

## Neural correlates of attachment trauma in borderline personality disorder: A functional magnetic resonance imaging study

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### Abstract

Functional imaging studies have shown that individuals with borderline personality disorder (BPD) display prefrontal and amygdala dysfunction while viewing or listening to emotional or traumatic stimuli. The study examined for the first time the functional neuroanatomy of attachment trauma in BPD patients using functional magnetic resonance imaging (fMRI) during the telling of individual stories. A group of 11 female BPD patients and 17 healthy female controls, matched for age and education, told stories in response to a validated set of seven attachment pictures while being scanned. Group differences in narrative and neural responses to “monadic” pictures (characters facing attachment threats alone) and “dyadic” pictures (interaction between characters in an attachment context) were analyzed. Behavioral narrative data showed that monadic pictures were significantly more traumatic for BPD patients than for controls. As hypothesized BPD patients showed significantly more anterior midcingulate cortex activation in response to monadic pictures than controls. In response to dyadic pictures patients showed more activation of the right superior temporal sulcus and less activation of the right parahippocampal gyrus compared to controls. Our results suggest evidence for potential neural mechanisms of attachment trauma underlying interpersonal symptoms of BPD, i.e. fearful and painful intolerance of aloneness, hypersensitivity to social environment, and reduced positive memories of dyadic interactions.

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### 1. Introduction

Borderline personality disorder (BPD) is characterized by extreme and enduring emotional instability involving a range of intense affects, including rage, panic, emptiness, loneliness, and characteristically

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multifaceted emotional pain and fear of abandonment (Lieb et al., 2004). Childhood maltreatment by a caregiver (emotional neglect, physical and sexual abuse) is one of the most important psychosocial risk and prognostic factors for BPD pathology (Zanarini, 2000; Zanarini et al., 2006).

Clinically, an essential dimension of BPD patients is their dysfunction of emotion-regulation systems combined with the inability to adjust emotional responses (Lieb et al., 2004). Studies using the startle reflex as a measure for emotional hyper-reactivity reported evidence that favored (Ebner-Priemer et al., 2005) and failed (Herpertz et al., 1999) to support this hypothesis. Two recent fMRI studies reported emotional hyper-reactivity as measured by increased amygdala activation in response to emotional pictures (Herpertz et al., 2001) or faces (Donegan et al., 2003). Two further recent studies investigated brain activation during processing of autobiographical memory. One study found less activation in emotion processing areas (Schnell et al., 2007) whereas an other study looking at unresolved life events compared to resolved life events found, among other regions, increasing activation of amygdala and anterior cingulate cortex (Beblo et al., 2006). Finally, reductions in amygdala (and hippocampal) volume have been reported for BPD patients (e.g. Driessen et al., 2000; Tebartz van Elst et al., 2001; Irlle et al., 2005). PET studies showed prefrontal dysfunction in BPD patients in response to listening to personal scripts of abandonment and abuse (Schmahl et al., 2003, 2004).

No patient study to date has examined neural patterns in relation to attachment, a basic behavioral system that processes relationship-based emotional experience and regulation.

Attachment theory provides a powerful framework for understanding the nature of close relationships, the links between mental representations in patterns of emotion regulation and psychopathology (Westen et al., 2006). Researchers have used two measurement strategies for assessing adult attachment, based on narrative assessment or self-report. In the present study we refer on the narrative tradition using interview assessments (George et al., 1996; George and West, 2003; Main et al., 1985). 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 (Main et al., 1985). Studies concur that the

unresolved attachment classification predominates in BPD patients, related particularly to lack of resolution of physical and sexual abuse (Fonagy et al., 2000; Agrawal et al., 2004). Attachment disorganization is considered to be one core feature in understanding BPD psychopathology in the context of affective and interpersonal problems (Fonagy et al., 2003; Gabbard, 2005).

The attachment relationship is an essential biological system that influences motivational and emotional processes related to survival (Bowlby, 1969). Animal studies suggest that limbic structures are involved in attachment deprivation (Insel, 1997; Bauman et al., 2004). Structural neuroimaging studies show reduced hippocampus and amygdala volumes in patients reporting traumatic attachment histories (Tebartz van Elst et al., 2003; Wignall et al., 2004).

Functional imaging studies investigating social attachments have focused on healthy subjects so far. Pictures of loved ones (e.g., spouse versus friend or own versus other baby) (e. g. Bartel and Zeki, 2004; Leibenluft et al., 2004) evoked cortical and subcortical responses, including the cingulate cortex, insula, basal ganglia, and orbitofrontal cortex. No fMRI studies have examined brain activation while subjects tell stories when the attachment system is activated.

fMRI data gathered while participants were speaking continuously demonstrated that this approach can be reliably applied to healthy controls and schizophrenic patients with severe formal thought disorder (Kircher et al., 2001). Recently, we measured attachment representation in an fMRI environment in which healthy participants told stories in response to the Adult Attachment Projective (AAP), a validated attachment measure described in detail below. We found robust activation of visual, motor and language related areas while talking to AAP pictures and activation of the right amygdala related to attachment status and involvement in the course of the task (Buchheim et al., 2006).

One key feature of interpersonal problems in BPD patients is their intolerance of aloneness (Gunderson, 1996). In a recent BPD study using the AAP measure in a non-fMRI-environment (Buchheim and George, *in press*), we examined different narrative responses to "monadic" attachment pictures (characters facing attachment threats alone) and "dyadic" attachment pictures (interaction between characters in an attachment context). Attachment related traumatic dysregulation was operationally defined as the frequency of occurrence of "traumatic fear indicators" in the narratives. The results showed a higher frequency of these words in unresolved patients than controls in response to stories to monadic pictures, but not to dyadic pictures.

In this study, we were interested to further investigate traumatic dysregulation in borderline patients by analyzing their neural activation patterns in response to the AAP, especially responses to stories associated with loneliness and abandonment (monadic pictures). According to Bowlby's (1969) conceptualization being alone is the single most frightening experience for primates. Thus, representations of being alone are thought to be the strongest activators of the attachment system. On the linguistic level, we predicted to find the same narrative patterns as in our behavioral study (Buchheim and George, *in press*). On the neural level we expected that patients would show greater activation of brain regions associated with fear and pain, for example, the amygdala or the anterior cingulate cortex, in response to monadic pictures.

## 2. Methods

### 2.1. Subjects

Thirteen female BPD patients were recruited from an inpatient psychiatric hospital and compared to 21 healthy female volunteers, matched for age and education. Controls were recruited for the study by an advertisement in a local newspaper and leaflets distributed in the Hospital of the University of Ulm. All control subjects were physically healthy, without a history of psychiatric disorder and did not use any medication. Clinical diagnoses of BPD patients were assessed by a trained psychiatrist (P.M.)<sup>2</sup> using the Structured Clinical Interview for DSM-IV (SCID-I and SCID-II) and the International Personality Disorder Examination (IPDE). Exclusion criteria of all subjects were serious medical or neurological illness (including comorbid psychotic disorders, bipolar disorder, PTSD and Dissociative Disorder), left handedness, metal in body, and language problems. 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 > 2mm, see below), and two patients classified as resolved (not enough to allow any substantial group inferences). Inclusion of this subgroup in a control analysis did not alter our results.

<sup>2</sup> P.M. has been trained and certified for reliable diagnosis in the SCID-rating by Prof. Wittchen, Munich, Germany and by A. Loranger MD, New York, regarding IPDE. In seven patients an experienced Master's level psychologist conducted a second SCID interview. Agreement between the raters was kappa=1.0 for both BPD and lifetime depressive episode.

Control analyses also demonstrated no influence for medication, therefore medicated and un-medicated BPD patients were combined into a single group for the main analyses. The final sample consisted of 11 BPD patients and 17 controls (see Table 1). Exclusion of the six subjects did not affect group homogeneity with respect to age (BPD: 27.8years±6.7, controls: 28.4years±7.5) and education (BPD: 10.8years±1.4, controls: 10.9years±1.6). Current depressive episode, current drug and/or alcohol dependency or abuse were exclusion criteria. Comorbidity in the final patient group included depression ( $n=6$ ), anxiety or panic disorder ( $n=2$ ), and somatoform disorder ( $n=3$ ). Seven patients (53.8%) had lifetime depressive episode(s), four (30.8%) had lifetime drug or alcohol abuse, five (38.5%) met current somatoform disorder criteria, three (23.1%) had current phobia or anxiety disorder, one patient (7.7%) fulfilled current dissociative disorder (44.5%). With respect to traumatic experiences in life cycle we documented life events, which have been identified as potential risk factors for the development of BPD (Paris, 1994). All but one patient reported one or more of these experiences ( $n=9$  sexual abuse,  $n=3$  violence,  $n=4$  parental neglect,  $n=5$  separation from parents,  $n=5$  psychiatric morbidity of parents,  $n=1$  single traumatic life event); but none of them fulfilled PTSD criteria. 45% (5/11) of the patients were treated with psychotropic medication, including low doses of neuroleptics (perazin, promethazine and chlorprothixene,  $n=3$ ), serotonin-reuptake inhibitors ( $n=2$ ) and lithium ( $n=1$ ). After complete description of the study to the subjects, written informed consent was obtained. The protocol was approved by the local institutional ethics committee.

### 2.2. Clinical assessment

The Dissociative Experience Scales (DES) (Bernstein and Putnam, 1986; Freyberger et al., 1999) (absorption, dissociative amnesia, depersonalization/derealization subscales) was applied as a measure of severity of dissociative symptoms. Severity of impulsiveness was assessed by using the Barratt Impulsiveness Scale (BIS-10) (Barratt, 1985).

### 2.3. Attachment measure

The Adult Attachment Projective (AAP) is a validated measure to assess narrative patterns using a set of eight pictures, one neutral and seven attachment scenes. The pictures depict theory-derived attachment events and are administered as follows: #2 "Child at Window"; #3 "Departure"; #4 "Bench"; #5 "Bed"; #6

Table 1  
Group comparison of clinical scales and attachment trauma scales

Variable	BPD ( <i>n</i> =11)		Controls ( <i>n</i> =17)		ES	Exact <i>U</i> -test	
	<i>M</i>	S.D.	<i>M</i>	S.D.		<i>Z</i>	<i>P</i>
<i>Clinical scales</i>							
State anxiety T1 (before fMRI)	49.8	10.9	37.4	5.3	1.58	2.92	0.002**
State anxiety T2 (after fMRI)	46.5	9.5	35.7	4.9	1.54	3.11	0.001***
GSI (SCL-90 General Symptom Index)	1.47	0.56	0.22	0.22	3.18	4.20	0.000***
Barrett Impulsivity Scale Total Score	84.8	11.3	67.4	10.0	1.66	3.39	0.000***
Dissociative Experience Scale Total Score	16.0	17.6	4.2	3.9	1.02	3.22	0.001***
<i>Attachment trauma scales in the Adult Attachment Interview</i>							
Score for loss experiences (scale 1–9)	5.10	2.08	3.18	2.24	0.88	2.16	0.030*
Score for abuse experiences (scale 1–9)	5.55	3.11	1.94	1.78	1.51	3.11	0.001***

*P* = significance of the two-tailed Exact test, \**P* ≤ 0.05, \*\**P* ≤ 0.01, \*\*\**P* ≤ 0.001.

“Ambulance”; #7 “Cemetery”; #8 “Corner”. There are four “monadic” and three “dyadic” scenes (Fig. 1). Individuals are instructed to tell a story: “Tell me what led up to that scene, what are the characters thinking or feeling, and what might happen next?” (George and West, 2001, 2003). Individuals are classified on the basis of verbatim narratives into one of two attachment groups: resolved and unresolved. Unresolved attachment in the coding system is defined as an individual’s failure to contain any frightening or threatening narrative material, including words and phrases such as death, attack, or devastation. This is termed attachment dysregulation (George and West, 2003). Stories are considered resolved when dysregulation is contained,

when characters utilize internal or relationship resources that provide help or care (Table 2).

A large-scale psychometric investigation of the AAP with 144 participants (George and West, 2003) showed excellent inter-judge reliability, test–retest reliability (retest after three months), discriminant validity and construct validity using the established Adult Attachment Interview (AAI) (George et al., 1996). The AAI is a validated semi-structured interview asking individuals to describe autobiographic childhood experiences with caregivers (e. g. separations, loss, abuse).

In this study, two blind, reliable AAP judges independently coded the transcribed verbatim AAP narratives. Inter-rater agreement was 100%. AAP validity was tested

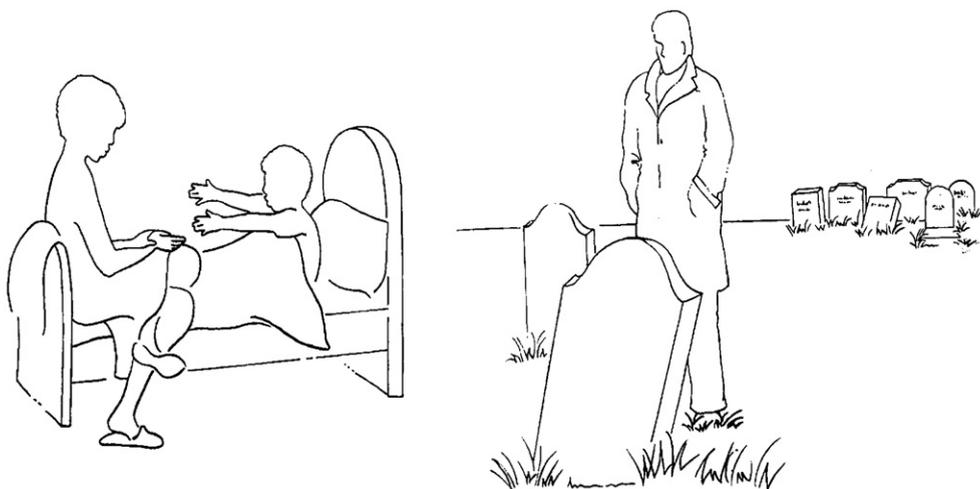


Fig. 1. Examples of two attachment pictures from the Adult Attachment Projective © George and West (2003): “Bed” (dyadic picture) and “Cemetery” (monadic picture). The AAP pictures depict events that according to theory and research activate the attachment system, for example, illness, solitude, separation, 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.

Table 2

Transcript example of a “Resolved” and “Unresolved” story to a “monadic” AAP picture “Bench

Resolved AAP story	Unresolved AAP story
<p><u>Normative dysregulation</u> (example of a control subject)</p> <p>“A women is <u>afraid</u>, feels bad, had a fight with a friend, sits on a bench to be alone and by herself. She is sitting and crying. Her friend was very disappointed that she has not told him the truth for several times, so he <u>broke up with her</u>. Now <u>she feels abandoned</u> and is <u>afraid</u> of the future. She thinks about the fight and realizes that she has to say sorry. But she is <u>afraid</u> that her friend would not talk to her, like her mother often did when she was young. She is <u>afraid</u>. She is sitting there for a long time, thinking about the problem. After a while she gets up and is trying to get in contact with the friend to talk about everything.”</p>	<p><u>Normative dysregulation</u> (example of a control subject)</p> <p>“She is very sad, wants to <u>hide herself under the bench</u>, she is very <u>frightened</u>, feels <u>abandoned</u> by everybody. Life can be so cruel. Her friend does not love her anymore, because she has overweight. Her mother <u>broke up</u> contact with her because she is not interested in her life anymore. She is <u>frightened</u> about the future and she doubts that she ever will meet someone who finds her attractive. I have no idea how this could end. I think she sits there for ever, I really don’t know.”</p> <p><u>Traumatic dysregulation</u> (example of a borderline patient)</p> <p>“She feels <b>homeless</b>, it seems that she is <b>incarcerated</b> in jail, wants to <b>escape</b> from this <b>isolation</b>, she thinks about <b>suicide</b>. It is also possible that she is in a <b>mental institution</b>, because she has already tried to commit <b>suicide</b> and now she has to be alone in an empty room. Nobody helps her, and she has no relatives or friends. I have no idea. (long pause) I think she only dreams of <b>running away</b>.”</p>

“Normative fear indicators” are underlined italics, “traumatic fear indicators” are bold.

based on convergent classifications with the AAI, administered one month after fMRI acquisition and classified by a blind trained AAI judge. The correspondence between the AAP and AAI resolved vs. unresolved categories was highly significant ( $kappa=0.70$ ).

Beyond overall classification we studied on a more detailed level, what kind of words with respect to attachment fear and trauma patients and controls used in their AAP stories. AAP judges differentiated between so called “normative” and “traumatic” fear indicators according a detailed manual (George and West, 2004). “Normative” fear indicators are defined as those typically present because of AAP picture “pull”, based on evaluations of several hundred stories in normative and clinical samples: statements like “talking to the deceased” in “Cemetery” or a character frightened by separation in “Bench” are coded as “normative” fear indicators (Table 2).

These markers do not have the same terrifying quality as “traumatic” fear indicators, such as the “deceased talking back to the living” in “Cemetery” or the girl in “Bench” described as suicidal and incarcerated. The two judges agreed 100% on these narrative indicators. The data we report here focus on the traumatic fear indicators because of the specific link between BPD and attachment trauma (Fonagy et al., 2000).

#### 2.4. Attachment task in an fMRI environment

Subjects were administered the fMRI-adapted version of the AAP. The detailed procedure is described else-

where (Buchheim et al., 2006). Subjects were first trained in the AAP story telling task prior to entering the scanner using two non-AAP “neutral” (i.e., not attachment scenes) pictures. The training procedure was repeated two more times, if necessary. During scanning, subjects were presented the standard AAP instruction (“what led up to that scene, what are the characters thinking or feeling, and what might happen next?”) for 10s and a fixation cross for 10s. This was followed by one of the seven AAP pictures (120s). Subjects were instructed to talk about the picture for 2min or as long as possible. A fixation cross was shown for 15s after picture presentation until beginning a new cycle of instruction and picture presentation. The total procedure included 9 pictures, 2 neutral and 7 standard AAP attachment stimuli. For detailed trial structure, see Fig. 2.

#### 2.5. Data acquisition

A 1.5-Tesla Siemens Magnetom Symphony scanner (Siemens, Erlangen, Germany), 64×64 voxels, FoV 192mm, slice thickness 4mm/1mm gap, 25 slices, TE/TR 40ms/2500ms, total acquisition time 25min (= 598 volumes, one session). The paradigm was presented with fMRI compatible video-goggles (Resonance Technologies, Northridge, CA). Speech was digitally recorded using an fMRI compatible microphone and Cool Edit Pro (Syntrillium Software Cop. Phoenix, Arizona as software). Head movement was minimized by using padded earphones fixating the head within the gradient insert coil.

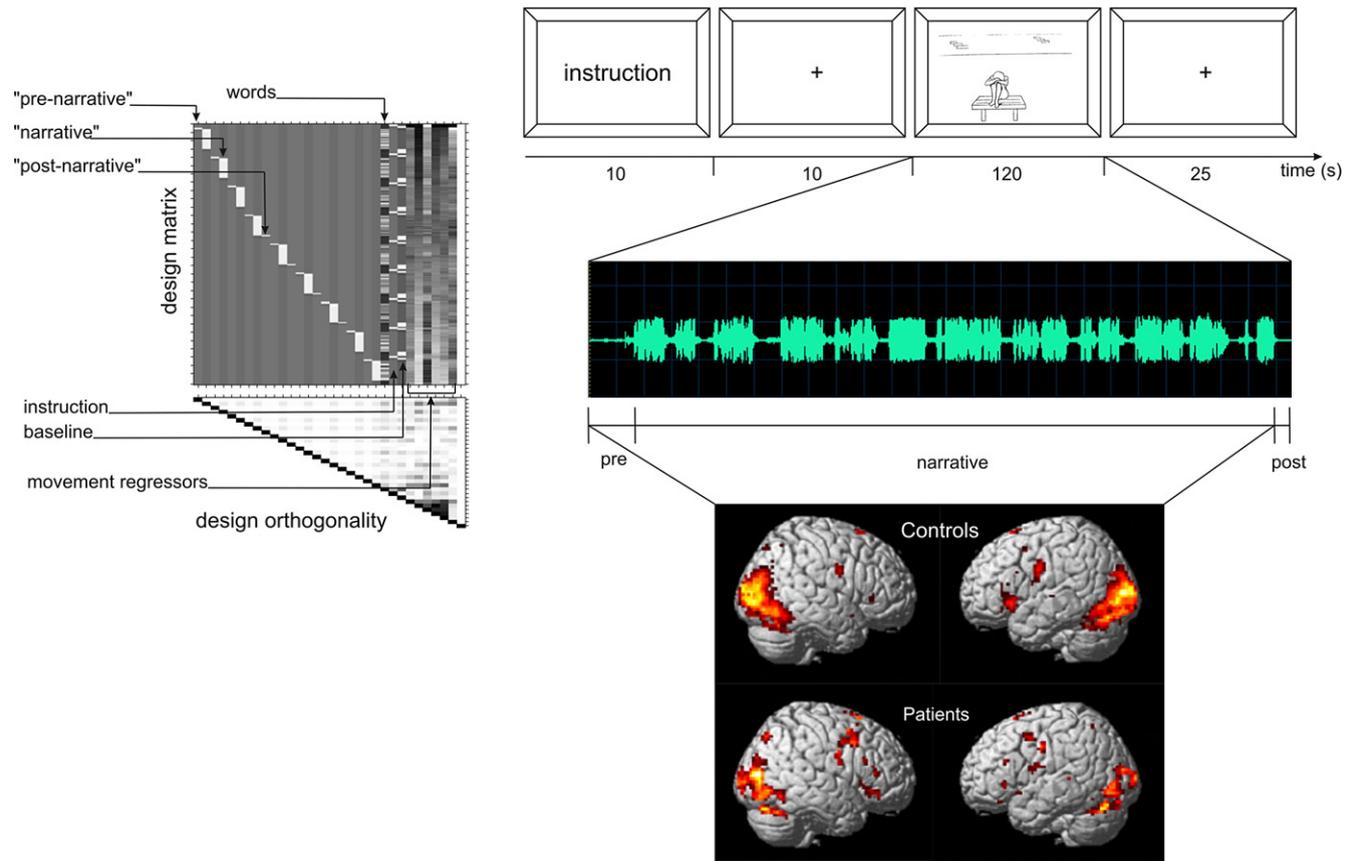


Fig. 2. Paradigm, modeling and main effects: right side: at the upper right the trial structure is depicted, demonstrating one of the monadic pictures. In the middle, the digital speech recording is shown. In the right lower part, the main effects of “picture” (see text) in the control and patient group are shown (one sample *t*-test,  $P < 0.001$  uncorrected, extent threshold 5 voxels, see also Table 4). On the left side the model in SPM is depicted. Pre-narrative, narrative and post-narrative were modeled as separate regressors. The fourth regressor modeled onset of every single word, the following two regressors modeled instruction and baseline. Moreover there are six regressors for movement parameters.

Table 3  
Three-group-comparison: occurrence frequency of traumatic fear indicators in the AAP

AAP picture	<i>R</i>		<i>U</i>		<i>B</i>		<i>R</i> × <i>U</i>	<i>R</i> × <i>B</i>	<i>U</i> × <i>B</i>	<i>R</i> × <i>U</i> × <i>B</i>
	Control resolved		Control unresolved		Borderline unresolved					
	(n=10)		(n=7)		(n=11)					
	<i>M</i>	S.D.	<i>M</i>	S.D.	<i>M</i>	S.D.	<i>P</i>	<i>P</i>	<i>P</i>	<i>P</i>
Monadic (alone) pictures	1.00	2.21	2.29	1.38	9.73	8.41	0.012*	0.000***	0.002**	0.000***
Window	0.40	1.26	0.71	1.89	2.27	3.50	0.743	0.004**	0.020*	0.003**
Bench	0.10	0.32	0.57	0.98	2.82	3.19	0.331	0.007**	0.117	0.011*
Cemetery	0.30	0.95	0.29	0.49	2.27	2.28	0.537	0.016*	0.032*	0.006**
Corner	0.20	0.63	0.71	0.95	2.36	2.80	0.250	0.061	0.305	0.064
Dyadic pictures	0.70	1.34	0.29	0.76	2.09	3.21	0.515	0.173	0.083	0.290
Departure	0.00	0.00	0.29	0.76	0.18	0.60	0.412	1.000	1.000	0.709
Bed	0.50	1.27	0.00	0.00	0.64	1.50	0.485	0.404	0.245	0.359
Ambulance	0.20	0.63	0.00	0.00	1.27	2.37	1.000	0.325	0.245	0.251

Mann–Whitney *U*-test: *P* = significance of the two-tailed Exact test; Kruskal–Wallis *H*-test: *P* = significance estimated in 100 000 Monte-Carlo trials; \**P* ≤ 0.05, \*\**P* ≤ 0.01, \*\*\**P* ≤ 0.001.

## 2.6. Data analysis

### 2.6.1. Behavioral scales

Group differences were analyzed using the Kruskal–Wallis *H*-test and the exact Mann–Whitney *U*-test (SPSS version 14). Non-parametric test procedures were used because of the non-normal distribution of the dependent variables. The magnitude of the group differences was expressed by the effect size (ES, Cohen's *d*).

### 2.6.2. Neuroimaging data

Analyses were carried out with SPM2 ([www.fil.ion.ucl.ac.uk](http://www.fil.ion.ucl.ac.uk)) and MATLAB 6.1 (MathWorks, Natick, Massachusetts). Preprocessing steps: 1) Motion correction by realigning them to the first volume of each session, 2) spatial normalization (3 × 3 × 3mm), and 3) smoothing (FWHM 8mm). Subjects with head movement of >2mm within a trial cycle were excluded from further analysis (four controls, no patients).

The regression model is depicted and explained in detail in the legend of Fig. 2. All regressors except those for motion were convolved with a function that modeled a prototypical hemodynamic response. The variance of each voxel was estimated for each trial according to the General Linear Model. Individual regionally specific effects of interest were calculated for each participant using linear contrasts, resulting in a *t*-statistic for every voxel.

The effects of interest in this study were those for monadic and dyadic pictures. The contrast for monadic pictures included pictures #2, #4 and #7; the contrast dyadic pictures included #3, #5 and #6. Picture 8 was excluded based on the coding results (see Results). We calculated the contrast “picture” = [(pre-speech) + (narrative)] versus base-

line, for each subject, thereby including any mental processes that occurred before the speaking phase.

Group differences were assessed at a second level using random effects analysis. Three analyses were performed. Analysis 1: main effects of “picture” were calculated using one sample *t*-tests. Analysis 2 (main analysis): one-way ANOVAs with three groups was calculated for monadic and dyadic “pictures” contrasts-resolved controls (*n* = 10), unresolved controls (*n* = 7) and unresolved patients (*n* = 11, medicated and un-medicated). Within the ANOVAs, patients were contrasted against both control groups combined as well as with each control group separately. A three-group analysis with two conditions was calculated to test for an interaction effect of group by picture category. Analysis 3 (control analysis): a one-way ANOVA with five groups was calculated in order to control for effects of attachment status and medication ((resolved controls (*n* = 10), unresolved controls (*n* = 7), resolved patients (*n* = 2, medicated), unresolved medicated patients (*n* = 4) and unresolved un-medicated patients (*n* = 7)).

*T*-statistics for each voxel were set at a threshold of *P* < 0.001, uncorrected for multiple comparisons. Results were corrected for extent threshold, resulting in *P* < 0.05 at the cluster level. Brain areas were identified using atlases (Talairach and Tournoux, 1988; Duvernoy, 1999).

## 3. Results

### 3.1. Behavioral data

BPD patients differed significantly from controls in all clinical scales (Table 1). The AAP classification

distribution was 10 resolved and 7 unresolved controls, and 2 resolved (included only in the fMRI control analysis) and 11 unresolved patients. The difference between the groups was significant. AAI analyses (Main

and Goldwyn, 1985) showed that patients were significantly more unresolved with respect to sexual abuse and loss through death of a significant person compared to controls (Table 1).

Table 4

Main effect of picture (pre-speech plus picture) from Analysis 1 for all, monadic and dyadic pictures in both groups, controls and patients

Region	BA	Controls			Patients		
		All	Monadic	Dyadic	All	Monadic	Dyadic
Dorsolateral prefrontal cortex	L 46	-54,30,12, 3.80					
	R 46						
Ventrolateral prefrontal cortex	R 9	54,3,42, 3.51					
	L 47	-54,27,3, 4.44	-54,18,-6, 3.92	-45,21,-9, 4.03	-54,30,0, 4.02		
	R 47	54,27,-6, 3.79					
	L 44	-39,9,33, 3.83					
Lateral prefrontal cortex	L 6	-48,3,48, 3.96					
	R 6	42,6,54, 3.79					
Superior frontal gyrus	6	0,6,6,63, 3.97	0,3,63, 3.76	0,15,63, 3.99			
	L 6	-3,15,66, 3.70					
	R 6	6,9,66, 4.53					
Medial prefrontal cortex	L 8	-3,21,48, 4.21					
	R 8	3,30,42, 3.68					
Precuneus	L 8	0,30,36, 3.75					
	L 7	-21,-66,48, 4.05	18,-75,51, 3.87	-21,-63,39, 3.60	-3,21,48, 4.30		
Precentral gyrus	R 7	24,-72,48, 4.82					
	L 6	-42,-9,33, 4.39	-45,-6,33, 3.95	-42,-9,33 4.00	-51,-9,39, 3.96	-51,-9,36, 4.00	-51,0,45, 3.50
Postcentral gyrus	R 6	54,-3,27, 3.98					
	L 4	-60,-3,18, 3.71					
Superior parietal lobe	L 7	-60,0,15, 3.67					
	R 7	-63,-9,18, 3.63					
Superior temporal gyrus	R 38	24,-63,54, 3.55					
Medial temporal gyrus	L 21	48,27,-12, 3.24					
Parahippocampal gyrus	R 28	-45,21,-9, 4.03					
Parahippo campal/ lingual gyrus	L 30	21,-27,-6, 4.18					
	R 30	-3,-42,3, 5.04					
Fusiform gyrus	R 19	6,-42,3, 4.31					
Cuneus	R 17	42,-78,-12, 4.26					
	L 17	-21,-87,24, 3.56					
Lingual gyrus	L 18	-15,-102,3, 3.67					
Occipital cortex	R 18	36,-90,9, 6.40	36,-90,9, 6.54	36,-90,6, 5.93	30,-84,9, 4.90	30,-84,9, 5.20	-21,-102,9, 4.55
	L 18	-30,-90,6, 6.27	-30,-90,6, 6.58	21,-84,-15, 4.32			
Cerebellum	L 19	-45,-81,-3, 5.96	-42,-75,-6, 4.84				-42,-75,-6, 4.93
	R 19	27,-69,42, 4.53					
Cerebellum	R	39,-66,-21, 5.60					
	L	33,-75,-24, 5.07					
		-24,-84,-21, 4.07					
		-39,-69,-24, 4.76					

For significant activated regions Talairach coordinates (x, y, z) as well as Z-value are given (one sample t-tests,  $P < 0.001$  uncorrected).

As predicted, BPD patients showed significantly more traumatic fear indicators in the monadic stories, and not in the dyadic ones, as compared to both control groups (Table 3). These results passed the Bonferroni criterion of simultaneous inference ( $P < 0.0167$ ). The strongest difference was found between

unresolved patients and resolved controls. The Kruskal–Wallis test showed significant differences in monadic pictures Window, Bench, and Cemetery. The difference for Corner did not reach statistical significance. Window, Bench, and Cemetery were selected for fMRI analysis.

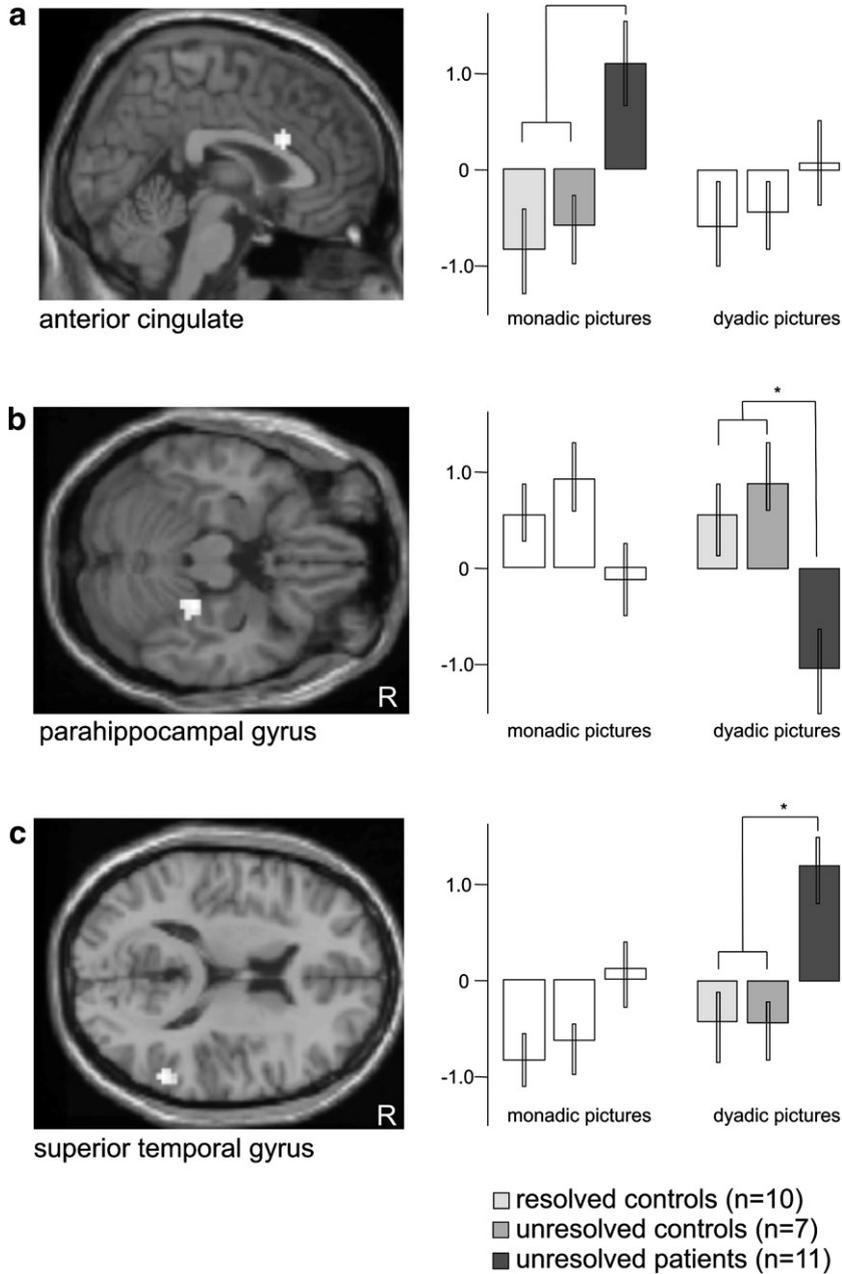


Fig. 3. a, b, c. Group differences for monadic and dyadic pictures. The results are from the second level analysis for monadic pictures ( $n=3$ ) or dyadic pictures ( $n=3$ ), respectively, thresholded at  $P < 0.001$  at the voxel level and  $P < 0.05$  at the cluster level (for exact location and  $z$ -values see text). The figure shows effect sizes, bars indicate 90% confidence interval (and resolved controls  $n=10$ , unresolved controls,  $n=7$ , unresolved patients,  $n=11$ ). Note, that the groups are grey scale coded only for the analysis in which the effect is significant at the chosen level of significance.

### 3.2. fMRI analysis

Analysis 1: both control and patient groups showed activations in visual (occipital), motor (precentral cortex, basal ganglia and cerebellum) and language related areas (temporal cortex), as well as in the anterior cingulate, superior and middle frontal gyrus (Fig. 2 and Table 4). This analysis was calculated to test replicability of our pilot study (Buchheim et al., 2006).

Analysis 2 (main analysis, Fig. 3): as hypothesized BPD patients showed significantly stronger activation of the anterior midcingulate cortex (aMCC,  $x=3, y=18, z=24, Z=4.43$ ) than controls in response to monadic pictures<sup>3</sup>. A similar activation trend for dyadic pictures was not significant.

In response to dyadic pictures, BPD patients showed less activation of the right parahippocampal gyrus (GH,  $x=33, y=-39, z=-15; Z=4.31$ ), and stronger activation of the right superior temporal sulcus (STS,  $x=60, y=-45, z=24; Z=4.52$ ) than controls. Again, similar activation trends for monadic pictures were not significant. This explains why the interaction effect of diagnosis by picture type was not significant. We calculated the same contrasts between the patient group (all unresolved) and each of the two subgroups of controls (resolved, unresolved) in order to test whether this effect was due to diagnosis or attachment classification. The results were the same, indicating a diagnosis effect. No other significant activations were found.

Analysis 3 (control analysis): the results of analysis 2 remained unchanged when including the two resolved patients and splitting the patient group by medication. The effects sizes of medicated and un-medicated patients did not differ significantly in all three regions of group differences. The effect sizes of the resolved patients were in between those of the unresolved patients and controls. Resolved patients may be more similar to healthy controls; however, there are too few patients ( $n=2$ ) to interpret this finding.

## 4. Discussion

This study investigated the neural correlates of attachment trauma in BPD patients versus controls while telling stories in response to attachment-activating scenes. As expected, BPD patients showed a higher

proportion of unresolved attachment classifications and more traumatic fear indicators in monadic pictures than controls. As hypothesized BPD patients showed significantly more dorsal anterior cingulate cortex activation than controls in response to “monadic” pictures. In response to dyadic pictures patients showed significantly more activation of the right superior temporal sulcus and less activation of the right parahippocampal gyrus.

### 4.1. Attachment trauma on a narrative level

In accordance with previous research (Fonagy et al., 2000; Agrawal et al., 2004), the majority of BPD patients were classified as unresolved. Convergent classifications between the scanner-administered AAP and the AAI administered outside the scanner confirm that the fMRI-AAP procedure was feasible also for BPD patients. The number of unresolved controls here, mostly due to loss experiences, is greater than the average percentage reported in healthy populations (George and West, 2003). Unresolved patients had significantly higher ratings for loss and abuse on the AAI scales compared to unresolved controls, indicating again that the combination of unresolved loss and abuse is more likely to contribute to pathological distress than experiences of loss alone (Lyons-Ruth et al., 2003).

The linguistic analysis of traumatic fear indicators provides a more specific understanding of attachment trauma in BPD patients. Unresolved BPD patients manifested significantly greater traumatic dysregulation in response to monadic pictures (Window, Bench, Cemetery), whereas normative dysregulation predominated in unresolved controls. For example, in Cemetery, patient stories described isolation, abandonment, murder, suicide, and dissociated imagery (e.g., figures floating above the ground). Controls predominantly described typical graveyard contact with the deceased (visit) or grief talk.

### 4.2. Neural correlates of attachment trauma

#### 4.2.1. Monadic pictures: anterior cingulate cortex

As expected BPD patients (unresolved) showed increased ACC activation in monadic pictures where traumatic dysregulation indicators were present. ACC activation is observed in response to pain and unpleasantness (Schnitzler and Ploner, 2000). ACC activation in healthy subjects is associated with social relationship stimuli, including intimate relationships (Bartel and Zeki, 2004), social exclusion (Eisenberger et al., 2003), and pictures evoking grief (Gündel et al., 2003). However, the ACC is not homogeneous (Vogt, 2005).

<sup>3</sup> Results for monadic pictures remain unchanged when including picture 8 into the analysis, i.e. when including all monadic pictures. This result was irrespective of the behavioural results, showing that pictures 2, 4 and 7 differentiate clearly between groups with respect to traumatic fear indicators.

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, involvement of aMCC in pain and fear avoidance is feasible. The observed ACC activation in our study was located in the aMCC. In the context of our study, we interpret this finding as a neural signature of pain and fear associated with attachment trauma. This pattern is consistent with our hypothesis and reports that abandonment fears are the most persistent long-term symptoms in BPD (Zanarini et al., 2003).

Our results are consistent with a FDG-PET study demonstrating increased baseline ACC metabolism in BPD patients (extending from aMCC into the medial prefrontal cortex) as compared to healthy controls (Juengling et al., 2003). However, they are not in accordance with findings from two recent functional PET studies (Schmahl et al., 2003, 2004). Women with BPD and a history of sexual abuse showed significantly less aMCC activation compared to women with sexual abuse without BPD. Nevertheless, there is a crucial difference to our study: subjects in the PET studies listened to pre-processed, scripted memories reintroduced during their neuroimaging experiment. The subjects in our study were instructed to respond spontaneously to attachment-activating pictures, which prevented anticipatory self-regulation.

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 (Schmahl et al., 2006). The authors interpret this pattern as an indicator of successful antinociception that patients have acquired by their experience of repetitive self-mutilation. We interpret our finding of clearly more dorsal aMCC activation as an indicator of unsuccessful coping with emotional pain. However we have to consider that 82% of our patients had experiences of sexual abuse compared to non-sexually abused controls. It may be that severe trauma (though not fulfilling PTSD criteria), more than a diagnosis of BPD per se, is associated with increased aMCC activation during emotional processing.

Furthermore, our specific stimuli indicating aloneness did not activate the amygdala compared to studies using more general emotional or psychophysical stimuli (Herpertz et al., 2001; Donegan et al., 2003; Schmahl et al., 2006).

#### 4.2.2. Dyadic pictures: superior temporal sulcus and parahippocampal gyrus

There were no specific hypotheses with respect to the neural response to dyadic pictures. However, we observed group differences that need to be explained. The STS is regularly activated in theory-of-mind tasks (Gallagher and Frith, 2003). It is a crucial part of a network involved in “thinking about others” (Saxe and Kanwisher, 2003). 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 (Fonagy et al., 2003). They often demonstrate a misleading hypersensitivity to others’ mental states that facilitates manipulating and controlling perceived threatening relationships. Based on this model, we interpret the increased STS activation in BPD patients as a neural indicator of fear-based hypervigilance in attachment relationships.

A second finding was the decreased activation of the parahippocampal gyrus in BPD patients compared to controls. Along with the hippocampus, this region is involved in memory processes (Eichenbaum, 2000). 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 (Erk et al., 2003). Reduced parahippocampal activation in BPD patients, thus, may be explained by reduced positive valence of memories of dyadic interactions. This interpretation is consistent with the finding that both resolved and unresolved controls in our study reported greater positive interactions in the dyadic narratives (i.e., warmth and mutuality) than the BPD patients.

#### 4.3. Limitations and conclusions

Several limitations of our study must be considered. First, speaking within the scanner is associated with movement; however, the amount of movement was comparable to other studies without speaking (Kircher et al., 2001). We used several measures to account for residual movement in our model, such as, including movement parameters as a covariate of no interest as well as modeling the onset of every spoken word. Furthermore, the activated regions were not those typically found for movement artifacts. Second, our sample size was not large enough to fill all four cells of the design. The control analyses showed that medication status and including the two resolved patients did not change our main results. Nonetheless, our findings must be examined using larger samples. Third, the influence

of lifetime psychiatric conditions in the patient group cannot be ruled out, although patients with current psychosis and substance abuse were excluded.

In conclusion, our behavioral results confirm that BPD pathology is associated with traumatic attachment fear related to autobiographic abuse and loss experiences. The monadic attachment pictures representing aloneness showed narrative and neural patterns of differentiation between patients and controls. The fact that such a differentiation was found only between (unresolved) patients and (resolved and unresolved) controls and not between controls with different attachment status can be interpreted such as that attachment disorganization and disease specific factors have additive effects. Our findings may provide evidence for possible mechanisms related to the fearful intolerance of aloneness in BPD patients (Gunderson, 1996). 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 (Fonagy et al., 2000) and addresses their poor contextualization of positive relationship memories (Levy et al., 2006).

Our results suggest evidence for potential neural mechanisms of attachment trauma underlying interpersonal symptoms of BPD. Moreover the findings indicate that we have developed a sensitive procedure capable to eliciting differences in patterns of brain activity between controls and individuals with BPD.

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