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Abstract	Borderline personality disorder (BPD) is a heterogeneous constellation of symptoms characterized by severe and persistent problems across interpersonal, cognitive, behavioral, and emotional domains of functioning [1, 2]. Diagnostic symptoms of BPD include: (1) frantic efforts to avoid abandonment, (2) a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation, (3) markedly and persistently unstable self-image or sense of self, (4) chronic feelings of emptiness, (5) transient, stress-related paranoid ideation or severe dissociative symptoms, (6) recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior, (7) impulsivity in at least two areas that are potentially self-damaging, (8) affective instability due to a marked reactivity of mood, and (9) inappropriate, intense anger, or difficulty controlling anger. These criteria are according to the DSM-IV, published in 2000 by the APA.
Keywords (separated by '-')	Anterior cingulate cortex - attachment representation - borderline personality disorder - fMRI - neuroimaging - unresolved trauma

Chapter 12
Neural Correlates of Emotion, Cognition, and Attachment in Borderline Personality Disorder and Its Clinical Implications

Anna Buchheim, Roberto Viviani, Carol George, Horst Kächele, and Henrik Walter

Keywords Anterior cingulate cortex • Attachment representation • Borderline personality disorder • fMRI • Neuroimaging • Unresolved trauma

Introduction

Borderline personality disorder (BPD) is a heterogeneous constellation of symptoms characterized by severe and persistent problems across interpersonal, cognitive, behavioral, and emotional domains of functioning [1, 2]. Diagnostic symptoms of BPD include: (1) frantic efforts to avoid abandonment, (2) a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation, (3) markedly and persistently unstable self-image or sense of self, (4) chronic feelings of emptiness, (5) transient, stress-related paranoid ideation or severe dissociative symptoms, (6) recurrent suicidal behavior, gestures, or threats, or self-mutilating behavior, (7) impulsivity in at least two areas that are potentially self-damaging, (8) affective instability due to a marked reactivity of mood, and (9) inappropriate, intense anger, or difficulty controlling anger. These criteria are according to the DSM-IV, published in 2000 by the APA.

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Lieb et al. [3] suggested clustering these criteria into four sectors of psychopathology because patients who manifest symptoms in all four areas simultaneously can be successfully discriminated from those with other forms of personality disorder. The first area is *affective disturbance*. Patients with BPD display a range of intense dysphoric affects, sometimes experienced as aversive tension, including rage, sorrow, shame, panic, terror, and chronic feelings of emptiness and loneliness. These individuals can be distinguished from other groups by the overall degree of their multifaceted emotional pain [4, 5]. Another aspect of their affective disturbance is their tremendous mood reactivity [6], as shown by their tendency to change from one interpersonally reactive mood state to another during the course of one day. The second area is *disturbed cognition*. According to Lieb et al. [3], patients show three levels of cognitive symptomatology [7]: (1) troubling but non-psychotic symptoms, such as overvalued ideas of being bad, experiences of dissociation in terms of depersonalization and derealization; (2) quasi-psychotic or psychotic-like symptoms – i.e., transitory, circumscribed, and somewhat reality-based delusions and hallucinations; and (3) genuine or true delusions and hallucinations. Serious identity disturbance is thought to be in the cognitive realm because it is based on a series of false beliefs (e.g., one is good one minute and bad the next). The third sector of their psychopathology is *impulsivity*. Patients show two types of impulsive behavior: (1) deliberately physically self-destructive, and (2) more general forms of impulsivity [3]. Self-mutilation, suicidal communication, and suicide attempts are the constituent elements of the first type of impulsivity, whereas the second type consists of behaviors like substance abuse, disordered eating, spending sprees, verbal outbursts, and reckless driving. The forth psychopathological symptom cluster includes *intense unstable relationships*, which are characterized by two separate but interlocking problems. The first is a profound fear of abandonment, which tends to manifest itself in desperate efforts to avoid being left alone [8] (e.g., calling people on the phone repeatedly or physically clinging to them). The second is a tumultuous quality to close relationships, which are marked by frequent arguments, repeated breakups, and reliance on a series of maladaptive strategies that can both anger and frighten others (e.g., highly emotional or unpredictable responses) [3].

Developmental Factors

BPD is a highly prevalent condition that affects approximately 1.3% of the population [9]. One of the most salient psychosocial factors associated with the development of BPD is early *childhood maltreatment*. Zanarini et al. [10, 11] found that of 358 patients with BPD, 91% reported having been abused, and 92% reported havening been neglected, before age 18. The BPD patients were significantly more likely than patients with other personality disorders ($n = 109$) to report having been emotionally and physically abused by a caretaker and sexually abused by a non-caretaker. They were also significantly more likely than other patients to report having a caretaker withdraw from them emotionally, treat them inconsistently, deny their thoughts and feelings, place them in the role of a parent, and fail to provide them with needed protection. Silk [12] reported that ongoing sexual abuse by a caregiver may be a strong determinant of specific aspects of the disordered interpersonal behavior and functioning found in female patients with BPD. The expectation that the world is an empty, malevolent place may have some of its roots in the repetition of sexual abuse experiences in childhood.

Rinne et al. [13] tested the hypothesis that severely abused borderline patients can be distinguished both from borderline patients without histories of severe abuse and from healthy control subjects by a hyperresponsive hypothalamic–pituitary–adrenal axis. Chronically abused BPD patients had a significantly enhanced adrenocorticotropin and cortisol response to the dexamethasone-suppressed corticotropin-releasing hormone challenge compared with non-abused subjects.

Hyperresponsiveness of the HPA axis in chronically abused BPD subjects might be due to the enhanced central drive to pituitary adrenocorticotropin release.

Although still a controversial point, traumatization might be one risk factor for developing BPD [14]. Indeed, 30–50% of BPD patients were found to fulfill criteria of posttraumatic stress disorder (PTSD) (e.g., [15]). A number of the DSM-IV diagnostic criteria for BPD are defined with reference to interpersonal behavior, such as a pattern of unstable and intense relationships, difficulty tolerating being alone, and frantic efforts to avoid real or imagined abandonment.

Attachment Theory

Attachment theory provides a powerful framework for understanding the nature of close relationships and the links between mental representations in patterns of emotion regulation and psychopathology [16]. Researchers have used two measurement strategies based on narrative assessment or self-report to assess adult attachment. In the study we demonstrate later [17], we refer on the narrative tradition using interview assessments [18–22]. This approach classifies attachment through examination of the person's state of mind with respect to attachment as expressed in linguistic qualities of the narratives. Classification falls into two main attachment groups: organized/resolved and disorganized/unresolved. Disorganized/unresolved individuals are flooded with painful affect, often evidenced through verbal descriptions of intense fear or linguistic disorientation [22]. Studies concur that the unresolved attachment classification predominates in BPD patients, related particularly to lack of resolution of physical and sexual abuse [17, 23, 24]. Attachment disorganization is considered to be one core feature in understanding BPD psychopathology in the context of affective and interpersonal problems (e.g., [17, 23, 25, 26]).

During the past few years, understanding of the underlying neurobiology of BPD has grown rapidly thanks to the application of functional neuroimaging techniques. Neuroimaging investigations are helpful to understand the underlying neural basis of the relationship between individual trauma and BPD by locating its putative functional and structural abnormality in a more general interpretive framework encompassing a wide range of psychiatric disorders [27]. Considerable empirical data have accumulated suggesting that a ventral system, in which the amygdala plays a pivotal role but includes wider portions of the medial and inferior temporal lobes, is involved in the appraisal of stimuli of emotional relevance, the generation of affective states, and the interplay between emotion and memory [28]. In contrast, psychological processes responsible for emotional control may be located in two distinct networks in the prefrontal cortex, with possible complementary roles [29], the first encompassing the dorsolateral prefrontal cortex (DLPFC) and the dorsal anterior cingulus, the second the rostral/subgenual anterior cingulate cortex (ACC). In this chapter, we focus on functional imaging studies only.

Neuroimaging Studies on Patients with Borderline Personality Disorder

According to Mauchnik and Schmahl [30], there are three domains of functional imaging findings investigating BPD: (1) affective dysregulation; (2) the complex of dissociation, self-injurious behavior, and pain processing; and (3) social interaction. By showing the involvement of the brain regions associated with the expression, control, and modulation of emotion and impulsivity in animals and humans, these studies have led to the hypothesis that dysfunctions in these networks may underlie some of the psychopathological symptoms seen in BPD (see also [31]).

Functional Imaging: Emotional, Cognitive, and Social Stimuli Studies

In general, neuroimaging studies measuring the *responsivity to emotional stimuli* provide support for the presence of a heightened responsivity to emotional stimuli among individuals with BPD. Herpertz et al. [32] examined amygdala and prefrontal cortex functioning in response to standardized emotional stimuli among right-handed female inpatients with BPD patients. Patients displayed a significantly greater activation of the amygdala in response to the negative compared to the neutral stimuli. In the control group, no such differences in amygdala activation occurred in response to the negative emotional stimuli.

In a related study, Donegan et al. [33] examined amygdala reactivity to pictures of human *facial expressions* of emotion in BPD participants and normal controls. Compared to the control group, BPD participants evidenced greater levels of left amygdala activation to sad, neutral, and fearful faces. Interestingly, the most striking difference between the groups occurred in response to neutral expressions. In evaluating the ambiguous "neutral" expressions, some of the BPD subjects disambiguated these expressions by projecting emotions or intentions into their descriptions of the neutral faces. Importantly, their attributions were uniformly negative, threatening, and untrustworthy. The strong negative reactions of these subjects to the neutral faces are consistent with the notion of transference in the psychotherapy. Findings from this study provide a foundation for elucidating the neural substrates of behavioral and emotional facets of BPD that contribute to disturbed interpersonal relations.

Another study tested a model of fronto-limbic dysfunction in facial emotion processing in BPD [34] focusing on emotions like *fear* and *anger*. BPD patients showed a significantly larger deactivation in the presence of fearful faces (relative to controls) in the bilateral rostral/subgenual ACC, and significantly greater activation in the right amygdala. There were no significant between-group differences in these areas in response to anger. The authors concluded that BPD patients exhibit changes in fronto-limbic activity in the processing of fear stimuli, with exaggerated amygdala response and impaired emotion modulation of ACC activity. The relative hyporesponsivity of the amygdala to anger might be related to an inability of BPD patients to manage socially undesirable behavior in interpersonal settings, including their own expressions of antagonistic thoughts and behaviors.

Affective dysregulation in BPD in response to both external stimuli and *memories* has been shown to be associated with functional alterations of limbic and prefrontal brain areas. In a recent functional magnetic neuroimaging (fMRI) study, Schnell et al. [35] examined in BPD patients and controls neuronal networks involved in autobiographical memory retrieval using pictures from the Thematic Apperception Test (TAT). In both groups, TAT stimuli activated brain areas known to be involved in autobiographical memory retrieval. In the TAT condition, compared to controls, BPD subjects displayed increased BOLD responses in the bilateral orbitofrontal and insular regions, in the left anterior cingulate and medial prefrontal cortex, as well as in the parietal and parahippocampal areas, which was consistent with a more aversive and arousing experience assessed by self-reports. The authors concluded that increased BOLD responses during TAT processing in BPD subjects were in line with previously reported changes in anterior cingulate and orbitofrontal cortices, which are known to be involved in memory retrieval. However, BPD subjects displayed hyperactivation in these areas for both TAT and neutral stimuli. The lack of selective activation of areas involved in autobiographical memory retrieval suggests a general tendency toward a self-referential mode of information processing in BPD, or a failure to switch between emotionally salient and neutral stimuli.

The importance of the presence or absence of *traumatic experiences* or *PTSD diagnosis* for BDP patients plays an important role, as evidenced in the following three studies.

Driessen et al. [36] recruited women with BPD who had experienced trauma (aged 21–40 years, mean 33 years) and who had various comorbidities. The authors interviewed the participants to obtain cues about *traumatic memories* and aversive non-traumatic memories, and observed them using fMRI during recall of those memories. The authors found an activation of the orbitofrontal cortex in both hemispheres and activation of Broca's area in patients with BPD without PTSD, only a minor activation of the orbitofrontal cortex and no activation of Broca's area in patients with BPD and PTSD. Because all BPD patients tested had experienced trauma but not all had PTSD, the authors argued that the presence or absence of comorbid PTSD may constitute an important subgroup.

In BPD patients listening to *personalized scripts of their own trauma* (e.g., childhood sexual or physical abuse), Schmahl et al. [37] found an activation in right DLPFC and deactivation in left DLPFC in women without BPD. There was also activation in right anterior cingulate and left orbitofrontal cortex in women without BPD. Women with BPD failed to show activation in the anterior cingulate gyrus and orbitofrontal cortex. No activity was seen in dorsolateral prefrontal gyrus in women with the diagnosis and treatment of BPD. The authors suggested that a dysfunction of the dorsolateral and medial prefrontal cortex, including ACC is correlated with the recall of traumatic memories in women with BPD. Here, these brain areas might mediate trauma-related symptoms, such as dissociation or affective instability.

Beblo et al. [38] aimed at investigating the neural correlates of the *recall of unresolved life* events in BPD patients and healthy controls. During fMRI, participants recalled unresolved and resolved negative life events. *Individual cue words* were used to evoke autobiographical memory. When contrasting unresolved and resolved life events, patients showed significant bilateral activation of frontotemporal areas including the insula, amygdala, and the ACC, the left posterior cingulate cortex, right occipital cortex, the bilateral cerebellum, and the midbrain. In healthy participants, no differential brain activation was related to these conditions. The authors concluded that the activation of both amygdala and prefrontal areas might reflect an increased effortful but insufficient attempt to control intensive emotions during the recall of unresolved life events in patients with BPD.

As mentioned, reduced *pain sensitivity* is a central aspect of dissociative states in BPD. Therefore, Schmahl et al. [4] investigated neural correlates of reduced pain sensitivity in BPD. A total of 12 non-medicated female patients with BPD and self-injuring behavior (SIB) and 12 age-matched healthy controls underwent a functional MRI scan while heat stimuli were applied to the individuals' hands. Patients with BPD had higher pain thresholds and smaller overall volumes of activation compared with healthy controls in response to identical temperature stimuli. In response to heat stimuli individually adjusted for equal subjective painfulness in all participants, the overall volume of activation was similar. However, the pattern of activation differed significantly, thus providing a possible circuit of pathologically reduced pain perception. In BPD patients as compared with healthy controls, there was increased activation in the DLPFC and decreased activation of the posterior parietal cortex. Additionally, pain evoked deactivation of the perigenual ACC and the amygdala in BPD patients. The interaction between increased pain-induced response in the DLPFC and deactivation in the ACC and the amygdala was suggested to be associated with an antinociceptive mechanism in patients with BPD. In BPD patients, this mechanism may modulate pain circuits, downregulation of the emotional components of pain, while sensory-discriminative processes remain intact.

Another brain area that may be relevant for BPD is the anterior insula, which has appeared as a key area associated with the processing of fairness *in social interactions*, subjective emotional awareness [39], facial emotion [40], and the appreciation of the intentions and emotional states of others [41] such as empathy [42, 43].

Individuals with BPD have shown an impaired ability to understand emotional information, in addition to problems with regulating emotions [44]. The emotional instability in BPD may be related to a heightened attention or sensitivity to social-emotional cues in interpersonal relations, a tendency to self-referential emotional processing or to dysregulated emotional processing mechanisms [6].

King-Casas et al. [45] found that individuals with BPD had reduced activity of the bilateral anterior insula during a trust game as compared to controls. These individuals also had problems in maintaining cooperation with their game partner and were further impaired in their ability to repair broken cooperation. The authors interpreted this as a consequence of the norms used in perception of social gestures being dysfunctional or missing in individuals diagnosed with BPD. This study suggests that activation of the anterior insula in a social context represents an evaluation of perceived or planned action. When an evaluation is perceived as negative, it may be associated with a feeling of discomfort. This implies that individuals with BPD may have problems in cooperation because they lack the "gut feeling" (corresponding to the anterior insula signal) that the relationship is in jeopardy and/or expect such behavior from the outset [46]. The fact that individuals with BPD were less likely to establish or maintain a cooperative relationship may then be the result of difficulties in trusting others.

In an fMRI study by Koenigsberg et al. [6], BPD persons responded to negative and positive *social-emotional* scenes with a hyperaroused visual processing system and with a more activated premotor cortex. In response to negative stimuli, persons with BPD appeared to show greater activity in the amygdala, fusiform, precuneus, and parahippocampal regions, while healthy controls mobilized dorsolateral and insular regions instead. The authors interpreted this as a use of a more reflexive, hypervigilant, and action-prone system to process social-emotional stimuli in BPD individuals, which may help explain the greater emotional sensitivity and reactivity seen in these individuals, whereas controls employ a more reflective and less reactive network [6].

Interpersonal problems in BDP patients recently have become a new focus of interest in neurobiological research [6, 45, 47, 48]. Patients frequently report that they are afraid of rejection and abandonment of significant others. As mentioned before, attachment disorganization is considered to be one core feature in understanding BPD psychopathology in the context of affective and interpersonal problems. Next, we will report in detail on one of our own studies on neural correlates of attachment trauma.

Borderline Personality Disorders and Neural Correlates of Attachment Trauma: An fMRI Study [AU1]

Introduction

Every developmental attachment study and approximately half of the attachment style studies (i.e., attachment conceived as a personality dimension) reported a strong association between BPD and indices of unresolved, fearful, preoccupied, or angry/hostile attachment [24, 49–54].[1] The association between BPD and unresolved and preoccupied attachment was recently confirmed in a recent meta-analysis of developmental attachment studies using the Adult Attachment Interview (AAI) [21, 22] to assess adult attachment in clinical and non-clinical samples [55]. Disorganized/unresolved individuals (i.e., dysregulated by emotional flooding) are flooded with painful affect, often evidenced through verbal descriptions of intense fear or linguistic disorientation while talking about traumatic attachment experiences, like abuse or loss [22], and disorganized in their attachment (BPD patients appear to be caught in a vicious cycle). Current situations and attachment figures (including adult romantic partners) likely activate past memories of abuse and aloneness, and attempts to organize current attachment relationships would therefore be derailed by chronic mourning of loss, abuse (i.e., unresolved state of mind), and a complex spectrum of assaults to attachment.

[1] In this section, we summarize parts of our paper published in *Psychiatry Research: Neuroimaging*, 2008, Ref. [17].

Bowlby [56] conceived of attachment as a key mechanism related to maintaining biological homeostasis, including the modulation of physiological stress and mental health. In a recent review, we reported current findings on attachment and neurobiology in fMRI research [57]. As this synopsis of findings in healthy subjects showed, researchers investigated very different *systems* (attachment, caregiving, sexual, affiliative, etc.), often by very different means and a variety of paradigms ranging from the presentation of individual photos of loved and unknown faces to more complex approaches (reflecting on attachment-relevant events, priming experiments). At present, the delineation of *a neuronal network* of attachment is not possible yet. The diversity of applied paradigms does not allow for a comparison of results. However, there is evidence across studies that brain regions like the amygdala and orbito/prefrontal cortices are involved in processing attachment-related stimuli. In addition, there are convergent results suggesting that, when caregiving is addressed, dopamine-associated regions of the reward system are active that differ from the neural correlates of the postulated "attachment circuitry."

These studies did not directly address the representational attachment system. Pictures of significant others are good fMRI stimuli, however, there is no corresponding methodology in attachment adult research using speech as the representational window to the internal working model of attachment.

Reliable analyses of fMRI data gathered during continuous overt speech have been demonstrated in healthy controls as well as in schizophrenic patients with severe formal thought disorder [58]. Inspired from that study, we recently demonstrated the feasibility of using an established attachment measure, the Adult Attachment Projective Picture System (AAP) [18, 19], in an fMRI environment while healthy subjects were telling stories to attachment pictures [59, 60]. Based on that pilot study, we investigated the functional neuroanatomy of *attachment trauma* in BPD patients [17].

Methodology

We decided to use the AAP [18, 19] because it provides (1) a set of eight standardized picture stimuli and (2) the possibility to code and classify individual story responses to these stimuli. This combination seemed feasible for use the measure in an fMRI environment.

The picture stimuli are line drawings of a neutral scene and seven attachment scenes (e.g., illness, separation, solitude, death, and threat). The stimuli are administered in a standard order: *Neutral* – two children playing ball; *Child at Window* – a child looks out a window; *Departure* – an adult man and woman stand facing each other with suitcases positioned nearby; *Bench* – a youth sits alone on a bench; *Bed* – a child and woman sit facing each other at opposite ends of the child's bed (Fig. 12.1); *Ambulance* – a woman and a child watch someone being put on an ambulance stretcher; *Cemetery* – a man stands by a gravesite head stone (Fig. 12.1); and *Child in Corner* – a child stands askance in a corner with hand and arm extended outward. In sum, the attachment pictures include four "monadic" scenes (individuals depicted alone) and three dyadic scenes (individuals depicted in potential attachment dyads). Individuals are instructed to tell a story about the scene, including the character(s)' thoughts and feelings, and the outcome of the story [18, 19].

The AAP classification system designates the four main adult attachment groups (secure, dismissing preoccupied, unresolved) from the transcribed verbatim narratives of the individual's response to the attachment picture stimuli, which are coded following a well-defined, validated manual [61]. A large-scale psychometric investigation of the AAP with 144 participants showed excellent inter-judge reliability, test–retest reliability (retest after 3 months), discriminant validity, and construct validity using the established AAI [18, 19].

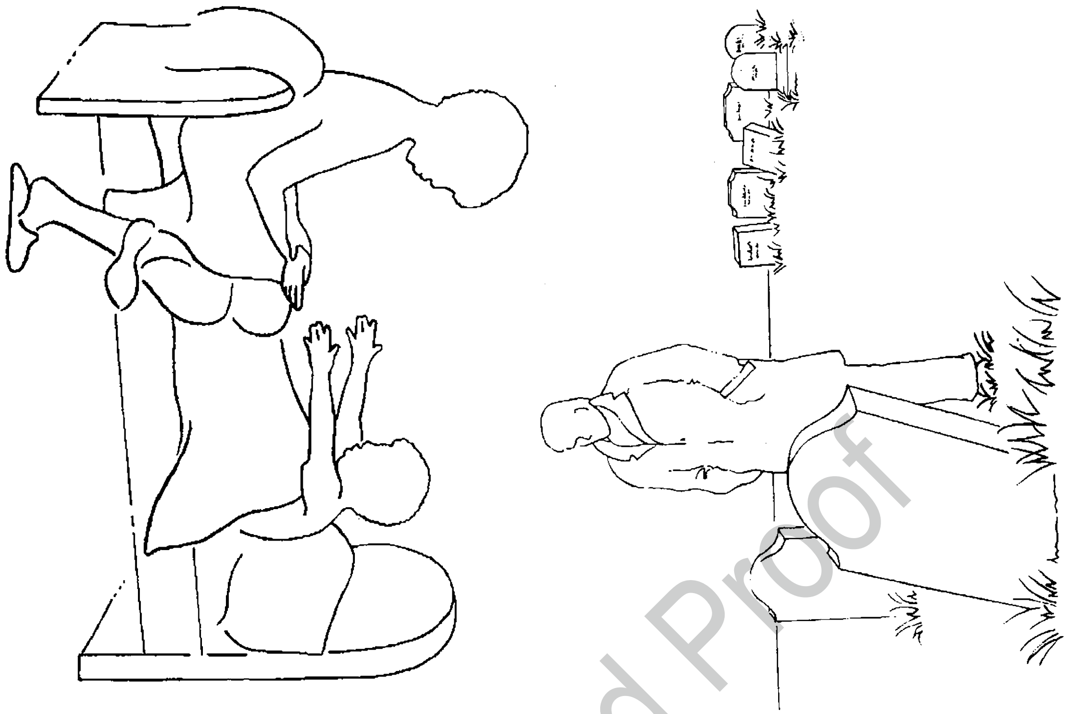


Fig. 12.1 Examples of two attachment pictures from the AAP "Bed" (*dyadic picture*) and "Cemetery" (*monadic picture*). The AAP pictures depict events that according to theory and research activate the attachment system, for example, illness, solitude, separation, loss, and abuse. The black and white line drawings contain only sufficient detail to identify an attachment scene. Facial expressions and other details are omitted or drawn ambiguously. The drawings were developed carefully to avoid gender and racial bias (Copyright © Carol George Ref. [63]

In our fMRI study, AAP classifications were coded by two independent reliable judges based on the transcribed verbatim AAP narratives subjects produced in the scanner. Inter-rater agreement was 100% (kappa = 1.00). Judges were blind to any identifying information about the subjects. The scanner-administered validity of the AAP was examined based on convergent classifications with AAIs administered outside the fMRI environment 1 month after fMRI acquisition, classified by an independent trained AAI judge also blind to all information about subjects. There was a high correspondence between the AAP and AAI "resolved" versus "unresolved" categories (kappa = 0.70).

Analyzing Attachment Trauma Based on the AAP Narratives

One of main features of the AAP coding system is the evaluation of attachment-based defensive processes. The AAP defines the defenses associated with unresolved attachment following Bowlby's [56] conceptualization of defensive exclusion in pathological mourning. He viewed defense as the regulating mechanism that maintained a steady representational state, the goal of which is representational, behavioral, and physiological homeostasis [62]. Pathological mourning, including the unresolved state of mind that we view as linked especially to chronic mourning, is associated with a particular form of defensive exclusion. Bowlby [56] termed this "segregated system." Homeostasis is extremely difficult to maintain in the face of threats to attachment, and Bowlby proposed that such memories and their associated affects must literally be segregated or blocked from conscious processing in order to prevent debilitating emotional dysregulation. Segregated systems defenses provide the individual with a rigid protection mechanism that works to prevent becoming overwhelmed and flooded by severe attachment distress, anger, sadness and fear.

The AAP operationally defines segregated systems in terms of a designated set of specific story response elements that are empirically and theoretically established indicators of attachment disorganization (termed “markers”). These include features of the response narrative that evidence danger, failed protection, helplessness, being out of control, isolation, spectral ideation, or response constriction. The AAP is judged “resolved” (i.e., re-integrated and contained as designated by the secure, dismissing, preoccupied classifications) or unresolved by evaluating if segregated systems markers are contained and re-organized in the narrative response. Resolution can take several forms, including descriptions of a character’s ability to think about attachment distress (descriptions of the character as taking constructive action, and depictions of others providing care. The failure to re-organize (i.e., being unresolved) is designated by uncontained dysregulation or constriction. Evidence of uncontained markers includes themes in which characters remain unprotected, descriptions of dysregulating distress are not diminished or transformed, or descriptions of frightening autobiographical experiences. Constricted responses are evidenced by the inability to engage in the narrative task in response to a picture stimulus, which is conceived as the individual totally shutting down attachment so as to block overwhelming feelings of being out of control and dangerously unprotected.

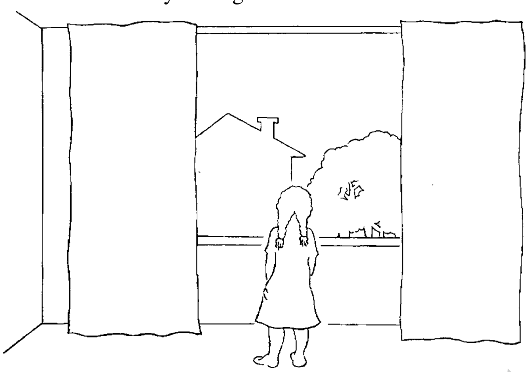
Classifying a transcript as resolved or unresolved is the first step in using the AAP. In our work, we have been interested in the patterns of dysregulation that appear in the previous transcript and beyond the classification category, in order to determine especially if there are different patterns in patient and non-patient responses. George [63] noted during the blind classification coding of several hundred AAPs in a range of different samples that some segregated systems markers were common and others were unusual. As a result, this author developed a supplementary set of AAP coding instructions that differentiated between what was considered “normative” (SS_{Norm}) and “traumatic” (SS_{Tr}) markers. Normative markers seemed to be related to the stimulus “pull,” for example, a death in *Ambulance* or the isolation associated with the breakup of teenage romance in *Bench*. Traumatic dysregulation markers (SS_{Tr}) were particularly frightening or bizarre responses to the AAP stimulus. These included themes of abuse, entrapment, abandonment, murder, suicide, or incarceration, or eerie descriptions of characters or events (e.g., girl floats over the bench). Some responses included descriptions of personal trauma (e.g., loss or abuse experiences), indicating merging with the depicted character and becoming flooded by personal memories. Table 12.1 provides examples that contrast SS_{Norm} and SS_{Tr} story responses to the AAP *Window*.

Both AAP judges also coded the AAP stories differentiating between normative and traumatic markers [63]. There was 100% inter-rater agreement in coding normative and traumatic markers (kappa = 1.00). The results presented next focus on the traumatic markers because of the specific link between BPD and traumatic childhood experience.

Hypotheses

We were especially interested in responses to monadic and dyadic attachment situations; that is, responses to stimuli portraying individuals as facing attachment threats alone versus in the presence of potential attachment figures. Given that one of the key features of BPD patients is their intolerance of aloneness [8], we predicted that AAP stimuli representing traumatic contents, such as aloneness, desperation, and physical threat, would elicit a significantly greater association with linguistic traumatic (and not only normative) dysregulation markers in the BPD group than controls. On the neural level, we hypothesized that BPD patients, as compared with controls, would show increased activation of brain regions associated with fear and pain (e.g., amygdala, ACC) during narration in response to these stimuli.

Table 12.1 Transcript examples of "resolved" and "unresolved" AAP *Window* story (Illustration: Copyright © Carol George Ref. [63])

Resolved AAP story	Unresolved AAP story
Normative dysregulation (example of a control subject)	Normative dysregulation (example of a control subject)
"A girl is *afraid*, feels bad, had a fight with her parents and has house arrest. She is looking out of the window and feels *terribly lonely* in her room alone by herself. She thinks about the fight and realizes that she has to say sorry. But she is *afraid* that her parents would reject her. She is standing there for a long time, thinking about the problem. After a while she leaves the room downstairs to her parents and tries to resolve the situation by talking to them."	"A girl is very sad, wants to *hide herself behind the curtain*, she is very *frightened*, feels *abandoned* by everybody, she has moved in a new neighborhood. Life can be so cruel. She is *frightened* about the future and she doubts that she ever will meet friends. I have no idea how this could end. I think she stand there forever, I really don't know."
	Traumatic dysregulation (example of a borderline patient) "She feels **homeless**, it seems that she is **incarcerated in that empty room** wants to **escape** from this **isolation**, **she thinks about suicide.** It is also possible that she is in a **mental institution**, because **she has already tried to commit suicide** and now she has to be **alone in an empty room**. I have no idea. (long pause) I think she only dreams of ***hiding and running away***."

"Normative dysregulation markers" are underlined italics, "traumatic dysregulation markers" are bold

Sample

Thirteen female BPD patients were recruited from an inpatient psychiatric hospital and compared to 21 healthy female volunteers, matched for age and education. Psychiatric diagnoses, including diagnostic criteria for BPD, were assessed by a trained psychiatrist using the Structured Clinical Interview I and II for DSM-IV [64]. We examined the groups in relation to important variables related to this study: movement parameters, balance of attachment classification groups in each sample, and patient medication. Six subjects were excluded from our main analysis: Four controls (movement > 2 mm, see following text), and two patients classified as resolved (not enough to allow any substantial group inferences). The final sample consisted of 11 BPD patients and 17 controls. Exclusion of the six subjects did not affect group homogeneity with respect to age (BPD: 27.8 years ± 6.7, controls: 28.4 years ± 7.5) and education (BPD: 10.8 years ± 1.4, controls: 10.9 years ± 1.6).

fMRI Procedure

The fMRI Attachment Paradigm procedure has been described elsewhere [59, 60]. In short, subjects were trained using two neutral non-AAP pictures before scanning. They were given the standard AAP instructions for story telling ("What led up to that scene; what are the characters thinking or feeling; what might happen next?"). They were asked to talk about each picture for 2 min, keeping their head as still as possible while speaking. Each picture trial during scanning consisted of the following sequence: Standard instruction (10 s); fixation cross (10 s), AAP picture (120 s), fixation cross (15 s) (Fig. 12.2).

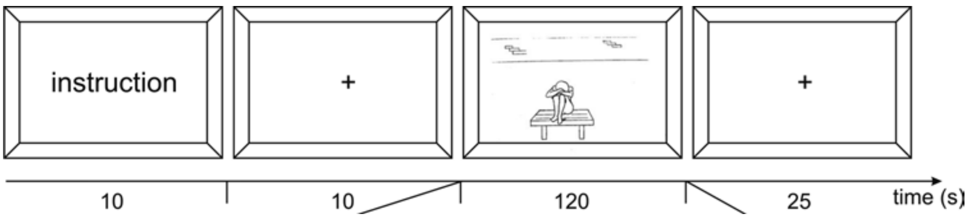


Fig. 12.2 fMRI study design

Results and Interpretations

Attachment Data

The AAP classifications for the sample were as follows: Controls, ten resolved and seven unresolved and for borderline patients, two resolved (excluded from further analysis, see earlier text), and 11 "unresolved." The predominant prevalence of unresolved attachment among the BPD patients in this study is comparable to other studies investigating clinical populations [24, 55, 65], whereas the number of unresolved control subjects (38%) is greater than the average percentage (19%) previously reported in healthy populations [55]. Analyses of the AAP linguistic traumatic markers showed greater traumatic dysregulation in the responses of BPD patients as compared to controls in response to the monadic pictures, independent of overall attachment classification. Significant differences were found for all monadic pictures. The differences for picture stimuli *Window*, *Bench,* and *Cemetery* were highly significant ($p<0.01$). Therefore, these three monadic pictures were selected for the fMRI analysis. There was no significant difference between the groups for any of the dyadic pictures.

Neuroimaging Data

Due to our attachment data showing significantly more traumatic dysregulation in the narratives to monadic pictures compared to dyadic one, we hypothesized on the neural level that BPD patients, as compared with controls, would show increased activation of limbic brain regions associated with fear and pain (e.g., amygdala, ACC) during narration in response to these monadic stimuli.

This hypothesis could be confirmed. As expected, BPD patients' responses to monadic pictures showed significantly stronger activation of the dorsal ACC than responses of the controls (Fig. 12.3).

ACC activation is observed in response to pain and unpleasantness [66]. ACC activation in healthy subjects is associated with social relationship stimuli, including intimate relationships [67], social exclusion [68], and pictures evoking grief [69]. However, the ACC is not homogeneous [70]. The subgenual ACC is mainly concerned with emotions, in particular the representation of autonomic afferences. The dorsal region posterior to the genu of the corpus callosum is divided into two subsections, the anterior and posterior midcingulate cortex (aMCC, pMCC). These are overlapping pain and fear sites. The aMCC is innervated by the midline and intralaminar thalamic nuclei belonging to the medial pain system, and also receives direct input from the amygdala. Thus, the aMCC is linked to pain, especially fear avoidance. The observed ACC activation in our study was located in the aMCC. We interpreted this finding as a neural signature of pain and fear associated with attachment trauma. This pattern was consistent with our hypothesis and reports that abandonment fears are the most persistent long-term symptoms in BPD [71].

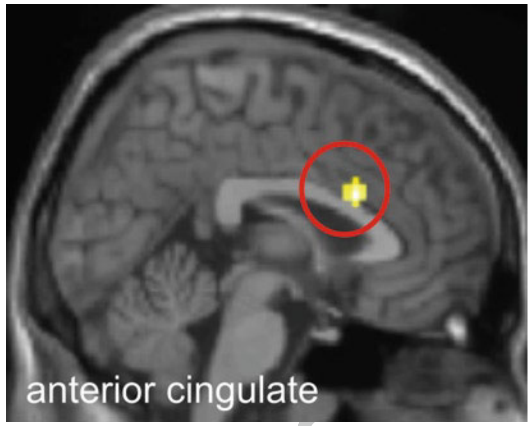


Fig.12.3 Traumatic markers monadic AAP pictures: increased activation in patients relative to controls in the ACC area (coordinates *x*, *y*, *z*: 3, 18, 24). Parametric map thresholded at $p<0.001$ uncorrected, cluster-level $p<0.05$

A recent fMRI study using heat stimuli in BPD patients found an interaction of increased pain-induced response in DLPFC and deactivation in the perigenual, ventral part of the ACC and the amygdala [4]. The authors interpreted this pattern as an indicator of successful antinociception that patients have acquired by their experience of repetitive self-mutilation. We interpreted our finding of clearly more dorsal aMCC activation as an indicator of unsuccessful coping with emotional pain. However, our specific stimuli portraying aloneness did not activate the amygdala, compared to studies using more general emotional or psychophysical stimuli [4, 32, 33].

We did not have a specific hypothesis for the dyadic picture stimuli because we did not find any significant differences in the "behavioral data" (i.e., attachment narratives to these pictures in the two groups).

However, we observed group differences that required explanation: BPD patients' responses to dyadic stimuli showed significantly stronger activation of the right superior temporal sulcus (STS) than controls. The STS has been shown to be regularly activated in theory-of-mind tasks [72]. It is a crucial part of a network involved in "thinking about others" [72]. Attachment researchers suggest that abusive childhood experiences of BPD patients lead to the inhibition of constructive "mentalizing" capacities used to reflect upon self and others. BPD patients show distorted, blocked, or "hyper-analytical" thinking processes when asked to describe attachment experiences [23, 73]. They often demonstrate a misleading hypersensitivity to others' mental states that facilitates manipulating and controlling perceived threatening relationships. Based on this model, we interpreted the increased STS activation in BPD patients as a neural indicator of fear-based hypervigilance in attachment relationships.

In a recent neuroimaging study by Takahashi et al. [74], the superior temporal gyrus (STG) subregion volumes in 20 teenagers with first-presentation BPD and 20 healthy controls were investigated. The authors stated that STG volume early in the course of BPD did not differ from that of healthy controls; however, BPD participants with violent episodes had a smaller left caudal STG volume compared with those without such episodes during the previous 6 months. The authors discussed that recent functional MRI studies also suggest the involvement of the STS region in emotional dysregulation and impulsivity in BPD (Fig. 12.4) [6, 75]. Taken together with our preliminary findings, future studies should evaluate the potential involvement of the STG in the neurobiological underpinnings of BPD.

Moreover, control subjects' responses to dyadic pictures showed significantly higher activation than BPD patients of the right parahippocampal gyrus (GH) (Fig. 12.5).

Along with the hippocampus, this region is involved in memory processes [76]. Recently, we have shown that this region is associated with a "subsequent memory effect" for neutral items that are encoded in a positive emotional context in healthy subjects [77]. Taken together, this suggests

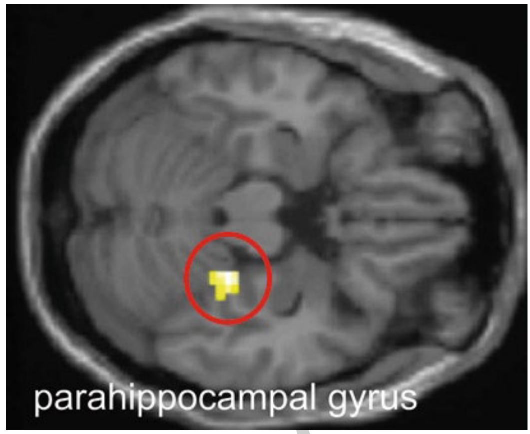


Fig. 12.4 Traumatic markers dyadic AAP pictures: increased activation in patients relative to controls in the superior temporal sulcus (coordinates x, y, z: 60, −45, 24). Parametric map thresholded at $p < 0.001$ uncorrected, cluster-level $p < 0.05$

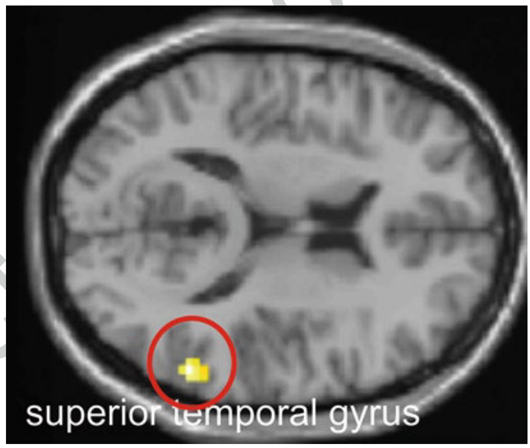


Fig. 12.5 Traumatic markers dyadic AAP pictures: increased activation in patients relative to controls, gyrus parahippocampalis (coordinates x, y, z: 33, −39, −15). Parametric map thresholded at $p < 0.001$ uncorrected, cluster-level $p < 0.05$

that the parahippocampal gyrus may mediate information about positive emotional information. Interestingly, in our AAP narratives of dyadic pictures, the unresolved control subjects describe overall positive dyadic interactions – interactions characterized by emotional warmth and mutuality. This impression was evidenced by higher scores on the AAP subscale *Synchrony*, the scale that evaluates dyadic stories for relationship mutuality (care for others or mutual enjoyment). Therefore, our finding regarding parahippocampal activation confirms that the control subjects' narratives are more associated with positive emotional memories compared to BPD patients, who show reduced activations. Our interpretation is also consistent with the fact that, on a descriptive level, the resolved control subjects showed the highest level of parahippocampal activation (i.e., more activation than unresolved controls).

Conclusions, Limitations, and Clinical Implications

Our finding of distinct prevalence patterns of linguistic markers in BPD provides a more detailed level of understanding of the organization and threats to attachment in BPD than exists in the literature to date [78]. In their selection of linguistic markers, unresolved BPD patients manifested more traumatic than normative attachment dysregulation, whereas normative dysregulation predominated in unresolved controls. Flooded and overwhelmed, the BPD patients in this study were not able to integrate organizing narrative elements (i.e., productive thinking, safety provided by an attachment figure, constructive action) into their monadic stories, and they remained dysregulated when attachment was activated.

On a neural level, the presentation of monadic pictures triggered traumatic dysregulation, and was accompanied by activation in brain regions associated with pain and fear. BPD patients showed significantly more activation in the dorsal ACC, a region associated with pain and fear. These findings may provide evidence on the possible mechanisms related to the fearful intolerance of aloneness in BPD patients [8].

Patients and non-patients did not differ in the number of traumatic markers in dyadic stories; on a neural level, patients showed hyperactivation of the right STS and hypoactivation of the right parahippocampal gyrus. The dyadic pictures, representing the quality of potential attachment interactions, differentiated on a neural level between the groups. This finding highlights borderline patients' hypersensitive attention to the social environment [23] and addresses their poor contextualization of positive relationship memories [25].

Several limitations should be stated when interpreting our findings. First, although we made every effort to exclude patients with current psychosis and substance abuse, the influence of lifetime psychiatric conditions in the patient group cannot be ruled out. Therefore, the neural results of attachment dysregulation may not be specific to BPD, but rather a feature of patients with multiple Axis I and Axis II disorders. Second, overt speech is necessarily accompanied by movement, which may have introduced artifacts in the neuroimaging data. However, we took a series of measures to eliminate the influence of movement as much as possible (exclusion of subjects, inclusion of movement parameters as covariate of no interest, modeling the onset of every spoken word). Moreover, the areas identified in the study did not involve regions typically affected by movement artifacts (see detailed model [17]).

Clinicians have stressed aloneness as one core deficit that should be addressed in the treatment of borderline patients [8, 23, 73]. This underscores the importance for therapists to think about BPD from an attachment theory perspective, and in particular of articulating aloneness in terms of "representational attachment isolation." A recent case study [78] discussed how the AAP, used as an attachment diagnostic tool at the outset of therapy, can provide clinicians with a realistic and enriching analysis of different levels of trauma in relation to the adverse childhood experiences that shape patients' styles of discourse, defense, and coping and add a new level of understanding regarding patients' frightened and distressed behavior in transference. Based on assessment of traumatic dysregulation, treatment could focus on helping a patient to understand step by step the representational contexts associated with attachment dysregulation and the intense emotional reactions of helplessness.

Outlook

The past years have rapidly increased our understanding of the neurobiological underpinnings of BPD. The presented results are encouraging and may be fruitful for the improvement of therapies for BPD patients. According to Mauchnik and Schmahl [30], it is important to stress the limitations and deficiency of controlled studies. To address this criticism, future functional MRI studies should work with clinical control groups as well as with additional dependent variables (i.e., behavioral, subjective, or physiologic variables), and patients should not be taking psychotropic medication. The approach of working with a focus on core dimensions of the disorder, as outlined in this chapter, shows promise as a research tool and to understand mechanisms of therapy. The complexity of BPD is best understood in terms of combinations of alterations in different neurobiological systems.

Neuroscience is already being integrated into psychotherapy. This inevitable process cannot and should not be reversed. Established knowledge about brain function has already become part of psychotherapeutic education in some centers, and this development should be encouraged. Noting that neuroimaging studies are increasingly used to study effects and mechanisms of psychotherapy, Walter et al. [79] suggested a working definition of neuropsychotherapy that includes the identification of mediators and functional targets, determination of new therapeutic routes to such targets, and, finally even the design of psychotherapeutic techniques. Most studies in this field have investigated the effects of cognitive and interpersonal psychotherapy in patients with depressive, anxiety, and obsessive compulsive disorders [80]. While these studies investigated short-time therapies, the first functional imaging study examining psychodynamic treatment was initiated by our large working group with chronically depressed patients during psychoanalytic treatment at the beginning and after 15 months of treatment [81]. In that longitudinal fMRI and EEG study, we used highly individually tailored stimuli (core-sentences) based on attachment narratives (Adult Attachment Projective System) and psychodynamic clinical interviews (Operationalized Psychodynamic Diagnostic, OPD) to capture individual relevant material, which might be crucial for the psychotherapeutic process. These data are about to be analyzed and will be published elsewhere.

[AU3]

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Author Queries

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Queries	Details Required	Author's Response
AU1	Footnote in section level heading has been moved to the end of the first sentence of the following para. Please check.	
AU2	Please provide closing parenthesis in the sentence starting "Resolution can take…"	
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AU4	Please provide journal abbreviation for Ref. [14].	
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