



## Reduced neural differentiation between self-referential cognitive and emotional processes in women with borderline personality disorder



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### ABSTRACT

Borderline personality disorder (BPD) is associated with disturbed emotion regulation. Psychotherapeutic interventions using mindfulness elements have shown effectiveness in reducing clinical symptoms, yet little is known about their underlying neurobiology. In this functional magnetic resonance imaging (fMRI) study, 19 female BPD patients and 19 healthy controls were compared during mindful introspection, cognitive self-reflection and a neutral condition. The activation pattern in the right dorsomedial prefrontal cortex (DMPFC) in BPD patients was different from that in healthy subject when directing attention onto their emotions and bodily feelings in contrast to cognitively thinking about themselves. Mindful introspection compared with the neutral condition was associated with higher activations in bilateral motor/pre-motor regions, left inferior frontal gyrus (IFG), and left posterior cingulate cortex (PCC), while cognitive self-reflection activated the right motor and somatosensory cortex, extending into the right supramarginal gyrus (SMG) and superior temporal gyrus (STG) in BPD patients compared with the controls. Results indicate that self-referential cognitive and emotional processes are not clearly differentiated in BPD patients at the neurobiological level. In particular, altered neural mechanism underlying self-referential thinking may be related to some aspects of the typical emotion dysregulation in BPD. Current data support the finding that mindful self-focused attention is effective in regulating amygdala activity in BPD as well as in healthy subjects.

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### 1. Introduction

Borderline personality disorder (BPD) is estimated to affect about 3% of the general population (Trull et al., 2010; Bohus and Kröger, 2011). It is the most common personality disorder, accounting for 10% of all psychiatric outpatients and about 20% of inpatients (Leichsenring et al., 2011). Individuals with a diagnosis of BPD suffer from dysfunctional emotion regulation, poor impulse control, and distorted self-image (Lieb et al., 2004). Difficulties specifically in the domains of self-focused attention and in regulating internal and external experiences play a central role in the disorder (Linehan, 1993a; Linehan, 1993b; Cheavens et al., 2005). Several forms of psychotherapeutic interventions are available for

patients with BPD (Binks et al., 2006). Amongst those, Dialectical Behavior Therapy (DBT) has proved efficacious in reducing clinical symptoms in BPD (Linehan, 1993a; 2006; meta-analysis: Kliem et al., 2010). One main component of successful DBT treatment is the training of mindfulness (e.g., Feliu-Soler et al., 2014).

The main goal of mindfulness practice is to reach a mental state in which one is attentive, aware, and accepting (non-judgmental) of the present moment, without becoming over-involved in cognitive or emotional reactions (Kabat-Zinn, 2003). Generally, mindfulness is conceptualized as a meditation technique. Yet, it has also been increasingly implemented in psychotherapy (Hofmann et al., 2010). In this context, a mindfulness approach aims at developing a general attitude to face emotional situations with a focus on the current experience (Bishop et al., 2004).

The functional relationship between mindfulness skills and BPD symptoms has been investigated prominently. Evidence suggests that low abilities in mindfulness may account for BPD-specific problems in emotion regulation, interpersonal function, and

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impulsivity (e.g., Wupperman et al., 2008, 2009; Fossati et al., 2011). In a preliminary study examining the mediating effect of mindfulness on BPD symptoms, Wupperman et al. (2013) suggested that typical dysregulated behaviors observed in BPD – for instance, self-injury, substance abuse, suicide attempts, or physical aggression (American Psychiatric Association, 2000) – were associated with a low level of mindfulness. The authors assumed a link between mindfulness deficits and BPD symptom severity. However, until now, the question of causality remains unanswered.

Mindful self-focused attention has been proposed as an adaptive regulation strategy for BPD patients in dealing with daily stressors. In a laboratory setting, Sauer and Baer (2012) found positive short-term effects of mindful self-focus in patients with BPD, who either were instructed to respond either with mindful self-focused attention or with ruminative self-focused attention during a distress-tolerance task after angry mood induction. The mindfulness group demonstrated more persistent toleration of distress and reported lower levels of anger (Sauer and Baer, 2012). Despite the empirical evidence, little is known about the neurobiological mechanisms underlying the effects of mindful self-focused attention in BPD.

In healthy participants, a mindful attitude has been linked to activation patterns in the medial and lateral prefrontal cortex (M/LPFC) (Creswell et al., 2007) as well as in parietal structures associated with attention (Dickenson et al., 2013). A mindfulness-close approach (e.g., affect labeling) has been further accompanied by reduced amygdala activations, suggesting less emotional arousal (Creswell et al., 2007; Lieberman et al., 2007). Additional support in this context was also provided by our previous study, where healthy subjects performed a self-reference task by making themselves aware of their emotions, bodily feelings, or cognitions (Herwig et al., 2010). In that study, similar to the above-mentioned findings, focusing on current emotions and bodily feelings in the absence of external stimuli was associated with reduced amygdala activity and enhanced activations in the medial and ventrolateral prefrontal cortex (M/VLPFC). This very basic task of a briefly induced period of mindful self-focused attention reduced amygdala activation, which is closely linked to (emotional) arousal. Prefrontal activity was further negatively correlated with trait mindfulness, pointing to a need to use a lower level of resources in high trait-mindful participants.

Hence, in the present study, we intended to examine the neurofunctional network activated in BPD patients while applying this basic mindfulness mechanism of introspection or directing attention towards current emotions and bodily feelings, and of cognitive self-reflection. We compared the involved circuits in BPD with those in matched healthy control subjects. Mainly, we were interested in whether the mechanism of mindful self-focused attention would have a comparable regulating effect on amygdala activity and also whether it would involve a similar regulating network of prefrontal areas in patients as that earlier observed in healthy participants (Herwig et al., 2010). In patients with BPD, unpleasant emotions often arise spontaneously without any explicit external trigger and are experienced as internally generated (Linehan, 1993a). For that reason, we aimed at focusing on inner processes, without external stimulation to avoid differential reactions towards (additional) negative external stimuli in BPD. Considering emotional dysregulation and disrupted self-related awareness (Lieb et al., 2004) as core features in BPD, we hypothesized limited regulatory control of the amygdala by prefrontal regions during mindful self-focused attention in patients relative to controls. Furthermore, given the negative correlation of PFC activity with trait mindfulness in healthy participants, we expected increased activations in PFC areas in BPD compared with control participants.

## 2. Methods

### 2.1. Participants

A total of 22 female BPD patients were recruited from in- and out-patient clinics at the Zurich University Hospital for Psychiatry, Switzerland, and via mailing lists. Three of these patients had to be excluded from analysis: one patient aborted the experiment and two further patients had to be excluded due to severe movement artifacts in their functional magnetic resonance images (defined as excessive head movements with more than 3 mm in translation and/or rotation). The remaining 19 patients were matched by age with a control group of 19 healthy female volunteers. All healthy control (HC) participants were screened for Axis-I psychiatric diagnoses (exclusion criterion) using the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1998) and were free of any medication (except for oral contraceptives). The two groups did not differ in age (ages 21–43, BPD mean age = 31.11, SD = 6.29; HC mean age = 29.37, SD = 4.48;  $t(36) = 0.98$ ,  $P = 0.333$ ). All subjects were right-handed according to a handedness questionnaire (Annett, 1970). The study was restricted to females because they account for approximately 75% of BPD patients in clinical settings (Oldham, 2004) and also to avoid potential gender-based differences. BPD diagnosis was made by the referring physicians using an extensive assessment, which included structured interviews, background and previous psychiatric records. A trained psychiatrist (A.B.B. and H.S.) then confirmed the diagnosis of borderline personality disorder according to ICD-10 and DSM-IV criteria (American Psychiatric Association, 2000) based on the patient records. To determine the current degree of clinical symptoms, BPD patients also completed a short version of the Borderline Symptom List (BSL-23) (Bohus et al., 2009; German version; Wolf et al., 2009), which is a self-rating questionnaire assessing state borderline disorder-typical symptomatology. Comorbid Axis-I diagnoses were evaluated using the German version (Ackenheil et al., 1999) of the M.I.N.I. for DSM-IV (Sheehan et al., 1998). Patients were excluded if they met DSM-IV criteria for present or previous bipolar disorder, schizophrenia, or schizoaffective disorder. Due to the known high rate of comorbid psychiatric disorders in BPD (Becker et al., 2000), we did not exclude patients with current depressive episodes (Gunderson et al., 2008). We also included patients reporting occasional use of cannabinoids and alcohol (Zanarini et al., 2011), but we excluded patients with an abuse/dependency of opioids and benzodiazepines and other psychotropic drugs. Sporadic low dose use of prescribed tranquilizers/benzodiazepines was allowed (< 3 mg lorazepam or equivalents per week), and patients were asked to abstain from intake of tranquilizers, cannabinoids and alcohol for at least 48 h before scanning. Among the BPD group, 14 subjects took psychotropic medication regularly (mainly antidepressants, see Table 1). One patient additionally took pramipexole intermittently (max 0.125 mg/day) for restless legs syndrome. In all patients, the dose of medication had been qualitatively and quantitatively stable for more than 1 month according to documentation at the time of participation. (For demographic details on the patient sample, refer to Table 1.) No active substance or alcohol consumption at the time of study was reported to assess the level of depression in the patient sample, we obtained ratings on the Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960), the Montgomery-Åsberg Depression Rating Scale (MADRS) (Montgomery and Åsberg, 1979) and the Beck Depression Inventory (BDI) (Beck et al., 1961). A positive family history of psychiatric disorders was present in 68% of the patients (mostly depression).

For all participants, general exclusion criteria (previous or current neurological disorders, head trauma, pregnancy, excessive consumption of alcohol, and contraindications to magnetic

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