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Emotion-modulated startle in major and minor depression: The role of mood severity in emotion reactivity

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Emotion-Modulated Startle in Major and Minor Depression: The Role of Mood Severity in Emotion Reactivity

by

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ABSTRACT

Major depressive disorder (MDD) is a disorder defined by mood disturbance, but the deficits in emotional reactivity that accompany MDD are not yet fully characterized. Researchers have utilized the emotion-modulated startle paradigm to investigate emotional responding among depressed individuals with mixed results. Inconsistent results may be due in part to the heterogeneity of mood disorders, including variation in mood severity. The current study utilized an emotion-modulated startle procedure with 33 individuals currently experiencing a major depressive episode, 25 individuals currently experiencing a minor depressive episode (mD), and 31 healthy controls. Severity of depression, anxiety, and positive and negative mood states were ascertained on the sample. Emotion-modulated startle failed to differentiate between mood disordered individuals and healthy controls. However, results found a significant association between abnormal patterns of emotion responding and positive affect (PA), such that individuals with low PA showed exaggerated responding to unpleasant stimuli. The results suggest that PA may be an important dimension in mood disorders that underlies abnormal emotional responses.

Introduction

Depression is one of the leading causes of disability worldwide (Murray & Lopez, 1997), and affects approximately one in five women and one in ten men in the United States (American Psychiatric Association [APA], 1994). MDD symptoms include persistent sad mood and/or loss of interest or pleasure in daily activities, as well as several associated somatic and cognitive symptoms, including loss of appetite, weight gain or loss, sleep difficulties, psychomotor agitation or retardation, lack of energy, feelings of worthlessness or guilt, concentration difficulties, and suicidal ideation (APA, 1994). MDD also has extremely high recurrence rates. Over 70% of depressed patients have more than one episode, and indeed, depressed patients may spend only 22% of the 12 years following a major depressive episode without symptoms (Judd et al., 1998). Furthermore, approximately 40% of individuals with three or more episodes of depression may relapse within 12 to 15 weeks of recovery (Keller et al., 1992; Mueller et al., 1996). Given the recurrent nature of MDD, it seems reasonable that depressed individuals possess one or more stable vulnerability traits that predispose them to repeated episodes of this disorder. One proposed vulnerability trait involves deficits in emotional responding.

There are conflicting views on how MDD influences emotion. Based in part upon the assumption that moods will facilitate reactions to like-valenced emotions (Rosenberg, 1998), researchers have suggested that MDD (and the associated depressed mood) may

facilitate negative emotions (e.g., Golin, Hartman, Klatt, Munz, & Wolfgang, 1977; Lewinsohn, Lobitz, & Wilson, 1973) or inhibit positive emotions (Berenbaum & Oltmanns, 1992; Sloan, Strauss, Quirk, & Sajatovic, 1997; Sloan, Strauss, & Wisner, 2001). However, as discussed in more detail below, growing evidence provides support for an alternative view of emotions in MDD, namely that MDD may involve inflexible responses across differing valence contexts, or emotion context insensitivity (ECI), (Rottenberg, 2005; Rottenberg, Gross, & Gotlib, 2005). The discrepancy between ECI (no mood enhanced reactivity in MDD) and the idea of mood-facilitated emotions raises the question of whether MDD represents a special case: Do the severe mood states in MDD have effects on emotional reactivity that are distinct from those of milder depressed mood? To date, no studies have examined whether ECI exists across the range of depressed mood. This study enrolled a sample with a wide range of depression severity and collected data on several severity metrics to examine the effects of depression severity on ongoing emotional reactivity. Emotional reactivity was probed using emotion-modulated startle paradigm, which has been extensively used to characterize motivation and pathophysiology of several clinical disorders (Grillon & Baas, 2003).

Depression: Symptoms versus Diagnosis

A longstanding debate in the literature concerns whether depression represents a distinct disease state (e.g., Judd, 1997) or whether the symptoms of depression are best thought of as existing along a continuum of severity (e.g., Cassano et al, 2004). The dimensional model of depression views the mood and physical symptoms of depression as existing along a continuum, with the diagnostic threshold placed somewhat arbitrarily—according to the number of symptoms and the level of impairment—at one

end of the continuum (e.g., Cassano et al, 2004; Prisciandaro & Roberts, 2005; Hankin, Fraley & Lahey, 2005). Many researchers utilize dysphoric populations (individuals who self-report low mood, but who do necessarily meet criteria for clinical depression) and generalize findings from this population to clinically depressed individuals (Vredenburg, Flett, & Krames, 1993). However, this methodology involves the assumption that dysphoria lies along the depression continuum and shares the same symptoms, mood states, and emotion regulation difficulties as diagnosable MDD (Coyne, 1993). There is some evidence to suggest that this generalization is valid and that dysphoric individuals and clinically depressed individuals resemble one another in several respects (e.g., Sweeney, Anderson, & Bailey, 1986). However, the literature using the dimensional model has measured severity in several ways, and there is no consensus on which severity measure, if any, represents the most effective means to elucidate the dimensional properties of depressed mood.

The disease state model, on the other hand, rejects the idea of a depressive continuum and argues instead that a clinically depressed person suffers from mood and physical symptoms that are qualitatively different than those symptoms of an individual with ordinary sad mood (e.g., Ottowitz, Dougherty, & Savage, 2002). This model of depression generally conceptualizes clinical depression as resulting from neurological, neuroendocrine, or other biologically linked etiologies (e.g., Ottowitz, et al., 2002; Arborelius, Owens, Plotsky, & Nemeroff, 1999; Drevets, 1998). Such models presume that more severe depression connotes a more chronic disease pattern (Judd, 1997). For example, those individuals exhibiting more “diseased” neurological or biological processes may be more likely to suffer from chronic, recurring depression, whereas those

exhibiting less “diseased” neurological processes may be less likely to experience more chronic forms of the disease. The disease model generally pays less attention to the conceptualization of subthreshold forms of depression, although, some commentators also formulate subthreshold depression within the disease framework (Judd, Akiskal, & Paulus, 1997).

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) currently lists one form of subthreshold depression, termed minor depressive disorder (mD), in the Appendix as a provisional diagnosis meriting further study (APA, 1994). Minor depressive disorder is defined as a period of two or more weeks during which at least two to four of the nine symptoms for a major depressive episode are present, and one symptom must be either depressed mood or lack of interest or pleasure in most or all daily activities (APA, 1994). Minor depression may differ from MDD by its general lack of neurovegetative symptoms (Rapaport et al., 2002.), but the lack of research on mD limits strong claims about symptomatic differences.

Evidence of mD prevalence rates are uncertain. Estimates vary depending on the degree of adherence to DSM-IV diagnostic criteria. Data from the nationally representative population of the National Comorbidity Survey found lifetime prevalence rates for mD with no prior history of MD of 10% (Kessler, Zhao, Blazer & Swartz, 1997). Those studies that follow DSM-IV criteria for mD found lower prevalence rates compared to those studies that diagnosed mD according to scores on depression severity scales, such as the BDI (e.g., 3.6% versus 12.9%; Newman, Sheldon, & Bland, 1998; Beekman, Deeg, & van Tilburg, 1995).

Research indicates that mD results in impairments similar to those of MDD, a pattern which would support the continuum view of depression. Individuals with mD often experience incomplete resolution of episodes as with MDD (Kessler et al., 1997). Minor depression can result significant functional disability and interfere with employment attendance to a similar degree as mild MDD (Cuijpers, de Graaf, & van Dorsselaer, 2004; Kessler et al., 1997). There is some evidence that individuals with mD may use outpatient services as frequently as individuals with MDD (Gonzalez-Tejera et al., 2005). Individuals with mD are at an increased risk for developing MDD compared to individuals with no depressive symptoms (Cuijpers et al., 2004). Indeed, the odds ratio for developing a first-time major depressive episode following a diagnosis of mD is as large as 5 (Fogel, Eaton, & Ford, 2006).

Existing data is unclear as to whether mD is a transient mood state preceding or following a major depressive episode or whether mD is a distinct disease with unique emotional correlates. Surprisingly, there have been virtually no direct comparisons of these conditions, and no laboratory studies that compare mD and MDD on emotional characteristics.

Emotional Reactivity in MDD

Emotion provides an important context for extending the continuity-of-depression debate into an important domain of clinical functioning. There has been active research on emotional reactivity in MDD, where three competing hypotheses for the emotional responding to positive and negative stimuli have emerged based on theory and research findings. These are described in turn.

The positive attenuation view hypothesizes that MDD individuals' responses to positively valenced stimuli are attenuated compared to the responses of non-depressed controls. For instance, compared to controls, MDD individuals have shown diminished emotion response to pleasant film stimuli (Berenbaum & Oltmanns, 1992). Likewise, depressed individuals also report reduced emotional responses to positive picture stimuli (Sloan, Strauss, Quirk, & Sajatovic, 1997; Sloan, Strauss & Wisner, 2001). The negative potentiation view theorizes that the emotional responses of MDD individuals to negatively valenced stimuli are potentiated or heightened compared to the responses of non-depressed controls. Little research has been conducted that supports this hypothesis and the negative potentiation hypothesis has not been supported when clinically diagnosed depression populations are used (Golin, Hartman, Klatt, Munz, & Wolfgang, 1977; Lewinsohn, Lobitz, & Wilson, 1973). Lastly, the emotion context insensitivity (ECI) theory argues that MDD individuals' core emotion deficit is a general failure to exhibit context-appropriate emotional reactivity to valenced stimuli in general (Rottenberg, Kasch, Gross & Gotlib, 2002; Rottenberg, Gross, & Gotlib, 2005).

There is growing evidence for ECI in MDD. For example, depressed patients have shown less electromyography (EMG) modulation to affective stimuli (Gehricke & Shapiro, 2000) and less facial reactivity to expressive faces (Wexler, Levenson, Warrenburg, & Price, 1994). In fact, a recent quantitative review found broad based support for the idea that MDD individuals display ECI in a variety of experimental contexts (Bylsma, Morris, & Rottenberg, in press). However, Bylsma et al. also found that the effect sizes were heterogeneous. It is possible that several factors influence the presence or absence of ECI among MDD samples and account for the heterogenous

findings. The goal of the current study is to utilize the emotion-modulated startle paradigm to examine abnormalities in emotion processing and emotion reactivity in MDD, as well as to examine the role of severity as a factor influencing the possible presence or absence of ECI in MDD.

Startle Paradigms and the Emotion-Modulated Startle Response

Laboratory assessment of the startle response has resulted in methods for examining automatic processes to aversive stimuli in humans and other species. In its most basic form, the startle response characterizes a defensive reflex to an aversive stimulus (e.g., a very loud sound). The startle response includes a cascade of evolutionarily adaptive behaviors, designed to protect the organism from harm, such as blinking of the eyes, a forward and downward movement of the head, and a drawing in of the shoulders (Landis & Hunt, 1939). In humans, the startle response is often quantified by the magnitude of the eye blink in response to the aversive stimulus, or startle probe, which is generally a brief burst of noise. Components of the startle response typically occur within 20ms of the aversive stimulus.

The startle paradigm has been extensively studied in both animals and humans (e.g., Koch & Schnitzler, 1997), and the neurological correlates of the startle response pattern are increasingly well understood (e.g., Lang, Bradley, & Cuthbert, 1998). Importantly, although the startle response can be elicited reliably in many contexts, the magnitude of the response is influenced by the current affective state of the organism. Specifically, numerous studies have found that emotional states elicited by affective stimuli (such as valenced pictures) reliably modulate the displayed amount of startle

amplitude in humans (Larson, Ruffalo, Nietert, & Davidson, 2000; Bradley & Lang, 2000; Bradley, Cuthbert, & Lang, 1990).

In healthy subjects, the "late" startle probe that is presented anywhere from 3 to 6 seconds after the onset of the valenced stimuli elicits a greater startle response if the subject is viewing unpleasant pictures (e.g., snakes, injured humans) than if the subject is viewing pleasant (e.g., families, food) or neutral pictures (e.g., landscape, garden tools), and pleasant pictures elicit smaller startle responses than neutral pictures. Thus, negative affect that is elicited by unpleasant pictures potentiates the startle response, while affect elicited by pleasant stimuli inhibits the startle response. This pattern of emotion-modulated startle does not appear to result from unequal allocation of attention to the startle probe (Vrana & Lang, 1990; Bradley et al., 1990).

The emotion-modulated startle response persists even in the presence of subjects' habituation to the startle probe, and is thus thought to represent underlying motivational processes (Lang, 1995). Indeed, the typical explanation for this pattern of emotion reactivity is that startle responses are compatible with aversive motivation (i.e., fight or flight mechanisms) and incompatible with appetitive motivational states (i.e., approach behaviors; Lang, Bradley & Cuthbert, 1998). This normative pattern of startle response can be conceptualized as normative emotion reactivity to affective stimuli. For the purposes of this proposal, a lack of context-appropriate emotion reactivity will refer to a subject's failure to display both potentiation in the context of unpleasant stimuli *and* inhibition in the context of pleasant stimuli.

Emotion-Modulated Startle Response and Psychopathology

The emotion-modulated startle paradigm has been widely used to demonstrate atypical patterns of emotion-modulated startle in several mental disorders (Grillon & Baas, 2003). Thus far, some evidence indicates disorder-specific patterns of atypical startle responding. A lack of startle potentiation during unpleasant picture viewing characterizes schizophrenic patients, who also display overall deficient habituation to the acoustic startle probe (Schlenker, Cohen, & Hopmann, 1995; Taiminen, et al, 2000). Psychopaths display an abnormal pattern of startle modulation compared to controls, generally showing equivalent startle responses for unpleasant stimuli and pleasant stimuli and heightened responding to neutral stimuli (Patrick, Bradley, & Lang, 1993). The modulated startle pattern of individuals with generalized anxiety disorder (GAD) generally indicates a higher overall startle, but no consistent pattern of reactivity differences (Grillon & Baas, 2003). However, research with other anxiety disorders has yielded consistent patterns that seem to differentiate these conditions. In some severe posttraumatic stress disorder patients there is larger potentiation during unpleasant pictures compared to controls and higher baseline startle responses compared to controls (Miller & Litz, 2004; Morgan, Grillon, Southwick & Charney, 1996). Studies have also found evidence for increased startle potentiation to feared stimuli in subjects with specific phobias and an increased baseline startle and increased startle potentiation in patients with panic disorder and social phobia (Hamm, Cuthbert, Globisch, & Vaitl, 1997; Larsen, Norton & Walker, 2002; Cuthbert, Lang, & Strauss, 2003). Thus, emotion-modulated startle patterns may be an appropriate and sensitive means to differentiate clinical disorders (such as mD and MDD).

Emotion Modulated Startle Response and MDD

Despite the general promise of the emotion-modulated startle paradigm, relatively little research has been conducted with it in depressed populations. Most of the existing studies are cross sectional in nature and have generated conflicting results (reviewed below). Consistent with the approach taken in this proposal, variation in depression severity both across and within studies may explain these discrepancies, with more severe, diagnosable depression being associated with more pronounced deficits in startle modulation.

Research with a sample of distressed college students—as indexed by high scores on the Depression scale of the Minnesota Multiphasic Personality Inventory—supported the negative potentiation hypothesis. Specifically, highly distressed individuals showed increased potentiation during negative imagery trials (Cook, Hawk, Davis, & Stevenson 1991). These results suggest that high levels of distress and possibly the presence of mD may actually potentiate responding to negative stimuli.

By contrast, in clinically depressed samples, findings from emotion-modulated startle studies are most consistent with ECI. For instance, Dichter and colleagues found, in two independent samples, a flattened pattern of startle (i.e., lack of inhibition for pleasant pictures and lack of potentiation for unpleasant pictures) among clinically depressed outpatients as compared to controls (Dichter et al., 2004; Dichter & Tomarken, 2008). In another early study of this type (Allen et al., 1999), clinically depressed inpatients showed a normative pattern of startle modulation; however, additional analyses suggested that results differed when patients were divided into groups based on the severity of the depressive symptoms, as indexed by scores on the Beck Depression

Inventory (BDI). Among subjects with severe BDI scores, startle magnitude was potentiated during pleasant pictures but not during unpleasant pictures. In more mildly depressed subjects with moderate and lower BDI scores, a pattern similar to the normative pattern of emotion-modulated startle reflex startle was observed, indicating context appropriate emotion reactivity. Therefore, the pattern of modulated startle exhibited by the severely depressed group in this study seems to conform with the ECI hypothesis, whereas the pattern of startle in the more mildly depressed sample does not support ECI. Although these internal analyses are limited by the small sample sizes involved (N's = 7), they illustrate the potential importance of symptom severity in modifying startle reactivity.

Kaviani and colleagues also observed effects of depression severity on emotion-modulated startle reflexes in a DSM-IV diagnosed, clinically depressed group (Kaviani, Gray, Checkley, Wilson, & Kumari, 2004). No significant differences in startle modulation were found between the depressed patients and the control group. However, when depressed participants were divided into low and high depressed groups on the Hospital Anxiety and Depression Scale (HADS), the low depressed group showed the normative pattern of modulated startle, which did not differ significantly from the startle pattern of controls, while the high-depressed group showed a flattened pattern of startle.

When depression severity was defined in terms of the number of previous depressive episodes, ECI was supported for a subgroup of depressed individuals who reported the most recurrent depressive episodes (Forbes et al., 2005). That is, when depressed patients were assigned to one of three severity groups based on the number of previous depressive episodes, those patients with episodes "too numerous to count"

displayed a flattened pattern of modulation. The group with one or two prior episodes and the group with three or more episodes displayed the normative pattern of startle modulation. The results of Forbes and colleagues again suggest that individuals with more severe MDD (for example, outpatients with multiple depressive episodes) lack context-appropriate emotion reactivity, whereas those with fewer episodes show intact emotion reactivity. Indeed in this study depressed participants as a whole showed a startle modulation pattern generally similar to that of controls. In summary, while the database of findings remains modest, MDD is sometimes associated with an absence of emotion modulated startle, and mild and moderate levels of MDD are sometimes associated with a more normative startle pattern. One critical limitation of prior studies of the emotion-modulated startle paradigm is that they have not fully represented the full range of depression severity; that is, no studies have included participants with both minor and major depression in the same sample. This kind of research design is needed to address the question of whether minor or mild mood disturbances have effects on emotional reactivity than are distinct from those seen in more severe diagnosable depression.

Specific Aims

Existing research of the emotion-modulated startle pattern of individuals with MDD has produced mixed findings. The current review suggests that this heterogeneity may be due to several factors, including the heterogeneity of depression, variations between studies in how severity is measured, and inconsistencies in how cut off points for low and high depression severity are used. The current study addressed the use of differing measures for depression severity by utilizing individuals with minor depression, as diagnosed according to DSM-IV-TR criteria (mD; APA, 1994), and by analyzing

emotional responding according to several different measures of symptom severity (e.g., amount of negative affect, lack of positive affect, presence and severity of comorbid anxiety). We predicted that levels of emotion-modulated startle would be linked to depression severity. By examining several measures of depression severity, we could identify the measure of severity that provides the clearest differences in context-appropriate emotional reactivity.

The general aim of this study was to investigate emotional reactivity across varying levels of severity. More specifically, we sought to clarify whether context-appropriate emotion reactivity varies according to DSM-IV diagnostic categories of depression and according to several alternative severity metrics. To achieve these aims, the following hypotheses were tested:

Hypothesis 1a: Startle modulation of depressed individuals will be significantly different from the startle patterns of control subjects and subjects with mD, such that MDD individuals will show flattened emotion-modulated startle responses relative to mD individuals and healthy controls.

Hypothesis 1b: It was predicted—based on Cook et al. (1991)—that individuals with minor depression would display greater negative potentiation compared to the responses of all other groups.

Hypothesis 2 (secondary): Measures of symptom severity will differentiate those with atypical emotion-modulated startle patterns from those with more typical emotion-modulated startle patterns.

The primary analyses focused on the magnitude of the startle response as a function of stimulus valence. Secondary analyses were conducted with skin conductance

and heart rate. Although the literature provided less guidance for predictions based on skin conductance and heart rate, we had similar hypotheses for these variables and expected that analyses would parallel results from startle.

Methods

Participants

Participants were recruited from fliers and online postings in and around the Tampa Bay community (Table 1). Over 460 potential participants were screened by telephone. Of those individuals, 159 were invited into the lab to complete the SCID. Of those participants who completed a SCID, approximately 52 were excluded for failing to meet inclusion or exclusion criteria. A further 21 individuals failed to attend the scheduled interview session for a variety of reasons (e.g., scheduling changes, failing to return calls to reschedule, etc). Participants were excluded for history of a major head injury, hearing impairment, diagnosis of bipolar disorder, substance abuse occurring within 6 months prior to entry into the study, or any history of primary psychotic symptoms.

Final participants were primarily females (77%) fluent in English and between the ages of 18 and 55. The final sample approximated the ethnic distribution of the Tampa Bay area: 59.8% Caucasian, 16.3% African American, 10.9% Latino/ Hispanic, 6.5% Asian, & 1.1% Native American. According to diagnoses based on DSM-IV-TR criteria, participants were experiencing a current Major Depressive episode (n = 33), a current Minor Depressive episode (n =25), or had no past or present psychopathology (i.e., no history of any Axis I disorder as assessed by the SCID, including past mD episodes; n = 31). Table 1 contains demographic information of the sample according to diagnostic

group. Participants were matched on age, ethnicity, gender, education level, income, and marital status (all *p*s > .11 for Cramer V tests).

Provisional DSM-IV-TR criteria recommend an absence of past episodes of MDD for an mD diagnosis. To improve study feasibility, we loosened this criterion and 36% of mD participants experienced at least one major depressive episode (MDE). In these included subjects we required a period of at least eight weeks with no residual depressive symptoms between the major depressive episode and the minor depressive episode. In all cases of mD with a past MDE, MDEs occurred at least one year prior to the current mD episode.

Table 1

Demographic Characteristics of the Sample

	Group		
Variable	MDD (*n* = 34)	mD (*n* = 26)	Controls (*n* = 32)
Age, M (SD)	29.88 (11.25)	25.85 (6.88)	26.72 (7.79)
% Caucasian	46.9%	73.1%	61.8%
% Female	88.2%	65.4%	75%
Education	5.29 (1.85)[a]	5.23 (1.75)[a]	5.63 (2.14)[a]
Income	5.31 (3.44)[b]	4.40 (3.07)[b]	5.93 (3.89)[b]
% Married	17.6%	19.2%	28.1%
% Antidepressants	14.7%	5.3%	3.7%[c]
% Psychotherapy	11.8%	5.3%	0%

[a]Education was assessed on an 8-point scale with higher numbers representing more education—a score of 5.63 reflects graduation from a 2-year or a technical college.
[b]Income was assessed on a 12-point scale—a score of 5.93 represents an income of between $25,000 and $34,999.
[c]One control participant was taking an antidepressant to (successfully) control migraine headaches.

Procedure Overview

Individuals responding to research ads were initially screened over the phone to determine potential eligibility. Screening questions were based on key diagnostic questions from the Structured Clinical Interview based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV-TR) Axis I Disorders, Research Version, Patient Edition with Psychotic Screen (SCID-I/P W/ PSY SCREEN; First et al., 2002). Based on this initial screening, potential participants were invited to complete a full SCID with a clinical doctoral student. Final diagnoses for study inclusion were made based on this SCID administration. Participants also competed a Beck Depression Inventory-II (BDI-II; Beck, Steer & Brown, 1996) at this session.

Participants deemed eligible based on the initial SCID interview were invited to return to the lab within one week to participate in the emotion-modulated startle procedure. The diagnostic interview was separated from the startle procedure to reduce participant burden and reduce the likelihood that the interview would in any way influence participants' emotion reactivity in the startle procedure.

Diagnostic Procedure

The SCID is a semi-structured interview designed to diagnose individuals based on the DSM-IV. Reliability and validity measures for the SCID differ according to population and diagnosis, but reliability for diagnosing MDD is relatively high with interrater reliability kappas ranging from .80 to .93 (Zanarini & Frankenburg, 2001; Zanarini et al., 2000; Skre, Onstad & Torgersen, 1991). Screening was conducted for the following diagnoses: bipolar I and II disorder, major depressive disorder, minor depressive disorder, dysthymic disorder, schizophrenia, schizoaffective disorder,

schizophreniform disorder, delusional disorder, brief psychotic disorder, substance dependence, social phobia, specific phobia, and obsessive compulsive disorder.

Ascertainment of Severity

The Beck Depression Inventory (BDI-II), a well-validated, 21-item, self-administered scale, was used to assess depression symptom severity. Scores range from 0 to 63 with higher scores representing more severity. Coefficient alphas for the BDI-II were high (alpha = 0.96). The test-retest reliability has also proven to be high at r = .93 (Beck, Steer, & Brown, 1996). The Beck Anxiety Inventory (BAI) is a 21-item self-administered questionnaire used to assess anxiety symptom severity. Symptoms are rated on a four-point scale, with higher scores indicating more severe anxiety symptoms (Beck, Epstein, Brown, & Steer, 1988). The internal consistency of the BAI for the current study was high (alpha = .92), and the BAI correlates highly with the SCL-90-R Anxiety Subscale (r = .81) (Steer, Ranieri, Beck, & Clark, 1993). The Positive and Negative Affect Schedule (PANAS) is a 20 item self-report scale, measuring dispositional forms of positive and negative affect (Watson, Clark, & Tellegen, 1988). The PANAS has successfully differentiated depression and anxiety in clinical samples (Dyck, Jolly, & Kramer, 1994; Jolly, Dyck, Kramer, & Wherry, 1994). The PANAS was also highly reliable, with a Cronbach's alpha of 0.90 for positive affect and 0.88 for negative affect.

Startle Session

Upon arrival to the startle procedure, participants completed a second BDI-II, a BAI, and a PANAS. Following completion of questionnaires, participants were seated approximately 1.5 feet from a 20-inch computer monitor placed on a table directly in front of the participant. Prior to picture presentation, electrodes were placed on the

subjects and impedances were checked. To familiarize participants with the procedure and to habituate participants to the startle probe, two sample neutral images were shown accompanied by inter-trial and picture-viewing startle probes and the participant completed two sets of ratings. Pictures were presented in 3 blocks of 12 pictures, with each block including four pictures of each valence. Pictures were presented in semi-random order with the constraint that no more than two pictures in a row were of the same valence. The picture presentation sequence was as follows: (1) 2-second baseline; (2) six-second picture viewing; (3) 20 seconds to rate the valence and arousal of the picture using the self-assessment manikin procedure (SAM; Lang, 1980; Hodges, Cook & Lang, 1985); (4) variable (15-second average) inter-trial intervals prior to presentation of the next picture.

The startle response was elicited by a binaural acoustic stimulus (50 milliseconds of white noise at 105db with an instantaneous rise time) during nine of the twelve images in each category, and during nine of the inter-trial intervals. Startle responses were probed at varying times between 3000 and 5500ms after picture onset to assess contextual affective processing and defensive versus appetitive motivational systems (Bradley, Cuthbert, & Lang, 1993). Probes also occurred randomly between 6000ms and 9000ms after picture presentation (inter-trial startles) for nine of the pictures (three of each valence category). These inter-trial startle probes were included to decrease the predictable anticipation of startle probes during picture viewing. Probe times were semi-random with the constraint that no more than two of each probe time occurred in a row.

Picture Stimuli. Pictures were 36 affective pictures designed to elicit positive, negative, or neutral affect from the International Affective Picture System (Center for the

Study of Emotion & Attention, 1999)[1]. Pictures were drawn from a recent study of startle modulation in depressed persons (Dichter & Tomarken, 2008). Pleasant and unpleasant pictures were matched on reported levels of arousal (Lang, Bradley, & Cuthbert, 2005). Following Dichter and Tomarken (2008), different sets of pictures were shown to males and females; these sets were matched on ratings of valence and arousal.

Startle Recording. Startle data were collected and analyzed following guidelines and recommendations set forth in Blumenthal and colleagues' committee report (2005). Stimulus control and physiological data collection utilized an IBM compatible computer running VPM data acquisition and reduction software (Cook, 1997). Data were collected and stored offline for later analyses. For measurement of the eyeblink component of startle reactivity, 2 "small" (4 mm) Beckman-type electrodes were placed 36mm apart just beneath the lower eyelid of the left eye to record the contraction of the orbicularis oculi muscle. Impedance for the electrode pair was less than 20 Ohms. EMG data were amplified using a high-resolution (A/D) converter. Next EMG signal was filtered to remove background noise and maximize the signal to noise ratio. Lastly, the signal was digitally smoothed.

Skin Conductance and Heart Rate Recording

Continuous physiological data, i.e., heart rate and skin conductance data, were collected and stored offline throughout the procedure. To measure cardiac activity, three "large" (8 mm) Beckman-type electrodes were placed between the participant's wrist and elbow. Additionally, two large electrodes were applied to the palm of the participant's non-dominant hand to measure skin conductance responses during picture display.

Initial heart rate deceleration (D1) magnitude as compared to baseline and subsequent acceleration (A1) compared to baseline were computed for each picture and averaged across valence conditions. Initial heart rate deceleration occurs within three seconds following picture onset and is generally conceptualized as representing sensory orienting responses, while acceleration occurs within two to five seconds following picture onset and is representative generally of emotional processing or defensive responding (Lacey & Lacey, 1970; Graham & Clifton, 1966; Sokolov, 1963). More specifically for the current study, the magnitude of D1 represents the degree of initial sensory orientation towards a stimulus, while the magnitude of A1 represents the degree of emotional processing of a stimulus. Initial deceleratory responses are generally greater for unpleasant than for pleasant pictures, while acceleratory responses are generally greater in the presence of pleasant stimuli (Lang, Greenwald, Bradley, & Hamm, 1993).

For skin conductance, the peak magnitude, average magnitude, and difference between baseline and peak magnitude for picture presentation (between two and six seconds following picture onset) were computed for each valence condition. Skin conductance is influenced solely by the sympathetic nervous system. Considerable evidence indicates that skin conductance increases in response to arousing stimuli and is greatest in response to the most arousing pleasant and unpleasant stimuli (Bradley, Codispoti, Cuthbert, & Lang, 2001).

Data Reduction

EMG signals for each individual were analyzed for onset latency and, most importantly for the purposes of the current study, for mean peak amplitude by condition. Peak magnitude was manually scored by determining peak amplitude between 20 and

120 ms following startle probe onset and subtracting onset EMG activity. Peak magnitude values were transformed into standardized *T* scores (with a mean of 50 and a standard deviation of 10) using the mean and standard deviation of startle responses during neutral pictures. This procedure accounts for arbitrary individual differences in baseline startle response values while preserving response differences between valence conditions. *T* scores were subsequently averaged across each valence condition. Eyeblink reflexes were excluded (treated as missing values) if the reflex occurred 20ms or earlier before the startle probe onset or if an unstable baseline period precluded the determination of startle onset. Trials with no perceptible eyeblink startle response were given a magnitude score of zero and were included in analyses. Twenty participants—termed non-responders—were excluded because their data did not yield startle responses for greater than 45% of trials. A Cramer's V analysis confirmed that there were no differences in the number of non-responders within each diagnostic group ($p = .97$). Approximately 22% (7) healthy controls were non-responders, 21% (7) of MDD individuals were non-responders, and 23% (6) of mD individuals were non-responders.

Hypothesis Testing

A repeated measures analysis of variance (ANOVA) was performed for each physiological variable with diagnostic group (control, MDD, mD) as the between-subjects variable and picture valence (pleasant, neutral, unpleasant) as the within-subjects variable. Assumptions of sphericity were met except when otherwise stated. Repeated measures ANOVAs were followed by one-way ANOVAs and paired sample *t* tests when appropriate. Additionally, subjects' ratings of picture valence and arousal were analyzed

separately using repeated-measures ANOVAs. Again, these were followed up by one-way ANOVAs and t tests when appropriate.

In order to test secondary hypotheses that measures of symptom severity would differentiate those with atypical emotion-modulated startle patterns from those with more typical emotion-modulated startle patterns, severity groups were created based on median splits of the severity measures for mD and MDD individuals combined. Three (severity group: high, moderate, controls) by three (picture valence: pleasant, neutral, unpleasant) ANOVA's were then conducted with each physiological measure of interest.

Results

Overview of Results

Initial analyses were conducted to assess the possible effect of demographic variables on the dependent variables and confirm the validity of the clinical diagnostic groups. Subjective ratings of picture valence and arousal were then analyzed to confirm that the intended manipulation was successful and to examine any possible differences between groups for these ratings. The primary results for startle are then presented, with repeated measures analysis of variance (ANOVA) of group effects on startle variables preceding repeated-measures ANOVA analyses of severity. These are followed by parallel secondary analyses of skin conductance and heart rate.

Effects of Demographic Variables

Repeated measures ANCOVAs were conducted for physiological variables by diagnostic group with gender, education level, ethnicity, income, treatment, and picture order entered individually as covariates. There were no significant interaction effects for these covariates on any of the physiological variables of interest, including baseline physiological measures (*p*s > .13). Therefore, these demographic variables were omitted from future analyses. Additionally, there were no significant effects of medication on physiological variables. However, for medication status, small cell sizes (see Table 1) made it difficult to assess possible medication effects due to low power. Because of the potential for antidepressant and anxiolytic medications to influence physiological measures, significant and trend-level effects were followed by analyses in which

medication status (as present or absent) was included as a covariate. Where such analyses resulted in changes to significant findings, these results are reported.

Clinical Characteristics of the Sample

Results of the questionnaire measures are listed in Table 2. Results confirmed diagnostic categorization of groups. As expected, a one-way analysis of variance (ANOVA) confirmed that Beck Depression Inventory (BDI) scores varied significantly among all three groups [F (2, 87) = 90.73, $p < .01$] such that MDD individuals had the highest BDI scores (indicating higher depression severity) followed by mD individuals and then control individuals. Beck Anxiety Inventory (BAI) scores also differed significantly between groups [F (2, 87) = 40.22, $p < .01$]. Follow-up tests indicated that MDD individuals and mD individuals endorsed significantly higher symptoms of anxiety than did healthy individuals ($p < .01$), but that scores did not differ significantly between MDD and mD individuals ($p = .34$).

Positive Affect (PA) scores also differed significantly between groups [F (2, 87) = 22.59, $p < .01$]. MDD and mD individuals both differed significantly from control individuals in the expected direction, showing significantly lower levels of PA ($p < .01$). MDD and mD individuals also differed significantly in terms of PA in the expected direction with mD individuals showing significantly higher PA compared to MDD individuals ($p < .05$). Negative Affect (NA) differed significantly between groups [F (2, 87) = 17.23, $p <. 01$], such that MDD and mD individual had significantly higher negative affect compared to healthy controls ($p < .01$). However, MDD and mD individuals not differ significantly in terms of NA ($p = .15$). Zero order correlations

between severity measures and all physiological measures are presented in the Appendices.

Table 2

Clinical Characteristics of the Sample

	Group		
	MDD	mD	Controls
	(*n* = 33)	(*n* = 25)	(*n* = 31)
Variable	Mean (SD)	Mean (SD)	Mean (SD)
BDI	29.03 (11.25)	19.52 (6.70)	2.29 (3.16)
BAI	16.51 (8.73)	13.88 (8.45)	1.52 (1.84)
PA	20.94 (6.27)	26.08 (6.68)	32.48 (7.60)
NA	20.76 (8.47)	18772 (5.76)	11.87 (2.60)

Note: BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory
PA = positive affect
NA = negative affect

Correlations between clinical characteristics are given in Table 3. All correlations among questionnaire measures reached significance and were in the expected directions.

Table 3

Correlations between Severity Measures

Variable	BDI	BAI	PA	NA
BDI		0.69*	-0.67*	0.62*
BAI			-0.44*	0.63*
PA				-0.40*
NA				

*$p < .01$
Note: BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory
PA = positive affect
NA = negative affect

Subjective Ratings of Picture Valence

Picture ratings of valence and arousal are presented in Table 3. Subjective ratings of picture valence confirmed that pictures differed according to valence condition. Likewise, analyses of subjective arousal ratings confirmed that pleasant and unpleasant pictures were matched on arousal. More specifically, a series of repeated measures ANOVAs were conducted to examine differences among subjective picture ratings between groups. Results indicated a significant main effect of Valence [F (2, 86) = 482.46, $p < .01$, $\hat{\varepsilon} = .85$] and Arousal [F (2, 86) = 92.21, $p < .01$, $\hat{\varepsilon} = .75$]. Valence ratings displayed the expected linear trend, with pleasant pictures receiving the highest ratings and unpleasant pictures receiving the lowest ratings of valence. Arousal ratings for pleasant pictures and unpleasant pictures were significantly higher than ratings for neutral pictures ($p < .01$), but did not differ significantly from each other, indicating that the valenced pictures were successfully matched on arousal. In addition, there was a small, significant group by picture valence interaction effect for arousal ratings [F (4, 170) = 2.76, $p < .05$, $\hat{\varepsilon} = .06$], such that MDD individuals rated unpleasant pictures as significantly more arousing than did mD individuals [t (1, 56) = 2.07, $p < .05$] or controls [t (1, 61) = 2.39, $p < .05$], but did not differ in the neutral picture or pleasant pictures.

Table 4

Self-Report Ratings

		Group		
		MDD	mD	Controls
		(*n* = 33)	(*n* = 25)	(*n* = 30)
Valence		Mean (SD)	Mean (SD)	Mean (SD)
	Pleasant	14.24 (2.38)	14.06 (2.80)	14.54 (2.59)
	Neutral	10.24 (1.22)	10.37 (1.22)	10.54 (1.84)
	Unpleasant	2.26 (2.77)	3.51 (2.78)	3.27 (2.53)
Arousal				
	Pleasant	12.60 (2.58)	12.49 (3.14)	13.47 (2.83)
	Neutral	6.14 (2.54)	7.35 (2.88)	6.78 (4.16)
	Unpleasant	14.10 (3.84)	11.74 (4.83)	11.65 (4.29)

*Ratings are based on a 0-20 scale.

Startle Magnitude

Table 5 lists the mean startle *T* scores by diagnostic group. A repeated-measures ANOVA for startle responses between diagnostic groups indicated the expected linear main effect for picture-type [*F* linear (1, 69) = 17.81, $p < .05$, $\hat{\varepsilon} = .21$]. Pairwise comparisons indicated that pleasant pictures differed significantly from unpleasant pictures ($p < .05$), with larger startle responses being elicited during unpleasant as compared to pleasant pictures. There was a trend towards lower startle responses during pleasant pictures as compared to neutral pictures ($p = .06$) and towards larger startle responses during unpleasant pictures as compared to neutral pictures ($p = .05$). Figure 1 shows the overall startle responses for each group according to picture type. Inconsistent with our primary hypothesis, there were no significant effects for diagnostic group [*F* (2, 72) = .71, $p = .59$], nor were there group by picture-valence linear or quadratic trends.

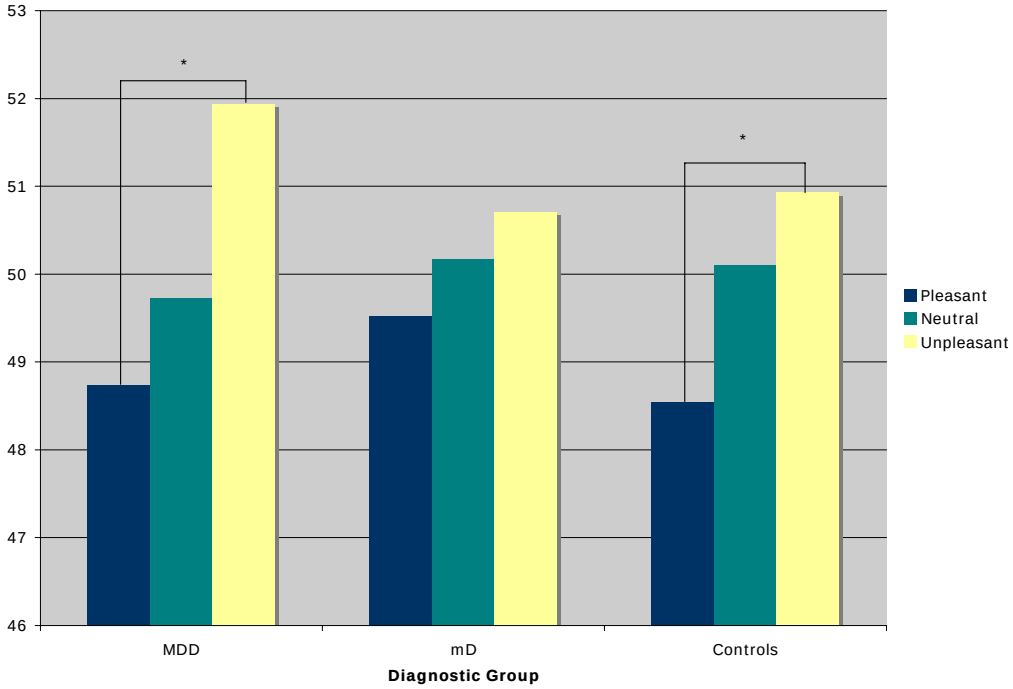

Figure 1. Mean standardized startle magnitudes according to diagnostic group.

To further examine the effects of diagnostic category on startle reactivity, we examined two other widely used startle metrics—startle amplitude and raw startle magnitude values—for possible group interaction effects. Startle amplitude is calculated in much the same way as startle magnitude with the exception that trials indicating no startle response are omitted from analyses. In this way, startle magnitude for only those pictures eliciting a response are utilized for analyses. Results of a repeated-measures ANOVA for startle amplitude failed to reveal significant group by picture valence interactions [F (4, 138) = 1.13, p = .35]. Likewise a repeated measure ANOVA was conducted using raw (unstandardized) startle magnitude values as the dependent variable and results again indicated only significant main effect for picture valence and no significant group by valence interactions [F (4, 138) = 1.59, p = .18]. Table 5 presents

amplitude and raw magnitude scores for each group. In summary, across the various startle metrics we obtained the expected valence modulation effects. However, the hypothesis that emotion-modulation of startle for depressed individuals would differ significantly from that of controls or that of mD individuals was not supported.

Table 5

Startle Magnitude

		MDD (n = 27)	mD (n = 20)	Controls (n = 25)
	Valence	Mean (SD)	Mean (SD)	Mean (SD)
Magnitude *T* Scores				
	Pleasant	48.74 (2.81)	49.52 (3.42)	48.54 (2.22)
	Neutral	49.73 (3.35)	50.17 (3.20)	50.10 (2.92)
	Unpleasant	51.94 (3.15)	50.71 (2.74)	50.93 (2.66)
Amplitude *T* Scores				
	Pleasant	48.54 (2.93)	49.56 (3.20)	48.67 (2.33)
	Neutral	49.57 (3.59)	50.19 (3.09)	49.89 (2.81)
	Unpleasant	52.15 (3.27)	50.49 (2.76)	50.91 (2.68)
Raw Scores				
	Pleasant	163.77 (145.88)	170.58 (161.08)	134.83 (107.49)
	Neutral	173.15 (151.47)	167.01 (140.02)	152.88 (122.85)
	Unpleasant	194.48 (180.17)	176.53 (149.32)	154.84 (134.20)

Startle Magnitude and Severity Measures

In order to test secondary hypotheses that measures of severity would differentiate atypical emotion-modulated startle responding from typical emotion-modulated startle responding, severity groups were created according to median splits on severity measures. To establish groups according to severity, mD and MDD individuals were first analyzed together and the median for each questionnaire score was attained. Minor and

major depressed individuals were then divided into two new groups based on these median splits and compared with the healthy control groups. Table 6 lists the resulting categorization of diagnostic groups according to severity measures. Analyses conducted with each of the three severity groups parallel those conducted with diagnostic groups.

Table 6

Re-categorization of Diagnostic Groups by Median Splits

		Group		
		MDD (n = 33)	mD (n = 25)	Controls (n = 31)
BDI Group		Mean (SD)	Mean (SD)	Mean (SD)
	Controls	0	0	31
	Moderate	10	20	0
	High	23	5	0
BAI Group				
	Controls	0	0	31
	Moderate	15	14	0
	High	18	11	0
PA Group				
	Controls	0	0	31
	Moderate	13	18	0
	High	20	7	0
NA Group				
	Controls	0	0	31
	Moderate	16	16	0
	High	17	9	0

Note: BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory
PA = positive affect
NA = negative affect

Specifically, three (severity group) by three (picture valence) ANOVA's were conducted to examine group differences in startle responses across picture valence. It was expected that the most severe groups (e.g., high BDI, high BAI, low PA, and high NA) would

show atypical emotion-modulation of startle responses (i.e., a failure to exhibit the normal pattern of valence modulation).

Before testing the hypothesis, we determined that in no case were there significant differences for inter-trial interval startle responses (*p*s > .25). Inconsistent with our hypothesis, severity analyses for BDI, BAI, PA, and NA revealed no significant interaction effects involving group (all *ps* > .38). However, severity analyses for PA revealed a trend towards group by picture valence interaction ($p = .11$). In fact, after controlling for medication status, results for the groups created by median splits of PA indicated a significant linear effect for picture valence by PA group [F linear (2, 57) = 5.36, $p < .05$, $\hat{\varepsilon} = .16$]. Follow-up paired comparisons indicated significant differences between groups for unpleasant pictures, such that individuals with the lowest PA scores showed the largest startle responses during unpleasant pictures as compared to healthy controls ($p < .05$) and those with medium PA scores ($p < .05$). Furthermore, paired sample t tests revealed the expected linear pattern—i.e., a difference between pleasant and unpleasant pictures [t (1, 48) = 3.26, $p < .01$]—for healthy controls, but not for those with mid-level PA scores. Specifically, within the moderate PA group, startle responses for pleasant and unpleasant pictures [t (1, 52) = -1.81, $p = .08$] and between unpleasant and neutral pictures [t (1, 52) = -.45, $p = .66$] were not significantly different. Thus, as shown in Figure 2, mood disordered persons who were moderately low in PA were the only group not to show the expected emotion-modulation by picture valence. Table 7 lists means of standardized T scores for startle magnitude according to PA group. In sum, among severity metrics, PA alone differentiated atypical from typical emotion-modulated startle responding, but the form of the interaction was unexpected.

Table 7

Standardized Startle Responses According to Positive Affect Scores

	Group		
	Low	Moderate	Controls
	(*n* = 18)	(*n* = 28)	(*n* = 25)
Valence	Mean (SD)	Mean (SD)	Mean (SD)
Pleasant	48.91 (3.07)	49.23 (3.18)	48.54 (2.22)
Neutral	49.17 (3.39)	50.30 (3.17)	50.10 (2.92)
Unpleasant	53.02 (2.51)	50.65 (2.67)	50.93 (2.66)

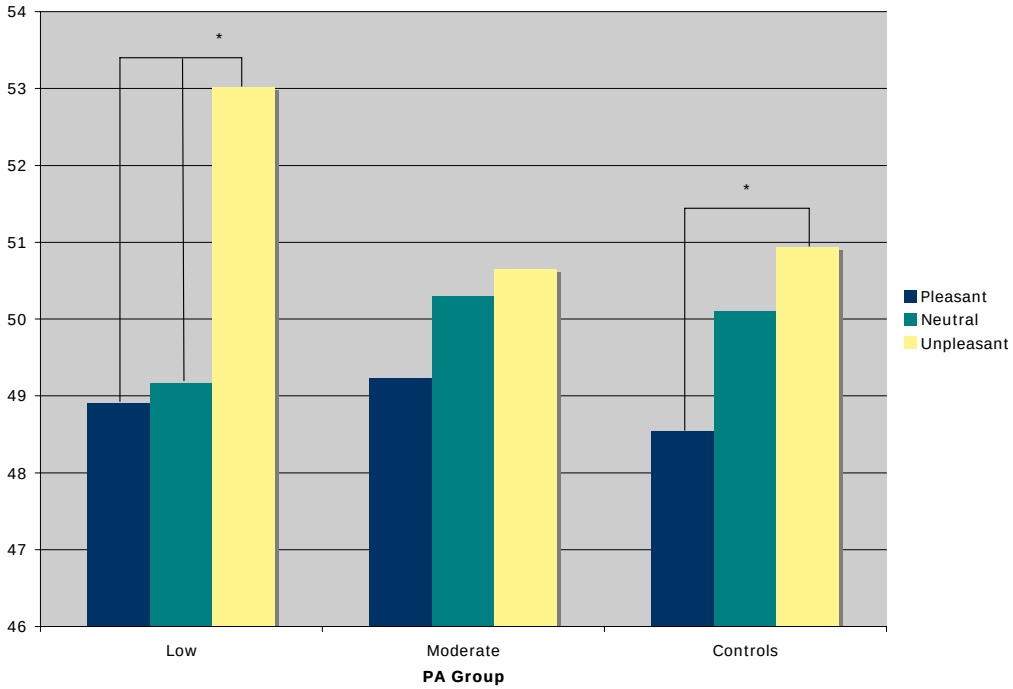

Figure 2. Startle magnitude according to PA group.

Skin Conductance Responses

The raw means for skin conductance reactivity, including average magnitude during picture display (Mean), peak magnitude (Peak), and the average difference between peak magnitude and the baseline conductance prior to picture display (Diff) are

presented in Table 8. In order to normalize skewness and kurtosis associated with raw skin conductance values, raw data was transformed in a linear natural log transformation.

Table 8

Skin Conductance Means

	Valence	MDD (n = 34) Mean (SD)	mD (n = 25) Mean (SD)	Controls (n = 29) Mean (SD)
Mean				
	Pleasant	.003 (.01)	-.002 (.01)	.001 (.01)
	Neutral	.001 (.02)	-.002 (.01)	-.003 (.01)
	Unpleasant	.016 (.03)	.013 (.03)	.019 (.06)
Peak				
	Pleasant	.013 (.02)	.006 (.01)	.009 (.01)
	Neutral	.011 (.02)	.005 (.01)	.005 (.01)
	Unpleasant	.033 (.05)	.029 (.05)	.037 (.08)
Difference				
	Pleasant	.014 (.02)	.008 (01)	.011 (.01)
	Neutral	.013 (.02)	.007 (.01)	.008 (.01)
	Unpleasant	.034 (.05)	.031 (.05)	.037 (.08)

*Note: Skin conductance values expressed in microsiemens (μS)

A series of repeated measures ANCOVAs was performed on transformed skin conductance scores with baseline skin conductance as a covariate to determine differences between picture types across diagnostic groups. The sphericity assumption was not met for average skin conductance, peak skin conductance, or the difference between peak skin conductance and baseline. Because the Greenhouse-Geisser Epsilons were low (0.53), adjustments were made using the Greehouse-Geisser correction. Prior studies of skin conductance patterns for emotion-modulated startle paradigms led to hypotheses of a quadratic effect for skin conductance, such that skin conductance would

be equivalently high for pleasant and unpleasant pictures, and low for neutral pictures (Lang, Greenwald, Bradley, & Hamm, 1993). Analyses yielded a significant quadratic effect for average skin conductance [F Quadratic (1.08, 85) = 6.32, $p < .05$, $\hat{\varepsilon} = .07$], peak skin conductance [F Quadratic (1.08, 85) = 7.14, $p < .01$, $\hat{\varepsilon} = .08$], and difference between peak skin conductance and baseline skin conductance [F Quadratic (1.06, 85) = 8.69, $p < .01$, $\hat{\varepsilon} = .10$]. However, pairwise comparisons indicated that skin conductance for unpleasant pictures was higher than for pleasant pictures and neutral pictures (ps < .05). Pairwise comparisons also indicated a similar pattern for peak skin conductance (p < .05). Lastly, the same quadratic trend was observed for skin conductance difference scores with all ps < .05.

Regarding emotion-modulated startle differences between diagnostic groups, it was hypothesized that MDD individuals would show a significantly different (non-quadratic) pattern of skin conductance responses as compared to mD and healthy controls. However, differences between groups for each skin conductance variable were not statistically significant (all ps > .90), nor were there any picture valence by group interactions for any of the skin conductance variables (ps > .60) or group by quadratic trends (ps > .52).

Relationships between Skin Conductance and Severity Measures

Analyses conducted with each of the three severity groups were similar to those conducted for startle responses. Specifically, three (severity group) by three (picture valence) ANOVAs were conducted to examine group differences in skin conductance responses across picture valence. Again, it was predicted that the most severe groups would show atypical emotion-modulation of startle responses compared to healthy

controls and moderately severe groups. Inconsistent with this hypothesis, there were no significant group by valence interactions for BDI (*p*s > .62), BAI (*p*s > .46), PA (*p*s > .67), or NA (*p*s > .69).

Cardiac Responses

Average heart rate values for each phase, including D1, A1, and a secondary deceleration (D2), are displayed in Figure 3. Because D2 values are not readily interpretable in this type of emotion-modulated paradigm, analyses focused on D1 and A1 values. Mean values by diagnostic group for D1 and A1 as a deviation from baseline values are presented in Table 9.

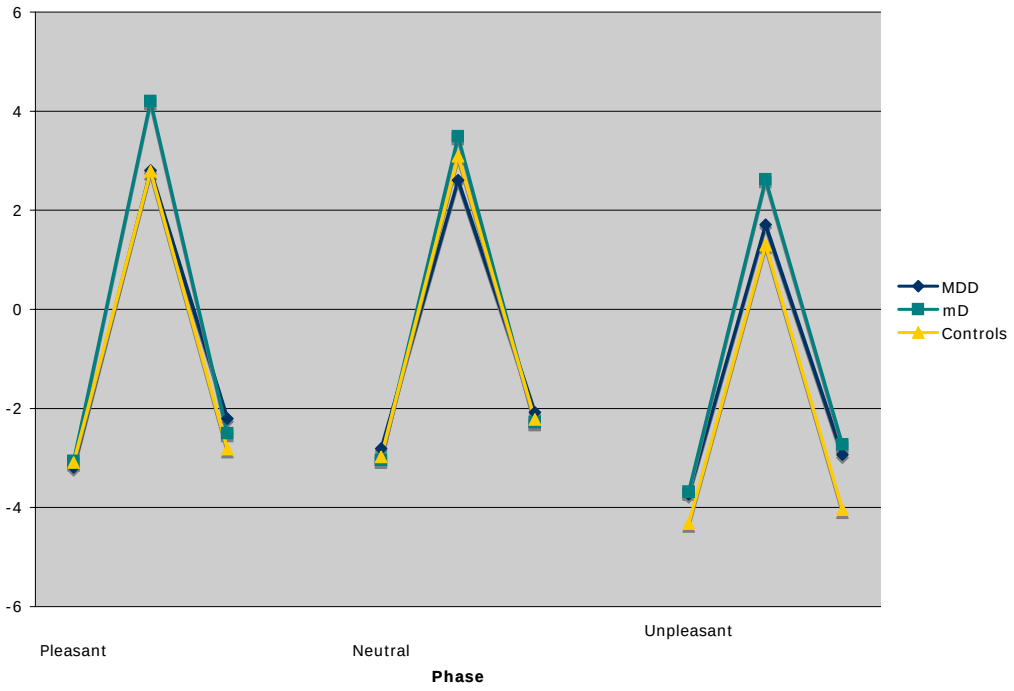

Figure 3. Heart phases (D1, A1, D2) by picture valence.

A series of repeated measures ANCOVAs (with baseline heart rate entered as a covariate) were conducted to examine whether heart phase magnitudes (D1, A1) differed

between diagnostic groups across picture valence. In line with previous hypotheses, it was predicted that MDD individuals would experience significantly smaller absolute heart phase magnitudes (signaling less sensory and emotional processing) compared to mD individuals and healthy controls. However, results failed to reveal a significant main effect for heart phase for group (D1: [F (2, 65) = .24, p = .79]; A1: [F (2, 65) = .44, p = .65]) or for group by picture valence (D1: [F (4, 128) = .91, p = .46]; A1: [F (4, 128) = 1.00, p = .41]). Furthermore, there were no linear by valence or quadratic by valence effects for picture valence, signaling that heart phase values did not differ significantly between picture valences. Values for D1 by picture valence and A1 by picture valence for each diagnostic group are displayed in Figures 4 and 5, respectively.

Table 9

Cardiac Measures by Diagnostic Group

		MDD	mD	Controls
	Valence	(n = 26)	(n = 17)	(n = 27)
D1		Mean (SD)	Mean (SD)	Mean (SD)
	Pleasant	-3.19 (2.27)	-3.06 (1.73)	-3.09 (1.59)
	Neutral	-2.81 (1.75)	-3.04 (1.87)	-2.98 (1.69)
	Unpleasant	-3.73 (2.16)	-3.68 (2.13)	-4.32 (2.27)
A1				
	Pleasant	2.80 (2.48)	4.20 (3.14)	2.79 (2.59)
	Neutral	2.61 (2.20)	3.49 (2.23)	3.09 (2.81)
	Unpleasant	1.71 (2.28)	2.62 (1.92)	1.30 (2.25)

Note: D1 = initial heart rate deceleration beats/min change from baseline
A1 = heart rate acceleration beats/min change from baseline

Relationship between Cardiac Responses and Severity

The typical pattern of cardiac responding to valenced pictures involves more initial heart rate deceleration (D1) for unpleasant pictures—indicating a greater sensory orienting response—than for pleasant pictures and larger subsequent acceleratory responses to pleasant pictures—representing greater emotional processing—than for unpleasant pictures (Lang, Greenwald, Bradley, & Hamm, 1993). In order to test the hypothesis that more severe groups would show equally small levels of sensory and emotional processing of valenced stimuli, a series of ANCOVA's was conducted for each heart phase variable by picture valence for each severity group, with baseline heart rate again entered as a covariate. In addition, within group linear trends by valence were examined to test the hypotheses that patterns of responding would differ across severity groups. Specifically, results of the ANCOVA failed to reveal significant group by picture valence effects for BDI group (D1: [F (4, 128) = 2.21, p = .08]; A1: [F (4, 128) = 1.45, p = .22]), for BAI group (D1: [F (4, 128) = 1.10, p = .36]; A1: [F (4, 128) = 1.18, p = .32]), or for NA group (D1: [F (4, 128) = 1.35, p = .26]; A1: [F (4, 128) = 1.86, p = .12]). However for PA group there were the hypothesized group by picture valence interactions for D1 [F (4, 128) = 4.17, $p < .01$, $\hat{\varepsilon}$ = .11] and A1 [F (4, 128) = 3.33, $p < .05$, $\hat{\varepsilon}$ = .09]). Mean cardiac values according to PA group are listed in Table 10. Although group by valence interactions for D1 were significant (Figure 5), follow-up paired comparisons indicated only trend level difference for D1 following unpleasant picture onset between those with low levels of PA and healthy controls (p = .09), such that individuals with low PA showed higher D1 values. Additionally, there was a trend for individuals with low

levels of PA to have higher A1 values during unpleasant pictures as compared to healthy controls (p = .08; Figure 6).

Table 10

Cardiovascular Measures by Positive Affect

	Valence	Low (n = 19) Mean (SD)	Moderate (n = 22) Mean (SD)	Controls (n = 27) Mean (SD)
D1				
	Pleasant	-3.51 (2.49)	-2.75 (1.64)	-3.09 (1.59)
	Neutral	-2.59 (1.49)	-3.09 (2.03)	-2.98 (1.69)
	Unpleasant	-3.20 (1.63)	-4.20 (2.49)	-4.32 (2.27)
A1				
	Pleasant	2.46 (2.11)	4.11 (3.25)	2.79 (2.59)
	Neutral	2.64 (2.31)	3.18 (2.26)	3.09 (2.81)
	Unpleasant	2.31 (2.22)	1.73 (2.19)	1.30 (2.25)

Note: Values are change in heart rate (in beats per minute) compared to baseline heart rate.

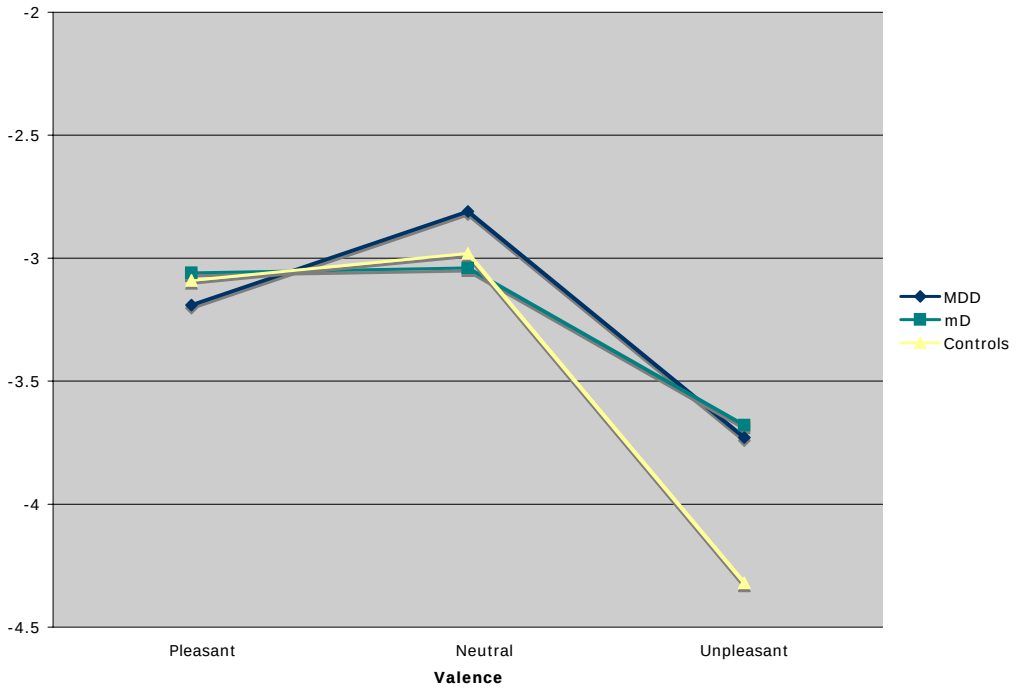

Figure 4. D1 cardiac responses by diagnostic group for each picture valence.

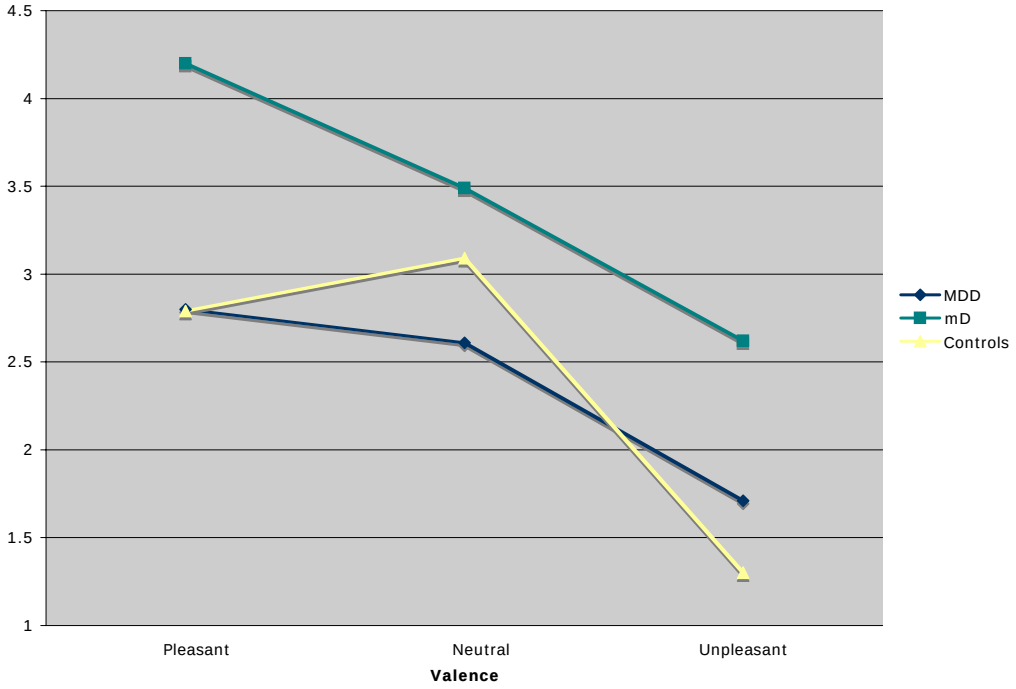

Figure 5. A1 cardiac responses by diagnostic group for each picture valence.

Lastly, individuals with moderate PA levels had significantly higher A1 values compared to healthy controls ($p < .05$) and compared to individuals with low levels of PA ($p < .05$; Figure 7). Only the group difference in A1 for unpleasant pictures survived covariation of medication status and remained significant ($p < .05$). In sum, these results suggest that compared to healthy controls, mood disordered individuals with low PA showed smaller sensory orienting responses and greater emotional processing during unpleasant pictures. Furthermore, results indicate that mood disordered persons with moderate levels of PA experienced significantly more emotional processing during pleasant pictures as compared to mood disordered individuals with low PA and healthy controls.

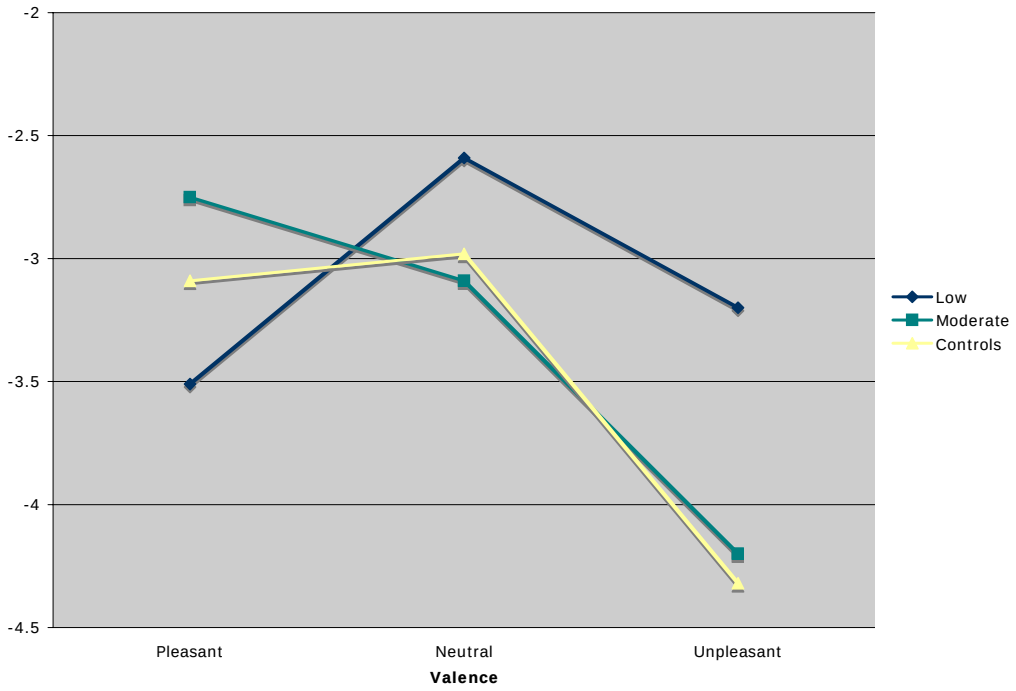

Figure 6. D1 Cardiac responses by PA group for each picture valence.

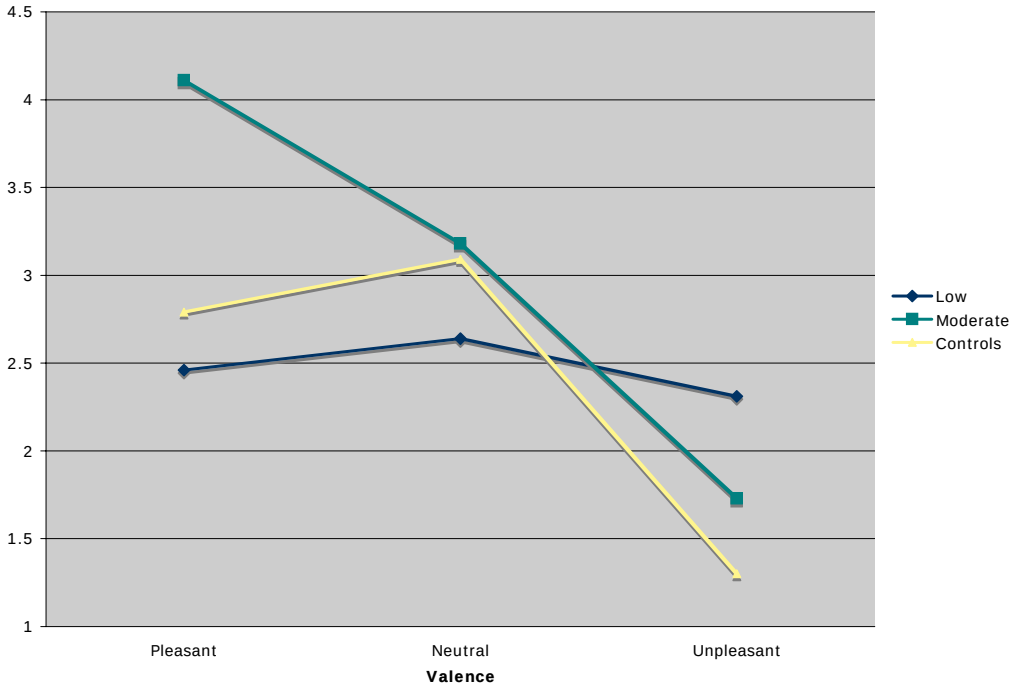

Figure 7. A1 Cardiac responses by PA group for each picture valence.

Discussion

Major depressive disorder is defined primarily by mood changes. However, research has not yet discerned how this chronic mood disturbance affects emotional responding. Furthermore, it is unclear whether subthreshold forms of depression, such as minor depression (mD), involve similar or different abnormalities in emotional responding as seen in MDD. The general aim of the current study was to examine abnormalities in emotional reactivity as a vulnerability and severity marker for MDD. It was predicted that MDD individuals would display abnormal (blunted) patterns of emotional responding compared to healthy controls, as well as mD individuals.

More specifically, this study was the first to examine the relationship between emotional reactivity to pleasant and unpleasant stimuli in a sample of carefully diagnosed MDD individuals, mD individuals, and healthy controls. The primary goal of the study was to discern diagnostic differences in emotion reactivity as a function of affective foreground, by utilizing the emotion-modulated startle eyeblink reflex. To clarify the role of severity in emotional reactivity, we analyzed startle to affective pictures as a function of several severity metrics, including depression severity, anxiety severity, and the strength of positive and negative mood states. To afford a more comprehensive assessment of psychophysiological responding, parallel analyses were conducted on heart rate and skin conductance.

Effects of the Paradigm

Several aspects of the results increase confidence that that the emotion-modulated startle paradigm was successfully applied. Results yielded the expected pattern of emotion modulation for startle reactivity. Standardized startle responses during negative pictures were significantly larger than startle responses occurring during pleasant pictures. Moreover, ratings of picture valence indicated that participants found unpleasant pictures significantly less pleasant than neutral and pleasant pictures. Additionally, participants found pleasant pictures to be equally arousing as unpleasant pictures, and both to be more arousing than neutral pictures. Skin conductance measures also displayed the expected quadratic pattern, such that measures were highest during unpleasant pictures and lowest for neutral and pleasant pictures. Lastly, heart rate variables showed the expected quadratic waveform across three phases of cardiac response. Taken together, these findings indicate that the manipulation of affective state produced the expected pattern of responses, suggesting that the internal validity of the paradigm was sound.

Effects of Diagnosis and Symptom Severity

The primary hypotheses predicted that MDD individuals would show less valence modulation when compared to mD individuals and controls across all physiological variables. However, analyses did not reveal significant group by picture valence interactions for any physiological variable of interest. In other words, in these data persons with MDD, as well as persons with mD, appeared to exhibit essentially normal valence modulation of startle, skin conductance, and heart rate responses.

It is unclear why MDD participants did not exhibit a lack of appropriate valence modulation across physiological indicators, especially in light of two recent studies which

found blunted startle modulation in MDD (Dichter & Tomarken, 2008; Dichter et al., 2004). However, previous research on the startle in MDD is not entirely uniform. In fact, two other previous studies found essentially normal emotion-modulated startle patterns in MDD individuals relative to healthy controls, and only abnormal startle modulation when depressive subgroups were analyzed (Allen et al., 1999; Kaviani et al., 2004). We anticipated this second possibility by performing a wide range of subgroup analyses focusing on several metrics of symptom severity.

More specifically, secondary analyses were conducted with various severity measures to test the hypothesis that the most severe group of mood-disordered individuals would show the clearest pattern of atypical (flattened) patterns of emotional responding across physiological variables. Results utilizing Beck Depression Inventory (BDI) scores, Beck Anxiety Inventory (BAI) scores, and negative affect scores (NA), as measured by the Positive Affect Negative Affect Scale (PANAS) as measures of severity were inconsistent with this hypothesis, and did not yield significant differences between severity groups. However, analyses conducted with positive affect (PA), as assessed by the PANAS, did predict differences in emotion-modulated startle responding as well as heart rate responses to affective pictures. These findings were novel in the literature and merit comment.

Specifically, mood disordered individuals with the lowest PA exhibited the largest startle responses to unpleasant pictures of the three severity groups. Thus, these individuals displayed increased reactivity for unpleasant pictures. Surprisingly, it was those mood disordered individuals with moderately low PA (and not the most severe group) that failed to show the typical pattern of emotion modulation for startle exhibited

by healthy persons. PA also differentiated patterns of cardiac responding between severity groups. Mood disordered individuals with the lowest PA showed atypical patterns of cardiac responses. The typical pattern of cardiac responding involves initial deceleration of heart rate in response to stimuli (D1), indicative of initial sensory orienting, and subsequent acceleration (A1), indicative of emotional processing (Lacey & Lacey, 1970; Graham & Clifton, 1966; Sokolov, 1963). In terms of emotion modulation, the typical pattern of heart rate responses involves heightened sensory orientation for unpleasant compared to pleasant pictures and heightened emotional processing of pleasant as compared to unpleasant pictures (Lang, Greenwald, Bradley, & Hamm, 1993). Mood disordered individuals with low PA showed equivalent sensory orientation for and emotional processing of both unpleasant and pleasant pictures. This suggests deficits in attending to emotional stimuli, such that the most severe group of mood disordered individuals exhibited decreased sensory orienting for unpleasant pictures, decreased emotional processing of pleasant stimuli, and increased emotional processing of unpleasant stimuli, resulting in a flattened pattern of heart rate responding across valence conditions (Figures 6 and 7). Past researchers have proposed models of emotional processing that are somewhat consistent with this pattern of biased attending towards negative stimuli (Beck, 1967).

Affect and Hedonic Capacity

Given past research in this area (e.g., Allen, et al., 1999) it is perhaps surprising that PA alone, and not BDI or NA, scores exerted influence on startle modulation and cardiac responses. However, there was a significant association between positive affect and startle responding to unpleasant pictures. A lack of PA as indicated by the PANAS,

can be conceptualized as representing a dimensional measure of anhedonia (Clark & Watson, 1991) or, similarly, impaired hedonic capacity (Meehl, 1962). Specifically, as anhedonia is defined by a lack of interest or pleasure, a lower score on the PA scale of the PANAS indicates higher levels of impaired hedonic capacity. Previous studies have found an effect for anhedonia on startle modulation, such that anhedonic individuals showed blunted emotional responding, as marked by a lack of startle modulation to both pleasant and unpleasant pictures (Kaviani et al., 2004; Larson, Nitschke, & Davidson, 2007).We did not replicate this flattened pattern of startle responses for persons with low PA. Instead, individuals with the lowest PA displayed higher startle responses during unpleasant pictures than did individuals with moderate PA and healthy controls. Individuals with the lowest PA also exhibited increased emotional processing of unpleasant pictures (as indicated by cardiac variables). Therefore, increased emotional processing of unpleasant stimuli may be related to a weak appetitive system, which leads to greater cardiac acceleration and higher levels of startle responding during unpleasant pictures.

In general, PA and NA have often been conceptualized as two independent affective dimensions (Tellegen, Watson, & Clark, 1999). However, NA and PA have been theorized to be reciprocally related in some instances of disturbed mood (Meehl, 1962). For example, the theory of aversive drift—first proposed as an explanation for the marked anhedonia seen in schizophrenia disorders—predicts that as the ability to feel pleasure decreases along the dimension of hedonic capacity, approaching anhedonia, individuals begin paying more attention to objects in the environment with negative affective tone (Meehl, 1962; Meehl, 2001). Consistent with this interpretation, in this

dataset we found that reports of PA and NA were moderately negatively intercorrelated (*r* = -.4). Thus, one potentially important finding of this study is that it suggests that more severe hedonic deficits in mood disorders result in higher levels of emotional processing for unpleasant stimuli. Future studies should further examine this association between greater emotional processing of unpleasant stimuli and dimensional hedonic capacity, and whether greater emotional processing of negative stimuli predicts the course of depression.

Conclusions

The current study did not reveal the expected differences in emotional responding between major and minor depression. These null findings for diagnostic group differences do not allow us to decide between the continuum and the disease model (whether MDD represents a distinct mood state with chronic, disease-like deficits in emotional responding or whether it is an arbitrary point along the continuum of disturbed mood). However, this study does suggest that qualitative features of depression such as symptom type (e.g., decreased hedonic capacity) may help to explain why findings for diagnostic group are often heterogeneous in the area of emotion.

Finally, there is relatively little research concerning the predictive ability of emotional responding in MDD and no research on mD. Given that some evidence indicates that anhedonia predicts a more recurrent course of MDD (Clark et al, 1984) and nonrecovery of MDD (Kasch et al., 2002), examination of the predictive validity of anhedonia severity for the spectrum of mood disorders is warranted. Given that the lack of positive affect seemed to be indicative of more severe deficits in emotional processing,

future studies should examine whether these deficits in emotional processing predict the development of or recovery from mood disorders.

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Appendices

Appendix A: Footnotes

[1]IAPS numbers of pictures used are as follows: neutral (2570, 2580, 7006, 7009, 7025, 7030, 7150, 7175, 7187, 7217, 7224, 7491 for males; and 2840, 5530, 5740, 6150, 7004, 7010, 7031, 7035, 7040, 7185, 7491, 9360 for females) pleasant (1650, 4320, 4653, 4689, 7501, 8080, 8180, 8260, 8300, 8380, 8470, 8501 for males; 4660, 5460, 5910, 7502, 8030, 8034, 8080, 8180, 8185, 8200, 8210, 8400 for females), and unpleasant (3015, 3053, 3060, 3071, 3080, 3170, 3530, 6260, 6313, 6570, 9410, 9570 for males; 2730, 3010, 3015, 3053, 3060, 3100, 3120, 6312, 9050, 9433, 9571, 9921 for females.

Appendix B: Additional Tables

Zero Order Correlations between Startle Responses and Severity Measures

Magnitude *T* scores		BDI	BAI	PA	NA
	Pleasant	0.05	-0.05	-0.06	-0.04
	Neutral	0.02	0.16	0.15	0.07
	Unpleasant	0.17	-0.04	-0.25*	0.02
Raw Scores					
	Pleasant	0.05	-0.02	0.03	0.16
	Neutral	0.03	-0.00	0.11	0.17
	Unpleasant	0.07	-0.01	0.01	0.18
Amplitude					
	Pleasant	0.04	-0.07	-0.04	-0.05
	Neutral	0.02	0.17	0.13	0.08
	Unpleasant	0.19	0.00	-0.27*	0.07

*$p < .05$

Note: BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory
PA = Positive Affect
NA = Negative Affect

Zero Order Correlations between Skin Conductance and Severity Measures

	Valence				
Mean		BDI	BAI	PA	NA
	Pleasant	0.02	-0.04	0.09	0.13
	Neutral	0.16	0.09	-0.05	0.26*
	Unpleasant	-0.09	-0.07	-0.04	-0.05
Peak					
	Pleasant	0.05	0.01	-0.00	0.14
	Neutral	0.13	0.13	-0.12	0.26*
	Unpleasant	-0.09	-0.05	-0.03	-0.06
Difference					
	Pleasant	0.07	-0.03	-0.00	0.15
	Neutral	0.14	0.14	-0.12	0.26*
	Unpleasant	-0.08	-0.04	-0.04	-0.06

*$p < .05$

Note: Skin conductance values expressed in microsiemens (μS)
BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory
PA = Positive Affect
NA = Negative Affect

Zero Order Correlations between HR Phase and Severity Measures

	Valence				
D1		BDI	BAI	PA	NA
	Pleasant	0.12	-0.04	0.07	-0.15
	Neutral	0.03	0.04	-0.03	-0.05
	Unpleasant	0.04	0.04	-0.11	-0.10
A1					
	Pleasant	0.02	0.03	0.06	0.06
	Neutral	-0.01	-0.06	0.02	0.15
	Unpleasant	0.13	0.12	-0.11	0.16

Note: BDI = Beck Depression Inventory
BAI = Beck Anxiety Inventory
PA = Positive Affect
NA = Negative Affect