



## Dialectical behavior therapy alters emotion regulation and amygdala activity in patients with borderline personality disorder



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### ABSTRACT

**Objective:** Siever and Davis' (1991) psychobiological framework of borderline personality disorder (BPD) identifies affective instability (AI) as a core dimension characterized by prolonged and intense emotional reactivity. Recently, deficient amygdala habituation, defined as a change in response to repeated relative to novel unpleasant pictures within a session, has emerged as a biological correlate of AI in BPD. Dialectical behavior therapy (DBT), an evidence-based treatment, targets AI by teaching emotion-regulation skills. This study tested the hypothesis that BPD patients would exhibit decreased amygdala activation and improved habituation, as well as improved emotion regulation with standard 12-month DBT.

**Methods:** Event-related fMRI was obtained pre- and post-12-months of standard-DBT in unmedicated BPD patients. Healthy controls (HCs) were studied as a benchmark for normal amygdala activity and change over time ( $n = 11$  per diagnostic-group). During each scan, participants viewed an intermixed series of unpleasant, neutral and pleasant pictures presented twice (novel, repeat). Change in emotion regulation was measured with the Difficulty in Emotion Regulation (DERS) scale.

**Results:** fMRI results showed the predicted Group  $\times$  Time interaction: compared with HCs, BPD patients exhibited decreased amygdala activation with treatment. This post-treatment amygdala reduction in BPD was observed for all three pictures types, but particularly marked in the left hemisphere and during repeated-emotional pictures. Emotion regulation measured with the DERS significantly improved with DBT in BPD patients. Improved amygdala habituation to repeated-unpleasant pictures in patients was associated with improved overall emotional regulation measured by the DERS (total score and emotion regulation strategy use subscale).

**Conclusion:** These findings have promising treatment implications and support the notion that DBT targets amygdala hyperactivity—part of the disturbed neural circuitry underlying emotional dysregulation in BPD. Future work includes examining how DBT-induced amygdala changes interact with frontal-lobe regions implicated in emotion regulation.

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### 1. Introduction

Borderline Personality Disorder (BPD) affects 2% of the population and is characterized by impulsivity and poor affect regulation

(Links et al., 1998), and severe morbidity and mortality, including reported suicide rates 50 times the general population (Skodol et al., 2002). BPD patients experience more frequent psychiatric hospitalizations, greater use of outpatient psychotherapy and emergency room use than individuals with any other psychiatric disorder (Bender et al., 2001; Lieb et al., 2004b).

Affective Instability (AI) is responsible for the considerable morbidity across psychiatric disorders including aggression, suicidality, and disrupted relationships. AI is defined as "rapid and reactive oscillations of intense affect, with a difficulty in regulating

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these oscillations or their behavioral consequences" (Marwaha et al., 2013). It is further characterized by heightened intensity of affect, usually in negative valence, rapid affective shifts lasting minutes to hours, hypersensitivity to environmental triggers, usually interpersonal in nature and, dysregulated affect modulation (Koenigsberg, 2010; Renaud and Zacchia, 2012; Carpenter and Trull, 2013; Links et al., 2008). AI contrasts with the affective/mood dysregulation seen in major depression and bipolar disorder where the mood disorder is sustained for days to weeks and relatively autonomous of environmental triggers.

While AI is expressed in other disorders, AI is at the core of BPD and subsumes many of the diagnostic criteria including affective lability, intense anger, chronic emptiness and behaviors like suicide and self-mutilation that may reflect misguided efforts to modulate strong and aversive emotional states (Linehan, 1993). Siever and Davis' (1991) psychobiological approach to the understanding of personality disorders highlights the dimension of AI in BPD.

Linehan's Biosocial Theory (1993) conceptualization of emotional dysregulation in BPD, overlaps with the construct of AI and delineates two components: a) heightened emotional responsivity characterized by high sensitivity to emotional stimuli and heightened emotional intensity, and b) difficulties in effortful modulation of negative affect. The emotional hyper-responsivity is postulated to be biologically mediated, arising from genetic vulnerabilities, intrauterine and/or early childhood events that interact with an "invalidating" environment (Linehan, 1993), as is supported by multiple studies indicating high rates of childhood trauma and neglect in this population (Fossati et al., 1999; Goodman et al., 2004). Empirical research on emotional hyper-responsivity in BPD includes subjective reports of heightened affective experiences to various emotional stimuli such as films, audiotapes, and pictures from the International Affective Picture System (IAPS) (Arntz et al., 2000; Herpertz et al., 1999; Yen et al., 2002). More recently, the use of objective psychophysiological parameters including affective startle modulation, skin conductance, and heart rate measures of emotional arousal have been employed, also revealing heightened responsivity in BPD, e.g., (Hazlett et al., 2007; Herpertz and Koetting, 2005). The second part of Linehan's Biosocial Theory focusing on difficulties in effortful modulation of negative affect is supported by neuroimaging data demonstrating inefficient regulatory control of the amygdala by prefrontal cortex (PFC) regions (Lis et al., 2007; Minzenberg et al., 2007; Wingenfeld et al., 2009; Silbersweig et al., 2007) and dysfunctional coupling of fronto-limbic structures (New et al., 2007).

Building on the substantial literature in both animals and humans that implicates amygdala in emotional processes, including the perception and production of emotion (Davidson et al., 1999), there is growing evidence supporting the role of amygdala in the emotion processing disturbances observed in BPD. Functional magnetic resonance imaging (fMRI) studies in BPD show increased amygdala activity to specific types of stimuli, e.g., "unresolved" life events (Schmahel et al., 2006), emotional faces (Donegan et al., 2003), positive and negative emotional pictures (Herpertz et al., 2001) and emotionally-triggering scripts (Beblo et al., 2006).

More recently, our group has demonstrated exaggerated amygdala response to repeated emotional pictures in two separate BPD studies. The first, in the largest sample size of unmedicated BPD patients ( $n = 33$ ) studied with fMRI to date (Hazlett et al., 2012) were compared with healthy controls (HC) and schizotypal personality disorder (SPD) patients while viewing socially-relevant IAPS pictures. The main finding was that compared with the other two groups, BPD patients failed to show amygdala habituation to repeated emotional (unpleasant and pleasant) but not neutral pictures. The second study, (Koenigsberg et al., 2014), using a similar IAPS habituation paradigm but an avoidant personality

disorder psychiatric-control group, examined functional connectivity differences between groups. The BPD group showed greater amygdala activity to unpleasant pictures collapsed across novel and repeated conditions compared with both the HC and avoidant groups and less functional connectivity between the midposterior insula and the left and right amygdala relative to the HC group (Koenigsberg et al., 2014). Taken together, these findings suggest that affective instability in BPD may be mediated by an overactive amygdala that manifests as increased emotionality, sensitivity and slow return to baseline.

In addition to functional differences in amygdala activity, some (Driessen et al., 2000; Tebartz van Elst et al., 2003) but not all (Goldstein et al., 2009; Rusch et al., 2003) structural MRI studies report significantly smaller amygdala volumes in BPD patients compared with HCs, with discrepant findings possibly due to posttraumatic stress disorder (PTSD) comorbidity (de-Almeida et al., 2012).

Dialectical Behavior Therapy (DBT) emphasizes the role of emotion regulation (Bohus et al., 2004; Linehan et al., 1991) and targets the acquisition of skills and techniques to encourage cognitive control over maladaptive behavioral patterns (Neacsiu et al., 2010). It has achieved widespread proliferation due to its robust empirical basis and exportability and is included as a component of the APA Practice Guideline for the treatment of BPD. With over 17 randomized clinical trials, DBT is the psychotherapy approach for BPD with the largest empirical base, however, minimal data exists regarding neurobiological mechanisms of change with DBT, or the existence of specific predictors for positive treatment response (Kleindienst et al., 2011) that might guide clinician treatment decisions.

While neuroimaging and psychophysiological studies of a psychotherapeutic treatment have been conducted in major depressive disorder (MDD) (Brody et al., 2001; Goldapple et al., 2004; Mayberg, 2003), few such studies exist in BPD. A small neuroimaging pilot on DBT (Schnell and Herpertz, 2007) highlights the role of amygdala normalization. This study scanned six BPD and six HC participants at five time points over a 12-week inpatient DBT program, with an IAPS paradigm. DBT treatment response was not operationalized but rather was defined as whether two of three treatment goals were met. DBT treatment decreased activity in anterior cingulate cortex (ACC), posterior cingulate, and insula to unpleasant stimuli. DBT responders (four of six) also demonstrated diminished activation in left amygdala and bilateral hippocampus (Schnell and Herpertz, 2007).

The present study examines DBT treatment effect on emotion regulation in unmedicated outpatients with BPD as measured by changes in the Difficulties in Emotion Regulation Scale (DERS) (Gratz and Roemer, 2004) and uses an emotional processing task to investigate amygdala changes after a standard 12-month course of DBT. A yoked HC group was included as a benchmark for normal amygdala activity and change over 12 months. Given our prior finding of exaggerated amygdala response and impaired habituation to unpleasant pictures in BPD, this investigation focused on the effects of DBT on the amygdala—our *a priori* region of interest. Individual differences in treatment response were also examined with correlations between the change in emotion regulation as measured by the DERS and amygdala activity from pre- to post-DBT treatment. Lastly, we examined change in emotion regulation with the DERS, independent of the amygdala as well, comparing baseline, 6, and 12 months. We hypothesized that the BPD patients would show a decrease in amygdala reactivity following treatment, and that the magnitude of this change would be associated with improved emotion regulation as measured by the DERS. In contrast, we hypothesized that the HC group would show consistent amygdala activation over time and their emotion regulation scores on

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