A Transdiagnostic Investigation of Amygdala-vmPFC Resting State Functional Connectivity and Emotional Distress in Daily Lives

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by

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The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled,

A Transdiagnostic Investigation of Amygdala-vmPFC Resting State Functional Connectivity and Emotional Distress in Daily Lives

Presented by Anne M. Merrill, a candidate for the degree of doctor of philosophy, and hereby certify that, in their opinion, it is worthy of acceptance.

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Professor John Kerns

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Professor Tim Trull

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Professor Bruce Bartholow

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Professor Donna Strickland

Dedication

Dedicated to my late mother, Mary Jo Drilling.

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Table of Contents

List of Tables and Figures

Abstract

Mood disorders, anxiety disorders and borderline personality disorder overlap in symptom criteria, are highly comorbid with one another, and group together in factor models of psychopathology (Kotov et al., 2011). These disorders of emotional distress are characterized by increased frequency and duration of intense negative affect, large abrupt shifts in affect (i.e., affective instability), and behavioral dysregulation (Selby, Anestis, Bender, & Joiner, 2009). Functional connectivity between the amygdala and the ventromedial prefrontal cortex (vmPFC) has been proposed as a possible endophenotype for emotion dysregulation. However, the relationship between amygdala-vmPFC connectivity and transdiagnostic symptoms of emotional distress is largely unknown. The present study used two powerful methodologies, fMRI and Ecological Momentary Assessment, to examine the relationship between amygdala-vmPFC resting state functional connectivity (rs-FC) and dysregulated moods and behaviors in daily lives. Twenty-seven women in treatment for a disorder of emotional distress completed clinical interviews, self-report questionnaires on symptoms and emotion regulation, resting state scans, and two weeks of frequent surveys assessing moods and behaviors. Results found that amygdala-vmPFC rs-FC was (a) correlated with frequency of behavioral dysregulation, including drinking alcohol to cope with distress, binge eating, and impulsivity, and (b) differentially correlated with anxiety and depression, replicating the results of previous research (Burghy et al., 2012). Results also found that another emotion circuit, the dACC-amygdala, was associated with negative affect and affective instability. The current research found evidence for neural mechanisms related to emotional and

behavioral dysregulation in daily lives of women with transdiagnostic disorders of emotional distress.

1. A Transdiagnostic Investigation of Amygdala-vmPFC Resting State Functional Connectivity and Emotional Distress in Daily Lives

Twenty-five percent of Americans meet diagnostic criteria for a mood or anxiety disorder annually (Kessler, Chiu, Demler, & Walters, 2005). These disorders include, among others, major depressive disorder (MDD), generalized anxiety disorder (GAD), Posttraumatic Stress Disorder (PTSD), and social anxiety disorder (SAD). While these disorders are diagnostically distinct in the DSM-5 (American Psychiatric Association, 2013), they have much in common and are all considered to be disorders of emotional distress (Watson, 2005). Disorders of mood and anxiety group together in factor models (Caspi et al., 2014; Krueger, 1999; Krueger & Markon, 2006), overlap in symptom criteria, and are highly comorbid (Kessler et al., 2005). Nearly 60% of individuals diagnosed with MDD will also meet criteria for an anxiety disorder in that same year (Kessler et al., 2003). Borderline personality disorder (BPD) is also closely related to this cluster of mood and anxiety disorders. At its core, BPD is largely thought to be a disorder of emotional distress and dysregulation (Linehan, 1993). When personality disorders are included in factor models of psychopathology, BPD loads on the factor of internalizing disorders, which is comprised of MDD and many of the anxiety disorders (Kotov et al., 2011). BPD is also highly comorbid with depressive and anxiety disorders, with 83% of individuals diagnosed with BPD also meeting criteria for a mood disorder and 85% also meeting criteria for an anxiety disorder (Tomko, Trull, Wood, & Sher, 2014). Thus, there is high comorbidity and overlap between mood disorders, anxiety disorders, and BPD as disorders of emotional distress (Watson, 2005).

Until recently, most research on emotional distress has focused on each distinct disorder, rather than studied the similar features of these disorders with a transdiagnostic approach. However, given the shared symptomatology of emotional distress disorders, there are likely to be shared mechanisms of emotional distress across these disorders. Emotional distress disorders are characterized by frequent and prolonged periods of intense negative affect, large shifts in affect from between hours and days (i.e., affective instability), and behavioral dysregulation, such as alcohol and drug use, binge eating, self-harm, and excessive interpersonal reassurance seeking (Selby, Anestis, Bender, & Joiner, 2009). In order to study the mechanisms underlying these behaviors, it has been recommended that research emphasize symptoms of emotional distress rather than diagnostic categories (Kotov et al., 2011; Sanislow et al., 2010).

Furthermore, research on emotional distress has typically used retrospective self-reports and laboratory methods, which have limited validity in assessing emotional distress symptoms due to memory biases in retrospective reports and the dynamic nature of affective instability. Ecological Momentary Assessment (EMA) allows for the real time assessment of multiple indices of emotion to better capture the nature of the emotional distress patterns (Trull & Ebner-Priemer, 2013; Trull & Ebner-Priemer, 2014). Considering both of these limitations of the existing literature, the present study includes participants across multiple diagnostic groups and uses EMA to assess symptoms of emotional distress in daily lives.

One important commonality among disorders of emotional distress is poor emotion regulation (Aldao, Nolen-Hoeksema, & Schweizer, 2010; Kring & Sloan, 2010; Taylor & Liberzon, 2007), which is viewed as a leading contributor to negative moods

and dysregulated behaviors (Aldao et al., 2010; Mennin, Holoway, Fresco, Moore, & Heimberg, 2007). Furthermore, many of the transdiagnostic symptoms seemingly indicate failures of emotion regulation. For example, individuals with emotional distress disorders have frequent intense negative affect with a delayed recovery time back to baseline (Watson, 2005; Aldao et al., 2010), as well as frequent shifts to negative mood states (i.e., affective instability; Trull et al., 2008). Negative mood states, affective instability, and poor emotion regulation characterize disorders of emotional distress (e.g., Carpenter & Trull, 2013). Furthermore, there is high variability, even within specific diagnostic groups, in the severity and frequency of these dysregulation symptoms. Therefore, to better understand and treat emotional distress disorders, we need to better understand the neural mechanisms underlying deficits in emotion regulation.

One proposed endophenotype for emotional distress is an altered relationship between the amygdala and the ventromedial prefrontal cortex (vmPFC; Etkin, Egner, Kalisch, 2011; Kim et al., 2011b; Milad & Quirk, 2012). The amygdala, a small almond-shaped structure located in the medial temporal lobe as part of the limbic system (Figure 1), has long been implicated to play a critical role in emotion (e.g., Adolphs, 2010; Armony, 2013; Morrison & Salzman, 2010). The amygdala is highly interconnected to the rest of the brain; the amygdala receives input from the sensory systems and sends output to many other structures and systems, including the prefrontal cortex and the hypothalamus (Tillman et al., 2018). There is evidence from human and animal studies that the amygdala is associated with processing both negative and positive valence stimuli (e.g., Cunningham & Kirkland, 2014; Janak & Tye, 2015), however the amygdala also appears to play an important role in emotional distress (Armony, 2013). For

example, amygdala damage leads to deficits in the experience of fear (Tranel, Gullickson, Koch, & Adolphs, 2006). Imaging studies show that the amygdala plays a crucial role in fear conditioning and fear extinction (Milad & Quirk, 2012). More recent research shows increased amygdala activation associated with the occurrence of negative affect (Bijsterbosch, Smith, Forester, John, & Bishop, 2014; Bishop, 2007; Gaffrey, Barch, & Luby, 2016). Not surprisingly, increased amygdala activity has been seen in individuals with disorders of emotional distress, including MDD (Hamilton et al., 2012; Zilverstand, Parvaz, & Goldstein, 2017), anxiety disorders (Heitmann et al., 2017; Kim et al., 2011b; Nitschke et al., 2009; Qin et al., 2014), and BPD (Schulze et al., 2011, Zilverstand et al., 2017). Therefore enhanced amygdala activity is likely to contribute to the increased emotional distress present in these disorders.

The amygdala is also directly connected to other emotion regions, including the ventromedial prefrontal cortex (vmPFC). The vmPFC and the dorsomedial PFC (dmPFC) are subdivisions of the medial PFC (Etkin et al., 2011; Figure 1). The vmPFC includes the ventral part of the pregenual cingulate, the subgenual cingulate, and the ventromedial portion of the frontal pole. The vmPFC is involved in higher order processes such as decision-making and emotion processing (Hebscher & Gilboa, 2016; Roy, Shohamy, & Wager, 2012). In emotion processing, several emotion researchers have posited that the vmPFC works with the amygdala in a circuit, with the vmPFC as a top-down regulator of amygdala activity (Motzkin, Philippi, Wolf, Baskaya, & Koenigs, 2015; Milad & Quirk, 2012; Roy et al., 2012). For instance, in this theorized circuit, the amygdala can be activated quickly in response to a potential threat and vmPFC activation follows to allow for a slower process of cognitive re-evaluation of the threat. Subsequently, the vmPFC

influences the amygdala output and related behavior (Kim et al., 2011b). In this way, the vmPFC is thought to be an integral component of fear conditioning and extinction and in emotional regulation more broadly.

There is evidence for this role of the vmPFC as an emotion regulator from both animal models and human imaging studies. In animal models, the rat infralimbic PFC is thought to be the homologue to the human vmPFC (Milad & Quirk, 2012; Peters, Kalivas, & Quirk, 2009). The infralimbic PFC is critical for the retrieval of fear extinction memories (Quirk & Mueller, 2008). Activation of the infralimbic PFC is associated with decreased conditioned fear response and decreased fear expression (Milad & Quirk, 2012). As the infralimbic PFC is thought to be the homologue to the human vmPFC, these results suggest that the vmPFC may also play a role in decreasing fear response and expression (Quirk & Beer, 2006). Human imaging studies provide support for this hypothesis. For example, functional activation of the vmPFC increases during fear extinction training and fear extinction recall, with greater activation during recall associated with more successful fear extinction (Schiller & Delgado, 2010). Moreover, the vmPFC is negatively correlated with skin conductance response (SCR), indicating that an objective rating of emotional response decreases as vmPFC activity increases (Schiller & Delgado, 2010). Findings from both the animal models of the infralimbic PFC and human imaging studies of the vmPFC demonstrate the regulatory role of the vmPFC in fear and emotional arousal.

In addition to this evidence that the amygdala and vmPFC are both independently implicated in fear learning and emotional functions, there is some research indicating that amygdala-vmPFC connectivity is critical for emotion. Animal lesion studies show

anatomical connections between the amygdala and the vmPFC, notably with afferent fibers to the amygdala originating in the mPFC, indicating a physical pathway for the vmPFC to regulate the amygdala (Ghashghaei & Barbas, 2002; Kim et al., 2011b). The amygdala and vmPFC are also functionally coupled during fear extinction tasks (Delgado, Nearing, Ledoux, & Phelps, 2008) and show a consistent pattern of inverse activation during fear learning and emotion tasks (Giustino & Maren, 2015; Kim et al., 2011b). Beyond anatomical and functional data, methods directly assessing the connectivity between the amygdala and the vmPFC provide even stronger evidence for this circuit. Diffusion tensor imaging, which assesses white matter integrity, and resting state data both show strong connectivity between the amygdala and the vmPFC (Etkin et al.,, 2011; Roy et al., 2009; Kim et al., 2011b). Therefore, imaging data from various methods point to the relationship between the amygdala and vmPFC as critical for fear extinction and emotional processing.

Moving beyond fear learning models, there is also evidence for the specific role of the amygdala and vmPFC in emotion regulation and symptoms of emotional distress. There is an intuitive translation of the fear learning research to emotion regulation. Fear extinction and emotion regulation both involve reappraisal of a potentially threating stimuli and are thought to have overlapping underlying neural mechanisms (Kim et al., 2011b). In fact, imaging studies on emotion regulation have found similar findings to those from the fear learning literature. Effective emotion regulation as measured through skin conductance response (SCR), leads to increased activation in the vmPFC and decreased activation in the amygdala (Schiller & Delgado, 2010). When participants are instructed to use emotion regulation strategies during functional task scans, they show

decreased amygdala activation and, in some studies, increased activity in the vmPFC (Johnstone, van Reekum, Urry, Kalin, & Davidson, 2007; Kim et al., 2011b; Klumpp, Bhaumik, Kinney, & Fitzgerald, 2018). In particular, Johnstone et al. (2007) reported that in people without depression that there was an inverse association between amygdala and vmPFC activity during emotion regulation. In contrast, they reported in people with major depression this association was positive. However, in contrast to these studies finding that vmPFC might be involved in explicit emotion regulation, meta-analytic reviews of emotional reappraisal have failed to find vmPFC activation for reappraisal (Buhle et al., 2014; Morawetz, Bode, Derntl, & Heekeren, 2017b). Based in part on this evidence, it has been suggested that amygdala-vmPFC connectivity might be critically involved in implicit (e.g., fear extinction) but not explicit (e.g., reappraisal) emotion regulation (Etkin, Buchel, & Gross, 2015). Possibly consistent with this, there is meta-analytic evidence that placebo expectancies of decreased pain result in increased activation of the vmPFC (Wager & Atlas, 2015). Thus while there is evidence that the vmPFC activity is associated with some types of emotion regulation, the nature of this relationship is not well understood.

As the above research tends to utilize task-based fMRI, there are other approaches to exploring the relationship between the vmPFC and the amygdala that more directly assess these regions as a circuit. Resting state connectivity or DTI measures allow for more information regarding the actual connection between the vmPFC and the amygdala. It is thought that studying the structural and functional connectivity between the vmPFC and the amygdala will provide more information regarding the circuit's role in emotional reactions and regulation than the activity of either region alone. When amygdala-vmPFC

connectivity is assessed with functional coupling methods, there is evidence that the strength of the inverse coupling between the amygdala and the vmPFC is increased during emotion regulation (Delgado et al., 2008; Kim et al., 2011b), indicating that emotion regulation is tied not only to activation in both areas, but the connection between them.

Amygdala-vmPFC connectivity has also been directly linked to symptoms of emotional distress, suggesting the possibility that a neural deficit in the top-down regulation of amygdala activity by the vmPFC may be a neuroendophenotype for emotional distress disorders (Diekhof, Geier, Falkai, & Gruber, 2011; Etkin et al., 2011; Giustino & Marren, 2015; Heitmann et al., 2017; Kim et al., 2011b; Milad & Quirk, 2012; Schiller & Delgado, 2010). As stated previously, resting state functional connectivity (rs-FC), compared to functional task data, is particularly well suited to answer questions into the specific nature of the relationship between the amygdala and vmPFC and has been recommended as a method by recent reviews (e.g., Kim et al., 2011b). rs-FC uses correlated time-series data between regions of the brain to show which regions are functionally connected (Thomason, Hamilton, & Gotlib, 2011). Importantly, rs-FC assesses spontaneous brain activity independent of tasks demands and has been found to be consistent with white matter connections between regions (e.g., Damoiseaux & Greicius, 2009).

Recently, a small number of resting state imaging studies have shown rs-FC between the amygdala and the vmPFC specifically related to symptoms of emotional distress. Importantly, however, the direction of the association has varied by study and by type of affect. In studies examining subclinical anxiety in psychiatrically healthy

participants, a less positive amygdala-vmPFC relationship has been correlated with higher levels of anxiety (Coombs, Loggia, Greve, & Holt, 2014; Kim, Gee, Loucks, Davis, & Whalen, 2011a). Similarly, Burghy et al. (2012) also found that, after partialling variance shared with depression, anxiety symptoms were associated with a more negative amygdala-vmPFC rs-FC. In contrast, Burghy et al. found that after partialling variance shared with anxiety, depression symptoms were associated with a more positive amygdala-vmPFC rs-FC. Hence, there is some evidence that anxiety and depression might be differentially associated with amygdala-vmPFC rs-FC. Further, it is possible that this differential association between anxiety and depression and amygdala-vmPFC rs-FC might result in non-significant associations between overall negative affect with amygdala-vmPFC rs-FC. In addition to potential differences between depression and anxiety, age of participants and study paradigms have also been suggested to contribute to the variability in the nature of the relationship between amygdala-vmPFC rs-FC and emotional regulation or distress (Gold et al., 2016). Another relevant factor might be that it has been suggested that the vmPFC might only be critical for implicit (e.g., fear extinction) but not explicit (e.g., reappraisal) emotion regulation (Etkin et al., 2015). Hence, it is not clear how this might affect the relationship between amygdala-vmPFC connectivity and emotional distress symptoms. Additionally, work using task-based functional connectivity has shown that the relationship between the amygdala and PFC changes directions with age, with a positive amygdala-vmPFC relationship seen in children and a negative amygdala-vmPFC relationship seen in healthy adolescents and adults (Gee et al., 2013). Finally, the resting state functional connectivity evidence of these emotion circuits is limited to studies using specific diagnostic groups rather than

considering the amygdala-vmPFC connectivity as a mechanism underlying transdiagnostic symptoms of emotional distress. Therefore, there is evidence that a neural deficit in the top-down regulation of amygdala activation by the vmPFC may be a neuroendophenotype for emotional distress, although the exact nature of this relationship is yet unknown.

In addition to the vmPFC, another region of the prefrontal cortex, the dorsal anterior cingulate cortex (dACC), is also thought to play an important role in emotional processing (e.g., Etkin et al., 2011). More specifically, the dACC has been suggested both to amplify negative emotion expression and also potentially to regulate the amygdala in a similar circuit to the vmPFC-amygdala. For example, patients with generalized anxiety disorder show decreased dACC-amygdala connectivity during attempts at emotion regulation (Etkin, Prater, Hoeft, Menon, & Schatzberg, 2010). Therefore, it has been posited that the vmPFC and the dACC might play complementary roles in emotion, with the vmPFC decreasing negative affect and the dACC increasing negative affect. However, the literature on the role of the dACC in emotion regulation is also somewhat complex. Although there is human evidence (and animal evidence from possibly homologous regions) for dACC being related to amplifying negative affect (e.g., dACC activation in instructed fear paradigms), there is also consistent evidence that some parts of the dACC are active during cognitive reappraisal (Buhle et al., 2014; Morawetz, Bode, Baudewig, & Heekeren, 2017a). Further, in a recent review, Zilverstand et al. (2017) reported that people with anxiety disorders have been frequently found to exhibit decreased dACC activity when attempting to use reappraisal to down-regulate negative affect. Hence, there is conflicting evidence that activating the dACC might amplify

negative affect or alternatively that it might be helpful for decreasing negative affect. Based on models of emotion regulation that posit a critical role for the anterior dACC in amplifying negative affect (Etkin et al., 2011), in the current research, in addition to examining amygdala-vmPFC connectivity, I also examined whether amygdala-dACC connectivity would be related to emotional distress symptoms.

To our knowledge, there are no previous studies examining reduced amygdala-vmPFC rs-FC and emotion regulation in a transdiagnostic group of emotional distress disorders. Moreover, although previous research suggests that the amygdala-vmPFC circuit plays a critical role in emotion regulation in some disorders of emotional distress, the relationship between this neural deficit and the symptoms people experience in their daily lives is largely unknown. Therefore, the current study will examine the relationship between amygdala-vmPFC rs-FC and emotional distress using ecological momentary assessment (EMA) to assess patterns of symptoms in people's typical lives. Critically, we are hypothesizing that amygdala-vmPFC rs-FC will be directly related to symptoms of emotional distress, such as negative affect, affective instability, and dysregulated behaviors across disorders in participants' daily lives. Although the primary hypotheses in this study are related to amygdala-vmPFC rs-FC, we will also examine rs-FC between the dACC and amygdala as a secondary circuit possibly relevant to disorders of emotional distress.

Although I am expecting that both emotional distress and behavioral dysregulation will be related to amygdala-vmPFC connectivity, there are also reasons to expect that emotional distress and behavioral dysregulation might be differentially associated with amygdala-vmPFC connectivity. Again, it has been suggested that

amygdala-vmPFC connectivity might only be critical for implicit emotion regulation. Hence, if emotional distress is largely related to impaired explicit emotion regulation (e.g., cognitive reappraisal), then emotional distress may not be associated with amygdala-vmPFC connectivity. Alternatively, in addition to research and theory suggesting that the vmPFC is important for emotion regulation, there is another well-established line of research and theory suggesting that the vmPFC is important for decision-making (Hiser & Koenigs, 2018). There is meta-analytic evidence that vmPFC activation is related to subjective value (Bartra, McGuire, & Kable, 2013), with processing subjective value thought to then be critical in guiding decision-making (Levy & Glimcher, 2012). Consistent with this, there is evidence that people with vmPFC damage exhibit impaired decision-making (e.g., Pujara, Wolf, Baskaya, & Koenigs, 2015). Hence, it is possible that amygdala-vmPFC connectivity might be related to increased behavioral dysregulation symptoms because altered connectivity directly affects decision-making rather than amygdala-vmPFC connectivity affecting emotional distress and then distally also affecting behavioral dysregulation.

Ecological momentary assessment (EMA) allows for the real time assessment of people's daily experiences in their real world environments and has many benefits over traditional laboratory measures and retrospective self-report (Trull & Ebner-Priemer, 2014). The valid assessment of clinical symptoms, such as negative affect, requires the measurement of subjective experience, physiological changes, and behavior (Lang, 1993; Levenson et al., 2008). EMA allows for these three types of variables to be assessed simultaneously. Moreover, with measures of subjective experiences, EMA improves upon traditional retrospective self-reports by decreasing or eliminating biases in memory.

In EMA, participants typically use electronic dairies or mobile phones to report on their subjective experiences while they occur. In retrospective reports, there are heuristic biases known to influence ratings of emotional events, such as the peak-end rule, which suggests that our memory is biased toward both peak emotion and emotion that occurs at the end of the mood episode (Fredrickson & Kahneman, 1993). There is also robust evidence that current mood state influences recall of emotion with a positive mood enhancing recall of positive emotions and a negative mood enhancing recall of negative emotions (Kihlstrom, Eich, Sandbrand, & Tobias, 2000). Methodologically, this is particularly concerning when studying individuals with disorders of emotion dysregulation as their frequent negative mood states could substantially bias their self-reports (for review of mood congruent memory in depression, see Blaney 1986; Dalgleish & Watts, 1990). Therefore, retrospective self-reports are a critically flawed method for examining mood symptoms in the lives of individuals with emotional dysregulation. In EMA, self-reports can be collected in real time, or close to real time, eliminating the influence of the heuristic biases of self-report. Empirically, momentary reports have in fact shown to be more accurate than retrospective self-reports of events, behaviors, and experiences (e.g., Solhan, Trull, Jahng, & Wood, 2009).

As stated previously, in addition to subjective experience, emotion should also be assessed through behavior and physiology. EMA diary methods can be supplemented with physiological measures, such as wearable physiological recording devices to corroborate self-report of clinical symptoms. Negative affect and affective instability are both a subjective experience within the individual and a physiological experience associated with increased physiological arousal. For example, negative emotional arousal

leads to increased heart rate, decreased heart rate variability, and increased respiration rate (Kreibig, 2010). Other physiological changes associated with negative emotion are electrodermal changes in the skin and increased skin conductance responses. However, these physiological changes may only be loosely coupled with subjective experiences and many studies have shown disagreement between physiological measures and self-report symptoms (Rachman & Hodgson, 1974). Therefore, combining participant report of emotion with physiological assessment is critical in improving the validity of studying emotions. With EMA, we can simultaneously collect mood ratings and physiological ratings while individuals are in their daily environment (e.g., Ebner-Priemer & Trull, 2009). Thus EMA methods can validly assesses clinical symptoms through improving upon self-reports of subjective experience and easily allowing physiology and behavior to be measured simultaneously.

An additional strength of EMA is that variables can be assessed repeatedly throughout the study period. The repeated assessments result in a time series that allows for the investigation of within-person processes. In addition to increased negative affect, emotional distress disorders are characterized by increased affective instability. Therefore, assessing one time point does not capture the changes that occur throughout the day. In the present study, self-reported mood and behavior was assessed at least six times a day. The repeated assessments will be used to study patterns of affective instability.

It is clear that EMA has many strengths as a research method and is particularly well-suited to study symptoms and behaviors associated with emotional distress. Therefore, this study aims to investigate the relationship between neural functioning and

symptoms of emotional distress in the daily lives of individuals with disorders of emotional distress. Emotional distress in daily life will be assessed with real-time mood ratings, supported by behavioral indicators of dysregulation.

Specifically, the primary goal of the study is to examine the relationship between amygdala-vmPFC resting state functional connectivity (rs-FC) and emotional distress symptoms in people's daily lives. Based on the previous literature, I predict that amygdala-vmPFC rs-FC, as indicated by an inverse relationship between the amygdala and the vmPFC, will be correlated with indices of emotion dysregulation collected during the 14 days of EMA data collection. Emotion dysregulation will be operationalized as increased negative mood ratings on self-reports, increased variability between mood ratings across surveys and more frequent behavioral dysregulation. For the momentary self-reports, I specifically predict that increased amygdala-vmPFC rs-FC will be associated with increased intensity and frequency of reported negative emotions and negative affect instability. However, recall that there is evidence that anxiety and depression might be differentially associated with amygdala-vmPFC rs-FC (Burghy et al., 2012) and that this could limit zero-order associations with overall negative affect. Hence, I will also follow the analyses of Burghy et al. and examine whether anxiety and depression would be differentially associated with amygdala-vmPFC rs-FC after removing shared variance. Behaviorally, I predict that amygdala-vmPFC rs-FC will be inversely correlated with using alcohol and other drugs to cope with emotion, binge eating, self-harm, reassurance seeking, self-reported impulsive acts, and endorsement of ruminative thoughts. Thus individuals with a more negative amygdala-vmPFC rs-FC will be experiencing relatively less negative affect and less affective instability than those

with a more positive amygdala-vmPFC rs-FC, and this will be evidenced through momentary self-report, physiological indices of mood, and behavioral dysregulation.

As secondary analyses, I will also explore the relationships between negative affect, affective instability, dysregulated behaviors, and emotion regulation strategies from retrospective self-reports to variables collected from EMA surveys. For example, rumination is frequently assessed in the literature using the ruminative responses scales (RRS; Treynor, Gonzalez, & Nolen-Hoeksema, 2003). However, to my knowledge, the RRS has not previously been validated with momentary reports of rumination. Considering the limitations of self-report, it is important to determine if rumination as captured on the RRS is related to frequency of rumination in everyday life. Therefore, this study will allow us to examine the utility of both laboratory-based self-reports and real time survey reports in capture indices of emotional distress.

2. Methods

Participants

Twenty-nine right-handed women in treatment for a disorder of emotional distress participated in this study (three additional participants completed the study procedures but were left-handed and were excluded from all analyses). Participants were recruited through advertisements in a weekly news bulletin distributed by the University of Missouri (i.e., MU info) and fliers posted in an outpatient community clinic. Participants met the general eligibility criteria if they: 1) were between the ages of 18 and 45, 2) were not pregnant or planning to become pregnant in the next month, 3) did not have a history of head trauma that had resulted in sustained impairment in mood, attention, or concentration, and 4) did not have a medical diagnosis of cystic fibrosis or diabetes, as these impact sympathetic nervous system activity, and 5) were not contraindicated for magnetic resonance imaging. Given the high heterogeneity of the sample across multiple diagnostic groups, the sample was limited to women. Demographic information for the sample is presented in Table 1. Additionally, all eligible participants met Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) criteria for a current mood disorder (Major Depressive Disorder current or recurrent with current symptoms, Bipolar I, or Bipolar II), a current anxiety disorder (Generalized Anxiety Disorder, Post-Traumatic Stress Disorder, or Social Anxiety Disorder), or Borderline Personality Disorder. Diagnostic eligibility was determined through diagnostic interviews completed by trained graduate research assistants (most conducted by Anne Merrill), comprised of the Mini-International Neuropsychiatric Interview (M.I.N.I. 7.0) and the Structured Interview for DSM-IV

Personality (SIDP-IV; Pfohl, Blum, & Zimmerman, 1997). As expected, comorbidity among the disorders was high and diagnostic groups are presented in Tables 2 and 3. Twenty-seven of the participants were taking psychiatric medication (Table 1.) This study was approved by the Institutional Review Board of the University of Missouri.

Measures

Self-report assessments. At initial assessment, participants completed a number of self-report questionnaires assessing psychopathology and emotion regulation. To assess current symptoms of mood and anxiety, participants completed the Depression, Anxiety, and Stress Scale (DASS-21; Lovibond & Lovibond, 1995a). The DASS-21 measures severity of core symptoms of depression, anxiety, and stress, and has been shown to be a reliable and valid measure of these three dimensions (Lovibond & Lovibond, 1995b). The depression and anxiety subscales of the DASS-21 correlate highly with the Beck Depression Inventory (Beck, Steer, & Brown, 1996) and Beck Anxiety Inventory, respectively (Beck & Steer, 1990; Lovibond & Lovibond, 1995b).

Participants also completed multiple questionnaires assessing various aspects of emotion regulation. For overall emotion regulation, participants completed the Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004). For specific emotion regulation strategies, participants completed the Ruminative Responses Scale which measures rumination (RRS; Treynor et al., 2003), the Emotion Regulation Questionnaire (ERQ) which measures suppression and reappraisal (Gross & John, 2003), the Acceptance and action Questionnaire (AAQ-II) which measures experiential avoidance (Bond et al., 2011), and the Five Facet Mindfulness Questionnaire which measures mindfulness (FFMQ; Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006).

There were also three measures of behavioral dysregulation. The first assessed frequency and quantity of alcohol use. Participants reported number of drinking occasions in the past year, typical number of drinks per drinking occasion, and number of binge drinking occasions (defined as more than 5 or more drinks) in the past year. Second, participants were asked to report frequency of drug use over the past year. The items assessed both specific drugs (e.g., marijuana, cocaine) as well as categories of drugs (e.g., opiates, amphetamines). Finally, participants completed the UPPS Impulsive Behavioral Scale (UPPS-P; Whiteside & Lynam, 2001). The UPPS-P measures impulsivity across dimensions of the Five Factor Model of personality.

Magnetic resonance imaging data collection and preprocessing. Imaging took place at the Brain Imaging Center on the University of Missouri campus. Scanning was performed using a Siemens Trio 3T scanner using an 8-channel head coil. Following previous research (Alexander & Brown, 2010; Deichmann, Gottfried, Hutton, & Turner, 2003), image slices were tilted 30 degrees toward the coronal plane from the Anterior Commissure-Posterior Commissure (AC-PC) line in order to minimize image distortions and signal losses by susceptibility gradients. Resting state functional scanning used a T2*-weighted gradient-echo echo-planar pulse sequence. The resting state parameters were TR 2000 ms, TE 30 ms, flip angle 90°, slice thickness 4.0 mm and the task parameters were 2000 ms, TE 25 ms, flip angle 70 deg, FOV 24 cm, 3.8 mm thickness, interleaved acquisition. Structural scanning used a high resolution T1-weighted sagittal scan (MPRAGE sequence), with 1 mm in-plane resolution and slice thickness.

Resting state data was preprocessed using SPM8 (Wellcome Trust Centre for Neuorimaging; http://www.fil.ion.ucl.ac.uk/spm/software/spm8/). Structural and

functional images were reoriented to align with the anterior commissure-posterior commissure (AC-PC) line. The images were corrected for slice acquisition timing with slice order interleaved from bottom to top. The realigned images were then coregistered with the participant's T1 image in order to better normalize each participant's data to the MNI template. Each participant's T1 image was then segmented into cerebrospinal fluid (CSF), white matter, and grey matter. Using the segmentation file that was produced, each participant's functional data were normalized to standard MNI template space. In the final step, a 6-mm spatial smoothing filter was applied to the images to help account for between-subject spatial differences.

Ambulatory assessment.

Smart phone data collection. Participants carried a smartphone (Motorola Droid MAXX, Android 4.4.4) for 14 days. The smartphone had a software app specifically designed for this study through a collaboration with computer scientist Dr. Yi Shang. Participants were instructed by Anne Merrill to use this app to complete surveys about their moods, behaviors, and experiences throughout the day, with Anne Merrill monitoring their completion of ambulatory assessment.

The protocol for survey initiation included a scheduled morning report, six random prompts throughout the day, and participant initiated prompts. This method is a combination of event-based reporting and scheduled sampling. Importantly, this method allows us to capture mood distress episodes as identified by the participant while also getting the benefits of random sampling. The scheduled morning report prompt was the first prompt of the day. The participant set the time for the morning report when they went to bed the prior evening based on when they expected to be awake the next day

(with the restriction that the morning report must be completed before noon). For the random prompts, the software stratified each day into 6 equal intervals and then randomly scheduled a prompt at time point within each interval. The beginning of the day was marked by the morning report (or noon if the participant failed to complete a morning report) and ended at 11:00pm. When a prompt was triggered, the phone alerted the participant through 6 seconds of vibrating and then an alarm that increased in volume. If the participant did not respond within 24 seconds, the alarm silenced and emitted reminder alarms at 5 and 10 minutes following the prompt time. If the survey was not initiated at any of the alarms, the survey was considered missed. For the participant initiated prompts, participants were instructed to initiate a survey when they experienced a marked change in their mood. Differences among the 3 types of surveys are shown in Appendix A.

Measures and variable creation.

Momentary affect assessment. For each survey, participants rated their experience of emotions over the last 15 minutes using 31 mood descriptors from the Positive and Negative Affect Schedule-Extended version (PANAS-X; Watson & Clark, 1999; Listed in Appendix A). Participants considered each mood descriptor and then rated the extent to which she felt this way from 1 to 5 (1 = very slightly or not at all, 5 = extremely). Variable creation for mood items followed previous research (Trull et al., 2008). To quantify affect, a general negative affect indicator was created by averaging the 21 negative affect trait descriptors together and a general positive affect indicator was created by averaging the 10 positive affect trait descriptors together. To quantify negative affective instability, we computed squared successive differences by subtracting the

negative affect score from one prompt earlier from the negative affect score of a given prompt and squaring this value (Trull et al., 2008). The PANAS-X was also scored in terms of the subscales of negative affect sadness, hostility, and fear, and affective instability was computed for each subscale.

Momentary behavioral dysregulation assessment. For behavioral dysregulation, participants were asked whether or not they had engaged in the following behaviors since the previous prompt: drinking alcohol to cope (i.e., "I drank alcohol because it would make me feel less distressed."), using drugs to cope, binge eating, non-suicidal self-injury, excessive reassurance seeking, and 4 items about general impulsive actions (e.g., "I did something without thinking;" Appendix A). Each measure of behavioral dysregulation is scored as a frequency and is corrected for number of surveys completed by each individual participant. Following the conceptualization and model testing of behavioral dysregulation used by Selby et al. (2009), a total behavioral dysregulation composite variable was also created from alcohol use, binge eating, self-harm, and excessive reassurance seeking.

Momentary rumination assessment. For rumination, participants were asked to rate agreement on a 1-5 scale of how much they agreed with two rumination statements: "How much are you focusing on your feelings right now?" and "How much are you focusing on your problems right now?"

Setting and life events. The last questions in the survey asked about current environment and possible life events that could influence affect. Participants indicated whom they had been with over the past 15 minutes and their current location (e.g., work, home). Participants also indicate if they have experienced life events that could

contribute to significant changes in affect such as receiving good or bad news or receiving praise or criticism.

Physiological data collection. During the 14 days of smart phone data collection, participants also wore two devices to monitor physiological responses. Both devices were worn while the participants were awake. The first was a Hexoskin smart shirt, which measured cardiac activity, respiration, and accelerometry. The second device was a sensor worn on the inner side of the left wrist (Q sensor Affectiva). The Q Sensor is designed to measure skin conductance, temperature, and 3-axis movement (Poh, Swenson, & Picard, 2010). The physiological data is beyond the scope of this dissertation and will be presented as part of future papers.

Procedure

Participants responded to study advertisements by phone or email. Interested participants were given more detailed information about the study and screened over the phone for study eligibility. The phone screening included questions assessing current treatment and diagnoses, current symptoms of emotional distress, and eligibility to undergo MRI scanning. Participants who were likely to meet full diagnostic criteria for a disorder of emotional distress as indicated by endorsing both current treatment for a disorder of emotional distress and current symptoms of emotional distress (e.g., frequent depression, frequent changing moods) were invited to the lab for session one.

Session one took approximately two hours. After providing written informed consent, participants completed the diagnostic interview to determine final eligibility for the remainder of the study (e.g., meeting DSM-5 criteria for a mood disorder, anxiety disorder, or BPD). If participants were eligible following the diagnostic interview, they

completed the self-report questionnaires on a computer. Due to the variability of time required to complete the interview, 8 participants completed the self-report questionnaires at session three rather than session 1. At the end of session one, participants were scheduled as soon as possible for the MRI session (i.e., session two), considering the limitations of both participants' schedules and scanner availability at the imaging center.

Session two took place at the Brain Imaging Center and took approximately 2 ½ hours. For the first 30 minutes, participants signed paperwork related to scanning procedures, prepped for the scan (removing all metal clothing and other items), and were oriented to general scanning procedures, as well as the two tasks to be completed in the scanner (which will not be part of this dissertation). Participants then spent approximately 1 hour and 45 minutes in the scanner completing the scans and tasks in the following order: structural scanning, task 1 functional scanning, task 2 functional scanning, resting state functional scanning, and diffusion tensor imaging. Participants were allowed to take breaks as necessary during the scan (for example, one person took 2 breaks to use the restroom). One participant did not complete the full scanning procedure by opting to not complete a second functional task to shorten the scan length due to physical discomfort (specifically a tight fit in the scanner). All participants completed the resting state scan.

After scanning was completed, participants were trained on the EMA portion of the study and assigned a study phone, Hexoskin shirt and device, and q sensor. Participants started the 14 days of EMA data collection on the same day as the scan unless they requested otherwise (2 participants requested a later start date). During the two weeks of data collection, participants' compliance was monitored daily and they

were contacted within 24 hours if they appeared to have substantial missing data. Participants were also instructed to contact the lab if they had any questions or concerns regarding the equipment or the surveys.

Participants came into the lab for session three after one week of data collection. Data from all devices was downloaded and checked to ensure participants were properly using all devices. Participants were paid based on their compliance with the phone surveys. If a participant's compliance was poor, there was a discussion of ways they could improve compliance for the second week. After 14 days of data collection, participants returned to the lab for session four. Participants were paid for the final week of the study (based on week two compliance), and returned all study equipment. Retention from session one to session four was 100%. Study timeline is illustrated in Table 5 below.

Data Processing and Analyses

Resting state functional connectivity

Resting state data was processed and analyzed using SPM8 (Welcome Trust Center for Neuroimaging, University College London, UK, http://www.fil.ion.ucl.ac.uk) and MATLAB (The Mathworks Inc., 2010). The primary variable computed from the resting state data is a temporal correlation between the vmPFC and the amygdala. We also examined the temporal correlation between the ACC and the amygdala. Our functional analyses followed the methods of Burghy et al. (2012) and Kim et al. (2011a). We used anatomical regions of interest (ROIs) for the right and left amygdala, the vmPFC, and the ACC (Table 6 and Figure 2). The amygdala ROIs came from the MarsBar toolbox of SPM (Tzourio-Mazoyer et al., 2002), specifically designed for ROI

analyses. All analyses were performed separately for the right and left amygdala, as is consistent with previous research (Roy et al., 2009; Kim et al., 2011a). The ROI for the vmPFC was defined based on a region found to be active in a meta-analytic review of previous emotion regulation research (Diekhof et al., 2011; Table 6). The ROI for the dACC was defined as a rectangle with a midpoint of x = 1, y = 38, z = 32 and dimensions of 18 x 12 x 14. The coordinates for the ROI were chosen to include activation peaks consistently found in previous research on fear and reappraisal, as reviewed by Kalisch and Gerlicher (2014). The ROI was defined as a rectangle (rather than a sphere) to best capture the shape of these previously established activation peaks. For the primary measure of functional connectivity between the amygdala and the vmPFC, we extracted the averaged signal time course from both the left and right amygdala and correlated them with time course data from the vmPFC ROI. In this model, time series data for global signal, white matter, CSF and six motion parameters for head movement were entered into the model as covariates of no interest. Therefore, we will have a score representing the strength of amygdala-vmPFC connection for each participant. This score will be used in additional analyses to test the hypotheses related to amygdala-vmPFC rs-FC and dysregulated moods and behaviors. Resting state functional connectivity between the amygdala and the ACC was calculated using the same method.

In addition to the correlation between the ROIs, I also ran a seed-based analysis to examine the relationship between the amygdala and each voxel of the rest of the brain. For this analysis, mean time series data extracted from the right and left amygdala ROIs were used as predictors to identify voxels that were correlated with amygdala activity. The same variables of no interest (global signal, white matter, CSF, and motion

parameters) were included as covariates in this model. The seed-based analysis generated maps showing which voxels in the brain had a significant relationship to activity from the amygdala. These maps were then analyzed at the group level, which resulted in a functional connectivity map showing all activation positively or negative associated with amygdala activity. These functional connectivity maps will also be used to examine how behavioral variables relate to connectivity between the amygdala and other areas of the brain.

E**MA data and correlations with amygdala-vmPFC rs-FC**

EMA data was analyzed at the person level. The key variables of interest are negative affect, affective instability, rumination, and behavioral dysregulation. Person level aggregates of these variables were obtained by averaging all momentary scores per day and then averaging all days per person.

3. Results

Affect and Behavior

Descriptive results.

Participants completed an average of 14.7 days in the EMA portion of the study with the fewest days being 11 and the most being 16. Most participants showed good compliance throughout the study, answering more than 75% of the random prompts. Two participants had compliance for random prompts below 60% and were excluded from all further analyses utilizing momentary data. After exclusion, average compliance for random prompts was 87.5%. This compliance rate is comparable with that reported in previous research (e.g., Hepp, Carpenter, Lane, & Trull, 2016). Within the 27 participants retained after exclusion based on random prompts, compliance for morning reports was very good with an average compliance of 97%.

Correlation between morning reports and random prompts. Affect at morning reports was highly correlated with affect at random prompts. Positive affect was correlated r_s = .73, negative affect was correlated r_s = .83, sadness was correlated r_s = .89, fear was correlated r_s = .83, and hostility was correlated r_s = .79. To examine relationships between momentary reports of emotion and functional connectivity, affect variables included both morning reports and random prompts (similar results were observed when morning reports and random prompts were examined independently).

Correlations within and between momentary assessment measures. Overall, and as expected, the subscales of negative affect were correlated with each other and not with positive affect. Affect and affective instability were also strongly correlated (r_s = .68), with increased negative affect related to increased affective instability (Table 7).

Hence, based on this it might be expected that mean negative affect and affective instability would be similarly associated with neural connectivity measures.

For momentary assessment of behavioral dysregulation, based on previous research (Selby et al., 2009), total behavioral dysregulation was represented with a composite score made up of alcohol use for coping, binge eating, and reassurance seeking and self-harm. This behavioral dysregulation composite score was also significantly correlated with impulsivity and drug use for coping. Overall, there were positive correlations between the momentary behavioral dysregulation measures. One exception is reassurance seeking, which was not significantly correlated with alcohol use, binge eating, self-harm or drug use (Table 8; as will be noted below, reassurance seeking was instead more strongly associated with negative affect).

As momentary affect and momentary behavioral dysregulation are broad indices of overall emotional distress, we expected that negative affect and affective instability would be correlated with dysregulated behaviors. Overall, there was a trend for positive correlations between negative affect, affective instability and behavioral dysregulation, however many of these correlations were not statistically significant (Table 9). Negative affect was significantly correlated with the composite behavioral dysregulation measure. It was also strongly associated with impulsivity; hence people reporting that they had recently done something impulsive was strongly associated with both behavioral dysregulation and emotional distress. Similarly, negative affective instability was significantly correlated with composite behavioral dysregulation, impulsivity. Finally, although reassurance seeking was somewhat weakly correlated with most other

behavioral dysregulation items, it was associated with mean negative affect and negative affect instability.

Correlations between momentary assessments and laboratory questionnaires.

A secondary goal of the study was to examine the validity of retrospective self-report measures and momentary assessments of emotional distress. Overall, we found the expected consistencies between symptoms and dysregulation reported on questionnaires completed at session 1 and momentary assessment of affect and behavioral dysregulation. Full results are presented in the Tables 10 and 11.

However, as one notable exception, the assessment of rumination at session 1 (RRS) was not significantly correlated with the assessment of rumination during the EMA surveys. Although the correlation is in the expected positive direction, it is notably weak compared to many of the other correlations seen across measures of analogous constructs. For example, impulsive behaviors as assessed on the DERS had a strong positive correlation with momentary assessment of impulsive actions ($r_s = 0.52$, $p < .01$). Furthermore, in contrast to momentary assessed rumination, the RRS questionnaire was significantly correlated with negative affect and negative affective instability, as would be expected of a measure of rumination. Hence, it is possible that the momentary assessment of rumination might not have effectively assessed negative rumination (I will return to this in the discussion)

Amygdala-vmPFC Resting State Functional Connectivity

Moving on to the resting state analyses, first, I examined the mean level of resting state correlation between the amygdala and the vmPFC in the current sample. Again, it is

relevant to note here that previous research has reported that amygdala-vmPFC connectivity tends to be positive early in life and then becomes more negative over time (Gee et al., 2013; Jalbrzikowski et al., 2017). In the current study, overall, the amygdala-vmPFC resting state correlation was not significantly different from 0 for either the right (M = 0.05, SD = 0.23) or the left (M = 0.02, SD = 0.25) amygdala (t = 1.07, p = .29; t = 0.38, p = .71, respectively). Hence, in this sample there was not an overall significant correlation between these two regions.

Next, I examined the primary hypothesis that amygdala-vmPFC rs-FC would be correlated with momentary assessment of affective and behavioral dysregulation. For overall mean negative affect (NA), as can be seen in Table 12, there was not a significant association between amygdala-vmPFC rs-FC and mean NA. Further, amygdala-vmPFC rs-FC was not significantly correlated with mean level of any specific negative emotion, although if anything the association tended to be largest with sadness. Further, there was not a significant association between amygdala-vmPFC rs-FC and mean positive affect (PA). Hence, there was no clear evidence that amygdala-vmPFC rs-FC was related to mean level of NA or PA in this study.

Next, I examined whether there were associations between rs-FC and affective instability. Overall, as can be seen in Table 12, there were no associations with instability of global NA or of PA. However, in examining specific negative emotions, there was a significant association between right amygdala-vmPFC rs-FC and instability of sadness. Hence, people with a more positive correlation between the right amygdala and the vmPFC exhibited more variability in their moment-to-moment experience of sadness. Note that this bears some similarity to the results of Burghy et al. (2012) who reported

that increased depression (but not anxiety) was associated with increased amygdala-vmPFC rs-FC. However on the whole amygdala-vmPFC connectivity did not tend to be strongly associated with total emotional distress.

Next, I followed the analyses of Burghy et al. (2012) and examined whether sadness and fear would be differentially associated with amygdala-vmPFC rs-FC after removing shared variance. As can be seen in Table 13, results were generally very consistent with Burghy et al. Sadness tended to be positively associated with amygdala-vmPFC rs-FC, with this being especially true for sadness instability (as was reported for the zero-order associations in Table 12). In contrast, both mean and instability of fear were significantly negatively associated with amygdala-vmPFC rs-FC. Hence, generally replicating the non-clinical results of Burghy et al. (2012), but here in a sample with emotional distress disorders, I also found that sadness and fear were differentially associated with amygdala-vmPFC rs-FC. One explanation for a lack of significant zero-order associations between amygdala-vmPFC rs-FC with overall negative affect (i.e., in Table 12) is that aspects of negative affect are differentially associated with amygdala-vmPFC rs-FC.

Next, I examined whether amygdala-vmPFC rs-FC was associated with behavioral dysregulation. As can be seen in Table 14, the composite measure of behavioral dysregulation (comprised of alcohol use, binge eating, reassurance seeking, and self-harm) was significantly associated with right amygdala-vmPFC rs-FC. Hence, people with a more positive correlation between right amygdala and vmPFC activity over time were more likely to engage in dysregulated behaviors. Therefore, being less likely to engage in dysregulated behaviors was associated with having a more inverse association

between amygdala and vmPFC rs-FC. In addition, there was also a trend for the composite measure of behavioral dysregulation to also be associated with left amygdala-vmPFC rs-FC (p = .105). I next examined associations with specific behavioral dysregulation items and amygdala-vmPFC rs-FC. In general, there is a trend for amygdala-vmPFC rs-FC to be associated with more frequently reported behavioral dysregulation items, such as binge eating and alcohol use. In particular, alcohol use was associated with amygdala-vmPFC rs-FC for both the right amygdala (at trend level) and the left amygdala. Similarly, binge eating was also associated with amygdala-vmPFC rs-FC for both the right and left amygdala. Finally, there was also a trend for right amygdala-vmPFC rs-FC to be associated with increased reports of impulsive behaviors. Hence, there was evidence that amygdala-vmPFC rs-FC was associated with behavioral dysregulation, especially for alcohol use and for binge eating. In contrast, there amygdala-vmPFC connectivity was not significantly associated with reassurance seeking. However, recall that reassurance seeking itself was not significantly associated with most other behavioral dysregulation items. Finally, amygdala-vmPFC connectivity was also not significantly associated with self-harm. However, very few people reported self-harm in the current study (n = 5). There was also no significant relationship between rs-FC and momentary reports of rumination (all ps > .50).

As stated previously, motion parameters were included as a covariate in data processing to ensure that potential differences in movement by participants did not contribute to findings in the data. However, as previous research has noted that this approach may not be sufficient (Power, Barnes, Snyder, Schlaggar, & Petersen, 2012), we also examined for possible correlations between motion and key variables of interest.

Motion was not correlated with behavioral dysregulation, neither the composite variable, alcohol use, binge eating, nor with affective instability in sadness (all *ps* > .50). Therefore, it is unlikely that potential differences in participant head movement is accounting for any of the significant correlations presented above.

Amygdala-ACC rs-FC

Thus far, I have reported that, as predicted, that amygdala-vmPFC rs-FC would be related to indices of emotional and behavioral dysregulation. Next, I examined whether rs-FC between the amygdala and another region, the anterior dorsal ACC, would also exhibit a similar relationship to emotional and behavioral dysregulation. As can be seen in Table 15, associations between amygdala-ACC rs-FC and emotional and behavioral dysregulation appeared to be quite different than they were for amygdala-vmPFC rs-FC. First, again note that associations for amygdala-vmPFC rs-FC with dysregulation variables tended to be positive (i.e., increased rs-FC associated with increased dysregulation). In contrast, the associations for amygdala-ACC rs-FC with dysregulation variables tended to be negative (i.e., decreased rs-FC associated with increased dysregulation). This appears to be, if anything, contrary to the hypothesis that increased rs-FC association between amygdala and dorsal ACC might be related to an amplification of negative affect. In addition, note that amygdala-vmPFC rs-FC tended to be, if anything, more associated with behavioral dysregulation variables than with mean negative affect or affective instability. In contrast, amygdala-ACC rs-FC was not significantly (or even at trend level) associated with the behavioral dysregulation composite variable, or with alcohol use or with binge eating. However, right amygdala-ACC rs-FC was associated at trend level with reassurance seeking and also associated

with reports of acting impulsively; again recall that both reassurance seeking and acting impulsively were moderately to strongly correlated with mean negative affect and affective instability. Consistent with this, right amygdala-ACC rs-FC was significantly negatively associated with negative affective instability, with decreased rs-FC associated with increased affective instability. In sum, results for amygdala-ACC rs-FC appear to be largely different than for amygdala-vmPFC rs-FC.

vmPFC-ACC rs-FC

Finally, considering that there were significant relationships between amygdala-vmPFC and amygdala-ACC functional connectivity and momentary assessments, we examined vmPFC-ACC rs-FC. There was a significant correlation between vmPFC-ACC rs-FC and alcohol use. However, overall, there were no other significant correlations between vmPFC-ACC rs-FC and any of the momentary measures of affect, affective instability, and behavioral dysregulation (Table 16).

Amygdala Seed to Whole Brain rs-FC

In addition to the rs-FC measure used above, seed-based analyses was also used to further explore the potential relationship between both the amygdala and the vmPFC and other regions of the brain. As can be seen in Tables 17 and 18, when the amygdala ROI was used as a seed, it was significantly correlated with activity in numerous brain regions, primarily in regions adjacent to the amygdala. The right and left amygdala are also closely linked, with both the right and left seed leading to bilateral amygdala activation. The right amygdala was also negatively associated with activation in the occipital lobe and the precuneus. The left amygdala was negatively associated with activation in the angular gyrus. Although previous research in healthy controls has found

more widespread significant functional connectivity for the amygdala (Roy et al., 2009), the regions that are significantly connected to the amygdala in the present study are consistent with those presented in previous research (Roy et al., 2009). As is consistent with ROI analyses reported earlier, neither the left or the right amygdala seeds were significantly correlated with activation in the vmPFC.

Amygdala connectivity predicting affect and behaviors. Next, I examined in whole-brain analyses the relationship between amygdala connectivity and momentary affective, affective instability, and dysregulated behaviors. There were no associations between emotional and behavioral indices and amygdala functional connectivity that passed significance threshold when corrected for family-wise error ($p < .05$, FWE corrected).

vmPFC Seed to Whole Brain rs-FC

I next examined connectivity of the vmPFC with other brain regions. Similar to the amygdala seed-based analyses, the vmPFC ROI was used as a seed to identify clusters in the brain with activation associated with the vmPFC. Full results are presented in Table 19. As expected, the vmPFC showed a strong positive association with some nearby regions of the limbic system, including the anterior cingulate and middle cingulate gyrus. However, as is consistent with the amygdala seed-based connectivity results, the vmPFC was not significantly related to activation in the amygdala. There were not significant findings for negative functional connectivity between the vmPFC and any regions.

vmPFC connectivity predicting affect and behaviors. Next, using the same method as the amygdala seed, I examined in whole-brain analyses the relationship between vmPFC connectivity and momentary affective, affective instability, and dysregulated behaviors.

There were no associations between emotional and behavioral indices and vmPFC functional connectivity that passed significance threshold when corrected for family-wise error ($p < .05$, FWE corrected).

4. Discussion

The current study found evidence that amygdala-vmPFC resting state functional connectivity is related to emotional and behavioral dysregulation in women with disorders of emotional distress. For emotional dysregulation, in zero-order analyses, functional connectivity was significantly correlated with instability of sadness. However, after removing shared variance, sadness and fear tend to be differentially related to amygdala-vmPFC rs-FC with sadness related to increased rs-FC, and fear related to decreased rs-FC, replicating previous research (Burghy et al., 2012). For behavioral dysregulation, amygdala-vmPFC rs-FC was positively correlated with reports of overall behavioral dysregulation, drinking alcohol to cope with distress, binge eating, and impulsive actions in participants' daily lives. The direction of this correlation indicates that individuals with stronger positive functional connectivity between the amygdala and vmPFC are more likely to engage in behavioral dysregulation. Accordingly, inverse amygdala-vmPFC rs-FC is associated with less frequent dysregulated behaviors, which fits with previous research indicating that a strong inverse relationship between the vmPFC and the amygdala is linked to effective emotion regulation (e.g. Heitmann et al., 2017; Schiller & Delgado, 2010). Overall, these behavioral results are consistent with the overall theorized role of the vmPFC as a regulator of the emotional responses originating in the amygdala. As this finding comes from a sample of participants diagnosed with anxiety disorders, mood disorders and borderline personality disorder, the present study suggests that amygdala-vmPFC rs-FC is a potential transdiagnostic mechanism related to dysregulated behaviors.

Alternatively, a quite different pattern of results was observed for the dACC. The present study found that amygdala-dACC rs-FC was negatively correlated with negative affect and affective instability. The direction of this correlation indicates that less positive functional connectivity was associated with more negative emotions and more affective instability. However, amygdala-dACC rs-FC was not significantly associated with behavioral dysregulation. Thus I see divergent patterns of results for the vmPFC and dACC, with the vmPFC-amygdala rs-FC positively associated with behavioral dysregulation and the ACC-amygdala rs-FC negatively associated with emotional dysregulation.

The present study supports the critical role of the vmPFC in behavior in disorders of emotional distress. In individuals with disorders of emotional distress, a stronger inverse relationship between the amygdala and vmPFC at rest is related to decreased likelihood of engaging in dysregulated behaviors, such as drinking to cope with distress, binge eating, reassurance seeking, and self-harm. One theory linking the vmPFC to behavioral dysregulation posits that dysregulated behavior is a consequence of negative emotions, likely due to poor emotion regulation. In this "emotional cascade model" (Selby et al., 2009), individuals experience negative affect and an inability to effectively regulate that affect may then lead to engaging in potentially harmful or risky behaviors. However, the present study does not provide support for this role of emotions as mediating the relationship between the vmPFC and behavior. In fact, the present study found minimal correlations between momentary affect and momentary dysregulated behavior, suggesting that dysregulated behaviors can occur in the absence of significant subjective emotional distress. Thus, rather than supporting the role of the vmPFC in

emotion regulation, the present study is more consistent with theories directly linking the vmPFC to behavioral outcomes, possibly through the role of the vmPFC in decision-making.

In addition to the theories suggesting that the vmPFC is important in emotion regulation, the vmPFC is also well-established as a critical region for reward-processing and decision making (Hiser & Koenigs, 2018). An important component of decision-making is valuation, a process of computing subjective value for alternative options based on values and goals. Valuation is linked to activation in the vmPFC (Levy & Glimcher, 2012). For example, the vmPFC is activated when individuals are deciding between different food items based on competing goals of health versus taste (Hare, Camerer, & Rangie, 2009). A meta-analysis supports the role of the vmPFC in subjective value (Bartra, McGuire, & Kable, 2013) and there is evidence that vmPFC damage is associated with impaired decision-making (e.g., Pujara et al., 2015). Alterations in decision-making are linked to increased risky behavior such as gambling and risky alcohol use (e.g., Harvanko, Schreiber, & Grant, 2013; Lawrence et al., 2009). In the present study, I found that individuals who had weaker inverse functional connectivity between the amygdala and vmPFC were more likely to decide to engage in dysregulated behaviors, specifically drinking alcohol to cope with negative emotions and binge eating. In deciding whether or not to drink alcohol to cope with negative emotions, an individual weighs and determines value of expected outcomes. Individuals who use alcohol to cope with negative emotions may have decision-making errors in inappropriately valuing short-term emotional changes over long-term emotional regulation, which may be similar to the concept of delay discounting seen in risky alcohol use (e.g., McCarthy, Niculete,

Treloar, Morris & Bartholow, 2012). Moreover, there is also evidence for deficits in valuation and decision-making in disorders that are characterized by increased behavioral dysregulation, such as mood and addiction disorders (Helie, Shamloo, Novak, & Foti, 2017). Overall, this line of research provides good support for the role of the vmPFC in decision-making that may be highly relevant to decisions to engage in behavioral dysregulation in individuals with disorders of emotional distress.

Further consistent with the theorized role of the vmPFC in decision-making and behavior, the vmPFC has been shown to be integral to active coping. For example, the vmPFC has been found to mediate the relationship between negative affect experienced from a goal setback and persistence to achieve that goal (Bhanji & Delgado, 2014). Thus when negative affect is experienced, the vmPFC is critical in influencing the subsequent behavioral outcomes. Theoretically, this is consistent with the present study, which is comprised of a sample of participants who are diagnosed with disorders of emotional distress, requiring some baseline level of negative affect. In fact, every participant in the present study endorsed at least one past episode of depression, indicating that this sample is prone to negative emotion. Thus the vmPFC may not be critical for the experience of negative emotion but rather the behavioral coping with that emotion. That is, individuals with a stronger inverse amygdala-vmPFC rs-FC may be more able to recruit the vmPFC for active coping and thus engage in more effective coping behaviors and less dysregulated behavior. Overall the present study is consistent with the theorized role of the vmPFC in behavior through decision-making processes and presents evidence that stronger inverse amygdala-vmPFC connectivity is associated with less behavioral dysregulation.

In contrast to behavioral dysregulation, the results for emotional dysregulation and its relationship to amygdala-vmPFC rs-FC were more complex. Overall, the present study arguably did not find strong evidence for a relationship between amygdala-vmPFC rs-FC and mean negative affect or affective instability in people's daily lives. On the one hand, there was a significant correlation between right amygdala-vmPFC rs-FC and affective instability in sadness, which could suggest an important relationship between amygdala-vmPFC rs-FC and some types of negative affect. Moreover, all participants in the presented sample had a history of major depression and it is possible that this contributed to us finding a result only for affective instability for sadness. However, there was not evidence for a relationship between amygdala-vmPFC rs-FC and mean negative affect, including sadness, fear, and hostility, or negative affective instability. When depressive and anxiety symptoms were examined separately, however, a different pattern of results emerged. Momentary reports of sadness were associated with increased positive amygdala-vmPFC connectivity, while momentary reports of anxiety (i.e., fear) were associated with increased inverse amygdala-vmPFC connectivity. This finding was consistent with Burghy et al. (2012), who found the same pattern in health young adults (also comprised primarily of women).

Thus for fear and anxiety, negative amygdala-vmPFC is associated with poor emotional outcomes. According to Burghy et al. (2012), the relationship between connectivity and anxiety is associated with cortisol levels in childhood and early adulthood following stressful life events, which disrupts the development of the amygdala-vmPFC circuit. This finding is also consistent with a resting state study that found that individuals with higher subclinical anxiety had negative amygdala-vmPFC rs-

FC (Kim et al., 2011a) and a study showing negative amygdala-vmPFC connectivity in individuals with social anxiety disorder (Young et al., 2009). Take together, these studies imply that when the amygdala and the vmPFC show good functional coherence, individuals experience less anxiety. The early evidence for the importance of the amygdala-vmPFC in emotion regulation came from translation research on fear extinction in rodents. Arguably, the experience and regulation of anxiety is conceptually closer to the fear extinction literature than regulating emotions such as sadness and depression. In general, this research showed that a lack of fear extinction is related to failures of activation in the vmPFC (Milad & Quirk, 2012), which is consistent with the finding in the present study that less vmPFC activation is associated with increased fear. Finally, there is also evidence that fear from a proximal threat is associated with reduction of vmPFC activation, possibly to inhibit complex cognitive processes and prepare an individual for a "fight-or flight" response (Mobbs et al., 2007). Taken together, this research corroborates existing evidence that negative amygdala-vmPFC connectivity is linked to increased fear and anxiety.

Alternatively, for depression, it appears that negative amygdala-vmPFC rs-FC is associated with better emotional outcomes. This finding provides some support of the theorized role of the vmPFC as a top-down regulator of negative affect generated in the amygdala. As this finding replicates the relationship found by Burghy et al. (2012), those authors theorize that depression is linked to functional connectivity through increased rumination. There is strong empirical support for the relationship between rumination and negative affect and depression (Aldao et al., 2010; Joormann & Gotlib, 2010; Joorman, & Vanderline, 2014). Burghy et al. (2012) proposes that positive functional connectivity

reflects increased rumination in individuals who are prone to feelings of depression and anxiety. Additional research has also found similar patterns with the Default Mode Network (DMN), with anterior regions in the DMN showing increased activation in individuals with depression in response to negative stimuli and a failure to reduce this activity during reappraisal (e.g., Mulders, van Eijndhoven, Schene, Beckmann, & Tendolkar, 2015; Sheline et al., 2009). In the present study, we did not find a relationship between connectivity and rumination, either with momentary assessment of rumination or with the Ruminative Responses Scale. Methodological considerations relevant for the assessment of rumination that will be considered in more depth below.

Importantly, the present study has replicated previous research in a sample of women with disorders of emotional distress utilizing EMA to capture emotional distress in daily lives. As much previous research has included healthy individuals with sub-clinical levels of depression or anxiety, studying these mechanisms in women with current diagnosed mood and anxiety disorders, is an important extension of this line of research. Previous research has also relied heavily on retrospective self-reports, which have limited validity for the assessment of emotional symptoms.

The current data also presents evidence that for transdiagnostic symptoms of non-specific negative affect, the vmPFC may not be critical for cognitive emotion regulation, a finding that is consistent with mounting evidence. Overall, support for the role of amygdala-vmPFC functional connectivity in emotional distress and regulation is mixed, both in terms of consistent effects and also direction of these effects. Although some research points to a role of the vmPFC in emotion regulation and disorders of emotional distress (e.g., Kim et al., 2011a; Klump et al., 2018; Motzkin et al., 2015), recent reviews

have failed to find consistent evidence implication amygdala-vmPFC rs-FC in depression (Brakowski et al., 2017) or supporting the vmPFC as a region critical for cognitive reappraisal (Buhle et al., 2014; Morawetz et al., 2017b). Furthermore, when evidence is found linking vmPFC-amygdala connectivity to emotion regulation, the direction of the vmPFC-amygdala functional connectivity is inconsistent, with evidence for both hyper-connectivity (i.e., a positive correlation between vmPFC and amygdala) and hypo-connectivity (i.e., a negative correlation between vmPFC and amygdala) in emotional dysregulation and disorders of emotional distress (e.g., Coombs et al., 2014; Fonzo & Etkin, 2017; Gold et al., 2016; Jalbrzikowski et al., 2017; Kim et al., 2011a). Furthermore, the basis for much of the theory of the vmPFC as an emotion regulation region comes from research on fear extinction in rodents and there is some question about the validity of the rodent homologue of the vmPFC (Myers-Schulz & Koenigs, 2012). As one explanation for the varied findings, it has been proposed that the vmPFC is important for implicit (e.g., fear extinction) but not explicit (e.g., explicit) emotion regulation (Etkin et al., 2015). The present study presents further evidence consistent with meta-analytic data that vmPFC activation is not strongly associated with transdiagnostic overall emotional distress or emotion regulation (Buhle et al., 2014; Morawetz et al., 2017b).

In an effort to understand the conflicting results in the previous literature, a critical examination of the evidence for the association between the vmPFC and emotion regulation reveals at least two factors that are worth additional discussion. As noted previously, there is evidence for both positive and negative amygdala-vmPFC connectivity. Although one contributing factor for this may be a differential pattern of results for depression and anxiety, there have also been inconsistent findings within

depression and within anxiety (e.g., Gold et al., 2016). One additional important factor may be the developmental nature of the amygdala-vmPFC connectivity. In healthy participants, there is evidence for positive amygdala-vmPFC connectivity in childhood that becomes negative with age, with the switch occurring sometime between age 10 (Gee et al., 2013) and 22 (Jalbrzikowski et al., 2017). There is also some evidence that a later developmental switch is associated with increased depression and anxiety (Jalbrzikowski et al., 2017). Thus when studying disorders of emotional distress, we may see age-related effects of the vmPFC-amygdala connectivity development. In the present study, amygdala-vmPFC connectivity ranged from positive to negative, with a mean of zero. As our study included some women in this young adulthood period (ages 18-22), we may expect that these women are still undergoing maturation of the amygdala-vmPFC circuit. Indeed, there is a trend toward a negative correlation between age and right amygdala- vmPFC (r_s = -.32, p = .09), indicating that as age increases, functional connectivity becomes more negative. Of note, amygdala-vmPFC rs-FC was still significant correlated with behavioral dysregulation when controlling for age. Due to the developmental nature of the vmPFC-amygdala functional connectivity, young adulthood may be a time when individuals with disorders of emotional distress are especially prone to behavioral dysregulation.

Another important factor to consider is the nature and locations of the vmPFC as a brain region. In the present study, I chose coordinates for our ROI based on a meta-analysis of the vmPFC, which identified a region of overlapping coordinates of significant activation from multiple lines of research (Diekhof et al., 2011). This consensus region was consistently associated with decreased negative affect from

research using paradigms for fear extinction, placebo control, and cognitive reappraisal. As I chose a vmPFC ROI that had strong support as a region with the best chances of finding a relationship with emotional distress, it is notable that such a relationship did not exist in this data and further supports the theory that the vmPFC may be critical for behavior but not overall negative emotion. However, it is also important to note that in the field, there is variability in the specific prefrontal subregions included in vmPFC ROIs, due to some disagreement about the exact boundaries of the vmPFC (Dixon, Thiruchselvam, Todd, & Christoff, 2017). Specifically, the vmPFC has been identified as voxels in Brodmann areas 10, 11, 25, and 32 (e.g., Diekhof et al., 2011; Etkin et al., 2011; Kim et al., 2011a; Schiller & Delgado, 2010; Zilverstand et al., 2017). As noted previously, it may be that different subregions of the vmPFC are involved in different cognitive and emotional processes. For example, one meaningful way to separate the vmPFC may be based on a division of peak areas tied to emotion, decision-making, and social cognition (Hiser & Koenigs, 2018). Alternatively, the posterior vmPFC may be associated with negative affect while the perigenual vmPFC is associated with positive affect (i.e., effective emotion regulation; Myers-Schulz & Koenigs, 2012). Noting the location of the vmPFC at the inferior boundary of the brain, it is also an area that can be subject to signal loss in fMRI. In the present study, we used a 30-degree tilt toward the coronal plan during scanning in order to minimize signal loss. Overall, the vmPFC is a complex region for research due to developmental changes into adulthood, poor anatomical boundaries, and divergent subregions involved in diverse cognitive processes.

The present study also found that amygdala-dACC connectivity was negatively correlated with affective instability, indicating that stronger positive amygdala-dACC

was associated with more emotional stability. Amygdala-dACC was also negatively correlated at a trend level with momentary reports of fear and showed a pattern of negative correlations with all assessments of negative affect. The dACC has a well-established role in emotion, although there are two divergent hypotheses about the nature of this role. One dominant model posits that the dACC can be distinguished from the vmPFC with the ACC involved in emotional expression and the vmPFC involved in emotion regulation (Etkin et al., 2011; Etkin et al., 2015). This model is built on previous research finding that positive ACC-amygdala functional connectivity is seen during emotional expression tasks. In this theory, the dACC is viewed as amplifying an emotional response. This model theorizes that the ACC plays a role in expression or amplifying emotion, such that increased ACC activation would lead to more negative emotion. In the present study resting state data, I found the opposite relationship, with amygdala-ACC rs-FC associated with decreased negative emotion. In this way, the present results are more consistent with the ACC as a regulator of negative affect, rather than an amplifier. While this finding is inconsistent with the role of the ACC proposed in the Etkin model, it is not wholly inconsistent with other research. Review papers also support the role of the ACC, particularly the dorsal ACC (dACC), in emotion regulation and cognitive reappraisal, with increased dACC activity related to effective emotion regulation (Buhle et al., 2014; Morawetz et al., 2017a; Morawetz et al., 2017b). dACC may also be reduced, rather than enhanced, in some anxiety disorders (Zilverstand et al., 2017). Overall, the negative association between amygdala-ACC rs-FC and negative moods supports the role of the ACC as an emotional regulation region.

There are some methodological limitations to the current study. In the current study, resting state data was collected for a period of 6 minutes. Although previous research has shown that scan lengths of 5 minutes have robust reliability and are often standard in resting-state fMRI studies (Van Dijk et al., 2010), there is also recent research to suggest that increasing scan length increases reliability. For example, test-retest reliability increased up to 20% as scan duration was increased from 5 minutes to 12 minutes, at which point reliability measures appeared to plateau (Birn et al., 2013). Although there is still some debate about the ideal scan duration, future protocols may benefit from adapting a longer scan duration.

Moreover, our seed-based analyses did not find any relationship between amygdala functional connectivity and emotion or behavioral dysregulation. Examination of the data revealed a number of positive and negative associations; however, nothing reached the level of significance required for recommended corrections for family-wise error. One limitation to consider is that the sample size of the present study may have been underpowered to detect such effects.

One advantage of this study was the ability to directly compare retrospective self-report measures of negative affect, emotional dysregulation, and emotion regulation strategies with analogous measures from momentary assessment. Overall, I found the expected patterns across variables of emotional distress from self-report questionnaires and momentary survey variables. For example, difficulties with emotion regulation as measured with the DERS showed a positive pattern of correlations with negative affect and negative affective instability. Mindfulness, as measured with the FFMQ had a pattern

of negative correlations with negative affect and negative affective instability, indicating that mindfulness was associated with less negative, more stable moods.

However, rumination, an important construct in disorders of emotional distress, was not correlated between laboratory questionnaires and momentary assessment. Rumination, defined as repetitive focus on the experience of a negative emotion and its causes and consequences (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008), is well-established as a pervasive ineffective emotion regulation strategies in disorders of emotional distress (Aldao et al., 2010; Joormann & Gotlib, 2010; Joorman, & Vanderline, 2014). Rumination has been found to prolong distress, increase anxiety and related avoidance (Nolen-Hoeksema & Watkins, 2011), and interfere with problem solving (Nolen-Hoeksema, 1991). Due to its role in disorders of emotional distress, rumination is an important component of the increased emotional and behavioral dysregulation observed in these disorders. Although rumination was directly assessed in the present study in a well-validated questionnaire (i.e., Ruminative Response Scale; RRS) and in momentary assessments, there was not a significant correlation between the two rumination measures. In fact, the correlation between the RRS and momentary impulsivity and momentary reassurance seeking was larger than the correlation between RRS and momentary rumination. Moreover, momentary rumination was not related to functional connectivity as seen with the other momentary variables of negative affect, negative affective instability and behavioral dysregulation.

This pattern of results indicates that the RRS and momentary assessment of rumination were unlikely to be capturing the same construct. In the momentary surveys, rumination was assessed with items asking participants how much they were focusing on

their feelings and their problems. As rumination is closely linked to negative affect (Nolen-Hoeksema & Watkins, 2011), we expected that rumination would be reported at surveys where participants also reported high levels of negative affect. However, momentary rumination was not associated with momentary negative affect and participants occasionally reported high degrees of focusing on their problems or feelings when experiencing high levels of positive affect. Alternatively, the RRS was strongly associated with momentary negative affect, providing validity to the RRS as a measure of rumination. Therefore, the lack of a relationship between the RRS and the momentary variable of rumination is likely reflecting an issue with the present method of assessing momentary rumination. As emotion regulation strategies are a critical area of study in disorders of emotional distress, this is a consideration to improve the assessment of rumination in future momentary assessment.

In sum, the present study extends the literature on important emotion neural circuits to transdiagnostic symptoms of emotional and behavioral dysregulation as experienced in daily life. I present evidence for an association between positive amygdala-vmPFC rs-FC and increased behavioral dysregulation, supporting the theorized role of the vmPFC as a "top-down" regulator of the amygdala. I also present evidence that the amygdala-vmPFC rs-FC may be differentially associated with symptoms of depression and anxiety and is not associated with non-specific negative affect. Alternatively, another emotion region, the dACC was found to be associated with negative affect and negative affective instability. As the present study used resting state analyses, these results provide insight into these circuits at baseline, as opposed to during created emotions from task-based protocols. Using EMA methods, the present study was

able to capture the day-to-day experiences of emotion and behavior in women with common disorders of emotional distress. Due to the complex nature of the activation patterns observed in these emotion circuits, future research should continue to use ecological assessments of symptoms to determine the functional effects of amygdala connectivity in disorders of emotional distress.

5. References

Adolphs, R. (2010). What does the amygdala contribute to social cognition? *Annals of the New York Academy of Sciences, 1191*, 42-61. doi:10.1111/j.1749-6632.2010.05445.x

Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2010). Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical Psychology Review, 30*, 217–237. doi:10.1016/j.cpr.2009.11.004

Alexander, W. H., & Brown, J. W. (2010). Competition between learned reward and error outcome predictions in anterior cingulate cortex. *NeuroImage, 49*, 3210-3218. doi:10.1016/j.neuroimage.2009.11.065

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Arlington, VA: American Psychiatric Publishing.

Armony, J. L. (2013). Current emotion research in behavioral neuroscience: The role(s) of the amygdala. *Emotion Review, 5*(1), 104-115. doi:10.1177/1754073912457208

Bartra, O., McGuire, J. T., & Kable, J. W. (2013). The valuation system: A coordinate-based meta-analysis of BOLD fMRI experiments examining neural correlates of subjective value. *NeuroImage, 76*, 412-427. doi:10.1016/j.neuroimage.2013.02.063.

Baer, R. A., Smith, G. T., Hopkins, J., Krietemeyer, J., & Toney, L. (2006). Using self-report assessment methods to explore facets of mindfulness. *Assessment, 13*, 27–45.doi:10.1177/1073191105283504

Beck, A. T. & Steer, R. A. (1990). Manual for the Beck Anxiety Inventory. The

Psychological Corporation: San Antonio, Tex.

Beck, A. T., Steer, R. A. & Brown, G. K. (1996). *Manual for Beck Depression Inventory-II.* San Antonio, TX: Psychological Corporation.

Bhanji, J. P. & Delgado, M. R. (2014). Perceived control influences neural responses to setbacks and promotes persistence. *Neuron, 83*, 1369-1375. doi:10.1016/j.neuron.2014.08.012

Bijsterbosch, J., Smith, S., Forester, S., John, O. P., & Bishop, S. J. (2014). Resting state correlates of subdimensions of anxious affect. *Journal of Cognitive Neuroscience, 26*(4), 914-926. doi:10.1162/jocna00512

Birn, R. M., Molloy, E. K., Patriat, R., Parker, T., Meier, T. B., Kirk, G. R., Nair, V. A., Meyerand, M. E., & Prabhakaran, V. (2013). The effect of scan length on the reliability of resting state fMRI connectivity estimates. *NeuroImage, 83*, 550-558. doi:10.1016/j.neuroimage.2013.05.099

Blaney, P. H. (1986). Affect and memory: A review. *Psychological Bulletin, 99*(2), 229-246. doi:10.1037/0033-2909.99.2.229

Bond, F. W., Hayes, S. C., Baer, R. A., Carpenter, K. M., Guenole, N., Orcutt, H. K., Waltz, T., & Zettle, R. D. (2011). Preliminary psychometric properties of the Acceptance and Action Questionnaire-II: A revised measure of psychological inflexibility and experiential avoidance. *Behavior Therapy, 42*, 676-688. doi:10.1016/j.beth.2011.03.007

Brakowski, J., Spinelli, S., Dorig, N., Bosch, O. G., Manoliu, A., Holtforth, M. G., & Seifritz, E. (2017). Resting state brain network function in major depression: Depression symptomatology, antidepressant treatment effects, future research.

Journal of Psychiatric Research, 92, 147-159. doi:10.1016/j.jpsychires.2017.04.007

Buhle, J. T., Silvers, J. A., Wager, T. D., Lopez, R., Onyemekwu, C., Kober, H., … Ochsner, K. N. (2014). Cognitive reappraisal of emotion: A meta-analysis of human neuroimaging studies. *Cerebral Cortex, 24*, 2981-2990. doi:10.1093/cercor/bht154

Burghy, C. A., Stodola, D. E., Ruttle, P. L., Molloy, E. K., Armstrong, J. M., Oler, J. A., … Birn, R. M. (2012). Developmental pathways to amygdala-prefrontal function and internalizing symptoms in adolescence. *Nature Neuroscience, 15*, 1736-1741. doi:10.1038/nn.3257

Carpenter, R. W. & Trull, T. J. (2013). Components of emotion dysregulation in borderline personality disorder: A review. *Current Psychiatry Reports, 15*(1), 335. doi:10.1007/s11920-012-0335-2

Caspi, A., Houts, R. M, Belsky, D. W., Goldman-Mellor, S. J, Harrington, H., Israel, S., … Moffit, T. E. (2014). The p factor: One general psychopathology factor in the structure of psychiatric disorders? *Clinical Psychological Sciences, 2*(2), 119-137. doi:10.1177/2167702613497473

Coombs, G., Loggia, M. L., Greve, D. N., & Holt, D. J. (2014). Amygdala perfusion is predicted by its functional connectivity with the ventromedial prefrontal cortex and negative affect. *PLoS ONE 9*(5): e97466. doi:10.1371/journal.pone.0097466

Cunningham, W. A. & Kirkland, T. (2014). The joyful, yet balanced, amygdala: Moderated responses to positive but not negative stimuli in trait happiness. *Scan, 9*, 760-766. doi:10.1093/scan/nst045

Dalgleish, T & Watts, F. N. (1990). Biases of attention and memory in disorders of anxiety and depression. *Clinical Psychology Review, 10*(5), 589-604. doi:10.1016/0272-7358(90)90098-U

Damoiseaux, J. S., & Greicius, M. D. (2009). Greater than the sum of its parts: A review of studies combining structural connectivity and resting-state functional connectivity. *Brain Structure and Function, 213*, 525-533. doi:10.1007/s00429-009-0208-6

Deichmann, R., Gottfried, J. A., Hutton, C., & Turner, R. (2003). Optimized EPI for fMRI studies of the orbitofrontal cortex. *Neuroimage, 19*, 430-441. doi:10.1016/S1053-8119(03)00073-9

Delgado M. R., Nearing, K.I., Ledoux, J. E., & Phelps, E. A. (2008). Neural circuitry underlying the regulation of conditioned fear and its relation to extinction. *Neuron, 59*, 829–38. doi:10.1016/j.neuron.2008.06.029

Diekhof, E. K., Geier, K., Falkai, P., & Gruber, O. (2011). Fear is only as deep as the mind allows: A coordinate-based meta-analysis of neuroimaging studies on the regulation of negative affect. *Neuroimage, 58*, 275-85. doi:10.1016/j.neuroimage.2011.05.073

Dixon, M. L., Thiruchsekvam, R., Todd, R., & Christoff, K. (2017). Emotion and the prefrontal cortex: An integrated review. *Psychological Bulletin, 143*(10), 1033-1081. doi:10.1037/bul0000096

Ebner-Priemer, U. W. & Trull, T. J. (2009). Ecological momentary assessment of mood disorders and mood dysregulation. *Psychological Assessment, 21*(4), 463-475. doi:10.1037/a0017075

Etkin, A., Buchel, C., & Gross, J. J. (2015). The neural bases of emotion regulation. *Nature Reviews Neuroscience, 16*, 693-700. doi:10.1038/nrn4044

Etkin A, Egner T, & Kalisch R. (2011). Emotional processing in anterior cingulate and medial prefrontal cortex. *Trends in Cognitive Sciences, 15,* 85–93. doi:10.1016/j.tics.2010.11.004

Etkin, A., Prater, K. E., Hoeft, F., Menon, V., & Schatzberg, A. F. (2010). Failure of anterior cingulate activation and connectivity with the amygdala during implicit regulation of emotional processing in generalized anxiety disorder. *American Journal of Psychiatry, 167*, 545-554. doi:10.1176/appi.ajp.2009.09070931

Fredrickson, B. L. & Kahneman, D. (1993). Duration neglect in retrospective evaluations of affective episodes. *Journal of Personality and Social Psychology, 65*, 45-55. doi:10.1037/0022-3514.65.1.45

Fonzo, G. A. & Etkin, A. (2017). Affective neuroimaging in generalized anxiety disorder: An integrated review. *Dialogues in Clinical Neuroscience, 19*, 169-179.

Gaffrey, M. S., Barch, D. M., & Luby J. L (2016). Amygdala reactivity to sad faces in preschool children: An early neural marker of persistent negative affect. *Developmental Cognitive Neuroscience, 17*, 94-100. doi:10.1016/j.dcn.2015.12.015

Gee, D. G., Humphreys, K. L., Flannery, J., Goff, B., Telzer, E. H., Shapiro, M., … Tottenham, N. (2013). A developmental shift from positive to negative connectivity in human amygdala-prefrontal circuitry. *The Journal of Neuroscience, 33*(10), 4584-4593. doi:10.1523/JNEUROSCI.3446-12.2013

Ghashghaei, H. T., & Barbas, H. (2002). Pathways for emotion: Interactions of prefrontal

and anterior temporal pathways in the amygdala of the rhesus monkey. *Neuroscience, 115,* 1261–1279. doi:10.1016/S0306-4522(02)00446-3

Giustino, T. F. & Marren, S. (2015). The role of the medial prefrontal cortex in the conditioning and extinction of fear. *Frontiers in Behavioral Neuroscience,* 9, 298. doi:10.3389/fnbeh.2015.00298

Gold, A. L., Shechner, T., Farber, M. J., Spiro, C. N., Leibenluft, E., Pine, D. S, & Britton, J. C. (2016). Amygdala-cortical connectivity: Associations with anxiety, development, and threat. *Depression and Anxiety, 33*(10), 917-926. doi:10.1002/da.22470.

Gratz, K. L. & Roemer, L. (2004). Multidimensional assessment of emotion regulation and dysregulation: Development, factor structure, and initial validation of the Difficulties in Emotion Regulation Scale. *Journal of Psychopathology and Behavioral Assessment, 26*, 41-54. doi:10.1023/B:JOBA.0000007455.08539.94

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology, 85*, 348-362. doi:10.1037/0022-3514.85.2.348

Hamilton, J. P., Etkin, A., Furman, D. J., Lemus, M. G., Johnson, R. F., & Gotlib, I. H. (2012). Functional neuroimaging of major depressive disorder: A meta-analysis and new integration of base line activation and neural response data. *American Journal of Psychiatry, 169*, 693-703. doi:10.1176/appi.ajp.2012.11071105

Hare, T. A., Camerer, C. F., & Rangel, A. (2009). Self-control in decision-making involves modulation of the vmPFC validation system. *Science, 324*, 646-648. doi:10.1126/science.1169957

Harvanko, A. M., Schreiber, L. R., & Grant, J. E. (2013). Prediction of alcohol and gambling problems in young adults by using a measure of decision making. *Journal of Addiction Medicine, 7*(5), 314-319. doi:10.1097/ADM.0b013e31829a2f32

Hebscher, M. & Gilboa, A. (2016). A boost of confidence: The role of ventromedial prefrontal cortex in memory, decision-making, and schemas. *Neuropsychologia, 90*, 46-58. doi:10.1016/j.neuropsychologia.2016.05.003

Heitmann, C. Y., Feldker, K., Neumeister, P., Brinkmannm L., Schrammen, E., Zwitserlood, P., & Straube, T. (2017). Brain activation to task-irrelevant disorder-related threat in social anxiety disorder: The impact of symptom severity. *NeuroImage: Clinical, 14*, 323-333. doi:10.1016/j.nicl.2017.01.020

Helie, S. Shamloo, F., Novak, K., & Foti, D. (2017). The roles of valuation and reward processing in cognitive function and psychiatric disorders. *Annals of the New York Academy of Sciences, 1395*, 33-48. doi:10.1111/nyas.13327

Hepp, J., Carpenter, R. W., Lane, S. P., & Trull, T. J. (2016). Momentary symptoms of borderline personality disorder as a product of trait personality and social context. *Personality Disorders: Theory, Research, and Treatment, 7*(4), 384-393. doi:10.1037/per0000175

Hiser, J. & Koenigs, M. (2018). The multifaceted role of the ventromedial prefrontal cortex in emotion, decision making, social cognition, and psychopathology. *Biological Psychiatry, 83*, 638-647. doi:10.1016/j.biopsych.2017.10.030

Jalbrzikowski, M., Larsen, B., Hallquist, M. N., Foran, W., Calabro, F., & Luna, B. (2017). Development of white matter microstructure and intrinsic functional

connectivity between the amygdala and ventromedial prefrontal cortex: Associations with anxiety and depression. *Biological Psychiatry, 82*(7), 511-521. doi:10.1016/j.biopsych.2017.01.008.

Janak, P. H. & Tye, K. M. (2015). From circuits to behaviour in the amygdala. *Nature, 517*(7534), 284-292. doi:10.1038/nature14188

Johnstone, T., van Reekum, C. M., Urry, H. L., Kalin, N. H., & Davidson, R. J. (2007). Failure to regulate: Counterproductive recruitment of top-down prefrontal-subcortical circuitry in major depression. *The Journal of Neuroscience, 27*(33), 8877-8884. doi:10.1523/JNEUROSCI.2063-07.2007

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition & Emotion, 24*, 281–298. doi:10.1080/02699930903407948

Joorman, J. & Vanderline, W. M. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clinical Psychological Science, 2*(4), 402- 421. doi:10.1177/2167702614536163

Kalisch, R. & Gerlicher, A. M. V. (2014). Making a mountain out of a molehill: One the role of the rostral dorsal anterior cingulate and dorsomedial prefrontal cortex in conscious threat appraisal, catastrophizing, and worrying. *Neurosceince and Biobehavioral Reviews, 42*, 1-8. doi:10.1016/j.neubiorev.2014.02.002

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Koretz, D., Merikangas, K. R., … Wang, P. S. (2003). The epidemiology of major depressive disorder: Results from the National Comorbidity Survey Replication. *The Journal of the American Medical Association, 289*(23), 3095-3105. doi:10.1001/jama.289.23.3095

Kessler, R. C., Chiu, W. T., Demler, O, & Walters, E. E. (2005). Prevalence, severity and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*, 617-627. doi:10.1001/archpsyc.62.6.617

Kihlstrom, J. F., Eich, E., Sandbrand, D., & Tobias, B. A. (2000). Emotion and memory: Implications for self-report. In A.A. Stone & J.S. Turkkan (Eds.), Science of self-report: Implications for research and practice, 81–99. Mahwah, NJ: Erlbaum.

Kim, M. J., Gee, D. G., Loucks, R. A., Davis, F. C., & Whalen, P. J. (2011a). Anxiety dissociates dorsal and ventral medial prefrontal cortex functional connectivity with the amygdala at rest. *Cerebral Cortex, 21*, 1667-1673. doi:10.1093/cercor/bhq237

Kim, M. J., Loucks, R. A., Palmer, A. L., Brown, A. C., Solomon, K. M., Marchante, A. N., & Whalen, P. J. (2011b). The structural and functional connectivity of the amygdala: From normal emotion to pathological anxiety. *Behavioral Brain Research, 223*, 403-410. doi:10.1016/j.bbr.2011.04.025

Kim M. J., & Whalen, P. J. (2009) The structural integrity of an amygdala-prefrontal pathway predicts trait anxiety. *The Journal of Neuroscience, 29*, 11614–11618. doi:10.1523/JNEUROSCI.2335-09.2009

Klumpp, H., Bhaumik, R., Kinney, K. L., & Fitzgerald, J. M. (2018). Principal component analysis and neural predictors of emotion regulation. *Behavioural Brain Research, 338*, 128-133. doi:10.1016/j.bbr.2017.10.024

Kotov, R., Ruggero, C. J., Krueger, R. F., Watson, D., Yuan, Q., & Zimmerman, M. (2011). New dimensions in the quantitative classification of mental illness.

Archives of General Psychiatry, 68, 1003-1011. doi:10.1001/archgenpsychiatry.2011.107

Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: a review. *Biological Psychology, 84*, 394-421. doi:10.1016/j.biopsycho.2010.03.010

Kring, A. M., & Sloan, D. M. (Eds.) (2010). *Emotion regulation and psychopathology: A transdiagnostic approach to etiology and treatment*. Guilford: New York.

Krueger, R. F. (1999). The structure of common mental disorders. *Archives of General Psychiatry, 56*, 921-926. doi:10.1001/archpsyc.56.10.921

Krueger, R. F. & Markon, K. E. (2006). Reinterpreting comorbidity: A model-based approach to understanding and classifying psychopathology. *Annual Review of Clinical Psychology, 2*, 111-113. doi:10.1146/annurev.clinpsy.2.022305.095213

Lang, P. J. (1993). The three-system approach to emotion. In N. Birbaumer & A. Oehan (Eds.), The structure of emotion: Psychophysiological, cognitive, and clinical aspects (pp. 18-30). Seattle, WA: Hogrefe & Huber.

Lawrence, A. J., Luty, J., Bogdan, N. A., Sahakian, B. J., & Clark, L. (2009). Problem gamblers share deficits in impulsive decision-making with alcohol-dependent individuals. *Addiction, 104*, 1006-1015. doi:10.1111/j.1360-0443.2009.02533.x

Levy, D. J. & Glimcher, P. W. (2012). The root of all value: A neural common currency for choice. *Current Opinion in Neurobiology, 22*, 1027-1038. doi:10.1016/j.conb.2012.06.001

Levenson, R. W., Ascher, E., Goodkind, M., McCarthy, M. E., Sturm, V. E., & Werner, K. (2008). Laboratory testing of emotion and frontal cortex. In B. Miller & G. Goldenberg (Eds.), *Handbook of Clinical Neurology, Third Series* (pp. 489-498).

New York: Elsevier. doi:10.1016/S0072-9752(07)88025-0

Linehan, M. M. (1993) *Cognitive–behavioral treatment of borderline personality disorder.* New York: The Guilford Press.

Lovibond, S. H. & Lovibond, P. F. (1995a). Manual for the Depression Anxiety Stress Scales. (2nd. Ed.) Sydney: Psychology Foundation

Lovibond, P. F. & Lovibond, S. H. (1995b). The structure of negative emotional states: Comparison of the depression anxiety stress scales (DASS) with the Beck Depression and Anxiety Inventories. *Behavioral Research and Therapy, 33(*3), 335-343. doi:10.1016/0005-7967(94)00075-U

Mauss, I. B., & Robinson, M. D. (2009). Measures of emotion: A review. *Cognition and Emotion, 32*(2), 209-237. doi:10.1080/02699930802204677

McCarthy, D. M., Niculete, M. E., Treloar, H. R., Morris, D. H. & Bartholow, B. D. (2012). Acute alcohol effects on impulsivity: Associations with drinking and driving behavior. *Addiction, 107*(12), 2109-2114. doi:10.1111/j.1360-0443.2012.03974.x

Mennin, D. S., Holoway, R. M., Fresco, D. M., Moore, M. T., & Heimberg, R. G. (2007). Delineating components of emotion and its dysregulation in anxiety and mood psychopathology. *Behavior Therapy, 38*, 284−302. doi:10.1016/j.beth.2006.09.001

Milad, M. R. & Quirk, G. J. (2012). Fear extinction as a model for translational neuroscience: Ten years of progress. *Annual Review of Psychology, 63*, 129-151. doi:10.1146/annurev.psych.121208.131631

Mobbs, D., Petrovic, P., Marchant, J. L., Hassabis, D., Weiskopf, N., Seymour, D., …

Frith, C. D. (2007). When fear is near: Threat imminence elicits prefrontal-periaqueductal gray shifts in humans. Science, 317, 1079-1081. doi:10.1126/science.1144298

Morawetz, C., Kellermann T., Kogler, L., Radke, S., Blechert, J., & Derntl, B. (2016). Intrinsic functional connectivity underlying successful emotion regulation of angry faces. *Social Cognitive and Affective Neuroscience, 11*(12), 1980-1991. doi:10.1093/scan/nsw107

Morawetz, C., Bode, S., Baudewig, J., & Heekeren, H. R. (2017a). Effective amygdala-prefrontal connectivity predicts individual differences in successful emotion regulation. *Social Cognitive and Affective Neuroscience*, 569-585. doi:10.1093/scan/nsw169

Morawetz, C., Bode, S., Derntl, B., & Heekeren, H. R. (2017b). The effect of strategies, goals and stimulus material on the neural mechanisms of emotion regulation: A meta-analysis of fMRI studies. *Neuroscience and Biobehavioral Reviews, 72*, 111-128. doi:10.1016/j.neubiorev.2016.11.014

Morrison, S. E., & Salzman, C. D. (2010). Re-valuing the amygdala. *Current Opinion in Neurobiology, 20*, 221-230. doi:10.1016/j.conb.2010.02.007

Motzkin, J. C., Philippi, C. L., Wolf, R. C., Baskaya, M. K., & Koenigs, M. (2015). Ventromedial prefrontal cortex is critical for the regulation of amygdala activity in humans. *Biological Psychiatry, 77*(3), 276–284. doi:10.1016/j.biopsych.2014.02.014

Mulders, P. C., van Eijndhoven, P. F., Schene, A. H., Beckmann, C. F., & Tendolkar, I. (2015). Resting-state functional connectivity in major depressive disorder: A

review. *Neuroscience and Biobehavioral Reviews, 56*, 330-344. doi:10.1016/j.neubiorev.2015.07.014

Myers-Schulz, B. & Koenigs, M. (2012). Functional anatomy of ventromedial prefrontal cortex: Implications for mood and anxiety disorders. *Molecular Psychiatry, 17*, 132-141. doi:10.1038/mp.2011.88

Nitschke, J. B., Sarinopoulos, I., Oathes, D. J., Johnstone, T., Whalen, P. J., Davidson, R. J., & Kalin, N. H. (2009). Anticipatory activation in the amygdala and anterior cingulate in generalized anxiety disorder and prediction of treatment response. *American Journal of Psychiatry, 166*, 302-310. doi:10.1176/appi.ajp.2008.07101682

Nolen-Hoeksema S., & Watkins E. R. (2011). A heuristic for developing transdiagnostic models of psychopathology: Explaining multifinality and divergent trajectories. *Perspectives on Psychological Science, 6*, 589–609. doi:10.1177/1745691611419672

Nolen-Hoeksema S, Wisco B. E., & Lyubomirsky S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400–424. doi:10.1111/j.1745-6924.2008.00088.x

Peters, J., Kalivas, P. W., & Quirk, G. J. (2009). Extinction circuits for fear and addiction overlap in prefrontal cortex. *Learning & Memory, 16,* 279-288. doi:10.1101/lm.1041309

Pfohl, B., Blum, N. S., & Zimmerman, M. (1997). *Structured interview for DSM-IV personality: SIDP-IV*. Washington, DC: American Psychiatric Press.

Poh, M. Z., Swenson, N. C., & Picard, R. W. (2010). A wearable sensor for unobtrusive,

long-term assessment of electrodermal activity. *IEEE Transactions on Biomedical Engineering, 57*, 1243-1252. doi:10.1109/TBME.2009.2038487

Power, J. D., Barnes, K. A., Snyder, A. Z., Schlaggar, B. L., & Petersen, S. E. (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage, 59*, 2142-2154. doi:10.1016/j.neuroimage.2011.10.018

Pujara, M. S., Wolf, R. C., Baskaya, M. K., & Koenigs, M. (2015). Ventromedial prefrontal cortex damage alters relative risk tolerance for prospective gains and losses. *Neuropsychologia, 79*, 70-75. doi:10.1016/j.neuropsychologia.2015.10.026

Qin, S. Young, C. B., Duan, X., Chen, T., Supekar, K. & Menon, V. (2014). Amygdala subregional structure and intrinsic functional connectivity predicts individual differences in anxiety during early childhood. *Biological Psychiatry, 75*, 892-900. doi:10.1016/j.biopsych.2013.10.006

Quirk G. J., & Beer, J. S. (2006). Prefrontal involvement in the regulation of emotion: convergence of rat and human studies. *Current Opinion in Neurobiology, 6*, 723–727. doi:10.1016/j.conb.2006.07.004

Quirk, G. J., & Mueller, D. (2008). Neural mechanisms of extinction learning and retrieval. *Neuropsychopharmacology, 33*, 56-72. doi:10.1038/sj.npp.1301555

Rachman, S. & Hodgson, R. (1974). Synchrony and desynchrony in fear and avoidance. *Behaviour Research and Therapy, 12*(4), 311-318. doi:10.1016/0005-7967(74)90005-9

Roy A. K, Shehzad, Z., Margulies, D. S., Clare Kelly, A. M., Uddin, L. Q., Gotimer, K.,

… Milhan, M. P. (2009) Functional connectivity of the human amygdala using resting state fMRI. *Neuroimage 45*, 614–626. doi:10.1016/j.neuroimage.2008.11.030

Roy, M., Shohamy, D., & Wager, T. D. (2012). Ventromedial prefrontal-subcortical systems and the generation of affective meaning. *Trends in Cognitive Sciences, 16*, 147-156. doi:10.1016/j.tics.2012.01.005

Sanislow, C. A., Pine, D.S., Quinn, K. J., Kozak, M. J., Garvey, M. A., Heinssen, R. K., Wang, P. S., & Cuthbert, B. N. (2010). Developing constructs for psychopathology research: Research domain criteria. *Journal Abnormal Psychology, 119*, 631-639. doi:10.1037/a0020909

Schiller, D., & Delgado, M. R. (2010). Overlapping neural systems mediating extinction, reversal and regulation of fear. *Trends in Cognitive Sciences, 14*, 268-276. doi:10.1016/j.tics.2010.04.002

Schulze, L., Domes, G., Krüger, A., Berger, C., Fleischer, M., Prehn, K., … Herpertz, S. C. (2011). Neuronal correlates of cognitive reappraisal in borderline patients with affective instability. *Biological Psychiatry, 69*, 564-573. doi:10.1016/j.biopsych.2010.10.025

Selby, E. A., Anestis, M. D., Bender, T. W., & Joiner, T. E. Jr. (2009). An exploration of the emotional cascade model in borderline personality disorder. *Journal of Abnormal Psychology, 118*, 375-387. doi:10.1037/a0015711

Sheline, Y. I., Barch, D. M., Price, J. L., Rundle, M. M., Vaishnavi, S. N., Snyder, A. Z.

… Raichle, M. E. (2009). The default model network and self-referential process in depression. *Proceedings of the National Academy of Sciences, 106*(6), 1942-1947. doi:10.1073/pnas.0812686106

Solhan, M., Trull, T. J., Jahng, S., & Wood, P. (2009). Clinical assessment of affective instability: Comparing EMA indices, questionnaire reports, and retrospective recall. *Psychological Assessment,* 21, 425–36. doi:10.1037/a0016869

Stevens, J. S., Jovanovic, T., Fani, N., Ely, T. D., Glover, E. M., Bradley, B., & Ressler, K. J. (2013). Disrupted amygdala-prefrontal functional connectivity in civilian women with posttraumatic stress disorder. *Journal of Psychiatry Research, 47*(10), 1469-1478. doi:10.1016/j.jpsychires.2013.05.031

Taylor, S. F., & Liberzon, I. (2007). Neural correlates of emotion regulation in psychopathology. *Trends in Cognitive Sciences, 11*, 413-418. doi:10.1016/j.tics.2007.08.006

Thomason, M. E., Hamilton, J. P., & Gotlib, I. H. (2011). Stress-induced activation of the HPA axis predicts connectivity between subgenual cingulate and salience network during rest in adolescents. *Journal of Child Psychology and Psychiatry, 52*(10), 1026-1034. doi:10.1111/j.1469-7610.2011.02422.x

Tillman, R. M., Stockbridge, M. D., Nacewicz, B. M., Torrisi, S., Fox, A. S., Smith, J. F., & Shackman, A. J. (2018). Intrinsic functional connectivity of the central extended amygdala. *Human Brain Mapping, 39,* 1291-1312. doi:10.1002/hbm.23917

Tomko, R. L., Trull, R. J., Wood, P. K., & Sher, K. J. (2014). Characteristics of

borderline personality disorder in a community sample: Comorbidity, treatment utilization, and general functioning. *Journal of Personality Disorders, 28*(5), 734-750. doi:10.1521/pedi_2012_26_093

Townsend, J. D., Torrisi, S. J., Lieberman, M. D., Sugar, C. A., Bookheimer, S. Y., & Altshuler, L. L. (2013) Frontal-amygdala connectivity alternations during emotion downregulation in bipolar I disorder. *Biological Psychiatry, 73*, 127-135. doi:10.1016/j.biopsych.2012.06.030

Tranel, D., Gullickson, G., Koch, M., & Adolphs, R. (2006). Altered experience of emotion following bilateral amygdala damage. *Cognitive Neuropsychiatry, 11*(3), 219-232. doi:10.1080/13546800444000281

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research, 27*, 247–259. doi:10.1023/A:1023910315561

Troy, A. S., Eilhelm, F. H., Shallcross, A. J., & Mauss, I. B. (2010). Seeing the silver lining: Cognitive reappraisal ability moderates the relationship between stress and depressive symptoms. *Emotion, 10*(6), 783-795. doi:10.1037/a0020262

Trull, T. J. & Ebner-Priemer, U. (2013). Ambulatory Assessment. *Annual Review of Clinical Psychology, 91*, 51-76. doi:10.1146/annurev-clinpsy-050212-185510

Trull, T. J. & Ebner-Priemer, U. (2014). The role of ambulatory assessment in psychological science. *Current Directions in Psychological Science, 23*(6), 466-470. doi:10.1177/0963721414550706

Trull, T. J., Solhan, M. B., Tragesser, S. L., Jahng, S., Wood, P. K., Piasecki, T. M., &

Watson, D. (2008). Affective instability: Measuring a core feature of borderline personality disorder with ecological momentary assessment. *Journal of Abnormal Psychology, 117*, 647-661. doi:10.1037/a0012532

Tzourio-Mazoyer, N., Landeau, B., Papathanassiou, D., Crivello, F., Etard, O., Delcroix, N., … Joliot, M. (2002). Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *NeuroImage, 15*, 273-289. doi:10.1006/nimg.2001.0978

Uchida, M., Biederman, J., Gabrieli, J. D. E., Micco, J., Los Angeles, C., Brown, A., … Whitefield-Gabrieli, S. (2015). Emotion regulation ability varies in relation to intrinsic functional brain architecture. *Social Cognitive and Affective Neuroscience, 10*, 1738-1748. doi:10.1093/scan/nsv059

Van Dijk, K. R., Hedden, T., Venkataraman, A., Evans, K. C., Lazar, S. W., & Buckner, R. L. (2010). Intrinsic functional connectivity as a tool for human connectomics: Theory, properties, and optimization. *Journal of Neurophysiology, 103*, 297–321. doi:10.1152/jn.00783.2009

Wager, T. D. & Atlas, L. Y. (2015). The neuroscience of placebo effects: Connecting context, learning and health. *Nature Reviews Neuroscience, 16*, 403-418. doi:10.1038/nrn3976

Watson, D., & Clark, L. A. (1999). The PANAS-X: Manual for the Positive and Negative Affect Schedule-Expanded Form. Unpublished manuscript, University of Iowa, Iowa City, IA.

Watson, D. (2005). Rethinking the mood and anxiety disorders: A quantitative hierarchical model for DSM-V. *Journal of Abnormal Psychology, 114*, 522-536.

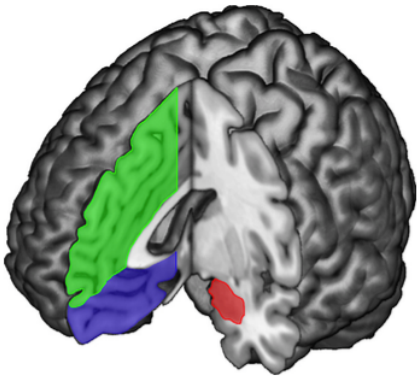
doi:10.1037/0021-843X.114.4.522

Whiteside, S. P., & Lynam, D. R. (2001). The Five Factor Model and impulsivity: Using a structural model of personality to understand impulsivity. *Personality and Individual Differences, 30*(4), 669-689. doi:10.1016/S0191-8869(00)00064-7

Young, K. S., Burklund, L. J., Torre, J. B., Saxbe, D., Lieberman, M. D., & Craske, M. G. (2017). Treatment for social anxiety disorder alters functional connectivity in emotion regulation neural circuitry. *Psychiatry Research: Neuroimaging, 261*, 44-51. doi:10.1016/j.pscychresns.2017.01.005

Zilverstand, A., Parvaz, M. A., & Goldstein, R. Z. (2017). Neuroimaging cognitive reappraisal in clinical populations to define neural targets for enhancing emotion regulation: A systematic review. *NeuroImage, 151*, 105-116. doi:10.1016/j.neuroimage.2016.06.009

Figure 1. *Amygdala and prefrontal cortex*



Note. Figure from Kim et al., 2011b; Illustrates the location of the amygdala (red) as well as a broad division of the PFC into ventromedial prefrontal cortex (blue) and dorsomedial prefrontal cortex (green).

Table 1. *Participant Demographic Information*

Variable	Participants (%)
Race/ethnicity (% Caucasian)	86.2
Mean (SD) age (years)	25.3
Annual Household Income	
Under $25,000	37.9
$25,001-$50,000	20.7
$50,001-$75,000	10.3
$75,001-$100,000	10.3
Over $100,000	10.3
Percent taking psychiatric medication	93.1
Anti-depressant (SSRI, MAOI)	82.8
Mood stabilizers	20.7
Beta blockers	0
Other anti-anxiety medication[1]	27.6

Note. n = 29; [1] Does not include SSRIs that may have been prescribed for anxiety.

Table 2. *Number of Participants in Each General Diagnostic Grouping*

Diagnostic Groups	n
Mood disorder	4
Anxiety disorder	9
Comorbid mood and anxiety	9
BPD with comorbid mood/anxiety	7

Table 3. *Number of Participants Meeting Criteria for Each Specific DSM-5 Diagnosis*

DSM-5 Diagnosis	n
Current Major Depressive Disorder	8
Current Major Depressive Episode	14
Lifetime Major Depressive Episode	29
Bipolar I or Bipolar II	6
Current Manic/Hypomanic Episode	0
Borderline Personality Disorder	7
Generalized Anxiety Disorder	21
Social Anxiety Disorder	9
Post Traumatic Stress Disorder	3
OCD	6
Panic Disorder	7
Alcohol Use Disorder	8
Substance Use Disorder	3
Eating Disorder	6
Avoidant Personality Disorder	2
Paranoid Personality Disorder	2
Dependent Personality Disorder	1
Obsessive-Compulsive Personality Disorder	3

Note. n = 29

Table 4. *Means and Reliability of Laboratory Questionnaires*

Measure and subscales	Mean (SD)	α
DASS-21	26.9 (12.3)	.90
Depression	9.8 (5.4)	.88
Anxiety	6.4 (4.2)	.72
Stress	10.8 (5.3)	.87
DERS		
Nonacceptance	18.4 (7.6)	.95
Goals	18.0 (5.1)	.91
Impulse	14.9 (6.1)	.91
Awareness	16.0 (4.9)	.80
Strategies	24.9 (8.0)	.91
Clarity	13.2 (4.6)	.84
RRS	61.1 (12.5)	.88
ERQ		
Reappraisal	23.4 (7.1)	.80
Suppression	17.9 (4.9)	.69
AAQ-II	35.6 (9.9)	.85
FFMQ		
Observe	25.2 (7.3)	.86
Describe	22.5 (8.8)	.93
Act with Awareness	21.3 (8.0)	.91
Nonjudge	18.3 (8.6)	.94
Nonreact	16.9 (5.9)	.91
UPPS-P		
Negative Urgency	29.4 (6.9)	.83
Lack of Premeditation	22.3 (4.0)	.63
Lack of Perseverance	21.4 (5.4)	.81
Sensation Seeking	30.8 (7.3)	.82
Positive Urgency	28.5 (6.1)	.77

Note. Subscales of the DERS: Nonacceptance = Nonacceptance of emotional responses, Goals = Difficulties engaging in goal directed behavior, Impulse = Impulse control difficulties, Awareness = Lack of emotional awareness, Strategies = Limited access to emotion regulation strategies, Clarity = Lack of emotional clarity; Subscales of the FFMQ: Observe = Observing, Describe = Describing, Act with Awareness = Acting with awareness, Nonjudge = Nonjudging of inner experiences, Nonreact = Nonreactivity to inner experience.

Table 5. *Study Timeline*

	Phone Screening	Session 1	Session 2	Session 3	Session 4
Study tasks completed	Initial eligibility assessment	Informed consent, diagnostic interview, self-report measures	MRI scanning, training of EMA devices and procedures, start of EMA data collection	Week 1 EMA data downloaded from all devices; compliance issues addressed, participant paid for EMA week 1	Participants paid for EMA week 2, debriefing
Payment	--	$20.00	$20.00	Up to $180.00	Up to $180.00
N in study:		N = 43	N = 32	N = 32	N = 32

Table 6. *MNI Coordinates of Regions of Interest (ROI)*

Region	Volume (mm)	Center of ROI (x y z)		
Right amygdala	1984	27	0.5	-18.8
Left amygdala	1760	-23.5	-2	-18.5
vmPFC	948	0	40	-18
ACC	5760	1	38	32

Figure 2. *Locations of ROIs in the left hemisphere*

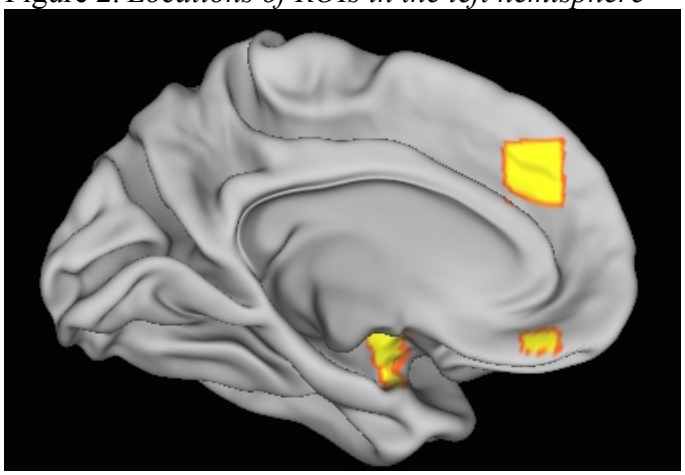


Table 7. *Correlations within Momentary Affect and Affective Instability*

	Affect					Affective Instability			
	NA	Sadness	Fear	Host	PA	NA	Sadness	Fear	Host
Affect									
NA	--								
Sadness	.81**	--							
Fear	.84**	.49**	--						
Host	.68**	.28	.60**	--					
PA	.33	.21	.25	.27	--				
Affective Instability									
NA	.68**	.39*	.67**	.65**	.26	--			
Sadness	.70**	.67**	.45*	.52**	.26	.65**	--		
Fear	.71**	.33	.90**	.57**	.03	.74**	.41*	--	
Host	.31	-.11	.27	.76**	.15	.63**	.18	.43	--
PA	.24	-.05	.30	.26	.64**	.39*	.30	.33	.31

Note. NA = negative affect total score, Sad = sadness subscale, Host = hostility subscale, PA = positive affect total score

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

Table 8. *Correlations within Momentary Behavioral Dysregulation*

Momentary Behavioral Dysregulation	Composite	Alcohol use	Binge eating	Reassurance Seeking	Self-harm	Impulsivity
Composite	--					
Alcohol use	.58**	--				
Binge Eating	.72**	.47*	--			
Reassurance Seeking	.33	-.19	-.02	--		
Self-harm	.48*	.13	.35	-.13	--	
Impulsivity	.68**	.40*	.53**	.38*	.08	--
Drug use	.50**	.43*	.13	-.03	.06	.39

Note. Composite score included alcohol use, binge eating, reassurance seeking, and self-harm

**$p < .01$, * $p < .05$, ^{t} $p \leq .10$

Table 9. *Correlations between Momentary Affect and Momentary Behavioral Dysregulation*

	Behavioral Dysregulation						
Momentary Affect	Composite	Alcohol use	Binge eating	Reassurance Seeking	Self-harm	Impulsivity	Drug use
Affect							
NA	.38*	.15	.19	.34 [t]	.05	.61**	.20
Sadness	.29	.19	.12	.21	.08	.52**	.28
Fear	.23	-.06	.08	.33 [t]	.03	.40*	.12
Hostility	.42*	.18	.27	.47**	-.02	.48**	.07
PA	-.07	-.24	.01	.13	-.04	.36*	-.10
Affective Instability							
NA	.37*	.06	.25	.36*	-.03	.73**	.27
Sadness	.50**	.20	.30	.38*	.24	.62**	.18
Fear	.15	-.16	-.06	.30	-.01	.42*	.17
Hostility	.26	-.01	.10	.43*	-.11	.55**	.15
PA	-.11	-.39*	-.09	.22	-.10	.33 [t]	-.18

Note. n = 30; NA = Negative affect total score, PA = positive affect total score; Composite score included alcohol use, binge eating, reassurance seeking and self-harm
**$p < .01$, * $p < .05$, [t] $p \leq .10$

Table 10. *Correlations between Momentary Affect and Affective Instability and Laboratory Questionnaires*

	Affect					Affective Instability				
	NA	Sad	Fear	Host	PA	NA	Sad	Fear	Host	PA
DASS	.29	.06	.30	.38 ^{t}	-.11	.44*	.07	.41*	.49*	.00
RRS	.46*	.48*	.26	.29	.07	.52**	.63**	.28	.17	.21
DERS										
NonA	.25	.33	.03	.11	.07	.24	.38*	.06	.07	.11
Goals	.41*	.18	.40*	.45*	-.09	.38	.12	.52**	.35	-.02
Impulse	.23	.02	.26	.38*	-.09	.52**	.33	.41*	.64**	.23
Aware	-.11	.33	-.03	.11	-.37 ^{t}	-.06	-.33	.10	.09	-.21
Strategies	.32	.29	.14	.41*	.00	.48*	.54**	.25	.50**	.21
Clarity	.24	.17	.19	.10	-.01	.18	.06	.11	.28	-.04
ERQ										
Reappraisal	-.37 ^{t}	-.27	-.46*	-.21	.07	-.26	-.08	-.38 ^{t}	-.11	-.07
Suppression	-.30	.18	-.42*	-.24	.24	-.29	-.05	-.43*	-.20	.07
FFMQ										
Observe	.14	.24	-.04	.03	.32	-.05	.20	-.11	-.04	.11
Describe	-.05	.01	-.11	-.24	.14	-.25	-.06	-.23	-.40*	.02
Act	-.26	-.22	-.11	-.27	-.20	-.44*	-.22	-.16	-.38 ^{t}	-.06
Nonjudge	-.30	-.38	-.14	-.23	-.34 ^{t}	-.19	-.52**	.21	-.06	-.13
Nonreact	.18	.31	-.02	.21	.28	.26	.50**	.03	.18	.17
AAQ	-.37 ^{t}	-.44*	-.22	-.26	-.11	-.43*	-.34 ^{t}	-.29	-.45*	-.25
UPPS										
Lack of premed	.13	.18	.04	.24	-.09	.17	.14	.13	.29	.05
Neg. urgency	.27	.29	.03	.43*	-.10	.48*	.29	.23	.50**	.01
Sensation seek	.07	.16	.00	-.05	.15	.17	.32	.00	-.09	.22
Lack of persev	.13	.19	-.01	-.04	.04	.28	.24	.11	.32	.15
Pos. urgency	.31	.28	.16	.40*	.07	.47*	.14	.29	.48*	.05

Note. n =27; Spearman correlations; NA = Negative affect total score, PA = positive affect total score; Subscales of the DERS: Nonacceptance = Nonacceptance of emotional responses, Goals = Difficulties engaging in goal directed behavior, Impulse = Impulse control difficulties, Awareness = Lack of emotional awareness, Strategies = Limited access to emotion regulation strategies, Clarity = Lack of emotional clarity; Subscales of the FFMQ: Observe = Observing, Describe = Describing, Act with Awareness = Acting with awareness, Nonjudge = Nonjudging of inner experiences, Nonreact = Nonreactivity to inner experience.

**$p < .01$, * $p < .05$, ^{t} $p \leq .10$

Table 11. *Correlations between Momentary Behavioral Dysregulation and Laboratory Questionnaires*

	Behavioral Dysregulation							
Questionnaires	Composite	Alcohol use	Binge eating	RS	SH	Impul.	Drug Use	Rumination
DASS	.09	.22	.02	.18	-.22	.35^{t}	.03	-.01
RRS	.36	.22	.21	.39^{t}	-.07	.50*	.24	.33
DERS								
NonA	-.01	.00	-.04	.23	-.15	.21	-.05	-.01
Goals	.21	.08	.07	-.03	.13	.37^{t}	.18	.24
Impulse	.46*	.40^{t}	.25	.01	.11	.59**	.36^{t}	.34
Aware	-.24	-.08	-.31	-.05	-.22	-.29	-.11	-.30
Strategies	.46*	.31	.23	.29	.00	.55**	.29	.29
Clarity	.24	.02	-.12	.53**	-.13	.33	.38^{t}	-.07
ERQ								
Reappraisal	.11	-.02	.16	.19	.22	-.20	-.27	-.31
Suppression	-.04	-.13	.16	.16	.11	-.25	-.32	-.18
FFMQ								
Observe	-.09	-.13	.07	.24	.04	.11	-.39^{t}	-.03
Describe	-.37	-.09	-.27	-.03	-.27	-.17	-.22	-.17
Act	-.16	-.01	-.08	-.43*	.12	-.32	-.10	.06
Nonjudge	-.28	-.24	-.42*	-.17	-.17	-.26	.03	-.44*
Nonreact	.34	.17	.42*	.18	.31	.18	-.09	.35
AAQ	-.11	-.10	.03	-.22	.24	-.37^{t}	-.21	-.37^{t}
UPPS								
Lack of premed	.14	.22	-.13	.22	-.29	.22	.19	.00
Neg. urgency	.39^{t}	.38^{t}	.22	.08	.01	.39*	.17	.08
Sensation seeking	.04	.17	-.01	.03	-.03	.17	.03	.23
Lack of persev	.14	.05	-.10	.20	-.20	.48*	.42*	-.05
Pos. urgency	-.02	-.01	-.08	.09	-.20	.26	.01	-.16

Note. N =27; Subscales of the DERS: Nonacceptance = Nonacceptance of emotional responses, Goals = Difficulties engaging in goal directed behavior, Impulse = Impulse control difficulties, Awareness = Lack of emotional awareness, Strategies = Limited access to emotion regulation strategies, Clarity = Lack of emotional clarity; Subscales of the FFMQ: Observe = Observing, Describe = Describing, Act with Awareness = Acting with awareness, Nonjudge = Nonjudging of inner experiences, Nonreact = Nonreactivity to inner experience; Composite = Alcohol use, binge eating, reassurance seeking, and self-harm

**$p < .01$, * $p < .05$, ^{t} $p \leq .10$

Table 12. *Correlations between Amygdala-vmPFC rs-FC and Momentary Affect and Affective Instability*

Momentary Affect	Mean (SD)	Right amygdala-vmPFC rs-FC	Left amygdala-vmPFC rs-FC
Affect			
Negative affect	1.45 (0.35)	.13	-.01
Sadness	1.61 (0.49)	.24	.04
Fear	1.40 (0.45)	-.09	-.18
Hostility	1.31 (0.30)	.11	.13
Positive affect	1.93 (0.51)	-.07	-.06
Affective instability			
Negative affect	0.20 (0.25)	.13	-.02
Sadness	0.50 (0.47)	.49*	.19
Fear	0.28 (0.39)	-.08	-.23
Hostility	0.27 (0.27)	.04	.05
Positive affect	0.63 (0.58)	.02	-.08

* $p < .05$

Table 13. *Correlations Between Amygdala-vmPFC Connectivity with Sadness and Anxiety After Removing Shared Variance Between Sadness and Anxiety*

	Right amygdala-vmPFC rs-FC	Left amygdala-vmPFC rs-FC
Sadness mean	.27	.20
Sadness instability	.58*	.32
Fear mean	-.42*	-.48*
Fear instability	-.46*	-.49*

* $p < .05$

Table 14. *Correlations between Amygdala-vmPFC rs-FC and Momentary Behavioral Dysregulation*

Behavioral Dysregulation	Mean (SD)	Right amygdala-vmPFC rs-FC	Left amygdala-vmPFC rs-FC
Composite	0.14 (2.91)	.45*	.32
Alcohol use	0.13 (0.23)	.33^{t}	.45*
Binge eating	0.04 (0.08)	.45*	.53**
Reassurance Seeking	0.02 (0.05)	.26	.01
Self-harm	0.00 (0.01)	.01	-.07
Impulsivity	1.21 (0.26)	.33^{t}	.18
Drug use	0.04 (0.13)	-.02	-.08

Note. BD = Behavioral dysregulation; Behavioral dysregulation variables are corrected for number of prompts completed by each participant.
**$p < .01$, * $p < .05$, ^{t} $p \leq .10$

Table 15. *Correlations between Amygdala-ACC rs-FC and Momentary Affect, Affective Instability, and Behavioral Dysregulation*

Momentary Variables	Right amygdala-ACC rs-FC	Left amygdala-ACC rs-FC
Affect		
Negative Affect	-0.28	-0.28
Sadness	-0.20	-0.31
Fear	-0.34[t]	-0.26
Hostility	-0.31	-0.22
Positive Affect	0.21	0.15
Affective Instability		
Negative affect	-0.42*	-0.12
Sadness	-0.23	-0.27
Fear	-0.40*	-0.23
Hostility	-0.33[t]	0.04
Positive Affect	0.08	0.31
Behavioral Dysregulation		
Composite	-0.12	-0.05
Alcohol use	-0.10	-0.09
Binge Eating	0.13	0.15
Reassurance seeking	-0.33[t]	-0.23
Self-harm	0.13	-0.08
Impulsivity	-0.41*	-0.11
Drug use	-0.08	-0.05

**$p < .01$, * $p < .05$, [t] $p \leq .10$

Table 16. *Correlations between vmPFC-ACC rs-FC and Momentary Affect, Affective Instability, and Behavioral Dysregulation*

Momentary Variables	vmPFC-ACC rs-FC
Affect	
Negative Affect	-0.06
Sadness	0.03
Fear	-0.20
Hostility	0.04
Positive Affect	-0.28
Affective Instability	
Negative affect	0.17
Sadness	0.20
Fear	-0.14
Hostility	0.12
Positive Affect	-0.32
Behavioral Dysregulation	
Composite	0.27
Alcohol use	0.57**
Binge Eating	0.13
Reassurance seeking	-0.08
Self-harm	0.19
Impulsivity	0.21
Drug use	0.17

**$p < .01$, * $p < .05$, ^{t} $p \leq .10$

Table 17. *Right Amygdala Seed-based Functional Connectivity*

Structure	Cluster size (voxels)	x	y	z	Z score
Positive					
Amygdala (R)	1241	26	0	-14	>8.0
Amygdala (L)		-30	-8	-14	7.71
Putamen (L)		-26	12	-10	6.78
Hippocampus (R)		26	-20	-14	6.74
Hippocampus (L)		-22	-20	-10	6.61
Putamen (R)		30	-8	2	6.42
Pallidum (R)		22	4	2	6.21
Thalamus (R)		18	-8	2	6.03
Superior temporal (R)		50	12	-22	5.69
Negative					
Occipital lobe (L)	73	-10	-68	14	6.10
Precuneus		-2	-64	38	5.43
Occipital lobe (L)	15	-26	-76	10	4.95

Note. Brain regions showing a significant positive or negative relationship with right amygdala ($p < .05$, corrected for family-wise error, extent threshold k = 10 voxels). For clusters with multiple peaks, one maxima (per each brain region) are listed. Coordinates are in MNI space.

Table 18. *Left Amygdala Seed-based Functional Connectivity*

Structure	Cluster size (voxels)	x	y	z	Z score
Positive					
Amygdala (L)	568	-22	0	-26	>8.0
Insula (L)		-30	16	-14	6.88
Putamen (L)		-22	12	-2	6.40
Fusiform (L)		-34	-20	-22	6.37
Thalamus (L)		-10	-12	2	5.43
Caudate (L)		-6	4	-6	5.12
Amygdala (R)	231	26	-4	-18	7.12
Putamen (R)		22	16	-10	6.63
Hippocampus (R)		30	-16	-18	6.43
Pallidum (R)		22	4	2	5.43
Insula (R)		38	8	-14	4.76
Negative					
Angular gyrus (R)	10	42	-44	42	5.65

Note. Brain regions showing a significant positive or negative relationship with left amygdala ($p < .05$, corrected for FWE, extent threshold k = 10 voxels). For clusters with multiple peaks, one maxima (per each brain region) are listed. Coordinates are in MNI space.

Table 19. *vmPFC Seed-based Functional Connectivity*

Structure	Cluster size (voxels)	x	y	z	Z score
Positive					
vmPFC	471	2	40	-18	>8.00
Anterior cingulate gyrus		2	44	6	6.07
Middle cingulate gyrus	51	-6	-32	30	5.62
Precuneus	17	6	-48	18	5.07

Note. Brain regions showing a significant positive or negative relationship with left amygdala ($p < .05$, corrected for FWE, extent threshold k = 10 voxels). For clusters with multiple peaks, one maxima (per each brain region) are listed. Coordinates are in MNI space.

Appendix A. Momentary surveys

Morning Report

Mood Items:

Rate degree of each emotion over the past 15 minutes on scale of 1 (very slightly or not at all) to 5 (extremely)

Negative Affect: afraid, ashamed, distressed, guilty, hostile, irritable, jittery, nervous, scared, upset, and frightened, shaky, angry, scornful, disgusted, loathing, sad, blue, downhearted, alone, lonely

Positive Affect: active, alert, attentive, determined, enthusiastic, excited, inspired, interested, proud, strong.

Impulsivity

Rating of 1 (very slightly or not at all) to 5 (extremely) over past 15 minutes.

"I felt and acted on a strong impulse"
"I did something without really thinking it through"
"I gave up easily"
"I did something for the thrill of it."

Situation and Setting:

In the PAST 15 MINUTES, WHO have you been with: (Check all that apply)

_ no one
_ partner/spouse
_ friend/acquaintance
_ other

WHERE is your current location? (Check all that apply)

_ home
_ work
_ bar/restaurant
_ outside
_ other public place
_ other

Random Assessments

Mood Items:

Rate degree of each emotion over the past 15 minutes on scale of 1 (very slightly or not at all) to 5 (extremely)

Negative Affect: afraid, ashamed, distressed, guilty, hostile, irritable, jittery, nervous, scared, upset, and frightened, shaky, angry, scornful, disgusted, loathing, sad, blue, downhearted, alone, lonely

Positive Affect: active, alert, attentive, determined, enthusiastic, excited, inspired, interested, proud, strong.

Impulsivity

Rating of 1 (very slightly or not at all) to 5 (extremely) over past 15 minutes.

"I felt and acted on a strong impulse"
"I did something without really thinking it through"
"I gave up easily"
"I did something for the thrill of it."

Behavioral Dysregulation items:

Rating of 1 (very slightly or not at all) to 5 (extremely) over past 15 minutes.

"How much are you focusing on your feelings right now?"
"How much are you focusing on your problems right now?"
"Since the last survey you answered, have you consumed alcohol?"
If yes, rating on a 1-4 scale "I drank alcohol because it would make me feel less distressed"
"Since the last survey you answered, ask someone you feel close to how they truly feel about you or whether they really care about you?"
"Since the last survey you answered, have a period of uncontrollable eating?"
"Since the last survey you answered, have you done anything to deliberately harm yourself (e.g., cutting your skin) without trying to kill yourself?"

Situation and Setting:

In the PAST 15 MINUTES, WHO have you been with: (Check all that apply)

_ no one
_ partner/spouse
_ friend/acquaintance
_ other

WHERE is your current location? (Check all that apply)

_ home
_ work
_ bar/restaurant
_ outside
_ other public place
_ other

Life events and experiences

Since the last prompt have you….
Had a disagreement (and with whom)
felt rejected (and by whom)
felt complimented or praised (and by whom)
felt "let down" by someone I depend on

experienced a loss
received bad/good news
slept (and for how long)

used caffeine (and how much)
used over the counter-medications (what and how much)
taken your medications as prescribed (if no, log changes)

Mood Change (initiated by participant)

Mood Items:

Rate degree of each emotion over the past 15 minutes on scale of 1 (very slightly or not at all) to 5 (extremely)

Negative Affect: afraid, ashamed, distressed, guilty, hostile, irritable, jittery, nervous, scared, upset, and frightened, shaky, angry, scornful, disgusted, loathing, sad, blue, downhearted, alone, lonely
Positive Affect: active, alert, attentive, determined, enthusiastic, excited, inspired, interested, proud, strong.

Impulsivity

Rating of 1 (very slightly or not at all) to 5 (extremely) over past 15 minutes.

"I felt and acted on a strong impulse"
"I did something without really thinking it through"
"I gave up easily"
"I did something for the thrill of it."

Behavioral Dysregulation items:

Rating of 1 (very slightly or not at all) to 5 (extremely) over past 15 minutes.

"How much are you focusing on your feelings right now?"
"How much are you focusing on your problems right now?"
"Since the last survey you answered, have you consumed alcohol?"
If yes, rating on a 1-4 scale "I drank alcohol because it would make me feel less distressed"
"Since the last survey you answered, ask someone you feel close to how they truly feel about you or whether they really care about you?"
"Since the last survey you answered, have a period of uncontrollable eating?"
"Since the last survey you answered, have you done anything to deliberately harm yourself (e.g., cutting your skin) without trying to kill yourself?"

Mood Change

How much did your mood change? (1 to 5)
Are you in a better or worse mood now than before?
If better,
What triggered your mood change?
Received good news
Someone complimented me

Used alcohol
Used drugs
Used prescribed medications
Had Sex
Spent time with someone close to me
Had a nice day or evening
Exercised
I did something I am proud of
Felt accepted and supported by someone
There were no triggers

If worse,
What triggered your mood change?

Lack of sleep
Argument or conflict
Used alcohol
Used drugs
Used prescribed medications
Problem at work or school
Stress
Received bad news
Upset mad at self
Felt rejected by someone
There were no triggers

Situation and Setting:

In the PAST 15 MINUTES, WHO have you been with: (Check all that apply)

_ no one
_ partner/spouse
_ friend/acquaintance
_ other

WHERE is your current location? (Check all that apply)

_ home
_ work
_ bar/restaurant
_ outside
_ other public place
_ other

VITA

Anne M. Merrill was born in Duluth, Minnesota in 1988. She graduated from Two Harbors High School in 2006. Anne received her undergraduate education at Carleton College, where she majored in Psychology and graduated in 2010. Anne began her graduate education in Clinical Psychology at the University of Missouri-Columbia in 2012. She is currently completing her pre-doctoral internship at the WJB Dorn VA Medical Center in Columbia, South Carolina.