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Affective lability and difficulties with regulation are differentially associated with amygdala and prefrontal response in women with Borderline Personality Disorder

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ABSTRACT

The present neuroimaging study investigated two aspects of difficulties with emotion associated with Borderline Personality Disorder (BPD): affective lability and difficulty regulating emotion. While these two characteristics have been previously linked to BPD symptomology, it remains unknown whether individual differences in affective lability and emotion regulation difficulties are subserved by distinct neural substrates within a BPD sample. To address this issue, sixty women diagnosed with BPD were scanned while completing a task that assessed baseline emotional reactivity as well as top-down emotion regulation. More affective instability, as measured by the Affective Lability Scale (ALS), positively correlated with greater amygdala responses on trials assessing emotional reactivity. Greater difficulties with regulating emotion, as measured by the Difficulties with Emotion Regulation Scale (DERS), was negatively correlated with left Inferior Frontal Gyrus (IFG) recruitment on trials assessing regulatory ability. These findings suggest that, within a sample of individuals with BPD, greater bottom-up amygdala activity is associated with heightened affective lability. By contrast, difficulties with emotion regulation are related to reduced IFG recruitment during emotion regulation. These results point to distinct neural mechanisms for different aspects of BPD symptomology.

1. Introduction

Borderline Personality Disorder (BPD) is characterized by strong, variable emotions and difficulties with self-regulation that impede functioning (Fletcher et al., 2014; Scott et al., 2013; Tragesser et al., 2007). Current theory suggests that emotional problems are central to BPD (Crowell et al., 2009; Jazaieri et al., 2013; Sebastian et al., 2013). Such problems manifest through intense and unstable emotions (i.e., affective lability) as well as through difficulties with top-down (i.e., volitional and cognitively-driven) emotion regulation, both within and across individuals (Linehan, 1993b; Linehan and Dexter-Mazza, 2007; Westen et al., 1997; Zittel Conklin et al., 2006). While some have concluded that affective lability and difficulties with emotion regulation are overlapping constructs (Marwaha et al., 2013), it is also possible that they are distinct, but difficult to discriminate, constructs. Consistent with this, affective instability and difficulty controlling emotions such as anger, are characterized as distinct yet meaningful diagnostic criteria for diagnosing BPD and such constructs map on closely to affective lability and difficulties with emotion regulation. The present study first sought to test whether symptomology related to affective lability and emotion regulation difficulties were related among individuals with BPD, and second, characterized these two dimensions using neuroimaging analyses focused on individual differences (Lenzenweger et al., 2008; Linehan and Dexter-Mazza, 2007).

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1.1. Affective lability in BPD

Affective lability, or the tendency to experience strong and variable emotions, disrupts functioning and well-being in BPD (Gunderson and Zanarini, 1989; Linehan, 1993a). Individuals with BPD experience greater affective lability than healthy individuals and individuals with other clinical disorders (Koenigsberg et al., 2002; Reich et al., 2012; Santangelo et al., 2014) and affective lability predicts worse outcomes, such as suicidal ideation and attempts, among individuals with BPD (Links et al., 2007; Wedig et al., 2012). While the amygdala has been linked to affective lability across various forms of psychopathology (Broome et al., 2015), the neural substrates underlying affective lability in BPD are not yet well-characterized.

The amygdala is critical for detecting, encoding and responding to social and emotional stimuli (Cunningham and Brosch, 2012; Kober et al., 2008; Phelps and LeDoux, 2005), particularly those that are ambiguous or unpredictable (Whalen, 2007). Individuals with BPD show reduced amygdala volumes compared to healthy controls (Ruocco et al., 2012; Schulze et al., 2016), and critically, have poorer white matter integrity in tracts connecting the amygdala to prefrontal regions important for regulating emotional responses (Lischke et al., 2015). Such structural alterations may explain at least in part why individuals with BPD amygdala show alterations in amygdala responses (Ruocco et al., 2013; Schulze et al., 2016), as well as amygdala habituation (Hazlett et al., 2012; Kamphausen et al., 2013), compared to healthy controls. While some studies have found that individuals with BPD show exaggerated amygdala responses when passively viewing emotional content (Donegan et al., 2003; Hazlett et al., 2012; Herpertz et al., 2001; Koenigsberg et al., 2009b; Niedtfeld et al., 2010), others have found blunted responses (Koenigsberg et al., 2009a; Smoski et al., 2011). These discrepancies might partially be due to affective lability among individuals with BPD resulting in variable amygdala responses both within and across individuals. Consistent with this, prior work has demonstrated that affective lability correlates with amygdala responses during passive viewing of aversive and neutral stimuli in BPD (Hazlett et al., 2012). This finding is intriguing but warrants follow-up because 1) it is unclear how to interpret amygdala responses to neutral images, and 2) amygdala responses were assessed solely during passive viewing and not during active regulation as well, making it unclear whether affective lability tracks with differences in bottom-up responding or top-down regulation.

In the present study, it was hypothesized that trait affective lability would track with amygdala responses during naturalistic emotional responding. Testing this hypothesis provides a critical check for models of BPD – if differences in affective lability do not correlate with amygdala recruitment in BPD, this would suggest that amygdala differences between BPD and controls are less clinically relevant than currently believed.

1.2. Difficulties with emotion regulation in BPD

Emotion dysregulation is a core feature of BPD (Fletcher et al., 2014; Scott et al., 2013; Stepp et al., 2014). In healthy adults, regulatory strategies such as reappraisal, which involves thinking about emotional events differently so as to alter their emotional import, recruit dorsal and lateral prefrontal (PFC) regions involved in cognitive control and attenuate amygdala responses (Buhle et al., 2013). Multimodal meta-analytic results have revealed something of a paradox with regards to lateral PFC in BPD – while individuals with BPD exhibit larger gray matter volumes in lateral PFC, they also show reduced lateral PFC activation (Schulze et al., 2016). With regards to reappraisal specifically, individuals with BPD report comparable reappraisal-related decreases in negative affect to controls, yet show different PFC and amygdala recruitment when reappraising (Koenigsberg et al., 2009a; Lang et al., 2012; Schulze et al., 2011). However, PFC effects differ across studies – two found that healthy controls recruited the anterior cingulate cortex (ACC) to a greater degree than did individuals with BPD during regulation (Koenigsberg et al., 2009a; Lang et al., 2012), while another found opposing results in the ACC and greater recruitment of dorsolateral and orbitofrontal cortex in healthy controls relative to individuals with BPD (Schulze et al., 2011). One possibility for these conflicting results is that prefrontal recruitment or prefrontal-amygdala functional connectivity – no work to date has examined reappraisal-related functional connectivity in BPD – during reappraisal may vary widely between different individuals with BPD and this variability has led to inconsistent findings across studies. Moreover, this variability in prefrontal recruitment might correspond to individual differences in trait difficulties in emotion regulation.

Clinical and neuroscientific evidence suggests that affective lability and difficulties with emotion regulation contribute to BPD but less is known about their neural substrates. The present study addressed this issue with a well-validated fMRI paradigm that has been used to study emotion regulation in healthy adults (Buhle et al., 2013) and individuals with BPD (Koenigsberg et al., 2009a; Lang et al., 2012; Schulze et al., 2011). In this paradigm, participants alternately respond to emotional stimuli in an unregulated way, to assess baseline emotional reactivity, or regulate their emotional responses using reappraisal (Buhle et al., 2013). Given that prior work has already compared individuals with BPD and healthy controls using this paradigm (Koenigsberg et al., 2009a; Lang et al., 2012; Schulze et al., 2011), and that the primary interest of the present study was to characterize within-disorder variability, the present study tested a large sample of women with BPD instead of comparing individuals with BPD to healthy controls. This large sample was critical for assessing individual differences (Yarkoni, 2009) and testing whether: (1) affective lability would be associated with heightened amygdala responses during naturalistic emotional responding, and (2) trait difficulties with regulating emotion would be associated with reduced prefrontal recruitment during emotion regulation.

2. Methods

2.1. Subjects

Sixty, medication-free adult females with BPD participated in this study (Table 1). Participants were a subgroup of individuals recruited through advertisements, clinician referrals and referrals from advocacy groups to be a part of a larger treatment study. All participants met DSM-IV criteria for BPD (American Psychiatric Association, 2000), as determined by the Structured Clinical Interview for DSM-IV (SCID), parts I and II (ICC=0.86). Exclusion

Table 1
Demographic characteristics of study participants.

	n	*Mean*	*SD*
Age	60	28.55	8.97
		n	%
Female		60/60	100
White		35/60	58
High school graduate or above		58/60	97
Single (includes separated and divorced)		47/60	78
Currently employed		38/60	63
History of psychiatric hospitalization		43/60	72