Major depressive disorder (MDD) is characterized by significant affective dysfunctions, including the cardinal symptom of anhedonia (American Psychiatric Association, 2013). Many factors have been implicated in depression etiology, including the presence of premorbid psychopathology, especially generalized anxiety disorder (GAD; Merikangas et al., 2003), and stressful life events (Monroe, Slavich, Torres, & Gotlib, 2007). An estimated 70% of first onset depressive episodes are preceded by recent stressors (Monroe & Harkness, 2005); however, most individuals experiencing life stress do not become depressed (Kessler, 1997). A large literature has emerged addressing how stressors can have high sensitivity but low specificity for predicting depression.

Diathesis–stress theories (Brown & Harris, 1978; Hammen, 1991; Monroe & Simons, 1991; Post, 1992) have addressed the specificity question by examining predisposing factors that may heighten the depressogenic effects of stress in a select few. These “stress modifiers” (Kessler, 1997, p. 207) include neuroticism (Kendler, Kuhn, & Prescott, 2004), negative attributional style (Kwon & Laurenceau, 2002), genetic vulnerability (Caspi et al., 2003), and premorbid psychopathology, including prior depression (Hammen, 1991) and anxiety (Frijts, Wittchen, Pfister, & Lieb, 2002; Hettema, Kuhn, Prescott, & Kendler, 2006). Speaking to the sensitivity issue is work exploring what stress properties or processes are potentially depressogenic. Life stress, for example, has been shown to blunt hedonic functioning (Berenbaum & Connelly, 1993), and stress-induced anhedonia has been proposed as a means by which life stress precipitates depressive episodes (Bogdan & Pizzagalli, 2006).

The present study experimentally investigated a proposed depressogenic stress process, stress-induced hedonic blunting, in a group known to be sensitive to the depressogenic effects of stress. We assessed effects of laboratory stress and neutral conditions on reward learning, a key aspect of hedonic functioning, in individuals with GAD, who are at increased depression risk after life stress (Hettema et al., 2006). Depression symptoms were ascertained at intake and at a one month follow-up. Before presenting our hypotheses, we review relevant work on GAD as a depression risk factor, stress-induced anhedonia as a depression pathway in GAD, and the reward learning paradigm for studying hedonic functioning in the laboratory.

**Generalized Anxiety Disorder as a Stress Modifier**

Generalized anxiety disorder (GAD) is characterized by chronic worry (American Psychiatric Association, 2013), and is a known depression risk factor. GAD and MDD are highly comorbid (Wittchen, Zhao, Kessler, & Eaton, 1994); GAD co-occurs with MDD more than any other anxiety disorder (Brown, Chorpita, & Barlow, 1998; Kessler, Chiu, Demler, & Walters, 2005), most frequently predating depression onset (Breslau, Schultz, & Peterson, 1995). This common sequential pathway is largely unexplained. Among the more compelling hypotheses is that GAD may sensitize individuals to the depressogenic effects of stress. Hettema et al. (2006) examined prior GAD and life stress as predictors of depression onset in a large twin sample (n = 8,068). Individuals with GAD were more vulnerable to depression after a stressful life event, regardless of its objective threat level. Although these findings support GAD as a stress-modifier, it is yet unclear what depressogenic stress processes are operating.
Stress-Induced Anhedonia as a Pathway to Depression

The processes by which stressful life events give rise to depressive episodes are not well understood. One candidate process involves stress-induced blunting of hedonic function (Berenbaum & Connelly, 1993; Bogdan & Pizzagalli, 2006; Pizzagalli, Bogdan, Ratner, & Jahn, 2007). Anhedonia, which is thought to represent impaired reward processing (Pizzagalli, Jahn, & O’Shea, 2005), has long been of interest among depression researchers as a symptom and risk factor (Meehl, 1975; Morris, Bylsma, & Rotenberg, 2009; Pinto-Meza et al., 2006; Schrader, 1997). Demonstrations of stress-induced anhedonia fed discussion of this process as a potential mechanism of depression development in humans (Bogdan & Pizzagalli, 2006) and other species (Anisman & Matheson, 2005). Berenbaum and Connelly (1993) examined hedonic functioning in healthy individuals before and after life stress in two samples. College students reported 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) compared individuals with high and low levels of perceived life stress and found that high perceived stress was associated with blunted hedonic function, as indexed by a behavioral (reward learning) laboratory task. These results suggest that stress blunts hedonic functioning, which is both a symptom and a risk factor for depression. However, no studies have examined this stress effect in groups known to be at increased depression risk.

Hedonic Functioning in GAD

Despite the strong relationship between anxiety and depression, relatively few studies examine hedonic functioning in anxiety disorders. Studies utilizing patient reports of anhedonia are mixed. Patients with GAD sometimes endorse low positive emotion on rating scales (Chambers, Power, & Durham, 2004), even apart from co-occurring depression symptoms (Power & Tarsia, 2007), but there are several null findings (Brown et al., 1998; Decker, Turk, Hess, & Murray, 2008). In laboratory studies, GAD patients report less positive emotion than controls in response to positive stimuli (Srivastava, Sharma, & Mandal, 2003), and experimentally induced worry—a key feature of GAD—decreases positive emotion reports (McLaughlin, Borkovec, & Sibrava, 2007). Notably, these mixed findings are based on self-report assessments of hedonic function, which measure the subjective component of hedonic functioning. In addition, strong inferences about hedonic functioning in GAD necessitate accounting for effects of current depression symptoms, which are highly comorbid with GAD and known to blunt hedonic functioning (Pizzagalli et al., 2005). Less is known about how past depression might alter hedonic functioning in anxious individuals, but some work suggests that hedonic deficits can remain upon depression remission (Pinto-Meza et al., 2006; Schrader, 1997). To our knowledge, no laboratory studies of GAD have assessed the effects of stress or past depression on hedonic functioning.

Laboratory Studies of Reward Learning

Recent methodological advances allow for objective laboratory assessments of hedonic function (Pizzagalli et al., 2005), including behavioral measures of reward learning. Reward learning paradigms assess a person’s ability to learn the reward value of environmental contingencies and modulate behavior appropriately to maximize reinforcement. From a behavioral perspective, lowered responsiveness to environmental rewards may lead to diminished engagement in pleasurable activities and reduced motivation to pursue rewarding outcomes (Depue & Iacono, 1989; Forbes & Dahl, 2005). Modified signal detection tasks can be used to assess reward learning by measuring the response bias that develops toward a more frequently or generously rewarded stimulus (Pizzagalli et al., 2005). Detection theory suggests that if one correct response is rewarded more often than another, people with robust reward learning will develop an implicit preference toward the more rewarded stimulus (Macmillan & Creelman, 1991), modulating behavior to maximize reward.

Individual differences in reward learning are clinically meaningful. For example, dysphoric individuals (Henriques, Glowacki, & Davidson, 1994; Pizzagalli et al., 2005) and individuals with MDD (Henriques & Davidson, 2000) show lower baseline reward learning compared to controls, a pattern that cannot be explained by task performance differences (for example, accuracy; Pizzagalli, Iosifescu, Hallett, Rainer, & Fava, 2008). Reduced reward learning also predicts elevated anhedonia symptoms one month later (Pizzagalli et al., 2005). Finally, reward learning paradigms also distinguish individuals with enhanced reward learning from controls. For example, one study found that individuals who were administered nicotine, which affects brain reward centers, showed greater reward learning than controls (Barr, Pizzagalli, Culhane, Goff, & Evins, 2008).

The Effect of Stress on Reward Learning

Two prior studies have found laboratory evidence that stress induces reduced reward learning. As noted previously, Pizzagalli et al. (2007) found blunted reward learning in individuals reporting high levels of perceived life stress in two independent samples. Bogdan and Pizzagalli (2006) found that lab-induced stress leads to reduced reward learning relative to a no-stress condition in healthy females. The study utilized a shock threat stressor condition whereby participants had two electrodes placed on their necks. While participants performed the computer-based signal detection task, an indicator on the computer screen displayed the likelihood of shock, ostensibly tied to task performance. In the control condition, participants always saw a very low shock likelihood. In the stress condition they saw fluctuating and higher levels of shock likelihood. Participants exhibited significantly lower reward learning in the stress condition than the control condition. Bogdan and Pizzagalli (2006) showed that healthy individuals experience stress-induced hedonic deficits and provided an innovative design and methodology to probe such effects in at-risk individuals.

The Present Study

This study was the first to our knowledge to examine the effects of stress on hedonic functioning in healthy individuals and individuals with analogue GAD. Our primary aims were to address whether (a) individuals with GAD exhibit lower reward learning compared to controls, (b) to examine the effects of stress on reward learning as a function of GAD status, and (c) to examine the
predictive relationship between reward learning and future depressive symptoms.

To achieve these aims, we assessed reward learning by indexing response bias on a signal detection task incorporating monetary rewards (used in Bogdan & Pizzagalli, 2006; Pizzagalli et al., 2005; Pizzagalli et al., 2007; Tripp & Alsop, 1999). We used a mental arithmetic task as the experimental stress condition. Bogdan and Pizzagalli (2006) found effects on reward learning for shock threat, but not negative performance feedback, which the authors speculated was due to negative feedback not generating sufficient anxious arousal and social evaluation. Prior work has found mental arithmetic generates significant increases in anxious arousal compared with baseline, including changes in affective ratings, heart rate, blood pressure, and skin conductance that are similar in magnitude to a shock stressor (Noteboom, Fleschner, & Enoka, 2001). Mental arithmetic in a socially evaluative context arguably has greater ecological validity than shock threat. Because previous work has found reduced reward learning to predict higher future anhedonia (Pizzagalli et al., 2005), we followed participants for one month and reassessed depression symptoms for longitudinal analyses.

We hypothesized that controls would exhibit the expected pattern of intact reward learning (i.e., developing a response bias) in the neutral condition, which would be blunted by a stressor. Given mixed findings and the lack of precendents, we tested two alternate hypotheses with regard to GAD effects: (a) the GAD group would exhibit an overall blunting in reward learning compared with controls, and (b) the GAD group would exhibit intact reward learning under neutral conditions, but greater stress-induced blunting than controls. Because current depression symptoms are known to blunt reward learning, we excluded participants with high levels of current depression and statistically controlled for depression symptoms in our main analyses. Because past depression is a potent risk factor for future depression, especially after a stressor (Kessler, 1997), and little is known about hedonic deficits that may remain as a consequence of prior depression, we also conducted exploratory analyses assessing effects of depression history on reward learning in the GAD group. Finally, we hypothesized that lower baseline reward learning would predict higher depression symptoms one month later in both groups, and explored the possibility that this relationship might be stronger in the at-risk group only.

Method

Participants

Participants were recruited from a research participant pool at the University of South Florida. We recruited females given the higher prevalence of depression and anxiety among females and findings that gender interacts with depression risk factors, such as stress and GAD (Hettema et al., 2006; Kendler et al., 2004). To focus on anxiety symptoms and reduce the potential confound of current depression on reward learning, we excluded people reporting either high depressive symptoms or a current depression diagnosis at intake. Initial prescreening ensured that all participants reported normal or corrected to normal vision, and no serious brain trauma or other neurological illness. Individuals meeting prescreen criteria were invited to participate in an online recruiting study for course credit. Participants were recruited based on their responses to recruiting study questionnaire measures of worry and depression symptoms, and were not informed of study eligibility criteria. Using cutoff scores established by previous studies (see below), participants reporting low levels of worry were recruited as controls, and participants with high worry levels were recruited for the GAD group. Eligible participants were invited to a laboratory session for course credit.

One hundred forty-seven participants attended laboratory sessions conducted from January to November 2009. Participants were typically young adults ($M = 20.80$, $SD = 4.59$, age range $18–47$). Reported ethnicity of the sample was $63.9\%$ White ($n = 78$), $11.5\%$ Hispanic/Latino ($n = 14$), $10.7\%$ Black/African American ($n = 13$), $7.4\%$ Multiracial ($n = 9$), $4.9\%$ Asian ($n = 6$), and $1.6\%$ American Indian/Alaskan Native (n = 2). Participants were mostly right-handed (90.2%).

Measures

Diagnostic and symptom assessments.

Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990). The PSWQ is a 16-item measure of trait worry. A cutoff score of $\geq 56$ 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 college samples (Behar, Alcaine, Zuiellig, & Borkovec, 2003). A cutoff score of $\leq 45$ was used to identify control participants. This cutoff score falls at the 50th percentile in community samples and reflects 98% specificity in identifying GAD cases (Behar et al., 2003). Thus, 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 midrange of worry scores, between 45 and 56), precluding inclusion in the control or GAD group. The PSWQ had excellent reliability in this sample ($\alpha = .95$).

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 GAD. To identify research analogue GAD, we used the authors’ recommended 5.7 cutoff, shown previously to yield 83% sensitivity and 89% specificity in identifying GAD cases (diagnosed by the Anxiety Disorders Interview Schedule; Brown, DiNardo, & Barlow, 1994). This cutoff has been previously used to identify college students with analogue GAD (Miranda & Mennin, 2007; Salters-Pedneault, Roemer, Tull, Rucker, & Mennin, 2006). The GAD-Q was reliable in this sample ($\alpha = .90$).

Beck Depression Inventory (BDI-II; Beck, Steer & Brown, 1996). The BDI-II is a well-validated 21-item scale of depression symptom severity. Coefficient alphas for the BDI-II are high ($\alpha = .91$; Beck, Steer, Ball, & Ranieri, 1996; current sample, $\alpha = .91$). As recommended by Dozois, Dobson, and Ahnberg (1998), a cutoff score of $< 20$ was used to screen out potentially high levels of depression during online recruitment. The BDI-II was readministered at the lab session, and we included cases with scores higher than the recruiting threshold ($\geq 20$) only if they did not meet diagnostic criteria for MDD (see IDD below).

Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988). The BAI is a 21-item scale assessing anxiety during the past week. Instructions were altered to assess symptoms over the
past two weeks to facilitate comparison with the BDI-II. Symptoms were rated on a 4-point scale, with higher scores indicating more severe anxiety. Internal consistency of the BAI is high (α = .92; present sample, α = .93).

**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 (α = .86). The IDD was used in the present study as a second tier of screening to exclude participants who likely had case-level depression.

**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 a major depressive episode (MDE; see secondary analyses). Internal consistency was excellent in the current sample (α = .91).

**Positive and Negative Affect Schedule-Trait (PANAS-T; Watson, Clark, & Tellegen, 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 is 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 = .89 and .87, respectively).

**Stress manipulation measures.**

**State Trait Anxiety Inventory, State version (STAI-S; Spielberger et al., 1983).** The original STAI 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, 1979). This scale demonstrated good reliability in the current sample (α = .89).

**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 nine 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 measures of anticipatory anxiety assessed participants’ level of anticipatory anxiety about completing the upcoming math task. The item used the probe question, “How ANXIOUS are you about the upcoming math task?” with responses on a visual scale ranging from 0 (not at all) to 9 (extremely). This question was repeated at reminder prompts at each 30-s break between trial blocks, totaling two ratings per condition.

**Math task appraisal questionnaire.** This questionnaire consists of eight items assessing participants’ perceptions and feelings about the impending math task. The questionnaire was modeled after that used by Tomaka, Blascovich, and colleagues (Tomaka, Blascovich, Kelsey, & Leiten, 1993; see Kelsey et al., 2000; Salomon, Clift, Karlstdottir, & Rottenberg, 2009 for adaptations).

**Behavioral measure of reward learning: Signal detection task.** A signal detection task indexed reward learning. As in prior studies (Bogdan & Pizzagalli, 2006; Pizzagalli et al., 2005; Tripp & Alsop, 1999), this method involved briefly presenting one of two stimulus types (a short line and long line) and asking participants to identify which of the two stimuli were seen. Only some correct responses were followed by a monetary reward (5 cents)—one stimulus type was scheduled to be rewarded for correct responses three times as often as the other stimulus. Creating an unbalanced reward schedule produces a response bias for the stimuli that is most often followed by the reward (Macmillan & Creelman, 1991). Conceptually, individuals with higher reward learning exhibit more of a response bias because they modulate their responses to maximize rewards (i.e., they will more often report seeing the stimulus that is more frequently paired with a reward). Individuals with lower reward learning do not exhibit the same response bias, but will perform adequately on the task (Pizzagalli et al., 2005; Tripp & Alsop, 1999).

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 three blocks of 100 trials, which were separated by 30 second breaks. Because participants completed the signal detection task twice (once in a neutral 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 (Bogdan & Pizzagalli, 2006).

Each trial began with a 1-s fixation on a point the middle of the computer monitor. 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 500 ms. 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 100 ms and then disappeared 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 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 (50 trials each per 100-trial block) in a quasi-randomized order; neither stimulus was presented more than 3 times in a row. Participants were instructed that not all correct identifications would be followed by a reward. Indeed, only 40 correct responses per each 100-trial block were scheduled to receive a reward. All other correct responses were unrewarded. 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 1500 ms, followed by a blank screen for 250 ms. If the correct identification was not scheduled to receive reward, no feedback was given and the screen was blank for 1750 ms. Figure 1 shows a schematic of a trial in which a reward is given for correct identification of a mouth (modified from Bogdan & Pizzagalli, 2006, p. 1148).

We scheduled the two stimuli versions (short and long) to be differentially rewarded to create conditions for a response bias to develop (Macmillan & Creelman, 1991). The version scheduled to be rewarded most often (30 of the 40 potential reward trials) was the “rich” stimulus, and the version associated with reward less often (10 of the 40 potential reward trials) was the “lean” stimulus. The assignment “rich” or “lean” was counterbalanced 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. 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 a more stringent test of response bias hypotheses.

**Procedure**

**Overview.** Participants provided written consent and completed the GAD-Q, IDD, IDD-L, BAI, PSWQ, and BDI-II. Participants who met diagnostic criteria for current MDD based on IDD responses were excused from further data collection (n = 4). Participants then completed the reward learning task in the stress and neutral conditions, and were dispersed monetary rewards won during the task after completing each condition (maximum compensation was $12). Two participants had incomplete response bias data because of technical difficulties, and one participant withdrew from the study before completing the task. Participants then completed a questionnaire packet unrelated to the current analyses and were compensated with course credit.

**Experimental protocol.** The lab visit lasted approximately 2.5 hours. Lab sessions were conducted by undergraduate or post-Bachelor’s research assistants who were blind to group status. Participants were told the study was examining “how anxiety affects task performance,” and the goal of the computer task was to win as much money as possible by correctly identifying stimuli (as in Bogdan & Pizzagalli, 2006). To establish credibility, participants were shown the cash they could win before the task. Participants were instructed to respond quickly and to “please do your best” on the task because their ability to perform well on the task was the study’s focus. Participants were told that not all of their correct responses would be rewarded.

Participants received instructions and completed 16 practice trials to gain familiarity with the task. Participants were seated approximately 20 in. from the computer screen. Following practice trials, the researcher left the room and remaining instructions were delivered via intercom from an adjacent observation room. Participants completed the signal detection task twice—once in a stress condition and once in a neutral condition (counterbalanced). Between conditions, participants traced shapes for five minutes to decrease carry-over effects.

Following Bogdan and Pizzagalli (2006), participants completed state measures (STAI-S, and SAM-A) at baseline, pretask, and posttask in each condition. Instructions on posttask measures were altered to assess affect during the computer task. Additionally, participants completed the Math Task Appraisal Questionnaire before performing the math task in each condition, and made anticipatory anxiety ratings during breaks between trial blocks.

**Stress condition.** Participants received instructions via intercom and performed the math stressor for 3 minutes. The task involved serial subtraction by 7 s from 3,796. Participants were told to face the camera, and that their performance would be monitored but not recorded. Participants were told to perform the task as quickly and accurately as possible. The experimenter announced each time the participant erred and instructed the participant to begin again at the correct total. Participants were also...
promoted to “Please work quickly,” if they did not answer in 3 seconds. Participants were told to “Please work faster,” midway through the task. Participants were prompted to “Look into the camera,” if looking away, and not to use fingers to count. After 3 minutes, participants were told that they would next perform the computer task, followed by a more difficult version of the math task (subtracting 13 instead of 7), which would be recorded and evaluated for speed, accuracy, and poise (Kelsey et al., 2000). Previous work has found that the addition of a second, subsequent videotaped mental arithmetic task increases participants’ stress ratings (Kelsey et al., 2000). Participants completed measures, and then performed the computer task. After the first 100 trials, during the 30-second break, a black bold font message appeared on a yellow computer screen saying the following:

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. A similar message appeared after the second block of 100 trials indicating the number of trials remaining, followed by another anticipatory anxiety rating. The purpose of these prompts was to remind participants of the impending stressor and to maintain anticipatory anxiety throughout the computer task. After completing the task, participants completed measures and performed the more difficult math task for 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, 2002). The intention of the task was to control for cognitive load and distraction, 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 without evaluation. Participants then completed measures and performed the computer task. After the first 100 trials, during the 30 second break, a black bold font message appeared on a yellow computer screen saying the following:

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 rate anticipatory anxiety. A similar reminder message appeared after the second block of 100 trials, followed by another anticipatory anxiety rating. After completing the third block of trials, participants completed posttask measures and pencil-and-paper arithmetic problems for one minute with no evaluation. Response bias during the neutral condition was used as a baseline measure of reward learning.

One month follow-up. Participants were invited via e-mail one month later to participate in a second online session for course credit. Some participants completed the follow-up measures in the laboratory for $10 cash compensation (the online system had closed). The follow-up measures included the BDI and other measures not relevant to these analyses.

Data Reduction

Deleted trials. Consistent with prior work (Bogdan & Pizzagalli, 2006), trials with RTs <150 ms or >1500 ms were excluded. Trials with nonallowed key presses (i.e., keys other than z or m) were also excluded. The total number of deleted trials per participants for any reason ranged from 0 to 42 (M = 4.83 SD = 6.85).

Excluded cases. Given that we allowed for variation between participants on the actual ratio of rich versus lean rewards received (we controlled only for a 3:1 ratio of opportunities for rich vs. lean rewards), we examined the total number of rewards received in each trial block for each participant. 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 (including both rich and lean reward trials) in any block were excluded from analyses (n = 14). Although this lower limit is more inclusive than that reported in a previous study (30 of 40 in each block; Barr et al., 2008), it was conservative enough to exclude participants who missed a great deal of trials in one or more blocks, or had low accuracy due to using a “strategy” like pressing the same key for most trials.

Response bias and discriminability calculations. Response bias and discriminability were calculated following past work using this task (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:

\[ H = \text{Hits} = \text{Correct identification of the rich stimulus} \quad (\text{rich rewarded more often}) \]

\[ F = \text{False alarms} = \text{Choosing the rich stimulus when the lean stimulus was presented} \]

\[ M = \text{Misses} = \text{Choosing the lean stimulus when the rich stimulus was presented} \]

\[ C = \text{Correct Rejections} = \text{Correct identification of the lean stimulus} \]

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

\[ \text{Response bias: } log b = 1/2\log[(H^*F)/(M^*C^R)] \]

Discriminability refers to the ability to discriminate between the two stimuli and measures overall performance. In the present context, discriminability measures were used to test for specificity of findings about the effects of stress on response bias.

\[ \text{Discriminability: } log d = 1/2\log[(H^*C^R)/(M^*F^A)] \]

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).
Results

Sample Characteristics

Participants who no longer met eligibility criteria for the control or analogue GAD groups at the lab session (PSWQ scores fell in the midrange, \( n = 21 \), or GAD subjects scoring below 5.7 on the GAD-Q, \( n = 26 \)), were excluded from analyses. Participants recruited for the control group were excluded if they met criteria for a past depressive episode according to the IDD-L (\( n = 4 \)). The final sample included 75 people (41 control, 34 GAD).

Controls and GAD groups did not differ on age (\( M = 21.07, SD = 5.13 \)), number of deleted trials (\( M = 4.83, SD = 6.85 \)), task accuracy rates (\( M = 76.5\%, SD = 6.4\% \)), or money earned in either condition (neutral \( M = $4.65, SD = .69 \); stress \( M = $4.66, SD = .42 \)). Nor did the groups differ in which study protocol version was used, indicating successful random assignment. The effect of group emerged, with the GAD group also reporting higher anticipatory anxiety ratings across both conditions than controls, \( F(1, 73) = 20.71, p < .01 \).

Stress Manipulation Analyses

Repeated measures analyses of variance (ANOVA) examined anticipatory anxiety ratings revealed a main effect of condition, \( F(1, 73) = 34.33, p < .01 \), where anticipatory anxiety was higher in the stress condition than the neutral condition. The GAD group also reported higher anticipatory anxiety ratings across both conditions than controls, \( F(1, 73) = 20.71, p < .01 \).

Arousal. A similar repeated measures ANOVA examining arousal (SAM-A scores) as the dependent variable revealed a main effect of condition, \( F(1, 72) = 5.80, p = .02 \), in both conditions eliciting greater increases in reported arousal from baseline to pretask, with stressor and neutral conditions eliciting similar baseline and posttask arousal as the neutral condition.

Math task appraisal and performance. Repeated measures analyses were performed for each Math Task Appraisal item with condition as within subjects and group as a between subjects factor. Main effects of condition and group are reported in Table 2. Main effects of condition were in the expected directions for all items: Participants overall appraised the stress condition as being more stressful than the neutral condition. An overall main effect of group showed the GAD group appraised both tasks (neutral and stress) generally more stressful than controls. One way ANOVAs revealed that the GAD group reported higher stressor appraisals than the control group, both in number of attempted tasks and neutral conditions eliciting similar baseline and posttask appraisal as the neutral condition.

Discriminability, Accuracy, and Reaction Time Analyses

Repeated measures ANOVAs were planned for discriminability and accuracy with group (control, GAD) as a between subjects factor, and condition (neutral, stress) and block (1, 2, 3) as within subjects factors. These analyses were performed to address the possibility that group differences in response bias might be accounted for by group differences in discriminability and accuracy (i.e., one group showed poor overall performance on the task). A similar analysis was performed with reaction time (RT) as the dependent variable. Accuracy analyses revealed no significant group effects. Discriminability analyses revealed a Group \( \times \) Condition interaction, \( F(2, 146) = 4.70, p = .01 \); however, follow-up univariate tests revealed no group differences in discriminability in any block in either condition. Reaction time analyses revealed a main effect of block, \( F(2, 146) = 23.24, p < .01 \).
9.80, $p < .01$, qualified by a Condition $\times$ Group $\times$ Block interaction, $F(2, 146) = 3.27, p = .041$; however, follow-up univariate analyses found no significant group differences in any block in either condition. In sum, the groups performed similarly on the task in both conditions, as assessed by discriminability, accuracy, and RT analyses.\footnote{We also followed up the Group $\times$ Condition $\times$ Block interactions for discriminability and RT with repeated measures analyses testing for Group $\times$ Block interactions in each condition separately. For discriminability, there were no main effects of block or group and no significant Group $\times$ Block interaction in the neutral condition (all $p$s $>.05$). In the stress condition, there was a Group $\times$ Block interaction, $F(2, 146) = 3.45, p = .034$. Bonferroni corrected post hoc tests found no group differences in discriminability and no differences between blocks (all $p$s $>.05$). When groups were considered separately, there was no block effect in either condition for the GAD group or controls (all $p$s $>.05$). For RT, there was a main effect of block in the neutral condition, $F(2, 146) = 5.96, p = .001$, and the stress condition, $F(2, 146) = 6.28, p = .002$, with RT means decreasing over time in both groups and both conditions. There were no main effects of group nor Group $\times$ Block interactions for RT in either condition (all $p$s $>.05$).}

**Table 2**

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<th>$df$</th>
<th>$p$</th>
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<tr>
<td>Group</td>
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<td>1.71</td>
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</table>

**Figure 2.** Stress manipulation effects on state anxiety scores.

**Group Differences in Reward Learning Under Stress and No-Stress Conditions**

Using data from the control group only, a repeated measures analysis of variance (ANOVA) with condition (neutral, stress) and block (1, 2, 3) as within subjects factors was performed to test for a main effect of condition (neutral, stress) on response bias. We found a main effect of block, $F(2, 80) = 9.23, p = .01$, and a main effect of condition, $F(1, 40) = 5.96, p = .019$. Bonferroni corrected comparisons revealed response bias scores in block 1 ($M = .012, SD = .172$) were significantly lower than block 2 ($M = .080, SD = .164$) and block 3 ($M = .129, SD = .157$), $p < .01$. The difference between blocks 2 and 3 was not significant. The significant increase in response bias across blocks indicates successful reward learning. The effect of stress was as we hypothesized, with response bias scores (i.e., reward learning) being lower in the stress condition ($M = .007, SD = .188$) compared with the neutral condition ($M = .140, SD = .243$), $F(1, 40) = 5.96, p = .019$.

To test for diagnostic group effects, an omnibus repeated measures analysis of variance (ANOVA) with group (GAD $n = 33$, Control $n = 40$) as a between subjects factor and condition (neutral, stress)
and block (1, 2, 3) as within subjects factors was performed to test for an interaction of group (between subjects) and condition (within subjects) on response bias. Current depression symptom scores were included as a covariate. To examine the potential influence of depression history in the GAD group, past depression status (past MDE+, past MDE−) was included as an exploratory factor. A main effect of block emerged, $F(2, 138) = 3.24, p = .042$, and a main effect of group, $F(1, 69) = 4.33, p = .041$, qualified by a Group × Condition interaction, $F(1, 69) = 9.01, p < .01$ as well as a Condition × Depression History interaction, $F(1, 69) = 4.84, p = .031$. Follow-up univariate tests (including covariates) revealed no differences between GAD group and controls on baseline response bias, $p > .05$. This result was contrary to the hypothesis of heightened baseline reward learning in the GAD group but partially supported the alternative idea that the GAD group would exhibit intact baseline reward learning but show enhanced stress-induced blunting. Unexpectedly, the GAD group showed higher (rather than lower) response bias scores during the stress condition than controls (see Figure 3), $F(1, 73) = 15.16, p > .01$.

To decompose the Group × Condition and Condition × Depression History interactions, separate analyses were performed using data from the GAD group only. A repeated measures ANOVA revealed a main effect of block, $F(2, 66) = 4.57, p = .014$, in the expected direction of response bias scores increasing over time, but no effect of condition. When depression history was included as a between subjects factor, there remained a main effect of block, $F(2, 64) = 4.54, p = .014$, and emerged a Condition × Depression History interaction, $F(1, 32) = 6.47, p = .016$. Follow-up univariate tests showed no differences in response bias between those with and without a history of depression in the neutral condition, $p > .05$. In the stress condition, those with a depression history had significantly lower scores than the never-depressed group, $F(1, 32) = 5.58, p = .024$. Separate repeated measures analyses were performed for those with and without past depression. For the GAD participants with past depression ($n = 17$), effects of block and condition were not significant, $ps > .05$. That is, there was no significant change in response bias scores from the neutral to stress conditions. Observed power for these analyses were .67 and .27, respectively. For the never-depressed GAD group, there was a significant effect of condition, $F(1, 16) = 5.28, p = .035$. Response bias for never-depressed GAD individuals was higher in the stress condition ($M = .23, SD = .05$) than the neutral condition ($M = .08, SD = .03$).

To gauge the GAD group effects in comparison with control participants, we compared mean response bias scores of the GAD groups with and without depression with that of the control group across all 3 blocks in each condition. There were no group differences in the neutral condition, $ps > .05$. In the stress condition, however, a main effect of group emerged, $F(2, 72) = 7.83, p < .01$. Post hoc Bonferroni corrected tests showed the never-depressed GAD group had higher response bias scores than both controls ($p < .01$) and GAD with past depression ($p = .042$). The control group and past depression group did not differ (see Figure 4).

### Reward Learning as a Predictor of Future Depression

To test whether reward learning predicted future depression symptoms, we performed Pearson correlation analyses for the GAD and control groups. Significant bivariate correlations were followed by partial correlation analyses controlling for initial depression levels. When the GAD group was followed up at one month ($n = 19$), reward learning in the neutral condition was unrelated to prospective depression symptoms ($p > .05$). However, reward learning in the stress condition predicted 1-month depression symptoms (BDI scores) such that higher reward learning in the stress condition predicted lower depression symptoms at one month ($r = -.45, p = .05$). This effect was reduced to a trend ($r = -.42, p = .086$) following for initial depressive symptom severity. In the control group ($n = 27$) reward learning in both conditions was unrelated to future depression symptoms. To further explore the relationship between stress-induced reward blunting and future depression in the GAD group, we computed an anhedonic subscale score from the two BDI anhedonia items and repeated the prospective analysis predicting anhedonic symptoms at one month. After controlling for initial anhedonic symptoms, higher reward learning in the stress condition predicted lower anhedonic symptoms one month later ($r = -.47, p = .05$).

### Discussion

This study was the first to investigate the effects of stress on reward learning in an anxious group that is actuarially predisposed to depression. We assessed reward learning via a computerized signal detection task in a neutral condition and laboratory stress condition among females meeting analogue GAD criteria and controls. The stressor manipulation, a mental arithmetic task, successfully elicited anxiety in both groups, with the GAD group reporting higher anxiety than controls in both conditions. Consistent with prior studies we found that controls displayed intact reward learning under neutral conditions and blunted reward learning under stress. This finding adds to growing evidence that stress blunts hedonic function (Berenbaum & Connelly, 1993; Bogdan & Pizzagalli, 2006; Pizzagalli et al., 2007).

Extending prior work, we proposed that stress-induced hedonic blunting may be particularly aberrant and depressogenic in individuals at elevated depression risk. We addressed prior mixed findings regarding hedonic function in GAD by testing two alternate hypotheses. First, we tested whether the GAD group would exhibit an overall blunting in reward learning compared to controls. This hypothesis was not supported, with the GAD group exhibiting intact reward learning in the neutral condition, similar to controls. Second, we tested whether the GAD group would exhibit intact reward learning under neutral conditions and an enhanced stress-induced blunting effect compared with controls. This hypothesis was partially supported: the GAD group showed intact baseline reward learning, but no evidence of stress-induced blunting. Instead, we found the opposite effect: in the stress condition, the GAD group exhibited higher reward learning than controls. It is noteworthy that the GAD group exhibited enhanced reward learning in the stressor condition despite experiencing the stressor as more stressful and having worse stressor math task performance.

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2 A separate analysis was performed with ethnicity, discriminability in both conditions, and baseline STAI scores in both conditions included as covariates. The group by condition interaction remained significant, $F(1, 64) = 5.74, p = .019$.

3 Protocol order (neutral or stress condition first) was entered as a covariate in a separate analysis and results were unchanged. A significant condition by depression interaction remained, $F(1, 31) = 6.40, p = .017$.
than controls. This is clearly counter to the notion that more sensitive stress responders would exhibit greater blunting of reward learning ability.

Our exploratory analysis of depression history shed more light on this unexpected finding. The stress-induced heightening of reward learning in the GAD group was driven by a subgroup of never-depressed GAD individuals, who showed higher reward learning under stress than those in the past depressed GAD group or the controls. This response pattern of stress-induced heightening is in striking contrast with the stress-induced blunting observed in controls, and was specific to the never-depressed GAD group. Importantly, our sampling and analytic strategies accounted for potential effects of current depression on reward learning, allowing stronger inferences about the effects of depression history in GAD on reward learning.

Baseline reward learning was similar among controls and both the past depressed and never-depressed GAD groups, suggesting that baseline reward learning is unaffected in GAD, regardless of depression history. That the past depressed GAD group showed intact baseline reward learning was somewhat surprising, given prior indications that that hedonic function may be impaired after depression remission (Schrader, 1997). Additionally, the lack of a stress-induced blunting in the past depressed group should be interpreted cautiously due to low power.

In our longitudinal analyses, we found that higher reward learning under stress predicted lower depression symptoms in the GAD group one month later. This suggests that the pattern of stress-induced hedonic blunting observed normatively in controls may be detrimental in GAD. Rather, heightened ability to learn reward contingencies in the face of stress predicted better outcomes in our GAD sample. This finding builds upon our cross-sectional results specifying never-depressed GAD individuals as the most likely to exhibit this stress-induced heightening of reward learning. Taken together, these findings suggest that enhanced hedonic functioning under stress may be an indicator of depression resistance in those with GAD.
Our findings in the control group are consonant with prior findings of stress-induced hedonic blunting (Berenbaum & Connelly, 1993; Bogdan & Pizzagalli, 2006). It may be that acute blunting of hedonic processes is adaptive in healthy individuals encountering a stressor. That is, short-term reduction of behavioral responses to environmental rewards may help healthy individuals focus efforts on effectively navigating a stressful context. That the stressful context had the opposite (heightening) effect in the never-depressed GAD group is intriguing. A growing literature suggests that resilience factors may “fit” with certain risk factors, but not be protective in others with a different risk profile (Davydov, Stewart, Ritchie, & Chaudieu, 2010). Following this view, one could hypothesize that the heightening of certain attentional or behavioral aspects of hedonic functioning, including reward learning, could serve as a natural inoculation against depression in this particular group, who may not necessarily report feeling increased hedonic tone during stress. This would account for our finding the stress-induced heightening effect only in the never-depressed group, who have presumably successfully navigated stress and avoided past depression.

Alternatively, heightened reward learning under stress could reflect a larger aberrant stress response. Prior work finds anxious individuals show a variety of aberrant responses under stressful conditions, such as higher reports of negative emotional reactivity to stress (as in this sample), and lack of autonomic reactivity to stress (Cohen et al., 1998). With this view, one could hypothesize that heightened reward responses under stress represent a misfiring of the emotion system when these at-risk individuals encounter stress. Following this view, however, one might expect hedonic heightening under stress to impede successful stress navigation, which is inconsistent with our findings that increased reward learning under stress predicted better prospective functioning. Notwithstanding this, replication of our finding is needed before firm conclusions can be drawn about whether the pattern of heightened stress-induced reward learning we observed in our never-depressed GAD participants is adaptive or detrimental. Either outcome could have important implications for our theoretical and clinical approaches to the development of depression in anxious individuals.

Suggestion for Future Studies

Our findings raise several questions for future studies, and our study has several notable limitations. First, our study sample was limited to non–treatment-seeking individuals meeting analogue criteria for GAD, with self-reported depression symptoms as our longitudinal outcome assessment. Given the time requirements of the experimental protocol, we opted to administer self-report diagnostic instruments in a single lab session rather than require an additional session to administer clinical diagnostic interviews. Our findings warrant future work assessing additional clinical characteristics and linking reward learning to additional functional outcomes in clinical samples. Replication of our longitudinal findings over a longer follow-up period are necessary before strong conclusions can be drawn about reward learning and depression resistance.

Second, our analyses of past depression were exploratory. Because we did not recruit participants based on past depression status, cell sizes of past depressed and never-depressed individuals were relatively small. Tests with larger sample sizes are needed to clarify whether the lack of stress-induced blunting in the past depressed GAD group reflected low power or inflexible stress responding. Likewise it is critical that future multimethod studies include both past depressed and currently depressed GAD groups to clarify the impact of depression comorbidity on reward function in GAD. Illustrating the promise of such an approach, we found anxious individuals who were not currently depressed showed similar emotion-modulated startle responses to healthy controls, while anxious individuals who were currently depressed exhibited a blunted startle response pattern typical of depressed groups (Taylor-Clift, Morris, Rottenberg, & Kovacs, 2011). Third, replication of our longitudinal findings in never-depressed GAD individuals as well as other at-risk groups would help characterize the extent to which stress-induced heightening of reward learning may be specific to GAD versus other depression risk factors. For instance, Berenbaum and Connelly (1993) found higher depression risk attributable to family depression history enhanced the hedonic blunting effect of life stress. It may be that depression risk conferred by certain risk factors can be mitigated by the presence of unique protective factors, which would not otherwise be favorable (i.e., for controls, who are not at heightened risk). Finally, the literature on resistance to stress-induced depression suggests that “bouncing back” from stress is an important predictor of depression resistance (Tugade & Fredrickson, 2004). Future studies examining the duration of the stress effect on reward learning, its relationship with other behavioral sequelae, and how these relate to future functioning would help delineate normative versus aberrant response patterns in controls and at-risk groups.

Summary

We investigated the effect of laboratory stress on reward learning in controls and GAD individuals with and without a history of depression. Consistent with previous work, controls displayed the expected response pattern of intact baseline reward learning and blunted reward learning under stress. Never-depressed GAD individuals also showed intact baseline reward learning, but showed heightened reward learning under stress. This heightened predicted better prospective functioning, suggesting this pattern may be adaptive for this group. Our findings have implications for our understanding of stress effects on hedonic functioning in healthy and at-risk anxious individuals.

References

nitive Therapy and Research, 31, 71–82. doi:10.1007/s10608-006-9063-4


Received November 10, 2013
Revision received March 31, 2014
Accepted April 9, 2014