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Increased neural sensitivity to self-relevant stimuli in Major Depressive Disorder

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Abstract

The current research examined how individuals with depression process emotional, self-relevant stimuli. Across two studies, individuals with depression and healthy controls read stimuli that varied in self-relevance while electroencephalogram (EEG) data was recorded. We examined the late positive potential (LPP), an event-related potential (ERP) component that captures the dynamic allocation of attention to motivationally salient stimuli. In study 1, participants read single words in a passive-viewing task. Participants viewed negative, positive, or neutral words that were either normative or self-generated. Exploratory analyses indicated that participants with depression exhibited affective modulation of the LPP for self-generated stimuli only (both positive and negative), and not for normative stimuli; healthy controls exhibited similar affective modulation of the LPP for both self-relevant and normative stimuli. In study 2, using a separate sample and a different task, stimuli were provided within the context of sentence stems referring to the self or other people. Participants with depression were more likely to endorse negative self-referent sentences and reject positive ones compared to health controls. Depressed participants also exhibited an increased LPP to negative stimuli compared to positive or neutral stimuli. Together, these two studies suggest that depression is characterized by relatively increased sensitivity to affective self-relevant stimuli, perhaps in the context of a broader reduction in emotional reactivity to stimuli that are not self-relevant. Thus, depression may be characterized by a more nuanced pattern based on the degree of stimulus self-relevance than either a global decrease or increase in reactivity to affective stimuli.

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Keywords

ERPs; LPP; DEPRESSION; SENTENCE PROCESSING; EMOTION; SELF-REFERENCE

1 Introduction

Major depressive disorder is the most common psychological diagnosis in the United States and is a major public health concern associated with loss of productivity, increased disability, and premature death (Lepine & Briley, 2011). Converging evidence from neurological, cognitive, and affective research on depression suggests an emerging endophenotype of blunted emotional reactivity to both pleasant and unpleasant environmental stimuli (Berghorst & Pizzagalli, 2010; Bylsma, Morris, & Rottenberg, 2008; Gaddy & Ingram, 2014; Khazanov & Ruscio, 2016; Rottenberg, Gross, & Gotlib, 2005); however, some previous research on emotional reactivity to negative stimuli have not shown this effect (e.g., Almeida, Versace, Hassel, Kupfer, & Phillips, 2010; Gaffrey et al., 2011; Suslow et al., 2010). The observed inconsistencies in the literature may be explained by maladaptive attentional biases specifically to personally-relevant information (Gaddy & Ingram, 2014). For healthy individuals, there is increasing evidence that self-relevance of stimuli is strongly associated with emotional arousal regardless of valence (Fields & Kuperberg, 2015b; Herbert, Herbert, Ethofer, & Pauli, 2011a; Herbert, Herbert, & Pauli, 2011b; Herbert, Pauli, & Herbert, 2011c), while individuals with depression seem to selectively focus on emotional self-relevant information (Bylsma, Taylor-Clift, & Rottenberg, 2011; Dai, Rahman, Lau, Sook Kim, & Deldin, 2015; Rottenberg et al., 2005; Sloan, 2005).

Emotional reactivity to self-relevant information may distinguish healthy individuals and those with depression, though, to our knowledge, no previous study has explicitly tested this claim. Some evidence suggests that individuals with depression overly attend to self-relevant stimuli regardless of valence (Bylsma et al., 2011; Koster, De Lissnyder, Derakshan, & De Raedt, 2011; Mor & Winquist, 2002; Sloan, 2005; Treynor, Gonzalez, & Nolen-Hoeksema, 2003). Previous work has demonstrated that individuals with depression have shown greater reactivity to positive emotional events in their daily lives compared to healthy controls (Bylsma et al., 2011), suggesting self-relevance is key in eliciting an emotional response in individuals with depression. Thus, while Beck's (1967) original model suggested that the hallmark of depression was a focus on all negativity, more contemporary research indicates that those with depression have more selective attentional biases to self-referential stimuli (Foland-Ross & Gotlib, 2012; Gaddy & Ingram, 2014; Goldstein & Klein, 2014; Ingram, Atchley, & Segal, 2011; Mehu & Scherer, 2015), which happen to typically be rated as negative (Dai et al., 2015; Sloan, 2005; Takano & Tanno, 2009). Thus, while healthy individuals may attend to all emotionally *or* idiographically salient information (e.g., Fields & Kuperberg, 2015a; Herbert et al., 2011c), individuals with depression may selectively attend to stimuli with personal salience *and* emotional content (Gaddy & Ingram, 2014).

Psychophysiological research has further elucidated attentional biases in major depression. The Late Positive Potential (LPP), an event-related potential (ERP) component associated with affective processes, has been increasingly useful in assessing differences in emotional reactivity between healthy controls and those with depression (Citron, 2012; Cuthbert, Schupp, Bradley, Birbaumer, & Lang, 2000). The LPP is maximal at centroparietal regions of the scalp and is thought to reflect the allocation of attention to information that is motivationally salient (Schupp, Flaisch, Stockburger, & Junghöfer, 2006). The LPP is enhanced by highly arousing emotional content, both pleasant and unpleasant, versus neutral, as these valences relate to approach and avoid mechanisms, respectively (Hajcak, Dunning, & Foti, 2009; Nowparast Rostami et al., 2016). The LPP does not solely equate to arousal and is better considered as a marker of attention, which has been influenced by bottom- up (e.g., stimulus properties, arousal) or top-down (e.g., volitional, task-related) effects (Hajcak, MacNamara, & Olvet, 2010; Krompinger, Moser, & Simons, 2008). The LPP has also been enhanced to self-relevant images and words regardless of valence (Herbert, Junghofer, & Kissler, 2008; Kissler, Assadollahi, & Herbert, 2006; Tempel et al., 2013). Tasks that involve extended processing or comprehension of self-relevant stimuli have enhanced this effect (Fields & Kuperberg, 2012, 2015a, 2015b; Herbert et al., 2011a; Herbert et al., 2011c).

Previous work has demonstrated that individuals with major depression generate more larger (i.e., more positive) LPP amplitudes to negative words than positive or neutral words and are more likely to endorse negative words as related to themselves; conversely, healthy controls elicit larger LPP amplitudes to positive words and they are more likely to endorse positive words as related to themselves (Auerbach, Stanton, Proudfit, & Pizzagalli, 2015; Deldin, Deveney, Kim, Casas, & Best, 2001; Gaddy & Ingram, 2014; Herbert et al., 2011a; Herbert et al., 2011c; Shestyuk & Deldin, 2010). What is unclear from this prior work, however, is how valence and self-relevance interact to affect the LPP differently across individuals with and without depression. Thus, the key aim of the two experiments reported here was to clarify the relation between self-reference and valence in attentional processing in depression. These studies examine a broadly similar question utilizing different methods and samples. In Study 1, participants viewed single words that were normatively rated as pleasant, unpleasant, or neutral as well as words that were self-generated to represent pleasant, unpleasant, and neutral mood states. This is the first study to examine how words varying in valence and self-relevance (in this case, self-generated) interact to modulate the LPP differently in individuals with and without depression. In Study 2, participants viewed words with positive or negative connotations presented in the context of sentences that either referred to the self or another person. This is the first study to examine how emotional sentence endings affect both behavioral and neural responses in individuals with and without depression. Sentences can disambiguate the intended meaning of words and enhance self-relevance beyond other forms of stimulus presentation (Bayer, Sommer, & Schacht, 2010; Kutas & Federmeier, 2011; Wlotko & Federmeier, 2012). Together, these studies address a gap in the literature regarding whether personal relevance and/or emotional content of stimuli are necessary in combination, or are sufficient variables on their own, to generate increased attention and neural activation in individuals with Major Depressive Disorder. Elucidating this relationship can enhance our understanding of attentional bias in depression as a target for treatment and prevention.

2 Study 1

To explore the differential processing of emotional words in individuals with and without depression, the major aim of Study 1 was to separate the self-relevant effects from valence effects. Previous studies have demonstrated that amygdala activity is enhanced while viewing idiographic (i.e., generated by the participant to represent their own emotional states) negative words alongside other normative words among individuals with depression, but not healthy controls (Shestyuk & Deldin, 2010; Siegle, Thompson, Carter, Steinhauer, & Thase, 2007). Thus, in this study, we explored the differences between stimuli that were normative (i.e. words previously rated to be positive, negative, or neutral) and idiographic (i.e. self-generated *and* referring to the self). This comparison builds on previous studies, which have not directly compared neural responses to both idiographic and normative stimuli, each across pleasant, neutral, and unpleasant valences. Comparison across these six categories varying in self-relevance and valence is essential to understanding the seemingly disparate effects of emotional reactivity in depression (e.g., potentiated reactivity to everyday pleasant life events versus attenuated reactivity to normative negative stimuli). The goal of this study was to further elucidate whether the personal relevance of stimuli is a key determining factor of abnormal emotional reactivity in depression. Given previous literature, we hypothesized that the LPP would be (a) attenuated in depression for affective normative stimuli, and (b) potentiated in depression for affective idiographic stimuli.

2.1 Method

2.1.1 Participants.—The present sample completed several tasks as part of an ongoing series of studies (e.g., Foti, Carlson, Sauder, & Proudfit, 2014). The depressed[i] group consisted of 39 women. Three participants with depression were excluded for greater than 50% artifacts in their ERP data, resulting in a final sample of 36 participants with depression. The inclusion criterion for the depressed group was a clinical diagnosis of unipolar depression (i.e., current depression and/or dysthymic disorder); exclusion criteria were the diagnosis of current generalized anxiety disorder (i.e., past six months), lifetime obsessive compulsive disorder, or more than one other current comorbid Axis I disorder. In light of research that antidepressant medication can alter the morphology of ERPs (d'Ardhuy et al., 1999), participants were excluded for reporting use of prescription of antidepressant medication within two months of study participation. Five participants with depression (14%) were engaged in psychotherapy at the time of the study. The healthy control group consisted of 34 adult women with no history of any Axis I disorder, no current prescription of psychiatric medication, and no history of any neurological illness. No healthy control participant reported being engaged in psychotherapy or pharmacotherapy. The depressed group was somewhat older ($M = 26.24$ years, $SD = 8.92$) than the control group ($M = 22.96$, $SD = 6.43$), though this difference was not statistically significant ($p = 0.08$, $d = 0.42$). There was a significantly greater number of Caucasian participants in the depressed group ($n = 26$; 74%) compared to the control group ($n = 14$; 48%), $\chi^2(1) = 3.89$, $p = 0.049$,

[i]A majority of depressed participants (66.7%) currently met criteria for current depression with no comorbid disorders. Of the remaining participants, 9 participants (25%) had one current comorbid diagnosis (e.g. dysthymia, specific phobia, panic, social phobia) and 3 participants (8.3%) had two current comorbid diagnoses (e.g. specific phobia, body dysmorphic disorder, opioid dependence).

though the effect size for this difference is small (ϕ = 0.24). Group differences in education were not significant, (*p* > 0.11). The institutional review board at Stony Brook University approved the research protocol, and all participants completed written informed consent prior to participation.

2.1.1.1 Recruitment and Diagnostic Procedures.: Depressed and healthy control participants were recruited from within Stony Brook University and the surrounding communities via fliers and internet advertisements. Psychological evaluations of all participants were made in a two-steps: (a) an initial telephone contact where we administered the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) and then (b) a more extensive Structured Interview for DSM Disorders (SCID; First, Spitzer, Gibbon, & Williams, 1997) for those who proceeded to the laboratory study. The MINI and SCID were completed by master's level graduate students with extensive experience with these instruments.

2.1.1.2 Symptom Measures.: Symptom severity was assessed using the Mood and Anxiety Symptom Questionnaire (MASQ), a 90-item scale designed in accordance with the tripartite model of depression and anxiety (Watson et al., 1995a; Watson et al., 1995b). Each item is rated on a five-point Likert-type scale representing the presence and severity of that symptom over the preceding week (1 = *not at all* to 5 = *extremely*). The MASQ contains four subscales: Anhedonic Depression (AD), Anxious Arousal (AA), the General Distress: Depressive Symptoms (GDD), and General Distress: Anxious Symptoms (GDA). We utilized the AD and GDD subscales to characterize depressive symptom severity in the depressed and control groups. In the current sample, the internal consistency was excellent for AD (α = 0.94) and GDD (α = 0.96). Due to collection constraints, ten participants did not complete the MASQ (one depressed, nine control), but were included in the final ERP analysis. Descriptive statistics for the MASQ can be found in Table 1. As would be expected, individuals in the depressed group reported significantly more severe symptoms of depression compared to the control group.

2.1.2 Procedure.

—The experiment was conducted in a single three-hour session. Participants completed informed consent procedures followed by the SCID. Next, the EEG recording session was conducted by a research assistant blind to group membership. Participants completed four tasks in a counterbalanced order, one of which was the emotional viewing task described below. Other tasks included a passive viewing, monetary feedback, and performance feedback tasks discussed elsewhere (Foti et al., 2014). After completing the task, participants were asked to rate all word stimuli on valence and arousal using the nine-point self-assessment manikin (Bradley & Lang, 1994, 1999), wherein larger scores correspond to greater negativity and arousal, respectively. Following the rating task, participants completed the MASQ. All participants were compensated for their time.

2.1.2.1 Normative Stimuli.: The task used affective words to elicit the LPP, modeled after the paradigm developed by Siegle and colleagues (2002). Thirty normative words were drawn from the ANEW (10 each of pleasant, neutral, and unpleasant)[ii]. Within each normative category, the selected words were balanced for emotional arousal, word frequency, and character length using the Balanced Affective Word List application (Siegle, 1994). We assessed the lexico-semantic qualities of the words using updated corpora so that the idiographic and normative words of this study were assessed against the same comparative samples and scale for descriptive purposes. Namely, in addition to length, we assessed frequency (Brysbaert & New, 2009), part of speech (Brysbaert, New, & Keuleers, 2012), concreteness (Brysbaert, Warriner, & Kuperman, 2014), and arousal and valence (Warriner, Kuperman, & Brysbaert, 2013), which are on the same 1 (positive) to 9 (negative) scale as Bradley and Lang (1994, 1999). We conducted a series of One-Way ANOVAs with each of these factors as the dependent variable and word type as the independent variable. We used Bonferroni correction on all pairwise comparisons. Results showed a main effect of valence [$F(2, 27) = 106.78$, $p < 0.001$, $\omega^2 = 0.87$], arousal [$F(2, 27) = 40.36$, $p < 0.001$, $\omega^2 = 0.72$], and concreteness [$F(2, 27) = 3.96$, $p = 0.030$, $\omega^2 = 0.16$], but neither frequency nor length (p's > 0.3, $\omega^2 < 0.05$). Pairwise comparisons showed that the selected negative words were rated as more unpleasant ($M = 7.12$, $SD = 0.32$) than neutral words ($M = 5.39$, $SD = 1.00$) and pleasant words ($M=2.68$, $SD= 0.08$); unpleasant words were rated as significantly more negative than neutral words (all p's < 0.001). In terms of arousal, the selected pleasant (M = 5.63, $SD = 0.61$) and neutral words ($M = 5.43$, $SD = 0.38$) were rated higher than neutral words ($M = 3.30$, $SD = 0.26$; both p's < 0.001), while pleasant and unpleasant words did not significantly differ from each other ($p = 0.83$). In terms of concreteness, neutral words were significantly more concrete ($M = 4.34$, $SD = 1.33$) than unpleasant words ($M = 3.06$, $SD = 1.17$; $p = 0.047$). The concreteness of pleasant stimuli ($M = 3.22$, $SD = 1.14$) did not significantly differ from unpleasant or neutral stimuli (all p's > 0.09). χ^2 tests did not reveal significant associations between stimulus category and parts of speech ($p = 0.24$, V < 0.1).

2.1.2.2 Idiographic Stimuli.: For idiographic words, participants generated a list of thirty words (3–11 letters long) in response to prompts to provide: “10 personally relevant negative words that best represent what you think about when you are upset, down, or depressed;” “10 personally relevant positive words that best represent what you think about when you are happy or in a good mood;” and “10 personally relevant neutral (i.e., not positive or negative) words that best represent what you think about when you are neither very happy nor very upset, down, or depressed.” These were then viewed during idiographic blocks of the task. We provided no additional constraints on stimuli in accordance with procedures described by Siegle and colleagues (2007). Of the 1420 stimuli that were generated across participants, nine participants duplicated four words from the normative list, and no participant duplicated more than one word.

We compared the categories of words using the ratings of concreteness, valence and arousal, frequency, length, and part of speech according to the norms established by Brysbaert and colleagues mentioned above (2009; 2012; 2014; 2013, respectively) using a series of 2 (Group: Depressed vs. Control) X 3 (Word Type: Positive, Negative, Neutral) univariate ANOVA on each variable (length, frequency, concreteness, arousal, valence), as there were

[ii]The following ANEW words were used: pleasant: 39, 69, 513, 754, 189, 241, 352, 530, 1003, 449; unpleasant: 584, 53, 111, 202, 216, 342, 604, 461, 462, 471; neutral: 651, 658, 710, 369, 416, 737, 578, 1026, 579, 1032. Parallel ANOVA using the ratings provided by the ANEW database showed comparable results to the ones presented below.

different availabilities of each variable depending on the word. We used Bonferroni correction for each pairwise comparison. For brevity, we only present the between-group differences that emerged as statistically significant. Appendices A and B present descriptive statistics for the idiographic words and a more thorough presentation of these assessments. There were no significant main effects or interactions of group on the length, frequency, or arousal (where available) of the generated words (all *p's* > 0.08). For concreteness, there was a significant interaction of Group and Word Type with a small effect size [$F(2, 1876) = 5.32$, $p = 0.005$, $\eta_p^2 < 0.006$] such that depressed individuals generated significantly more concrete neutral words than did healthy controls, $p < 0.001$. Finally, there was a significant interaction of Group and Word Type on valence ratings [$F(2, 1715) = 5.06$, $p = 0.006$, $\eta_p^2 < 0.006$] such that the depressed group generated significantly more negatively-rated neutral words than the healthy group ($p = 0.007$) while the control group generated somewhat more negatively rated negative words than the depressed group at a non-significant trend-level ($p = 0.076$). No other significant main effects, interactions, or pairwise comparisons between groups approached significance. Negligible differences emerged in terms of parts of speech, about which Appendix B provides more information.

2.1.2.3 Task.: Following questionnaires and diagnostic procedures, all participants completed the passive viewing task while EEG was recorded. Normative words were consistent across participants while the idiographic words that the participant viewed were specific to those that she provided. Prior to the task, participants read a list of all 30 normative words to reduce the novelty of the stimuli. During recording, idiographic and normative words were presented in separate blocks, as were pleasant, unpleasant, and neutral words (e.g., normative, pleasant words were in a different block than normative, neutral). At the beginning of each block, participants were presented with the following instructions: "The following words will be more [pleasant/unpleasant/neutral] to view," depending on the content of the block. Participants were instructed to "simply view the words." Each word was presented in random order twice per block for a total of 120 trials each (60 idiographic, 60 normative). Each trial began with a fixation point ("+") that was presented for a random duration of 2000–2500ms, followed by one word for 2000ms. At the end of each block, participants received a short break. Blocks were counterbalanced across participants. All stimuli were presented as white text on black background and occupied approximately 6° of the visual field horizontally and 2° of field vertically using Presentation software (Neurobehavioral Systems, Inc., Albany, CA).

2.1.2.4 Apparatus.: EEG was recorded using a custom cap (Cortech Solutions, Wilmington, NC, USA) and the ActiveTwo Biosemi system (BioSemi, Amsterdam, Netherlands). Recordings were taken from 34 scalp electrodes based on the 10/20 system, as well as two electrodes placed on the left and right mastoids. Ocular movement was recorded from electrodes 1 cm above and below the left eye, and near the outer canthi of both eyes.

2.1.2.5 Psychophysiological Recording and Data Reduction.: Offline analysis was performed using Brain Vision Analyzer software (Brain Products, Munich, Germany). EEG was digitized at 24-bit resolution with a sampling rate of 1024 Hz. Each electrode was measured online with respect to a common mode sense electrode forming a monopolar channel. All data were re-referenced offline to averaged mastoid electrodes and band-pass filtered between 0.01 and 30 Hz. EEG was segmented for 500 ms prior to word onset and continued for 2000 ms after to retain flexibility in processing. Each trial was corrected for blinks and eye movements using the method developed by Gratton, Coles, and Donchin (1983). Specific channels in each trial were rejected using a semi-automated procedure with physiological artifacts identified by: a step of more than 50 μV between sample points, a difference of 300 μV within a trial, and a maximum difference of less than 0.5 μV within 100-ms intervals. Remaining artifacts were removed using visual inspection. On average, 19.65 ($SD = 0.86$) trials were retained for each condition across participants, exceeding the suggested minimum of 8 trials for a reliable LPP (Moran, Jendrusina, & Moser, 2013).

Stimulus-locked ERPs were averaged separately for each trial type (e.g., pleasant normative, pleasant idiographic, etc.). Visual inspection indicated the LPP to be maximal at centro-parietal sites across the full sample, consistent with previous research (e.g., Cuthbert et al., 2000; Foti, Hajcak, & Dien, 2009; Weinberg & Hajcak, 2011). Thus, we scored the LPP as the average pooled activity at CP1 and CP2. While the LPP is apparent in the ERP waveform as a sustained positivity, studies have demonstrated that the LPP represents the summed activity of posterior components that overlap in time (Foti et al., 2009; Weinberg & Hajcak, 2011). To add this time course, the LPP was scored as the average activity across three representative time windows: 400–600, 600–800, and 800–1000 ms.

2.1.2.6 Data Analysis.: EEG data from the above windows and electrodes was entered into a 3 (Word Type: pleasant, neutral, unpleasant) × 2 (Personal Relevance: normative, idiographic) × 3 (Time: 400–600, 600–800, 800–1000) × 2 (Group: Depressed vs. Control) mixed-model ANOVA. Greenhouse-Geisser correction was used where appropriate. Where indicated by the omnibus ANOVA, we conducted orthogonal follow-up contrasts of arousal (pleasant/unpleasant vs. neutral) and word type (pleasant vs. unpleasant). We also conducted exploratory analyses to investigate word type, personal relevance, and time effects in the healthy control and depressed groups separately. Significant interactions with group were examined using follow-up within-subjects ANOVA and paired samples *t*-tests, with Bonferroni correction for all follow-up tests.

2.2 Results

2.2.1 Valence Ratings.

Ratings of valence and emotional arousal were available for 25 controls and 31 participants with depression (see Table 2). The results of the mixed-model ANOVA for valence ratings yielded a significant main effect of Personal Relevance [$F(1, 54) = 24.15$, $p < 0.001$, $\eta_p^2 = 0.31$], such that idiographic words were rated as more pleasant than normative words overall. There was also a significant main effect of Word Type [$F(2, 108) = 831.78$, $p < 0.001$, $\eta_p^2 = 0.94$], which may be explained considering both a significant two-way interaction of Personal Relevance and Word Type [$F(2, 108) = 23.03$, $p < 0.001$, $\eta_p^2 = 0.30$], and a significant three-way interaction between Personal Relevance, Word Type, and Group, [$F(2, 108) = 4.39$, $p = 0.015$, $\eta_p^2 = 0.08$]. The results of post-hoc *t*-tests are also presented in Table 2. The depressed group rated normative pleasant stimuli as significantly more unpleasant, and normative unpleasant stimuli as significantly less unpleasant than did the healthy controls; no other valence ratings rose to a level of significance. The two groups did not significantly differ on their ratings of idiographic stimuli.

2.2.2 Arousal Ratings.

—There was a significant main effect of Personal Relevance [$F(1, 54) = 59.15$, $p < 0.001$, $\eta_p^2 = 0.52$], indicating that idiographic words were rated as more arousing than normative words overall. There was also a significant main effect of Word Type [$F(2, 108) = 123.95$, $p < 0.001$, $\eta_p^2 = 0.70$], indicating emotional words were rated as more arousing than neutral words, and a significant interaction between Word Type and Personal Relevance [$F(2, 108) = 5.25$, $p = 0.007$, $\eta_p^2 = 0.09$] such that idiographic emotional words were rated as the most arousing. No interactions with Group were significant (*p's* > 0.08).

2.2.3 LPP.

—ERP waveforms to idiographic and normative words are presented in Figure 1. There was a significant main effect of Time [$F(2, 130) = 8.51$, $p < 0.001$, $\eta_p^2 = 0.12$] wherein the LPP was more positive in the middle time window (600–800ms) compared to the early (400–600ms) and late (800–1000ms) time windows [$F(1, 65) = 47.04$, $p < 0.001$, $\eta_p^2 = 0.42$]. There was also a significant main effect of Word Type [$F(2, 130) = 4.51$, $p = 0.013$, $\eta_p^2 = 0.06$], such that the LPP was larger for pleasant and unpleasant versus neutral words [$F(1, 65) = 10.47$, $p = 0.002$, $\eta_p^2 = 0.14$]; pleasant and unpleasant did not differ from one another ($p = 0.84$). There was a significant main effect of Personal Relevance [$F(1, 65) = 37.19$, $p < 0.001$, $\eta_p^2 = 0.36$], wherein the LPP was increased to idiographic words compared to normative words overall. The main effect of Group was not significant, $p = 0.76$.

None of the higher order interactions with Group were significant, all *p*'s > 0.10. Exploratory analyses were conducted based on inspection of the waveforms and our hypotheses regarding increased reactivity to idiographic stimuli. Considering the pattern of main effects of Time (i.e., maximal from 600–800ms), Word Type (pleasant, unpleasant, neutral), and Personal Relevance (idiographic > normative), we calculated two interaction contrasts: (1) the interaction between group, personal relevance, time (600–800 ms vs. 400–600/800–1000 ms), and arousal (pleasant/unpleasant vs. neutral). This contrast fit the data well [$F(1,65) = 6.97$, $p = 0.010$, $\eta_p^2 = 0.10$]; and (2) the analogous test with a contrast of valence (pleasant vs. unpleasant) rather than arousal did not fit the data, [$F = 0.45$, $p = 0.51$]. Therefore, group differences in LPP modulation by personal relevance were specific to the middle time window (600–800ms) and high-arousal words[iii].

Next, we conducted follow-up Word Type × Personal Relevance repeated-measures ANOVA for both groups within the middle time window. The results showed that healthy participants elicited a larger LPP for idiographic compared to normative words [$F(1, 33) = 11.22$, $p = 0.002$, $\eta_p^2 = 0.25$] and for arousing compared to neutral words [$F(1, 33) = 5.12$, $p = 0.030$,

[iii]Given potential group differences in age, we included age as a covariate in the main analyses. Including age as a covariate did not affect the significance of group effects in the omnibus ANOVA (main effect of Group was not significant [$F(1, 64) = 0.03$, $p = 0.86$, $\eta_p^2 < 0.01$]; main effect of Age was not significant [$F(1, 64) = 0.19$, $p = 0.66$, $\eta_p^2 < 0.01$]; and none of the higher order interactions with Group were significant, all *p*'s > 0.10). The interaction contrast between group, personal relevance, time (600–800 ms vs. 400–600/800–1000ms), and arousal (pleasant/unpleasant vs. neutral) still fit the data well, $F(1, 64) = 6.62$, $p = 0.012$, $\eta_p^2 = 0.09$. Age did not correlate with any LPP variable in the middle time window, all *r*'s <.19, all *p*'s > 0.10.

η_p^2 =.13], though these variables did not interact ($p = 0.86$). Similarly, the depressed group generated a larger LPP to idiographic than to normative words [$F(1, 35) = 8.35$, $p = 0.007$, $\eta_p^2 = 0.19$] and for arousing than to neutral stimuli, [$F(1, 35) = 6.23$, $p = 0.017$, $\eta_p^2 = 0.15$]. Unlike controls, however, there was a significant interaction of arousal and personal relevance, [$F(1, 35) = 4.23$, $p = 0.047$, $\eta_p^2 = 0.11$] (Figure 2). For idiographic words, the depressed group exhibited a larger LPP for pleasant and unpleasant words compared to neutral stimuli [$F(1, 35) = 14.61$, $p < 0.001$, $\eta_p^2 = 0.29$]; pleasant and unpleasant did not differ from one another, $p = 0.83$. For normative words, LPP amplitude did not differ across valence or arousal, all p's > 0.56. Thus, those in the depressed group showed emotional modulation of the LPP for idiographic but not normative words. No other main effect or interaction approached significance.

2.3 Study 1 Discussion

The results from Study 1 indicate a distinct pattern of abnormal emotional reactivity in individuals with depression: participants in the depressed group exhibited relatively normal affective modulation of the LPP for high-arousal, self-relevant words within a mid-latency time window, while no such elevation of the LPP was apparent for normative emotional words. This effect contrasts with participants in the healthy control group, who showed a similar increase in LPP amplitude for positive and negative versus neutral stimuli, regardless of self-relevance. These group differences in the LPP to arousing stimuli occurred despite a lack of significant group differences in arousal ratings for either normative or idiographic words. Thus, emotional modulation does not seem to be broadly dysfunctional in depression, or specific to negative valence; rather, individuals with depression modulated reactions only when stimuli were emotional and personally salient. These effects are consistent with the Emotion Context Insensitivity model (Rottenberg et al., 2005) in that those with depression demonstrated blunted emotional reactivity to pleasant and unpleasant stimuli, which has been demonstrated in previous work (Foti, Olvet, Klein, & Hajcak, 2010). However, this is the first study to provide electrophysiological evidence that emotional blunting in depression may be specific to normative stimuli, as reactivity to personally salient emotional stimuli remained intact. Additionally, this study was the first to identify these effects in the mid-latency time window. This finding was unexpected and requires replication in future studies.

3 Study 2

To further explore processing of personally salient words in depression, we completed a second study investigating the role of self-evaluative linguistic processing in adults with depression. This study was conducted as an independent project with different recruitment and inclusion criteria (discussed further below). The goal of this study, similar to Study 1, was to examine emotional reactivity to normative vs. idiographic stimuli in adults with major depression and healthy controls. In this study, participants completed a task similar to the Self-Referential Encoding Task (SRET; Derry & Kuiper, 1981) in that they were asked to affirm the veracity of sentences that contained a self-referent frame (e.g., "I think of myself as a…") with a sentence-final word that was either positive or negative (e.g., "loser;" "winner"). These self-evaluative statements were contrasted with neutral evaluations of others (e.g., "Picasso was an artist"). This task is distinct from the SRET in two important ways: (a) the sentences included judgements of others while the SRET focuses solely on whether the word is relevant to the participant, and (b) the use of sentences for statements about the self can disambiguate the meaning and intention of a word, which can facilitate processing of self-relevance (Bayer et al., 2010; Kutas & Federmeier, 2011; Wlotko & Federmeier, 2012). We focused on the LPP elicited by explicitly self-referential stimuli (i.e., whether or not they pertain to the respondent). Given the results of Study 1 demonstrating the importance of self-relevant stimuli and prior research demonstrating that those with depression have more selective attentional biases specifically to *negative* self-referential stimuli, we hypothesized that participants with depression would affirm a higher proportion of negative sentences and would have an increased LPP to negative final words than healthy controls. We also hypothesized that healthy controls would have a larger LPP to positive final words than participants with depression.

3.1 Method

3.1.1 Participants.—Similar to Study 1, this study was conducted as part of an ongoing series of studies in the lab using ERPs to examine the interaction of language and emotion in depression (e.g., Atchley et al., 2012). Forty participants (20 depressed and 20 never-depressed, age-matched controls) participated in this study and were eligible after completing all screening procedures. Two control and three depressed participants were removed for insufficient usable trials (< 10) due to artifact or failure to respond (discussed further below). Thus, the final sample included 17 participants with current depression (14 women) and 18 never-depressed controls (12 women and one person who did not report gender). Inclusion criteria for participants in both groups were: between the ages of 20 and 65, completed at least 12th grade, no reported history of neurological disorders or intellectual disability, and, for the depressed group, no current comorbid diagnoses (confirmed via structured interview, discussed further below). The depressed group reported having no prior engagement with psychotherapy. Neither group reported use of psychotropic medications. Control group participants had no prior history of any Axis I disorder. Additionally, included participants reported no history of major head trauma, were right handed, and were native speakers of English according to self-reports. Both groups were matched on age ($M = 32.0$ years (both groups), $SD_{depressed} = 11.5$, $SD_{control} = 11.1$; $p = 0.82$, $d = 0.07$) and both ethnicity and gender (p's > 0.7, $\phi < 0.1$). The Institutional Review Board at the University of Kansas approved all aspects of the study, and participants completed verbal and written consent prior to participation.

3.1.1.1 Recruitment and Diagnostic Procedures.: Patient participants were recruited from a local community mental health facility, and age-matched healthy controls responded to advertisements posted on the University of Kansas campus and surrounding area. Similar to Study 1, psychological evaluations of all participants were made in two steps: first via an initial telephone interview to attain a brief history of symptoms and then a follow-up, more extensive interview using the SCID (First et al., 1997). The SCID and all other diagnostic procedures were completed by trained graduate student clinicians.

3.1.1.2 Symptom Severity.: Severity of Depression was assessed using the Beck Depression Inventory (BDI; (Beck & Steer, 1990).[iv] Each control participant completed the

BDI while three individuals in the depressed group did not. As expected, the depressed group reported higher BDI scores (*M* = 22.87, *SD* = 11.92) than did the healthy control group (*M* = 4.12, *SD* = 3.16; [t (16) = 7.55, $p < 0.001$, d = 2.15]).

3.1.2 Procedure.—The study was conducted across two sessions that occurred at least 24 hours apart. In the first session, the participants completed self-report questionnaires and trained graduate student clinicians administered the SCID. During the second session, participants completed a series of cognitive tasks, including the sentence processing experiment described below, while continuous EEG was recorded. Participants were seated in a comfortable chair in a dimly lit room. They placed their head in a chin-rest 51cm in front of an LCD monitor where stimuli were presented.

3.1.2.1 Stimuli.: Participants were presented 48 sentences that ranged in length from 4–6 words. Half of the sentences (*n* = 24) ended with neutral filler items while the stem either referred to well-known individuals (e.g., "Michael Jordan was a basketball star") or a group (e.g., "Nurses tend to be helpful"). The second half of sentences (*n* = 24) were self-referent wherein they beg an with a sentence-stem in the first person (e.g., "I think of myself as a …"). Twelve final words were negative (e.g. "failure," "stupid") and twelve were positive (e.g. "winner," "fun"). All sentence-final words were 4–10 letters long (*M* = 6.3, *SD* = 1.53). The positive and negative sentence final words were adapted from the ANEW database (Bradley & Lang, 1999) while neutral words were generated in the lab;[v] the valence of all three word types were confirmed via ratings of undergraduate volunteers not otherwise associated with the study. For consistency, as with Study 1, we confirmed ratings of frequency, part of speech, concreteness, and valence and arousal, using norms developed by Brysbaert and colleagues (2009; 2012; 2014; 2013, respectively). A series of one-way ANOVA with Word Type (sentence ending) as the independent variable showed a significant main effect of concreteness [$F(2, 43) = 4.86$, $p = 0.013$ $\omega^2 = 0.14$] and valence [$F(2, 43) = 52.58$, $p < 0.001 \omega^2 = 0.69$], but neither frequency, arousal, nor length (Fs < 1.3, p's > 0.29, $\omega^2 < 0.04$) across sentence endings. Post-hoc tests with Bonferroni correction showed that neutral sentence endings were significantly more concrete (M = 3.53, *SD* = 1.17) than negative endings (M = 2.38, *SD* = 0.74) and positive endings (*M* = 2.51, *SD* = 1.06, p's < 0.05), while positive and negative words did not significantly differ in terms of concreteness (p = 1.0). In terms of valence, positive endings were rated significantly more positively (*M* = 7.48, *SD* = 0.60) than neutral (*M* = 5.86, *SD* = 1.51) and negative endings (*M* = 2.75, *SD* = 0.44), and neutral words were rated significantly more positively than negative words (p's ≤.001). Excluding the sole sentence-final verb, the proportion of nouns and adjectives did

[iv]We also administered the Beck Anxiety Inventory (Beck & Steer, 1990). The depressed group reported significantly greater anxiety (M = 19.95, SD =10.6) than the control group [t (18) = 6.79, $p < 0.001$, d = 2.19]. Five depressed participants experienced severe anxiety (scores > 30), and an additional 6 experienced moderate anxiety (scores > 17). Significance was not altered when these scores were entered as a covariate into the analyses. It is unclear why these scores were as high as they were while participants denied additional anxious symptoms on the SCID. One possibility is that the present sample was somewhat older and severely depressed, both of which can reduce the discriminability of depressive and anxious symptoms as measured by the BAI and BDI (Brenner, 2011).

[v]The following words were used as sentence endings in Study 2, as coded by Warriner, et al. (2013): Neutral: 6999, 2357, 5130, 855, 8787, 11250, 2835, 11940, 12288, 9409, 11069, 2235, 11345, 621, 5272, 8019, 13107, 11039, 4265, 5759, 5142, 1295, 8404; Negative: 6333, 11966, 4437, 13097, 2973, 10101, 7783, 7208, 13270, 12956, 1374, 6087; Positive: 5906, 7266, 10122, 2193, 5881, 4960, 11354, 12024, 1490, 5008, 6982. An additional neutral word, "Missouri," had no available ratings of concreteness or valence, but did have a rating of frequency and was coded as a noun.

not significantly differ as a function of word type [χ^2 (2) = 5.50, $p = 0.064$, $\phi = 0.35$], with a slightly higher proportion of neutral nouns ($n = 17$) than adjectives ($n = 7$).

3.1.2.2 Task.: On each trial, stimuli were presented one word at a time for 350 ms using rapid serial visual presentation (RSVP; i.e. with no interstimulus interval), in order to reduce eye movements (Young, Atchley, & Atchley, 2009). RSVP has been used previously in assessing late components associated with semantic and affective evaluation (e.g., Herbert et al., 2008). Responses were collected after sentence completion while a blank screen was presented for 2000 ms. Participants were asked to rate whether each sentence was true via the number pad of a USB keyboard, wherein 1 was coded as "yes" and 2 was coded as "no." The task began with a practice round of ten trials to orient the participant to the task; the sentences in the practice block were neutral and not used in the main task. Sentences were presented in random order.

3.1.2.3 Apparatus.: All EEG equipment and software were manufactured by Compumedics Neuroscan (Charlotte, NC). The EEG were recorded using 32 Ag-AgCl electrodes mounted in an elastic cap (Quick Cap) according to the international 10–20 system. Impedances were kept below 5 kΩ. Additional electrodes were placed above and below the left eye and at the outer canthi to monitor blinks and saccades, respectively. Signals were amplified with a Synamps amplifier and signals were recorded at 250 Hz. All stimuli were presented using E-Prime 1.1 (Psychology Software Tools, Inc., Pittsburgh, PA) as black text on white background, size 18 Courier New font via an LCD computer screen.

3.1.2.4 Psychophysiological Recording and Data Reduction.: Offline, signals were band pass filtered from 0.01 to 50 Hz and were re-referenced to averaged mastoids. Ocular artifacts were corrected using the proprietary covariance protocol within CURRY software (Semlitsch, Anderer, Schuster, & Presslich, 1986). Any trials containing ±70 μV after correction were removed from analyses, as were trials in which participants did not respond. ERPs were time-locked to the onset of sentence-final words, with a 200ms baseline period and extending for 1000ms. Previous research indicates that the LPP is maximal at around 400–600ms in central posterior electrodes (e.g., Cuthbert et al., 2000; Foti et al., 2009; Weinberg & Hajcak, 2011). Accordingly, inspection of waveforms confirmed that this window encompassed the maximal amplitudes of this component. We used the mean amplitude of the window from 400–650ms at electrode CPz, where the LPP was maximal. Inspection of the data did not indicate the presence of the LPP in any other window or electrode for either group using similar methods to Study 1. We confirmed this by conducting parallel mixed model repeated measures ANOVA (discussed below) in additional time windows of 650–850ms and 850–1050ms, but the main effects and interactions of valence and group at these times did not approach significance. For brevity, we report only the results of the ANOVA of the 400–650ms time window discussed in-text.

3.1.2.5 Data Analysis.: We extracted the percentage of affirmations (i.e., "yes" responses) that participants made as well as response time (RT) for each stimulus category. Percentage of affirmations, RT, and LPP amplitudes were entered into parallel 2 (group: depressed vs.

controls) × 3 (valence: positive, negative, and neutral) mixed-model, repeated measures ANOVA. Planned comparisons were conducted using Bonferroni correction.

3.2. Results

3.2.1 Behavioral data.

3.2.1.1 Affirmed Statements.: There was no main effect of group ($p = 0.40$), but there was a significant main effect of valence [$F(2, 66) = 103.48$, $p < 0.001$, $\eta_p^2 = 0.76$], which can likely be best explained in light of a Group × Valence interaction [$F(2, 66) = 6.98$, $p < 0.001$, $\eta_p^2 = 0.21$]. Planned comparisons revealed that the control group affirmed negative statements ($M = 0.13$, $SE = 0.07$) less than neutral ($M = 0.95$, $SE = 0.01$) and positive statements ($M = 0.93$, $SE = 0.04$; p's < 0.001); affirmations of positive and neutral statements did not significantly differ ($p = 1.0$). The depressed group also affirmed fewer negative statements ($M = 0.32$, $SE = 0.07$) than positive ($M = 0.67$, SE = 0.04) or neutral statements ($M = 0.94$, SE = 0.02; p's < 0.01). The control group affirmed positive statements more frequently than the depressed group ($p < 0.001$), and the depressed group affirmed negative sentences more frequently than the control group, though at a non-significant trend-level ($p = 0.080$; Figure 2).

3.2.1.2 RT.: The results of the ANOVA revealed a significant main effect of Group [$F(1, 33) = 11.57$, $p = 0.003$, $\eta_p^2 = 0.24$] and a significant main effect of Word Type [$F(2, 66) = 13.00$, $p < 0.001$, $\eta_p^2 = 0.28$], which can be best explained within a Group × Word Type interaction [$F(2, 66) = 9.71$, $p < 0.001$, $\eta_p^2 = 0.23$]. The control group did not significantly differ in terms of reaction time for any word type (all p's = 1.0). However, the depressed group responded to neutral endings significantly faster ($M = 674.93$, $SE = 40.33$) than to positive ($M = 843.99$, $SE = 45.98$) and negative statements ($M = 867.19$, $SE = 47.41$; p's < 0.001). The depressed group also responded to positive and negative stimuli in similar response times, $p = 1.0$. When compared directly, the control group was significantly faster at responding to positive ($M = 608.91$, SE = 44.68) and negative endings (M = 618.76, SE = 46.07; both p's = 0.001) than the depressed group. Healthy controls also responded to neutral stimuli (M = 601.46, SE = 39.20) in a similar time to the depressed group, $p = 0.2$. See Figure 2.

3.2.2 LPP.—Results of the ANOVA for the LPP revealed a non-significant, trend-level main effect of group [$F(1, 33) = 3.50$, $p = 0.070$, $\eta_p^2 = 0.10$], a non-significant main effect of word type [$F(1, 33) = 1.20$, $p = 0.28$, $\eta_p^2 = 0.03$], and a significant Group × Word Type interaction [$F(2, 66) = 3.27$, $p = 0.044$, $\eta_p^2 = 0.09$]. Planned comparisons showed that, for individuals with depression, the LPP was larger for negative statements than for both positive and neutral statements, p's < 0.05. Additionally, the LPP to negative stimuli for was larger for individuals with depression than for healthy controls ($p = 0.010$); the LPP to neutral and positive statements did not significantly differ between the two groups (p's > 0.36)[vi]. See Figure 3.

[vi]For consistency with Study 1, we examined the potential impact of age on the results of the analyses, which revealed an identical pattern of statistical significance. Namely, for behavioral affirmations, the main effect of word type remained significant [$F(2, 64) = 7.18$, $p = 0.002$, $\eta_p^2 = 0.18$], while the main effect and Group and Age were not [Fs < 0.98, p's > 0.2, η_p^2s < 0.03]. However, maintained a significant interaction of group and Word Type [$F(2, 64) = 9.25$, $p < 0.001$, $\eta_p^2 = 0.22$]. For response time data, the

3.3 Study 2 Discussion

The results of Study 2 demonstrated that participants with depression were significantly more likely to affirm negative self-referential statements and less likely to affirm positive self-referential statements compared to healthy controls. Additionally, the depressed group was slower to respond to both positive and negative self-statements compared to the healthy controls; reaction time to neutral sentences did not significantly differ between the two groups indicating differences were unlikely due to psychomotor delay or impaired verbal abilities. Moreover, for individuals with depression, the LPP was largest for self-referent sentences with a negative final word while the control group showed no demonstrable effect of sentence type. The negative self-referential statements likely elicited sustained elaborative processing specifically in the participants with depression and not healthy controls. These results are consistent with maladaptive self-focused attention, a hallmark symptom of depression (Bylsma et al., 2008; Bylsma et al., 2011; Koster et al., 2011; Mor & Winquist, 2002; Treynor et al., 2003).

4 General Discussion

The goal of the present pair of studies was to examine emotional reactivity to valenced self-relevant stimuli in major depression. In Study 1, participants with depression exhibited an increased LPP to pleasant and unpleasant idiographic (i.e., self-generated) stimuli compared to idiographic neutral stimuli and all normative stimuli. In contrast, healthy controls exhibited similar patterns of reactivity to valenced compared to neutral words across both idiographic and normative word types. These data provide direct support for a moderating role of self-relevance on stimulus processing in depression. Complementary findings emerged in Study 2: participants with depression were characterized by a reduced tendency to affirm self-relevant sentences that ended with a positive word (e.g., "I think of myself as a winner") and exhibited a larger LPP to the same sentence stems that ended with a negative word (e.g., "I think of myself as a loser."). Healthy controls, however, elicited a comparable LPP for both negative and positive sentence-final words. This finding indicates that, unlike participants with depression, healthy participants processed emotional words equivalently across emotional content in a self-referential context and the emotional salience was similar for statements about the self and others.

The findings of these studies contribute to the literature in several ways. First, emotional reactivity in depression appears to be context-specific rather than globally impaired. The present studies support previous research, which has demonstrated that individuals with depression tend to exhibit attentional bias to stimuli that are both negative *and* self-relevant (Sloan, 2005; Takano & Tanno, 2009), while self-relevance *or* emotional content may often

main effect of Group remained significant [$F(1, 32) = 19.49$, $p = 0.003$, $\eta_p^2 = 0.25$], as did the interaction of Group and Word Type [$F(2, 64) = 9.16$, $p < 0.001$, $\eta_p^2 = 0.22$], and Word Type and Age [$F(2, 64) = 3.25$, $p = 0.045$, $\eta_p^2 = 0.09$], though the main effect of sentence type was no longer significant and the main effect age did not approach significance ($F < 1.0$, p's > 0.5, η_p^2s < 0.019). Finally, For LPP amplitudes, the interaction of Group and Word Type remained significant [$F(2, 64) = 3.39$, $p = 0.040$, $\eta_p^2 = 0.10$], while the main effect of Group approached significance, [$F(1, 32) = 3.44$, $p = 0.073$, $\eta_p^2 = 0.10$]. The main effects of Word Type, Age and the interaction of Age X Word Type were also not significant (Fs < 1.4, p's > 0.2, η_p^2s < 0.03). Age did not significantly correlate with LPP amplitudes in any valence (rs < 0.2; p's > 0.2).

be sufficient for attentional bias in healthy controls (Citron, 2012; Gaddy & Ingram, 2014; Kircanski & Gotlib, 2015). The implications of these findings are discussed further below.

4.1 Implication of Healthy Control Data

For healthy controls, the results of Study 1 are consistent with previous research showing an increased LPP to personally-relevant stimuli (Fields & Kuperberg, 2012; Herbert et al., 2011a; Herbert et al., 2011b; Herbert et al., 2011c), with participants showing a larger LPP to self-referent versus normative stimuli regardless of valence (c.f. Fields & Kuperberg, 2015a). In Study 2, however, the LPP was not modulated by self-reference or valence for healthy control participants, counter to hypotheses. One possible explanation is the differences in task. For example, Delaney-Busch, Wilkie, and Kuperberg (2016) demonstrated that both valence and arousal effects are impacted by task demands, such as semantic versus valence coding instructions. Here, Study 1 presented single words in a passive-viewing paradigm while Study 2 required a response in agreement of the total sentence. By presenting the words in the context of sentences, never-depressed individuals may engage in elaborative processing, even without the quality of self-relevance (Schupp et al., 2006). Additionally, the findings in Study 2 may be driven by the process of judging the veracity of sentences within the task. For healthy controls, this process may reduce the emotional impact of the affective word as their evaluative scope was spread beyond the emotional content of the final word, while participants with depression have a narrower scope that is not modulated by sentence context (Bayer et al., 2010; Harmon-Jones, Gable, & Price, 2012; Martin-Loeches et al., 2012). The judgment of veracity, rather than content, may also explain why the hypothesized self-related positivity bias observed in other work (Fields & Kuperberg, 2015a, 2015b) was not observed here.

4.2 Implications of Depressed Group Data.

In Study 1, participants with depression exhibited blunted effects of valence: in comparison to the healthy control group, normative positive words were rated as less pleasant and normative negative words were rated as less unpleasant. Participants with depression also exhibited blunted emotional modulation of the LPP for normative words, with intact modulation apparent only for negative and positive idiographic words. In Study 2, however, individuals with depression exhibited an increased LPP specifically to negative, and not positive, endings to self-referential sentences. These differences in the LPP to valence specificity may be explained by the context in which the words were processed and the task used (Delaney-Busch et al., 2016; Fields & Kuperberg, 2015a; Hinojosa, Mendez-Bertolo, & Pozo, 2010), as similar inconsistencies have been observed in previous work using different tasks. For example, Auerbach and colleagues (2015) found a larger LPP in individuals with depression than healthy controls when participants were asked to classify a word as relevant to them, whereas Deldin and colleagues (2001; 2005) did not observe between-group differences in two samples that completed a working-memory task that involved paying attention to the orthography of the word than judging its content. For the present studies, Study 1 employed words that were idiographic and presented without context, whereas Study 2 presented words that were explicitly self-referent via sentence context and additionally required a judgment. The difference in tasks may also contribute to why the LPP to negative words was significantly greater for the depressed group than controls for

Study 2. Together, the increased LPP for individuals with depression in both studies were a result of a combination of both valence and self-relevance.

The results of these studies may reflect self-focused cognitive distortions, including rumination, that have been proposed as an endophenotype of depression (Berghorst & Pizzagalli, 2010; Koster et al., 2011; Takano & Tanno, 2009; Treynor et al., 2003). Previous work utilizing the same task as Study 1 found that amygdala activity to self-relevant, emotionally valenced words was more sustained in the depressed group and that this effect correlated with self-reported rumination (Siegle et al., 2007). As indicated here, emotional information must contain an element of personal relevance in order to activate attentional biases in individuals with depression. This specific focus may partially explain the equivocal results of treatments for depression that target cognitive biases to general negative information (Cristea, Kok, & Cuijpers, 2015), while therapies targeting bias to self-relevant negative information (i.e., ruminative processes) have shown greater promise (Watkins, Baeyens, & Read, 2009; Watkins et al., 2011; Watkins et al., 2007). The present data suggest that therapeutic interventions for depression should focus less on reappraisal of all negative stimuli, and more specifically on self-referential stimuli and experiences. Future work should further investigate attentional bias to negative personal relevance within depression, including specific assessment of rumination, in order to better understand and expand the present findings.

It is important to note that the group differences in these studies indicate selective deficits to self-relevant information and not broad impairments of information processing. More specifically, in both studies, there was no main effect between depressed and healthy control participants on overall LPP amplitude. In Study 2, participants with depression were slower to respond to emotional stimuli than healthy individuals; however, they responded comparably to neutral stimuli, indicating that these results are unlikely due to general psychomotor slowing or impaired verbal processing. The differences seen here are thus likely specific to processing negative self-referent stimuli and not general cognitive deficits, consistent with previous research (Bowie, Gupta, & Holshausen, 2013; Foland-Ross & Gotlib, 2012; Gaddy & Ingram, 2014).

4.3 Limitations.

The current findings are qualified by several limitations. First, the samples in these studies were small, limiting interpretability of effect sizes. The findings from the present studies should be considered tentatively and with a focus on the provided effect sizes. Moreover, the sample in Study 1 was entirely composed of women while the sample of Study 2 was approximately 75% women, which further limits the generalizability of these findings. Both labs recruited from departmental and community clinics in rural towns where women are simply more likely to pursue treatment and sign up for studies of this nature (Afifi, 2007; Clement et al., 2015). Nonetheless, gender is known to be an important moderator in the prevalence of depression as well as its cognitive underpinnings (Johnson & Whisman, 2013; Yuan et al., 2009) and results should be considered with this sample composition in mind. The two studies presented in this paper were conducted at different time points and in different laboratories, and thus the two samples also differed in diagnostic inclusion criteria sociodemographic composition. The sample in Study 1 was younger and more ethnically heterogeneous than the sample in Study 2. In Study 1, the depressed sample was somewhat older and ethnically homogenous than the control sample. It will be important to test the generalizability of the current findings to larger and more diverse samples in future work. In study 2, we did not control for years of education of participants beyond ensuring they had completed 12th grade.

Secondly, the results presented here should be qualified by the limitations present in the tasks employed. For Study 1, it is reasonable to assume, as with all affective research, that the normative stimuli may vary in personal relevance across participants. Future studies assessing the differences in emotional reactivity to normative versus idiographic stimuli could require participants to rate the self-relevancy of normative stimuli in order to further disentangle normative and idiographic effects. With regard to the task used in Study 2, future studies should also include a greater variety of sentence stems and completions (e.g., sentences with self- and other-reference with positive/negative/neutral endings and/or compare idiographic endings with normative endings) in order to confirm and expand the effects observed in the present study. The focus of the current manuscript was on self-relevance, for which the LPP has shown particular sensitivity. Therefore, it is important to confirm the present effects with additional tasks, components (e.g., the Early Posterior Negativity, N400), and/or psychophysiological measures that have also shown sensitivity to emotional processing in a variety of populations (Bayer et al., 2010; Kutas & Federmeier, 2011). Additionally, although Study 2 attained response time data, future studies could insert a pause prior to response collection for each statement in order to control for motor response contamination, or counterbalance which finger or hand is used to respond. The use of these other methods and components in future research will help to support and better understand the mechanisms that underlie the attentional biases to personally-relevant emotional information in depression observed in the present studies (e.g., Auerbach et al., 2015; Krompinger & Simons, 2009; Shestyuk et al., 2005).

Finally, though the stimuli in both studies were generally matched across categories and valences, neutral words in both studies tended to be more concrete, which can attenuate the expression of the LPP (Kaltwasser, Ries, Sommer, Knight, & Willems, 2013; Kanske & Kotz, 2007; Lee et al., 2010). In the case of Study 1, the depressed individuals generated significantly neutral words that were significantly more concrete and negatively-rated than did the control group. While the effect sizes in those interactions were negligible (both $\eta_p^2 <$ 0.006, where .0099 is considered the threshold for a "small" effect (Richardson, 2011)), and the pattern of LPP amplitudes did not correspond to the patterns of these ratings, the interaction did rise to a level of significance and, thus, we cannot unequivocally state that the two groups generated analogous corpora. Concreteness and other lexico-semantic variables are important avenues for future research in linguistic and emotional processing in depression.

4.4 General Conclusions.

In sum, the two studies presented in this article highlight the interaction of both emotional valence and self-relevance for emotional reactivity in depression. Namely, we show that those with depression exhibit a bias to stimuli that are both emotional and self-relevant, such that reactivity is intact for negative self-relevant information but not normatively negative or neutral self-relevant information. Concurrently, the data suggest that self-relevance alone may be sufficient to increase attention to stimuli in healthy control participants in some contexts. These results underscore self-focus as a vulnerability factor for depression, particularly for negative information.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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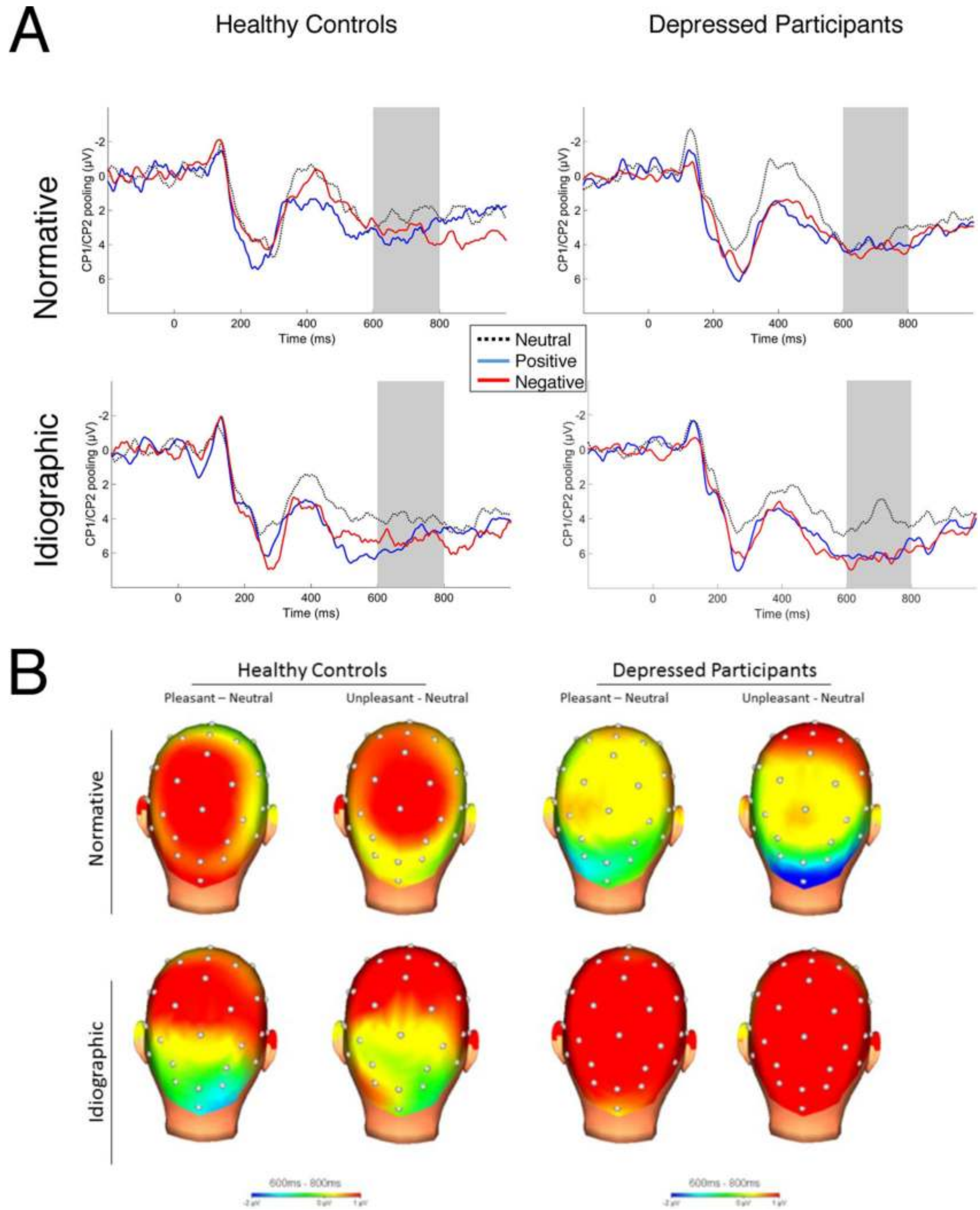

Fig. 1.

A. Grand average waveforms from CP1 and CP2 presenting the results of Study with the analyzed window of the LPP highlighted. Normative words are in the upper row while idiographic words are in the lower row; healthy controls are in the left column while depressed participants are in the right column. Note that negative polarity is up. Dashed gray lines are trials with neutral words, solid blue lines represent trials with pleasant words, while solid lines represent trials with positive words **B.** Topographic maps depicting the subtraction neutral from pleasant (left) and from unpleasant words (right) for healthy controls (two leftmost maps) and depressed individuals (two rightmost maps). Normative words are in the top row while idiographic words are in the lower row.

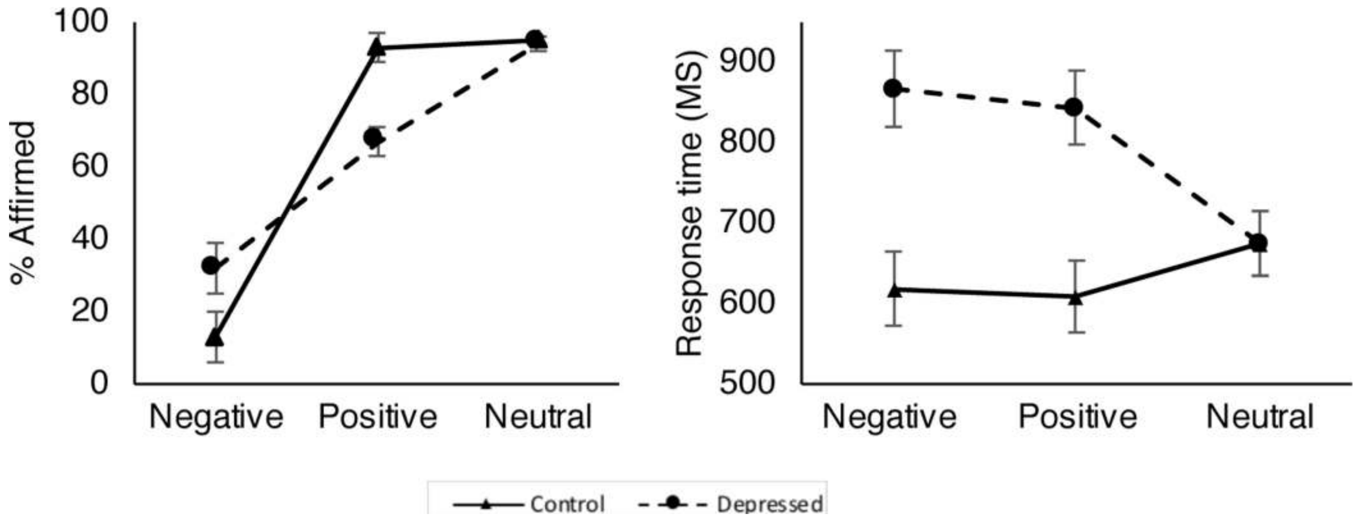

Fig. 2.

Line graphs depicting behavioral response for Study 2 with percent affirmations (**left**) and response time to each sentence type (**right**). Note that depressed individuals (**dashed line**), compared to healthy controls (**solid line**) were slower and more likely to affirm negative statements and reject positive statements; there was no significant difference between the groups' behavior for neutral statements. Error bars represent 1 SEM.

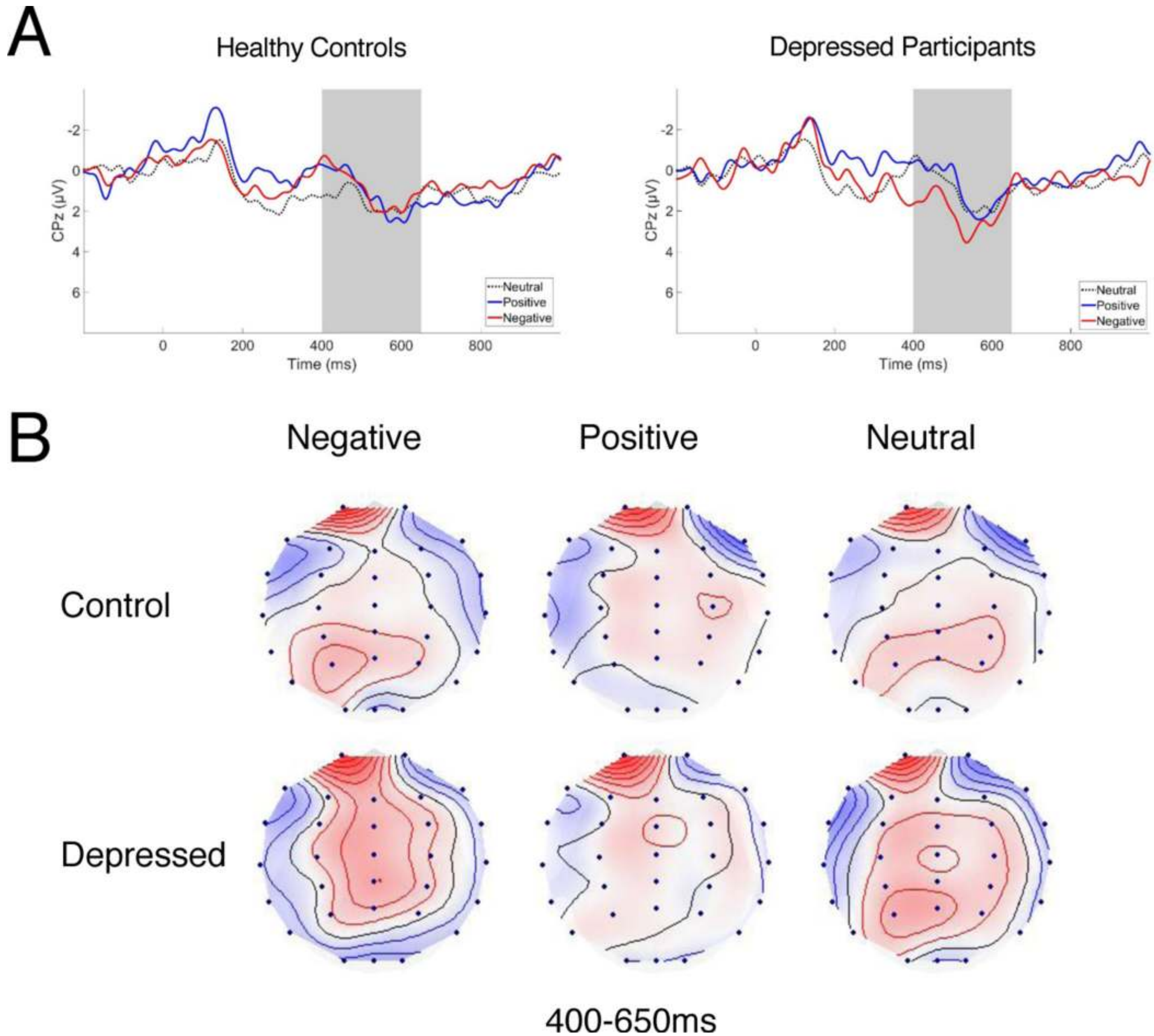

Fig. 3.

A.Grand average waveforms depicting from electrode CPz from Study 2 with the analyzed window of the LPP highlighted. Healthy controls are in the left column while depressed participants are in the right column. Dashed gray lines indicate trials with neutral words, red solid lines represent trials with unpleasant stimuli, while solid blue represent trials with pleasant stimuli. Note that negativity is facing up. **B.** Topographical maps depicting the areas of activation for the analyzed window with red indicating positive polarity and blue represents negative.

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Table 1

Sample symptom characteristics for Study 1 from the Mood and Anxiety Symptom Questionnaire.

	Depression (*n*=36)		**Controls (*n*=34)**		**Group Comparison**
Symptoms	***M***	***SD***	***M***	***SD***	**Cohen's *d***
Anhedonic Depression	65.00	12.55	39.23	11.57	2.14***
General Distress: Depression	38.45	11.59	18.19	3.92	2.61***
Anxious Arousal	30.45	10.92	20.69	4.08	1.30***
General Distress: Anxiety	25.33	8.57	16.15	4.10	1.45***

*** p<.001

Table 2

Results of Valence and Arousal rating tasks for both groups from Study 1

	Depression(n=31)		Controls(n=25)		Group Comparison
Word Type	***M***	***SE***	***M***	***SE***	***t* (*p*)**
Normative					
Pleasant	3.24	.22	2.58	.17	−2.27 (.027) *
Neutral	4.79	.06	4.91	.08	1.16 (n.s.)
Unpleasant	7.35	.18	7.86	.15	2.11 (.040) *
Idiographic					
Pleasant	1.83	.11	1.78	.14	−0.30 (n.s.)
Neutral	4.63	.15	4.54	.17	−0.40 (n.s.)
Unpleasant	7.67	.14	7.76	.21	0.38 (n.s.)
Arousal	*M*	*SE*	*M*	*SE*	*t*
Normative					
Pleasant	4.19	.31	5.38	.35	2.56 (.013) *
Neutral	1.69	.18	2.05	.21	1.31 (n.s.)
Unpleasant	5.19	.33	4.93	.47	−0.47 (n.s.)
Idiographic					
Pleasant	5.93	.32	6.72	.35	1.65 (n.s.)
Neutral	2.46	.25	2.51	.29	0.12 (n.s.)
Unpleasant	5.99	.35	6.05	.38	0.12 (n.s.)

Note: Greater values correspond to increases in unpleasantness and arousal; only significant p-values are shown, all others are > 0.10); all degrees of freedom = 54.

* $p < 0.05$