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Neural Correlates of Emotional Action Control in Anger-Prone Women with Borderline Personality Disorder

Running head: Emotional action control in BPD

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Abstract

Background: Difficulty in controlling emotional impulses is a crucial component of borderline personality disorder (BPD) that often leads to destructive, impulsive behaviors against others. In analogue to recent findings in aggressive samples, deficits in prefrontal-amygdala coupling during emotional action control may account for these symptoms.

Methods: To study the neurobiological correlates of altered emotional action control in BPD, 30 medication-free, anger-prone, female BPD-patients and 28 age- and intelligence-matched healthy women took part in an Approach-Avoidance task while lying in the MR-scanner. The task required controlling fast behavioral tendencies to approach happy and avoid angry faces. Additionally, saliva testosterone and self-report tendencies to act out anger were collected before the task and correlated with behavioral and fMRI data.

Results: BPD-patients reported increased tendencies to act out anger and were faster in approaching than avoiding angry faces compared to healthy women, suggesting deficits in emotional action control in BPD. On a neural level, controlling fast emotional action tendencies was related to enhanced activation in the antero- and dorsolateral prefrontal cortex across groups. Healthy volunteers showed a negative coupling between the left dorsolateral prefrontal cortex and right amygdala, whereas this was absent in BPD-patients.

Limitations: Specificity of results for BPD and sex differences remain unknown due to lack of clinical control groups and male participants.

Conclusion: The results indicate reduced lateral prefrontal-amygdala communication during emotional action control in anger-prone BPD-patients. The findings provide a possible neural mechanism underlying difficulties with controlling emotional impulses in BPD.

Introduction

Borderline personality disorder (BPD) is a severe mental disorder characterized by instability of affect, self-image, and personal goals along with interpersonal dysfunctions and high levels of hostility, impulsivity, and risk-taking behavior [1]. Enhanced difficulty in controlling emotional impulses is a crucial component of BPD [2]. Unfortunately, the patients' impulsive responses are often directed against other individuals, thereby obstructing healthy social relationships [3]. Investigating the neurobiological correlates of altered social emotional behavior in BPD is of high relevance as an increased knowledge of underlying mechanisms may guide the development of new mechanism-based treatment [4]. In the present study, we investigated these neurobiological correlates in a group of female BPD-patients who performed an experimental task that requires rule-driven control of emotional behavior.

Previous studies with BPD-patients found altered reactivity to emotional stimuli in several brain regions including prefrontal areas and the amygdala [5]. While increased amygdala activation has been associated with emotional hypersensitivity, decreased activity in the (dorsolateral) prefrontal cortex (PFC) [5,6] and reduced prefrontal-amygdala functional and structural connectivity [7] suggest deficient or ineffective communication between these regions in BPD-patients. In studies with healthy participants, the dlPFC as well as the lateral anterior PFC (aPFC) have been found to be crucially involved in the control of emotionally relevant actions by down-regulating the amygdala [8-12]. A recent investigation found reduced lateral aPFC activation and aPFC-amygdala coupling in aggressive male offenders during emotional action control [12]. This suggests that an inefficient inhibition of the amygdala by lateral PFC regions could be a neurobiological correlate underlying decreased cognitive control of emotional behavioral tendencies [9-10], especially in individuals with a tendency to act out aggressively their feelings of anger or threat [12]. Testosterone modulates

lateral PFC-amygdala connectivity [11-12]. This hormone has been linked to the tendency to approach interpersonal threats and to act out aggressively [13-15]. Interestingly, testosterone levels have recently been reported to be enhanced in female BPD-patients [16-18]. Taken together, these findings raise questions about whether a) lateral PFC activity and PFC-amygdala connectivity are altered when BPD-patients have to control emotionally relevant actions b) and whether such alteration may be related to the patients' aggression and endogenous testosterone levels [3].

To address these questions, anger-prone (see Methods) female BPD-patients and female healthy volunteers took part in an Approach-Avoidance task during which they were instructed to respond to briefly presented happy and angry facial expressions with approach and avoidance movements [9-12, 19]. During affect-congruent conditions, participants could follow their emotional tendency to approach happy and avoid angry faces, whereas they had to control their emotional action tendencies during affect-incongruent conditions in order to perform the counterintuitive action of avoiding happy and approaching angry faces. In previous studies, healthy volunteers responded slower and showed stronger aPFC activations in trials requiring emotional action control (affect-incongruent versus congruent trials) [9-11]. Using this task, deficient aPFC-amygdala coupling has been found in highly aggressive male offenders [12] suggesting less prefrontal regulation of emotional actions [10].

Here, we investigated whether similar reductions in the communication between the prefrontal cortex and amygdala during emotional action control could be found in anger-prone female BPD-patients. We hypothesized that BPD-patients would show deficits in cognitive control of emotional action tendencies as reflected in reduced behavioral and lateral prefrontal congruency-effects compared with healthy volunteers. In addition, we expected reduced PFC-amygdala coupling during affect-incongruent (versus affect-congruent) condition. Based on previous research, we additionally assessed whether these alterations could be related to

patients' elevated levels of endogenous testosterone [17] and the strength of their tendency to act out their feelings of anger.

Methods and Materials

Participants

30 medication-free female BPD-patients (BPD; $M_{\text{age}}=26.9$, $SD=6.1$, range=18–40 years) and 28 age- and intelligence-matched healthy women (CON; $M_{\text{age}}=26.5$, $SD=5.7$, range=19–48 years) took part in the study (see Table 1; originally, $N=32$ BPD and $N=30$ CON were measured; $N=4$ participants had to be excluded due to head movements or joystick malfunctioning).

Exclusion criteria comprised of: neurological disorders, alcohol/drug abuse in the last two months or alcohol/drug dependence in the last 12 months, a lifetime diagnosis of schizophrenia, schizoaffective or bipolar disorder, severe medical illness, or psychotropic medication for at least two weeks prior to participation. Only patients were included who currently fulfilled at least five DSM-IV criteria of BPD *including* BPD-criterion 8 “anger proneness” given the focus of the current study, and to avoid excessive heterogeneity [20]. Healthy controls had never received a psychiatric diagnosis (assessed by structured interviews, see below) or undergone a psychotherapeutic or psychiatric treatment.

The study was part of the KFO-256 [21], a German consortium on mechanisms underlying emotion dysregulation in BPD. Participants were recruited through a KFO-256 general recruitment unit with psychometric data of all participants being monitored in a central data bank. Samples across KFO-256 studies may show overlap in participants. The study was approved by the Ethics Committee of the Medical Faculty of the University of Heidelberg. Participants provided written informed consent. Details on the experimental protocol are provided in the Supplementary Information.

Measures

All patients and healthy volunteers took part in an extensive onsite diagnostic interview to assess BPD and other current and lifetime psychiatric disorders. Interviews consisted of the Structured Clinical Interview for DSM-IV [SCID-I for axis-I disorders; 22] and the International Personality Disorder Examination [IPDE for axis-II disorders; 23]. They were performed by experienced diagnosticians (AA, SC, KH, DG, FK, see Acknowledgement) who had at least a M.Sc. in Psychology or M.D. and underwent standardized training resulting in high inter-rater reliabilities ($ICC \geq .91$ for both the number of BPD criteria and the dimensional score assessed by the ZAN-BPD scale). Body-mass index was calculated according to height and weight measurements on the study day. Possible confounders of testosterone data (menstrual cycle, contraceptive intact, smoking) were assessed in a standardized questionnaire. Raven's progressive matrices [24] were used as an estimate for intelligence. BPD symptom severity was assessed with the Zanarini Rating Scale for BPD [25], depressiveness with the Beck Depression Inventory [26], Attention Deficit Hyperactivity Disorder (ADHD) symptoms with the Self-Rating Behavior Questionnaire for ADHD [27], trait anxiety with the State-Trait-Anxiety Inventory [28], and the State-Trait-Anger Expression Inventory [29] for the disposition to act out feelings of anger.

Testosterone Levels

A saliva sample was collected prior to the experiment (1.30–2.00p.m.) in 2-ml polypropylene tubes and immediately frozen at -20°C for biochemical analysis. Testosterone concentration was measured using a competitive chemiluminescence immunoassay (LIA) with a sensitivity of 0.0025ng/mL (IBL) and intra- and inter-assay coefficients between 10%

and 12%. As testosterone levels were skewed, log-transformed and z-standardized (per group) values were used.

Approach-Avoidance Task

The experiment was based on a 2x2-design with the factors congruency and facial affect. Participants had to categorize the affect of angry and happy faces (presentation time: 100ms) by either pushing a joystick away from themselves or pulling it towards themselves as soon as the face appeared [9-12]. After having moved the joystick, they had to return it to the starting position before the end of the inter-trial interval (2-4sec). The task consisted of 16 blocks with 12 trials/block. Each block started with a written instruction indicating the required responses, i.e., pulling for happy and pushing angry faces (congruent condition) or vice versa (incongruent condition), and ended with a baseline period (black screen; 21-24sec). The sequence of blocks (incongruent/congruent) was counterbalanced across participants. Within each block, facial affect and sex were presented in a pseudorandomized order (<4 sequential presentations of the same affect and/or sex). The task lasted for 35min starting with a joystick calibration and training (4 blocks/8 trials with different stimuli). See Supplementary Information for details.

Data Acquisition

Stimulus presentation and acquisition of joystick positions (Fiber Optic Joystick, Current Designs, sampling rate: 550Hz; placed on the participants' abdomen) were controlled by Presentation software (Version 16.3, Neurobehavioral Systems). Functional images were acquired in a 3-Tesla whole-body MR scanner (Tim Trio; Siemens) equipped with a 32-channel head coil using a multi-echo GRAPPA sequence (TR=2,190ms, TEs=9.3/20.9/32/44ms; 34 transversal slices, ascending acquisition, distance factor=17%,

effective voxel size=3.3x3.3x3.0mm³, FoV=212mm [30]). After completion of the task, isotropic high-resolution structural images were recoded using a T1-weighted coronal-oriented MPRAGE sequence (TR=2,300ms, TE=2.98ms, 240 sagittal slices, effective voxel size=1.0x1.0x1.0mm³, FoV=256mm).

Data Analysis

BPD-Symptomatology. Two sample t-tests were used to analyze group differences in BPD-symptom severity, depressiveness, ADHD symptoms, trait anxiety, tendencies to act out anger, and, testosterone ($p < .05$ and Cohen's d as effect size).

Behavioral Data. Trials with incorrect responses, reaction times <100ms or >1,500ms, or with joystick peak velocities or path lengths $> \pm 3SDs$ of the participant-specific data distribution were excluded. To investigate emotional action control, we calculated difference scores by subtracting the mean reaction time (time from stimulus presentation until movement onset) for affect-congruent conditions from affect-incongruent conditions. These difference scores were then submitted to a group (BPD, CON) by affect (happy, angry) analysis of variance (ANOVA) employing a two-tailed $p < .05$ significance threshold. Effect sizes of significant results are reported as proportion of explained variances (η^2). The sphericity assumption was not violated ($\epsilon = 1.0$). For further analysis of interaction effects, Dunn's Multiple Comparisons with Bonferroni correction for multiple testing were used as post-hoc tests.

FMRI Data. Statistical parametric mapping (SPM8, www.fil.ion.ucl.ac.uk/spm/software/spm8/) was used for preprocessing and analyzing imaging data following previously described procedures for multi-echo GRAPPA MR sequences ([30], Supplementary Information).

For each participant, a design matrix was constructed by modeling face presentation onset and reaction time (convolved with the canonical hemodynamic response function) as separate regressors for the four combinations of affect (angry, happy) x movement (approach, avoid), two regressors for the excluded trials (misses) and the instructions/feedback (information), and regressors for the movement parameters and the signal intensities in white matter, in cerebrospinal fluid, and in the proportion of MR image outside the skull ([31], Supplementary Information). Finally, fMRI time series were high-pass filtered (cutoff 120s) and temporal autocorrelation was modeled as a first-order autoregressive process.

In line with previous publications [9-12], consistent effects across participants and between groups were assessed in a random effects multiple regression analysis with the estimated effects of the eight conditions based on the group x affect x movement interaction.

As we were interested in neural correlates of emotional action control, analyses were focused on the congruency effect, i.e., task-related differences of affect-incongruent (avoid-happy, approach-angry) vs. affect-congruent (approach-happy, avoid-angry) trials across groups and for each group separately. We performed a hypothesis-driven region-of-interest (ROI) analysis [see 8-12] on the left and right aPFC [32] and dlPFC [33] as well as an exploratory whole brain analysis. We assessed congruency effects within one group and tested whether those effects were specific to that group and thus significantly weaker in the other group. This was done by applying a strict family-wise error (FWE) voxel-level correction for multiple comparisons ($p_{\text{FWE}} < .05$ based on recent recommendations [34]) on the effect of interest (group-specific congruency effect) and masking that contrast with the group x congruency contrast (at $p < .05$ uncorrected; also see 12]. Please note that Bonferroni-corrected p-values of ROI analysis are reported.

Furthermore, psychophysiological interaction analyses (PPIs; [35]) were performed to test whether the coupling of aPFC and dlPFC with the amygdala (ROI [36]) during the

congruency effect was different between groups. To define the volumes-of-interest (VOI), voxels within a sphere of 8mm radius around to peak voxel of the congruency effect across both groups were selected (left aPFC: $x=-24$, $y=52$, $z=6$ and left dlPFC: $x=-32$, $y=52$, $z=22$; see Results). Participant-specific contrast images were generated describing the PPI between the time courses of the VOIs and affect-incongruent vs. affect-congruent conditions.

We additionally performed explorative correlations analyzing associations of behavioral and fMRI data with testosterone and tendency to act out anger ($p<.05$).

Results

BPD-Symptomatology. Besides significantly higher levels of BPD-symptom severity, depressiveness, ADHD symptoms, and trait anxiety (all $ps<.001$), BPD-patients reported stronger outwardly directed anger ($p=.003$) and had significantly increased testosterone levels ($p=.023$) compared with healthy volunteers (see Table 1 for statistical details).

Table 1

Behavioral Data. Mean reaction times are presented in Table 2. The analysis of difference scores (incongruent minus congruent trials) revealed a significant group x affect interaction ($F(1,56)=5.72$, $p=.020$, $\eta^2=.09$). Post-hoc tests showed significantly larger difference scores for happy than angry faces in both groups ($ps<.01$) and a significant group effect for angry faces ($p<.05$; Figure 1). The negative mean difference score of BPD-patients ($M=-0.045$, $SE=0.014$) suggested relatively faster approach vs. avoidance responses to angry

faces, an effect that was absent in healthy volunteers ($M=-0.001$, $SE=0.015$; $p>.05$). This effect in BPD-patients is opposite to previously reported emotional action tendencies in healthy samples to avoid rather than approach signals of interpersonal threats [19] and may support the role of aggression in BPD [3]. Effects remained significant after controlling for depressiveness, ADHD symptoms, and trait anxiety.

Figure 1 and Table 2

FMRI Data. The multiple regression analysis revealed a significant congruency effect (contrast: incongruent > congruent trials) across both groups in the left dlPFC (BA46 extending into BA10; peak voxel: $x=-32$, $y=52$, $z=22$; ROI: $p_{FWE}=.002$, $k=181$; Figure 1B-C and Table 3 for significant whole brain results) and in the left lateral aPFC (BA10; $x=-24$, $y=52$, $z=6$; ROI: $p_{FWE}=.050$, $k=51$). In the left dlPFC, this effect was driven by healthy volunteers (BA46 extending into BA10; $x=-32$, $y=54$, $z=12$; ROI: $p_{FWE}<.001$, $k=31$; Figure 1C) and it was significantly weaker in BPD-patients (as the reported result in healthy volunteers remained after masking the main effect in healthy volunteers by group (CON>BPD) x congruency interaction thresholded at $p<.05$ following [9-12]).

Furthermore, BPD-patients activated a relatively wide network during incongruent compared to congruent trials. There was a significant congruency effect in a more posterior located cluster in the right dlPFC (BA46; ROI: $p_{FWE}<.001$, $k=39$; Figure 1C), which was significantly weaker in healthy volunteers (as the reported result remained after masking the effect in BPD-patients by the group (BPD>CON) x congruency effect thresholded at $p<.05$).

Additionally, BPD-patients showed a significant congruency effect in parts of the right middle and inferior frontal gyri, right supra marginal, left inferior temporal, bilateral fusiform gyri, and in several clusters of the occipital cortex including the precuneus and cuneus (all $p_{FWE} < .05$; Table 3). The described effects were evoked by both happy and angry faces according to post-hoc conjunction analyses (all $ps < .001$ [37]).

Figure 2 and Table 3

Connectivity analysis with the left aPFC ($x=-24, y=52, z=6$) as seed region did not reveal any significant effects. However, using left dlPFC ($x=-32, y=52, z=22$) as seed region on the congruency effect indicated a group difference with the right amygdala (ROI: $x=34, y=0, z=-20, p=.005, k=4$) with healthy volunteers showing a negative coupling between the left dlPFC and right amygdala (ROI: $x=34, y=0, z=-20, p_{FWE}=.03, k=10$), while BPD-patients showed no differential connectivity effect (Figure 1D-E).

Correlation Analyses. The tendency to act out anger modulated the group (BPD>CON) by congruency effect (incongruent > congruent trials) in the left aPFC (ROI: $x=-28, y=52, z=10, p_{FWE}=.021, k=11$) and the right amygdala (whole brain: $k=52, x=30, y=-8, z=-12, p_{FWE}=.002$). Post hoc analyses revealed that these effects were mainly driven by angry faces: In healthy volunteers, congruency effects decreased in the left aPFC and increased in the right amygdala with an increasing tendency to act out anger. Contrary to this, congruency effects were unrelated to aPFC activations in BPD-patients and decreased in the right amygdala with an increasing tendency to act out anger (Figure 2). No associations were found between the tendency to act out anger and behavioral data (all $p > .05$), and no significant

association was found with testosterone, except positive correlations with the behavioral tendency to approach rather than avoid happy and angry faces (BPD: $r=.50$, $p=.005$, CON: $r=.35$, $p=.072$; Supplementary Figure 1).

Discussion

The present study aimed to test neural correlates of aggression in female BPD-patients during emotional action control. The results pointed at several behavioral and neural deficits of emotional action control in BPD-patients: Behaviorally, the patients showed increased self-reported tendencies to act out feelings of anger and relatively faster approach than avoidance behavior for angry faces. At the neural level, they showed a reduction in the negative prefrontal-amygdala coupling that was observed in healthy participants during emotional action control. We will discuss these effects in relation to current literature below.

In line with the expected deficits in cognitive control of emotional action tendencies and previous findings in anger-prone or aggressive individuals [38-40], BPD-patients showed relatively faster approach than avoidance responses to angry faces. Our data add to previous reports of an increased likelihood to detect subtle signals of facial anger [41-42], a stronger initial orientation towards negative emotional faces [43], and an increased percentage of attention shifts towards threatening emotional faces [44-45] in BPD. Together these studies suggest a hypersensitivity for negative or threatening emotional information as well as difficulties in the control of emotional impulses, two symptoms which we have recently proposed as possible mechanisms for the increased tendency to act out aggressively in response to interpersonal threats or provocations [3]. Both, threat hypersensitivity and the reduced or slower avoidance of interpersonal threat stimuli may be related to growing up in an unpredictable, invalidating, and abusive environment [46]. Experiences like these, which are

reported by the majority of BPD-patients, may not foster avoidance of potential interpersonal threats as a favorable option and could generally hinder the development of an efficient and reliable emotion action control system [47]. However, so far it remains an open question whether deficits in emotion action control are rather a risk factor or a consequence of negative social experiences throughout life and may be modulated by specific interventions.

In the current study, we were primarily interested in studying the neural correlates of deficient emotional action control in BPD-patients using fMRI. Importantly, the negative connectivity between the lateral PFC and amygdala in healthy volunteers was absent in BPD-patients. This connectivity pattern has previously been shown to relate to lateral PFC inhibition of the amygdala which can facilitate emotional action control [10]. A similarly reduced – albeit more anterior – PFC-amygdala coupling was recently found in aggressive male delinquents as well as a lack of communication from the aPFC to the amygdala in a sample susceptible to develop affective disorders during emotional action control [10,12]. This suggests that deficiencies in the communication between these regions are a common neurobiological correlate for difficulties in emotional impulse control [19]. This is supported by further similarities between our data and increased behavioral approach tendencies in anger-prone or aggressive individuals [19,38-39]. Deficits in dlPFC-amygdala communication – but not PFC activation per se – have also been reported in BPD-patients during (negative) affect regulation [48-49] and thus highlight the centrality of emotion dysregulation for this disorder and its treatment [47].

Furthermore, both groups replicated previously reported anterior and dorsal lateral PFC activations in trials that required control of fast emotional action tendencies [8-12,19]. The aPFC is known to facilitate the selection of responses by integrating and coordinating different cognitive processes [50], while the dlPFC seems critically involved in executive processes, particularly during continuous updating and manipulation of stimuli in working

memory [51] and emotion regulation [8]. BPD-patients did not show blunted PFC activations while overriding fast emotional action tendencies, but increased activations in the PFC as well as in a broad network of brain regions involved in the processing of visual (occipital cortex) and facial (fusiform face area) information and emotion processing (precuneus, cuneus), amongst others. Interestingly, the current results are highly similar to a recently reported network of activations in highly aggressive men performing the same task [12]. Finally, it is well worth considering the associations between self-reported tendencies to act out anger and lateral PFC and amygdala activations: In healthy volunteers, the tendency to act out anger was negatively related to left lateral aPFC and positively to amygdala activations for approach of angry faces. This indicates that healthy volunteers who are less able to recruit prefrontal areas to down-regulate the amygdala while approaching angry faces are those who are less able to refrain from acting out feelings of anger. Contrary to this, in BPD-patients with a high tendency to act out anger, approaching angry faces was associated with decreased amygdala responses, without a significant prefrontal effect. Acting out to interpersonal threat may hence be a way to regulate aversive states of anger or other negative emotions by reducing arousal, inner tension, and increased limbic activation. This suggests a similar regulatory function of aggressive and auto-aggressive, self-injurious behaviors [52]. Clinically, the current results may suggest a stronger treatment focus on feelings of anger as well as the emotional action control ability in BPD-patients. While facial signals of anger are threatening for the majority of individuals and typically induce fear and avoidance, anger-prone individuals, such as BPD patients, interpret them as provocative and exhibit appetitive motivation and approach/attack behavior [53]. Learning strategies to avoid or withdraw from potentially threatening interpersonal situations could therefore be important for specific interventions in those BPD-patients with increased tendency to act out anger.

Despite several strengths of the current study, such as the inclusion of a large sample of medication-free BPD-patients and a well-matched healthy control group, several limitations need to be considered. First, BPD-patients had a number of comorbid disorders, which confirms the representativeness of the current sample, but may question the specificity of the results for BPD. Therefore, more studies in which clinical control groups as well as male participants are included are needed. Second, it would be interesting for future research to investigate whether approach-avoidance tendencies change as a function of psychotherapy. Third, important differences between the current and former studies with male aggressive delinquents [12,38] have to be noted: Although all BPD-patients reported current anger-proneness, only one patient fulfilled the criteria for antisocial personality and no information was available on psychopathic traits (while high levels of psychopathy were reported in [12,38]). Despite prominent differences between anger-prone BPD and psychopathy, the current results may however indicate a shared mechanism for deficits in emotional impulse control. Although problems in anger regulation are experienced by more than 70% of BPD patients [54], the restriction on anger-prone patients may limit the generalizability of the current results. This is important to mention since no differences were found in the response to angry faces in one previous behavioral study on emotional action control in an unselected sample of BPD-patients [55]. Fourth, except for the correlations with the tendency to act out anger, we did not find any emotion-specific neural congruency effects. This is unexpected when considering that behavioral group differences were only found for angry faces. It remains unclear whether the differences between neural and behavioral effects are due to a greater sensitivity in the neural data or are related to the Approach-Avoidance task, which may not fully differentiate between automatic and effortful stages of socio-emotional behaviors. Fifth, for time reasons, we did not include neutral facial expressions or a non-emotional control task as congruency effects have previously not been found in control tasks or for neutral faces [11-12,38] and because BPD-patients are known to interpret neutral faces

as aversive [56]. Finally, despite its general association with approach-related behavior, we could not replicate modulatory effects of testosterone on aPFC activations found in male participants [11-12] calling for further studies to clarify sex-specific effects of testosterone on neural correlates of cognitive control of emotional action tendencies.

Taken together, the present results show deficits in emotional action control in female anger-prone BPD-patients. Highly similar to male aggressive offenders, they were relatively faster in approaching than avoiding angry faces. Crucially, deficits in emotional action control in anger-prone individuals have, across diagnoses, been associated with a reduced lateral PFC-amygdala communication. These findings may represent a common mechanism underlying difficulties in controlling emotional impulses.

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Tables

Table 1. Demographic and psychometric information (mean \pm one standard deviation) as well as comorbid disorders (current (lifetime)) of patients with borderline personality disorder (BPD; $N=30$) and healthy volunteers (CON; $N=28$). ZAN-BPD: Zanarini Rating Scale for Borderline Personality Disorder; BDI-II: Beck Depression Inventory, revised; STAXI: State-trait Anger Expression Inventory; STAI: State-trait Anxiety Inventory; ADHD: attention deficit hyperactivity disorder; ADHD-SR: Self-Rating Behavior Questionnaire for ADHD; PTSD: posttraumatic stress disorder; PD: personality disorder.

	BPD	CON	T	p	d
Age (years)	26.9 \pm 6.1	26.5 \pm 5.7	0.28	.784	0.07
Intelligence (Raven)	54.2 \pm 4.2	54.1 \pm 4.1	0.09	.928	0.02
Body-mass index (kg/m ²)	23.0 \pm 2.9	22.0 \pm 2.5	1.40	.169	0.37
Salivary testosterone (pg/ml)	26.9 \pm 33.5	11.1 \pm 12.3	2.34	.023	0.62
BPD symptom severity (ZAN-BPD)	13.2 \pm 5.0	0.5 \pm 0.8	13.18	<.001	3.46
Depressiveness (BDI-II)	27.5 \pm 10.7	3.9 \pm 3.4	11.12	<.001	2.92
ADHD (ADHD-SR)	14.45 \pm 1.5	6.4 \pm 1.1	4.32	<.001	1.14
Trait Anxiety (STAI)	59.5 \pm 6.8	29.4 \pm 5.9	18.03	<.001	4.74
Anger Out (STAXI)	15.1 \pm 4.5	11.7 \pm 3.8	3.10	.003	0.82
Affective disorders	8 (22)	0 (0)			
Substance disorders	0 (3)	0 (0)			
Anxiety disorders	12 (15)	0 (0)			
PTSD	7 (8)	0 (0)			
Social phobia	5 (7)	0 (0)			
Somatoform disorders	3 (3)	0 (0)			
Eating disorders	7 (12)	0 (0)			
Antisocial PD	1 (1)	0 (0)			
Avoidant PD	10 (10)	0 (0)			

Table 2. Reaction times (\pm one standard error) for each group (patients with borderline personality disorder, BPD and healthy volunteers, CON) and factor in the Approach-Avoidance task.

	BPD	CON
Happy – Approach	578 (15)	562 (15)
Happy – Avoid	654 (20)	619 (21)
Angry – Approach	602 (17)	601 (21)
Angry – Avoid	627 (18)	598 (18)

Table 3. Clusters showing significantly larger activations for the affect-incongruent vs. affect-congruent conditions across groups, in healthy volunteers (CON) and BPD patients (BPD)

Note. Coordinates are defined in MNI space (X, Y, Z). P-values represent FWE-corrected voxel-level corrected values. K: cluster size, L: left, R: right, aPFC: anterior prefrontal cortex.

	BA	Side	X	Y	Z	K	T	P _{FWE}
<i>Congruency effect across groups</i>								
<i>VOI on aPFC</i>	10	L	-24	52	6	51	3.66	.025
<i>VOI on dlPFC</i>	46	L	-32	52	22	181	5.27	.001
<i>Whole brain effects</i>								
Calcarine Sulcus	17	L	-4	-78	10	76	6.05	.001
Superior occipital cortex	17	L	-10	-98	8	7	5.62	.004
Inferior temporal cortex	37	L	-50	-50	-24	17	5.62	.004
Cuneus	18	R&L	2	-82	22	39	5.57	.004
Dorsolateral prefrontal cortex	46/(10)	L	-32	52	22	6	5.27	.015
<i>Congruency effect in CON</i>								
<i>VOI on dlPFC</i>	46	L	-32	54	24	31	5.43	<.001
<i>Whole brain effects</i>								
Dorsolateral prefrontal cortex	46/(10)	L	-32	54	24	12	5.43	.008
<i>Congruency effect in BPD</i>								
<i>VOI on dlPFC</i>	46	R	26	42	24	39	5.39	<.001
<i>Whole brain effects</i>								
Superior occipital cortex/ precuneus	7/18/19	R	22	-76	32	180	6.57	<.001
Middle/ superior occipital cortex	18/19	L	-32	-84	12	107	6.35	<.001
Cuneus/ calcarine sulcus	17/18	L&R	-6	-80	22	159	6.24	<.001
Middle frontal gyrus	8	R	32	16	60	99	6.21	<.001
Lingual gyrus/ fusiform gyrus	18/19	L	-18	-70	-12	59	6.04	.001
Middle frontal gyrus	9	R	28	26	34	28	5.94	.001
Middle occipital cortex	19	L	-30	-64	26	37	5.38	.001
Inferior occipital cortex	37	L	-48	-64	-14	26	5.7	.003
Fusiform gyrus	37	L	-38	-44	-26	6	5.67	.003
Dorsolateral prefrontal cortex	46	R	26	42	24	42	5.66	.003

Superior occipital cortex	19	L	-14	-92	22	17	5.65	.003
Inferior temporal gyrus	37	L	-48	-52	-26	9	5.55	.005
Calcarine sulcus	17/18	R	12	-86	6	27	5.47	.007
Precuneus		R	12	-56	42	5	5.45	.007
Supra marginal gyrus	40	R	54	-46	42	5	5.33	.012
Inferior frontal gyrus	45	R	48	40	10	13	5.29	.014
Superior occipital cortex	18	L	-12	-96	12	6	5.23	.018

Figure Legend

Figure 1 A. Difference scores for reaction times \pm one standard error (affect-incongruent minus affect-congruent conditions) of patients with BPD (BPD) and healthy volunteers (CON). Note that the behavioral congruency effect for both emotions is influenced by a general movement effect (i.e., generally larger reaction times for avoid than approach joystick movements which is typically found in the MR version of the Approach-Avoidance task; also see: <http://www.ingevolman.com/Projects/suppl-to-volman-et-al-submitted>); **: $p < .01$, *: $p < .05$. B. Bar graph showing the mean activation \pm one standard error of the active voxels within the left dorsolateral PFC for affect-incongruent vs. affect-congruent conditions for each affect (happy, angry) and group (BPD, CON). C. Brain regions reflecting increased activations for affect-incongruent vs. affect-congruent conditions across groups (ALL), in healthy volunteers (CON), and in patients with BPD (BPD). For visual purposes, activations are presented at $p < .001$ and $k > 10$. D. Group difference on the congruency-related left dorsolateral PFC-amygdala connectivity, $p < .001$ for visual purposes. E. Bar graph showing the strength of the congruency-specific changes \pm one standard error in the dorsolateral PFC-amygdala connectivity for healthy volunteers (CON), which was not present in patients with BPD (BPD). *: $p < .05$.

Figure 2. Modulation of the congruency effect by the tendency to act out anger in the left amygdala for angry faces in patients with BPD (BPD) and healthy volunteers (CON). For visual purposes, activation is presented at $p < .001$. Scatterplots reflect correlations between the significant amygdala cluster for approach minus avoidance of angry faces and self-reported, z-standardized tendency to act out anger. BPD: $r = -.35$, $p = .06$, CON: $r = .52$, $p = .005$, $z = -3.19$, $p = .001$.