Acute Stress Reduces Reward Responsiveness: Implications for Depression

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Abstract

Background: Stress, one of the strongest risk factors for depression, has been linked to "anhedonic" behavior and dysfunctional reward-related neural circuitry in preclinical models.

Methods: To test if acute stress reduces reward responsiveness (i.e., the ability to modulate behavior as a function of past reward), a signal-detection task coupled with a differential reinforcement schedule was utilized. Eighty female participants completed the task under both a stress condition, either threat-of-shock (n = 38) or negative performance feedback (n = 42), and a no-stress condition.

Results: Stress increased negative affect and anxiety. As hypothesized based on preclinical findings, stress, particularly the threat-of-shock condition, impaired reward responsiveness. Regression analyses indicate that self-report measures of anhedonia predicted stress-induced hedonic deficits even after controlling for anxiety symptoms.

Conclusions: These findings indicate that acute stress reduces reward responsiveness, particularly in individuals with anhedonic symptoms. Stress-induced hedonic deficit is a promising candidate mechanism linking stressful experiences to depression.

Introduction

Diathesis-stress models postulate that both biological and environmental factors influence the development of psychiatric disorders, including depression (Millon and Davis 1999). These theories suggest that diatheses, including genetic (Caspi et al 2003; Kendler and Karkowski-Shuman 1997) and neurobiological (Davidson et al 2002; Holsboer 2000) predispositions, influence one's vulnerability to the destabilizing effects of stress. Consistent with this view, stress has been strongly associated with depression in both retrospective and prospective research (Brown and Harris 1978; Monroe and Hadjiyannakis 2002; Van Praag et al 2004). Specifically, severe, chronic, and dependent psychosocial stressful life events have been linked to depression onset (Brown and Harris 1978, 1989; Kendler et al 1999). Despite the impressive predictive value of stressful events for depression and the suggested causality (Kendler et al 1999), the mechanisms by which stress is associated with depression are poorly understood.

Findings emerging from preclinical research offer potential insight into these mechanisms. Animal models of depression have demonstrated that stress induces anhedonic-like behavior (Anisman and Matheson 2005). Various procedures, including chronic mild stress (Willner 2005), learned helplessness (Henn and Vollmayer 2005), inescapable stress (Zacharko et al 1983), and early separation (Matthews and Robbins 2003) have been shown to decrease animals' sensitivity to reward. Importantly, animal research suggests that only stressors affecting dopaminergic transmission in pathways associated with reward (Schultz 2002; Wise 2004), result in anhedonic behavior (Zacharko et al 1983). These preclinical findings are particularly intriguing in light of the role of anhedonia in depression (American Psychiatric Association 2000).

Surprisingly, and in contrast with the animal literature, little translational human research has investigated the interplay of stress and anhedonia. One notable exception found that samples of U.S. Army cadets and college students reported a decreased ability to experience pleasure following a stressful period (field training exercises and final examinations, respectively) compared to a control period (Berenbaum and Connelly 1993). Further highlighting a potential link between anhedonia and stress, depressed individuals with anhedonia reported higher subjective ratings of stressful events (Willner et al 1990). Moreover, melancholia, a subtype of depression characterized by anhedonia, is often accompanied by hypercortisolemia (Gold and Chrousos 1999). Taken together, preclinical evidence and limited human research invite the possibility that stress might increase the likelihood of depression development by inducing anhedonia.

As an initial test of this hypothesis, the present study aimed to investigate whether acute stress induced hedonic deficits in healthy female controls. Only females were included because depression occurs nearly twice as often in women compared with men (Kessler et al 1993) and gender differences in behavioral and biological stress responses have been described in both the animal (Faraday 2002; Tinnikov 1999) and human (Maciejewski et al 2001; Weiss et al 1999) literature. To elicit acute stress, two widely used laboratory stress-induction paradigms, threat-of-shock and negative performance feedback, were utilized. Prior findings indicate that both paradigms reliably induce negative affect and anxiety (Grillon et al 1993; Stroud et al 2002). To objectively assess hedonic behavior, a signal-detection task was utilized to measure reward responsiveness, which can be conceptualized as an individual's propensity to modulate behavior according to rewarded experience (Pizzagalli et al 2005a). Given animal research and the

limited human findings reviewed above linking stress to anhedonic-like behavior, we hypothesized that individuals will demonstrate impaired reward responsiveness and reward learning under a stress compared with a no-stress condition. Moreover, we hypothesized that stress induced impairments in reward responsiveness will be particularly pronounced in individuals reporting anhedonia in daily life.

Methods and Materials

Participants

Eighty-three female participants aged 18–25 were recruited from the community and introductory psychology courses. All were right-handed (Chapman and Chapman 1987) and reported no color blindness, past or present neurological, psychiatric, hormonal, or metabolic disturbances. For their time, participants received either course credit or $10/hour as well as money ($10.60) "won" during the task. Participants who did not believe the stress manipulation (n = 2) or did not understand the experiment (n = 1) were excluded. Thus, data from 80 subjects were utilized for analyses. Participants were randomly assigned to either a negative performance feedback (n = 42; age: 21.26 ± 2.37) or threat-of-shock (n = 38; age: 22.05 ± 2.24) manipulation.

The study was approved by the Committee on the Use of Human Subjects at Harvard University.

Task

The computer task, which was adapted from prior research (Pizzagalli et al 2005a; see also Tripp and Alsop 1999), was presented on a PC using E-prime software (version 1.1; Psychology Software Tools, Inc, Pittsburgh, Pennsylvania). The task consisted of

300 trials, which were divided into 3 blocks of 100 trials. Blocks were separated by a 30-second break. Each subject completed the computer task twice: in a stress and no-stress condition, the order of which was counterbalanced across subjects. To reduce carry-over effects between conditions, two different stimuli (a nose and mouth; see below) were utilized as targets. Stimuli were counterbalanced across conditions and subjects.

Trial Presentation (Figure 1A)

Each trial began with the presentation of a fixation cross for 1.0 –1.4 sec in the middle of the screen (Figure 1A). The fixation cross was replaced by a mouthless (or noseless) face presented in the center of the screen. After 500 ms, either a short mouth (10.00 mm) or nose (5.00 mm); or a long mouth (11.00 mm) or nose (5.31 mm) was presented for 100 ms. (The length of stimuli were determined through pilot testing to minimize potential differences in response bias and discriminability between the nose and mouth stimuli.) Importantly, the difference in stimulus length was small, making the discrimination between a short or long mouth (or nose) difficult. The mouthless (or noseless) face remained on the screen for an additional 1500 ms. Participants were instructed to identify which stimulus (long or short) was presented by pressing the '1' or '4' key (counterbalanced across subjects and between conditions) on a button response box. Within each block, the short and long stimuli were presented equally often in a pseudo-randomized sequence with the constraint that no more than three instances of the same stimulus were presented consecutively. For each block, reward feedback ("Correct!! You won 5 cents") was presented after 40 correct trials according to a controlled reinforcement schedule. Critically, one stimulus (hereafter labeled as the "rich stimulus")

was disproportionately rewarded compared to the other (hereafter labeled as the "lean stimulus") for correct responses with a ratio of 3 to 1. Thus, during each block, a participant received 30 reward feedbacks for correct identifications of the rich stimulus while receiving only 10 reward feedbacks for correct identifications of the lean stimulus. The controlled reinforcement schedule used guaranteed that reward feedback for correct responses was given according to a pseudo-randomized schedule. If a participant failed to make a correct response for a trial in which feedback was scheduled, reward feedback was delayed until the next correct identification of the same stimulus type (rich or lean). Reward feedback was presented for 1500 ms and was followed by a blank screen for 250 ms. If feedback was not given (i.e., the subject was inaccurate or was accurate but no feedback was scheduled), a blank screen was displayed for 1750 ms.

Stress Manipulation

Two stress manipulations were used; threat-of-shock and performance feedback (Figure 1B, 1C). Throughout the experiment, a multicolored bar was utilized to signal the presence of the stressor. For participants in the threat-of-shock manipulation (no shock was ever actually delivered), this bar represented the likelihood that they would receive an "unpleasant but not painful" electrical shock via the electrodes attached to the back of their neck (see Procedure). Participants were instructed that the likelihood they would receive a shock was dependent upon their performance, such that they were more likely to receive a shock if they were performing worse than past participants. In the performance feedback manipulation, the bar represented the participant's percentile ranking relative to past participants. These stressful manipulations and instructions were

utilized to emphasize psychosocial (i.e., evaluative), and dependent (i.e., contingent on the individuals' own behavior) aspects of stress, which have been strongly linked to depression onset in humans (Kendler et al 1999).

For both stress manipulations, an indicator mark on the bar represented the participant's current level, i.e., the likelihood of receiving a shock in the threat-of-shock manipulation or their percentile ranking in the performance feedback manipulation. To maintain the stress manipulation throughout the experiment, the location of the indicator mark was updated after every 10 trials according to a fixed pattern, independent of actual performance. To minimize task distraction a 2-sec window was provided during which the indicator mark moved before the next trial started. For the stress condition of the threat-of-shock manipulation, the indicator mark oscillated within the region indicating a 50–75% likelihood of receiving an electrical shock. In the no-stress condition, the indicator mark moved within the 0–25% region labeled "safe." Participants were told that if the indicator mark was within the "safe" region it would be impossible for them to receive a shock.

Subjects assigned to the performance feedback manipulation received poor performance feedback during the stress condition. To this end, the indicator mark fluctuated within the region indicating that the participant was performing within the 25th–50th percentiles of past participants. In the no-stress condition of the performance feedback manipulation the indicator mark moved within the 75th–100th percentile.

Procedure

After providing informed written consent, participants were given verbal instructions. Subjects were told that the aim of the study was to win as much money as

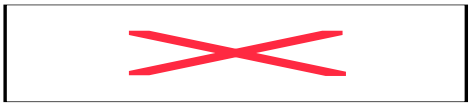
possible and that the best way to do so was to correctly identify as many stimuli as possible. Additionally, participants were informed that not every correct response would receive a reward. To assess the effects of stress on self-report measures of affect, subjects completed the state form of the Spielberger Trait Anxiety Inventory (STAI; Spielberger et al 1970) and the Positive and Negative Affect Scale (PANAS; Watson et al 1988) four times: immediately before (pre-task) and after (post-task) the stress and no-stress conditions. 1 For participants assigned to the threat-of-shock manipulation, for both the stress and no-stress condition, 8-mm electrodes (Coulborn, V91-93, V91-33) were attached immediately after the pre-task administration of the PANAS and STAI scales and removed immediately after completion of the post-task PANAS and STAI scales. To avoid confounding effects due to asymmetrical placement on the body (Simpson et al 2001), electrodes were attached to the neck.

After completion of pre-task PANAS and STAI measures, written instructions for the signal-detection task were presented on the computer screen, followed by practice trials. Participants were allowed as many practice trials as necessary. Following completion of the signal-detection task during the first condition (stress or no-stress), participants completed the post-task STAI and PANAS assessments. Between the two conditions, participants completed a variety of self-report measures, including the Chapman and Chapman (1987) handedness scale, Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al 1995), and the Beck Depression Inventory II (BDI-II; Beck et al 1996), among others. The second condition (stress or no-stress) was presented at least 30 min after completion of the first condition. Before beginning the second condition, the respective instructions and practice trials were provided. The state

forms of the STAI and PANAS scales were administered again immediately before and after the second condition. Following completion of the entire study, participants were debriefed and remunerated.

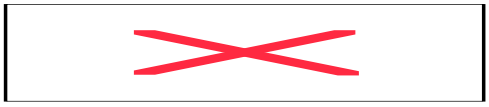
Data Reduction

The main variable of interest was response bias, which is an empirically-based measure of reward responsiveness. Response bias assesses participants' systematic preference for the response paired with the more frequent reward, and is calculated as:

Response Bias: 

As evident from the formula, a high response bias emerges with (a) large numbers of correct identifications of the rich stimulus and misses for the lean stimulus (incorrectly identifying the lean stimulus as the rich stimulus), which result in a large numerator; and (b) small numbers of misses for the rich stimulus and correct identifications of the lean stimulus, which result in a smaller denominator. To further evaluate response bias findings, analyses were also performed on accuracy (percentage of correct responses) for each stimulus (rich or lean) type.

To test the specificity of putative findings, control analyses were performed on discriminability. Discriminability provides a measure of a participants' ability to discriminate the two stimuli and is a measure of overall task performance or difficulty. Discriminability was calculated according to the following formula:

Discriminability: 

Response bias and discriminability were derived from the behavioral model of signal detection (Macmillan and Creelman 2005).

Statistical Analyses

To remove outliers, trials with RTs less than 150 ms or longer than 1500 ms were first excluded. Next, for each subject, trials with RTs (following natural log transformation) falling outside the mean ± 3 SD were considered as additional outliers and excluded. Overall, 1.32% of trials were excluded. To assess the general effects of acute stress on affect and task performance, analyses of variance (ANOVAs) were performed on the entire sample (n = 80).

For the signal-detection task, ANOVAs with Condition (stress, no-stress), and Block (1,2,3) as repeated measures and Stress Manipulation (threat-of-shock, negative performance feedback) as a between-subject factor were performed for response bias and discriminability separately.2 To further assess the unique effects of the two stress manipulations on response bias and discriminability, Condition x Block ANOVAs were repeated separately for the threat-of-shock (N = 38) and performance feedback (N = 42) manipulations. For accuracy scores, an ANOVA with Condition (stress, no-stress), Stimulus Type (rich, lean), Block (1,2,3) and Stress Manipulation as factors was performed.

For each self-report measure of affect (PANAS PA, PANAS NA, and STAI), a separate ANOVA with Condition (stress, no-stress) and Time (pre-task, post-task) as repeated measures and Stress Manipulation (threat-of-shock, negative performance feedback) as a between-subject factor was performed. Throughout, the Greenhouse-Geisser correction was applied when applicable. Post-hoc Newman-Keuls tests were utilized in case of significant ANOVA effects.

To investigate whether self-report measures of mood were associated with response bias, Pearson correlations were run between BDI/MASQ scores and total response bias within the stress and no-stress conditions. As in prior studies (Joiner et al 2003; Pizzagalli et al 2005a), an anhedonic subscore of the BDI was computed by summing items #4 (loss of pleasure), #12 (loss of interest), #15 (loss of energy), and #21 (loss of libido). For the MASQ, the four subscales—anhedonic depression (AD), general depression (GDD), anxious arousal (AA), and general anxiety (GDA)—were considered (Watson et al 1995). Finally, to test the a priori hypothesis of a link between anhedonia and stress, hierarchical regression analyses were run to evaluate if anhedonic depression (as measured by the MASQ and BDI) uniquely predicted response bias during the stress condition after controlling for response bias in the no-stress condition (entered in the first step) and MASQ measures of anxiety (AA and GDA; entered in the second step).

Results

The Effects of Stress on Response Bias

The three-way ANOVA with Condition (stress, no-stress), Block (1,2,3), and Stress Manipulation (threat-of-shock, negative performance feedback) revealed a main effect of Block [$F(2,156) = 32.73$, $p < .001$], due to increases in response bias over time (block 3 > block 1; block 2 > block 1; Newman-Keuls: p's > .001). More importantly, the main effect of Condition was also significant [$F(1,78) = 5.39$, $p < .03$], due to lower response bias during the stress (0.08 ± 0.16) than no-stress (0.16 ± 0.17) condition (Fig. 2A).

When considering the two stressor manipulations separately, Condition x Block ANOVAs revealed that the main effect of Condition was significant only for the threat-

of-shock manipulation [$F(1,37) = 6.47$, $p < .02$; stress: 0.08 ± 0.14, no-stress: 0.17 ± 0.13]. On an individual level, 28 of the 38 subjects (74%) in the threat-of-shock manipulation showed lower response bias in the stress than no-stress condition (binomial $P(28/38) < .002$). To examine the contribution of each stimulus type on response bias, a Stimulus Type (rich, lean) x Block x Condition ANOVA was conducted on accuracy scores. Critically, a significant Stimulus Type x Condition interaction emerged [$F(1,37) = 10.39$, $p < .01$; see Figure 2B].3 Post-hoc Newman-Keuls tests revealed that accuracy for the rich stimulus was significantly higher in the no-stress relative to the stress condition ($p < .02$); for the lean stimulus, accuracy was higher in the stress compared to the no-stress condition ($p < .03$).

In light of the response bias findings, correlation and regression analyses were performed to investigate whether individual differences in anhedonic symptoms predicted response bias in the threat-of-shock manipulation. Consistent with our hypotheses, negative correlations emerged between mean response bias during the stress, but not no-stress, condition and (1) BDI anhedonic subscore ($r = -.33$, $p < .05$) and (2) MASQ anhedonic depression subscale ($r = -.30$, $p < .08$; Table 1). Highlighting the specificity of these findings, hierarchical regression analyses clarified that MASQ anhedonic epression predicted mean response bias during the stress condition even after controlling for mean response bias during the no-stress condition and MASQ anxiety measures (GDA, AA), [$\Delta R2 = .14$, $\Delta F(1,32) = 5.36$, $p < .03$]. When considering the BDI anhedonic subscore score, a similar pattern emerged [$\Delta R2 = .09$, $\Delta F(1,33) = 3.47$, $p < .08$].

Control Analyses

Discriminability. The three-way ANOVA with Condition, Block, and Stress Manipulation as factors revealed only a significant main effect of Block [$F(2, 156)$ _ 5.01, p _ .01; _: 0.93], due to greater discriminability in block 2 (0.43 _ 0.18) relative to block 1 (0.38 _ 0.14; Newman-Keuls: p _ .01; see Figure 2C). When considering the two stressor manipulations separately, the main effect of Condition was not significant for the threat-of-shock [$F(1, 37)$ _ .06, p _ .81] or the performance feedback [$F(1,37)$ _ 2.19, p _ The mean response bias (averaged across blocks) was considered.

Self-Report Measures of Affect. To test the effects of stress on affect, Condition (stress, no-stress) x Time (pre-task, posttask) x Stress Manipulation (threat-of-shock, negative performance feedback) ANOVAs were performed for NA, PA, and STAI scores separately. For the sake of brevity, only effects involving Condition are reported. For STAI, the Condition x Time interaction was significant [$F(1,78) = 8.54$, $p < .01$]. For PANAS NA, the Condition x Time interaction approached significance [$F(1,78) = 3.31$, $p < .08$]. As expected, the stress condition led to increases of NA and STAI (post > pre, Newman-Keuls: p's < .02). Moreover, STAI scores were significantly higher after the stress than no-stress condition (Newman-Keuls: p's < .01; Fig. 3B). For PANAS PA, a significant Condition x Time x Stress Manipulation emerged [$F(1,78) = 4.83$, $p < .04$]. Follow-up Condition x Time ANOVAs conducted for each stress manipulation separately revealed, however, no significant findings.

Discussion

Anhedonia has long been recognized as a potential trait marker of depression (Loas 1996; Meehl, 1975). More recently, anhedonia has come under renewed attention as a particularly promising depressive phenotype (Hasler et al 2004; Pizzagalli et al

2005a) because it is: 1) a cardinal symptom of depression (American Psychiatric Association 2000); 2) heritable (Farmer 2003); 3) associated with dysfunctions in brain reward pathways (Anisman and Matheson 2005); 4) a predictor of poor outcome (Kasch et al 2002); and 5) often a precipitant of depression onset (Dryman and Eaton 1991). However, although preclinical findings suggest that stress plays a major role in the emergence of anhedonia (Anisman and Matheson 2005), the mechanisms by which hedonic deficits arise in humans remain largely unknown.

The goals of the present study were to: 1) test whether acute stress impairs reward responsiveness, an empirical measure of hedonic capacity, in healthy female controls; 2) assess the effects of two different psychosocial stress manipulations on reward responsiveness; and 3) evaluate associations between self-reported anhedonia and levels of reward responsiveness under stress and no-stress conditions. Consistent with prior research, both stress manipulations successfully induced negative affect and anxiety (Grillon et al 1993; Rhudy and Meagher 2003; Stroud et al 2002). As in prior studies from our laboratory, which assessed subject samples different from the one considered here (Pizzagalli et al 2005a; Pizzagalli, Ratner, Jahn, unpublished observation), reliable response bias development and stimulus-dependent changes in accuracy indicated that participants modified their behavior according to reinforcement history. Thus, both the stress induction and reward responsiveness task were successful.

Consistent with our main hypothesis, preclinical investigations (Anisman and Matheson 2005; Henn and Vollmayr 2005; Willner 2005) and limited human research (Berenbaum and Connelly 1993), subjects, particularly in the threat-of-shock manipulation, displayed significantly lower response bias in the stress compared to the

no-stress condition indicating that acute stress reduced reward responsiveness in healthy female controls. Notably, for both stress manipulations, analyses on discriminability scores revealed no significant differences between the stress and no-stress condition suggesting no global effects of stress on task performance. Further highlighting specific hedonic impairments rather than a global performance deficit, the stress condition was associated with significantly lower accuracy for the rich stimulus but significantly higher accuracy for the lean stimulus.

Interestingly, negative correlations emerged between self report measures of anhedonia and response bias during the stress, but not no-stress, condition. Accordingly, individuals reporting greater anhedonic symptoms in their daily life showed the strongest hedonic deficits in the face of an acute stressor. Highlighting the specificity of this link, anhedonic symptoms predicted stress-induced hedonic deficits even after controlling for response bias in the no-stress condition and anxiety symptoms.

Collectively these findings suggest that acute psychosocial stressors with evaluative and dependent features4 led to transiently blunted hedonic capacity in psychiatrically healthy female participants, particularly in those reporting hedonic deficits. In light of the observations that both stress (Monroe and Hadjiyannakis 2002) and anhedonia (Dryman and Eaton 1991) often precede depression onset, the present findings provide a potential mechanism—stress-induced hedonic deficits—by which stress may lead to depression onset. In addition to this study, two independent lines of evidence suggest that these effects might be particularly deleterious for individuals with biological vulnerabilities featuring anhedonic traits (Farmer et al 2003; Oquendo et al 2004). First, a family history of depression has been found to confer an increased

vulnerability to stress-induced hedonic deficits (Berenbaum and Connelly 1993). Second, animals bred for depression demonstrate increased stress-induced anhedonic-like behavior (Overstreet et al 1997) and blunted dopamine responses to reward (Yadid et al 2001).

Interestingly, in a recent study using the same signal-detection task without any acute stressor, we observed that subjects who appraised recent situations in their life as stressful, unpredictable, and uncontrollable had significantly lower reward responsiveness than comparison subjects (Pizzagalli, Ratner, Jahn, unpublished observation). Although in the present study we did not assess the participants' appraisal of how uncontrollable or unpredictable the acute stressors were, findings from these independent studies suggest that both sustained laboratory stressors with psychosocial components as well as perceived stress in daily events were associated with similar reductions in hedonic capacity. In addition to providing important convergent evidence, these findings emphasize the ecological validity of laboratory stressor paradigms.

Candidate Neurobiological Mechanisms

Due to the purely behavioral nature of this study, no conclusive statements about putative neurobiological mechanisms underlying the link between acute stress and anhedonia can be advanced. Extrapolating from extensive preclinical findings, we suggest, however, that stress may induce hedonic deficits by altering the rewarding properties of stimuli through dysfunction within dopaminergic tracts and structures associated with reward processing, most notably the mesocorticolimbic pathways (Anisman and Matheson 2005). Generally, animal research suggests that enhanced

mesolimbic dopamine transmission promotes approach-related behaviors while stress-related dysfunctions are associated with decreased hedonic capacity (Cabib and Puglisi-Allegra 1996; Di Chiara et al 1999; Pani et al 2000). Interestingly, stress-induced mesolimbic hypodopaminergic but mesocortical hyperdopaminergic transmission have been associated with deficits in motivated behavior (Cabib et al 2002). Neuroimaging techniques probing neurochemical (Koepp et al 1998; Pruessner et al 2004) and functional (e.g., Knutson et al 2001) aspects of the mesocorticolimbic system will be needed to test whether the present stress-induced hedonic deficits may be due to transiently decreased mesolimbic and/or increased mesocortical dopamine function.

In addition to potential modulation within mesocorticolimbic pathways, a second, but not mutually exclusive, mechanism linking stress and anhedonia might involve prefrontal cortex (PFC) regions. Specifically, a large body of electroencephalographic (EEG) literature suggests that the left and right PFC are critically implicated in approach-related and withdrawal-related affect, respectively (Davidson 2004; Gotlib et al 1998; Henriques and Davidson 2000; Pizzagalli et al 2002, 2005b). Consistent with an asymmetrical involvement in approach-related affect, we recently found that resting (task-free) EEG hypoactivity in left dorsolateral PFC regions (as well as medial orbitofrontal regions) was associated with decreased reward bias in a monetarily reinforced task (Pizzagalli et al 2005b). Based on these EEG findings as well as animal data indicating asymmetrical dopaminergic activation in response to stressors (Carlson et al 1988, 1993), we speculate that acute stressors may induce hypoactivation in the left prefrontal cortex and thus induce blunted reward responsiveness. Alternatively, based on reports that acute administration of the stress hormone cortisol leads to increased right PFC activation

(Tops et al 2005), a region critically implicated in anxiety and withdrawal-related affect (Davidson 2004; Pizzagalli et al 2002), reduced appetitive behavior during acute stressors may arise due to increased inhibitory effects of right PFC regions over homologous left PFC regions subserving approach-related affect (Daskalakis et al 2002; Allison et al 2000; Sullivan 2004). Measurements of brain electrical activity in similar laboratory based reward task in conjunction with acute stressors will be needed to test these alternative hypotheses.

Limitations and Future Directions

The limitations of this study deserve mention. First, although the affective responses to the stress manipulations were as hypothesized, no physiological measures (e.g., skin conductance and cortisol) were collected to confirm the effects of the stress manipulation. Second, although the present findings are in line with extensive preclinical evidence emphasizing stress-mediated hedonic deficits, due to their purely behavioral nature, they cannot provide any evidence about putative neural mechanisms linking stress and blunted hedonic capacity. Third, only female participants were considered, a choice motivated by the increased prevalence of depression in women compared with men following stressful life events (Maciejewski et al 2001). Although the present findings highlight a potential vulnerability to stress induced hedonic deficits in females, future studies will be needed to evaluate whether these findings extend to males. Fourth, although both stressor manipulations led to similar decreases in hedonic capacity during the stressful condition, this reduction was not statistical significant for the performance feedback manipulation. The reasons for this null finding are not entirely clear.

Possibly, the anxiety and negative affect generated by the threat-of-shock manipulation coupled with the evaluative aspects of the stressor may be required to induce hedonic deficits. Future studies will be needed to identify the specific aspects of psychosocial stressors that lead to hedonic deficits. Limitations notwithstanding, the present findings indicate that acute stress impaired hedonic capacity, particularly in subjects reporting elevated levels of anhedonic symptoms, raising the possibility that stress-induced hedonic deficits may be a candidate mechanism underlying the etiology and pathophysiology of depression.

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Table 1. Pearson Correlations between Measures of Mood and Response Bias During the Stress and No-Stress Conditions for the Threat-of-Shock (n = 38) Manipulation

	Stress RB	Control RB
MASQ AD	-0.30*	-0.24
MASQ GDD	-0.31	0.01
MASQ AA	-0.14	0.15
MASQ GDA	-0.12	-0.11
BDI	-0.16	-0.17
BDI Anhedonic Score	-0.33*	0.02

BDI, Beck Depression Inventory-II (Beck et al 1996). BDI Anhedonic Score = sum of items 4 (loss of pleasure), 12 (loss of interest), 15 (loss of energy), and 21 (loss of interest in sex). MASQ, Mood and Anxiety Symptom Questionnaire (Watson et al 1995). AD, Anhedonic Depression; GDD, General Distress Depression; AA, Anxious Arousal; GDA, General Distress Anxiety. *$p < .10$, **$p < .05$.

Figure Legends

Figure 1. (**A**) Schematic representation of the task design and trial presentation; in this example, the mouth version of the task is shown. (**B**) Example of the no-stress condition for the performance feedback manipulation (with mouth version). (**C**) Example of the stress condition for the threat-of-shock manipulation (with nose version). During the experiment, facial features were presented in white against a black background, and the bar used to signal the presence of the stressor was multicolor.

Figure 2. Overall effect of task manipulation on behavioral measures. (**A**) Response bias (entire sample; *n*_80); (**B**) accuracy (threat-of-shock manipulation; *n* _ 38); (**C**) discriminability (entire sample; *n* _ 80). Error bars represent standard errors. The black bars represent the stress condition while the light gray bars represent the no-stress condition.

Figure 3. Overall effect of task manipulation on self-reported measures of affect and anxiety for the entire sample (*n*_80). (**A**) Negative affect (NA) and (**B**) STAI anxiety. Error bars represent standard errors. The black bars represent the stress condition while the light gray bars represent the no-stress condition.

Figure 1

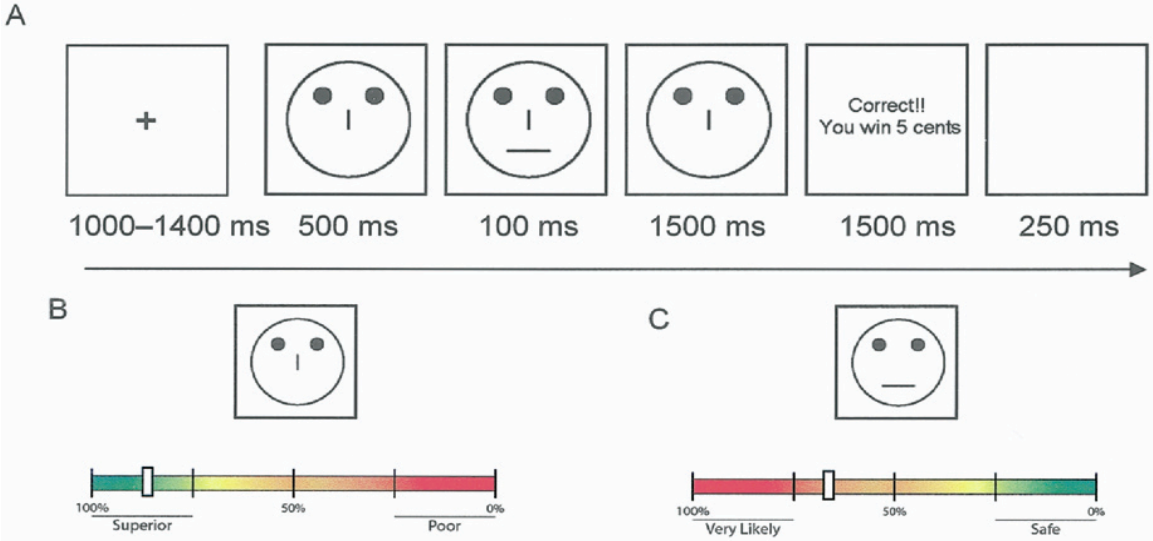
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Figure 2

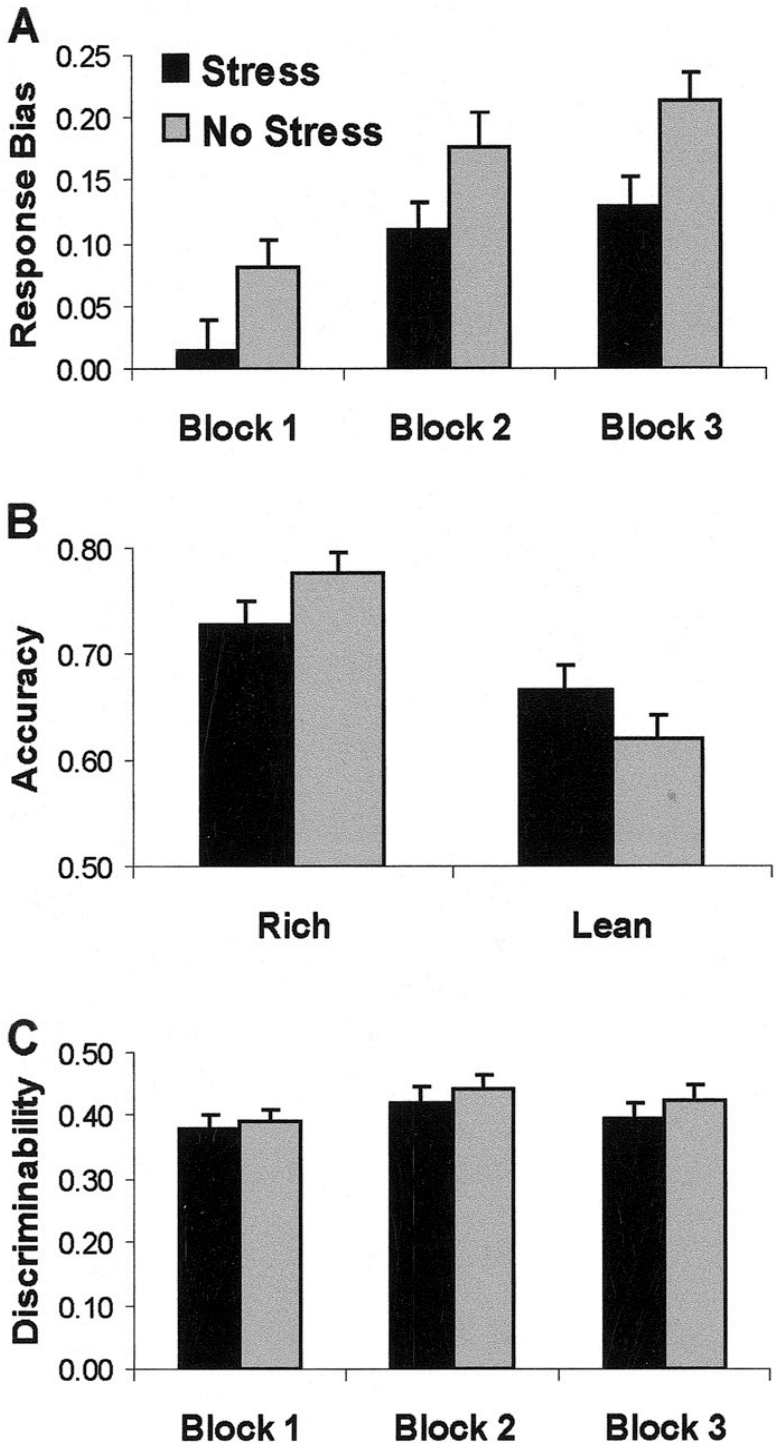
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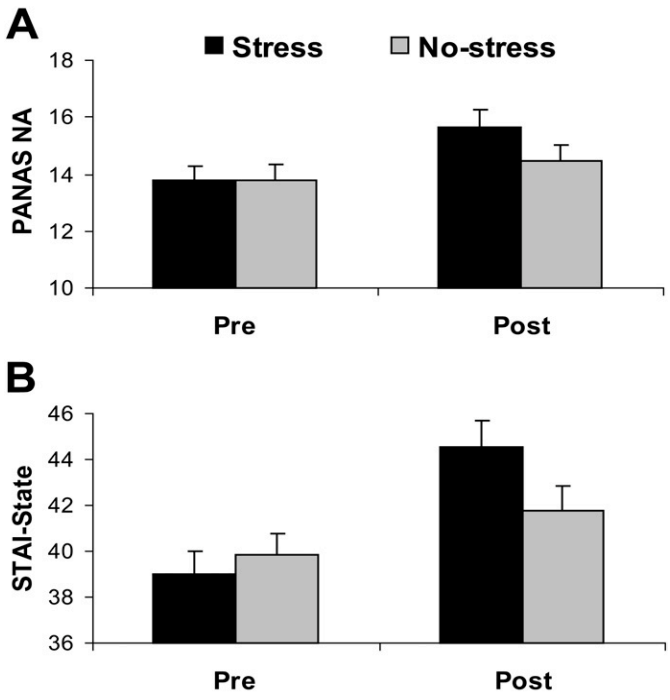
Figure 3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