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Dissociation proneness and pain hyposensitivity in current and remitted borderline personality disorder

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Abstract

Background: Stress-related dissociation has been shown to negatively co-vary with pain perception in current borderline personality disorder (cBPD). While remission of the disorder (rBPD) is associated with normalized pain perception, it remains unclear whether dissociation proneness is still enhanced in this group and how this feature interacts with pain sensitivity.

Methods: Twenty-five cBPD patients, 20 rBPD patients and 24 healthy controls (HC) participated in an experiment using the script-driven imagery approach. We presented a personalized stressful and neutral narrative. After listening to the scripts, dissociation and heat pain thresholds (HPT) were assessed.

Results: Compared to HC, cBPD patients showed enhanced dissociation and exhibited significantly enhanced HPT in the neutral condition, whereas rBPD participants were in between. After listening to the stress script, both clinical groups exhibited enhanced dissociation scores. Current BPD participants responded with significantly higher HPT, whereas rBPD only showed a trend in the same direction. However, both BPD groups showed significantly increased HPT compared to the HC in the stress condition, but did not differ from each other. Dissociation proneness correlated significantly positively with pain hyposensitivity only in cBPD.

Conclusion: Dissociation proneness is enhanced in both BPD groups. This feature is clearly positively related to pain hyposensitivity in cBPD, but not in rBPD. However, the data indicate that stress causes the pain perception in rBPD to drift away from that obtained in HC. These results highlight the volatile state of BPD remission and might have important implications for the care of BPD patients in the remitted stage.

Significance: Both current (cBPD) and remitted borderline personality disorder (rBPD) patients show enhanced proneness to dissociation. This feature is significantly linked with pain hyposensitivity in cBPD in a paradigm that induces stress using a script-driven imagery approach, whereas this connection cannot be observed in rBPD. However, in the stress compared to the neutral condition, rBPD participants also show

Robin Bekrater-Bodmann and Herta Flor contributed equally.

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pain hyposensitivity compared to healthy controls. This study provides new insights into the pain processing mechanisms of BPD and its remission.

1 | INTRODUCTION

Borderline personality disorder (BPD) is characterized by a prolonged pattern of maladaptive behaviour, including impairments in self-image, interpersonal functioning, affectivity and inhibition (American Psychiatric Association, 2013). Another prominent BPD feature is pain hyposensitivity, which has been demonstrated using various types of stimulation procedures (e.g. Bekrater-Bodmann et al., 2015; Ludäscher et al., 2007; Ludäscher et al., 2010; Schmahl, Elzinga, et al., 2004; Schmahl, Greffrath, et al., 2004), and which appears to be specific for BPD compared to other stress-related mental disorders (Schmahl et al., 2010). Pain hyposensitivity is positively related to dissociation (Bohus et al., 2000; Ludäscher et al., 2007), describing perceived detachment from reality in a dysfunctional attempt to cope with emotional stress. Self-injurious behaviour, involving the infliction of pain on oneself (e.g. Bohus et al., 2000; Ludäscher et al., 2007) is often performed to release the aversive tension associated with dissociation (Kleindienst et al., 2008; Schmahl & Baumgartner, 2015) and is not perceived as painful. Since BPD is often associated with early traumatic stress, pain hyposensitivity has been viewed as an acquired coping response (Bohus et al., 2000).

Only a few studies investigated the course of BPD, which is often characterized by symptomatic remission defined as a state in which patients no longer fulfilled diagnostic BPD criteria for at least 2 years. About 99% of BPD patients fulfilled at least temporarily the remission criteria over the course of 16 years. However, recurrence of the disorder can be observed in up to 36% of the cases (Zanarini, Frankenburg, Reich, & Fitzmaurice, 2012). Thus, the state of BPD remission seems rather elusive in terms of stable clinical improvement.

Pain perception, at least to a certain degree, returns to normal when BPD is remitted (Bekrater-Bodmann et al., 2015), with heat pain thresholds (HPT) no longer being statistically different from those of healthy controls (HC). However, recent findings revealed enhanced stress responsivity in remitted BPD compared to HC, as remitted BPD patients react with an increased urge for self-injurious behaviour to the induction of stress (Willis et al., 2018). Thus, despite symptomatic remission, stress regulation deficits may still exist in remitted BPD. However, while previous studies investigated the stress-relieving effect of pain (Willis et al., 2018) in current (cBPD) and remitted BPD (rBPD) patients, it remains open whether pain perception in both groups is differentially influenced by dissociation proneness. The responses in rBPD are of particular importance in this context, because these might give insight into the nature of still existing stress regulation deficits in symptomatic BPD remission.

In this study, we investigated HPT in both cBPD and rBPD patients and its relationship to the response to the experimental induction of dissociation by script-driven imagery (Ludäscher et al., 2010; Shalev, Orr, & Pitman, 1992). In order to evaluate specificity of the expected findings for the pain domain, we also assessed warm perception thresholds. We hypothesized that HC would show significant differences in dissociation and pain sensitivity compared to cBPD patients in a neutral condition, whereas rBPD would not differ from HC. However, for the stress condition, we hypothesized that rBPD patients should respond similarly to the cBPD patients with enhanced dissociation and elevated pain thresholds, whereas HC should not show changes in these measures. We further expected a significant positive relationship between dissociation proneness and pain hyposensitivity in both BPD groups.

2 | METHODS

2.1 | Participants

Participants with current BPD were recruited from online announcements, flyers and the pool of in- and out-patients of the Department of Psychosomatic Medicine and Psychotherapy at the Central Institute of Mental Health and of the Department of General Psychiatry at the University of Heidelberg. Remitted BPD patients from the pool of patients formerly treated at the Central Institute of Mental Health were asked to participate in the study, whereas HC were recruited through the local resident's registration office. Recruitment of all participants in our study was undertaken by the central office of the KFO 256, a Clinical Research Unit funded by the German Research Foundation (DFG) for investigating the mechanism of disturbed emotion processing in BPD (Schmahl et al., 2014). Hence, all projects linked to the KFO 256 included participants from a joint database.

We performed an a priori sample size calculation based on large effects for script-driven imagery on pain in cBPD (Ludäscher et al., 2010; Cohen's $d = 1.46$). For rBPD, we only can estimate this effect and assume a smaller one of $d = 1$. HC and rBPD previously showed a medium effect size for differences in pain perception (Bekrater-Bodmann et al., 2015; $d = 0.48$). The linear relationship between dissociation and pain perception in cBPD has been shown to be medium to large (r between .54 and .83, mean $r = .69$; Bekrater-Bodmann et al., 2015; Ludäscher et al., 2007); given the low levels and low variance of dissociation in rBPD, the previously reported non-significant relationships with pain

(Bekrater-Bodmann et al., 2015) have to be evaluated with care so that we assume in our dissociation induction experiment a mean correlation of at least $r = .55$. Assuming an α of .05 and a power of 80%, at least 19 participants per group had to be included to detect the smallest of expected effects (G*Power v3.1.9.4, Faul, Erdfelder, Buchner, & Lang, 2009).

In total, we included 69 participants, 25 with cBPD (mean (M) age = 27.44 years, standard deviation (SD) = 6.87), 20 with rBPD (M age = 30.10 years; SD = 4.83) and 24 HC (M age = 27.67 years; SD = 5.75). All participants were female and there was no significant group difference in age, $F_{2,66} = 1.31$, $p = .28$. Except for two left-handed and three ambidextrous rBPD subjects as well as three subjects with missing data (two cBPD, one HC), all participants were right-handers by self-report. Eighteen (72%) patients with cBPD, 15 (75%) participants with rBPD and seven (29%) HC had already participated in another study on pain perception (Bekrater-Bodmann et al., 2015). All participants were fluent in the German language.

The diagnosis of BPD according to DSM-5 (American Psychiatric Association, 2013) was assessed with the International Personality Disorder Examination (IPDE; Loranger, 1999). Trained psychologists with at least a master's degree conducted the assessments. Participants had to fulfil five or more IPDE criteria for at least the last 5 years for inclusion in the cBPD group, whereas participants who had fulfilled full BPD diagnostic criteria (i.e. IPDE ≥ 5 criteria) once in their life and who fulfilled three or less criteria throughout 2 years prior to participation were considered rBPD. Particularly, self-harming behaviour must not have been shown more than twice within the last 2 years (in the present rBPD sample, only one patient reported such behaviour in the last 12 months, whereas all cBPD patients answered this question in the affirmative, according to a custom-made self-rating questionnaire for the assessment of NSSI behaviour (Kleindienst et al., 2008; Reitz et al., 2015; Willis et al., 2018). The validity of the criteria for symptomatic remission was confirmed by a previous longitudinal BPD study (Zanarini et al., 2014). However, symptomatic remission of BPD cannot be regarded as the recovery of the disorder (Zanarini et al., 2014). We did not include participants with scars at the palmar side of the hands due to the potential interference with painful stimulation. Further exclusion criteria were a lifetime diagnosis of schizophrenia or bipolar-I disorder, substance dependence within 2 years prior to study participation, current substance abuse, pregnancy, history of epilepsy, brain trauma or tumour or other significant neurological or medical conditions. Highly potent psychotropic medication (such as neuroleptics) had to be discontinued at least 2 weeks and pro re nata medication (such as sedative-hypnotics or benzodiazepines) at least 2 days before and throughout study participation. Selective serotonin reuptake inhibitors (SSRIs) were allowed to be taken during study participation (in this study, three cBPD and one rBPD subjects reported current intake of SSRIs), as SSRIs are often used to treat anxiety disorders and

depression commonly co-occurring with BPD (Ripoll, 2013; Stoffers & Lieb, 2015), and thus, discontinuation is not recommended. Current and lifetime comorbid mental disorders and medication of the participants are given in Table 1. The study was approved by the ethics review board of the Medical Faculty Mannheim, Heidelberg University, and adhered to the Declaration of Helsinki in its current form. All participants gave written informed consent before study participation.

2.2 | Script-driven imagery

Script-driven imagery has been previously used to experimentally induce dissociation in cBPD patients (Barnow et al., 2012; Bichescu-Burian, Steyer, Steinert, Grieb, & Tschoke, 2017; Krause-Utz et al., 2018; Ludäscher et al., 2010; Winter et al., 2015). This approach has been shown to activate memories, which can be evaluated using affective self-report measures and psychophysiological assessments (Bichescu-Burian et al., 2017). Since mentally imagined interaction with a stimulus can induce similar emotional reactions as a real interaction with the same stimulus (Lang, 1979), our subjects were instructed to vividly imagine autobiographical events. For this purpose, the participants were asked to describe autobiographical situations in which they experienced low or high tension due to emotional stress. The order of script preparation (neutral first) was fixed. After giving the instruction for preparing a script, the subjects completed the short version of the Dissociation Tension Scale (DSS-4; Stiglmayr, Schmahl, Bremner, Bohus, & Ebner-Priemer, 2009) to assess the baseline level of dissociation. The DSS-4 is the short form of the Dissociation-Tension Scale acute (DSS-acute; Stiglmayr, Braakmann, Haaf, Stieglitz, & Bohus, 2003), and represents an instrument for repeated assessment of dissociation during experimental and real-life settings. The DSS-4 contains four items that assess somatoform dissociation (reduced auditory sensory perception), analgesia, depersonalization and derealization. Dissociation scores are calculated as means of these four items of the DSS-4. Then, the investigator started to ask for some examples of emotionally neutral situations in the participant's daily life, along with additional questions about experiences in a specific situation in the recent past. The participant was asked to detail the situation and it was assessed how (a) stressful, (b) relevant for her personal life and (c) emotionally upsetting the situation was using a visual analogue scale (VAS, 100 mm, with the endpoints 'not at all' and 'very strong'). Neutral scripts had to have a value of 20/100 or below on the VAS targeting stress. For three cBPD participants, who were not able to report a situation below this value, even when several events had been evaluated, a value of <35/100 on the VAS was accepted. Valence and arousal of the situation were rated using the non-verbal

	cBPD <i>N</i> = 25	rBPD <i>N</i> = 19 ^a	HC <i>N</i> = 24
Comorbidities, <i>n</i> (%)			
Comorbid major depression (current)	4 (16%)	0 (0)	0 (0)
Major depression (lifetime)	22 (88%)	14 (73.7%)	0 (0)
Comorbid anxiety disorders and phobias (current)	16 (64%)	6 (31.6%)	0 (0)
Comorbid posttraumatic stress disorder (current)	9 (36%)	0 (0)	0 (0)
Posttraumatic stress disorder (lifetime)	10 (40%)	5 (26.3%)	0 (0)
Other comorbid disorders	11 (44%)	1 (5.3%)	0 (0)
Medication, <i>n</i> (%)			
None	13 (52%)	15 (78.9%)	23 (95.8%)
Selective serotonin reuptake inhibitors	3 (12%)	1 (5.3%)	0 (0)
Neuroleptics	6 (24%)	1 (5.3%)	0 (0)
Benzodiazepines	3 (12%)	2 (10.5%)	0 (0)
Proton pump inhibitor	0 (0)	0 (0)	1 (4.2%)
Oral contraceptives	3 (12%)	1 (5.3%)	0 (0)
Thyroid hormones	4 (16%)	2 (10.5%)	0 (0)
Asthma medication	1 (4%)	1 (5.3%)	0 (0)

Abbreviations: cBPD, current borderline personality disorder; HC, healthy control; rBPD, remitted borderline personality disorder.

^aOne participant in the rBPD group was not included due to insufficient data collection.

TABLE 1 Comorbid mental disorders and medication of the samples

Self-Assessment Manikin scales (Bradley & Lang, 1994). The scales were later converted to ratings ranging from 1 (pleasantness/high arousal) to 9 (unpleasantness/low arousal). The participants were then asked to tell the story in detail in first-person perspective and in the present tense with a focus on sensations, thoughts and emotions (Lanius et al., 2001; Ludäscher et al., 2010; Pitman & Orr, 1993), not exceeding about 60s. The story was written down and then read to the participant who was allowed to change the content, if desired. The finalized script was read again by the experimenter, whereas the participant was instructed to relive the situation as vividly as possible. Then, the DSS-4 was again used to assess state dissociation.

Subsequently, an emotionally stressful script, which was selected to not contain traumatic elements, was constructed and transcribed in the same way. The participants were instructed to remember aversive emotionally upsetting situations, which caused stress ratings of >80/100. Due to inability to report an everyday stressful situation fulfilling this criterion in six participants (two subjects from each group), a story with a stress rating value of >70/100 was accepted. Trauma-related situations were explicitly excluded in order to ensure at least partly comparable emotionally stressful scripts between BPD participants and HC. For this purpose, we used the Posttraumatic Stress Diagnostic Scale (German version

by Ehlers, Steil, Winter, & Foa, 1996) to check the stressful narrative and excluded it and assessed another situation in case of positive ratings.

In all groups, the participants predominantly chose narratives about routines of daily life for the neutral script and interpersonal conflicts for the stressful script (a detailed content analysis is given in Table S1). The specific values characterizing neutral and stressful scripts (provided in Table S2) indicate that the stress script was rated as significantly higher in all assessed variables (DSS-4 score, inner tension rating, perceived stress, personal relevance, emotional upsetting, perceived valence and perceived arousal) compared to the neutral script across all groups. Except for reported dissociation and tension, the groups did not significantly differ in their ratings of the stories, suggesting comparable stimulus material for the experimental sessions.

2.3 | Warm perception and heat pain threshold assessment

For the assessment of the participants' warm perception (WPT) and heat pain thresholds (HPT) we used a contact thermode (30x30 mm, Thermal Sensory Analyzer, Medoc Advanced Medical Systems Ltd, Ramat Yishai, Israel).

The order of threshold assessment was fixed, starting with the assessment of WPT. The thermode was attached to the left thenar eminence of each participant's hand and the temperature was increased continuously by 1.2°C/s for warm perception and 3.0°C/s for heat pain (Leung, Wallace, Schulteis, & Yaksh, 2005). All participants were instructed to immediately respond to the onset of warm or heat pain perception with a mouse-click, which recorded the temperature before returning to the baseline point (32°C) for the next trial. For WPT and HPT, five trials were performed, and the mean of the last four trials served as threshold value.

2.4 | Experimental procedure

Each participant came for three assessments on separate days (Figure 1). At least 1 day before the first of two experimental sessions, an emotionally neutral and an emotionally stressful script were assessed by a trained experimenter (RBB), based on the procedure described by Ludäscher et al. (2010). The transcription of the collected narratives, read by a female German native speaker, was recorded and digitally stored. The experimental sessions were performed on two consecutive days. Before presentation of the personalized scripts in randomized order, we assessed state dissociation using the DSS-4. Each script was played twice in order to enhance the

intensity of the induced state (Ludäscher et al., 2010). The participants were instructed to carefully listen to the scripts and to imagine themselves as vividly as possible in the situation so that they relived it. Immediately after presentation of the scripts, dissociative responses were again assessed with the DSS-4. Due to a later implementation of vividness ratings, only a subsample of participants (15 cBPD, 15 rBPD, 11 HC) was specifically asked for the vividness of the imagery (using a numeric rating scale ranging from 0 = 'not at all' to 9 = 'as if it were real') (Ludäscher et al., 2010). Immediately after the ratings, we assessed WPT and HPT as described earlier.

2.5 | Statistical analyses

We entered DSS-4 dissociation data in a 2 (factor *point in time*; pre and post script) \times 2 (factor *condition*; neutral and stress) \times 3 (factor *group*; cBPD, rBPD and HC) mixed-model ANOVA. We report on test statistics and effect sizes (η^2) and used Bonferroni correction (p_{Bonf} ; α of .05) whenever post hoc tests were performed. Significant interactions were further analysed by simple effects analyses. In order to analyse whether or not substantial dissociation was induced, we used a composite dissociation score: in an attempt to account for group-specific differences in the extent of dissociation, we subtracted the mean of the DSS-4 score after script

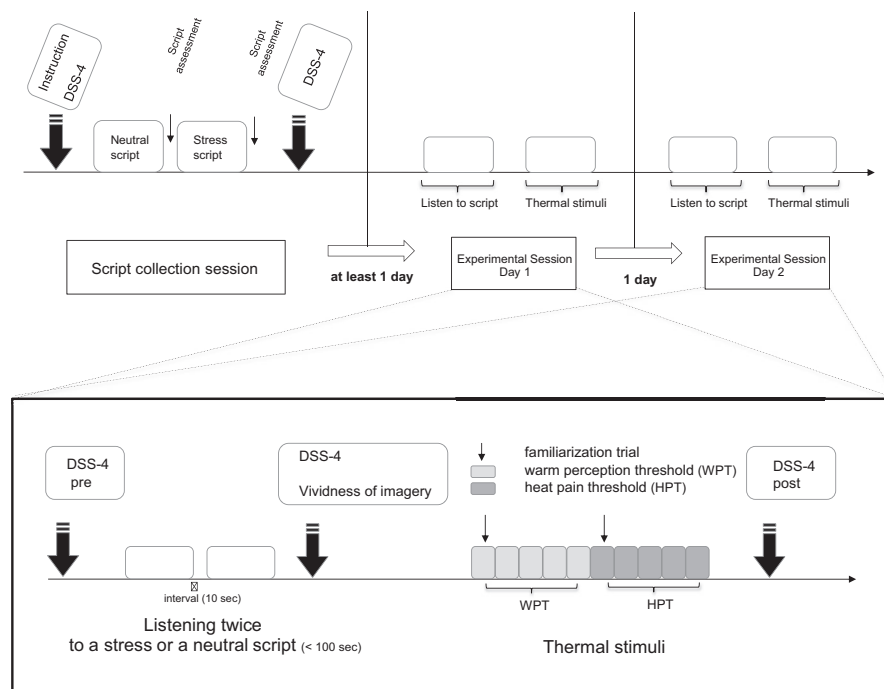


FIGURE 1 Study design. This study took place on 3 days. First, at least 1 day before the first of two experimental sessions, two autobiographical scripts with neutral and stress content were obtained (Script collection session). The experimental sessions were implemented on two subsequent consecutive days. State dissociation (assessed by the Dissociation Tension Scale, DSS-4) before and after listening to the personalized scripts and vividness of imagery were assessed. After the psychometric assessments, warm perception threshold (WPT) and heat pain threshold (HPT) were assessed. The duration of each script was less than 100 s. Each of the two scripts was played twice

presentation from the reported mean of the dissociation score before listening to the script in each group, separately for the stress and the neutral condition (i.e. induced dissociation (ID) = mean of DSS-4_{post_stress/neutral} minus mean of DSS-4_{pre_stress/neutral}). Then we subtracted the value obtained in the neutral condition from the value obtained in the stress condition (i.e. the composite dissociation score ID_{composite} = ID_{stress} minus ID_{neutral}). ID_{composite} has a possible range from -18 to +18, with positive values representing stronger induced dissociation in the stress condition compared to the neutral condition, controlled for individual differences, and thus, the score reflects *dissociation proneness*. We used one-sample *t*-tests with the test value 0 for each group in order to test for significant dissociation proneness. We report on test statistics, p_{Bonf} and Cohen's *d* (based on *n*, *M* and *SD*) as a measure of effect size. The vividness scores were similarly analysed using a mixed-model ANOVA, excluding the factor *point in time*.

Previous results indicated that thermal pain threshold assessment might underestimate the extent of pain hyposensitivity especially in cBPD (Bekrater-Bodmann et al., 2015), since the increase in temperature stops for safety reasons when a temperature of 52°C is reached although the subjects may not yet have reached the pain threshold. Twenty-two participants (2 HC, 6 rBPD and 14 cBPD) had at least one trial where the thermode stopped heating. In an attempt to compensate for the underestimation of HPT, we rounded these trials to 54°C (i.e. adjusted HPT), which is still in the range of C nociceptor responsiveness (e.g. Van Hees & Gybels, 1981). Non-significant Kolmogorov–Smirnov tests (group-wise; $H_{20-24} \leq 0.16$; all $p \geq .12$) indicated that the normal distribution assumption was not violated by this procedure. Furthermore, missing data in single trials (due to technical reasons) were replaced by the individual's mean per condition (which was the case in 2.5% of all trials). Again, we used a mixed-model ANOVA by entering the factors *group* and *condition*. The mean effect for condition was decomposed for each group by applying dependent sample *t*-tests (one-tailed, uncorrected *p* value). For WPT, we performed an identical analysis. In order to further separately analyse the pattern of

HPT data in the neutral and the stress condition, we used independent *t*-tests. Note that the results for these analyses are also reported for the non-adjusted HPT data (see Table S4).

Finally, we performed two-tailed Pearson correlation analyses in order to examine the relationship between the composite dissociation score (ID_{composite}; see above for calculation procedure) and changes in HPT (HPT in the stress condition minus HPT in the neutral condition; positive values in the resulting score thus represent higher HPT in the stress compared to the neutral condition). We provide the correlation coefficient *r* and the two-sided *p* value for each group separately (uncorrected). All statistical analyses were carried out with IBM SPSS Statistics (v22.0).

3 | RESULTS

3.1 | Induction of dissociation

M and *SD* of induced dissociation data are provided in Table 2. The ANOVA revealed a significant main effect for the factor *condition* ($F_{1,66} = 9.52$, $p = .003$, $\eta^2 = 0.13$), with higher dissociation ratings in the stress compared to the neutral condition. Furthermore, there was a significant main effect for the factor *group* ($F_{2,66} = 15.07$, $p < .001$, $\eta^2 = 0.31$). Post hoc comparisons revealed that cBPD reported significantly higher dissociation compared to HC ($p_{\text{Bonf}} < .001$) and rBPD ($p_{\text{Bonf}} = .001$), whereas HC and rBPD did not significantly differ ($p_{\text{Bonf}} = .83$). Moreover, there was a significant main effect for the factor *point in time* ($F_{1,66} = 21.19$, $p < .001$, $\eta^2 = 0.24$), which was driven by significantly higher dissociation ratings after compared to before listening to the script. However, there also was a significant *point in time* * *condition* interaction ($F_{1,66} = 23.86$, $p < .001$, $\eta^2 = 0.27$). The subsequent simple effects analysis revealed that the main effect for *point in time* solely relied on the increase in dissociation in the stress condition ($p_{\text{Bonf}} < .001$), whereas there was no significant change in the neutral condition ($p_{\text{Bonf}} = .45$). There also was a significant *point in time* * *group* interaction ($F_{2,66} = 5.53$, $p = .006$, $\eta^2 = 0.14$). A simple effects analysis

TABLE 2 Mean and standard deviation of state dissociation, heat pain thresholds (HPT) and warm perception (WPT) after listening to the stress script and neutral script (experimental sessions)

	cBPD (N = 25)		rBPD (N = 20)		HC (N = 24)	
	Neutral script M (SD)	Stress script M (SD)	Neutral script M (SD)	Stress script M (SD)	Neutral script M (SD)	Stress script M (SD)
DSS-4 pre	1.44 (1.73)	1.15 (1.46)	0.16 (0.33)	0.19 (0.52)	0.03 (0.15)	0.04 (0.16)
DSS-4 post	1.30 (1.75)	2.46 (2.16)	0.19 (0.49)	1.01 (1.60)	0.05 (0.15)	0.05 (0.16)
HPT	48.39 (4.08)	49.90 (3.63)	46.36 (4.17)	47.77 (4.68)	44.89 (3.19)	44.55 (3.25)
WPT	34.20 (1.43)	34.96 (1.75)	34.48 (1.98)	34.51 (1.57)	33.78 (0.81)	33.73 (0.45)

Abbreviations: cBPD, current borderline personality disorder; DSS-4, Dissociation Tension Scale-4 (0, not at all – 9, very strong); HC, healthy control subjects; HPT, heat pain thresholds; M, mean; N, sample size; rBPD, remitted borderline personality disorder; SD, standard deviation; WPT, warm perception thresholds.

revealed that cBPD reported stronger dissociation compared to rBPD and HC (all $p_{\text{Bonf}} \leq .001$ before and after listening to the scripts), whereas HC and rBPD did not significantly differ (all $p_{\text{Bonf}} \geq .37$). The simple effects analysis for the significant *point in time* * *condition* * *group* interaction ($F_{2,66} = 8.20$, $p = .001$, $\eta^2 = 0.20$) further showed that cBPD reported significantly higher dissociation compared to rBPD and HC (all $p_{\text{Bonf}} \leq .009$), whereas there was no significant difference between rBPD and HC (all $p_{\text{Bonf}} \geq .14$), regardless of *point in time* and *condition*. However, as depicted in Figure 2a, the slope from pre to post script in rBPD under neutral conditions resembles the slope obtained in HC, whereas in the stressful condition, the slope obtained in the rBPD resembles that from the cBPD. This suggests that BPD-specific responses (regardless of whether the state of the disorder is current or remitted) cause the significance in the two- and three-way interactions involving the factor *group*.

In an attempt to further examine this interpretation, we separately tested $\text{ID}_{\text{composite}}$ against 0 in the three groups. Both cBPD ($M = 1.45$, $SD = 1.73$; $t_{24} = 4.19$, $d = 0.84$, $p_{\text{Bonf}} < .001$) and rBPD ($M = 0.80$, $SD = 1.32$; $t_{19} = 2.71$, $d = 0.61$, $p_{\text{Bonf}} = .042$), but not HC ($M = -0.01$, $SD = 0.14$; $t_{23} = -0.37$, $d = -0.08$, $p_{\text{Bonf}} = 1.00$), showed significant positive scores, indicating substantial dissociation proneness only in the clinical groups, albeit different in extent. This indicates that both BPD groups respond with dissociation when stress is induced. These data are visualized in Figure 2b. Note that vividness of imagery during the experimental sessions was comparable between groups and conditions, as revealed by non-significant main and interaction effects for this measure (see Table S3).

3.2 | Heat pain and warm perception thresholds

For HPT, there was a significant main effect for *condition* ($F_{1,66} = 4.12$, $p = .046$, $\eta^2 = .06$) which was driven by elevated HPT in the stress compared to the neutral condition. However,

this effect was mainly associated with the cBPD participants, as revealed by a significant increase of HPT in the stress compared to the neutral condition only in this group ($t_{24} = 1.81$, $p = .041$, $d = 0.34$). For rBPD, there only was a trend in the same direction ($t_{19} = 1.60$, $p = .064$, $d = 0.38$), and in HC, no significant changes were observed ($t_{23} = -0.81$, $p = .21$, $d = -0.17$). We further found a significant effect of *group* ($F_{2,65} = 10.32$, $p < .001$, $\eta^2 = 0.24$) with cBPD having significantly higher thresholds compared to HC ($p_{\text{Bonf}} < .001$). Remitted BPD did not significantly differ from cBPD ($p_{\text{Bonf}} = .14$) or HC ($p_{\text{Bonf}} = .08$). The interaction *condition* * *group* missed significance ($F_{2,66} = 2.08$, $p = .13$, $\eta^2 = 0.06$). M and SD of HPT data for each group are given in Table 2. Note that the main effects of the factors *condition* and *group* were specific for the nociceptive domain, since an analysis using WPT did not reveal significant main effects (both $p \geq .06$, $\eta^2 \leq 0.08$; M and SD are given in Table 2). The pattern of results is similar for the non-adjusted HPT data (see supplement).

In order to further analyse the pattern of results for HPT, we performed t -tests in the groups separately comparing the HPT in the neutral and stress condition. For the neutral condition, we found HPT to be significantly higher for cBPD versus HC ($t_{47} = 3.34$, $d = 0.96$, $p_{\text{Bonf}} = .005$), whereas there was no significant difference between cBPD and rBPD ($t_{43} = 1.64$, $d = 0.50$, $p_{\text{Bonf}} = .32$) or between rBPD and HC ($t_{42} = 1.33$, $d = 0.40$, $p_{\text{Bonf}} = .58$). For the stress condition, however, we found significantly higher HPT for both cBPD compared to HC ($t_{47} = 5.43$, $d = 1.55$, $p_{\text{Bonf}} < .001$) and rBPD compared to HC ($t_{42} = 2.68$, $d = 0.80$, $p_{\text{Bonf}} = .031$) but not between cBPD and rBPD ($t_{43} = 1.72$, $d = 0.51$, $p_{\text{Bonf}} = .28$, see Figure 3). The pattern of significances remains valid also for the non-adjusted HPT data (see supplement).

3.3 | Relationship between dissociation proneness and heat pain thresholds

Pearson correlation analyses revealed that dissociation proneness correlated significantly positively with induced changes

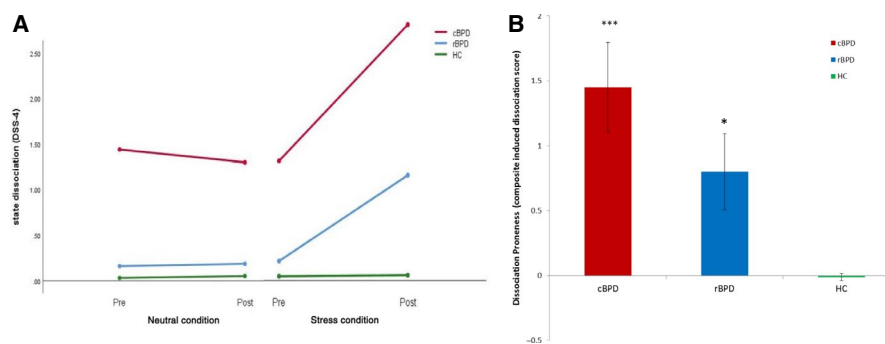


FIGURE 2 State Dissociation slopes and dissociation proneness in current borderline personality disorder (cBPD), remitted borderline personality disorder (rBPD) and healthy controls (HC). (a) State dissociation slopes (mean values). (b) Dissociation proneness (mean values); error bars indicate the standard error of the mean. *** $p < .001$; * $p < .05$ (2-tailed one-sample t -test with test value 0)

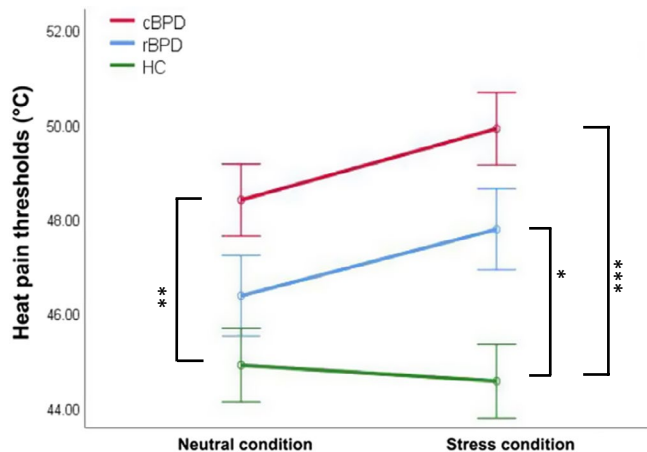


FIGURE 3 Heat pain thresholds in the neutral and the stress condition. cBPD, current borderline personality disorder; rBPD, remitted borderline personality disorder; HC, healthy controls. Error bars indicate the standard error of the mean. *** $p < .001$; ** $p < .01$; * $p < .05$

in HPT in participants with cBPD ($r_{23} = .40, p = .047$), whereas there were no significant relationships in rBPD ($r_{18} = .22, p = .36$) and HC ($r_{22} = -.37, p = .08$). The scatter plot for cBPD is given in Figure 4.

4 | DISCUSSION

In this study, we investigated the relationship between dissociation proneness and pain hyposensitivity in patients with current and remitted BPD as well as HC as a non-clinical control group. Recordings of autobiographical stressful narratives, compared to neutral narratives in the control condition, were used to induce dissociation on two consecutive days. This procedure reliably induced dissociation in both clinical groups. We found that cBPD participants displayed reduced heat pain perception compared to HC, replicating previous results (Bohus et al., 2000; Ludäscher et al., 2010; Niedtfield et al., 2010; Russ et al., 1992; Schmahl,

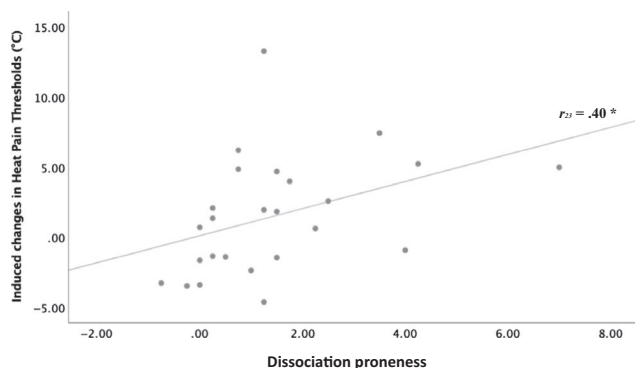


FIGURE 4 Relationship between dissociation proneness and heat pain threshold changes in the stress versus neutral condition in participants with current borderline personality disorder. * $p < .05$

Greffrath, et al., 2004; Schmahl et al., 2010; Schmahl, Vermetten, Elzinga, & Bremner, 2004). Remitted BPD participants were in between, and did not differ significantly from either cBPD or the HC in the neutral condition. However, after listening to the stressful script, rBPD participants showed significantly reduced pain sensitivity compared to HC, perceptually resembling cBPD participants, even though the overall level of pain hyposensitivity was lower. In cBPD, but not in rBPD, dissociation proneness was significantly positively related to pain hyposensitivity. These results suggest that BPD-specific altered pain sensitivity is associated with trait dissociation proneness in the current stage of the disorder; in rBPD patients, however, pain hyposensitivity is present under stressful, but not neutral, conditions (although weaker in extent compared to cBPD), independent of dissociation proneness. These results are indicative of differential mechanisms of pain perception in the clinical groups, and highlight the elusive state of BPD remission in terms of stable clinical improvement.

4.1 | Dissociation proneness

The results might help to resolve some of the inconsistencies about the relationship between stress, dissociation and pain in BPD reported before. Stress-related pain hyposensitivity has been reliably associated with cBPD (e.g. Bohus et al., 2000; Russ et al., 1992; Schmahl, Greffrath, et al., 2004; Schmahl et al., 2010). For dissociation, however, the empirical evidence is rather inconsistent: while state dissociation has been found to be more reliably correlated with pain hyposensitivity (Bekrater-Bodmann et al., 2015; Ludäscher et al., 2007), for trait dissociation, there are mixed results (Bekrater-Bodmann et al., 2015; Defrin et al., 2019; Ludäscher et al., 2007, 2015), highlighting the dissociable nature between trait and state stress responses in cBPD. By introducing the measure of dissociation proneness, we offer a new variable for experimental investigations, reflecting the level of state dissociative responses corrected by individual trait differences. Although prospective studies have to further evaluate the validity of this measure, the differences between cBPD and rBPD in this study indicate that stress and dissociation independently contribute to BPD-specific pain hyposensitivity. It would be particularly interesting to test for relationships between this measure and recently identified central (Kraus et al., 2009; Schmahl et al., 2006) and peripheral physiological (Defrin et al., 2019) correlates of cBPD-associated pain hyposensitivity and the potential underlying mechanisms.

4.2 | Altered pain sensitivity and its potential importance for NSSI behaviour

Non-suicidal self-injurious behaviour (NSSI) is often performed in cBPD in a dysfunctional attempt to cope with stress

(Reitz et al., 2012, 2015). It has been shown that individuals who have higher pain thresholds are more likely to engage in NSSI, and repeated NSSI might in turn lead to elevated pain thresholds over time (Hooley, Ho, Slater, & Lockshin, 2010). This bi-directional link of nociception and behaviour might be the basis for operant learning mechanisms underlying dysfunctional coping strategies such as self-harm. Dissociation has been identified to be an important mediator for the relationship between pain perception and NSSI in cBPD (Ludäscher et al., 2010). The present data, however, indicate that stress-responses other than dissociation might play a role for this relationship: when the disorder is in its remitted stage, we found stress-associated hyposensitivity in rBPD which cannot completely be explained by still enhanced dissociation proneness. Enhanced stress reactivity in rBPD and associated increase in the urge for NSSI (Willis et al., 2018) might reflect the stability of learned dysfunctional coping behaviour beyond the disorder's current stage. This interpretation, together with the present's studies results regarding altered stress-related pain sensitivity in rBPD, might be of importance for therapeutic considerations for individuals in the remitted stage. Longitudinally, NSSI has been found to be associated not only with dissociative symptoms but also with female gender, severity of dysphoric cognitions, major depression and a history of childhood and adult sexual abuse (Zanarini, Laudate, Frankenburg, Reich, & Fitzmaurice, 2011). Although Zanarini et al. (2011) did not differentiate between BPD in the current and the remitted stage, other reports of the same cohort suggest very high rates of—at least temporarily stable—symptomatic remission (Zanarini et al., 2012), indicating that the identified predictors of NSSI might also be crucial for rBPD. While this study's results suggest that dissociation might play a minor role in rBPD, enhanced stress levels due to dysfunctional cognitions, mood disorders and a history of adverse experiences might still affect pain perception which in turn might reduce the inhibition threshold to engage in NSSI (see Hooley et al., 2010). However, it is remarkable that only one out of 20 rBPD patients in this study reported self-harming behaviour in the last 12 months (compared to 100% of the cBPD patients), suggesting rather high competence of rBPD patients to deal with adverse effects of everyday life stressors. The identification of successful coping strategies might be of interest for future studies on therapeutic aftercare for BPD patients in the remitted stage of the disorder.

4.3 | Limitations and perspective

Several limitations of our study must be noted. Firstly, although we implemented a randomized order of scripts, the participants could predict the content to a certain degree. After the experiment, some participants with current and

remitted BPD spontaneously reported that they prepared themselves for the second experimental session, be it settling in anticipation of a stressful script or keeping relaxed in anticipation of a neutral script. This might have interfered with the induction of dissociation, as the scores we assessed were relatively low (increase of about 1.2 averaged sum score points in the DSS-4) compared to other studies (Bichescu-Burian et al., 2017; Krause-Utz et al., 2018; Ludäscher et al., 2010, with converted values of 1.5 and higher). The purposeful exclusion of traumatic events might account for the rather low scores in this study, while increasing the ecological validity of findings. However, the slightly lower dissociation level cannot really explain the small effect sizes. While Ludäscher et al. (2010) reported effect sizes larger than 1 for pain modulation by the script-driven imagery approach, we found rather small effect sizes for both BPD groups between $d = 0.3$ and 0.4 . The reasons for these lower effects need to be further investigated. Secondly, our approach to round HPT for participants who reached the safety limit of the thermode might have induced a bias in our data. Although we used a stimulation procedure described before (Leung et al., 2005), the heating rate of $1.2^{\circ}\text{C}/\text{s}$ might not have been optimal in the present context. Slower heating rates induce temporal summation resulting in increased pain perception and accordingly reduced pain thresholds (Arendt-Nielsen & Petersen-Felix, 1995; Eide, 2000; Vierck, Cannon, Fry, Maixner, & Whitsel, 1997), which might be beneficial for the investigation of pathologically enhanced HPT. It might be useful to carefully adapt the pain stimulation procedure for populations with mental disorders in general and BPD in particular in prospective studies. Alternatively, ceiling effects could be avoided in the future using other types of painful stimulation such as mechanical, chemical or electrical stimulation (Ludäscher et al., 2007; Magerl, Burkart, Fernandez, Schmidt, & Treede, 2012), where the thermal-specific stimulation restrictions are not given. However, the similarity of result patterns for adjusted (results section) and non-adjusted data (supplement) suggests robustness of effects, which in fact might remain underestimated in this study. Finally, future studies should validate our results with physiological measures of stress, since we can only indirectly conclude that dissociation proneness as defined in this study is a consequence of stress reactivity. Moreover, prospective studies should implement longitudinal designs in which dissociation proneness and pain perception can be evaluated over an extended period of time, from the disorder's current stage into remission. Without longitudinal data, we do not know whether rBPD patients had similarly severe BPD symptoms, compared to the cBPD group, when they were in their current stage, or had simply been milder cases, with less pronounced dissociation symptomatology (Löffler, Kleindienst, Cackowski, Schmidinger, & Bekrater-Bodmann, 2019).

5 | CONCLUSION

Taken together, our results suggest enhanced dissociation proneness not only in cBPD, but also in rBPD. However, the interaction with pain perception might be rather complex. Compared to HC, remitted BPD react with pain hyposensitivity under stressful compared to neutral conditions, although smaller in extent compared to cBPD. While this feature is clearly positively related to dissociation proneness in cBPD, this association cannot be observed in rBPD. However, the data indicate that stress causes the pain perception rBPD to drift away from that of the HC. The clinical value of these findings as well as its importance for therapeutic considerations in the aftercare of BPD needs to be further evaluated in the future.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

AUTHOR CONTRIBUTIONS

All authors contributed significantly to the study. RBB and HF conceived and designed the experiments. RBB and BYC performed the experiments. RBB, BYC, SH and IS analysed the data. RBB, BYC, HF, SH and IS wrote the paper. All authors have discussed the results and commented on the manuscript.

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