measures of reward processing in major depressive disorder. A simple gambling task was used to elicit feedback negativity (FN), an ERP component elicited by feedback indicating gain versus loss, in 27 patients with major depression and 27 healthy participants. We found that participants with depression were characterized by reduced FN responses, especially towards monetary gains, but not losses, compared with healthy individuals. In addition, the amplitude of FN to gain feedback in participants with depression was related to anhedonia severity and depressive symptoms. These findings indicate an association between low hedonic capacity and reduction in FN. As a neural measure of reward sensitivity, FN may be generated in part by reward-related activity.

1. Introduction

Depression is a leading cause of disability worldwide and is associated with a variety of symptoms. While depressed mood is a common component, depression is characterized by the absence of goal-directed behavior, e.g., anhedonia, failure to engage socially, and psychomotor retardation. Specifically, a large proportion of these symptoms may be driven at least in part by reward-related abnormality (Eshel & Roiser, 2010; Nestler & Carlezon, 2006). It has been hypothesized that dysfunctional reward circuitry may account for anhedonia (Der-Avakian & Markou, 2012). Understanding the link between anhedonia and reward deficits in depression may provide new insights for diagnosis and treatment.

Recent work has assessed neural sensitivity to rewards using feedback negativity (FN), or feedback Error-Related Negativity (fERN), which is derived from the observation of a relatively negative deflection in the ERP for feedback in response to monetary gains and losses between 230 and 330 ms (Gehring & Willoughby, 2002; Goyer, Woldorf, & Huettel, 2008; Hewig et al., 2007; Holroyd, Hajcak, & Larsen, 2006; Miltner, Braun, & Coles, 1997; Nieuwenhuis, Yeung, Holroyd, Schurger, & Cohen, 2004; Sato et al., 2005; Yeung & Sanfey, 2004). FN has been interpreted as a negative-going ERP component that reflects the phasic activity of the midbrain dopamine system (Holroyd & Coles, 2002). Previous studies have found evidence to suggest that FN may be a neural process tracking the occurrence of unfavorable outcomes (Holroyd & Krigolson, 2007; Holroyd, Nieuwenhuis, Yeung, & Cohen, 2003). However, recent work has emphasized...
the role of positive feedback in FN responses (Baker & Holroyd, 2011; Foti, Weinberg, Dien, & Hajcak, 2011; Holroyd, Krigolson, & Lee, 2011; Holroyd, Pakzad-Vaezi, & Krigolson, 2008; San Martin, Manes, Hurtado, Isla, & Ibáñez, 2010). A study which used Temporal-spatial Principal Components Analysis (PCA) to investigate the underlying structure of the ERP response to monetary feedback identified a positive deflection at fronto-central recording sites in FN time range (Foti et al., 2011). Moreover, this component in the time range of the FN was not only enhanced by monetary gains compared to losses (Carlson, Foti, Mujica-Parodi, Harmon-Jones, & Greg Hajcak, 2011; Foti et al., 2011; Holroyd et al., 2008, 2011), but also correlated with brain activation in the mesocorticlimbic reward circuit, including the ventral striatum and the caudate (Carlson et al., 2011; Foti et al., 2011); these areas are associated with reward processing and show reduced functioning in depression (Foti et al., 2006; Pizzagalli et al., 2009a; Steele, Kumar, & Ebmeier, 2007). Based on this data, FN may be conceptualized as a positivity that is sensitive to unexpected positive feedback, but not negative feedback.

Given the association between FN and reward processing, FN may be a useful measure of abnormalities of reward sensitivity in depression. Studies have found support for a reduced FN response in adolescents at risk of depression (Foti, Kotov, Klein, & Hajcak, 2011) and also in younger samples in late childhood to early adolescence (Bress, Smith, Foti, Klein, & Hajcak, 2012). Moreover, depressive symptoms were also found to be associated with blunted FN responses (Foti & Hajcak, 2009). Finally, self-reported sadness after a mood induction task predicted FN responses (Foti & Hajcak, 2010), and lower FN amplitudes predicted depression onset in later life (Bress et al., 2013). Together, these findings suggest that FN may be a biomarker for studying change in reward sensitivity in depression. However, most of the aforementioned studies did not include individuals with clinical diagnoses of depression. In addition, although anhedonia is a core symptom of depression (APA, 1994) and is closely related to reward-related deficits (Der-Avakian & Markou, 2012), there has been no investigation to examine the extent to which anhedonia and FN are associated in depressed adults. Whether abnormal reward processing relates to depressive symptoms in depressed patients, especially for those with high levels of anhedonia, remains poorly understood.

The present study sought to examine FN responses to monetary gains and losses in patient with depression and healthy individuals and to explore the associations between depressive symptoms and neural sensitivity to rewards. A simple gambling task was used to elicit FN and self-reported scales were used to evaluate hedonic capacity and other emotional information in the participants. We hypothesized that, consistent with findings from non-clinical studies, the magnitude of FN would be attenuated in patients with depression compared to healthy individuals. Furthermore, based on the notion that FN reflects reward-related processing abnormalities, we hypothesized that the magnitude of FN would be related to clinical symptoms, especiallyhedonic capacity in patients with depression.

2. Methods

2.1. Participants

Twenty-seven patients with depression were selected from the outpatient clinic of the Guangzhou Psychiatric Hospital. All patients met the diagnostic criteria for Major Depressive Disorder according to DSM-IV (APA, 1994) were free from other Axis I disorders and psychotic features, and all had a score of at least 17 on the Hamilton Depression Scale for Depression (HRSD) (Hamilton, 1960). Patients who had received electroconvulsive therapy in the past six months were excluded. The mean HRSD score for depressed participants was 29.29 (standard deviation (SD) = 10.72; range 18–65) and the length of the current depressive episode was 1.8 years (y) (SD = 2.01 y). In the depressed sample, 21 patients received antidepressant medications, with a cumulative treatment duration of 17.14 months (SD = 6.08). We recruited 27 healthy controls matched for age, gender, handedness and years of education from the local community. Healthy participants were screened for psychopathological disturbances using a phone interview based on DSM-IV criteria. The Beck Depression Inventory (BDI) (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) was used to evaluate the intensity of depression before the experiment. All healthy participants were not taking any medication and had no history of psychiatric illness, neurological disease, major physical illness or drug abuse.

2.2. Task

The simple gambling task was similar to the version used in previous studies (Bress et al., 2012; Foti et al., 2007; Foti et al., 2011). The participants were asked to choose one of two doors shown side by side on a computer screen by clicking the left or right mouse button. After the participants made a choice, a fixation mark appeared for 1000 ms, which was followed by a feedback on the screen for 2000 ms. The feedback consisted of either a green “+”, indicating a gain of 1 Chinese Yuan (about 0.16 USD) or a red “−”, indicating a loss of 0.5 Chinese Yuan (about 0.08 USD). These values were chosen in order to give gains and losses equivalent subjective values (Tversky & Kahneman, 1992). After the feedback, a fixation mark appeared for 1500 ms, followed by a message “Click for the next round,” which remained on the screen until the participants responded. The task consisted of 40 trials; 20 gain and 20 loss feedback trials were presented to each participant in a random order.

2.3. Emotion assessment instruments

General hedonic tone over the past week (state levels) was measured using the Snath-Hamilton Pleasure Scale (SHAPS) (Snath et al., 1995), which covers four domains of hedonic experiences: interests/past times, social interaction, sensory experience, and food/drink. The scale contains 14 items and a higher score indicates more anhedonic symptoms. The Chinese version used for the present study has been validated in Chinese samples (Liu, Wang, Zhu, Li, & Chan, 2012). The Cronbach’s alpha in the present sample was 0.93.

The Temporal Experience of Pleasure Scale (TEPS) (Gard, Gard, Kling, & John, 2006) was used to evaluate different components of the long-term experience of pleasure, namely the anticipatory and consummatory pleasurable experiences among the participants. The original English version of the TEPS has good internal consistency and test-retest reliability. The present study used a 20-item Chinese version that was modified from the original English version (18 items) (Gard et al., 2006). A lower total score in the scale indicates a higher level of anhedonia. The Chinese version of the TEPS has been shown to possess adequate reliability in previous studies (Chan et al., 2010; Chan, Shi, et al., 2012; Chan, Wang, et al., 2012). Cronbach’s alphas for the TEPS-ANT (anticipatory pleasure) and the TEPS-CON (consummatory pleasure) in the present sample were 0.77 and 0.75, respectively.

Symptoms of depression, anxiety and stress reactivity were measured using the short-form of the Depression Anxiety Stress Scale (DASS-21) (Lovibond & Lovibond, 1995). The scale contains 21 items and each item on the DASS includes four response categories describing increasing severity of depression, anxiety and stress response. The version used for the present study has been validated in the Chinese population (Chan, Xu, et al., 2012). Cronbach’s alphas for depression, anxiety and stress subscales in the present sample were 0.92, 0.88 and 0.87, respectively.

2.4. Procedure

The study was approved by the ethics committee of the Guangzhou Medical University and informed consent was obtained from all participants. After completing the self-reported scales, the experimental task was administered to each participant.

2.5. EEG recording and analysis

Electroencephalography (EEG) recordings were obtained using 64 Ag/AgCl electrodes in the International 10/20 system positions. Electrooculography (EOG) was recorded from electrodes placed above and below the left eye and at the outer edge of both eyes to monitor horizontal and vertical eye movements. The ground electrode was placed at the frontal pole (Fpz). All electrode recordings were referenced to an electrode placed on the left mastoid and data were also recorded from the right mastoid, which enabled computation of a linked mastoid reference online. Data were recorded at a rate of 500 Hz with an online 100 Hz low-pass filter using a Neuroscan Synamps System and the appropriate software. Impedances were kept below 10 kΩ. Stimulus timing was controlled by E-Prime Software.

EEG data were re-referenced to the numeric mean of the two mastoids. The digitized signals were filtered using a 4th order digital Butterworth filter (24 dB) with a pass band of 0.10–30 Hz. The EEG was segmented for each trial, beginning 200 ms before feedback onset and continued for 800 ms following feedback onset. Ocular artifacts were corrected using the eye movement correction algorithm.
described by Gratton, Coles, & Donchin (1983). The data were baseline corrected by subtracting from each sample the mean voltage associated with that electrode during the 200 ms interval preceding stimulus onset. Trials with muscular and other artifacts were discarded using a ± 100 μV threshold level and a ± 50 μV step threshold as rejection criteria. The mean number of trials per condition after artifact rejection was 18.39 (SD = 1.05). Most of the participants had between 15 and 20 usable trials for both gain and loss feedback, and only two participants had fewer than 15 usable trials (one had nine usable lose trials while the other had 12 usable gain trials). According to the previous data suggesting that the error-related negativity can be quantified using a minimum of between six and eight trials (Oblatt & Hajcak, 2009), we retained all participants for further analysis. The EEGLAB Matlab toolbox (Delorme & Makeig, 2004) and the ERPLAB software (http://erpinfo.org/erplab) were used for EEG offline processing and analysis. Statistical analysis of the EEG data was restricted to channel FCz, where FN is maximal (Holroyd & Krigolson, 2007; Milner et al., 1997). In the first step, we analyzed the different waveforms of the feedback-locked ERP components and the ERPs separately for gain and loss responses in a manner that was consistent with previous reports (Bress et al., 2013). ERP activity was quantified on gain and loss responses as the average amplitudes from 250 ms to 350 ms after stimulus onset. A principal components analysis (PCA) was conducted to obtain the spatial distribution of these temporal factors using all recording electrodes. Promax rotation and Infomax rotation were used. The demographic and self-report data are summarized in Table 1.

### 3. Results

#### 3.1. Demographic and baseline clinical information

The demographic and self-report data are summarized in Table 3. Patients with depression showed significantly higher levels of state (measured by the SHAPS) and trait anhedonia (measured by the TEPS) than healthy controls (all ps < .001). The depressed group reported significantly more symptoms of depression, anxiety and stress reactivity (measured by the DASS) than healthy controls.

#### 3.2. Mean FN amplitude analysis

Fig. 1 presents feedback-locked ERP averages for gain and loss feedback for the two groups and shows the difference waves obtained by subtracting gains from losses between the two groups at FCz.

For the responses for gain and loss feedback, ANOVA with group (depressed group, healthy controls) and feedback (gain, loss) as factors showed a significant main effect for feedback (F(1,52) = 104.568, p < 0.001, partial r² = 0.668) and interaction effect of feedback and group (F(1,52) = 6.263, p = 0.016, partial r² = 0.107). Post hoc analyses found that larger amplitude waves were elicited by feedback indicating gains than losses for both groups (all ps < 0.001). Compared with the healthy controls (mean = 23.058 μV, SD = 9.096 μV), the depressed group (mean = 16.776 μV, SD = 7.253 μV) displayed blunted responses to gain feedback. For the loss feedback, no significant difference between the two groups emerged (p = 0.328). In addition, T test showed that the amplitude of difference waves (losses minus gains) was significantly reduced in the depressed group (mean = -0.663 μV, SD = 4.667 μV) when compared with the healthy controls (mean = -7.893 μV, SD = 4.911 μV) (T(52) = -5.545, p < 0.001).

Correlations analysis showed that, for the depressed group, high levels of trait anhedonia measured by the TEPS (r = 0.463, p = 0.015), anticipatory anhedonia measured by the TEPS-ANT (r = 0.413, p = 0.032), consummatory anhedonia measured by the TEPS-CON (r = 0.464, p = 0.015) and depressive symptoms measured by the HRSD (r = -0.430, p = 0.025) were associated with reduction in response to gain feedback (Fig. 2). No other significant correlation emerged. Because anhedonia is often correlated with depressive symptoms, partial correlation controlling for depressive symptom severity was conducted for the TEPS, TEPS-ANT, TEPS-CON scores and FN responses to gain. Only the TEPS, TEPS-CON scores and the mean amplitudes on gain trials retained a statistical trend (r = 0.361, p = 0.076; r = 0.360, p = 0.077).

For the healthy controls, no significant correlation emerged between the self-report measure of emotional information and the mean amplitude of responses to gain or loss feedback. However, high levels of consummatory anhedonia were associated with a reduction of the difference wave amplitudes (losses minus gains) in the healthy controls (r = -0.440, p = 0.022) (Fig. 3).

#### 3.3. PCA results

Table 1 presents feedback-locked ERP averages for gain and loss feedback for the two groups and the difference waves obtained by subtracting gains from losses between the two groups at FCz.

ANOVA with feedback (gain, loss) as the within-subject factor and group (depressed group, healthy controls) as the between-subject factor loadings, the peak amplitude of the factor was used for further analysis (Carlson et al., 2011; Dien, Michelson, & Franklin, 2010; Foti & Hajcak, 2009).

Repeated-measures analysis of variance (ANOVA) with group (depressed group, healthy controls) and feedback (gain, loss) as factors for FN on gain and loss trials and independent-sample t test for the difference waves were performed. The Greenhouse-Geisser correction for repeated measures was applied where appropriate and post hoc Bonferroni tests were performed in cases of significant ANOVA effects. Pearson correlation analysis was used to investigate the association between depressive symptoms (measured by the HRSD), anhedonia severity (measured by SHAPS, TEPS, TEPS-ANT, and TEPS-CON), amplitude of responses to gain and loss feedback, and the difference wave amplitudes (losses minus gains) for the two groups.

<table>
<thead>
<tr>
<th>PCA factor</th>
<th>Corresponding ERP component</th>
<th>Variance explained (%)</th>
<th>Peak latency (ms)</th>
<th>Peak channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>TF4S1</td>
<td>P200</td>
<td>2.2</td>
<td>178</td>
<td>FCz</td>
</tr>
<tr>
<td>TF1S1</td>
<td>FN</td>
<td>10.5</td>
<td>326</td>
<td>FCz</td>
</tr>
<tr>
<td>TF3S1</td>
<td>P300</td>
<td>3.4</td>
<td>622</td>
<td>FCz</td>
</tr>
<tr>
<td>TF2S1</td>
<td>Slow wave</td>
<td>2.2</td>
<td>646</td>
<td>Cz</td>
</tr>
</tbody>
</table>
individuals. We found that patients with depression had reduced FN, calculated as the difference between monetary losses and gains. When responses to losses and gains were examined separately, patients with depression had a smaller FN to gains than healthy controls, indicating a blunted neural response to gains. For the role of anhedonia and depressive symptoms in reward processing, state anhedonia, trait anhedonia and depressive symptoms in patients with depression were associated with FN responses to gains by using conventionally averaged ERP measure. In addition, high levels of trait anhedonia in healthy controls, especially for consummatory anhedonia, was associated with the blunted FN

4. Discussion

In the present study, event-related potentials were used to examine the neural responses to reward information and the influence of hedonic capacity on neural responses to monetary gains and losses in patients with depression and healthy controls.

Table 2

<table>
<thead>
<tr>
<th>PCA factor</th>
<th>Corresponding ERP component</th>
<th>Variance explained (%)</th>
<th>Peak latency (ms)</th>
<th>Peak channel</th>
</tr>
</thead>
<tbody>
<tr>
<td>TF5SF1 P200</td>
<td>1.2</td>
<td>220</td>
<td>C2</td>
<td></td>
</tr>
<tr>
<td>TF2SF1 FN</td>
<td>9.1</td>
<td>306</td>
<td>FCz</td>
<td></td>
</tr>
<tr>
<td>TF3SF1 P300</td>
<td>1.4</td>
<td>446</td>
<td>Cz</td>
<td></td>
</tr>
<tr>
<td>TF1SF1 Slow wave</td>
<td>12.9</td>
<td>552</td>
<td>FCz</td>
<td></td>
</tr>
</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Measures</th>
<th>Depressed group (N=27)</th>
<th>Healthy controls (N=27)</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>11/16</td>
<td>12/15</td>
<td>χ² = 0.07, df = 1, p = 0.78</td>
</tr>
<tr>
<td>Age (years)</td>
<td>30.66 ± 10.14</td>
<td>34.14 ± 10.16</td>
<td>t(52) = −1.26, p = 0.21</td>
</tr>
<tr>
<td>Education (years)</td>
<td>12.37 ± 3.50</td>
<td>13.22 ± 2.62</td>
<td>t(52) = 0.31, p = 0.78</td>
</tr>
<tr>
<td>Estimated I.Q.</td>
<td>107.07 ± 16.01</td>
<td>100.92 ± 16.73</td>
<td>t(52) = −0.64, p = 0.52</td>
</tr>
<tr>
<td>Self-reported experience of emotion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHAPS (14–56)</td>
<td>28.59 ± 7.15</td>
<td>22.44 ± 8.44</td>
<td>t(52) = −2.88, p &lt; 0.01</td>
</tr>
<tr>
<td>TEPS total score</td>
<td>72.29 ± 14.37</td>
<td>82.77 ± 9.81</td>
<td>t(52) = −3.12, p &lt; 0.01</td>
</tr>
<tr>
<td>TEPS-ANT (11–66)</td>
<td>39.66 ± 7.59</td>
<td>45.22 ± 6.17</td>
<td>t(52) = −2.94, p &lt; 0.01</td>
</tr>
<tr>
<td>TEPS-CON (9–54)</td>
<td>32.62 ± 7.57</td>
<td>37.55 ± 5.85</td>
<td>t(52) = −2.68, p &lt; 0.01</td>
</tr>
<tr>
<td>DASS total score</td>
<td>27.49 ± 14.78</td>
<td>5.92 ± 6.64</td>
<td>t(52) = −6.91p &lt; 0.01</td>
</tr>
<tr>
<td>DASS-D (0–21)</td>
<td>9.31 ± 4.91</td>
<td>1.14 ± 2.10</td>
<td>t(52) = −7.93, p &lt; 0.01</td>
</tr>
<tr>
<td>DASS-A (0–21)</td>
<td>8.58 ± 5.82</td>
<td>1.85 ± 2.47</td>
<td>t(52) = 5.52, p &lt; 0.01</td>
</tr>
<tr>
<td>DASS-S (0–21)</td>
<td>9.19 ± 5.12</td>
<td>2.92 ± 3.09</td>
<td>t(52) = 5.78, p &lt; 0.01</td>
</tr>
</tbody>
</table>

Clinical characteristics

<table>
<thead>
<tr>
<th>Measures</th>
<th>Depressed group (N=27)</th>
<th>Healthy controls (N=27)</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDRS-baseline (0–64)</td>
<td>29.29 ± 10.72</td>
<td>22.44 ± 8.44</td>
<td>t(52) = −2.88, p &lt; 0.01</td>
</tr>
<tr>
<td>Duration of illness (years)</td>
<td>1.80 ± 2.01</td>
<td>1.14 ± 2.10</td>
<td>t(52) = −7.93, p &lt; 0.01</td>
</tr>
<tr>
<td>Cumulative episodes treated (months)</td>
<td>17.14 ± 6.08</td>
<td>10.16 ± 6.73</td>
<td>t(52) = −6.91p &lt; 0.01</td>
</tr>
</tbody>
</table>

Data are presented as n or mean ± SD.
Notes: SHAPS, Snith-Hamilton Pleasure Scale; TEPS-ANT, Temporal Experience of Pleasure Scale – Anticipatory Pleasure Subscale; TEPS-CON, Temporal Experience of Pleasure Scale – Consummatory Pleasure Subscale; DASS, Depression Anxiety Stress Scale; DASS-D, DASS Depression subscale; DASS-A, DASS Anxiety subscale; DASS-S, DASS Stress subscale.
difference waves by employing both the average ERP component and PCA-yielded factor measures.

The findings in the present study are consistent with recent reports (Baker & Holroyd, 2011; Foti et al., 2011; Holroyd et al., 2008, 2011; San Martin et al., 2010), which suggested that the variation in FN amplitudes stemmed from neural activity associated with positive rather than negative feedback. Previous studies often used a difference wave approach to study FN responses to gain or loss feedback. However, these findings are limited by the fact that the difference wave approach cannot attribute that variation to a specific outcome. Consistent with previous findings in non-clinical samples (Bress et al., 2012; Foti et al., 2011), when FN was quantified as the amplitude difference between gain and loss feedback, FN amplitudes were less negative in patients with depression than healthy controls. Considering the feedback type, we found blunted FN responses to gain, but not to loss feedback in patients with depression compared to healthy controls. The findings were not affected by the particular time window we selected from 250 ms to 350 ms after feedback presentation for the FN, because a similar pattern of effects was observed by using the PCA peak amplitude measure which can exclude the effects of potentially overlapping components (Dien, 2010a). FN is traditionally thought to reflect the degree of negative prediction error, a signature when events are worse than expected, due to decreased dopaminergic activity emanating from the anterior cingulate cortex (ACC) (Holroyd & Coles, 2002; Nieuwenhuis, Holroyd, Mol, & Coles, 2004). As a modification to this theory, researchers suppose that FN may also reflect reward-related activity of the striatum (Carlson et al., 2011; Foti et al., 2011; Holroyd et al., 2008), and emerging evidence suggests that dopamine encode a reward prediction error, while serotonin may encode a punishment prediction error or regulate the prediction to future reward (Cools, Robinson, & Sahakian, 2008; Daw, Kakade, & Dayan, 2002; Miyazaki, Miyazaki, & Doya, 2012). Similarly, EEG studies have shown that negative and positive feedback trigger
distinct functional processes (Baker & Holroyd, 2011; Holroyd et al., 2008). Although a major puzzle about the impact of negative and positive outcomes on the FN remains, the finding in this study emphasized valence specificity in the FN responses to reward-related feedback in patients with depression.

Consistent with previous findings in non-clinical children (Bress et al., 2012) and adolescents with depression onset in later life (Bress et al., 2013), this study demonstrated the link between depressive symptoms and reduced FN responses in currently depressed patients, and this study is also the first to show that trait anhedonia may affect the neural activities related to feedback processing in this population. In this study, patients with high levels of depressive symptoms and anhedonia displayed more blunted FN responses to gain feedback. After correcting for the influence of depression severity, the effect of anhedonia on feedback processing retained a trend significance. As core symptoms of depression, depressed mood and anhedonia are correlated closely with each other, making it difficult to completely disentangle their contributions towards findings in depressed patients. Of note, a similar relationship between anhedonia and FN responses was also observed in healthy controls, suggesting that high levels of trait anhedonia may be associated with blunted FN difference waves, which further supports the link between anhedonia and FN responses. Anhedonia is undoubtedly involved in reward processing and largely related to reward anticipation, salience and decision making (Der-Avakian & Markou, 2012), but its contributions to scalp-recorded ERPs in clinical samples remain less well studied. Interestingly, a few studies have reported that FN responses in patients with depression may be different from those reported in other psychiatric disorders. Patients with schizophrenia (Horan, Foti, Hajcak, Wynn, & Green, 2012) and autism (Larson, South, Krauskopf, Clawson, & Crowley, 2011) may have normal FN responses to reward feedback. It seems that FN responses may also be potentially useful in delineating the scope of reward-related feedback sensitivity impairments in different psychiatric conditions. The incorporation of FN into tasks which quantify the difference between positive and negative feedback in electrophysiological investigation on anhedonia may produce new data in understanding the clinical presentation and biological basis of major depression.

This study attempts to understand the neural mechanisms underlying the disturbances in feedback processing in depressed patients with relatively high HRSD scores (mean = 29.29). The insensitivity to reward feedback demonstrated by the depressed group is broadly consistent with considerable evidence of dysfunctional self-reported and physiological responses to pleasant or rewarding stimuli in this population (Clark, Chamberlain, & Sahakian, 2009; Eshel & Roiser, 2010; Forbes et al., 2009; Kumar et al., 2008; Pizzagalli et al., 2009a). However, findings in previous studies which focus on errors and negative feedback (Mies et al., 2011; Ruchsow et al., 2004, 2006; Santesso et al., 2008; Steele et al., 2007; Taylor Tavares et al., 2008; Tucker, Luu, Frishkoff, Quiring, & Poulsen, 2003) mainly demonstrated enhanced electrophysiological responses to negative feedback. Factors such as differences in depressive symptom severity, the use of antidepressants and specific symptoms of depression (e.g., anhedonia, apathy and psychomotor retardation), are thought to influence the neural response to feedback processing (Mies et al., 2011; Schrijvers et al., 2009; Tucker et al., 2003). For example, depressive symptom severity may affect FN responses to negative feedback in that
depressed patients in remission (Santesso et al., 2008) and moderately depressed patients (Mies et al. 2011; Tucker et al., 2003) have been reported to show an enhanced FN responses to negative feedback, while an attenuated FN amplitude has been reported in more severely depressed patients (Mies et al. 2011; Schrijvers et al., 2009; Tucker et al., 2003). In addition, the use of different types of medication influence the response of error-related negativity (ERN), an ERP component which follows response errors and is thought to share a neural source network with FN (Gentsch, Verkes, Ruijt, & Sabbe, 2004; Johannes, Wieringa, Nager, Dengler, & Munte, 2001; Schrijvers et al., 2008) and norepinephrine reuptake inhibitors may increase ERN (Jocham & Ullsperger, 2009; Riba, Rodriguez-Fornells, Morte, Munte, & Barbanoj, 2005). In this study, the relatively severe depressive symptoms of participants in the patient group and antidepressant treatment might have influenced the results.

Limitations of the present study include our focus on enrolling patients with DSM-IV current major depression, thus precluding our ability to generalize these results to patients with subsyndromal depression. Our results suggest no significant association between anxiety, stress levels and electrophysiological sensitivity to rewards. It is possible that a ceiling effect had occurred in measuring these affective characteristics due to the fact that the patient sample had moderate to severe depression. Thus, more research is needed to clarify whether this affective characteristic may have an effect in other depression-related conditions such as comorbid depression and anxiety. In addition, most of our patients were on medication. In future studies, it will be important to explore the effect of antidepressant on FN amplitudes and determine whether it is a concomitant or a consequence of depressive symptoms. Taken together, as a neural measure of reward sensitivity, FN responses are attenuated in patients with depression and we demonstrate a link between FN and hedonic tone. The specific relationship between trait anhedonia and the neural responses to monetary gains but not losses indicates that FN seems to be generated in part by reward-related activity.

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