2010

The effect of stress on hedonic capacity in generalized anxiety disorder: A prospective experimental study of one potential pathway to depression

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The Effect of Stress on Hedonic Capacity in Generalized Anxiety Disorder:

A Prospective Experimental Study of One Potential Pathway to Depression

by

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A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Arts
Department of Psychology
College of Arts and Sciences
University of South Florida

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Date of Approval:
November 20, 2009

Keywords: major depressive disorder, reward, anhedonia, response bias, longitudinal

To A.J.M.

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The Effect of Stress on Hedonic Capacity in Generalized Anxiety Disorder:

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ABSTRACT

A growing body of work links psychopathology to changes in hedonic capacity following stressors. This was the first experimental study of the effects of stress on hedonic capacity in an analog generalized anxiety disorder (GAD) sample (a high worry group). Specifically, we utilized an experimental manipulation of stress and a behavioral index of anhedonia to test the hypothesis that individuals with GAD, who are at higher risk for developing depression symptoms, exhibit greater stress-related deficits in hedonic capacity than do nonanxious controls. Further, this study assessed whether stress-induced hedonic deficits predicted future depression. Controls exhibited the expected reward learning pattern in the baseline condition, demonstrating intact hedonic responding, as well as the expected pattern of behavioral anhedonia under stress. Contrary to predictions, worriers demonstrated intact hedonic capacity under stress. The stress effect in worriers was modulated by past depression diagnostic status; whereas worriers with no past depression demonstrated blunted baseline hedonic capacity and heightened hedonic capacity under stress, worriers with past depression demonstrated the normative response pattern. Blunted baseline response bias predicted higher future depression in both groups. We discuss the differential stress effects on behavioral hedonic capacity found as a function of worry, the role of past depression as a moderator of stress effects among worriers, and the need for future work to further explicate the mechanisms that may modulate reward response under stress.

Introduction

Major Depressive Disorder

Major depressive disorder (MDD) is a common psychiatric syndrome characterized by significant affective dysfunctions, including the cardinal symptoms of persistent low mood and/or a marked decrease in the experience of pleasurable activities (*Diagnostic and Statistical Manual of Mental Disorders, DSM-IV-TR,* American Psychiatric Association [APA], 2000). Associated MDD symptoms include fatigue, lack of concentration, appetite changes, sleep disturbance, feelings of worthlessness, psychomotor agitation or retardation, and thoughts of suicide. MDD tends to be recurrent and imposes a high long-term disease burden, leading many researchers to conceptualize it as more of a chronic condition (e.g., diabetes) than as an acute syndrome (Vos, Haby, Barendregt, Kruijshaar, Corry, & Andrews, 2004). Given the debilitating nature and high prevalence of MDD, investigators have sought variables that predict its onset and course.

Many factors have been implicated in the etiology of depression, including genetic variations (Caspi et al., 2003), personality factors (Kendler, Neale, Kessler, & Heath, 1993), stressful life events (Monroe, Slavich, Torres, & Gotlib, 2007), and previous onset of other psychopathology, especially generalized anxiety disorder (GAD; Merikangas et al., 2003). In fact, many depression investigators agree that single risk factors (e.g., gender) are rarely sufficient to explain MDD and that it is useful to consider

how multiple risk factors interact to produce depression outcomes (Hammen, 2005; Luyten, Blatt, & Houdenhove, 2006; Monroe & Simons, 1991).

One rich and compelling set of theories that address the interaction of depression risk factors are diathesis–stress theories (e.g., Brown & Harris, 1978; Hammen, 1991; Post, 1992). Diathesis–stress theories generally posit that predisposing individual difference variables interact with environmental factors to produce a depressive episode (Monroe & Simons, 1991). Diathesis–stress models thus provide a natural theoretical backbone for research aimed at understanding how risk factors, such as stress and GAD, interact and create potential pathways to depression.

Overview of the Literature Review

The current study takes an experimental, process-level approach to examining how stress interacts with a key proposed diathesis (premorbid GAD) to form a potential pathway to depression. First, diathesis–stress models of depression are described as well as how these models have been tested. Next, we discuss findings from longitudinal, naturalistic studies that suggest GAD may modify the depressogenic effects of stress, enhancing vulnerability to a depressive episode following stress. Then, anhedonia, a key feature of depression, is considered and findings about its role in the stress–depression relationship are discussed. Lastly, the purpose and rationale for a laboratory study of the stress–depression relationship is given as well as a discussion of how the present design advances the literature on stress, GAD, and depression.

Two Methods to Study the Stress–Depression Relationship

Both field and laboratory methodologies have been used to study the stress-depression relationship. There has been particular interest in longitudinal, epidemiological field studies of the impact of stressful life events on the development of depressive episodes (reviewed in Hammen, 2005; Kessler, 1997; Mazure, 1998). A substantial literature has emerged which examines the phenomenological and temporal relationship between life stress and depression in studies that retain high ecological validity. Laboratory stress studies employ experimental control of stress, allowing researchers to isolate specific processes or mechanisms involved in stress responding and potentially affording stronger causal inferences than field studies. Whereas the cost of a laboratory model is uncertain ecological validity, the benefit is the ability to explicate theory and findings of naturalistic life stress studies by experimentally testing hypotheses about causal processes. As discussed below, there is already strong evidence in the non-experimental life stress literature that stress and other risk factors are related to subsequent depression. Experimental studies are needed to examine potential causal mechanisms underlying this large effect. Though the present study takes an experimental approach, the non-experimental life stress literature is important to review because 1) findings from the non-experimental life stress literature inspired much of the theoretical basis of the present study, and 2) little experimental literature on stress and depression bears strongly on this topic.

Diathesis–Stress Models of Depression

Diathesis–stress models in the depression arena (e.g., Brown & Harris, 1978), have been used to explicate the role of stressful life events in the development of depressive episodes. Consistent with diathesis–stress models, life stress is consistently associated with onset of a depressive episode (Kessler, 1997; for a review, see Mazure, 1998). Although initial findings in this area were tempered by varied operationalizations of life stress (e.g., acute versus chronic; Monroe & Simons, 1991) and research designs which offered limited ability to draw causal inferences about life stress and depression (Kessler, 1997), recent work has moved away from simple dose-response models of stress and depression and towards more complex models that focus on the interaction between risk factors, stressors, and depression (e.g., Monroe & Harkness, 2005). Although a complete review of major views and relevant findings is beyond our present scope, it is useful to note two major themes of this literature: a) the life stress–depression relationship is dynamic, and that b) other variables (e.g., risk factors) likely interact with life stress, enhancing or blunting its depressive effects (for reviews see Hammen, 2005; Mazure, 1998; Monroe & Harkness, 2005).

Variables that Modify the Depressive Effects of Stress

An estimated 70% of first onset depressive episodes are preceded by recent major life events (Monroe & Harkness, 2005). However, "the majority of people exposed to all but the most extreme stressful life experiences do not become depressed. An attempt is made to explain this finding and, more generally, individual differences in stress reactivity by searching for characteristics of the individual or the environment in which

the individual is embedded that modify stress effects" (Kessler, 1997, p. 207). Thus, individual difference (e.g., genes, personality traits) or situational variables (e.g., poverty or other long term chronic stress), can influence whether a major life stressor induces a depressive episode. These variables have been defined by Kessler (1997) as "aspects of the personal and situational environments of people exposed to stressful events that are associated with variation in the impact of these events on their probability of becoming depressed" (p. 201). These factors are sometimes referred to as "stress modifiers" and "stress-buffering factors, vulnerability factors, or stress–diathesis factors" (Kessler, 1997, p. 207). Recent work has emphasized a dynamic, interactive relationship between the individual and the environment (e.g., Luyten et al., 2006) and has begun to examine how these factors can interact to modify the effect of stress on depression. In other words, the key question is about what factors predispose certain people to become depressed after a stressor. One line of research, for instance, looks at depression itself as a predisposing factor because depression often leads to subsequent stress (stress generation; Hammen, 1991). Researchers have examined several other factors which may modify the effect of stress on depression including neuroticism (e.g., Kendler, Kuhn, & Prescott, 2004), negative attributional style (e.g., Kwon & Laurenceau, 2002; Reff, Kwon, & Campbell, 2005); genetic vulnerability (e.g., Caspi et al., 2003) as well as several forms of premorbid psychopathology, including anxiety psychopathology (e.g., Friis, Wittchen, Pfister, & Lieb, 2002; Hettema, Kuhn, Prescott, & Kendler, 2006).

Generalized Anxiety Disorder as a Risk Factor for Depression

Generalized anxiety disorder (GAD), a diagnosis characterized by at least six months of anxiety symptoms, including chronic, uncontrollable worry (DSM-IV, APA, 2000), is a known risk factor for depression that may sensitize people to the depressive effects of stress. GAD and MDD are often comorbid (Kessler, Chiu, Demler, & Walters, 2005; Wittchen, Zhao, Kessler, & Eaton, 1994). Specifically, MDD is more highly related to GAD than any other anxiety disorder (Brown, Chorpita, & Barlow, 1998; Kessler, Chiu, et al., 2005), with the most common pattern of onset being GAD predating the first onset of depression (Breslau, Schultz, & Peterson, 1995). Though substantial evidence suggests that GAD and MDD share a common genetic diathesis (e.g., Kendler, Kessler, Walters, & MacLean, 1995; Kendler, Gardner, Gatz, & Pedersen, 2007) and a shared "general distress" component (Mineka, Watson, & Clark, 1998), much is still unknown about the comorbidity of these two disorders. For example, why does GAD so often predate its comorbid counterpart, MDD?

Given the possibly shared diathesis of GAD and MDD, their high comorbidity rate, and their often sequential onset (i.e., that GAD often predates depression), work is needed to investigate potential pathways that exist from premorbid GAD to depression. In a recent study that specifically investigated whether GAD and stress may interact to predict depression onset, Hettema et al. (2006) examined prior GAD diagnosis, stressful life events, and depression onset in a large twin sample (*N*=8,068). Individuals with prior GAD were more vulnerable to the "depressogenic" effects of stressful life events, regardless of the level of objective threat imposed by the event. These findings suggest that GAD may sensitize individuals to the depression-causing effects of stressful life

events (Hettema et al., 2006). Previous findings in the same sample implicated neuroticism as a stress-modifier as well; individuals with higher levels of neuroticism were also more sensitive to the depression-inducing effects of stressful life events (Kendler et al., 2004). Hettema et al. (2006) suggested, "neurotic traits index one's genetic susceptibility to either GAD or MDD, with other factors (modifier genes or environmental factors such as stressful life events) determining the often observed sequence of GAD predating MDD" (Hettema et al., 2006, p.794). That is, higher neuroticism enhances the depressogenic effects of life stress, especially among those who have already developed GAD, which is a "more proximal and potent risk factor for MDD" (Hettema et al., 2006, p.794). In sum, neuroticism and premorbid GAD may interact with stress to form a pathway to depression.

The Contributing Role of Neuroticism

Depression researchers have increasingly examined ways that neuroticism may operate to increase depression vulnerability. Hammen (2005) notes the potential for neuroticism to inform diathesis-stress theories of depression "because of its implication for understanding stress generation and stress reactivity, and as a candidate for aspects of genetic risk for depression" (Hammen, 2005). Neuroticism may for example reflect the working of an underlying genetic factor (Kendler et al., 1993), which modifies the effects of stress on depression (Kessler, 1997). For instance, Caspi et al. (2003) found that a polymorphism of the serotonin transporter gene (5-HTTLPR), which has been associated with neuroticism (Schinka, Busch, & Robichaux-Keene, 2004; Sen et al., 2004; cf., Risch et al., 2009), moderated the effects of stress on the subsequent development of

depression. Further, Jacobs et al. (2006) found that the relationship of 5-HTTLPR to the depressive effects of stressful life events was accounted for by neuroticism. The authors suggest that 5-HTTLPR may be responsible for how people characteristically react to and manage stress (Jacobs et al., 2006). In sum, neuroticism may represent an underlying genetic factor which predisposes some individuals to the depressogenic effects of stress, accounting for the relationship between life stress and impending depression (Caspi et al., 2003; Jacobs et al., 2006; Kendler et al., 2004). In light of these findings and the strong relationship that neuroticism has with both depression and anxiety, a measure of neuroticism will be included in the current study design (see Morris, Bylsma, & Rottenberg, 2009 for a review of neuroticism and depression course).

Hedonic Capacity and the Development of MDD

Decreased hedonic capacity, or anhedonia, has long been of interest among depression researchers (e.g., Meehl, 1975). Anhedonia is a cardinal feature of depression and represents a deficit in reward processing (e.g., Forbes & Dahl, 2005; Pizzagalli, Jahn, & O'Shea, 2005). Reward processing and approach behavior are thought to be products of a theorized approach system seated in the brain (i.e., behavioral activation system, BAS; Carver & White, 1994; Gray, 1981), which governs all manner of approach-related, reward-relevant behaviors. Deficits in BAS, specifically low levels of approach tendencies in the trait-like reward system, are related to current and prospective depression (Kasch, Rottenberg, Arnow, & Gotlib, 2002). Similarly, low approach tendencies (low BAS) may not normalize even upon recovery from depression, with anhedonia levels remaining constant even with decreases in depression symptoms (Pinto-

Meza et al., 2006; Schrader, 2004). Relatedly, lower levels of trait positive affect predict a worse course of depression (Morris et al., 2009). Taken together, these findings suggest that deficits in hedonic capacity may be etiologically significant for depression (for a review from a developmental psychopathology perspective, see Forbes & Dahl, 2005).

The Effect of Stress of Hedonic Capacity

In two field studies of hedonic capacity in healthy individuals, Berenbaum and Connelly (1993) examined hedonic capacity before and after experiencing life stress. College students reported experiencing less pleasure in their daily lives during a stressful period (exam week), and Army cadets reported less pleasure in response to an amusing film after a stressful training weekend. Pizzagalli et al. (2007) report similar findings when comparing individuals with high and low levels of perceived life stress, as indexed by the Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983): compared with low perceived stress, high perceived stress was related to blunted reward responding indexed via a laboratory task. These findings expose one possible pathway from stress to depression if even a moderate life stressor (e.g., exam week) can lead to hedonic blunting, which is etiologically linked to depression. Stress-induced anhedonia has also been observed in animal studies of depression, where various stressors elicit depressotypic behaviors in laboratory animals (see Anisman & Matheson, 2005). These findings suggest, again, that a normative effect of stress may be the induction of acute anhedonia, that is, an immediate decrease in hedonic capacity.

Bogdan and Pizzagalli (2006) suggested that based on previous work, "preclinical evidence and limited human research invite the possibility that stress might increase the

likelihood of depression development by inducing anhedonia" (p. 1147). This hypothesis can be extended to include findings from the life stress literature, which speak to why only vulnerable individuals develop MDD in response to stress. That is, the life stress literature tells us that some individuals (e.g., persons with GAD) are at a greater risk of developing MDD as a result of stress, and the literature on anhedonia tells us that deficits in hedonic capacity are relevant to the development of depression. Might be it be the case that for certain individuals stress leads to more pronounced drops in hedonic capacity, rendering these individuals more vulnerable to developing a full blown depressive episode? Such a model offers a theoretical framework for testing hypotheses about a potential pathway from GAD to depression. Specifically, individuals with GAD may be especially vulnerable to future depression because they are especially susceptible to pronounced stress-induced hedonic deficits.

Studying Hedonic Capacity in the Laboratory

Recent methodological advances allow for improved experimental manipulation and assessment of hedonic capacity (e.g., Pizzagalli et al., 2005). Researchers have begun to utilize behavioral measures of anhedonia, or reduced reward responsiveness. Behavioral anhedonia paradigms often include a task where some sort of reward is offered and the response to the reward or sensitivity to the reward is indexed. These behavioral anhedonia measures have been shown to distinguish depressed from healthy individuals as well as predict future depression. Both dysphoric individuals (Henriques, Glowacki, & Davidson, 1994; Pizzagalli et al., 2005) and individuals with MDD (Henriques & Davidson, 2000) show a decreased response bias toward reward on

laboratory tasks when compared to healthy controls, a pattern that cannot be explained by depression-related differences in task performance (e.g., accuracy; Pizzagalli et al., 2005; 2009). Importantly, reduced reward responding has been shown to predict greater levels of depression symptoms one month later (Pizzagalli et al., 2005). Depressed children show similar alterations in reward response, which are also predictive of future depression (Forbes, Shaw, & Dahl, 2007). Finally, behavioral anhedonia paradigms also distinguish individuals with enhanced reward responsiveness from controls. Barr et al. (2008) found that individuals who were administered nicotine, a drug that affects brain reward centers, showed significantly greater reward responsiveness than controls. Laboratory probes of anhedonia, therefore, appear to be well-suited to study hedonic capacity experimentally, as well as the individual differences that might exist between groups of healthy and at-risk individuals.

Laboratory Investigations of Stress and Hedonic Capacity

Recently, Bogdan and Pizzagalli (2006) used a behavioral measure of anhedonia and found that lab-induced stress leads to reduced hedonic capacity. Specifically, healthy female participants showed decreased hedonic capacity under laboratory induced stress when compared to a no-stress condition. Because the present study draws upon the Bogdan and Pizzagalli design, the methodology and findings of Bogdan and Pizzagalli (2006) are reviewed in some detail.

Bogdan and Pizzagalli (2006) operationalized hedonic capacity by using a signal detection task to index response bias toward reward. Signal detection tasks have been previously used as implicit tests of response bias toward reward (e.g., Pizzagalli et al.,

2005) to objectively measure individuals' propensity to change response patterns based on the presence of reward. Detection theory suggests that if one correct response is rewarded more often than another, people will begin to prefer that stimulus over the one that is less often rewarded (i.e., they develop a response bias; Macmillan & Creelman, 1991). Response patterns of individuals high in reward responsiveness demonstrate their ability to modulate behavior in order to maximize reward. Alternatively, individuals low in reward response (i.e., anhedonia) will not effectively modulate behavior to maximize reward. The use of response bias on a signal detection task to measure reward response thus potentially represents an "objective, laboratory-based measure of hedonic capacity" (Pizzagalli et al., 2005, p.320).

In a healthy female sample, Bogdan and Pizzagalli (2006) induced stress in two experimental conditions and then used a signal detection task to measure response bias. In one stressor condition, participants performed the signal detection task under shock threat via two electrodes placed on their necks. While participants performed the computer-based signal detection task, an indicator on the computer screen displayed the likelihood that they would receive shock, ostensibly as a result of their performance on the task. Individuals in the control condition always saw a very low likelihood while individuals in the stress condition saw fluctuating higher levels of likelihood of shock. Individuals in the shock threat condition showed a significant reduction in response bias on the signal detection task compared to controls, although there were no differences in discriminability (i.e., the stressor did not just make them perform poorer on the task in general). In the other stressor condition, individuals received feedback on their performance on the signal detection task via an indicator on the computer screen. The

indicator displayed feedback as to the individuals' performance compared to previous participants (i.e., ranging from "poor" to "superior"). The decreases in reward response due to negative feedback did not reach statistical significance, which the authors conjectured may be a result of this stressor not producing the necessary level of anxiety and negative affect that, when "coupled with the evaluative aspects of the stressor may be required to induce hedonic deficits" (Bogdan & Pizzagalli, 2006, p. 1152). Overall, Bogdan and Pizzagalli (2006) showed that healthy individuals experience hedonic deficits as a result of stress and provided an innovative design and methodology to probe such effects in at-risk individuals.

The Present Study

The present study aimed to test a model where at-risk individuals experience enhanced deficits in hedonic capacity as a result of stress. Previous evidence suggests that stress can lead to depression, that individuals with GAD are at greater risk of developing depression as a result of stress, and that stress leads to reduced hedonic capacity, which has been implicated in the etiology of depression. This study extended previous work by Bogdan and Pizzagalli (2006) and examined individual differences in the effects of stress on hedonic capacity in healthy individuals and individuals with GAD. To our knowledge, this was the first study to examine the impact of stress on hedonic capacity in a group at elevated risk for developing depressive symptoms.

The central study aim was to test whether individuals with GAD exhibit greater stress-induced hedonic deficits than control individuals. To reduce the potential confound of current depression on reward responding, the study excluded cases reporting a current

depression diagnosis. Further, data on the MDD history of each participant was collected to test for effects of past depression on stress-induced anhedonia, as past depressive episodes themselves can influence the effects of stress on depressive symptoms (Kessler, 1997). Given that gender has been found to interact with risk factors for depression including stress, neuroticism, and GAD (e.g., Hettema et al., 2006; Kendler et al., 2004), female participants were the focus here to simplify our modeling. We expected stress-induced reductions in hedonic capacity in the control group, and that this effect would be larger in the GAD group. Secondary analyses of neuroticism as a potential mediator of these effects were planned, as neuroticism is a shared vulnerability factor for both anxiety and depression and because it has been shown to moderate the effects of stress on depression in naturalistic studies (Hutchinson & Williams, 2007; Kendler et al., 2004). Finally, participants were followed over one month and reassessed on levels of depression symptoms to permit prospective analyses. Based on previous work that hedonic deficits predict higher anhedonia levels one month later (Pizzagalli et al., 2005), it was expected that reductions in hedonic capacity in the stress condition would predict elevated anhedonia and depressive symptoms prospectively in both groups, with the GAD group showing a stronger predictive effect. To achieve this aim, a behavioral measure of anhedonia was acquired from an analog GAD group and control participants during a baseline no-stress condition as well as in a stress condition (order counterbalanced). Behavioral anhedonia was indexed by participants' ability to modulate responses to maximize reward (i.e., response bias) on a signal detection task incorporating tangible reward for correct responses (used in Bogdan & Pizzagalli, 2006, Pizzagalli et al., 2005; Pizzagalli et al., 2007; Tripp & Alsop, 1999). The signal detection

task was presented in three blocks of 100 trials. The study was essentially a 2 x 2 x 3 factorial design with group (control, GAD) as a between-subjects factor and condition (no stress, stress) and block (1, 2, 3) as within subjects repeating factors. Hedonic capacity (as indexed by response bias on the signal detection task) was the dependent variable. Finally, stress-induced behavioral anhedonia was investigated as a predictor of prospective depression symptoms (particularly anhedonia) and anxiety symptoms, measured at a one month follow-up session.

Hypotheses

H1 = *In the control group, exposure to stress will lead to a decrease in hedonic capacity as measured by response bias on the signal detection task (See Figure 1).*

H2 = *Compared to controls, individuals in the worry/GAD group will exhibit greater hedonic deficits as a result of stress. Therefore, the worry/GAD group will exhibit a greater reduction in response bias during stress than the control group (See Figure 1).*

H3 = *Stress-induced hedonic deficits will predict elevated levels of depression and anhedonia symptoms one month later. This effect will be seen in both groups, with the worry/GAD group showing an enhanced effect compared with controls. Prospective anxiety symptoms will also be investigated as an exploratory outcome variable.*

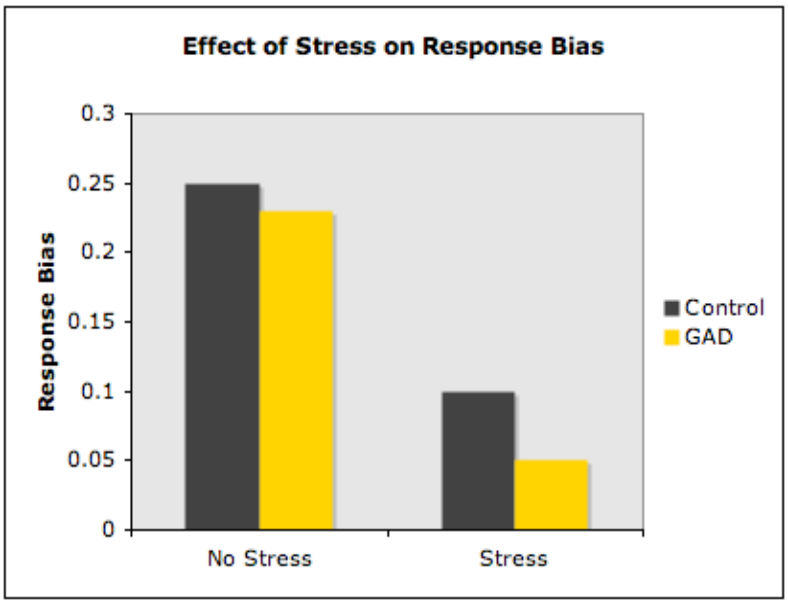

Figure 1. Expected results for hypotheses 1 and 2.

Method

Overview

The study consisted of three sequential phases: an online recruiting phase, a laboratory phase, and a follow up phase. Based on questionnaire responses in the online recruiting phase, potentially eligible participants were invited to participate in the laboratory session. At the lab session, participants were further screened for eligibility using self-report measures, and those who met criteria for participation completed the experimental protocol the dependent variables were measured in both control and experimental conditions. Participants who completed the lab session were invited to participate in a one-month follow up consisting of self-report measures. Follow up measures were completed online or in the laboratory, depending on whether the follow up session occurred when online forms were available via the subject pool.

Participants

Participants were recruited from an undergraduate research participant pool at the University of South Florida. Initial online pre-screening ensured that all participants were female, reported normal or corrected to normal vision, and reported no current diagnosis of depression, serious brain trauma, or other neurological illness. All individuals meeting pre-screen criteria were invited to participate in the online recruiting study for course credit. Participants were recruited via email based on their responses to questionnaire

measures of worry and depression symptoms, and were not informed of study eligibility criteria. Using cutoff scores established by previous studies (see Measures), participants reporting low levels of worry were recruited for the control group, and participants with high levels of worry were recruited for the GAD group. Participants with high levels of current depression symptoms were excluded. Eligible participants were asked to come to the laboratory session in exchange for course credit.

One hundred twelve participants attended laboratory study sessions, which were conducted over a nine month period from January to October 2009. Participants were ages 18-47 (M = 20.81, SD= 4.80). Among participants were 36 freshman (32.1%), 34 sophomores (30.4%), 23 juniors (20.5%), 16 seniors (14.3%), and 3 who responded "other" (2.7%). Reported ethnicity of the sample was 61.6% Caucasian (n=69), 12.5% Hispanic/Latino (n=14), 11.6% Black/African American (n=13), 8.9% Multi-racial (n=10), 3.6% Asian (n=4), <1% American Indian/Alaskan Native (n=1), and <1% Unknown or not reported (n=1). Participants were predominantly right-handed (92%). Thirty-four participants were excluded from analyses for various reasons (see Table 1), resulting in a final sample size of N=78.

Table 1. Participants excluded from analyses and reasons for exclusion

Total *N* = 112	*n* excluded	Reason for exclusion	Number excluded by group	
N = 93	19	Midrange worry scores (PSWQ 46-55)		
N = 92	1	Inconsistent scores on PSWQ/GAD-Q		
			Worry/GAD (*n*=48/30)	Control (*n*=44)
N = 90	2	Meets current MDD criteria (IDD)	2/2	
N = 89	1	Incomplete data (technical difficulties)	1/1	
N = 89	1	<50% overall accuracy	1/1	
N = 79	9	Received <20 rewards in any block	5/4	4
N = 78	1	Outlier: response bias *z*-score >4		1
Final *N* = 78			Final *n*=39/22	Final *n*=39

Measures

Eligibility Measures for Study Group Inclusion.

Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990). The PSWQ is a 16 item measure of trait worry. A cutoff score of ≥56 was used to recruit participants for the GAD group. This score yields 90% sensitivity and 75% specificity in identifying GAD cases (diagnosed by the GAD-Q-IV; Newman et al., 2002) in a college sample (Behar, Alcaine, Zuellig, & Borkovec, 2003). A cutoff score of ≤ 45 was used to identify control participants. This cutoff score falls at the 50th percentile in a community sample and reflects 98% specificity in identifying individuals with GAD (Behar et al., 2003), which means the controls recruited for the present study were unlikely to have significant GAD symptoms. The PSWQ was readministered at the lab session. Participants were excluded if they no longer met PSWQ eligibility criteria (i.e.,

PSWQ scores fell in the mid-range of worry scores (between 45 and 56), precluding inclusion in the control or GAD group. The PSWQ had acceptable reliability in this sample ($\alpha = .73$).

Generalized Anxiety Disorder Questionnaire (GAD-Q-IV; Newman et al., 2002). The GAD-Q is a 9 item paper-and-pencil diagnostic measure for current generalized anxiety disorder. The authors recommend a dimensional scoring system of 0-13 with a cutoff of 5.7 yielding 83% sensitivity and 89% specificity in identifying GAD cases (as diagnosed by the Anxiety Disorders Interview Schedule; Brown, DiNardo, & Barlow, 1994). This method has been previously used to identify college students with analog GAD (Miranda & Mennin, 2007; Salters-Pedneault, Roemer, Tull, Rucker, & Mennin, 2006). Turk et al. (2005) found that the 5.7 cutoff led to 33% of an unselected sample meeting criteria for analog GAD. In Salters-Pedneault et al. (2006), 26% of an unselected sample met criteria for analog GAD (31% of females—59 out of 190—met criteria). The GAD-Q was reliable in this sample ($\alpha = .743$). The current study used the 5.7 cutoff to identify research analog cases of GAD. In addition, inclusion in the GAD group required participants to score consistently on the GAD-Q and the PSWQ, that is, to also have high worry scores (PSWQ scores ≥ 56) at the time of the lab session.

Thirty participants initially met criteria for the GAD group, using the 5.7 cutoff on the GAD-Q diagnostic measure. Because prior analog GAD research has also been conducted using the PSWQ instrument, hypotheses were also tested also in the larger group of high worriers selected by the PSWQ. Forty-eight participants met initial criteria for the worry group utilizing the ≥ 56 cutoff score on the PSWQ as criteria for inclusion.

Pervasive worry is the cardinal feature of GAD, so the group selected by the PSWQ is conceptually similar to the group selected by the GAD-Q.

Beck Depression Inventory (BDI-II; Beck, Steer & Brown, 1996). The BDI-II was used primarily to screen out individuals with very high levels of current depression symptoms. The BDI-II is a well-validated 21-item self-administered scale of depression symptom severity. Scores range from 0 to 63 with higher scores representing more severity. Coefficient alphas for the BDI-II are high in previous studies ($\alpha = .91$; Beck, Steer, Ball, & Ranieri, 1996) and in the current sample ($\alpha = .90$). The test-retest reliability is also high ($r = .93$; Beck et al., 1996). The BDI-II measures depressive symptoms during the last two weeks. As recommended by Dozois, Dobson, and Ahnberg (1998), we utilized a cutoff score of <20 to screen out potentially high levels of dysphoria or clinical depression during the online phase. The BDI-II was readministered at the lab session, and we included cases with scores higher than the recruiting threshold (≥20) only if these cases did not meet diagnostic criteria for MDD (see IDD below).

Inventory to Diagnose Depression (IDD; Zimmerman & Coryell, 1987a). The IDD is a 22 item self-report measure to diagnose major depressive disorder. In a college sample, it demonstrates 70% sensitivity and 87.5% specificity in identifying depression cases diagnosed via a structured clinical interview (Goldston, O'Hara, & Schartz, 1990). The IDD was reliable in this sample ($\alpha = .84$). The IDD was used in the present study as a second tier of screening to exclude participants who likely had case-level depression. Participants who met IDD criteria for a current depressive episode were excused from further data collection. The IDD also generates a continuous symptom score (range 0-88) with high scores representing higher current depression symptom severity.

Other Lab Session Measures.

Demographics and Health Questionnaire. Participants completed a questionnaire targeting demographic information (e.g., age, gender) and health inclusion criteria (e.g., brain trauma, normal vision).

Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988). The BAI is a 21-item self-administered questionnaire of anxiety symptoms during the past week. In the present study, instructions were altered to assess anxiety symptoms over the past two weeks to facilitate comparison with the BDI-II. Symptoms were rated on a four-point scale, with higher scores indicating more severe anxiety symptoms. Previous studies show the internal consistency of the BAI is high ($\alpha = .92$), and the BAI correlates highly with the SCL-90-R Anxiety Subscale ($r = .81$) (Steer, Ranieri, Beck, & Clark, 1993). The BAI demonstrated excellent reliability in this sample ($\alpha = .92$).

Mood and Anxiety Symptom Questionnaire (MASQ; Watson et al., 1995). The MASQ is a 90 item measure of depression and anxiety symptoms which was designed in line with the tripartite model of anxiety and depression. The MASQ assesses symptoms over the past week and has several subscales assessing general distress - mixed symptoms (MASQ-GDM), general distress - anxious symptoms (MASQ-GDA), general distress - depressive symptoms (MASQ-GDD), anxious arousal (MASQ-AA), and anhedonic depression (MASQ-AD). It has sound psychometric properties (Keogh & Reidy, 2000; Watson et al., 1995), and demonstrated good reliability in this sample ($\alpha = .88$).

Inventory to Diagnose Depression, Lifetime (IDD-L; Zimmerman & Coryell, 1987b). The IDD-L is the lifetime version of the IDD and was used to determine whether or not each participant had a past history of major depression (see secondary analyses). Internal consistency was excellent in the current sample (α = .91).

Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983). The PSS is a widely used 14 item self-report measure of perceived life stress during the last month. The PSS has previously shown strong psychometric properties in samples of college students (Cohen et al., 1983), and showed good reliability in this sample (α = .86).

State Affect Measures for Stressor Manipulation.

State Trait Anxiety Inventory, State version (STAI-S; Spielberger et al., 1983). The STAI-S is a 20 item self-report measure of anxiety symptoms experienced at the present moment. An abbreviated form was used in the present study, including only the 10 STAI state items from Spielberger's State Trait Personality Inventory (STPI, Spielberger et al., 1979). This scale demonstrated good reliability in the current sample (α = .90).

Positive and Negative Affect Schedule-State Instructions (PANAS-S; Watson, Clark, & Tellegen, 1988). The PANAS-S is a 20 item self-report measure of positive and negative affect experienced at the present moment. This measure has demonstrated excellent psychometric properties in previous samples and is a valid measure of the two independent constructs of positive and negative affect (Watson et al., 1988). Reliability in the current sample was excellent for PA (α = .90) and good for NA (α = .79).

Self Assessment Manikin-Arousal (SAM-A; Bradley & Lang, 1994). The SAM-A is a paper-and-pencil picture-based scale that depicts 5 figures ranging from unaroused to extremely aroused. Responders choose between 9 responses (one for each picture and one in between each picture) to indicate which of the figures best represents their current level of arousal.

Anticipatory Anxiety Rating. During the computer task, single item assessments of anticipatory anxiety were administered to assess participants' level of anticipatory anxiety about completing the upcoming math task. Participants were presented with a visual scale ranging from 0 (not at all) to 9 (extremely) and asked to respond by keystroke to the question, "How ANXIOUS are you about the upcoming math task? Using the scale below, type the number on the keyboard that describes how anxious you feel right now." Ratings were made following reminder prompts at each 30 second break between trial blocks, totaling two ratings per condition.

Stressor Task Appraisal Measure.

Math Task Appraisal Questionnaire. This questionnaire consists of 8 items assessing participants' perceptions and feelings about the impending math task. The questionnaire is modeled closely after the appraisal measure used by Tomaka, Blascovich, and colleagues (Tomaka, Blascovich, Kelsey, & Leitten, 1993; see also Kelsey et al., 2000; Salomon, Clift, Karlsdottir, & Rottenberg, 2009 for more recent adaptations).

Trait Measures.

State Trait Anxiety Inventory, Trait version, form Y (STAI-T; Spielberger et al., 1983). The STAI-T is a widely used measure of trait anxiety symptoms. Responders answer 20 items assessing anxiety symptoms in terms of how they *generally* feel. The STAI-T has excellent psychometric properties and demonstrates convergent validity with other indices of anxiety symptoms. The STAI-T demonstrated excellent reliability in this sample ($\alpha = .93$).

Temporal Experience of Pleasure Scale (TEPS; Gard, Gard, Kring, & John, 2006). The TEPS is an 18 item self-report measure of anticipatory and consummatory pleasure. The TEPS demonstrates adequate internal consistency, good test-retest reliability, and convergent validity with other anhedonia measures (Gard et al., 2006). In the current sample, the TEPS demonstrated adequate internal consistency ($\alpha = .76$).

NEO-PI-Five Factor Inventory (NEO-PI-FFI; Costa & McCrae, 1992). The NEO-PI-FFI is a widely used 60 item measure of personality including indices of neuroticism, extraversion, openness, agreeableness, and conscientiousness. The NEO-PI-FFI shows solid psychometric properties in samples of adolescents and college students (McCrae & Costa, 2004). The current study utilized the neuroticism (NEO-N) and extraversion (NEO-E) subscales, which demonstrated good reliability in the current sample ($\alpha = .85$ and .77, respectively).

Behavioral Inhibition/ Activation System Scales (BIS/BAS; Carver & White, 1994). The BIS/ BAS is a 24 item self-report measure of behavioral approach (BAS) and inhibition (BIS) tendencies. The BIS/BAS scale has shown adequate reliability in

previous samples (Carver & White, 1994), and both BIS and BAS subscales demonstrated good reliability in the current sample (α = .82 and.81, respectively).

Positive and Negative Affect Schedule-Trait Instructions (PANAS-T; Watson et al., 1988). The PANAS-T is a 20 item self-report scale measuring dispositional forms of positive and negative affect (Watson et al., 1988). The PANAS has successfully differentiated depression and anxiety in clinical samples (Dyck, Jolly, & Kramer, 1994; Jolly, Dyck, Kramer, & Wherry, 1994). The PANAS is also highly reliable, with a Cronbach's alpha of .89 for positive affect and .85 for negative affect (Crawford & Henry, 2004). In the current study, both PA and NA demonstrated high reliability (α = .88 and .88, respectively).

Behavioral Measure of Hedonic Capacity.

Signal Detection Task. A signal detection task was used to index participants' ability to modulate responses based on reward, or reward responsiveness (Pizzagalli et al., 2005). As in prior studies (e.g., Bogdon & Pizzagalli, 2006; Pizzagalli et al., 2005; Tripp & Alsop, 1999), this method involved briefly presenting one of two stimulus types (e.g., a short line and long line) and asking participants to respond as to which of the two stimuli were seen. The two stimulus types were presented equally often. Only some correct responses were followed by a monetary reward (5 cents)—one stimulus type (e.g., either the short line or the long line) was scheduled to be rewarded for correct responses three times as often as the other stimulus. Creating an unbalanced reward schedule between the two types of correct responses produces a systematic preference—or response bias—for the stimuli that is most often followed by the reward (Macmillan &

Creelman, 1991). Conceptually, individuals with higher reward responsiveness exhibit more of a response bias because they modulate their responses to increase the chances of receiving the reward (i.e., they will more often report seeing the stimulus that is more frequently paired with a reward). Individuals with lower reward responsiveness do not exhibit the same response bias, but will perform adequately on the task (Pizzagalli et al., 2005; Tripp & Alsop, 1999). Response bias on the signal detection task, therefore, was a behavioral measure of reward responsiveness, or hedonic capacity.

The method for this study drew heavily upon Tripp and Alsop (1999), Pizzagalli et al. (2005), and Bogdon and Pizzagalli (2006). The signal detection task was presented on a PC via E-prime software (version 2.0, Psychological Software Tools, Inc., Pittsburgh, PA). The task included 3 blocks of 100 trials, which were separated by 30 second breaks. Because participants completed the signal detection task twice (once in a no stress condition and once in a stress condition), two target types were used (nose or mouth on a schematic face) and were counterbalanced across group and condition to minimize carry-over effects (Bogdan & Pizzagalli, 2006).

Each trial began with a fixation point at the middle of the screen for 1 second. The fixation point was then replaced with a schematic representation of a face that was missing a feature (without a nose or a mouth) for 500ms. The missing feature then appeared either as a long version (13 mm for mouths; 6.5 mm for noses) or a short version (12 mm for mouths; 6 mm for noses) for 100ms and then disappears again, leaving the mouthless or noseless face on the screen for 1500 ms. The participant then responded as to whether it was the long or short stimulus that was presented on the face by pressing either the ‘z’ or ‘m’ key (counterbalanced across participants). Participants

were instructed to keep their index fingers on the z and m keys throughout the task, and the keys were marked with brightly colored stickers to aid in this. Short and long stimuli were presented equally often in a quasi-randomized order— such that neither version was presented more than 3 times in a row. Participants were instructed that not all of the correct identifications would be followed by a reward. Indeed, only 40 correct identifications were followed by a reward. If a participant identified a stimulus correctly and a reward was scheduled, the phrase "Correct!! You won 5 cents!" was presented in the center of the screen for 1500ms and followed by a blank screen for 250ms. If the correct identification was not scheduled to receive reward, no feedback was given and the screen was blank for 1750ms. Figure 2 shows a schematic of a trial with consecutive screens and the length of time they are seen in a trial where a reward is given for correct identification of a mouth (modified from Bogdan & Pizzagalli, 2006, p. 1148).

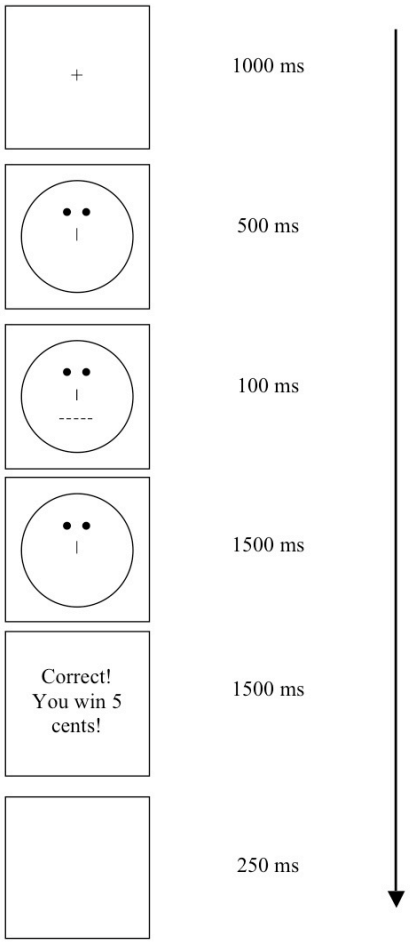

Figure 2. Trial schematic

As previously stated, creating the necessary conditions for response bias to occur requires scheduling the two versions of the target stimuli (short and long) to be differentially rewarded (Macmillan & Creelman, 1991). The version scheduled to be rewarded most often (30 out of 40 trials) is referred to as the "rich" stimulus, and the version associated with reward less often (10 out of 40 trials) is the "lean" stimulus. The assignment of each stimulus to be "rich" or "lean" was counterbalanced across condition so that each participant encountered both long and short versions of the stimuli as the

"rich" stimulus. Importantly, we diverged from previous studies in not using a controlled reinforcer procedure, or missed reward replacement. That is, previous studies attempted to control the 3:1 ratio of rich rewards versus lean rewards by replacing scheduled reward trials if the participant did not provide the correct response and receive the scheduled reward (i.e., offering additional reward opportunities until a fixed ratio of received rewards was met). The current study controlled only the potential for receiving 3 rich rewards for every 1 lean reward. The advantage of our design is that the participant's reward ratio was contingent upon her own performance, allowing for individual variation in the exact ratio of rich to lean rewards, and serving as a more stringent test of response bias hypotheses.

Procedure

Overview. Upon arrival at the laboratory, participants provided written consent, including consent to be videotaped and consent to be contacted for follow up study participation. Participants completed the Demographics and Health Questionnaire, GAD-Q, IDD, IDD-L, and BAI, and the PSWQ and BDI-II were re-administered. Participants who met diagnostic criteria for current major depression based on IDD responses were excused from further data collection. Participants then completed the behavioral measure of hedonic capacity in the stress and no stress conditions (counterbalanced), and were given monetary rewards earned directly after completing each computer task (the maximum compensation was $12 per participant). Participants then completed the BISBAS, PSS, STAI-T, TEPS, NEO-FFI, PANAS-T, and MASQ, and were compensated for participation with course credit.

Experimental Protocol. All lab sessions were conducted by undergraduate or post- Bachelor's level research assistants who were blind to participant group status. Research assistants attended an introductory training session with the principal investigator (~2 hrs), followed by a supervised practice session with another research assistant standing in as the participant. Research assistants were required to demonstrate mastery of experimental scripts and protocol administration including stressor task administration prior to data collection, and all first administrations were supervised by the principal investigator.

Participants were told that the study was examining "how anxiety affects task performance." The signal detection task was referred to as a "computer task" and participants were told that the goal in the computer task was to win as much money as possible and that the best way to do this was to correctly identify as many stimuli as possible (as in Bogdan & Pizzagalli, 2006). To establish credibility, participants were shown six $1 bills they may win by performing well on the computer task. Participants were instructed to respond as quickly as possible and were told to "please do your best" on the task because their ability to focus and perform well on the task was the focus of the study. Participants were told that not all of their correct responses would be rewarded.

Participants received instructions on the signal detection task and completed sixteen practice trials to gain familiarity with the task. Participants were seated approximately 20 inches from the computer screen. Following the practice trials, the research assistant left the study room and all other instructions were delivered via intercom from an adjacent observation room. Participants then completed the signal detection task twice—once in a stress condition and once in a no stress condition

(counterbalanced). Between the stress and no stress conditions, participants traced geometric shapes for five minutes as a buffer task to decrease carry-over effects from the previous condition.

Following Bogdan & Pizzagalli (2006), participants completed state affect measures (PANAS-S, STAI-S, and SAM-A) at baseline, pre-task, and post-task in each condition. Instructions on the post-task measures were altered to assess affect during the computer task. Additionally, participants made anticipatory anxiety ratings during breaks between computer task trial blocks.

Stress Condition. To extend prior work, the current study utilized a mental arithmetic task as the experimental stress condition. Bogdan and Pizzagalli (2006) found that shock threat had effects on reward responsiveness, but a negative performance feedback condition did not. Threat of shock is a highly arousing stressor which was also tied to performance on the signal detection task within their design. Bogdan and Pizzagalli (2006) speculated that receiving negative feedback was not successful in inducing decrements in reward responsiveness because it did not sufficiently involve elements of anxious arousal and social evaluation. Therefore, we selected a mental arithmetic task as the stressor because it is more ecologically valid than shock threat and involves elements of both social evaluation and anxious arousal. Indeed, mental arithmetic has been shown to elicit similar levels of anxious arousal to a shock stressor (Noteboom, 2001).

Participants completed baseline state measures. They then received instructions via intercom and performed mental arithmetic task for 3 minutes. The task involved serial subtraction by 7s from 3,796. Participants were told to face the video camera, and that

they would be observed but not videotaped during the task. Participants were told to perform the task as quickly and accurately as possible. Errors were monitored by the experimenter and announced to the participant with instructions to begin again at the correct subtraction total. Participants were also prompted to "Please work quickly," if they did not produce a complete answer in 3 seconds. Participants were told to "Please work faster," 90 seconds or mid-way through the task. Participants were prompted to "Look into the camera," if looking away, and were not allowed to use fingers to count. After 3 minutes, participants were told that they would next perform the computer task, followed by performing a more difficult version of the math task (subtracting 13 instead of 7), which would be videotaped and evaluated for speed, accuracy, and poise (as in Kelsey et al., 2000). Previous work has found that the addition of a second, subsequent videotaped mental arithmetic task increases participants' subjective ratings of the stressfulness of the task (Kelsey et al., 2000). Participants completed pre-task state measures and the task appraisal measure, and then performed the computer task. After the first block of 100 trials, during the 30 second break, a black bold font message appeared on a bright yellow computer screen saying,

> *"You have just completed the first 100 trials of this task. There are 200 trials remaining before you begin the *MORE DIFFICULT MATH TASK * that will be VIDEOTAPED and EVALUATED. Please continue to do your best on this task."*

Then, a black screen appeared requesting participants to respond by key press to the anticipatory anxiety rating. Similarly, a message appeared after the second block of 100 trials referring to 200 completed trials and 100 remaining to complete, followed by another anticipatory anxiety rating. The purpose of these prompts was to remind

participants of the impending stressor and to maintain and assess anticipatory anxiety throughout the computer task. After completing the third block of trials, participants completed post-task state measures. Participants then performed the more difficult mental math task (subtracting 13s). Because anticipatory anxiety was the variable of interest and the math task functioned only at this point to retain credibility for future tasks, participants were not prompted as frequently to work quickly during the task or to look into the camera, and the task only lasted one minute.

No Stress Condition. Participants completed paper-and-pencil arithmetic problems of similar difficulty to those used in the stress condition for 3 minutes. Participants were informed that their responses would not be graded for accuracy. This type of control condition has been used in previous studies employing a mental arithmetic stressor (e.g., Domes, Heinrichs, Reichwald, & Hautzinger, et al., 2002). The intention of the task was to control for cognitive load (i.e., it is not a relaxation task) and distraction (i.e., it provides distraction from rumination upon previous task performance or worry about future performance) without purposely or systematically evoking a particular emotion. After 3 minutes, participants were told that they would next complete the computer task, followed by performing more paper-and-pencil arithmetic again without evaluation. Participants then completed pre-task measures and the task appraisal measure, and then performed the computer task. After the first block of 100 trials, during the 30 second break, a black bold font message appeared on a yellow computer screen saying,

> *"You have just completed the first 100 trials of this task. There are 200 trials remaining before you do written math again. Please continue to do your best on this task."*

Then participants were asked to make an anticipatory anxiety rating. A similar reminder message appeared after the second block of 100 trials, which referred to the 200 completed trials and 100 remaining, followed by another anticipatory anxiety rating. After completing the third block of trials, participants completed post-task measures. Participants then began the pencil and paper arithmetic problems and continued for 1 minute with no evaluation. Response bias during the no stress condition was used as a baseline measure of reward responsiveness for each participant. The lab visit lasted approximately 2.5 hours. One participant did not complete the experimental portion of the protocol due to technical difficulties. See Figure 3 for a laboratory protocol example in descending chronology for a participant in the no-stress condition first and stress condition second.

- Initial Laboratory Protocol
    - Demographic, diagnostic and symptom measures
    - Instructions and practice with computer task
- No Stress condition
    - No stress condition Baseline state measures
    - No stress math task (written math- 3 min.)
    - Instructions to anticipate doing written math again after computer task
    - Pre-task State measures and measure of task appraisal
    - Computer task (20-30 min.)
        - Single item anxiety rating after each block of trials
    - Post-task State measures
    - Monetary compensation
    - Written math (1 min.)
- Buffer task
    - Shape tracing (5 min.)
- Stress condition
    - Stress condition Baseline State measures
    - Stress math task (mental math- 3min.)
    - Instructions to anticipate doing more difficult math task with videotape after computer task
    - Pre-task State measures and measure of task appraisal
    - Computer task (20-30 min.)
        - Single item anxiety rating after each block of trials
    - Post-task State measures
    - Monetary compensation
    - Mental math (1 min.)
- Self-report measures (20-30 min)

Figure 3. Laboratory study protocol

Follow Up Study. Participants were contacted via email one month following their participation in the lab session and invited to participate in a second online session for course credit. If the follow up session was scheduled to occur outside the period when online data collection was available, participants completed paper-and-pencil measures in

the laboratory for $10 cash compensation. This follow-up session involved completion of the following measures: the GAD-Q, IDD, BAI, BDI-II, STAI, TEPS, PSWQ, PANAS, MASQ, and PSS. Participants were debriefed via email following follow up study participation.

Data Reduction

Deleted Trials. Consistent with previous studies utilizing the signal detection paradigm (Bogdan & Pizzagalli, 2006), trials with reaction times <150 ms or >1500 ms were excluded. Trials with incorrect key presses were also excluded with one exception: If a participant consistently pressed a neighboring key (i.e., "x" instead of z for several trials, where the intention of the key press was clear) and the trials were NOT scheduled to receive a reward (i.e., the person would not have been rewarded even if z had been pressed), the trials were counted as correct responses for the purposes of accuracy. Any incorrect key presses that were random or occurred in a trial scheduled to receive a reward were excluded. The total number of deleted trials per participants for any reason ranged from 0 to 42 (M=4.64, SD = 6.77).

Excluded Cases. Consistent with prior work (Barr et al., 2008), participants were excluded for performing at less than chance accuracy rates (<50% accuracy). To ensure that included participants received adequate numbers of rewards to create the desired reward differential in each block of trials, participants receiving fewer than 20 of 40 (50%) potential rewards in any one block were excluded from analyses. Although this lower limit is more liberal than that reported in a previous study (30 out of 40 in each block; Barr et al., 2008), it was conservative enough to exclude participants who 1)

missed a great deal of trials in one or more blocks, 2) used a "strategy" like pressing the same key for most trials, or 3) performed well in one condition and at chance levels in other condition (i.e., where combined accuracy may have been slightly greater than chance).

Response Bias and Discriminability Calculations. Response bias and discriminability were calculated following past work using this task (e.g., Bogdan & Pizzagalli, 2006). Calculation formulas were derived from signal detection theory (Macmillan & Creelman, 1991). For clarity, components of the formulas are defined below in both traditional signal detection terms (e.g., hits, misses) and in terms specific to the task in this study:

H = Hits = Correct identification of the rich stimulus (rich = rewarded more often)

F = False alarms = Choosing the rich stimulus when the lean stimulus was presented

M = Misses = Choosing the lean stimulus when the rich stimulus was presented

C = Correct Rejections = Correct identification of the lean stimulus

Response bias in the present context is defined as the tendency to systematically prefer the rich stimulus over the lean stimulus. It is represented by the following formula:

Response bias: $\log b = \frac{1}{2}(H * F / M * CR)$

Discriminability refers to the ability to discriminate between the two stimuli and measures overall performance. In the present context, discriminability measures will be used to test for specificity of findings about the effects of stress on response bias. That is, by demonstrating that stress does not affect overall task performance but does affect response bias, one can infer that the effect of stress is specific to response bias.

Discriminability: $\log d = \frac{1}{2}(H * CR / M * FA)$

Following previous work, 0.5 was added to each cell of the decision matrix to allow for calculations where the cells contain zeros (see Pizzagalli et al., 2007).

Overview of Analyses

Stress Manipulation Analyses

Repeated measures analyses of variance (ANOVAs) tested for significant stress manipulation effects on each dependent measure of self-reported state anxiety, negative affect (NA), positive affect (PA), and arousal (STAI-S, PANAS-S-NA, PANAS-S-PA, SAM-A) using Group (control, worry) as a between subjects factor and Condition (no stress, stress) and Time (baseline, pre-task, post-task) as repeated within subjects factors. A successful stressor manipulation would be indicated by a Condition x Time interaction, which would be decomposed using follow up contrasts and graph inspection. Scores on the PANAS-S-NA, STAI-S, SAM-A were expected to increase from baseline to pre-task (and to decrease on the PANAS-S-PA) to a greater degree in the stress condition than in the no stress condition (although Bogdan & Pizzagalli, 2006, did not find significant reductions in PA in the stress conditions). Similar analyses were planned examining stressor effects on task appraisal (MTAQ) and Anticipatory Anxiety Ratings taken during the computer task.

Hypothesis Testing

H1 = *In the control group, exposure to stress will lead to a decrease in hedonic capacity as measured by response bias on the signal detection task.*

Using data from the control group only, a repeated measures analysis of variance (ANOVA) with Condition (no stress, stress) and Block (1, 2, 3) as within subjects factors was planned to test for a main effect of Condition (no stress, stress) on response bias. Alpha was set at $p<.05$ *a priori*. A main effect of Condition (no stress, stress) in the hypothesized direction would indicate that the stress condition was associated with significantly lower response bias scores than the control condition. Planned comparisons were used to test for the expected increases in response bias across blocks.

H2 = *Compared to controls, individuals in the worry/GAD group will exhibit greater hedonic deficits as a result of stress. Therefore, the worry/GAD group will exhibit a greater reduction in response bias during stress than the control group.*

A repeated measures analysis of variance (ANOVA) with Group (control, worry/GAD) as a between subjects factor and Condition (no stress, stress) and Block (1, 2, 3) as within subjects factors was planned to test for an interaction of Group (between subjects) and Condition (within subjects) on response bias. A significant interaction would be followed up by planned contrasts to determine whether the worry/GAD group exhibited significantly lower response bias scores in the stress condition compared to controls. Planned contrasts were used to test for the expected increases in response bias across blocks.

H3 = *Stress-induced hedonic deficits will predict elevated levels of depression and anhedonia symptoms one month later. This effect will be seen in both groups, with the*

worry/GAD group showing an enhanced effect compared with controls. Prospective anxiety symptoms will also be investigated as an exploratory outcome variable.

Correlation analyses were planned for each group separately to test whether mean response bias scores in the stress condition predicted follow-up depression, anhedonia, and anxiety scores. Significant relationships would be followed up by hierarchical regression analyses entering baseline symptoms into the regression model at step 1 and response bias under stress at step 2 to test for prediction of future symptoms beyond initial symptom levels. We expected that lower response bias in the stress condition would predict higher depression and anhedonia at one month follow-up in both groups. As a follow up, to test the hypothesis that the worry/GAD group might show an enhanced predictive effect compared to controls, the Chow test (Chow, 1960) was planned to statistically test the hypothesis that the two groups differed on the set of coefficients in the regression models.

Discriminability, Accuracy, and Reaction Time Analyses

Repeated measures ANOVAs were planned for discriminability and accuracy with Group (control, worry) as a between subjects factor, and Condition (no stress, stress) and Block (1, 2, 3) as repeating within subjects factors. Non-significant findings on these tests would help exclude the possibility that group differences in response bias were driven by group differences in discriminability and accuracy (i.e., if one group showed poor overall performance on the task). A similar test was performed with reaction time as the dependent variable.

Secondary Moderation Analyses

Secondary analyses were planned to test for potential moderation of the relationship between condition and response bias in each group. Neuroticism, history of depression, and measures of life stress would be investigated as potential moderators.

Results

Checking Model Assumptions and Assessing Outliers

General Linear Model assumptions were evaluated for the main continuous outcome variable (response bias scores) separately for each condition. Initial visual inspection of histograms suggested normally distributed data in the stress condition, but slight positive skew in the no stress condition. Shapiro-Wilk tests of normality confirmed non-normality in the no stress condition ($W = .948$, $p = .003$), along with significant skewness and kurtosis values. Outlier analyses revealed one significant outlier (z-score > 4) in the no stress condition. When this outlier was removed, the distribution normalized and skewness, kurtosis, and normality test statistics values were no longer significant. All further analyses were performed with this outlier omitted. The assumption of independence of observations was met as part of the design: the behavior and responses of each participant was independent of all others. The assumption of homogeneity of variance was met based on nonsignificant Levene's test statistics for dependent variable scores at all levels of the independent variables. Visual distribution inspection of all secondary dependent variables (accuracy, reaction time, discriminability) suggested normally distributed data.

Sample Characteristics

Data are presented for 39 controls and 39 high worry participants. Randomization to experimental condition was successful: control and worry groups did not differ in assignment to counter-balanced experimental protocols, Cramer's $V = .384$, $p = .118$. Groups also did not differ on characteristics such as ethnicity, year in school, handedness, or age, all *p*s >.05. In the worry group, 22 met criteria for GAD according to the GAD-Q cutoff score. Worry group participants were more likely to meet criteria for a past episode of major depression according to the IDD-L (n=18) compared to controls (n=4), $\chi^2(1, N=78) = 12.41$, $p<.001$. The worry group reported significantly higher current depression, anxiety, and anhedonia symptoms, as well as higher trait negative affect, neuroticism, and perceived stress, and lower trait positive affect (see Table 2).

Table 2. Group differences in symptoms and trait variables

Measure	Control group		Worry group				
	M	*SD*	*M*	*SD*	*F*	*df*	*p*
PSWQ	35.51	5.25	64.08	6.14	487.86	1,76	<.001
BDI-II	4.67	3.88	13.26	7.57	39.82	1,76	<.001
BAI	5.67	4.58	16.39	12.03	27.01	1,75	<.001
GAD-Q total	0.90	1.05	6.58	2.85	138.03	1,76	<.001
IDD total score	16.62	12.86	32.67	19.08	32.36	1,76	<.001
MASQ-GDD	16.54	2.58	23.59	6.77	36.90	1,76	<.001
MASQ-GDA	14.49	2.83	22.71	6.22	56.67	1,76	<.001
MASQ-AA	20.26	5.50	26.49	8.58	14.59	1,76	<.001
MASQ-AD	46.44	11.60	60.08	13.26	23.29	1,76	<.001
PSS	18.21	5.34	26.56	5.96	42.48	1,76	<.001
TEPS total score	81.08	11.22	85.54	10.73	3.22	1,76	.077
TEPS-A	46.38	6.40	49.26	7.37	3.38	1,76	.070
TEPS-C	34.69	7.21	36.28	6.29	1.077	1,76	.303
PANAS-T-PA	35.59	7.32	31.21	5.85	8.541	1,76	.005
PANAS-T-NA	12.08	1.86	18.36	5.68	43.08	1,76	<.001
STAI-T	30.59	5.05	46.59	8.82	96.56	1,76	<.001
BIS	19.49	3.54	24.28	2.31	50.28	1,76	<.001
BAS	42.18	4.14	42.41	5.57	.043	1,76	.836
NEO-N	13.97	5.08	26.08	6.68	81.07	1,76	<.001
NEO-E	32.77	5.86	30.08	6.40	3.75	1,76	.056
NEO-C	35.49	6.64	35.38	6.62	.005	1,76	.946
NEO-O	29.85	6.16	30.41	5.58	.180	1,76	.673
NEO-A	33.33	6.70	32.71	6.10	.182	1,75	.671

PSWQ: Penn State Worry Questionnaire, BDI-II: Beck Depression Inventory, BAI: Beck Anxiety Inventory, GAD-Q total: Generalized Anxiety Disorder Questionnaire total score, IDD total score: Inventory to Diagnose Depression total score, MASQ: Mood and Anxiety Symptom Questionnaire, MASQ-GDD: MASQ General Distress Depression subscale score, MASQ-GDA: MASQ General Distress Anxiety subscale score, MASQ-AA: MASQ Anxious Arousal subscale, MASQ-AD: MASQ Anhedonia subscale, PSS: Perceived Stress Scale, TEPS: Temporal Experience of Pleasure Scale, TEPS-A: TEPS Anticipatory subscale, TEPS-C: TEPS Consummatory subscale, PANAS-T-PA: Positive and Negative Affect Schedule, Trait Positive Affect scale, PANAS-T-NA: Positive and Negative Affect Schedule, Trait Negative Affect scale, BIS: Behavioral Inhibition scale, BAS: Behavioral Activation scale, NEO-N: Neuroticism, NEO-E: Extraversion, NEO-C: Conscientiousness, NEO-O: Openness, NEO-A: Agreeableness.

Stress Manipulation Analyses

State Anxiety. Repeated measures analyses were performed for STAI-S scores to assess stressor manipulation effects on state anxiety reports. There were main effects for Condition, F (1, 75) = 30.22, p<.001, partial η^2 = .287, and Time, F(2,150) = 64.376, p<.001, partial η^2 = .462, qualified by a Condition x Time interaction, F(2,150) = 34.29, p<.001, η^2 = .314, in which the stress condition generated greater increases in reported state anxiety than the no stress condition. In other words, our intended manipulation of state anxiety was successful. A main effect of Group, F(1, 75) = 53.67, p<.001, partial η^2 = .417, along with Group x Condition, F(1, 75) = 6.36, p = .014, partial η^2 = .078, and Group x Time interactions, F(2, 150) = 3.35, p = .038, partial η^2 = .043, show the worry group reported higher anxiety scores than controls overall in both conditions with more dramatic increases in anxiety that were especially apparent in the stress condition (see Figure 4a).

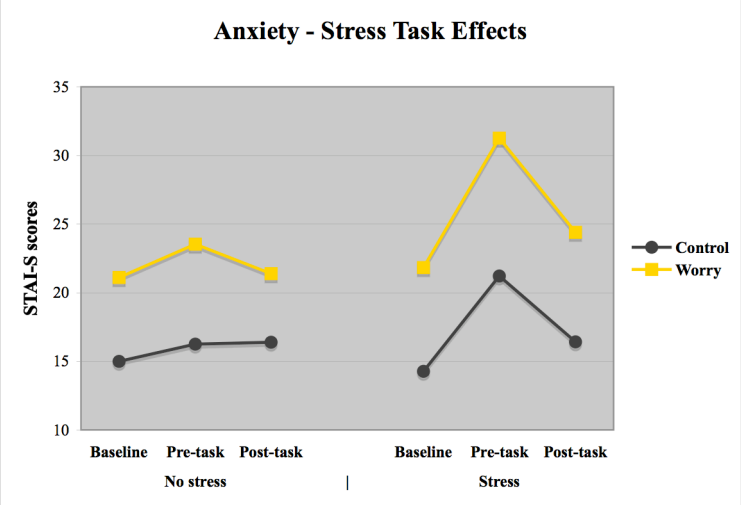

Figure 4a. Stress manipulation effects on state anxiety

Negative Affect. Analyses for NA revealed similar effects with main effects of Group, $F(1, 75) = 43.33$, $p<.001$, partial $\eta^2 = .366$, Condition, $F(1, 75) = 34.12$, $p<.001$, partial $\eta^2 = .313$, and Time, $F(2, 150) = 33.05$, $p<.001$, partial $\eta^2 = .306$, qualified by interactions of Group x Condition, $F(1, 75) = 8.08$, $p = .006$, partial $\eta^2 = .097$, and Group x Time, $F(2, 150) = 6.88$, $p = .001$), partial $\eta^2 = .084$, Condition x Time, $F(2, 150) = 37.90$, $p<.001$, partial $\eta^2 = .336$, and Group x Condition x Time, $F(2, 150) = 6.39$, $p = .002$, partial $\eta^2 = .079$. Again, decomposition of the Condition x Time interaction indicated the stressor manipulation was successful in producing greater NA increases from baseline in the stress condition than the no stress condition. Again, the worry group reported a greater manipulation effect than the control group (see Figure 4b).

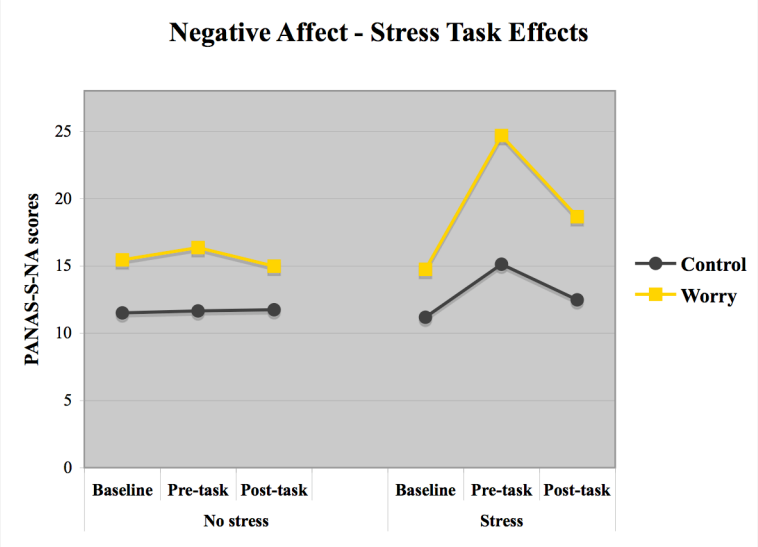

Figure 4b. Stress manipulation effects on negative affect

Positive Affect. A main effect of Time, $F(2, 148) = 35.76$, $p<.001$, partial $\eta^2 = .326$, qualified by a Condition x Time interaction, $F(2, 148) = 3.49$, $p = .033$, partial $\eta^2 = .045$, indicated successful PA reduction in the stress condition, where reports of PA

decreased from baseline only in the stress condition for both groups. A significant main effect of Group, $F(1, 74) = 7.76$, $p = .007$, partial $\eta^2 = .095$, indicated the worry group reported lower PA overall (see Figure 4c).

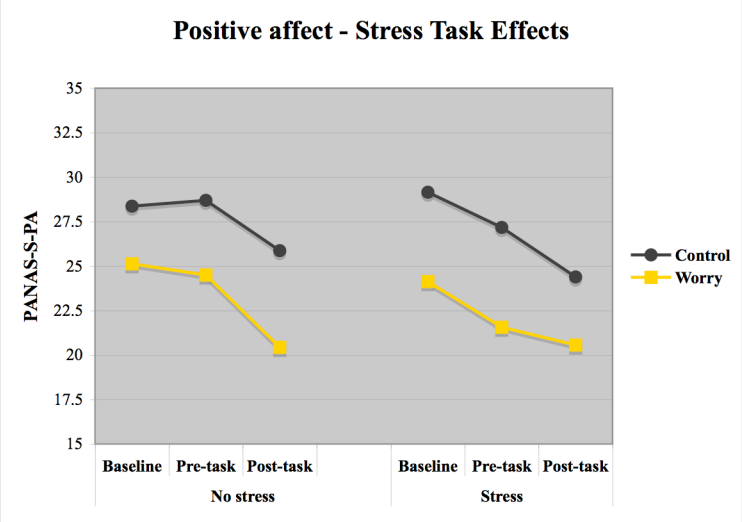

Figure 4c. Stress manipulation effects on positive affect

Arousal. Analyses for arousal ratings indicated successful manipulation of arousal, with an effect of Time, $F(2, 148) = 45.58$, $p = .001$, partial $\eta^2 = .381$, qualified by a Group x Condition x Time interaction, $F(2, 148) = 3.93$, $p = .022$, partial $\eta^2 = .050$. Decomposition of the interaction indicated the stress condition generated larger arousal increases from baseline than the no stress condition in both groups. The worry group reported slightly larger increases from baseline in the stress condition, but this appears driven by group differences in baseline arousal ratings in the stress condition rather than differences in stress condition pre-task ratings (see Figure 4d). Thus, the stressor task was reported as more arousing than the no stress task for both groups.

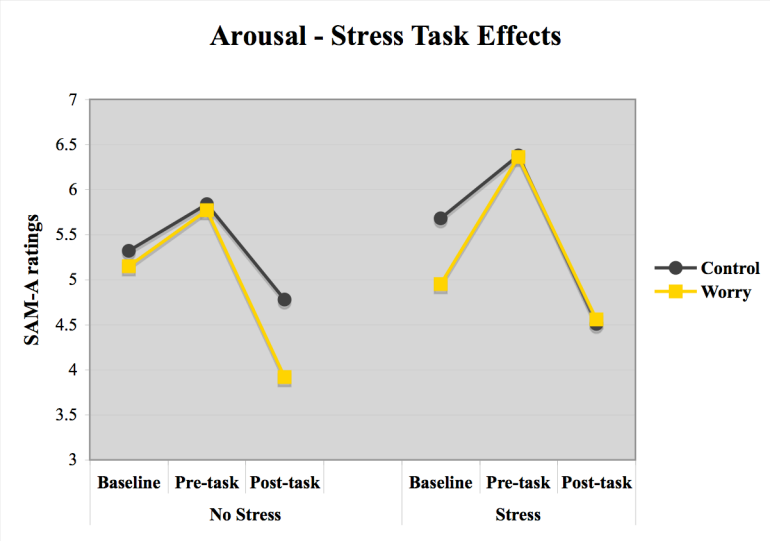

Figure 4d. Stress manipulation effects on arousal

Math Task Analyses – Appraisal, Anticipatory Anxiety, and Performance

Appraisal. Repeated measures ANOVAs were performed for MTAQ items, with Condition (no stress, stress) as a within-subjects factor and Group as a between-subjects factor. Main effects of Condition indicated that participants appraised the stressor (mental) math task as significantly more *demanding*, *stressful*, and *threatening* than the no stress (written) math task, and participants reported feeling more *nervous*, less *eager*, less *confident*, less *looking forward to* the stressor math task than the no stress math task (see Table 3). Participants in the worry group found both math tasks more *stressful* and *threatening*, and reported feeling less *eager*, less *confident*, less *looking forward to*, and more *nervous* about both math tasks than controls. Groups did not differ on how *demanding* they found the task, suggesting that the math task were not simply more difficult for one group than the other. Interestingly, the item *able to cope* showed main

effects of Condition and Group, qualified by a Group x Condition interaction, $F(1, 74) = 14.64$, $p<.001$, partial $\eta^2 = .165$.

Table 3. Group and condition effects on math task appraisal

Appraisal item	*F*	*df*	*p*	partial η^2
Demanding				
Condition	97.64	1,74	<.001	.569
Group	.134	1,74	.715	.002
Stressful				
Condition	90.57	1,74	<.001	.550
Group	22.90	1,74	<.001	.236
Threatening				
Condition	81.35	1,74	<.001	.524
Group	10.90	1,74	<.001	.128
Nervous				
Condition	47.52	1,74	<.001	.391
Group	13.92	1,74	<.001	.158
Eager				
Condition	19.42	1,74	<.001	.208
Group	6.40	1,74	.014	.080
Confident				
Condition	95.08	1,74	<.001	.562
Group	15.65	1,74	<.001	.175
Looking forward to				
Condition	41.39	1,74	<.001	.359
Group	9.72	1,74	.003	.116
Able to cope				
Condition	53.34	1,74	<.001	.419
Group	36.89	1,74	<.001	.333

Post hoc Bonferroni corrected follow up tests revealed that while both groups reported feeling less able to cope in the stress versus no stress condition (*p*s<.01), the worry group reported feeling less able to cope than controls in the no stress condition, $F(1, 75) = 12.57$, $p<.001$), and stress conditions, $F(1, 75) = 27.72$, $p<.001$. Worry group participants reported significantly greater decreases in ability to cope (no stress: $M =$

4.32, *SD* = .78, stress: *M* = 3.05, *SD* = 1.18) in the stress condition than controls (no stress: *M* = 4.84, *SD* = .437, stress: *M* = 4.45, *SD* = .83). In sum, both groups appraised the stressor task more negatively than the no stress task, with the worry group reporting more negative appraisals overall. Interestingly, *able to cope* was the only appraisal item where the stressor condition had more dramatic appraisal effects for the worry group.

Anticipatory Anxiety. A repeated measures ANOVA was performed with Group as a between subjects factor and Condition and Time (1, 2) as repeating within-subjects factors. As Anticipatory ratings were only made during each condition (i.e., no baseline ratings were made), a main effect of Condition would indicate successful manipulation. Analyses revealed main effects of Condition, $F(1, 76) = 48.86$, $p<.001$, partial $\eta^2 = .391$, and Group, $F(1, 76) = 19.67$, $p<.001$, partial $\eta^2 = .206$, qualified by a significant Group x Condition interaction, $F(1, 76) = 4.05$, $p = .048$, partial $\eta^2 = .051$. Anticipatory Anxiety ratings in the stress condition were higher for both groups than in the no stress condition, suggesting a successful manipulation of anticipatory anxiety. The lack of a significant Time effect suggested that the manipulation was successful at maintaining consistent anxiety levels throughout the computer task. The worry group had higher overall anticipatory anxiety, and larger increases in the stress condition than the control group (see Figures 4e and 4f).

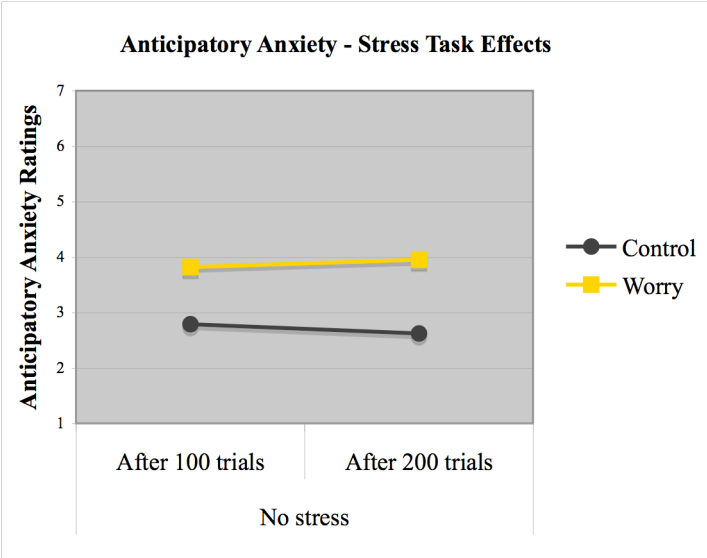

Figure 4e. Stress manipulation effects on anticipatory anxiety in the no stress condition

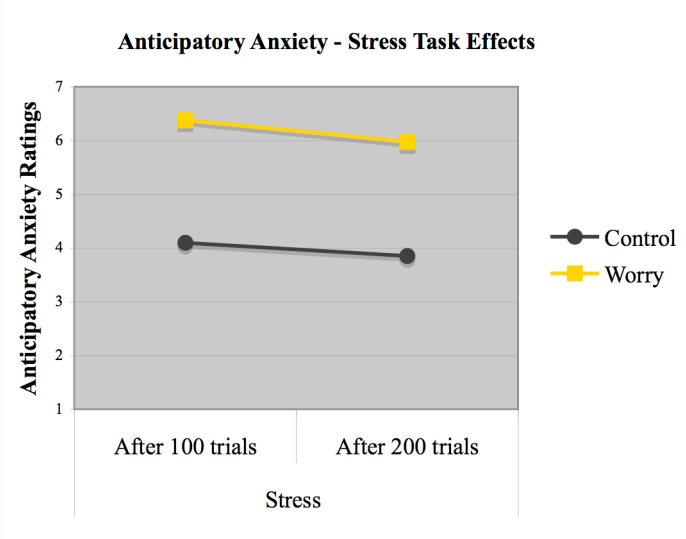

Figure 4f. Stress manipulation effects on anticipatory anxiety in the stress condition

Performance. One-way ANOVAs were performed to test for group differences in math task performance on the stressor mental math task occurring before the computer task (subtraction of 7s) and after the computer task (13s). Worry and control groups did

not differ in number of math problems attempted or correctly solved in either task, *p*s>.05.

Cross-sectional Analyses

Hypothesis 1. *In the control group, exposure to stress will lead to a decrease in hedonic capacity as measured by response bias on the signal detection task.*

Using data from the control group only, a repeated measures ANOVA was performed with Condition (no stress, stress) and Block (1, 2, 3) as within-subjects repeating factors to test for a main effect of Condition (no stress, stress) on response bias. Consistent with hypothesis 1, the Condition main effect was significant, $F(1, 38) = 4.43$, $p = .042$, partial $\eta^2 = .104$, with planned comparisons revealing the expected pattern of decreased response bias in the stress condition (see Figure 5). A main effect of Block also emerged, $F(2, 76) = 10.02$, $p<.001$, partial $\eta^2 = .209$, with planned contrasts revealing Block 1< Block 2< Block 3, all *p*s<.05, suggesting a pattern of increasing response bias across blocks in both conditions.

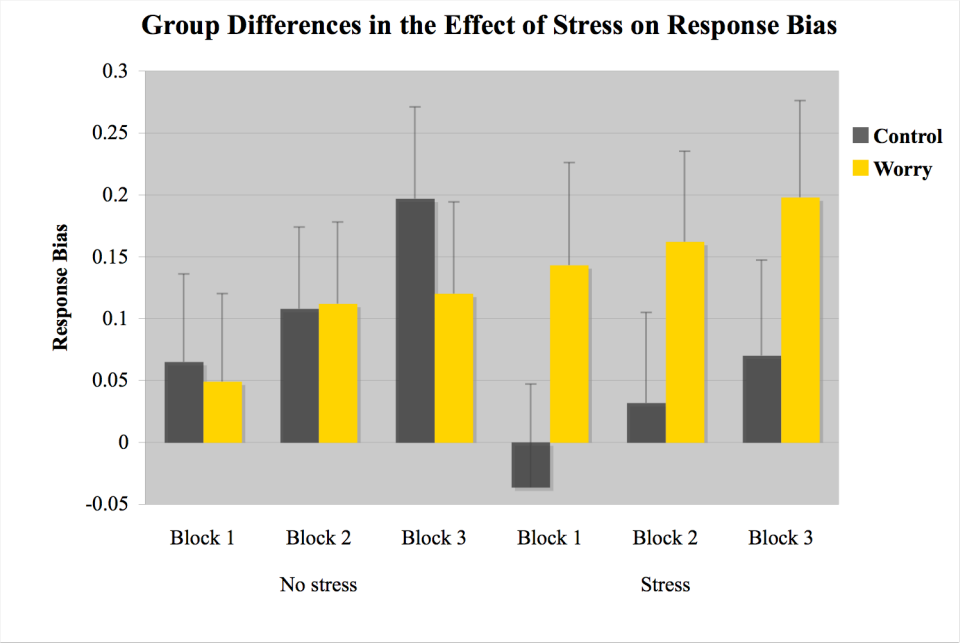

Figure 5. Group differences in the effect of stress on response bias

Hypothesis 2. *Compared to controls, individuals in the worry/GAD group will exhibit greater hedonic deficits as a result of stress. Therefore, the worry/GAD group will exhibit a greater reduction in response bias during stress than the control group.*

A repeated measures ANOVA was performed with Group (control, worry) as a between-subjects factor and Condition (no stress, stress) and Block (1, 2, 3) as repeating within-subjects factors to test for a Group x Condition interaction. A significant main effect of Block emerged, $F(2, 152) = 12.25$, $p<.001$, partial $\eta^2 = .139$, with planned contrasts revealing the expected Block 1< Block 2< Block 3 pattern of increasing response bias, all ps<.01.A significant main effect of Group, $F(1, 76) = 4.34$, $p = .041$, partial $\eta^2 = .054$, was qualified by a significant Group x Condition interaction, $F(1, 76) = 6.655$, $p = .012$, partial $\eta^2 = .081$. Follow up tests revealed no group differences in mean response bias scores in the no stress condition, $p>.05$. However, in the stress condition

the worry group had significantly higher mean response bias scores, $F(1, 76) = 9.95$, $p = .002$ (see Figure 5). Visual inspection of graphs showed that although the hypothesized interaction was significant, the form of the interaction was opposite our expectation—the worry group showed intact hedonic capacity during the stress condition. A repeated measures ANOVA performed separately for the worry group indicated that the effect of Condition was nonsignificant ($p = .13$). Thus, for worry group members response bias scores were unchanged across conditions, while control participants exhibited expected decreases under stress.

Parallel tests of Hypothesis 2 were performed comparing controls to the worry subgroup meeting GAD diagnostic criteria (n=22). Similar to previous analyses, a significant effect of Block emerged, $F(2, 118) = 6.54$, $p = .002$, partial $\eta^2 = .100$, with planned contrasts showing marginally significant differences between blocks, Block 1 < Block 2 (p=.055) and Block 2 < Block 3 (p=.050). Also similar to previous analyses, a significant main effect of Group, $F(1, 59) = 7.98$, p=.006, partial $\eta^2 = .119$, was qualified by a marginally significant Group x Condition interaction, $F(1, 59) = 3.69$, $p = .059$, partial $\eta^2 = .059$. Follow up tests revealed a similar pattern to worry analyses; the GAD group showed significantly higher response bias scores in the stress condition, $F(1, 59) = 9.32$, $p = .003$, and no group differences in the no stress condition. Again, separate analyses in the GAD group revealed no condition-related changes in response bias among GAD individuals ($p = .419$), suggesting a similar pattern of stable response bias under stress. In sum, analyses of GAD individuals were similar to worry group analyses, with the GAD group showing static response bias scores in the stress condition. Given the

similarity of results for GAD and worry groups further analyses focused upon the larger high worry group.

Given group differences in reported increases in state anxiety, negative affect, arousal, and negative task appraisal (as well as decreases in positive affect and positive task appraisals), repeated measures analyses were repeated in the full sample including each of these measures as covariates. Results remained unchanged, with none of the covariates emerging significant in the model (all *p*s>.05) and the Group x Condition interaction reported above remaining significant in each analysis (all *p*s<.05). These results suggest that group differences in response bias were unlikely to be due to elevated task anxiety or negative task appraisals in the worry group.

Discriminability, Accuracy, and Reaction Time analyses. Separate repeated measures ANOVAs were performed for discriminability, accuracy, and reaction time with Group as a between-subjects factor, and Condition and Block as repeating within-subjects factors. No significant effects were found for Group, Condition, Block, or any interaction for discriminability, suggesting that participants in both groups were able to discriminate short and long stimuli similarly across blocks and stressor conditions. In reaction time analyses, an effect of Block was found, $F(2, 152) = 5.64$, $p = .004$, partial $\eta^2 = .069$, with post hoc Bonferroni corrected tests revealing mean differences between Block 1 and Blocks 2 and 3 (1< 2 and 3) but no difference between Blocks 2 and 3. This suggests that overall participants in both groups became faster at responding after Block 1 in both conditions, and maintained this pace throughout the next two blocks of that condition. Group, Condition, and interaction effects were all non-significant, ruling out the possibility that group and condition effects on response bias reflect group differences

in overall task performance.

Moderation Analyses. Several individual difference variables were chosen *a priori* as potential moderators of the stress effect on response bias. Selection of factors was based on established links with depression risk that might serve as modifiers of the stress—depression relationship (neuroticism, past depression history), or links to reduced laboratory hedonic capacity by prior studies (perceived life stress, Pizzagalli et al., 2007). Because the study design involved within-subjects conditions, the method of Judd, Kenny, and McClelland (2001) was utilized, which allows tests of whether the magnitude of an experimental within-subjects effect (i.e., the change between conditions) is moderated by a variable that remains stable across conditions. In this method, the change in the dependent variable due to condition was regressed upon individual difference variables that were stable across conditions. According to Judd et al. (2001) significant regression coefficients would indicate significant moderation of the experimental effect by the individual difference variable. Separate analyses were performed for each group. Due to differences in directionality of the experimental effect among groups (i.e., increases versus decreases from baseline), change scores were computed as baseline – stress for controls, and stress – baseline for the worry group to achieve positive change scores for both groups.

Control Group Moderation Analyses. Among controls, the mean change in response bias from the baseline to stress condition was a decrease of .101 (SD = .299), with a trend toward higher levels of neuroticism predicting less decrease from baseline to the stress condition (R^2 = .094, $F(1, 37) = 3.86$, p = .052, r = -.307). To investigate this effect further, the control group was divided based on a median split of neuroticism

scores and ANOVAs compared the low (<13) and high (13+) scoring neuroticism groups on baseline and stress response bias means. Groups did not differ on levels of response bias in the stress condition. The high neuroticism group had significantly lower baseline response bias (M = .064, SD = .127) than the low neuroticism group (M = .192, SD = .233), $F(1, 37) = 4.66$, p = .037. Thus, among controls, higher neuroticism individuals showed low levels of baseline response bias with little change in the stress condition, whereas lower neuroticism was associated with higher baseline response bias and a greater decrease from baseline during the stress condition. All other potential moderators (perceived stress, past depression) were nonsignificant.

Worry Group Moderation Analyses. In the worry group, neither perceived stress nor neuroticism was related to change from baseline to stress conditions. Report of a past depressive episode (defined by IDD-L diagnosis) moderated the changes in response bias among worriers. A positive depression history was related to less change from baseline to stress conditions, R^2 = .188, $F(1, 37) = 8.58$, p = .006, r = -.434. Follow up ANOVAs comparing individuals with a past episode (n=18) to never depressed individuals (n=21) on response bias indicated that past depressed individuals had higher baseline response bias (M = .162, SD = .169) than individuals with no past episode (M = .035, SD = .159), $F(1, 37) = 5.82$, p = .021 (see Figure 6). Individuals with a past episode also had lower response bias scores in the stress condition (M = .097, SD = .210) than those with no prior episodes (M = .229, SD = .215). In sum, people high in worry exhibited a response bias pattern similar to controls if they had a past episode of depression (with mean response bias higher at baseline and decreasing in the stress condition). Worry group

members with no depression history showed blunted baseline response bias and dramatically increased response bias in the stress condition (see Figure 6).

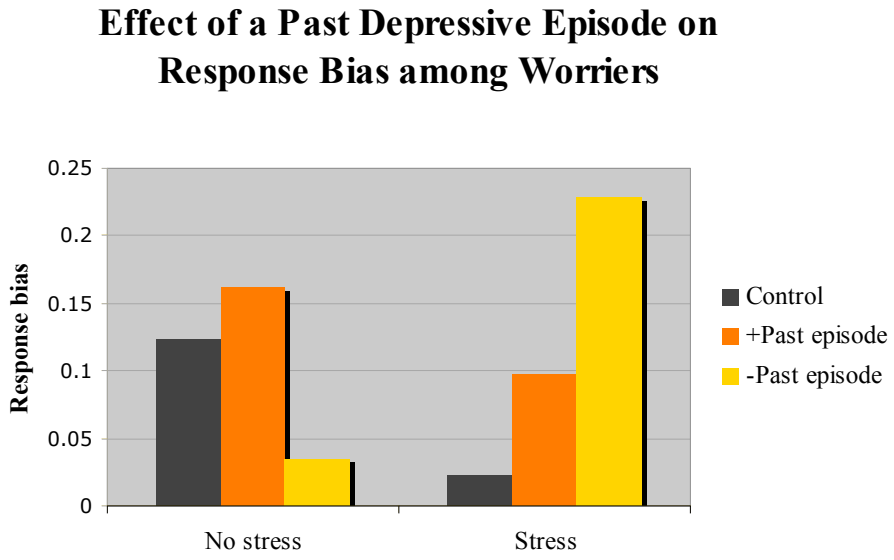

Figure 6. Moderation of response bias by past depression in the worry group

Exploratory Analyses Correlating Response Bias and Trait Measures. Response bias (baseline or stress) was unrelated to perceived stress (PSS), trait anhedonia (TEPS), behavioral approach or avoidance (BIS, BAS), trait positive affect (PANAS-T–PA), or extraversion (NEO-E). Response bias in the stress condition was positively correlated to neuroticism (NEO-N, r = .242, p=.033), and marginally correlated with trait anxiety (STAI-T, r = .211, p = .064).

Longitudinal Analyses

Hypothesis 3. *Stress-induced hedonic deficits will predict elevated levels of depression and anhedonia symptoms one month later. This effect will be seen in both*

groups, with the worry/GAD group showing an enhanced effect compared with controls. Prospective anxiety symptoms will also be investigated as an exploratory outcome variable.

Thirty-four participants (20 controls, 13 worry) completed follow measures of depression (BDI-II), anxiety (BAI), and anhedonia (MASQ-AD). Follow up measures were completed between 24 and 107 days following the lab visit (M=39.29, SD = 15.63). Follow up completers did not differ from non-completers on initial group status, $\chi^2(1, N=78) = 1.91$, $p>.05$. One way ANOVAs found no differences between completers and non-completers on initial BDI-II, BAI, PSWQ, IDD-L, IDD, or response bias scores in either condition, all ps>.05.

Correlation analyses using the entire sample revealed no significant relationship of response bias in the stress condition to any of the follow up measures (BDI-II, BAI, MASQ-AD). Results were unchanged when number of follow up days was controlled in a partial correlation analysis. When groups were analyzed separately, response bias in the stress condition was marginally negatively related to future BDI-II scores in the control group, with higher stress response bias predicting lower future depression scores. Among worriers, stress response bias showed a trend level positive relationship to anhedonia (MASQ-AD) in the worry group with higher stress response bias predicting higher future depression symptoms (see Table 4). Thus, Hypothesis 3 was not supported.

Table 4

Correlation analyses (controls *n*=20 above diagonal, worry *n*=14 group below)

Measure	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.
1. Baseline response bias	-	-.249	-.112	-.111	-.079	-.238	-.451*	-.161	-.311	-.287
2. Stress response bias	-.151	-	-.080	-.129	-.155	.015	-.407†	-.303	-.333	-.348
3. BDI-II	.122	-.085	-	.590**	.787**	.414**	.567**	.549*	.497*	.527*
4. BAI	.266	-.260	.752**	-	.563**	.032	.327	.771**	.379	.292
5. IDD total score	-.013	-.137	.528**	.384*	-	.367*	.526*	.442	.497*	.392
6. MASQ-AD	.092	-.012	.603**	.305	.281	-	.650**	-.020	.353	.793**
7. Follow up BDI-II	-.252	.398	.544*	.069	.071	.352	-	.516*	.752**	.725**
8. Follow up BAI	.119	-.139	.526	.345	.331	.314	.615*	-	.715**	.280
9. Follow up IDD total	-.468	.507†	.427	-.053	-.112	.465	.825**	.292	-	.559*
10. Follow up MASQ-AD	-.502	.510†	.571*	.103	.108	.523	.801**	.371	.756**	-

† $p<.08$, * $p<.05$, ** $p<.01$

BDI-II: Beck Depression Inventory, BAI: Beck Anxiety Inventory, IDD total score: Inventory to Diagnose Depression total score, MASQ-AD: Mood and Anxiety Symptom Questionnaire – Anhedonia subscale score.

Baseline Response Bias as a Predictor of Current and Future Depressive Symptoms. Some studies report that higher baseline response bias (specifically the change in response bias from Block 1 to Block 3) predicts lower current and future depression symptoms, (Pizzagalli et al., 2005), while others find no relationship (Bogdan & Pizzagalli, 2006). In the current sample, baseline (no stress) response bias was unrelated to current depression, anhedonia, and anxiety measures, but was negatively related to future MASQ-AD anhedonia symptoms (r = -.374, p = .035), with a trend for BDI-II scores (r = .326, p = .060). Results were virtually unchanged when number of days to follow up was partialled out. Lower levels of (or blunted) baseline response bias predicted higher depression and anhedonia symptom levels at follow up.

Hierarchical regression analyses were run for follow up depression and anhedonia measures including their initial values as step 1 predictors to assess whether baseline response bias predicted follow up symptoms after accounting for initial symptom levels. Because there were no group differences in baseline response bias, these analyses were performed in the entire sample. Analyses for future anhedonia (MASQ-AD) in the entire sample found no significant effects for baseline response bias after accounting for baseline symptoms (p>.05). Baseline response bias predicted follow up BDI-II scores even when baseline BDI-II scores were included in the model (see Table 5). This result held when number of follow up days was included in the model. When group status and interaction terms were added to the analysis, results were also unchanged, with group and all interaction terms nonsignificant. In sum, even after controlling for initial depression

symptoms, blunted baseline response bias predicted higher depression symptom levels one month later.

Table 5

Regression analyses predicting future depression symptoms

Predictors	$R^2\Delta$	$F\Delta$	*df*	*B*	*SE B*	β	*t*	*p*
Analyses for BDI-II								
Step 1	.393**	20.744	1,32					
Constant				1.999	1.078		1.854	.073
Baseline BDI-II				.506	.111	.627	2.555	<.001
Step 2	.084*	4.999	1,31					
Constant				2.987	1.108		2.695	.011
Baseline BDI-II				.492	.105	.610	4.694	<.001
Baseline response bias				-6.794	3.039	-.291	-2.236	.033

*p<.05, **p<.01

Discussion

The primary aim of this study was to investigate the effect of stress on hedonic capacity among individuals with GAD, a group at greater risk for depression following stress. Low hedonic capacity, or anhedonia, may be etiologically significant in the development of depression (e.g., Forbes & Dahl, 2005). Previous work suggests life stress may reduce hedonic capacity (Berenbaum & Connelly, 1993), and recent experimental studies have induced anhedonia behaviorally via a laboratory stressor (Bogdan & Pizzagalli, 2006). We sought to conceptually replicate stress-induced anhedonia with a more ecologically valid laboratory stressor, to extend the paradigm to investigate GAD in an analog sample (a high worry group), and to examine stress-induced anhedonia as a predictor of future depression symptoms. Secondary analyses examined potential moderators of the effect of stress on hedonic capacity.

Consistent with hypotheses and prior work, control participants demonstrated the expected baseline reward learning pattern, increasingly modulating their behavior to maximize rewards at baseline, and exhibiting behavioral anhedonia under stress. Contrary to hypotheses, worriers did not exhibit enhanced hedonic blunting under stress, instead showing intact hedonic responding under stress. Surprisingly, when depression history was considered, worriers with no past depression history exhibited *enhanced* hedonic responses under stress. Our hypothesis that the magnitude of stress-induced anhedonia would predict higher future depression symptoms was not supported. However, blunted

baseline hedonic responses predicted higher levels of depression symptoms one month later. Results of the current study suggest 1) previous findings of laboratory stress-induced anhedonia generalize to a more ecologically valid stressor, 2) a normative consequence of stress may be a temporary blunting of hedonic capacity, and 3) this effect may be moderated by neuroticism, 4) stress may operate differently among worriers, who display intact hedonic responding under stress, 5) past depression may moderate stress effects in worriers, and 6) blunted baseline hedonic capacity predicts future depression symptoms. Each of these points is discussed in turn, followed by limitations and suggestions for future study.

Replication with a More Ecologically Valid Stressor

Bogdan and Pizzagalli (2006) found threat of shock to induce behavioral anhedonia in healthy controls. By replicating this effect with the mental math stressor, the current study extended this paradigm to a different class of stressors. First, mental math is a more ecologically valid stressor with verbal, interpersonal, and evaluative components that more closely mimic a broader range of life stressors than the threat of physical harm. One could argue that to the extent that the mental math task more closely approximates actual life stressors than shock threat, the stress-induced anhedonia effect generalizes to a more ecologically valid stressor.

Second, the current results demonstrate the effect generalizes to anticipatory anxiety of a delayed threat—where the anticipated threat is not immediate. In the Bogdan and Pizzagalli (2006) study, participants completed the response bias task while continually viewing the likelihood that they might receive a shock purportedly based on

their own performance. Participants were therefore anticipating an immediate threat (i.e., shock that could occur any second). In the current study, participants anticipated a delayed threat. Participants completed an observed and evaluated mental math task during which they were frequently prompted for speed and accuracy by a voice over an intercom. Upon completion, they were told to anticipate performing an even more difficult version of this task and were continually reminded of that anticipated task while the dependent variable (response bias) was being measured. Naturally-occurring life stress often involves either anticipating the delayed threat of a potentially negative outcome (e.g., medical test results, company lay offs, an upcoming public speaking engagement) or anticipating immediate threat during an acute stressor (e.g., the act of public speaking, an interpersonal confrontation). Taken together with previous results, the current findings suggest that both immediate and delayed threats can impair hedonic capacity.

Stress-Induced Anhedonia May be Normative

The finding of stress-induced anhedonia in control participants is consistent with prior experimental and nonexperimental findings of reduced hedonic capacity during stress (e.g., Berebaum & Connelly, 1993; Bogdan & Pizzagalli, 2006; Henriques & Davidson, 1994), adding to a growing body of work that suggests experiencing stress temporarily reduces individuals' experience of and responses to reward stimuli. From an evolutionary perspective, it makes good sense that organisms would temporarily down regulate pursuit of rewards under stressful conditions (e.g., in the presence of a predator discontinue search for food or a mate, see Nesse, 2001). The current study and Bogdan

and Pizzagalli (2006) add to literature demonstrating that threatening stressors that elicit anxiety states induce behavioral anhedonia.

How does the temporary stress-induced anhedonia seen in healthy persons relate to the pervasive hedonic blunting exhibited during a depressive episode? Depressed persons demonstrate baseline hedonic deficits in the laboratory (Henriques & Davidson, 2000), consistent with the idea that their hedonic deficits can be long lasting. Recent work suggests that resolution of depressed mood states may be associated with a normalization of baseline hedonic response (Vrieze, Pizzagalli, Demyttenaere, & Claes 2009). Thus, there is evidence that behavioral anhedonia can be long lasting while a person is in a mood episode and can be induced temporarily by anxiety-provoking stressors in healthy persons. It is unknown, however, whether hedonic deficits accompany other negative mood states (e.g., sad mood) that occur outside of depressive episodes at low levels of severity (e.g., mood fluctuations in healthy persons). Although the current study found no relationship of baseline hedonic capacity to current reports of depression symptoms, which is consistent with Bodgan and Pizzagalli (2006), others have found higher baseline hedonic responding related to lower current depression symptoms (Pizzagalli et al., 2005). As anhedonia is increasingly being considered etiologically significant in the development of depression, understanding normative variations in hedonic capacity—and the mood or emotion states that can elicit these changes—can inform our understanding of the development of persistent anhedonic responding seen in MDD.

Stress-Induced Anhedonia is Moderated by Neuroticism

Secondary moderation analyses indicated that controls characterized by high neuroticism demonstrated blunted baseline hedonic capacity that showed little change under stress, whereas lower neuroticism exhibited the normative response pattern of higher baseline response bias and a greater decrease from baseline during stress. In the context of a life stress literature that suggests that individuals with higher neuroticism are at greater risk of developing depression after a stressor (see Kessler, 1997), these results suggest that one way neuroticism may influence the stress–depression relationship is by blunting baseline hedonic capacity. The pattern of blunted hedonic capacity at baseline is similar to the pattern seen in depressed samples (e.g., Pizzagalli et al., 2005). At the same time, there was no relationship between response bias and current depression or anxiety symptoms, even though these constructs were both correlated with neuroticism in this sample (rs = .66 and .57, BDI-II and BAI respectively, ps<.001). Neuroticism, a known risk factor for both depression and anxiety, was investigated as a stress moderator because of strong prior links to enhancing the depressogenic effects of life stress. The current study offers preliminary evidence that high neuroticism may be linked to blunted baseline reward functioning, and although neuroticism levels were not related to hedonic capacity during stress in this sample, more evidence is needed before concluding that no relationship exists.

Intact and Hyper-Hedonic Stress Response in Worriers

Given prior findings that GAD increases the depressogenic effects of stress (Hettema et al., 2006), it was hypothesized that compared to controls individuals high in

trait worry (an analog GAD group) would exhibit a more dramatic decrease in hedonic capacity following stress. Although worriers exhibited baseline hedonic capacity similar to controls, contrary to expectation, they exhibited *intact* hedonic capacity following stress. Depression history was investigated as a potential moderator of stress effects on hedonic capacity. Surprisingly, worriers with a history of depression displayed the normative pattern of baseline reward learning and behavioral anhedonia under stress, while worriers without past depression displayed *blunted* baseline hedonic capacity and *enhanced* hedonic responses under stress.

The differential effects of stress on hedonic capacity may seem counterintuitive at first glance, as one might assume that individuals at risk for psychopathology (especially depression) should display deficient—not intact or enhanced—hedonic responding under stressful conditions. In considering this surprising effect, it is first important that we were able to rule out several methodological or third variable interpretations. First, there were no group differences in any other dependent variable measured during the signal detection task (accuracy, discriminability, reaction time), which suggests that the stress effect is specific to hedonic response in this case, and not driven by group differences in task performance. Second, although worriers reported higher depression symptoms, which typically would be expected to blunt hedonic responding, depression symptoms did not relate to behavioral anhedonia on this task. Finally, even though worriers reported the stressor task to be more anxiety-provoking than controls, the magnitude of participants' anxious responses to the stressor were unrelated to hedonic responses, preventing this from explaining the pattern of group differences in hedonic capacity in the current study.

Mainstream theoretical accounts of anxiety disorders, including GAD, have generally not integrated reward system functioning, working under the assumption that anxiety is functionally unrelated to hedonic capacity (e.g., Borkovec's GAD avoidance theory, see Borkovec, Alcaine, & Behar, 2004, cf. Kashdan & Hofmann, 2008). There are few studies exploring reward response in anxiety disorders, and none that explore hedonic capacity under stress. Observed aberrations in hedonic capacity are generally considered a direct function of unipolar or bipolar mood disorder comorbidity (see Mineka, Watson, & Clark, 1998; McIntyre et al., 2006), and aside from mood disorder comorbidity, anxious groups typically do not report global deficits in hedonic capacity (Dyck et al., 1994). However, the emotion dysregulation model of GAD put forth by Mennin and colleagues (2005; 2008) theorizes broadly that GAD is associated with hyperreactivity to various emotional contexts and is a useful framework for considering aberrant reward responding in GAD. The emotion dysregulation theory suggests that in GAD worry functions to dampen or suppress emotional hyperarousal that GAD individuals find aversive. Although the preponderance of evidence in support of this theory has investigated hyperreactivity in negative contexts, there is some evidence that individuals with GAD may be more reactive to pleasant emotions as well. In one study, analog GAD participants were more responsive a pleasant piece of music than controls, reporting significant reductions in physiological anxiety symptoms following the manipulation whereas controls reported no changes (Mennin et al., 2005). Additionally, individuals with GAD report experiencing emotional situations as more intense than controls (without regard to valence), and report being more fearful of experiencing positive emotions than controls (Turk, Heimberg, Luterek, Mennin, & Fresco, 2005).

Taken together with these findings, the current results adds to this preliminary evidence that analog GAD may be associated with increased hedonic responses under certain circumstances.

An evolutionary perspective is also potentially helpful for understanding these results. As described in a previous section, it may be adaptive for organisms to suspend reward learning under conditions of stress, which accounts for controls experiencing intact hedonic responding at baseline and blunted hedonic responding under stress. Thus, the demonstration of intact hedonic responding under stress among worriers (or enhanced responses in the never-depressed subgroup), may represent a maladaptive response pattern characteristic of GAD and high worry groups. By not responding appropriately to an environmental threat (in this case by increasing reward learning even when experiencing a stressor as more frightful than controls do), worriers may be exhibiting a unique brand of context insensitivity (see Rottenberg, 2005 for context insensitivity theory of depression). If personal resources are being allocated toward potential rewards during a threatening time, the individual may be less able to deal with the threat (i.e., more vulnerable to potential negative outcomes as a result). Mennin's emotion regulation theory (e.g., Mennin et al., 2005; 2008) posits broadly that GAD is associated with emotional inflexibility, with diminished ability to respond adaptively to and regulate emotions in a given context. However, this and other theoretical accounts of anxiety have focused mainly upon negative emotions and lack specific predictions about responses to positive stimuli or rewards. The current findings suggest that GAD and worry may be associated with maladaptive responses to threat, in the form of intact reward learning during a time when this response may be detrimental.

The Effect of Past Depression on Hedonic Responses under Stress among Worriers

Given previous findings relating current depression to blunted hedonic capacity (e.g., Pizzagalli et al., 2005), one could argue that past depression might be expected to continue to blunt baseline hedonic capacity, especially in individuals at risk for depression. However, our results suggest the opposite effect: among those at risk for depression by way of analog GAD a past depressive episode was associated with a response pattern similar to controls, with mean response bias higher at baseline and decreasing in the stress condition, and those with no depression history showed blunted baseline response bias and dramatically increased bias in the stress condition (see Figure 6). This finding is puzzling, especially given the lack of effects for current depression symptoms. Both groups (worriers with and without depression history) are at increased risk for depression, but only the worriers without depression history exhibit strong aberrations in reward response. Could these group differences be indicative of two distinct subgroups? Perhaps hedonic capacity operates differently in worriers before and after depression onset. That is, prior to depression onset worriers may show blunted baseline hedonic capacity that is heightened under stress, but exposure to a depressive episode may lead to enduring changes in how stress affects hedonic capacity.

Other depression risk factors, such as family history of depression have been shown to further blunt hedonic capacity following stress. Berenbaum and Connelly (1993) examined non-depressed people and found that individuals with and without a family history of depression had similar intact hedonic capacity in a control condition, and although both groups showed decreased hedonic capacity in the stress condition, this

effect was enhanced for individuals at risk for depression. That is, the presence of a depression risk factor was associated with enhanced blunting of hedonic capacity under stress. In combination with the current findings, hedonic responding under stress may be differentially influenced by various depression risk factors (i.e., past depression, worry, family history of depression), perhaps suggesting that individual factors may affect the stress-hedonic response relationship distinct ways, increasing depression risk via unique mechanisms.

Predicting Future Depression

Examining how reward biases relate to future depression can elucidate what response bias patterns are potentially linked with an important clinical outcome. Hedonic capacity in the no stress baseline condition, but not in the stress condition, predicted future depression symptoms. In the entire sample, lower baseline hedonic capacity was related to worse outcomes (higher depression symptoms) at follow up, even after accounting for initial symptom levels. This is consistent with results from a prior study of behavior hedonic capacity (Pizzagalli et al., 2005), as well as previous work utilizing other indices of reward responding and positive emotionality that suggest that higher levels of baseline levels of hedonic capacity are associated with positive mental and physical health outcomes (see Morris et al., 2009). Prediction of symptoms via a behavioral measure of hedonic capacity (such as the task utilized in the current study) is particularly informative, as it provides a more objective, implicit assessment of reward responding than self-report assessments (see Pizzagalli et al., 2005). This finding adds to other evidence that pre-morbid hedonic functioning may be etiologically significant in

the development of depression (e.g., Forbes & Dahl, 2005), with lower baseline hedonic responding related to higher depression risk.

Limitations and Future Directions

The current study had a number of features that limit the generalizability of these results. First, only females undergraduates were included, which precludes generalization to male or community samples. Second, although the laboratory stressor used in the current study is more ecologically valid than the threat of shock stressor used in Bogdan & Pizzagalli (2006), it is still artificial and does not resemble many real life stressors. Future studies examining daily life stressors, perhaps utilizing experience-sampling techniques, will be needed to understand how these results map onto behaviors outside the laboratory. Additionally, broader behavioral correlates of baseline hedonic capacity need to be examined in order to generalize performance on a response bias task to reward response in the individual's actual environment. Third, to increase the feasibility of the study we used self-report instruments to select our sample; one should be cautious about generalization to DSM syndromes until results are replicated in samples constituted by diagnostic interview measures of GAD as well as current and past MDD. Finally, future studies are needed to replicate and explicate the novel findings of this study, specifically increased hedonic capacity under stress among worriers, and the role of past depression in modulating this effect.

Summary and Conclusions

The present study aimed to test a model where at-risk individuals experience enhanced deficits in hedonic capacity as a result of stress. Extending a previous study of stress-induced hedonic deficits in healthy controls (Bogdan & Pizzagalli, 2006), this was the first study to examine the impact of stress on hedonic capacity in a group at elevated risk for developing depressive symptoms. A behavioral measure of anhedonia was acquired from an analog GAD sample (a high worry group) and control participants during baseline no-stress and stress conditions. Hedonic capacity was indexed by participants' ability to modulate responses to maximize reward on a signal detection task incorporating tangible reward for correct responses. controls exhibited the expected reward learning pattern in the baseline condition, demonstrating intact hedonic responding, as well as the expected pattern of behavioral anhedonia under stress. Contrary to predictions, worriers demonstrated intact hedonic capacity under stress. This effect was modulated by past depression diagnostic status, where worriers with no past history of a depressive episode demonstrated blunted hedonic capacity at baseline and heightened hedonic capacity under stress. Alternatively, worriers with a positive life history of depression demonstrated a response pattern more similar to controls. For both groups, blunted baseline measures of hedonic capacity predicted higher depression scores at follow up. Stress appears to operate differently on behavioral hedonic capacity in worried and control groups, and this group effect is even more striking when history of depression is accounted for. Future studies are needed to further explicate the mechanisms by which reward response may be modulated differentially under stress

among worriers and non-worriers, as well as how this might change as a function of having experienced a depressive episode.

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