Disconnected self: influence of dissociation on emotional distractibility in Borderline Personality Disorder: a neuroimaging approach

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CHAPTER 6

Dissociation in Borderline Personality Disorder: Disturbed cognitive and emotional inhibition and its neural correlates

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Abstract

Background: Evidence is heterogeneous regarding whether patients with Borderline Personality Disorder (BPD) display disturbed emotional inhibition in the Emotional Stroop Task. Previous findings suggest that state dissociation may influence cognitive inhibition of task-irrelevant material, particularly with negative content. **Methods:** Our aim was to examine performance in an Emotional Stroop Task including negative, neutral, and positive words in BPD patients and healthy controls during functional magnetic resonance imaging. In advance, half of the BPD patients underwent a dissociation induction using script-driven imagery. **Results:** BPD patients without dissociation induction showed behavioral performance comparable to that of healthy controls but displayed stronger neural responses, especially to positive stimuli, in the superior temporal gyrus, dorsomedial prefrontal cortex, and anterior cingulate cortex. BPD patients with dissociation induction showed overall slower and less accurate responses as well as increased reaction times for negative versus neutral words compared with BPD patients without dissociation induction. Moreover, they showed comparatively decreased neuronal activity in the fusiform gyrus and parietal cortices independent of valence, but elevated activity in the left inferior frontal gyrus in response to negative versus neutral words. **Conclusion:** In conclusion, experimentally induced dissociation in BPD was associated with inefficient cognitive inhibition, particularly of negative stimuli, in the Emotional Stroop Task.

Keywords: Emotion, Memory, Emotional Stroop, Executive functioning, Cognitive functioning, State dissociation, Script-driven imagery

6. 1. Introduction

Emotion dysregulation is considered to be a core feature of Borderline Personality Disorder (BPD) (Koenigsberg et al., 2002; Zittel Conklin et al., 2006; Glenn and Klonsky, 2009). BPD patients have been found to show intensive and prolonged reactions to aversive stimuli (Herpertz et al., 1997; Wagner and Linehan, 1999; Stiglmayr et al., 2005). Hence, emotional information may capture more attention in BPD patients than in healthy controls, even when this emotional information is irrelevant to the target task (for a review, see Winter et al., 2014). The paradigm most often employed to study this hypothesis of impaired *emotional inhibition* is the Emotional Stroop Task (EST; Mathews and MacLeod, 1985). In the EST, participants are required to name the color of emotional or neutral words. The longer a participant takes to name the color of a word, the more the stimulus' content is thought to capture the participant's attention. Results however are heterogeneous: some studies show that BPD patients have longer reaction times compared to healthy individuals when naming emotional vs. neutral stimuli, especially for negative words (Arntz et al., 2000; Sieswerda et al., 2007; Wingenfeld et al., 2009a), but also for positive words (Sieswerda et al., 2007). In juxtaposition, other studies have not found significant differences between BPD patients and healthy controls for this paradigm (Sprock et al., 2000; Domes et al., 2006; Minzenberg et al., 2008; Wingenfeld et al., 2009b). In addition, inconsistent findings were reported when using functional magnetic resonance imaging (fMRI) to study emotional inhibition. Stronger interference of word content during color naming in the EST is usually associated with increased activity in the anterior cingulate cortex (ACC) and frontal areas including the inferior frontal gyrus (IFG) - areas (among others) active in tasks requiring to divert attention - as well as in areas involved in semantic processing such as the lateral inferior parietal cortex and the superior temporal gyrus (Whalen et al., 1998; Britton et al., 2009; Hart et al., 2010; Mincic, 2010; Ovaysikia et al., 2011). In BPD, one study found that patients lacked differential activation in relevant brain regions including the ACC and prefrontal cortex in response to negative compared to neutral stimuli, suggesting a smaller difference between emotional and neutral stimuli in the EST (Wingenfeld et al., 2009b). Using a modified EST, another study found decreased medial orbitofrontal and subgenual ACC activation as well as increased activity in the insula, dorsal ACC, and lateral orbitofrontal areas in BPD patients in comparison with healthy controls, pointing to increased recruitment of areas associated with diverting attention (Silbersweig et al., 2007). The factors that underlie these inconsistent reports have yet to be established. Some authors suggest that methodological limitations and modifications the original EST study design may explain these inconsistencies (Domes et al., 2006; Minzenberg et al., 2008; Wingenfeld et al., 2009a).

Personal stimulus relevance, anxiety, childhood trauma, Axis I comorbidity and overall prolonged reactions times in BPD may have masked a possible effect of emotional words (Domes et al., 2006; Sieswerda et al., 2007; Wingenfeld et al., 2009a).

So far, no studies have tested whether the current presence of dissociation, hereafter referred to as "state dissociation", may contribute to inconsistencies in EST performance. Dissociation is defined as a "disruption of and/or discontinuity in the normal integration of consciousness, memory, identity, emotion, perception, body representation, motor control, and behavior" (APA, 2013; p. 291). State dissociation is transiently experienced by two thirds of all BPD patients and has manifold manifestations, including derealization, depersonalization, and amnesia (Zanarini et al., 2000; Zanarini et al., 2008; Korzekwa et al., 2009). Two streams of research suggest that dissociation may influence BPD patients' EST performance. One suggests that inefficient inhibition of task-irrelevant information regardless of valence (further referred to as *cognitive inhibition*) may be a characteristic of BPD patients who exhibit high levels of state dissociation. Only one study to date has investigated the association of this cognitive function and dissociation in BPD, though it observed dissociation solely as a trait but not as a state (Haaland and Landro, 2009). This study found that BPD patients with high levels of trait dissociation performed worse than healthy controls in all tested domains, including executive functioning and, more specifically, performance on a non-emotional Stroop task. This suggests also impairments in cognitive inhibition in BPD patients with high levels of trait dissociation. In this regard, it is interesting to note that BPD patients had overall longer reaction times than healthy controls in most studies using the EST even in response to non-emotional words (Arntz et al., 2000, Domes et al., 2006, but not Wingenfeld et al., 2009b). No study so far has investigated whether this result is associated with high state dissociation in BPD. The second stream of research suggests that dissociation can have an impact on the processing of affect-laden materials. BPD patients with high levels of state dissociation lacked differential reactions to an conditioned stimulus paired with an aversive event (CS+) compared to a neutral stimulus (CS-) in an aversive conditioning paradigm (Ebner-Priemer et al., 2009). Also, state dissociation in BPD was associated with decreased startle responses but increased skin conductance in response to aversive pictures (Barnow et al., 2012). An fMRI study found that state dissociation correlated negatively with activity in the amygdala, hippocampus, ACC and insula during distraction from negative pictures in an emotional working memory task in BPD patients (Krause-Utz et al., 2012). Thus, a valence-specific effect of negative materials on cognitive inhibition may be found in BPD patients with high state dissociation.

To our knowledge, no studies have experimentally manipulated the levels of state dissociation and its effect on task-irrelevant emotional information in BPD yet.

In sum, there is a lack of evidence regarding the association of high state dissociation and (1) inefficient cognitive inhibition over task-irrelevant information and (2) a smaller difference between the inhibition of emotional content compared with neutral content in the EST in BPD. To examine these research gaps, we used personalized script-driven imagery - which has been shown to be capable of inducing high state dissociation (Lanius et al., 2002; Ludäscher et al., 2010) - combined with the EST and related memory tasks (recall and recognition). We hypothesized that dissociation induction in BPD would be associated with (1) inefficient cognitive inhibition over task-irrelevant information as reflected in overall slower reaction times and more errors in the EST and the succeeding memory tasks, as well as altered task-related neural activity e.g. in the ACC, the inferior parietal cortex, the superior temporal gyrus, and the IFG in the EST (Whalen et al., 1998; Britton et al., 2009; Hart et al., 2010; Mincic, 2010; Ovaysikia et al., 2011), and that (2) dissociation induction in BPD would be associated with smaller difference in the inhibition of negative stimuli (compared to neutral stimuli) in the EST, i.e. a smaller difference between reaction time latencies and response accuracy for negative versus neutral words, and smaller differential neuronal task-related activity in these brain regions when comparing negative to neutral words.

6.2. Methods

6.2.1. Sample

The participants comprised 40 women with BPD and 20 healthy controls (HC) between 18 and 45 years of age. Due to movement artefacts during fMRI scanning, four subjects were excluded from the analysis. The final sample included 19 HC, 19 BPD patients who did not undergo dissociation induction (BPDn), and 18 BPD patients who underwent dissociation induction (BPDd). General exclusion criteria were serious somatic illnesses, traumatic brain injuries, current and lifetime psychotic or bipolar-I disorder, psychotropic medication (within 4 weeks prior to the study), developmental disorders, substance dependency during the last year, and substance abuse within two months prior to the study. For MRI, exclusion criteria were metal implants, pregnancy, left-handedness, and claustrophobia. BPD patients had to fulfil the DSM-IV criteria for BPD, including the criterion for stress-related dissociation. Further exclusion criteria for HC were any current or previous mental disorder. BPD patients were randomly assigned to either the BPDn or BPDd group.

Clinical diagnoses were assessed by trained diagnosticians using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; Wittchen et al., 1997) and the BPD section of the International Personality Disorder Examination (IPDE; Loranger, 1999). Self-report measures included questionnaires on BPD symptom severity [Borderline Symptom List short version (BSL-23; Bohus et al., 2009)], childhood trauma [Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003)], trait dissociation [Dissociative Experience Scale (DES; Bernstein and Putnam, 1986)], severity of depressive mood [Beck Depression Inventory (BDI; Beck et al., 1961)], as well as trait and state anxiety [State Trait Anxiety Inventory (STAI; Spielberger et al., 1970)]. Questionnaire data were collected in a 3-day period before or after the experiment. Demographic data and clinical characteristics of the final sample are reported in Table 6.1.

Table 6.1.
Demographic and clinical variables (means ± standard deviation) in healthy controls (HC), Borderline Personality Disorder patients after dissociation induction (BPDd) and Borderline Personality Disorder patients without dissociation induction (BPDn)

	HC (*n*=19)	**BPDn (*n*=19)**	**BPDd (*n*=18)**	**Statistics**
Age – years	28.74 (8.07)	28.05 (7.82)	27.61 (5.95)	HC = BPDn = BPDd
BSL-23 - mean score	0.08 (0.02)	1.65 (0.62)	2.05 (0.80)	HC < BPDn = BPDd
DES - total score	3.20 (2.49)	28.74 (14.30)	32.96 (16.28)	HC < BPDn = BPDd
CTQ - total score	34.47 (11.67)	66.29 (18.97)	59.13 (25.64)	HC < BPDn = BPDd
BDI - total score	1.67 (2.22)	22.19 (11.24)	24.23 (11.78)	HC < BPDn = BPDd
STAI - trait	29.18 (4.83)	58.16 (9.80)	58.75 (7.20)	HC < BPDn = BPDd
- state	29.99 (5.48)	52.32 (9.84)	54.92 (9.59)	HC < BPDn = BPDd
Years of education, *n (%)*				
Less than 9 years	1 (5.3)	2 (10.5)	2 (11.1)	$\chi^2=3.053$
9 years	2 (10.5)	1 (5.3)	0 (0)	df=6
10 years	4 (21.1)	5 (26.3)	3 (16.7)	p= 0.802
13 years	12 (63.2)	11 (57.9)	13 (72.2)	
Co-morbidities, *n (%),*				
major depressive disorder		1 (5.3)	2 (11.1)	
dysthymia		1 (5.3)		
panic disorder		4 (21.1)	3 (16.7)	
social phobia		5 (26.3)	8 (44.4)	
specific phobia		2 (10.5)	3 (16.7)	
obsessive compulsive disorder		3 (15.8)		
posttraumatic stress disorder		7 (36.8)	8 (44.4)	
somatization disorder			1 (5.6)	
pain disorder			2 (11.1)	
unspecific somatoform disorder			1 (5.6)	
anorexia nervosa			2 (11.1)	
bulimia nervosa		1 (5.3)	1 (5.6)	
binge eating disorder			3 (16.7)	

BDI=Beck Depression Inventory; BSL-23=Borderline Symptom List-23; CTQ=Childhood Trauma Questionnaire; DES= Dissociative Experience Scale; STAI=State Trait Anxiety Inventory; RT= reaction time; Post-hoc *t*-test at $p<0.05$ Bonferroni-corrected.

State dissociation and tension were measured using the fMRI-suited DSS-4 (Stiglmayr et al., 2009). The five items in this measure ask for current depersonalization, derealization, analgesia, somatoform dissociation, and tension on a Likert scale ranging from 0 to 9.

Demographic data did not differ between the three groups. As expected, BPD patients had higher scores than HC for clinical variables (BSL-23, DES, CTQ, BDI, and STAI), whereas there were no significant differences in these clinical variables between the BPDn and the BPDd group. All subjects received monetary remuneration for participation in the study. The study was approved by the ethical board of Heidelberg University, Germany, and was conducted according to the declaration of Helsinki at the Central Institute of Mental Health in Mannheim. Written informed consent was obtained from the participants.

6.2.2. Dissociation induction

Dissociation was induced through script-driven imagery (Lanius et al., 2002; Ludäscher et al., 2010). Studies showed that this dissociation induction can lead to disruptions in mental processing, comparable to those reported in naturally occurring dissociation (Ludäscher et al., 2007; Ludäscher et al., 2010). With the help of a clinician (F.S. or D.W.), a 30-s script of a well-remembered recent autobiographical memory was prepared for each participant. For the HC and BPDn groups, an autobiographical memory of a non-emotional everyday episode was collected. For the BPDd group, an autobiographical memory of a non-trauma-related episode in which dissociation was experienced was collected. To examine the validity of the dissociation induction scripts, the finalized scripts were read back to the BPDd group and an increase of at least 1.5 on the DSS was set up as the criterion. A person, unknown to the participants, read the scripts aloud to record them on audio tape. An illustration of the study design can be found in Figure 6.1.

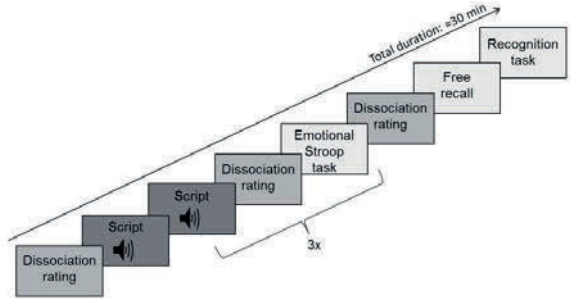

Figure 6.1. Study design–overview. The EST was presented in a block design, with 10 trials of one-word valence (negative, neutral, positive) each, and eight blocks after each script presentation. Valence order was fixed and counterbalanced to control for effects of mood carryover.

During fMRI, the script was presented via headphones, twice before the EST and two further times between the EST blocks. The rationale behind this repeated script presentation was that we aimed to maintain high levels of induced dissociation throughout the whole experiment (compensating for the fact that task performance might lead to a reduction of dissociation).
To measure the level of state dissociation, we used the DSS-4, which also includes a tension rating (0-9 Likert scale), inside the MR scanner immediately before fMRI, after each script presentation, and at the end of the EST.

6.2.3. Emotional Stroop Task

We used an adapted version of the EST (Mathews and MacLeod, 1985; Williams et al., 1996). Negative, positive and neutral words were presented in blue, red, green or yellow. Each color was assigned to a button, which participants were able to press with their right index, middle, ring, or little finger. The participants were given the task of pressing the button that corresponds to the word's printed color. Words were derived from the *Aachener Emotionale Wortliste* (Aachen's emotional word list; Böcker et al., 2014; see Supplementary Table S6.1 for information on stimulus characteristics). Twenty words were included in each category, with comparable ($p < 0.05$) word length for positive, negative, and neutral words and with comparable valence intensity for the positive and negative words. Each word was presented four times (once in each of the four colors) for 1500 ms. Blocks of 10 words of one particular valence (block design) were presented. Block order was fixed, with each valence following each other valence equally often, so that mood carryover effects were equally distributed. Inter-trial intervals between two words were jittered, ranging from 200 to 400 ms, with a mean of 300 ms. The total duration of the EST including dissociation induction was approximately 20 min, depending on the duration of the individual dissociation rating duration. Before the task began, color naming was trained in 20 trials with non-word stimuli.

Immediately after the EST and still lying inside the MR scanner, participants were asked to report all the words they remembered from the color naming task in an incidental free recall task. Subsequently, the 60 old and 60 new words comparable in word length, and valence ratings were presented randomly for a recognition task. Participants were asked to 9 report via button press if a word occurred in the color naming task or not. The software Presentation (http://nbs.neuro-bs.com/) was used for all stimulus presentations.

6.2.4. fMRI scan protocol and data analysis

MRI was conducted using a 3 Tesla Siemens TRIO-Scanner (Siemens, Erlangen). Head cushions and headphones were used to reduce head movement artefacts and scanning noise. Blood oxygen level-dependent (BOLD) signal was measured with 36 3-mm transversal slices

covering the entire brain using gradient-echo echo-planar imaging [EPI, T2-weighted contrast, field of view = 192×192 mm, voxel size 3×3×3 mm³, 64×64 voxel matrix, flip angle= 80°, spin echo time (TE) = 30 ms, inter-scan repetition time (TR) = 2000 ms]. After functional scanning, a high resolution anatomical scan as an individual template for functional data was acquired using three-dimensional magnetization prepared rapid acquisition gradient echo (MPRAGE, T1-weighted contrast, voxel size 1×1×1 mm³).

6.2.4.1. Statistical analysis of behavioral data

Means of all dissociation and tension ratings after script presentation were calculated. To check if dissociation increased in BPDd, time × group interactions of DSS-4 ratings were calculated using repeated measures analyses of variance (rm-ANOVAs), including the within-subject factor "time" (pre-script presentation, mean postscript presentation) and the between-subject factor "group" (HC, BPDn, BPDd). Post-hoc Bonferroni-corrected *t*-tests were performed in case of a significant interaction effect. To assure that, at any time during the EST, dissociation induction was sufficient, we ran the manipulation check analysis again using all DSS-4 ratings separately in the factor "time" (pre-script measurement and each of the four post-script measurements). Reaction times (RTs) in the EST and the recognition task were examined for outliers ± 2 SD, which were replaced by the mean of the group. To test for group differences and valence × group interactions in RTs and accuracy measures, rm-ANOVAs including the within-subject factor "valence" (negative, neutral, positive) and the between-subject factor "group" (HC, BPDn, BPDd) were conducted. In case of significant effects, post-hoc Bonferroni-corrected *t*-tests were applied to follow up subgroup differences between HC vs. BPDn and BPDn vs. BPDd and to follow up the interaction of valence and group regarding valence differences (negative-neutral, positive-neutral) in each group. All behavioral analyses were performed with IBM SPSS Statistics 20 (IBM, USA) with a statistical significance level of $p < 0.05$, with Greenhouse-Geisser correction when necessary.

6.2.4.2. Statistical analysis of fMRI data.

The first four volumes were discarded to minimize T1 effects. FMRI data were analyzed using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). EPI time series were preprocessed according to common practice: slice time correction, spatial realignment to the mean image to correct for head motion; coregistration onto participants' segmentated high resolution T1 scan, normalization to the standard brain of the Montreal Neurological Institute (MNI) space; and smoothing with a Gaussian kernel with a full-width at half-maximum of 6 mm. First level analyses were modeled using separate regressors for scripts, ratings, finger responses and the six motion parameters, as well as negative, neutral and positive word blocks (10 words trials per block),

correcting for global signal intensity variation and low-frequency fluctuations with a high-pass filter of 620-s cutoff. For group (second) level analyses, a full factorial model with the factors "group" (HC, BPDn, BPDd) and "valence" (negative, neutral, positive) was calculated. In this model, group differences in the neural activity while performing the EST across all valence conditions (i.e., including the regressors modelling negative, neutral and positive word blocks) were examined: Differences in neural activity between HC vs. BPDn and BPDn vs. BPDd, which were the group comparisons of interest, were analyzed via *t*-tests. In addition, differences in valence processing in each group were calculated by *t*-tests per group within the full factorial model. Also, interactions of group and valence were calculated by planned *t*-test according to the mentioned hypotheses. Whole brain second level analyses were performed with a threshold of $p < 0.001$, $k > 10$ voxel, uncorrected for multiple comparisons at the voxel level following Lieberman and Cunningham (2009) to balance Type I and Type II errors. For the central results, post-hoc correlational analyses were performed by extracting beta values from the respective peak voxel in the respective first level contrasts and correlating them with the corresponding behavioral data in SPSS.

6.2.4.3. Post-hoc analysis controlling for early childhood traumatization, depressive mood, anxiety, and tension.

Several variables have been previously described to influence EST performance (Williams et al., 1996) and thus have been considered in studies on the EST and emotional inhibition in BPD: traumatic experiences (Sieswerda et al., 2007; Wingenfeld et al., 2009a), depression (Gotlib & McCann, 1984; Gotlib & Cane, 1987), anxiety (Domes et al., 2006; Sieswerda et al., 2007) and the current state (Dorahy et al., 2005, 2006) have been associated with slower RTs to negative stimuli. Thus, post-hoc data analyses were run in order to control for the influence of clinical variables (early childhood traumatization, depressive mood, anxiety, and tension to model current emotional state) on main findings in BPD patients. To include tension as a covariate, it was necessary to correct tension ratings for dissociation ratings using partial correlations, as tension and dissociation ratings were highly correlated in the current study, indicating a high level of multicollinearity between these self-report measures (mean correlation $r = 0.727$, $p < 0.001$, when averaged across all measurements after script presentation), which is in line with previous findings and conceptualizations (Stiglmayr et al., 2008; APA, 2013). Behavioral analysis for the EST and the subsequent memory tasks, as well as fMRI data analyses of BPDn vs. BPDd, were repeated with the following covariates: CTQ, BDI, trait STAI, state STAI, and tension ratings (DSS-4 item). More details of these analyses can be found in the Supplementary material.

6.3. Results

6.3.1. Manipulation check: dissociation induction

Means, SDs and statistical analyses of dissociation and tension ratings (DSS-4scores) are summarized in Table 6.2a. There was a time × group interaction, namely that in BPDd, dissociation and tension ratings increased after dissociation induction, but no significant change in dissociation and tension ratings was observed for HC and BPDn. The interaction remained significant when considering each time point of dissociation ratings separately in the factor "time" (F4.2,112.8 = 19.40, $p < 0.001$, $\eta^2 = 0.42$; data not presented in Table 6.2a). All dissociation ratings after script presentation were higher than those before script presentation in BPDd ($p < 0.001$) and there were no such significant differences in BPDn and HC. This suggests successful experimental induction of dissociation in BPDd.

Table 6.2a.
Behavioral data of the measures of dissociation induction, the Emotional Stroop Task and related memory tasks in healthy control participants (HC), patients with Borderline Personality Disorder without dissociation induction (BPDn) or with dissociation induction (BPDd) [Means ± SD]

	HC (*n*=19)	**BPDn (*n*=19)**	**BPDd (*n*=18)**	**Main effect Group**	**Main effect Time**	**Interaction group x time**
DSS-4 dissociation						
before scripts	0.22 (4.78)	1.51 (1.68)	2.08 (1.77)	$F_{2,53}$=33.26, p<0.001, η^2=0.56	$F_{1,53}$=63.19, p<0.001, η^2=0.54	$F_{2,53}$=44.41, p<0.001, η^2=0.63
after scripts	0.20 (.41)	2.06 (2.10)	5.75 (1.81)			
Tension Ratings						
before scripts	1.47 (1.78)	3.32 (2.41)	3.83 (2.31)	$F_{2,53}$=17.72, p<0.001, η^2=0.40	$F_{1,53}$=15.54, p<0.001, η^2=0.23	$F_{2,53}$=18.11, p<0.001, η^2=0.41
after scripts	1.20 (1.85)	3.53 (2.47)	6.57 (1.91)			
Emotional Stroop Task				**Main effect Group**	**Main effect Valence**	**Interaction group x valence**
Reaction times (ms)						
negative words	684.69 (85.45)	679.36 (112.77)	836.51 (170.94)	$F_{2,53}$=6.92, p=0.002, η^2=0.20	$F_{1.7,91.1}$=13.44, p<0.001, η^2=0.20	$F_{3.4,91.1}$=5.91, p=0.001, η^2=0.18
neutral words	680.69 (91.52)	667.44 (99.91)	781.28 (158.58)			
positive words	676.59 (88.92)	673.73 (108.43)	797.41 (153.19)			
accuracy (%)						
negative words	98.88 (1.38)	98.49 (1.59)	95.69 (4.18)	$F_{2,53}$=9.06, p<0.001, η^2=0.24	$F_{1.7,89.5}$=0.47, p=0.597, η^2=0.01	$F_{3.4,89.5}$=0.98, p=0.412, η^2=0.04
neutral words	97.96 (1.51)	98.36 (1.87)	95. 97 (3.70)			
positive words	98.68 (1.21)	98.29 (1.33)	95.28 (4.63)			
Free recall (%)						
negative words	16.32 (8.31)	17.89 (10.04)	12.78 (7.90)	$F_{2,53}$=3.07, p=0.055, η^2=0.10	$F_{2,106}$=38.72, p<0.001, η^2=0.42	$F_{4,106}$=0.27, p=0.899, η^2=0.01
neutral words	5.26 (5.89)	6.58 (7.27)	2.50 (3.93)			
positive words	7.89 (6.52)	11.58 (10.94)	6.94 (7.10)			
Recognition task						
Reaction times (ms)						
negative words	868.37 (101.32)	854.25 (104.90)	954.08 (127.19)	$F_{2,53}$=4.14, p=0.021, η^2=0.14	$F_{2,106}$=5.52, p=0.005, η^2=0.10	$F_{4,106}$=0.66, p=0.620, η^2=0.02
neutral words	837.07 (102.10)	832.19 (138.51)	927.46 (129.69)			
positive words	844.19 (126.92)	861.38 (114.76)	947.14 (117.53)			
accuracy (%)						
negative words	71.32 (10.32)	75.26 (12.27)	66.94 (11.55)	$F_{2,53}$=2.29, p=0.112, η^2=0.08	$F_{2,106}$=7.16, p=0.001, η^2=0.12	$F_{4,106}$=1.31, p=0.271, η^2=0.05
neutral words	67.37 (10.94)	67.50 (44.43)	63.47 (11.79)			
positive words	67.63 (10.78)	74.87 (11.92)	66.94 (10.56)			

Note: significance level p<0.05, reaction times refer to correct responses; %=correct responses, DSS-4=Dissociation Tension Scale Short Version, ms=milliseconds, SD=standard deviation

6.3.2. Emotional Stroop Task

Descriptive statistics and interference statistics (*F*-, *t*-, *p*-values) for behavioral performance (accuracy, RTs) are summarized in Table 6.2a and Table 6.2b. Comparisons between negative-positive words are reported additionally in the Supplementary Table S6.2.

Table 6.2b.
Behavioral data of interference in the emotional Stroop task and related memory tasks in healthy control participants (HC), patients with Borderline Personality Disorder in the neutral (BPDn) or dissociation condition (BPDd) [Means ± standard deviation; reaction times refer to correct responses]

	HC (*n*=19)	**BPDn (*n*=19)**	**BPDd (*n*=18)**	**Significant post-hoc group comparison (Tukey HSD)***
Emotional Stroop task				
Reaction times - ms				
negative - neutral words	4.00 (39.36)	11.70 (29.68)	55.23 (52.08)***	BPDd>HC**,
positive – neutral words	-4.10 (32.76)	6.07 (22.61)	16.13 (29.62)*	BPDd>BPDn**
accuracy - % correct				BPDd>HC$^{(*)}$
negative - neutral words	0.92 (2.31)	0.13 (2.50)	-0.27 (2.93)	
positive – neutral words	0.72 (1.68)$^{(*)}$	-0.07 (2.58)	-0.69 (3.41)	
Free recall – % correct				
negative - neutral words	11.05 (9.51)***	11.32 (9.55)***	10.28 (7.37)***	
positive – neutral words	2.63 (8.72)	5.00 (10.80) $^{(*)}$	4.44 (7.45)*	
Recognition task				
Reaction times– ms				
negative - neutral words	31.30 (58.39)***	22.07 (59.26)	26.62 (62.20) $^{(*)}$	
positive – neutral words	14.41 (62.80)	29.20 (49.20)	19.69 (57.89)	
accuracy - % correct				
negative - neutral words	3.95 (12.73)	7.76 (8.82)**	3.47 (12.22)	
positive – neutral words	0.26 (12.66)	7.37 (7.57)***	3.47 (9.48)	

***p<.001, **p<.01, *p<.05, $^{(*)}$p<.01

The interaction of valence and group as well as the main effect of group regarding RTs in the EST were significant. Only BPDd revealed longer RTs for negative than for neutral words, while there were no significant differences between RTs to positive words and RTs to neutral words in all groups (see Figure 6.2). Figure 6.2C further illustrates that the RT difference of negative compared to neutral words was larger in BPDd than in BPDn and HC and that there was a trend for RT difference of positive compared to neutral words was in BPDd than in HC.

In addition, RTs were longer in BPDd than in BPDn, though RTs for HC and BPDn did not differ significantly (Figure 6.2A). For accuracy measures in the EST there was no significant interaction between group and valence. There was a significant group effect for accuracy. BPDd responded less accurately than BPDn in the EST, but BPDn and HC performed comparably (Figure 6.2B).

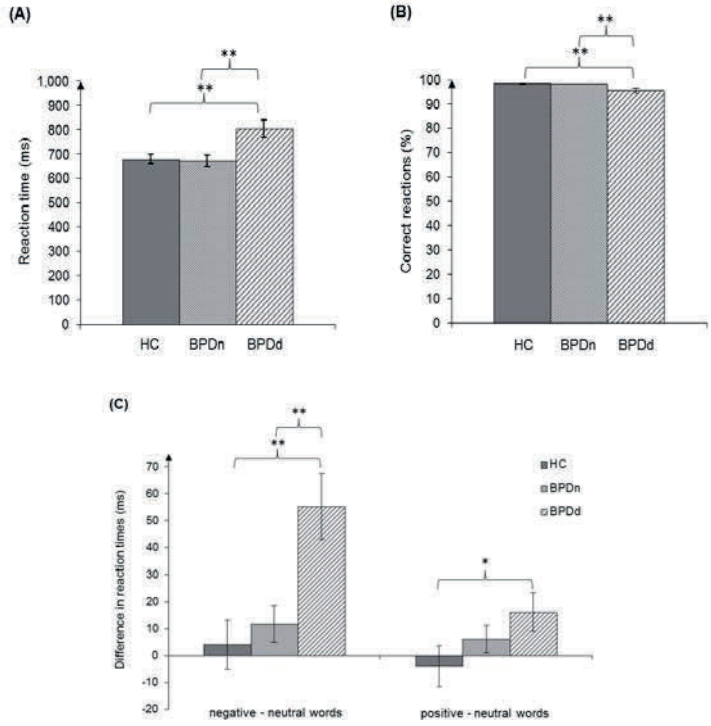

Figure 6.2. Group differences in mean reaction times (A) and accuracy (B) in the emotional Stroop task independent of stimulus valence and (C) in reaction time latencies of emotional versus neutral words in the emotional Stroop task. Note: ***p<0.001, ** p<0.01, * p<0.05, (*) p<0.10. Significance level p<0.05. BPDd= patients with Borderline Personality Disorder with dissociation induction, BPDn = patients with Borderline Personality Disorder without dissociation induction, and HC = healthy controls.

In the recall task, there was no significant interaction between valence and group. BPDd recalled fewer words than BPDn (trend towards a group effect) but word recall among BPDn and HC did not differ significantly. In the recognition task, there was no significant interaction effect between valence and group for RTs. There was a significant group effect for RTs, namely that BPDd responded slower than BPDn, while BPDn and HC performed comparably. There was neither a significant interaction effect of group and valence nor a main effect for group in accuracy in the recognition task.

6.3.4. Functional MRI during the Emotional Stroop Task

With respect to neuronal activity during EST performance, there were significant group differences across all valence conditions (see Table 6.3).

Table 6.3.
Group differences in neural activation in response to words independent of valence in the Emotional Stroop Task. Whole-brain fMRI data at a threshold of p<.001, k>10 voxel-uncorrected.

Anatomical label	BA	Cluster size	MNI x	MNI y	MNI z	*T* value (peak voxel)	*Z* value (peak voxel)
HC – BPDn							
r. cerebellum	-	20	24	-70	-50	3.85	3.76
BPDn – HC							
r. middle occipital gyrus*	18	40	30	-94	1	4.96	4.78
			21	-100	4	3.62	3.54
l. precentral gyrus	4	28	-48	-16	40	4.77	4.60
l. calcarine fissure	18	44	-15	-100	-2	4.61	4.46
l. inferior occipital gyrus	18		-27	-94	-5	4.15	4.04
l. middle occipital gyrus	19		-33	-88	4	3.43	3.37
l. inferior occipital gyrus	37	10	-39	-64	-8	4.23	4.11
l. middle occipital gyrus	39	61	-36	-70	22	4.02	3.92
l. middle occipital gyrus	19		-39	-67	7	3.81	3.72
l. middle temporal gyrus	39		-45	-64	19	3.67	3.59
BPDn – BPDd							
l. fusiform gyrus	19	20	-30	-73	-8	4.79	4.62
l. inferior temporal gyrus	37	12	-42	-64	-8	4.52	4.38
l. superior parietal lobe	7	74	-27	-55	49	4.27	4.15
			-27	-64	52	3.99	3.89
r. superior parietal lobe	7	18	27	-55	49	4.06	3.96
l. inferior parietal lobe	40	49	-45	-43	46	4.05	3.94
l. fusiform gyrus	37	51	-33	-46	-17	3.93	3.84
l. fusiform gyrus	19		-30	-49	-8	3.90	3.80
others: n.s.							

Note: BA= Brodman area; BPDd = borderline personality disorder (BPD) patients after dissociation induction; BPDn = BPD patients without dissociation induction; HC = healthy controls; l.= left; n.s. = not significant; r. = right; *would survive FWE-correction at $p<.05$ peak voxel level

BPDn showed increased activity in occipital areas and the left precentral gyrus, as well as decreased activity in the cerebellum compared with activity in HC. BPDd showed decreased brain activation in the left fusiform gyrus (Figure 6.3A), the bilateral superior parietal cortex, including the intraparietal sulcus (IPS), the inferior parietal gyrus and the temporal gyrus, when compared with BPDn. A positive correlation between neural activation in the left fusiform gyrus and RTs across all valence conditions failed statistical significance (p = 0.180). Complete results for valence differences per group can be found in Table 6.4.

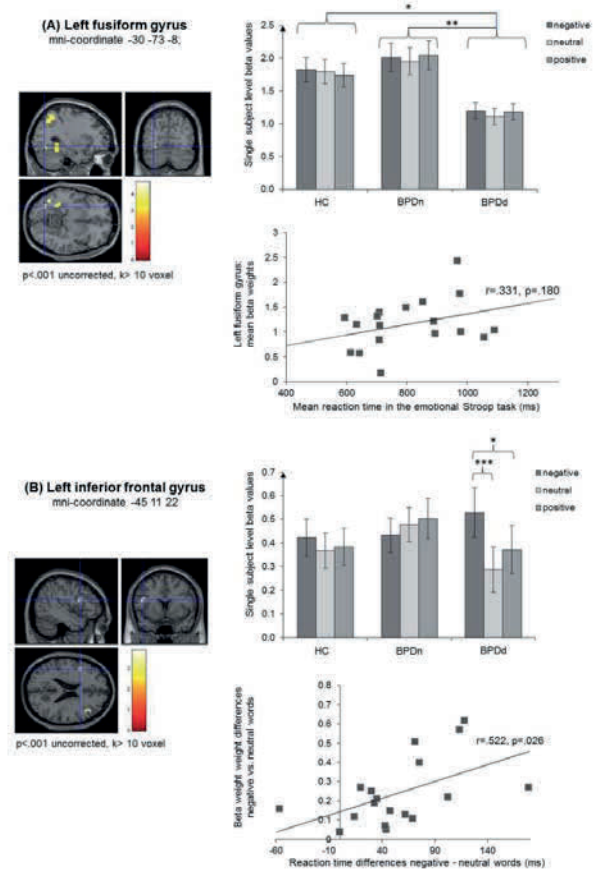

Figure 6.3. Neural activation in response to the emotional Stroop task. (A) Neural activation in response to the Emotional Stroop Task (EST) is higher in patients with borderline personality disorder who did not undergo dissociation induction (BPDn) than in patients who underwent dissociation induction (BPDd) in the left fusiform gyrus (contrast BPDd>BPDn; displayed on the left). After extracting beta values from the respective peak voxel of the single subject fMRI analysis, post-hoc analyses revealed that reduced neural activation in the left fusiform gyrus is specific for BPDd (right top) but not correlated with prolonged reaction times in the EST independent of valence. (B) Neural activation differences in response to negative compared to neutral words in the EST are larger in BPDd than in BPDn in the left inferior frontal gyrus (group level contrast $BPDd_{negative–neutral}$>$BPDn_{negative–neutral}$; displayed on the left). After extracting beta values from the respective peak voxel of the single subject fMRI analysis, post-hoc analyses revealed that this activation difference is specific for BPDd (right top) and correlates in this group with prolonged reaction times in response to negative versus neutral words (right bottom). *p<0.05, **p<0.01, and ***p<0.001, HC=healthy controls

Table 6.4. *Whole-brain data from group level analyses of the EST (p<.001, k>10 voxel uncorrected).*

Anatomical label	BA	Cluster size	MNI x	MNI y	MNI z	*T* value (peak)	*Z* value (peak)
HC: negative – neutral: n.s.							
HC: positive – neutral: n.s.							
BPDn: negative – neutral: n.s.							
BPDn: positive – neutral:							
r. superior temporal gyrus*	22	74	48	-31	4	5.58	5.32
r. superior temporal gyrus*	22	12	51	-10	-11	4.89	4.69
l. superior temporal gyrus	22	34	-54	-7	-11	4.78	4.61
r. supplementary motor area	8	18	9	17	52	4.03	3.93
l. middle temporal gyrus	22	35	-57	-43	1	3.80	3.72
			-51	-37	-2	3.67	3.59
l. orbital inferior frontal gyrus	47	10	-39	23	-14	3.67	3.59
r. superior frontal gyrus	8	11	15	29	46	3.58	3.50
r. medial superior frontal gyrus	9		9	32	40	3.44	3.37
BPDd: negative – neutral:							
l. inferior frontal gyrus	9	508	-42	11	25	5.47	5.23
/ pars triangularis*	47		-39	29	4	4.82	4.65
	46		-51	26	16	4.77	4.60
r. inferior frontal gyrus	45	47	42	23	19	4.72	4.56
l. middle occipital gyrus	19	87	-33	-79	1	4.38	4.25
	18		-30	-88	-5	3.56	3.48
l. inferior temporal gyrus	19	70	-48	-58	-11	4.34	4.22
l. fusiform gyrus	37		-36	-58	-11	3.50	3.43
l. cerebellum			-45	-64	-23	3.39	3.33
l. middle temporal gyrus	39	95	-57	-55	7	4.28	4.16
			-63	-43	7	4.14	4.02
l. superior temporal lobe	40	68	-54	-46	22	3.87	3.78
l. cerebellum			-6	-79	-26	4.20	4.08
r. cerebellum		126	3	-79	-17	3.97	3.87
r. cerebellum			24	-76	-35	4.20	4.08
			30	-79	-26	4.10	3.99
			15	-79	-29	4.02	3.92
l. middle temporal gyrus	39	25	-48	-64	19	4.08	3.97
l. medial superior frontal gyrus	9	45	-6	53	34	3.97	3.87
			-15	56	31	3.62	3.54
l. middle temporal gyrus	21	16	-54	-19	-5	3.89	3.80
r. fusiform gyrus	37	13	33	-49	-17	3.81	3.72
l. thalamus		11	-27	-22	10	3.66	3.58
l. inferior parietal lobe	7	15	-27	-73	43	3.54	3.46
l. thalamus		11	-3	-22	4	3.41	3.34
BPDd: positive – neutral: n.s.							

Note: l=left; r=right; *survive FWE-correction at *p*<.05 peak voxel level

A complete description of supra-threshold clusters for group differences in neuronal activity in response to emotional compared to neutral words is provided Table 6.5.

Table 6.5.
Group differences in neural activation in response to emotional versus neutral words in the emotional Stroop task. Whole-brain fMRI data from group level analyses at a threshold of p<.001, k>10 voxel uncorrected

Anatomical label	**BA**	**Cluster size**	**MNI**			***T* value (peak)**	***Z* value (peak)**
			x	**y**	**z**		
HC-BPDn: negative-neutral: n.s.							
HC-BPDn: positive-neutral: n.s.							
BPDn-HC: negative-neutral							
r. superior temporal gyrus	41	14	48	-7	-11	4.10	4.00
BPDn-HC positive-neutral							
r. superior temporal gyrus*	22	37	48	-31	4	4.89	4.71
			57	-22	-2	3.41	3.35
medial superior frontal gyrus	9	32	0	47	37	4.47	4.33
l. superior frontal gyrus	9	25	-18	50	34	4.31	4.19
r. anterior cingulate	32	21	12	35	16	4.23	4.11
l. medial superior frontal gyrus	10	14	-9	53	13	3.64	3.56
r. medial frontal gyrus	24	10	9	29	37	3.61	3.54
BPDn-BPDd: negative-neutral: n.s.							
BPDn-BPDd: positive-neutral: n.s.							
BPDd-BPDn: negative-neutral							
l. inferior frontal gyrus pars opercularis	9	11	-45	11	22	3.88	3.79
r. middle frontal gyrus	45	10	42	20	19	3.56	3.49
r. middle frontal gyrus	46		45	32	22	3.36	3.30
BPDd-BPDn: positive-neutral: n.s.							

Note: BA= Brodman area; l.= left; n.s. = not significant; r. = right; *would survive FWE-correction at *p*<.05 peak voxel level

For completeness, analyses comparing both emotional valences with each other are reported in the Supplementary Table S6.3. Our analysis revealed that BPDn, compared with HC, exhibited increased neuronal activity to negative vs. neutral as well as positive vs. neutral words in the right superior temporal gyrus.

They also showed increased activation in response to positive vs. neutral words in the dorsolateral (Brodmann area (BA) 9, superior frontal gyrus) and dorsomedial prefrontal cortex (BA 10/24, medial frontal gyrus) and ACCs. BPDd showed increased neuronal response to negative vs. neutral stimuli in the IFG (BA 9) and dorsolateral prefrontal cortex (BA 46, middle frontal gyrus) than did BPDn. Differences in neural activity according to valence in the left IFG per group are presented in Figure 6.3B. In BPDd, higher activation in this brain area in response to negative compared to neutral words was associated with greater RTs to negative words than to neutral words.

6.3.5. Post-hoc analysis controlling for trauma, depression, anxiety, and tension

Post-hoc behavioral analysis controlling for CTQ, BDI, trait STAI, and state STAI scores as well as tension residuals mainly confirmed the described behavioral results. The differences were the following: This analysis revealed a group effect for recall performance ($F2,48 = 3.62$, $p = 0.033$, $\eta^2 = 0.13$), with fewer words recalled in BPDd than in BPDn ($p = 0.037$) but no significant difference between word recall in BPDn and HC. Also, the group effect for RTs in the recognition task remained significant ($F2,48 = 3.92$, $p = 0.026$, $\eta^2 = 0.14$), even though post-hoc tests now only showed a trend ($p = 0.074$) for BPDd to respond more slowly than BPDn. Furthermore, the analysis revealed a trend for a group effect in recognition accuracy ($F2,48 = 2.81$, $p = 0.070$, $\eta^2 = 0.10$), with BPDd recognizing fewer words than BPDn ($p = 0.092$) and no significant difference between BPDn and HC. Comparing BPDd to BPDn in overall neural response during EST performance across all three valence conditions, the results could be replicated at a reduced threshold of $p < 0.005$, $k > 10$ voxel, uncorrected for multiple comparison (Lieberman and Cunningham, 2009), and no replication was possible for the right superior parietal lobe. With respect to the different valences, BPDd still showed enhanced neural processing of negative vs. neutral words in the left IFG and, for a reduced threshold of $p < 0.005$, $k > 10$ voxel, in the right dorsolateral prefrontal cortex (BA46, middle frontal gyrus) when compared to BPDn. No further significant group differences in valence processing were revealed in this post-hoc analysis. In sum, the major behavioral results and, at a more liberal threshold, also the neuroimaging results remained significant after controlling for CTQ, BDI, trait STAI, and state STAI scores as well as tension residuals.

6.4. Discussion

This study investigated BPD patients' performance on the EST after dissociation induction compared to those without dissociation induction and compared with healthy controls.

These were the main results:

(1) Cognitive inhibition was impeded in BPD patients only after dissociation induction. Reactions were slower and less accurate in the EST. These effects were also observed in the subsequent free recall task. Across all valences during the EST, BPD patients who did not undergo dissociation induction showed predominantly stronger occipital activity than healthy control participants. BPD patients who underwent dissociation induction exhibited reduced brain activity in the fusiform gyrus and in the inferior and parietal and temporal cortices compared to patients who did not undergo dissociation induction.

(2) With respect to altered emotional inhibition, BPD patients who did not undergo dissociation induction revealed enhanced neuronal activity in response to positive compared to neutral stimuli in the superior temporal gyrus, the dorsolateral and dorsomedial prefrontal cortex, and the ACC as compared to healthy controls. Furthermore, BPD patients revealed less inhibition of negative stimuli after dissociation induction. They demonstrated prolonged reactions in the EST and exhibited increased neuronal activity particularly in the IFG and dlPFC in response to negative stimuli when compared to BPD patients without dissociation induction.

BPD patients who did not undergo dissociation induction did not differ from healthy controls in terms of behavioral measures. On the neural level, they showed stronger activity in predominantly occipital areas compared to healthy controls. In BPD, previous studies found enhanced occipital activity during the processing (Koenigsberg et al., 2009a) as well as already during anticipation (Scherpiet et al., 2014) of emotional stimuli. These authors interpreted this finding in terms of higher vigilance for emotional stimuli. Previously, enhanced occipital activity was indeed associated with enhanced attentional requirements in visual tasks (Hopfinger et al., 2000; Kelly et al., 2008; Rauss et al., 2009). Thus, our finding may be interpreted in terms of increased recruitment of attentional resources to potentially emotional stimuli in the absence of a behavioral consequence. With respect to BPD patients after dissociation induction, the results are consistent with our first hypothesis that BPD patients show inefficient cognitive inhibition of task-irrelevant information in the EST after dissociation induction independent of stimulus valence. Our findings are in line with studies examining nonclinical participants with dissociation proneness and studies examining clinical participants with dissociative disorders, which suggests that these populations are less efficient in suppressing both emotional and non-emotional distracting material (Freyd et al., 1998; DePrince and Freyd, 1999; Elzinga et al., 2000, 2003; Chiu et al., 2010, 2012). In our study, after dissociation induction patients showed reduced activity in the fusiform gyrus.

This area has been shown to be involved in color processing (Beauchamp et al., 1999; Chao & Martin, 1999; Kellenbach et al., 2001) and word recognition (Nobre et al., 1994; Pammer et al., 2004; Binder et al., 2006), among others. Also, the superior parietal cortex was less activated in BPD patients with dissociation induction than in BPD patients without dissociation induction. The superior parietal cortex is associated with attention (LaBar et al., 1999; Schultz and Lennert, 2009), in particular language processing (Majerus et al., 2006), working memory (LaBar et al., 1999; Todd & Marois, 2004), and sensory-motor coordination (Sakai et al., 2002; Grefkes & Fink, 2005), among others. Being less activated in BPD patients after dissociation induction, the left inferior parietal cortex and the left inferior temporal gyrus have been associated with language processing (Cohen et al., 2000; Simon et al., 2002; Ravizza et al., 2004). Thus, the current findings suggest that inhibition of task-irrelevant information is less efficient in BPD patients during dissociative states, which is likely reflected in reduced activity in the fusiform gyrus as well as the superior and inferior parietal cortex.

For BPD patients without dissociation induction, our findings are consistent with previous studies which found no behavioral differences between BPD patients and healthy controls performing the EST under neutral conditions (Sprock et al., 2000; Domes et al., 2006; Minzenberg et al., 2008; Wingenfeld et al., 2009b). Nevertheless, BPD patients without dissociation induction compared with healthy controls showed enhanced neural activity in the ACC, superior temporal gyrus, dmPFC, and dlPFC, particularly in response to positive versus neutral words. These are areas associated with executive functions including interference inhibition of distracting emotional stimuli and emotion down-regulation (Whalen et al., 1998; Britton et al., 2009; Hart et al., 2010; McRae et al., 2010; Mincic, 2010; Ovaysikia et al., 2011; Kanske et al., 2011; Dorfel et al., 2014). This supports the idea that BPD patients differ from healthy controls in the processing of positive stimuli (Sieswerda et al., 2007). Our findings suggest that BPD patients may exhibit exacerbated neural processing of positive words and may recruit more neural resources to prevent the occurrence of inhibitory deficits (for positive words) on the behavioral level. One possible explanation of this may be that positive stimuli are more ambiguous for BPD patients than for healthy controls (Thome et al., 2016), which could be related to a negative self-image in BPD (Rüsch et al., 2007; Lynum et al., 2008; Kopala-Sibley et al., 2012). This ambiguity may thus lead to more interference and more recruitment of cognitive resources in the EST. We did not replicate attenuated differential activity in response to negative vs. neutral stimuli in the ACC as observed in a previous study in BPD (Wingenfeld et al., 2009b), which may be due to methodological differences in the respective study designs, such as the current study's inclusion of positive words.

After dissociation induction, BPD patients revealed prolonged reactions and heightened IFG activity in response to negative words when compared to neutral words in the EST in comparison to BPD patients without dissociation induction. Since a respective valence effect was not present in the succeeding memory tasks, our finding suggests that alterations associated with high state dissociation in BPD become selectively observable in the process of emotional inhibition. Furthermore, these findings are inconsistent with our second hypothesis that BPD patients after dissociation induction would show a smaller difference in the inhibition of negative compared to neutral information in the EST compared to BPD patients without dissociation induction. Namely, BPD patients after dissociation induction showed behaviorally less emotional inhibition of negative stimuli, which was not the case for BPD patients without dissociation induction. After dissociation induction, BPD patients compared with BPD patients without dissociation induction showed increased activity primarily in the left dorsolateral and inferior frontal gyrus (BA 9/46) in response to negative vs. neutral words. The left IFG is associated with verbal processing and executive functions such as response inhibition, especially with respect to the EST (Britton et al., 2006; Britton et al., 2009; Mincic, 2010; Ovaysikia et al., 2011) and has revealed increased neural activity in BPD patients while they listened to dissociation-inducing scripts (Ludäscher et al., 2010). Due to correlations of stronger activity in the IFG and slower reactions to negative compared to neutral words in BPD patients after dissociation induction, this neural activity may imply that these patients required more neural resources to inhibit negative, task-irrelevant stimuli less successfully. This finding suggests that the left IFG may be a neural substrate for disturbed inhibition of negative stimuli in BPD during induced dissociative states.

In sum our findings are in line with the concept presented by Dorahy (2006) for individuals with clinically relevant dissociation proneness. Dorahy argues that cognitive processes such as directing awareness are dependent on the context which the stimuli are presented in. In a threat-related context, for example, awareness may be directed to threat-related stimuli. Since dissociative states are rather aversive in BPD, it may be possible that during dissociative states the may be more prone to process negative information.

The study's main behavior results and, at a lowered threshold, fMRI results were largely replicated when measures of early childhood traumatization, depressive mood, anxiety, and the specific effect of tension were included as covariates. BPD patient groups also did not differ in demographic data, number of patients with comorbid posttraumatic stress disorder, psychometric measures, or initial dissociation and tension ratings. This suggests that these variables may not have sufficiently accounted for the observable effects.

However, it is still possible that further variables not considered may have been relevant. For example, seven and eight patients in the BPDn and BPDd groups respectively had comorbid posttraumatic stress disorder. However, due to power constraints in a possible subgroup analysis, we suggest that further studies need to address if comorbid posttraumatic stress disorder alters or even determines the influence of induced dissociation on emotional inhibition in BPD. Findings from this study cannot be generalized to all BPD patients as the study sample was composed solely of female BPD patients with high levels of trait dissociation. Thus, this study does not offer conclusions regarding how male BPD patients or those with a low tendency to dissociate perform in the EST. Also, we applied a comparatively liberal threshold for the fMRI data. Thus, a replication of the findings is particularly relevant (Lieberman and Cunningham, 2009). In addition, our stimulus material was counterbalanced for valence and emotional stimuli were comparable in valence intensity, but we did not account for stimulus arousal. Accordingly, we cannot rule out the possibility that stimulus arousal may have contributed to the findings as this was suggested before (Schimmack, 2005; Dresler et al., 2009). Further, dissociation induction may likely have induced stress or negative mood. We considered that dissociation is related to stress in BPD and that dissociation ratings are positively correlated with tension ratings in BPD patients (APA, 2000; Stiglmayr et al., 2008). Even though we attempted to correct for the specific effect of tension, shared mechanisms may account for the observable effects in this study. Since only three patients had a current episode in our study, it remains an interesting topic for future research to assess if the presence of mood disorders has an impact on dissociation induction. It may be discussed whether experimentally induced dissociation is comparable to naturally occurring dissociation. In this study, we examined that a dissociative state occurred via self-report, an approach used previously to infer the role of state dissociation in emotion processing and cognitive functioning in BPD (Ebner-Priemer et al., 2009; Barnow et al., 2012; Krause-Utz et al., 2012). The DSS-4 (Stiglmayr et al., 2009) used in our study was demonstrated to have good - excellent inner consistency and reliability, to discriminate between diagnostic groups and to be sensitive in change in symptomatology. Physiologically, higher scores in this measure were associated with higher pain thresholds (Ludäscher et al., 2010), probably corresponding to a naturally occurring dissociative symptom called analgesia (Ludäscher et al., 2007). We therefore argue that if participants show high DSS-4 scores, they experience dissociation as they would experience it naturally. However, this aspect of the current study's design remains an unaddressed and interesting question for future studies to examine if neuropsychological test performance and neural correlates of induced and naturally occurring dissociation correspond.

As the findings from this study are in line with studies in nonclinical individuals with high dissociation proneness and patients with dissociative disorders, the effects of state dissociation on cognitive and emotional inhibition may not be specific to BPD patients and may be found in other clinical populations with dissociative feature. This is particularly relevant as we did not assess the presence of dissociative disorders apart from transient dissociative states according to the IPDE in our sample. It would be interesting to replicate the finding in other samples in which dissociation can be induced, too, such as in patients with posttraumatic stress disorder or dissociative disorders. Even though we discussed our findings in the framework of inhibition of task-irrelevant material, we cannot infer which specific process is altered by dissociation. It may well be that dissociation is already associated with impaired processing of emotional content or so called "over-modulation" (Lanius et al., 2010) or response execution, which may have led to e.g. longer reaction times in our study. Further studies need to clarify this issue, dismantling the effect of (induced) dissociation on sensory processing, emotion processing, executive functioning, learning and memory as well as motor responding.

In summary, the current study suggests that BPD patients under induced dissociative states show inefficient cognitive inhibition of task-relevant material and impaired inhibition of negative stimuli. These findings offer first experimental evidence for impaired emotional and non-emotional inhibition during high state dissociation in BPD. Thus, we recommend that state dissociation should be measured in studies examining cognitive functioning in BPD. Also, if replicated, the findings of this study may have implications for psychotherapy in BPD patients as these individuals may have difficulty in adequately processing new information and emotional experiences during high state dissociation. This may be a contributing factor regarding the tendency of BPD patients who to show high state dissociation to be predictive of poor psychotherapy outcome (Kleindienst et al., 2011; Kleindienst et al., 2016).

Future studies are therefore needed to clarify which processes are relevant for psychotherapy as well as the maintenance of BPD psychopathology (such as emotion regulation and emotional learning) and whether they are affected by high state dissociation.

Conflict of interest:
None.

Supplementary material

Table S6.1.

Length, valence and frequency of the word stimuli derived from the German Aachener Emotionale Wortliste (Aachen's emotional word list; Böcker, Gruber, Gauggel, in preparation)

	Length		Valence		Frequency	
	letters	*Sd*	*-3 to 3*[a]	*Sd*	*Log*	*Sd*
Negative words						
Emotional Stroop task	5.05	0.80	-1.84	0.30	0.97	0.44
Recognition task	5.05	0.78	-.194	0.38	0.97	0.50
Neutral words						
Emotional Stroop task	5.05	0.80	0.23	0.15	0.97	0.45
Recognition task	5.05	0.78	0.22	0.12	1.07	0.47
Positive words						
Emotional Stroop task	5.05	0.80	1.62	0.21	0.97	0.46
Recognition task	5.05	0.78	1.30	0.27	1.14	0.47

[a]data was collected on a 7-point scale ranging from 1 to 7 and transformed to a scale ranging from -3 to + 3 to assure comparability between valences

Additional information: Post hoc analysis controlling for early childhood traumatization, depressive symptoms, anxiety, and tension.

To control for the influence of early childhood traumatization, depressive symptoms, state and trait anxiety, as well as tension on main findings, the following reanalysis was applied: first, tension ratings were corrected for dissociation ratings, as both measures were highly correlated in the current study (mean correlation r=.727, p<.001, when averaged across all measurements after script presentation). We used a regression analysis with tension ratings as the dependent variable and DSS-4 ratings as independent variable and extracted the unstandardized residuals per participants. Then, the following analyses were performed at the same statistical significance levels as in the respective analyses of behavioral and fMRI data.

Behavioral data. For the dependent measures of the EST and the subsequent memory tasks, rm-ANOVAS were repeated with CTQ, BDI, trait STAI, and state STAI values as well as with tension residuals as covariates.

fMRI data. As it is not possible in SPM8 to include multiple covariates in the ANOVA group level model we used for the fMRI analysis, we needed to calculate the respective contrasts at single subject level (see below for model and test specifications for the group comparison across and considering differential activity between valences in the EST).

Then, at group level, we only repeated the contrast BPDn vs. BPDd and renounced the analysis of HC vs. BPDn as here, group differences in the designated covariates may mask an effect of group in the reanalysis so that the results are not interpretable. In order to include covariates for overall emotional Stroop task performance group comparison (independent of valence), a new single subject level model needed to be calculated as it is not possible in SPM8 to include multiple covariates in the ANOVA group level model we used for the fMRI analysis. This model included one regressor each for scripts, ratings, and responses as well as only one regressor for all task blocks instead of three separate regressors for blocks of each valence. Afterwards, between groups comparison was performed between BPDn and BPDd using a t-test for independent samples with CTQ, BDI, STAI state, and STAI trait values as well as tension residuals per participant as covariates. We did not calculate the contrasts of HC vs. BPDn as group differences in the designated covariates may mask an effect of group in the reanalysis so that the results are not interpretable. To be able to include covariates for group comparisons of valence effects, first contrast between responses to negative vs. neutral and positive vs. neutral words were calculated on single subject level for the original single subject model. Second, for group level comparison between BPDn vs. BPDd, independent sample t-tests with CTQ-, BDI-, STAI state, and STAI trait values as well as tension residuals per participant as covariates were conducted. We again did not calculate the contrasts of HC vs. BPDn as group differences in the designated covariates may mask an effect of group in the reanalysis so that the results are not interpretable.

Table S6.2.

Behavioral data of interference of negative compared to positive stimuli in the EST and related memory tasks in healthy control participants (HC), BPD patients in the neutral (BPDn) or dissociation condition (BPDd) [Means ± SD; reaction times refer to correct responses]

	HC (*n*=19)	**BPDn (*n*=19)**	**BPDd (*n*=18)**	**Significant post-hoc group comparison (Tukey HSD)***
Emotional Stroop task				
Reaction times **-** ms	8.10 (23.96)	5.63 (27.34)	39.10 (50.26)**	BPDd>HC*, BPDd>BPDn*
accuracy **-** % correct	0.20 (1.63)	0.20 (1.92)	0.42 (1.82)	
Free recall – % correct	8.42 (8.17) ***	6.32 (11.65)*	5.83 (9.89)*	
Recognition task				
Reaction times – ms	24.18 (77.57)	-7.13 (54.45)	6.93 (63.83)	
accuracy **-** % correct	3.68 (8.31) (*)	0.40 (10.04)	0.00 (9.96)	

***p<.001, **p<.01, *p<.05, (*)p<.10

Table S6.3.

Neural activation in response to negative versus positive words in the emotional Stroop task per group and in group comparison.

Anatomical label	BA	Cluster size	MNI x	y	z	*T* value (peak voxel)	*Z* value (peak voxel)
HC negative –positive: n.s.							
HC positive – negative: n.s.							
BPDn negative – positive: n.s.							
BPDn positive – negative: n.s.							
BPDd negative – positive:							
r. cerebellum		51	27	-76	-32	4.50	4.36
l. inferior frontal gyrus	9	14	-42	11	25	4.08	3.98
l. inferior frontal gyrus	47	49	-36	26	4	4.02	3.92
			-42	32	1	3.88	3.78
r. anterior cingulate	33	15	6	5	25	3.99	3.89
r. superior frontal gyrus	6	17	9	11	64	3.91	3.81
l. putamen		11	-18	14	10	3.90	3.81
l. cerebellum		13	-39	-58	-26	3.69	3.61
medial cerebellum		41	0	-55	-47	3.63	3.55
			-3	-49	-38	3.62	3.54
			6	-52	-38	3.56	3.49
medial cerebellum		13	6	-76	-17	3.49	3.42
			-3	-76	-11	3.38	3.32
l. inferior parietal lobe	40	12	-54	-46	22	3.47	3.41
BPDd: positive - negative: n.s.							
BPDn-HC: neg. – positive: n.s.							
BPDn-HC: positive – neg.: n.s.							
BPDd-BPDn:negative –positive:							
r. Pons		10	12	-40	-41	3.71	3.63
l. Putamen		11	-18	8	-2	3.51	3.44
BPDd-BPDn: positive -neg.: n.s.							

Note: Whole-brain fMRI data from group level analyses at a threshold of $p<.001$, $k>10$ voxel uncorrected; BA= Brodman area; BPDd = borderline personality disorder after dissociation induction; BPDn = borderline personality disorder without dissociation induction; HC = healthy control participants; l.= left; n.s. = not significant; r. = right