Emotional learning during dissociative states in borderline personality disorder

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Background: Neurobiological findings and clinical data suggest that dissociative experience inhibits conditioning processes, but experimental studies are lacking. The aim of our study was to determine whether high states of dissociative experience would specifically alter emotional learning, but not declarative knowledge. **Methods:** We used an aversive differential delay conditioning procedure in 33 unmedicated patients with borderline personality disorder (BPD) and 35 healthy controls. **Results:** Patients with BPD who had high state dissociative experiences (BPD D+) showed diminished acquisition of differential aversive delay conditioning with respect to emotional learning compared with those who did not experience dissociative symptoms (BPD D–) and healthy controls (skin conductance response; interaction dissociation × quadratic time × type, $p = 0.009$). Specifically, the control group and the BPD D– subgroup showed an increase in valence and arousal to the conditioned stimulus (CS+) during the conditioning procedure (all $p < 0.012$) and demonstrated differential skin conductance responses in the acquisition and extinction phases. In contrast, the BPD D+ subgroup showed no increase in valence and arousal to CS+ or differential response regarding skin conductance. We examined general psychopathology, trauma history, perceptual differences and posttraumatic stress disorder as confounding factors, but we found no evidence of bias. **Limitations:** Subdividing the BPD group reduced power. In addition, because our sample included only women, the generalizability of our results is constrained. Furthermore, we performed no separate analysis of the influence of different aspects of dissociation on the learning process. **Conclusion:** Emotional, amygdala-based learning processes seem to be inhibited during state dissociative experience. State dissociative experience may alter acquisition and extinction processes and should be closely monitored in exposure-based psychotherapy.

Contexte : Selon des observations et des données cliniques neurobiologiques, les états dissociatifs inhiberaient les processus de conditionnement, mais les études expérimentales sur le sujet font défaut. La présente étude avait pour but de déterminer si les états hautement dissociatifs peuvent altérer spécifiquement certains apprentissages émotionnels, sans influer sur le savoir déclaratif. **Méthodes :** Nous avons utilisé une technique de conditionnement différé aversif différentiel chez 33 patientes atteintes d'un trouble de personnalité limite non traitées pharmacologiquement et chez 35 témoins en bonne santé. **Résultats :** Les patientes atteints d'un trouble de personnalité limite et présentant un état hautement dissociatif (D+) ont manifesté une acquisition plus lente du conditionnement différé aversif différentiel en ce qui a trait à l'apprentissage émotionnel, comparativement aux patientes qui ne présentaient pas de symptômes dissociatifs (D–) et aux témoins en bonne santé (réponse de conductance cutanée; dissociation de type « temps quadratique » vis-à-vis des interactions, $p = 0{,}009$). Plus spécifiquement, le groupe témoin et le sous-groupe de patientes D– ont présenté une augmentation de la valence et de l'éveil au stimulus conditionné (SC+) durant l'étape de conditionnement (tous $p < 0{,}012$) et ont manifesté des réponses de conductance cutanée différentielles durant les phases d'acquisition et d'extinction. En revanche, le sous-groupe de patientes D+ n'a manifesté aucune augmentation de valence et d'éveil au SC+, ni aucune réponse différentielle en ce qui a trait à la conductance cutanée. Parmi les facteurs de confusion, nous avons analysé la psychopathologie générale, les antécédents de traumatisme, les différences perceptuelles et les troubles de type stress post-traumatique, mais nous n'avons relevé aucun signe de

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biais. **Limites :** La division du groupe atteint d'un trouble de personnalité limite a réduit la puissance de l'étude. De plus, étant donné que notre échantillon n'incluait que des femmes, nos résultats sont plus difficilement généralisables. En outre, nous n'avons effectué aucune analyse distincte de l'influence de divers aspects de la dissociation sur le processus d'apprentissage. **Conclusion :** Les processus d'apprentissage émotionnels qui dépendent de l'amygdale semblent être inhibés chez les participants présentant un état dissociatif. Les états dissociatifs peuvent perturber les processus d'acquisition et d'extinction et méritent d'être surveillés étroitement lors de psychothérapies par exposition.

Introduction

Neurobiological findings[1–9] and clinical data[10,11] suggest that conditioning processes are inhibited by dissociation. Regarding neurobiological processes, the corticolimbic disconnection model of dissociation[12] hypothesizes that the medial prefrontal cortex inhibits the amygdala, resulting in a reduced emotional experience and a dampened autonomic output. Recent studies have partially confirmed this dissociation model. Individuals with depersonalization disorder showed reduced autonomic and emotional responses to unpleasant pictures[1] and facial expressions of disgust[2] but not to neutral stimuli, suggesting a selective inhibition of emotional processing. They also showed an absence of subjective emotional experience and no activation of brain regions involved in normal emotional processing (insula and occipitotemporal cortex) when viewing aversive pictures[3] or during encoding and recognition of emotional verbal material.[4] Similarly, individuals who had posttraumatic stress disorder (PTSD) with present-state dissociative experiences exhibited reduced heart rates and increased activation in the dorsolateral and medial frontal cortices compared with a nondissociative PTSD subgroup in a traumatic script-driven symptom-provocation paradigm.[5,7] Likewise, an inverse relation between dissociation severity and cortisol stress reactivity during a psychosocial stress paradigm has been shown in people with dissociative disorders and people with PTSD.[8] Our group has recently demonstrated that individuals with borderline personality disorder (BPD) exhibit reduced startle response amplitude during states of dissociative experience.[9] This is in accordance with the corticolimbic disconnection model of dissociation,[12] since the startle reflex can be directly modified by the central nucleus of the amygdala.[13]

With respect to clinical findings, dissociative experience has been identified as a predictor of poor outcome in behavioural treatments for panic disorder[10] and obsessive–compulsive disorder.[11] This may be explained by the reduced emotional engagement during dissociative experience, as emotional engagement is thought to be crucial for successful exposure therapy.[14] To our knowledge, there are no experimental studies investigating the influence of dissociation on classical conditioning processes (see Giesbrecht and colleagues[15] for a review on experimental studies on dissociation).

The neural circuitry underlying classical conditioning has been well characterized, and emotional and cognitive/declarative learning components can be distinguished.[16,17] Emotional learning is largely based on a pathway connecting the amygdala and the medial frontal cortex,[18–21] whereas the cognitive components can be related to the lateral frontal cortex and the hippocampus.[16,17] Accordingly, selective damage of the amygdala in humans leads to impaired emotional learning (no acquisition of skin conductance responses) but intact cognitive/declarative knowledge, whereas selective damage of the hippocampus leads to impaired cognitive/declarative knowledge but intact emotional learning.[16]

To determine whether emotional learning depends on dissociative state, we conducted a differential aversive Pavlovian delay conditioning procedure. We chose to study patients with BPD, in which dissociation is commonly observed clinically and is a diagnostic criterion of this disorder. We assumed that present state dissociative experience would specifically alter amygdala-based emotional learning but not hippocampus-based cognitive/declarative knowledge. Specifically, we hypothesized that patients with BPD who had high states of dissociative experience during the experiment would exhibit diminished acquisition of differential conditioning regarding emotional learning (valence, arousal, skin conductance response) compared with patients with BPD and healthy controls who did not experience dissociative symptoms during the experiment. We furthermore hypothesized that the groups would not differ with regard to cognitive/declarative knowledge (contingency awareness).

Methods

Participants

We conducted the study at the Central Institute of Mental Health, Mannheim, Germany. We recruited participants with BPD from consecutively admitted patients to a dialectical behaviour therapy treatment program or via announcements on the Internet. We randomly selected healthy controls from the local resident register. Trained psychologists administered the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I)[22] and the International Personality Disorder Examination (IPDE).[23] Inter-rater reliability was good: SCID-I $\kappa = 0.69$; IPDE $\kappa = 0.77$. We included patients aged 18–45 years who met full DSM-IV diagnostic criteria for BPD and who were free of psychotropic medications for at least 4 weeks before the experiment. We excluded patients with comorbid schizophrenia (current, lifetime), bipolar disorder (current, lifetime) and current major depression or current alcohol/drug abuse. Exclusion criteria for the control group were any current or past Axis-I or Axis-II disorder, and current or past psychotherapy. We also excluded participants with colour blindness. We matched patients and controls for age, sex and race. We paid all

patients and controls for participating in the study (10 ≠/h). We used tercile splitting to divide patients with BPD into 2 subgroups: those with no present state dissociative experiences (BPD D–) and those with severe present state dissociative experiences (BPD D+). All participants provided written informed consent after receiving a complete description of the study. The ethical review committee of the University of Heidelberg, Germany approved the study.

Psychometric measures

We assessed present state dissociative experience using the state version of the Dissociation-Tension-Scale acute.[24] This self-rating scale consists of 19 items assessing psychological (e.g., derealization, depersonalization, amnesia) and somatic dissociation (e.g., perception of pain, vision and hearing). We derived all items from the Dissociative Experiences Scale[25] and the Somatoform Dissociation Questionnaire.[26] Reliability analysis of the Dissociation-Tension-Scale acute[27] resulted in a Cronbach's α of 0.94 (internal consistency) and a split-half reliability (Guttman) of $r = 0.93$. We assessed trait dissociation using the German adaptation of the Dissociative Experiences Scale,[28] handedness using the Edinburgh Handedness Inventory[29] and global borderline psychopathology using the Borderline Symptom List.[30] We assessed hearing thresholds of all participants using a simplified version of a published procedure (www.neurobs.com/ex_files/expt_view?id=69; Neurobehavioral Systems).

Experimental design

Participants completed an aversive differential delay conditioning procedure. We used an aversive sound (baby cry) rather than an electric shock as the unconditioned stimulus because patients with BPD have exhibited altered pain thresholds.[31] Previous work indicated that this baby cry was subjectively perceived to be highly aversive and that stable sympathetic differential conditioning responses could be elicited.[32] We presented the unconditioned stimulus binaurally via headphones. We calibrated volume to 95 dB using a sound level metre (Brüel and Kjær, type 2206. The conditioned stimuli (CS) were 2 neutral inkblots (7.5 × 5.5 cm), which had been used previously.[33]

The conditioning task consisted of a habituation phase, an acquisition phase and early and late extinction phases. In the habituation phase, both inkblots were presented 4 times each to diminish preconditioning differences. In the acquisition phase, one of the inkblots (positive conditioned stimulus [CS+]) was sometimes paired with the unconditioned stimulus, whereas the other inkblot (negative conditioned stimulus [CS–]) was never paired with the unconditioned stimulus. Specifically, in 12 trials, we paired the CS+ with the baby cry (unconditioned stimulus), whereas in 6 trials, the CS+ was not followed by the unconditioned stimulus. In trials in which we paired the CS+ with the unconditioned stimulus, the skin conductance response to the CS+ overlapped in time with the skin conductance response to the unconditioned stimulus. Therefore, we used only the trials using the CS+ alone to test for the acquisition of conditioned response in the acquisition phase. All later analyses refer to trials using the CS+ alone.[15] We used the early and late extinction phases to test how the conditioned response to the CS+ diminished over time. We presented 4 trials with the CS+ and 4 trials with the CS– in each extinction phase without any unconditioned stimulus. We counterbalanced the inkblots among participants and presented them in pseudorandom order with the constraint of a maximum of 2 consecutive presentations of either the CS+ or CS– The randomly generated intertrial interval was between 15 and 30 seconds. The duration of the CS was 0.6 seconds, and that of the unconditioned stimulus was 3.5 seconds administered with a delay of 0.5 seconds after CS onset.

Procedure

The experiment took place in a sound-attenuated, temperature-controlled room with participants seated upright in a comfortable armchair. Prior to and after the conditioning procedure, we administered state questionnaires and rated the CS on 6-point Likert scales according to valence (end points: pleasant = 1, unpleasant = 6) and arousal (end points: relaxing = 1, exciting = 6). To mitigate the influence of the experimental instructions,[34] we did not obtain ratings during the experiment, nor did we inform participants about contingencies between stimuli or the different experimental phases. After completing the differential learning task, participants rated the subjective contingency awareness, defined as the estimated probability that the unconditioned stimulus would occur after a given CS (100-point Likert scale; end points: low probability = 1, high probability = 100).

Apparatus and physiologic recordings

We controlled stimulus delivery using Presentation software (Neurobehavioral Systems). We recorded physiologic data at a rate of 256 Hz in continuous mode using the Vitaport II system and vitagraph software, version 4.61 (Becker Meditec). We measured skin conductance using Ag/AgCl-electrodes (10-mm diameter, Marquette Hellige) filled with an isotonic electrodermal response jelly TDE-246 (Steffens; identical to Grass EC-33) and placed on the thenar and hypothenar eminences of the nondominant hand (constant voltage method with 0.5 V). We assessed arm movement as a control measure using a 2-dimensional accelerometer.

Physiologic data transformation

We performed the parameterization of the electrodermal activity according to published guidelines[35] with the software program EDR-PARA (Dr. F. Schäfer, Institut für Psychologie, Universität Gesamthochschule Wuppertal, Germany). We defined phasic skin conductance responses as the response magnitude (maximum deflection) within a 1- to 4-second timeframe (first interval response). We scored skin conductance responses lower than 0.05 μS as zero. We considered the interval response to be missing when the skin

conductance response was clearly initiated before CS onset. If such an anticipatory response was superimposed on a stimulus-related response, we used the scoring method (B), described by Boucsein.[35] We log-transformed skin conductance responses after adding 1 to reduce skewness.[35]

Statistical analyses

In a first step, we conducted a repeated-measures analysis of variance (ANOVA) with the factors group (BPD, control), type (CS+, CS–) and time (habituation, acquisition, early extinction, late extinction; pre and post conditioning procedure, respectively) and the covariate dissociation (continuous format) for each outcome measure (valence, arousal, contingency awareness, skin conductance response). We tested sphericity of the variance–covariance matrix using the Mauchly test. If the assumption of sphericity tended to be violated ($p \leq 0.10$), we used a Greenhouse–Geisser adjustment of degrees of freedom. If the type × time × dissociation interaction was significant (specifically the quadratic effect for skin conductance response), we continued with further analyses. For these further analyses we used tercile splitting, which enabled us to test and graphically represent if learning processes still work during clinically relevant dissociative states. We performed 2-tailed Student *t* tests, and we calculated effect sizes (*d*) according to published procedures.[36] In case of heteroscedasticity, we calculated *t* statistics according to Satterthwaite approximation. For cases of deviation from normal distribution, we used Wilcoxon signed rank tests. We performed statistical analyses using SPSS 14.0 (SPSS Inc.). An α level of 0.05 determined statistical significance.

Results

Participants

We recruited a total of 85 participants (patients with BPD and healthy controls). Owing to technical problems (defective memory card; detached electrodes), we had to exclude 10 participants. In addition, 6 participants (all patients with BPD) did not tolerate the aversive sound and left the experiment before testing. There was no group difference between withdrawing and participating individuals with BPD regarding dissociative experience, age, education and BPD symptomatology. We excluded 1 healthy control participant who showed no skin conductance responses throughout the entire experiment (mean skin conductance level 0.96, standard deviation [SD] 0.008 μS). Our final sample included 33 women with BPD and 35 female controls, for a total of 68 participants.

The breakdown of comorbid Axis I disorders in the BPD group was as follows: major depressive disorder (present 0%, lifetime 88%), PTSD (present 46%, lifetime 49%), anxiety disorder other than PTSD (present 61%, lifetime 64%) and eating disorders (present 18%, lifetime 52%).

The mean age of participants in the BPD group was 27.8 (SD 6.8) years compared with a mean age of 28.7 (SD 7.6) years in the control group ($t_{66} = 0.5$, $p = 0.60$). All but 2 participants (1 Asian participant in each group) were white; race was self-designated by participants. One participant in the control group and 2 in the BPD group were left-handed. Years of education differed significantly between both groups (mean 12.4, SD 2.8 yr in the BPD group v. mean 15.9, SD 1.7 yr in the control group; $t_{50.1} = 6.1$, $p < 0.001$); this factor was not related to the main outcome variables.

Of the 33 participants with BPD, the BPD D– subgroup comprised 11 women and the BPD D+ subgroup comprised 10 women. The remaining 12 women had medium dissociated experiences (BPD D^{medium}). Table 1 shows that the BPD D– group exhibited similar present state dissociative experiences to the control group (both 0.12), whereas the BPD D+ group (3.10) was clearly above the published cut-off of 2.7 for severe dissociative experience. Data for the BPD D^{medium} group are not provided in this paper, but are available on request.

Control variables

To ascertain whether the BPD subgroups specifically differed in present state dissociative experiences, we compared the dissociation and confounding variables between the groups. As displayed in Table 1, patients with BPD who had high versus low present state dissociative experiences significantly differed regarding state (Dissociation-Tension-Scale acute) and trait dissociative experiences (Dissociative Experiences Scale). We observed a trend for altered hearing threshold, which was not surprising given that impaired hearing is a somatoform aspect of dissociative experience. However, the sound level of the unconditioned stimulus remained more than 40 times above the reduced hearing threshold level in the BPD D+ group (42 dB v. 95 dB), and heightened hearing threshold was not accompanied by a reduced perceived aversiveness of the unconditioned stimulus (regarding psychological and physiologic parameters) in the BPD D+ subgroup.

To ascertain whether the BPD subgroups specifically differed in present state dissociative experiences, we also analyzed general psychopathology, including severity of borderline symptoms (dissociative items were excluded), number of comorbid Axis-I disorders, number of comorbid Axis-II disorders, experience of trauma and current or lifetime PTSD, as a possible confounding variable (Table 1). We found no significant group differences. Furthermore, we evaluated whether participants in the BPD D+ group perceived the stimuli and the conditioning procedure as equally aversive. Findings on emotional valence, arousal and skin conductance response to the unconditioned stimulus revealed no differences between the BPD D+ and the BPD D– groups (Table 1). We observed no subgroup differences regarding general skin conductance level and the skin conductance response to CS+ and CS– before conditioning (habituation phase).

Emotional learning: skin conductance response

The 2 × 2 × 4 factorial ANOVA for skin conductance response with the factors group (BPD, control), type (CS+, CS–) and

time (habituation, acquisition, early extinction, late extinction) and the covariate dissociation (continuous format) showed a significant effect for the interaction type × quadratic time × dissociation ($F_{1–65} = 7.2$, $p = 0.009$), indicating that differential conditioning was influenced by dissociation. Furthermore, data analyses revealed a significant effect for the interaction type × quadratic time ($F_{1–65} = 6.2$, $p = 0.015$), indicating successful differential conditioning among all participants and a significant effect for group ($F_{1–65} = 5.3$, $p = 0.024$) and phase ($F_{1–65} = 12.9$, $p = 0.001$).

To analyze the effect of state dissociation in greater detail, we examined the BPD D+ and BPD D– subgroups (see Fig. 1). The control group exhibited no differential skin conductance response (CS+ v. CS–) in the habituation phase ($t_{34} = 0.2$, $p = 0.74$, $d = 0.06$), but significant differences during acquisition ($t_{34} = 2.3$, $p = 0.029$, $d = 0.38$) and early extinction ($t_{34} = 2.5$, $p = 0.017$, $d = 0.43$), whereas a statistical trend with a small effect size appeared in late extinction ($t_{34} = 1.8$, $p = 0.08$, $d = 0.30$). The BPD D– group exhibited no differential skin conductance response (CS+ v. CS–) in the habituation phase ($t_9 = 1.7$, $p = 0.13$, $d = 0.52$) or in the acquisition phase ($t_9 = 1.5$, $p = 0.16$, $d = 0.48$), for which the effect size was medium. Differential conditioning was evident in the early extinction phase ($t_9 = 2.2$, $p = 0.05$, $d = 0.70$) with a high effect size, but not in the late extinction phase ($t_9 = 0.6$, $p = 0.54$, $d = 0.20$). The BPD D+ group did not exhibit a differential response in the habituation ($t_{10} = 0.6$, $p = 0.56$, $d = 0.26$), acquisition ($t_{10} = 0.6$, $p = 0.58$, $d = 0.04$), early extinction ($t_{10} = 0.6$, $p = 0.59$, $d = 0.11$) or late extinction phases ($t_{10} = 1.3$, $p = 0.22$, $d = 0.17$). This indicates that participants in the BPD D+ group did not acquire a differential conditioning response, as measured via skin conductance.

Emotional learning: emotional valence ratings

The 2 × 2 × 2 factorial ANOVA with the factors group, type and time (pre v. post) and the covariate dissociation (continuous format) showed a significant type × time × dissociation interaction ($F_{1–65} = 8.4$, $p = 0.005$), indicating that differential conditioning was influenced by dissociation. Further analyses revealed a significant type × time interaction ($F_{1–65} = 26.1$, $p < 0.001$), indicating successful overall differential conditioning regarding emotional valence for all participants and a main effect for group ($F_{1–65} = 25.6$, $p < 0.001$).

To further evaluate differential conditioning (Fig. 2) in the BPD subgroups, we calculated single pre–post comparisons (Student *t* tests). The control group exhibited a significant pre–post increase in valence ($t_{34} = 2.8$, $p = 0.008$, $d = 0.48$) of the CS+, indicating that controls perceived the CS+ to be more negative after the conditioning procedure. There were no significant pre–post differences in emotional valence with the CS– ($t_{34} = 0.7$, $p = 0.45$, $d = 0.13$). This finding was

Table 1: Demographic and psychometric measures among participants, by acute dissociative experience

Measure	Group; mean (SD)*			BPD D+ v. BPD D–	
	BPD				
	Nondissociative (BPD D–)	Dissociative (BPD D+)	Healthy controls	Test	*p* value
Dissociative experience					
DSS (state)	0.12 (0.11)	3.10 (1.60)	0.12 (0.22)	$t_{10.1} = 6.2$	< 0.001
DES (trait)	15.9 (11.5)	35.5 (12.7)	3.32 (3.01)	$t_{19} = 3.7$	0.002
Hearing threshold level, dB	33.3 (4.62)	42.0 (13.6)	32.7 (11.2)	$t_{12.5} = 2.0$	0.07
General psychopathology					
Borderline Symptom List[30]	1.77 (0.48)	2.09 (0.53)	0.74 (0.31)	$t_{19} = 1.4$	0.17
Cormorbidity					
No. Axis-I disorders	1.30 (0.82)	1.00 (0.89)	—	$t_{19} = 0.8$	0.44
No. Axis-II disorders	0.50 (0.53)	0.64 (0.67)	—	$t_{19} = 0.6$	0.61
PTSD: current, %†	50	27	—		0.39
PTSD: lifetime, %†	50	36	—		0.67
Trauma, %†	100	82	6		0.48
Baseline reactivity					
US valence‡	5.70 (0.5)	5.45 (0.7)	4.86 (1.0)	$t_{19} = 0.9$	0.36
US arousal§	5.20 (0.9)	5.18 (0.9)	4.51 (1.5)	$t_{19} = 0.1$	0.96
US log (SCR+1)	0.36 (0.2)	0.37 (0.2)	0.27 (0.2)	$t_{19} = 0.2$	0.88
CS (habituation) log (SCR+1)	0.09 (0.1)	0.05 (0.1)	0.05 (0.1)	$t_{19} = 1.3$	0.20
Skin conductance level	0.94 (0.2)	0.85 (0.2)	0.83 (0.2)	$t_{19} = 1.2$	0.23
Declarative knowledge					
CS+ contingency awareness	67 (23)	51 (29)	49 (9.2)	$t_{19} = 1.6$	0.13
CS– contingency awareness	17 (22)	29 (27)	9 (17)	$t_{19} = 1.1$	0.30

BPD = borderline personality disorder; BPD D+ = borderline personality disorder, dissociative subgroup; BPD D– = borderline personality disorder, nondissociative subgroup; CS = conditioned stimulus; CS+ = positive conditioned stimulus; CS– = negative conditioned stimulus; DES = Dissociative Experiences Scale;[25] DSS = Dissociation-Tension-Scale acute;[24] PTSD = posttraumatic stress disorder; SCR = skin conductance response; SD = standard deviation; US = unconditioned stimulus.
*Unless indicated otherwise.
†Fisher exact test.
‡Measured on a 6-point Likert scale: 1 = pleasant, 6 = unpleasant.
§Measured on a 6-point Likert scale: 1 = relaxed, 6 = excited.

expected, given that the CS– was not paired with the unconditioned stimulus, whereas the CS+ was combined with the unconditioned stimulus. Similar to the control group, the BPD D– group acquired a conditioned response to the CS+, shown by a significant pre–post increase in valence ($t_9 = 3.3$, $p = 0.009$, $d = 1.04$) and no significant pre–post differences in CS– ($t_9 = 1.8$, $p = 0.11$, $d = 0.56$). In contrast, the BPD D+ group did not acquire a conditioned response. There were no significant pre–post increases regarding the CS+ ($t_{10} = 0.0$, $p = 1.00$, $d = 0.01$) and CS– ($t_{10} = 0.3$, $p = 0.77$, $d = 0.09$).

Emotional learning: arousal ratings

The $2 \times 2 \times 2$ factorial ANOVA for arousal with the factors group, type and time (pre v. post) and the covariate dissociation (continuous format) showed a significant type × time × dissociation interaction ($F_{1–65} = 9.1$, $p = 0.004$), signifying that differential conditioning was influenced by dissociation. Further analyses revealed a significant type × time interaction ($F_{1–65} = 12.6$, $p < 0.001$), indicating successful overall differential conditioning regarding arousal for all participants and main effects for group ($F_{1–65} = 29.7$, $p < 0.001$), type ($F_{1–65} = 7.5$, $p = 0.008$) and time ($F_{1–65} = 4.8$, $p = 0.031$).

To further evaluate differential conditioning (Fig. 2) in the BPD subgroups, we calculated single pre–post comparisons (Student t tests). Regarding the CS+, the control group exhibited a significant pre–post increase in arousal ($t_{34} = 3.3$, $p = 0.002$, $d = 0.56$), and, as expected, no significant pre–post differences regarding the CS– ($t_{34} = 0.3$, $p = 0.79$, $d = 0.04$). Similar to the control group, the BPD D– group acquired a conditioned response to the CS+, indicated by a significant pre–post increase in arousal ($t_9 = 3.2$, $p = 0.012$, $d = 1.00$), and no

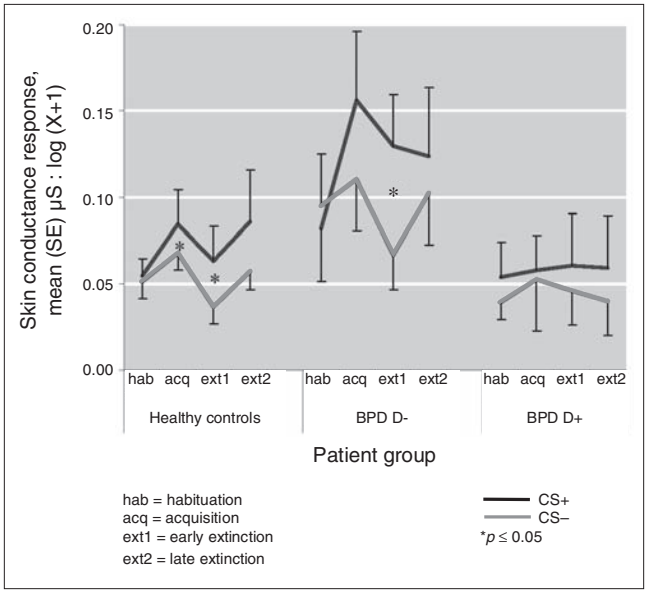

Fig. 1. Conditioned skin conductance responses averaged for habituation, acquisition, early and late extinction for the following groups: healthy controls and patients with borderline personality disorder (BPD), both those with no dissociative symptoms (BPD D–) and those with high state dissociative experience (BPD D+). The $2 \times 2 \times 4$ factorial analysis of variance for skin conductance response with the factors group (BPD, control), type (CS+, CS–) and time (habituation, acquisition, early extinction, late extinction) and the covariate dissociation (continuous format) showed a significant effect for the interaction type × quadratic time × dissociation ($F_{1–65} = 7.2$, $p = 0.009$), signifying that differential conditioning was influenced by dissociation. In the control group, differences between CS+ and CS– were significant in the acquisition ($p = 0.033$) and in the early extinction phases ($p = 0.019$). Differences in the BPD D– group were present only in the early extinction phase ($p = 0.05$); however, effect sizes for CS+ and CS– differences were small to medium for the acquisition phase. We found no significant differences in the BPD D+ group (all $p > 0.20$). SE = standard error. *$p \leq 0.05$.

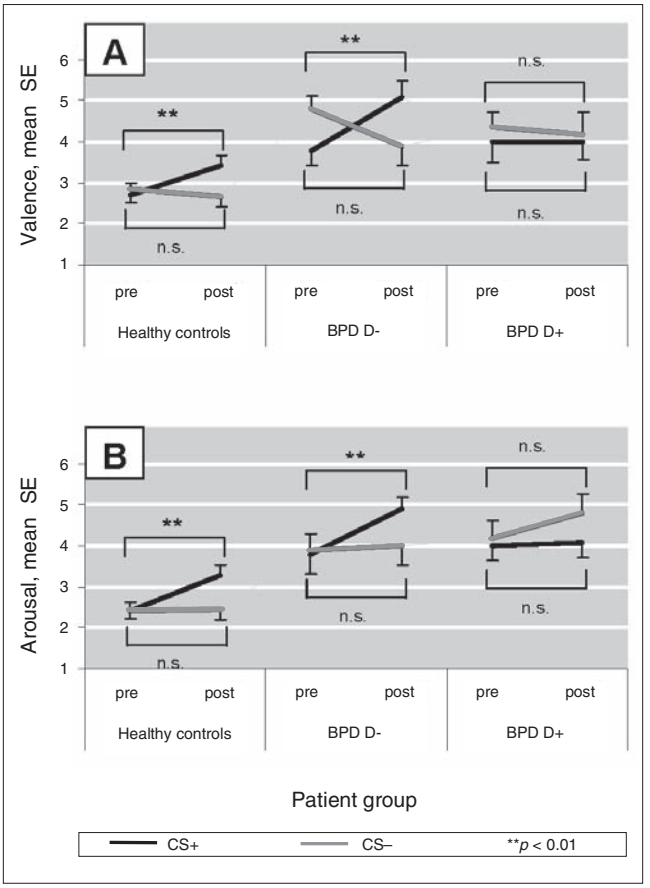

Fig. 2. Ratings for valence and arousal before (pre) and after (post) the conditioning procedure for all groups: healthy controls and patients with borderline personality disorder (BPD), both those with no dissociative symptoms (BPD D–) and those with high state dissociative experience (BPD D+). Both $2 \times 2 \times 2$ factorial analyses of variance with the covariate dissociation (continuous format) showed a significant type × time × dissociation interaction (valence $F_{1–65} = 8.4$, $p = 0.005$; arousal $F_{1–65} = 9.1$, $p = 0.004$), signifying that differential conditioning was influenced by dissociation. Participants in the control group ($n = 35$) and in the BPD D– group ($n = 10$) had significant pre–post differences in valence (control $p = 0.008$; BPD D– $p = 0.009$) and arousal (control $p = 0.002$; BPD D– $p = 0.012$) for CS+, signifying successful emotional learning. The BPD D+ group ($n = 11$) did not show any significant pre–post difference regarding valence ($p = 1.00$) or arousal ($p = 0.867$). SE = standard error. *$p < 0.01$.

significant pre–post differences in the CS– ($t_9 = 0.2$, $p = 0.86$, $d = 0.06$). In contrast, the BPD D+ group did not acquire a conditioned response. There were no significant pre–post increases regarding the positive ($t_{10} = 0.2$, $p = 0.87$, $d = 0.05$) and negative conditioned stimuli ($t_{10} = 1.0$, $p = 0.36$, $d = 0.28$).

Cognitive/declarative knowledge

The 2 × 2 factorial ANOVA for contingency awareness with the factors group (BPD, control) and type (CS+ v. CS–) and the covariate dissociation (continuous format) showed a significant type × dissociation interaction ($F_{1–65} = 6.5$, $p = 0.013$), signifying that differential conditioning was influenced by dissociation. Further analyses revealed significant main effects for group ($F_{1–65} = 7.7$, $p = 0.007$) and type ($F_{1–65} = 94.8$, $p < 0.001$).

To further evaluate differential conditioning (Fig. 2B) in the BPD subgroups, we calculated between-group differences but found no significant effects regarding contingency awareness (BPD D+ v. BPD D–: CS+ $p = 0.13$; CS– $p = 0.30$). Within-subject comparison for contingency awareness of CS+ and CS– revealed significant differences for the control group ($t_{34} = 7.58$, $p < 0.001$, $d = 1.28$) and the BPD D– group ($t_9 = 5.51$, $p < 0.001$, $d = 1.74$), but only a statistical trend for the BPD D+ group ($t_{10} = 1.87$, $p = 0.09$, $d = 0.56$) with a medium effect size.

Discussion

Our findings support our hypothesis that patients with BPD who have high state dissociative experiences exhibit diminished acquisition of differential aversive delay conditioning with respect to the emotional aspects of learning (skin conductance response, self-report of valence and arousal) compared with healthy controls and individuals with BPD who do not experience dissociative symptoms. Specifically, the control group and the BPD D– subgroup demonstrated differential skin conductance responses in the acquisition (control group only) and the extinction phases (control and BPD D– groups) and showed an increase in valence and arousal to the CS+ during the conditioning procedure. In contrast, the BPD D+ group failed to report higher negative valence and higher arousal ratings to the CS+ after the conditioning procedure or any differential response regarding skin conductance. Since this is, to our knowledge, the first published conditioning study investigating the influence of dissociation on emotional learning and the first study investigating conditioning processes in patients with BPD, we cannot compare our findings to similar studies. However, from a theoretical point of view, previous studies proposing inhibited amygdala processing during dissociative states[9,12] and studies indicating that the amygdala is necessary for the acquisition and expression of conditioned responses[15,37,38] are consistent with our results. We did not find any indications that general psychopathology or perceptual difficulties might explain conditioning deficits in patients in the BPD D+ group. Even though the hearing threshold was minimally altered, the BPD D+ group showed intact unconditioned responding. Intact unconditioned responding has previously been reported in studies of animals[18,37] and humans[15,20,32] with lesion or inactivation of the amygdala.

We also compared indices of declarative knowledge. The findings were inconsistent, as the 2 × 2 factorial ANOVA showed a significant type × dissociation interaction, whereas we did not find significant differences regarding contingency awareness between the BPD D+ group versus the BPD D– group. However, we cannot exclude the possibility that the absence of group differences may reflect insufficient power, given the small sample size. Therefore, the finding of unimpaired cognitive/declarative knowledge among participants in the BPD D+ group remains preliminary.

Limitations

There are several limitations to our study. First, although the sample size was relatively large compared with many other psychophysiological studies, subdividing the BPD group on the basis of dissociative experience in the secondary analyses reduced power. Because of the small sample size in subgroups we did not use a Bonferoni correction for multiple testing to avoid type II errors. The chosen strategy of using the upper and lower tercile was the best compromise between sample size and natural occurrence of clinically relevant dissociation. Splitting the groups based on a published cut-off score of 2.7[24] for acute severe dissociative experience resulted in too few participants with severe dissociative experiences ($n = 5$) for statistical comparison. However, using only the 5 patients with severe dissociation yielded similar but more pronounced findings (data available on request). A median split resulted in subgroups of equal size, but dissociative scores in the BPD subgroup below the median was still 3-fold higher than in the control group, whereas dissociative experience in the BPD subgroup above the median was below the published cut-off. Second, because this was a female sample, the generalizability of the findings is constrained. However, this also reduced heterogeneity, which may be useful in the light of data revealing robust differences between sexes in emotional responding.[39] Third, there is a tremendous overlap between BPD and dissociative disorder,[40,41] whereas the exact numbers depend on the population studied. Furthermore, these disorders share high rates of developmental traumata. Future research should include a comparison group with dissociative disorders to clarify the generalizability of our findings, and should assess the comorbidity of dissociative disorders within the BPD group. Fourth, several authors conceptualize qualitatively distinct forms of dissociation.[26,42] For example, Stiglmayr and colleagues[27] differentiate psychological and somatoform dissociation, whereas Holmes and coworkers[42] distinguish detachment and compartmentalization. We calculated subscores for psychological and somatoform dissociation,[26] which correlated highly ($r = 0.89$). This is in line with Stiglmayr and colleagues,[24] who revealed a single factor solution of dissociation in patients with BPD using the Dissociation-Tension-Scale acute. Therefore, we performed no separate analysis on the influence of different aspects of

dissociation on learning processes. Finally, it may be questioned if the effects found could also be attributed to trait dissociative experience instead of state dissociative experience. That dissociative experience is highly variable over time within patients with BPD,[43] and that state (Dissociation-Tension-Scale acute) and trait (German version of the Dissociative Experiences Scale) dissociative experience in our sample exhibited a shared variance below 50% ($r = 0.678$, $p < 0.001$) suggests that effects in our study may appropriately, though perhaps not definitely, be considered to be caused by state dissociative experience. This approach is similar to previous studies of our working group, investigating the influence of state dissociative experience on the startle response and its habitation.[9]

Clinical implications of our findings should be considered. Even though our findings are solely related to the acquisition of new unconditioned–conditioned stimuli associations, recent studies indicate that the amygdala is also necessary in extinction.[44] Therefore, dissociation may alter acquisition as well as extinction processes. As stress is known to trigger dissociative symptoms,[43] dissociation should be closely monitored in exposure therapy and optionally limited by pharmacotherapy.[45] Taken together, findings from the present study point to dissociative experience as an important psychopathological factor associated with diminished emotional learning processes in BPD.

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