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Increased Perceived Stress is Associated with Blunted Hedonic Capacity: Potential Implications for Depression Research

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Abstract

Preclinical studies suggest that stress exerts depressogenic effects by impairing hedonic capacity; in humans, however, the precise mechanisms linking stress and depression are largely unknown. As an initial step towards better understanding the association between stress and anhedonia, the present study tested, in two independent samples, whether individuals reporting elevated stress exhibit decreased hedonic capacity. The Perceived Stress Scale (PSS) measured the degree to which participants appraised their daily life as unpredictable, uncontrollable, and overwhelming. Hedonic capacity was objectively assessed using a signal-detection task based on a differential reinforcement schedule. Decreased reward responsiveness (i.e., the participants' propensity to modulate behavior as a function of reward) was used as an operational measure of hedonic capacity. In both Study 1 (n = 88) and Study 2 (n = 80), participants with high PSS scores displayed blunted reward responsiveness and reported elevated anhedonic symptoms. Additionally, PSS scores predicted reduced reward responsiveness even after controlling for general distress and anxiety symptoms. These findings are consistent with preclinical data highlighting links between stress and anhedonia, and offer promising insights into potential mechanisms linking stress to depression.

Keywords

Affect; Anhedonia; Depression; Dopamine; Reward; Stress

Introduction

The role of stress in the development, expression, and exacerbation of depression is well established (Brown & Harris, 1989; Kendler et al., 1995; Hammen, 2005). Epidemiological research has found that stress can induce depressive symptoms (Lloyd, 1980; Kendler, Karkowski & Prescott, 1999) and is associated with poorer treatment prognosis and more frequent relapse (Tennant, 2002). Importantly, the impact of a particular stressor varies across individuals. As a result, the likelihood for a depressive episode is hypothesized to increase when individuals perceive stress as uncontrollable, unpredictable, and severe, and deem coping resources as insufficient (Akiskal and McKinney, 1973; Hammen, 2005). Perception of

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uncontrollability of stressors, in particular, has been found to have profound physiological, cognitive, and motivational consequences (Breier, 1989; Dickerson & Kemeny, 2004; Maier & Walkins, 2005; Seligman, Maier & Geer, 1968) and increase vulnerability to emotional disorders (Chorpita & Barlow, 1998). In spite of this association between stress and depression, the mechanisms underlying this link remain largely unknown.

A convergence of several independent lines of evidence raises the possibility that anhedonia – the loss of pleasure or lack of reactivity to pleasurable stimuli (American Psychiatric Association, 2000) – might be a promising link between stress and depression. First, various animal models show that exposure to uncontrollable and unpredictable stressors induce depression-like, particularly "anhedonic", behavior (e.g., Anisman & Matheson, 2005; Seligman, Maier & Geer, 1968; Weiss & Simson, 1985) and dysfunctions in dopaminergic reward pathways (Cabib & Puglisi-Allegra, 1996; Pani, Porcella & Gessa, 2000). These preclinical findings are intriguing because depression has been not only associated with dysregulated stress responsiveness (Ehlert, Gaab & Heinrichs, 2001; Gold & Chrousos, 1999) but also with dysfunctions in the brain reward system (e.g., Keedwell, Andrew, Williams, Brammer & Phillips, 2005; Tremblay, Naranjo, Cardenas, Herrmann & Busto, 2002).

Second, the personality trait of "locus of control" (Rotter, 1966) has been found to influence reactivity to both stressors and reinforcements. Specifically, an external locus of control (i.e., a tendency to attribute consequences and events to external factors such as luck, other people, or uncontrollable forces) has been associated with (1) a reduced anticipation that a specific behavior will lead to a reward (e.g., Rotter, 1966); (2) increased psychological and biological stress reactivity (e.g., Bollini, Walker, Hamann, & Kestler, 2004; Kobasa, 1979); and (3) dysregulation of plasma concentrations of dopamine metabolites (De Brabander & Declerk, 2004). These findings suggest that individuals characterized by low perception of control are less responsive to rewards and more sensitive to stressors, possibly due to subtle differences in the mesolimic dopamine reward system (Declerck, Boone, & De Brabander, 2006).

Third, individuals suffering from melancholic depression, a subtype of depression characterized by anhedonic features, often show hypercortisolemia (Gold & Chrousos, 1999; Ehlert et al., 2001; Gold & Chrousos, 2002) and report higher levels of subjective severity, but not number, of minor daily stressors compared to control individuals and individuals with nonmelancholic depression (Willner, Wilkes & Orwin, 1990). Along similar lines, participants with social anhedonia reported higher perceived stress than control participants despite comparable exposure to life stressors (Horan et al., 2007).

Finally, limited empirical evidence indicates that acute stressors can decrease hedonic capacity in humans. In an influential paper, Berenbaum & Connelly (1993) reported that an acute stressor (military training) reduced self-reported rating of pleasure in response to an enjoyable movie (Study 1). These findings were replicated in a second study, in which a different acute stressor (final examinations) reduced self-reported pleasure and positive affect in an undergraduate sample. In this second study, a 1-item perceived stress score was unrelated to pleasure ratings. Interestingly, in both studies, the deleterious effects of the acute stressor were greatest in participants with a familial history of depression, indicating that stress-induced reduction in hedonic capacity may be particularly pronounced in individuals with increased vulnerability to depression. Recently, we experimentally extended the Berenbaum & Connelly's (1993) findings by showing that an acute laboratory stressor (threat-of-shock) reduced an objective measure of hedonic capacity, particularly in participants reporting elevated baseline anhedonic symptoms (Bogdan & Pizzagalli, 2006). Collectively, these lines of evidence suggest that both acute stressors as well as low perception of control over stressors might lead to blunted hedonic capacity and a diminished ability to experience pleasure.

The goal of the present studies was to test the hypothesis that a low perception of control over ongoing stressors might be associated with a reduced hedonic capacity. Unlike prior research (Berenbaum & Connelly, 1993), hedonic capacity was objectively assessed using a signal-detection task that measured participants' propensity to modulate behavior as a function of reward (Bogdan & Pizzagalli, 2006; Tripp & Alsop, 1999; Pizzagalli, Jahn, O'Shea, 2005). Based on the evidence reviewed above, we hypothesized that participants perceiving their lives as uncontrollable, unpredictable, and stressful would display reduced hedonic capacity. This hypothesis was tested in two independent studies.

STUDY 1

Methods

Participants—Eighty-eight Harvard University undergraduates (48 female; age: 22.20, SD: 4.42) participated in this study. All participants provided informed written consent and were right-handed (Chapman & Chapman, 1987). Study remuneration consisted of course credit or $5. In addition, participants received money (on average $6) as part of the experimental task. For motivational reasons, participants were told that their performance dictated how much money they "won" during the task, but in actuality, this amount was predetermined. All aspects of the study were approved by the Committee on the Use of Human Subjects in Research at Harvard University.

Tasks and Procedures—Participants completed a signal-detection task designed to assess reward responsiveness (Pizzagalli et al., 2005). Reward responsiveness, an individual's propensity to modulate behavior according to reward history, was used to operationalize hedonic capacity. The signal-detection task employed an asymmetric reinforcement schedule to produce a response bias for selecting the more frequently rewarded of two possible stimuli (Tripp & Alsop, 1999). The task involved three blocks of 100 trials. At the beginning of each trial, an asterisk was presented for 500 ms, followed by a mouth-less cartoon face. After a delay of 500 ms, either a short mouth (11.5 mm) or a long mouth (13 mm) was presented for 100 ms. For each trial, the participants' objective was to decide, via button press (either the "z" or the "/" key on a standard keyboard), whether a short mouth or a long mouth appeared. Throughout the task an equal number of long and short mouths appeared according to a pseudorandomized sequence. Correct identification of either the short or long mouth was rewarded ("Correct!! You won 5 Cents") three times as often as correct identification of the other mouth, resulting in a more frequently rewarded "rich stimulus" and a less frequently rewarded "lean stimulus".

The reward feedback was presented for 1750 ms immediately after the correct response. Both the mouth rewarded more frequently and the keys used to identify each mouth were counterbalanced across participants. To guarantee the proper reward ratio, only 40 correct trials (30 rich, 10 lean) per each 100-trial block were rewarded. Participants were informed that they would not receive reward feedback after all correct responses.

The signal-detection task has been empirically validated by findings suggesting that individuals with elevated depressive symptoms (Pizzagalli et al., 2005) as well as unmedicated individuals with unipolar depression (Pizzagalli et al., in preparation) are characterized by impaired reward responsiveness. Critically, in prior independent samples, reward responsiveness was negatively correlated with anhedonic symptoms, rather than overall depression severity (Bogdan & Pizzagalli, 2006; Pizzagalli et al., 2005), and predicted anhedonic symptoms (assessed by summing the items "loss of pleasure", "loss of interest", "loss of energy" and "loss of interest in sex" in the Beck Depression Inventory; Beck, Steer, & Brown, 1996) one month later, even when adjusting for general negative affectivity (Pizzagalli et al., 2005). These findings are intriguing, particularly because BDI items assessing loss of interest or pleasure in

appetitive, sex, social activities, and work activities best characterized anhedonic depressed inpatients in a clinical sample (Fawcett, Clark, Schetner, & Hedeker, 1983). Overall, these findings indicate that this task provides an objective assessment of participants' hedonic capacity, correlating specifically with self-report of anhedonia as opposed to general symptoms of distress.

Following the signal-detection task, participants completed several questionnaires, including the Perceived Stress Scale (PSS; Cohen, Kamarck & Mermelstein, 1983), the Beck Depression Inventory II (BDI-II; Beck, Steer, & Brown, 1996), and the Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995). The BDI-II is a reliable and well-validated self-report instrument of depressive symptomatology used to assess levels of depressive symptoms. The MASQ is a reliable self-report measure with four subscales assessing symptoms specific to either anxiety (Anxious Arousal, AA) or depression (Anhedonic Depression, AD), as well as non-specific distress symptoms (General Distress Anxiety, GDA and General Distress Depression, GDD).

The PSS was selected to assess individual differences in stress appraisal. This instrument was chosen because (a) it is among the most widely used self-report assessments in studies of stress and health; (b) its validity has been shown in numerous studies investigating stress hormones, illness, and bodily symptoms; and (c) it has higher heritability estimates compared to other scales assessing stress perception (Cohen et al., 1983; Vedhara et al., 2003; Ebrecht, Hextall, Kirtley, Taylor, Dyson & Weinman, 2004; Federenko, Schlotz, Kirschbaum, Bartels, Hellhammer & Wust, 2006). Moreover, perception of uncontrollability has been found to robustly activate the physiological stress responses (Breier, 1989; Dickerson & Kemeny, 2004) and increase vulnerability for anxiety and depressive disorders (Chorpita & Barlow, 1998).

The PSS consists of 14 items, which include statements such as: "*In the last week, how often have you felt that you were unable to control the important things in your life?*" or "*In the last week, how often have you found that you could not cope with all the things that you had to do?*" Each item is scored on a 5-point Likert scale, ranging from 0 (never) to 4 (very often). Prior work suggests that the scale has adequate internal and short-term reliability (coefficient alpha reliability: 0.84; two-day test-retest reliability: 0.85; Cohen et al., 1983; Hewitt, Flett & Mosher, 1992).

Data Reduction and Statistics—Following established procedures, performance in the signal-detection task was analyzed with respect to response bias (log *b*) and discriminability (log *d*) (Davison & Tustin, 1978), which were computed as:

$$\log b = \frac{1}{2}\log\left(\frac{Rich_{correct} * Lean_{incorrect}}{Rich_{incorrect} * Lean_{correct}}\right)$$

$$\log d = \frac{1}{2}\log\left(\frac{\mathrm{Rich}_{correct} * \mathrm{Lean}_{correct}}{Rich_{incorrect} * Lean_{incorrect}}\right)$$

These formulae were adjusted using the so-called "log-linear rule", which involves adding 0.5 to every cell of the detection matrix. This adjustment allows the computation of response bias and discriminability in cases that contain a zero in one cell of the formula (Hautus, 1995). Response bias indicates the systematic preference for the response paired with the more frequent reward ("rich stimulus"), and was the main variable of interest. Discriminability as well as accuracy for the rich and lean stimuli were analyzed to rule out task-unspecific group differences.

In the present sample, inter-item reliability of the PSS (Cronbach's alpha coefficient: 0.82) mirrored the satisfactory reliability reported elsewhere (Cohen et al., 1983). To identify subjects reporting high vs. low perceived stress and maximize the number of subjects included in the analyses, a median-split approach on PSS scores was used. This approach is in line with prior studies that have used the PSS scale categorically to identify low vs. high PSS scorers (e.g., Kuiper, Olinger, & Lyons, 1986; Maes, Van Bockstaele, & Van Gastel, 1999; van Eck, Berkhof, Nicolson, & Sulon, 1996).

For response bias and discriminability mixed analyses of variance (ANOVA) were conducted with *Group* (high PSS, low PSS) and *Block* (1,2,3) as factors. For accuracy, *Stimulus* (Rich, Lean) was included as an additional factor. To test whether groups differed in anxiety-specific, depression-specific, or general distress symptoms, a *Group* (high PSS, low PSS) × *MASQ Subscale* (GDA, AA, GDD, AD) was performed. When appropriate, the Greenhouse-Geisser correction was applied. Post-hoc Newman Keuls tests were run after significant ANOVA effects. Throughout, effect sizes (partial eta^2) are reported.

In a second, complementary approach, a set of hierarchical regression analyses were performed to investigate whether differences in stress perception uniquely predicted response bias. Since prior studies have shown that measures of perceived stress can contain components of non-specific distress and negative affect (e.g., Watson & Pennebaker, 1989), the regression analyses adjusted for distress and anxiety symptoms, as assessed by the MASQ AA and GDA subscales. To this end, GDA and AA were simultaneously entered in the first step of the regression followed by PSS group (dummy coded) to predict: (a) development of response bias (Block 3 - Block 1); or (b) response bias at the end of the experiment (Block 3). A hierarchical regression was used instead of the analysis of covariance (ANCOVA) to prevent confounds caused by the covariate (e.g., GDA and AA) correlating with the independent variable (PSS score) (Cohen & Cohen, 1983; Miller & Chapman, 2001).

Results

Demographic and self-report data—Using a median split approach, participants with relatively higher PSS scores (n = 42; mean PSS score: 28.19±5.11; range: 23-43) and those with relatively lower PSS scores (n = 45; 17.24±4.26; range: 4-22) were identified. The high and low PSS groups did not differ with respect to age (22.26±5.66 vs. 22.13±5.32; $t(85) = 0.11$, $p = 0.90$), gender ratio (female/male: 24/18 vs. 23/22; Fisher exact test, $p > 0.14$), and smoking status (smoker/non-smoker: 2/40 vs. 3/42; Fisher exact test, $p = 0.32$). High PSS participants reported significantly higher BDI scores (11.71±8.01 vs. 4.68±3.94, $t(85) = 5.20$, $p < 0.001$).

The *Group* (high PSS, low PSS) × *MASQ Subscale* (GDA, AA, GDD, AD) ANOVA revealed significant main effects of *MASQ Subscale* ($F(3,255) = 613.20$, $p < 0.001$, partial eta$^2 = 0.878$, $\varepsilon = 0.58$) and *Group* ($F(1,85) = 36.24$, $p < 0.01$, partial eta$^2 = 0.299$). Interestingly, the main effect of *Group* was qualified by a significant *Group* × *MASQ Subscale* interaction ($F(3,255) = 11.73$, $p < 0.01$, partial eta$^2 = 0.121$, $\varepsilon = 0.92$). As shown in Fig. 1A, although groups differed on all four MASQ subscales (post-hoc Neuwman Keuls *p*s < 0.01), differences were most pronounced for the general depression (GDD) and anhedonic depression (AD) subscales.

ANOVA analyses: Effects of PSS on task performance Exploratory analyses revealed no gender effects on response bias; accordingly, gender was not considered in the analyses.

Response Bias The *Group* × *Block* interaction was the only effect emerging, $F(2,170) = 4.98$, $p < 0.01$, partial eta$^2 = 0.055$, $\varepsilon = 0.92$ (Fig. 2A). Post-hoc Newman Keuls tests indicated that low, but not high, PSS participants had significantly higher response bias in Blocks 3 compared to both Block 1 ($p < 0.0005$) and Block 2 ($p < 0.03$). In Block 3, high PSS participants displayed significantly lower response bias than low PSS participants ($p < 0.007$). Further analyses

indicated that, compared to low PSS participants, high PSS participants had significantly lower increases from Block 1 to 3 [-0.02±0.24 vs. 0.12±0.27; $t(85) = -2.58$, $p < 0.015$] and from Block 2 to 3 [-0.03±0.21 vs. 0.09±0.22; $t(85) = 2.63$, $p < 0.010$], highlighting impaired reward learning.

Discriminability No significant effects emerged (*Block:* $F(2,170) = 2.21$, $p > 0.10$; *Group:* $F(1,85) = 0.06$, $p > 0.80$; *Group × Block:* $F(2,170) = 0.41$, $p > 0.60$). Based on these findings, discriminability was not considered in Study 2.

Accuracy The *Group × Block × Stimulus* ANOVA revealed a significant *Stimulus* effect ($F(1,85) = 82.86$, $p < 0.001$, partial $eta^2 = 0.494$), due to higher accuracy for the rich compared to the lean stimulus. Critically, the *Group × Block × Stimulus* interaction was also significant, $F(2,170) = 3.21$, $p < 0.05$, partial $eta^2 = 0.036$. Follow-up ANOVAs performed for the rich and lean stimuli separately indicated that this effect was a result of a significant *Group × Block* interaction for the lean ($F(2,170) = 4.25$, $p < 0.017$), but not rich ($F(2,170) = 0.55$, $p > 0.90$) condition. This interaction was due to increases in lean accuracy across the blocks for high, but not low, PSS participants (Fig. 2B). Post-hoc tests revealed, however, no significant differences.

Regression analyses Two hierarchical regressions were performed to examine whether PSS group explained significant variance in response bias after adjusting for individual differences in anxiety symptoms and general distress. PSS group uniquely predicted both response bias development ($\Delta R^2 = 0.049$, $\Delta F(1,83) = 4.37$, $p < 0.040$) as well as the response bias at the end of the experiment (Block 3) ($\Delta R^2 = 0.054$, $\Delta F(1,82) = 4.96$, $p < 0.030$) even after controlling for the MASQ GDA and AA subscores.

STUDY 2

Methods

Study 2 provided a conceptual replication of Study 1, and involved a re-analysis of recent data from our laboratory (Bogdan & Pizzagalli, 2006). The new analyses assessed whether participants with high PSS scores are characterized by reduced hedonic capacity, a topic not investigated in Bogdan & Pizzagalli (2006). Data from 80 female participants were available. All participants were right-handed (Chapman & Chapman, 1987); reported no past or present neurological, psychiatric, hormonal, or metabolic disturbances; and were recruited from the community and introductory psychology courses. Their mean age was 21.64 years (S.D.: 2.33). Using a median-split procedures, 36 participants were included in the high PSS group (mean PSS: 30.06±5.49; range: 24-48), whereas 38 participants were included in the low PSS group (mean PSS: 17.26±3.83; range: 5-22).

The task, procedure, and data analyses were identical to Study 1, with one main exception. In Study 2, participants completed the reward task under both a stress (threat-of-shock or negative performance feedback) and no-stress condition, the order of which was counterbalanced across participants. To allow comparability with Study 1, only data from the no-stress condition were considered here. In the no-stress condition, participants were instructed that (a) it would be impossible for them to receive a mildly aversive, but not painful, shock; *or* (b) their performance was within the 75th –100th percentile of past participants.

Results

Demographic and self-report data—As in Study 1, high PSS subjects reported significantly higher BDI scores compared to low PSS subjects (12.39±6.24 vs. 4.79±4.54, $t(72) = 6.01$, $p < 0.001$). Further replicating findings from Study 1, the *Group × MASQ*

Subscale ANOVA revealed significant effects of *MASQ Subscale* ($F(3,213) = 412.77$, $p < 0.001$, partial $eta^2 = 0.853$ $\varepsilon = 0.61$), *Group* ($F(1,71) = 58.14$, $p < 0.01$, partial $eta^2 = 0.450$), and, more importantly, *Group* × *MASQ Subscale* ($F(3,255) = 5.67$, $p < 0.006$, partial $eta^2 = 0.074$, $\varepsilon = 0.61$). Although groups differed on all MASQ subscales (post-hoc Neuwman Keuls *p*s < 0.01), as in Study 1, the largest group differences emerged for the GDD and AD subscales (Fig. 1B).

ANOVA analyses: Effects of PSS on task performance Exploratory analyses revealed no differences in response bias between participants completing the no-stress condition before or after the stress condition (all *F*s < 0.584, all *p*s > 0.55). Consequently, condition order was not further considered.

Response Bias The ANOVA revealed a significant *Block* effect ($F(2,144) = 15.06$, $p < 0.001$, partial $eta^2 = 0.173$), due to a systematic increase in response bias over blocks. Importantly, a reliable *Group* effect also emerged ($F(1,72) = 5.95$, $p < 0.02$, partial $eta^2 = 0.076$), due to significantly higher response bias in low than high PSS participants (Fig. 3A). When considering development of response bias across the blocks, no significant group differences emerged [all *t*s(72) < 1.63, $p > 0.100$)].

Accuracy As in Study 1, the *Stimulus* effect was significant ($F(1,72) = 61.27$, $p < 0.001$, partial $eta^2 = 0.460$), due to higher accuracy for the rich compared to the lean stimulus. In addition, the *Group* × *Block*, *Block* × *Stimulus*, and more importantly, the *Group* × *Stimulus* interactions were significant [all *F*s > 3.44, all *ps* < 0.037). Newman-Keuls post-hoc tests exploring the latter interaction indicated that, compared to low PSS participants, high PSS participants had significantly higher accuracy for the lean stimulus ($p < 0.005$; Fig. 3B). No group differences emerged for the rich stimulus ($p > 0.40$). For both groups, accuracy was significantly higher for the rich than lean stimulus (both *ps* < 0.0005).

Regression analyses—As in Study 1, two hierarchical regressions were performed to examine whether PSS group explained unique variance in response bias after adjusting for individual differences in general distress and anxiety symptoms, as assessed by the MASQ GDA and AA subscales. Findings revealed that PSS group was a significant predictor of response bias at the end of the experiment (Block 3), $\Delta R^2 = 0.053$, $\Delta F(1,70) = 4.02$, $p < 0.050$. For Response Bias development (Block 3 – Block 1), however, the model was not significant (ΔR^2=0.014, $\Delta F(1,70) = 0.99$, $p > 0.30$).

Integration of Study 1 and 2—Study 1 and 2 were not only performed on independent samples but also differed with respect to experimental design. Specifically, half of the subjects in Study 2 performed the signal-detection task after exposure to an acute stress manipulation. To evaluate whether this difference diminished comparability between studies, an ANOVA with *Study* (Study 1, Study 2) and *Group* (high PSS, low PSS) as between-subject factors and *Block* (1,2, 3) as repeated measure was performed on response bias data. The only significant findings were the main effects of *Block* ($F(2,314) = 13.576$, $p < 0.001$), *Group* ($F(1,157) = 5.84$, $p < 0.02$), and the *Group* × *Block* interaction ($F(2,314) = 4.29$, $p < 0.015$), which was due to increasing group differences across the blocks (Table 1). The main effect of *Study* or the *Study* × *Group* × *Block* interaction were not significant (all *F*s < 2.12, all *p*s > 0.12). Compared to low PSS subjects (n = 83), high PSS subjects (n = 78) showed significantly lower reward learning (response bias Block 3 – response bias Block 1: 0.13±0.24 vs. 0.03±0.23; $t(159) = -2.72$, $p < 0.008$).

General Discussion

A large body of research suggests that uncontrollable stressful events are particularly potent depression antecedents. Specifically, human and animal data indicate that lack of control over stressors exacerbates stress responses and predicts depression (Seligman et al., 1968; Breier, 1989; Brown & Harris, 1989; Anisman & Matheson, 2005; Hammen, 2005). However, the precise mechanisms linking stress and depression, remain largely unexplored in humans.

Inspired by preclinical evidence indicating that stressors can induce anhedonic-like behavior in animals, the main goal of the present studies was to test the hypothesis that elevated levels of perceived stress would be associated with reduced hedonic capacity in a non-clinical population. This hypothesis was confirmed in two independent samples.[1] Participants who appraised recent situations in their life as stressful, unpredictable, and uncontrollable had significantly lower reward responsiveness than comparison participants. Since reward responsiveness was measured as the degree of response bias toward the more frequently rewarded alternative, participants with high PSS scores had a diminished propensity to modulate behavior as a function of prior exposure to reinforcements (i.e., exhibited reduced hedonic capacity). Consistent with this conclusion, in both Study 1 and 2, participants reporting elevated PSS scores showed *higher* accuracy for the less frequently rewarded ("lean") stimulus compared to low PSS participants, further emphasizing that their performance was less influenced by the asymmetric reward contingency.[2] Critically, in both studies, high PSS scores predicted blunted response bias at the end of the experiment even after controlling for general distress and anxiety-specific symptoms (anxious arousal), suggesting that perceived stress plays a unique role in hedonic capacity.

Before further discussion of these findings is provided, two important limitations of the current study are worth noting. First, because the present signal-detection task included only a reward manipulation, we cannot fully rule out the possibility that participants reporting elevated perceived stress might be less responsive to any form of feedback, irrespective of reward. Although a modified task incorporating various forms of feedback (e.g., punishment, reward, and abstract feedback) will be required to test these alternative interpretations conclusively, recent findings from our laboratory highlight a rather specific link between anhedonia and response bias, as assessed through the present paradigm. As mentioned above, in an independent sample, decreased reward responsiveness was associated with elevated levels of self-reported anhedonic symptoms (e.g., loss of pleasure, energy, interest, and libido) and predicted anhedonic symptoms one month later, even after adjusting for initial anhedonic symptoms and general negative affect (Pizzagalli et al., 2005). Based on these prior findings and preclinical evidence indicating that uncontrollable stressors decrease animals' sensitivity to reward (Zacharko, Bowers, Kokkinidis, Anisman, 1983; Henn & Vollmayer, 2005; Willner, 2005), we believe that the interpretation of decreased hedonic capacity in participants with high PSS scores is the most parsimonious explanation. Second, although we were able to statistically control for concurrent distress and anxiety symptoms, the correlational nature of our studies does not allow us to determine whether reported global stress indicated by the PSS led to decreased hedonic capacity on the reward responsiveness task or whether pre-existing anhedonia resulted in greater perception of stress. As a result, the study goal was not to make

[1] In Study 1, the main finding emerging from the ANOVA on response bias scores was a significant *Group* × *Block* interaction, which was due to lower response bias at the end of the experiment (Block 3) as well as impaired reward learning in participants with elevated PSS scores. In Study 2, only a main effect of *Group* emerged, indicating that participants with high PSS scores had a diminished response bias overall. Although findings from both studies converge in suggesting decreased hedonic capacity in participants with high PSS scores despite differences in the experimental design, the reason for this difference in significant effects is not entirely clear.

[2] The lack of group differences in discriminability as well as the finding of higher accuracy for the less frequently rewarded stimulus in participants with high PSS scores rule out the possibility that the response bias findings were confounded by non-specific factors (e.g., differences in task difficulty or task disengagement).

a directional claim of causality, but instead to test the *a priori* hypothesis that individual differences in perceived stress would be associated with reduced hedonic capacity.

Whereas the correlational and cross-sectional nature of the present study does not allow conclusions about possible mechanisms underlying stress-depression relations, recent animal and human work has begun to elucidate this important association. In animals, chronic stressors have been found to impact the mesocorticolimbic dopamine pathways implicated in reward processing (Wise, 2004; Schultz, 2002) and induce anhedonic-like symptoms (Cabib & Puglisi-Allegra, 1996; Moore, Rose, & Grace, 2001). Of relevance to the present study, this animal research suggests that stressor controllability is an important factor influencing the relationship between stress, dopamine, and hedonic behavior. Specifically, uncontrollable stressors result in a reduction of dopamine release in the mesoaccumbens dopamine system and impaired responding to reward while controllable stressful experiences can produce the opposite effects (Cabib & Puglisi-Allegra, 1996; Moore et al., 2001). Although caution should be used when extrapolating from non-human research, it is interesting to note that, in healthy humans, exposure to uncontrollable stress elicits stronger neuroendocrinological and behavioral responses (increased ratings of lack of success, lack of control, helplessness, and depression) than identical amounts of controllable stress (Breier, 1989; Breier, Albus, & Pickar, 1987).

Findings from recent experimental studies in humans are also consistent with the hypothesis that stressors can reduce hedonic capacity. For example, in a study using the signal-detection task, we recently reported that an acute laboratory stressor lead to blunted hedonic capacity in healthy controls (Bogdan & Pizzagalli, 2006). These findings replicated and extended a prior report showing that naturalistic acute stressors reduced self-report ratings of pleasure and positive affect (Berenbaum & Connelly, 1993). Notably, in Berenbaum and Connelly (Study 2), perceived stress was not associated with reduced hedonic capacity, but rather with increased negative affect. In the present study, perceived stress was associated with increased negative affect and anhedonia (as assessed by the MASQ AD subscale) as well as reduced hedonic capacity in a signal-detection task. Methodological differences in the assessment of perceived stress might explain this discrepancy (PSS in the present study vs. a 1-item scale in Berenbaum and Connelly). More importantly, in the present study, hedonic capacity was assessed using a laboratory-based approach, and a well-validated measure of anhedonia derived from the MASQ (Watson et al., 1995), whereas Berenbaum and Connelly used self-repot ratings of adjectives (e.g., “happy”, “joyful”; Study 1) or individually tailored scales listing activities associated with pleasure (Study 2). Despite these methodological differences, the present findings replicate prior observations linking perceived stress and negative affect (Berenbaum and Connelly, 1993), and provide new evidence that perceived stress is linked to blunted hedonic capacity

Conclusion—The present findings indicate that individual differences in *perceived* stress are associated with a reduced ability to modulate behavior as a function of prior reinforcement history. Although these findings raise the possibility that perceived stress may exert depressogenic effects by reducing individuals' propensity to modulate behavior as a function of reward-related cues, future prospective studies will be required for a conclusive test of this hypothesis.

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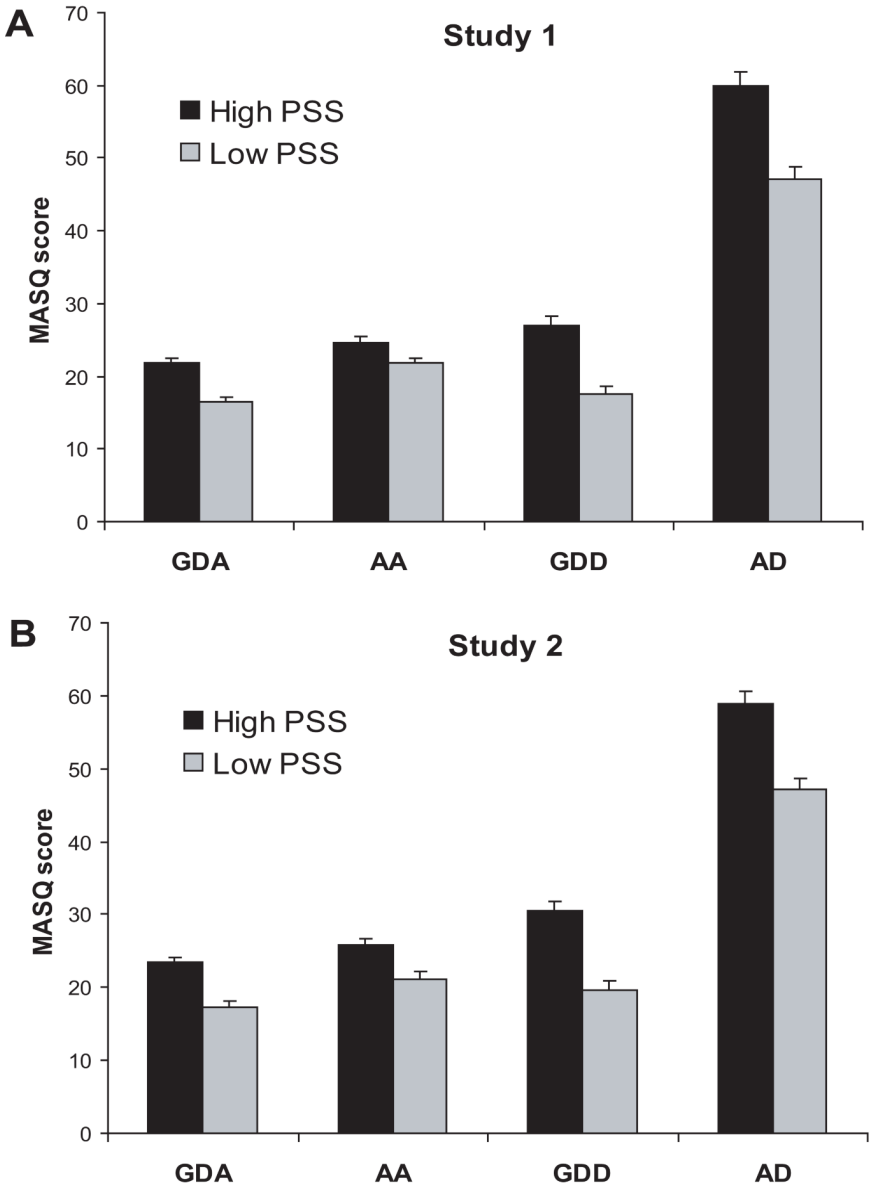

Fig. 1.

Mean score on the MASQ subscales for high PSS and low PSS participants in **(A)** Study 1 (high PSS: n = 42; low PSS: n = 45), and **(B)** Study 2 (high PSS: n = 36; low PSS: n = 38). Error bars denote S.E.

MASQ: Mood and Anxiety Symptom Questionnaire (Watson et al., 1995); GDA: General Distress Anxiety; AA: Anxious arousal; GDD: General Distress Depression; AD: Anhedonic Depression.

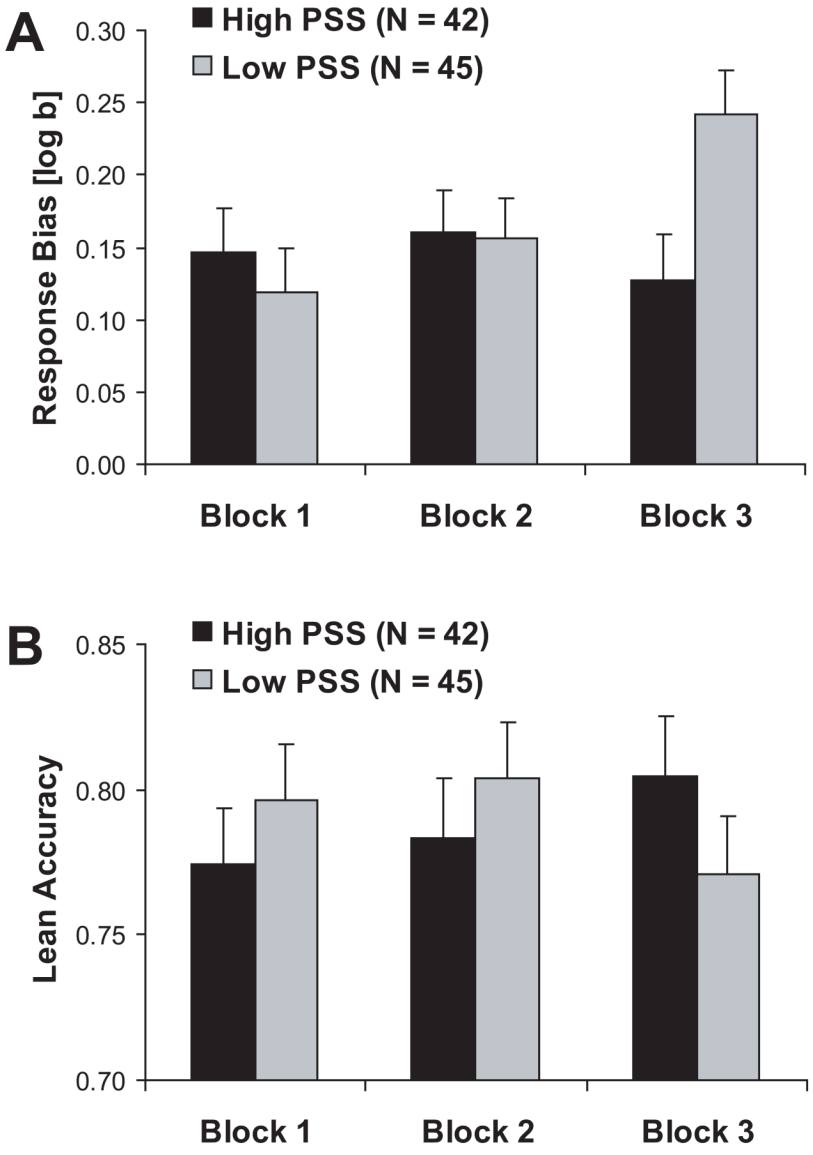

Fig. 2.

(A) Mean response bias, and **(B)** accuracy for the lean stimulus for high PSS (n = 42) and low PSS (n = 45) participants in Study 1. Error bars denote S.E.

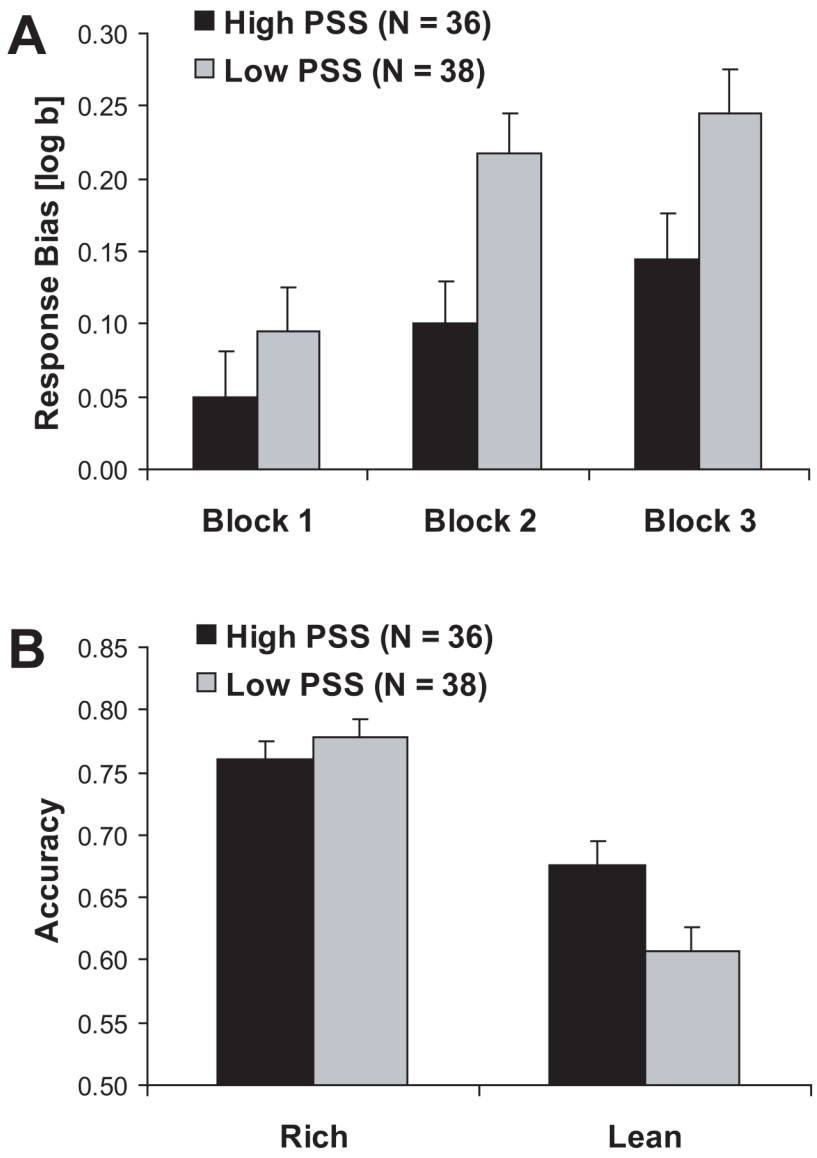

Fig. 3.

(A) Mean response bias, and **(B)** accuracy for the rich and lean stimulus for high PSS (n = 36) and low PSS (n = 38) participants in Study 2. Error bars denote S.E.

Table 1

Mean (and S.D.) response bias as a function of block for high PSS (n = 78) and low PSS (n = 83) subjects across Study 1 and 2.

	High PSS (n = 78) (Mean ± S.D.)	**Low PSS (n = 83) (Mean ± S.D.)**
Block 1	0.10±0.19	0.11±0.19
Block 2	0.13±0.21	0.18±0.20
Block 3	0.13±0.20	0.24±0.19