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The effects of social exclusion on response inhibition in borderline personality disorder and major depression

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ABSTRACT

It is a prevalent notion that borderline personality disorder (BPD) is characterized by deficits in executive functions (EF) like inhibition. Yet experimental studies yield inconsistent results. However, despite emotional dysregulation being a core feature of BPD, most paradigms did not control for emotional state or comorbid mental disorders. In the present study, subjects with BPD and comorbid MDD (BPD+MDD), with major depression (MDD) and healthy controls (HC) partook in a social exclusion paradigm combined with an inhibition task. We expected inhibition to be more strongly impaired in BPD+MDD than in depression and HC when experiencing negative emotions. Respecting inhibition, depressed patients performed best while (BPD +MDD) patients performed worst. Surprisingly, MDD & HC participants' performance improved during social exclusion, but this was not the case for BPD+MDD. Inhibition deficits were correlated with childhood trauma. These results challenge the hypothesis that an induction of negative emotion results in inferior inhibition in (BPD+MDD). Instead, patients with (BPD+MDD) seem to suffer from a more general inhibitory dysfunction. Importantly, (BPD+MDD) patients were not able to improve their performance during social exclusion like HC and MDD patients did. These findings need to be investigated further, particularly regarding the efficiency of neural networks regulating inhibition and effects of trauma.

1. Introduction

Borderline personality disorder is a debilitating mental illness which encompasses a multitude of symptoms. Core features pertain to emotional stability, interpersonal relations and impulsive behavior (American Psychiatric Association, 2013).

In the last years there has been increasing interest in executive dysfunctions (EF) as a possible key moderator in the development of BPD (Judd, 2005; Haaland and Landrø, 2009; Bazanis et al., 2002). A growing body of literature links BPD with impairments of executive functions like planning (Beblo et al., 2006; Dinn, 2004), cognitive flexibility, and inhibition (Rentrop et al., 2007; Black et al., 2009). Yet importantly, there are inconsistent results regarding a deficit concerning domains of EF in BPD (for a review see McClure et al., 2015). It has been suggested that comorbid psychopathologies like depression or ADHD could account for the mixed results. Both major depression and ADHD are often characterized by impairments in EF (for depression e.g. Aker et al., 2016; Snyder, 2013; for ADHD e.g. Salomone et al., 2016). What is more, Fertuck et al. (2006) found no differences in performance between depressed patients and depressed patients with comorbid BPD in tests of cognitive flexibility and inhibition, therefore "deficits found in previous BPD samples may reflect their susceptibility to co-occurring MDD".

Furthermore, van Eijk et al. (2015) suggested impairments in response inhibition in patients with BPD when comorbid ADHD is controlled. This was also demonstrated by Lampe et al. (2007). Likewise, a recent study by Krause-Utz et al. (2013) linked response inhibition deficits in BPD with co-occurring ADHD and furthermore emphasized the importance of the assessment of stress levels at the present time.

This argument is in accordance with clinical observations and neuropsychological studies which argue that BPD is characterized by emotional dysregulation and impulsivity, wherein emotional responses are inflexible, rigid and overarousing (Linehan, 1993; Putnam and Silk, 2005; Berlin et al., 2005). Despite the fact that disruption in emotion regulation is a core feature in BPD psychopathology, most of the

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previous neuropsychological studies did not control for a possible emotional influence on BPD patients' abilities pertaining to EF in general or response inhibition in particular. An exception is a study by Domes et al. (2006) which showed a relation of failed inhibition and unstable affect in this patient sample. It can be speculated that negative emotional context may interfere with EF such as response inhibition in BPD, leading to conflicting results in the field. For example, BPD patients did poorly in emotional Stroop tasks (Sieswerda et al., 2007; Arntz et al., 2000), negative priming and directed forgetting of negative stimuli (Domes et al., 2006), yet they performed just as well as healthy controls in an emotionally neutral Stroop design (Kunert et al., 2003). Previous studies which explored the connection of negative emotions and executive functioning usually induced cognitive stress (e.g. serial additions of numbers when faced with time pressure and noise (Krause-Utz et al., 2016, 2013, 2012)). These paradigms bare little representative status of the negative emotions and triggers for tensions of patients' everyday lives. Clinical observations and psychotherapeutic treatments rather emphasize the aspects of social and interpersonal stressors (like social exclusion) and the emotions they provoke (Linehan, 1993). In the light of interpersonal stress, BPD patients suffer from a pronounced emotional reactivity and enduring negative affect which they find hard to regulate (e.g. Bohus and Kröger, 2011).

According to neuroimaging studies (see review by Krause-Utz et al., 2014), borderline patients show structural and functional aberrations of fronto-limbic networks of fundamental importance for inhibition and affect regulation. In a study by Jacob et al. (2013), borderline patients performed just as well as HC, yet they exhibited relatively weaker activations of the inferior frontal cortex (IFC) and stronger activations of the subthalamic nucleus – allowing speculation that a recruitment of subcortical structures served as a compensation for less efficient frontal regions. Silbersweig et al. (2007) also documented decreased prefrontal activations in BPD patients who performed a Go/NoGo-task.

These findings stress the need for neuropsychological studies assessing the influence of negative emotions on response inhibition. As borderline individuals are prone to sentiments like isolation and readily feel rejected and abandoned, the Cyberball game is an especially appropriate method to induce negative emotions in this sample. It addresses core insecurities and experiences associated with the aetiology of BPD and depressive disorders (e.g. Ayduk et al., 2008; Slavich et al., 2010). There is also a significant body of research using this paradigm with BPD and MDD individuals as well as HC (e.g. Jobst et al., 2015; Domsalla et al., 2013; Otten and Jonas, 2012).

On the basis of the mentioned previous findings we expected that the induction of negative emotions by the Cyberball game results in inferior inhibitory performance in BPD patients, but not in healthy controls. To control for a possible influence of major depression on emotion regulation and response inhibition, patients with MDD were also included. As BPD is of high prevalence in women, we decided to restrict our sample to female participants.

Since BPD and major depression have high comorbidity rates (e.g. lifetime rates of occurrence at 82%, see Zanarini et al., 1998) we decided to only include BPD patients with an acute comorbid MDD.

2. Methods

2.1. Ethics statement

All experiments were approved by the Ethics Commission of the Medical Faculty, University Hospital Frankfurt and are in compliance with the Declaration of Helsinki. Written informed consent was obtained from all participants of the experiments.

2.2. Participants

22 healthy adult female volunteers (HC), 20 female patients with major depression (MDD) and 22 female patients with major depression and comorbid BPD (BPD+MDD) were recruited. Diagnoses were made in accordance with the DSM-IV-criteria. To validate the diagnostic process, SCID-I and -II interviews were performed by trained interviewers. There was no difference in the mean age between the groups ($F(2, 61) = 1.43$, $p = 0.246$, $r = 0.21$; HC: $M = 30.50$, $SD = 10.06$, MDD: $M = 31.75$, $SD = 11.34$, BPD+MDD: $M = 26.73$, SD = 8.83). All participants were right-handed and had normal or corrected-to-normal visual acuity.

The healthy control group consisted solely of college students. A quarter of the BPD+MDD patients and half of the MDD patients also were college students while respectively half of the patients had a college diploma. The pharmacotherapy administered were SSRI for approximately a third of the patient sample (BPD + MDD =8; MDD =7).

Subjects were excluded if they reported substance abuse or consumption of promethazine and benzodiazepines during the last 48 h, a history of schizophrenia and psychotic symptoms, bipolar disorder, neurological diseases, or closed head injury. All subjects additionally completed the German version of the Beck Depression Inventory (BDI-II, Hautzinger et al., 2006). Furthermore, all participants completed the short version of the Borderline Symptom List (BSL-23, Bohus et al., 2008), the Childhood Trauma Questionnaire (CTQ, Bernstein and Fink, 1998), the Borderline Personality Inventory (BPI, Leichsenring, 1997), an ADHD self-report questionnaire (Rösler et al., 2008) and the Need Threat Scale (NTS, van Beest and Williams, 2006), an account of affect and cognition during the Cyberball game. There was no assessment of intelligence, but a chi-squared test of education level yielded no significant differences between the groups.

2.3. Experimental design

The experiment encompassed three parts: the Cyberball game, a Go/NoGo Task and a rating of one's current emotional state.

Cyberball is a virtual ball-tossing game wherein participants are made to believe that they are playing with other real persons over the internet. All participants played 8 blocks of Cyberball. Each block consisted of 35 ball tosses. If the participant received the ball, they could throw it to either one of the other two players whom they selected via button press. Unbeknownst to the participants, the game was split into two conditions, namely social inclusion and exclusion, which were presented in a pseudo-randomized order. During social inclusion, participants received 33% of the total ball tosses (thus, an equal share). During social exclusion, participants received the ball only once at the beginning of each block and were then excluded for the rest of the block. After each Cyberball block subjects engaged in one block of the Go/NoGo task and one block of the rating of affect (Fig. 1).

The Go/NoGo task involved two kinds of stimuli: a NoGo stimulus (x) and Go stimuli (all other letters of the alphabet). The stimuli were presented for 1.1–1.3 s, followed by a fixation cross for 200–400 ms. Participants were instructed to respond to Go-stimuli only and as fast as possible via button press. Response inhibition is operationalized as the ability to appropriately withhold responses to NoGo stimuli. Every block of the Go/NoGo task started with 16 Go stimuli. After a break of 10 s (during which a fixation cross was displayed) 10 Go and 6 NoGo stimuli were presented in pseudo-randomized order.

The Self-Assessment Manikin (SAM) by Bradley and Lang (1994) is a non-verbal pictorial assessment technique that measures the pleasure, arousal, and dominance associated with a participant's affective reaction. In total, there were 8 ratings during the experiment.

The experiment was programmed and presented using "Presentation" (Neurobehavioral Systems, Albany, USA). A keyboard with three designated response buttons was used as input device (right hand to respond).