Background: Early traumatization and additional post-traumatic stress disorder are frequent in patients with borderline personality disorder (BPD). The purpose of this study was to investigate neural correlates of traumatic memory in BPD with and without posttraumatic stress disorder (PTSD) using functional magnetic resonance imaging (fMRI).

Methods: We studied 12 traumatized female patients BPD, 6 of them with and 6 without PTSD. According to an autobiographical interview key words (cues) were defined for traumatic and for negative but nontraumatic episodes. In a block-designed fMRI task patients recalled these episodes. Contrasts between trauma condition and non-trauma condition were analyzed.

Results: Analyses for all subjects revealed activation of orbitofrontal cortex areas in both hemispheres, anterior temporal lobes, and occipital areas. In the subgroup without PTSD, activation of orbitofrontal cortex on both sides and Broca's area predominated. In the subgroup with additional PTSD, we observed right more than left activation of anterior temporal lobes, mesiotemporal areas, amygdala, posterior cingulate gyrus, occipital areas, and cerebellum.

Conclusions: Dependent on absence or presence of additional PTSD different neural networks seem to be involved in the traumatic memory of patients with BPD. Biol Psychiatry 2003;00:000–000 © 2003 Society of Biological Psychiatry

Key Words: Posttraumatic stress disorder, borderline personality disorder, fMRI, trauma, memory
were reported (Bremner et al 1999b; Lanius et al 2001, 2002, 2003; Rauch et al 1996; Shin et al 1997, 1999). Grossly summarizing these studies revealed that trauma-related stimuli compared with neutral stimuli in patients with PTSD compared with healthy controls were associated with greater activation of limbic and paralimbic areas and with decreased activation of (medial) prefrontal cortical areas and of Broca’s area.

The purpose of the present study was to investigate neural activation patterns of traumatic memory compared with the recall of negative (aversive) but nontraumatic autobiographical events in BPD patients with and without additional PTSD. We hypothesized 1) that traumatic memory in BPD patients is associated with activation patterns different from those associated with negative but nontraumatic memory and 2) that additional PTSD modifies these patterns.

Methods and Materials

Subjects

Twelve Caucasian, 21-year-old to 40-year-old, female traumatized BPD patients were included in the study. All of them were treated for BPD as inpatients in the Gilead Hospital or in the Ev. Johannes Hospital, Bielefeld, Germany, during 2001 and 2002. All patients met DSM-IV criteria of BPD, assessed by the treating psychotherapists within the first week after admission. Participants were neither pregnant nor had any of the following current or previous medical conditions, which were assessed by their medical history, by careful clinical examination, and by laboratory means: endocrine system disorders, malignant diseases, liver cirrhosis, neurologic diseases, loss of consciousness (lifetime), or mental retardation. Further exclusion criteria were current infectious diseases, anorexia, schizophrenia, schizoaffective disorders, and major depressive disorder with psychotic symptoms. Clinical diagnoses of alcohol and/or drug dependence during the 6 months before the study also led to exclusion. Eight patients had occasionally received psychotropic medication during the 1-week to 7-week period before the study, but all subjects had been drug-free for at least 7 days before the assessments.

Informed written consent to participate in the study was obtained from all subjects.

Subjects received financial remuneration for their efforts (maximum $50 to $100 with the amount depending on the distance from home) when patients were discharged during the study. The study was accepted by the Institutional Review Board (IRB) (University of Muenster Ethics Committee) on July 17, 2000.

Clinical Assessment and Memory Testing

The clinical assessment was similar to that in a previous study (Driessen et al 2000), but participants completed the full Structured Clinical Interview for DSM-IV (SCID) (Wittchen et al 1997). Current psychopathology was assessed by the Beck Depression Inventory (BDI) (Beck and Steer 1994), the Symptom Checklist (SCL-90-R) (Franke 1995), and the Dissociative Experiences Scale (DES) (Bernstein and Putnam 1986; German version by Freyberger et al 1999). Traumatization history was assessed by the 28-item version of the Childhood Trauma Questionnaire (CTQ) (Bernstein and Fink 1998) and the Impact of Event Scale (IES-R) (Maercker and Schu¨tzwohl 1998). In all subjects, urinary drug screenings (Triag¨e-Test, Merck, Germany) and a venous blood sample were obtained as clinical routine. No pathologic measures were found in any participant. To control for declarative memory, the Wechsler Memory Scale (WMS-R) (H¨artner et al 2000; Wechsler 1987) was administered.

Autobiographical Interview and Traumatic Memories

The method of script-driven stimulation has been applied not only in neuroimaging studies of traumatized subjects (Bremner et al 1999a; Lanius et al 2002, 2003) but also in those of other psychiatric and neurologic conditions like addictive disorders (Kilts et al 2001) and epilepsy (Jokeit et al 2001). Basing on these experiences, we applied a semistructured autobiographical research interview (Fischer-Rosenthal 1991; Hopf 1991; Witzel 1985) 1 week before fMRI acquisition. The interview covered the whole life span (childhood, youth, early adulthood, adulthood) and dimensions, such as family, social contacts, significant others, school, partnership, and employment, for each episode separately. Relevant single events were assessed with a focus on those with a positive or negative emotional impact and on traumatic events. The complete interview was recorded and typewritten. Four episodes between age 12 and age 18 were selected, with two nontraumatic and two traumatic events. Nontraumatic episodes were defined as being of negative emotional relevance for the subjects; however, these episodes were neither evaluated as traumatic by the subject nor did they fulfill the criterion A of DSM-IV PTSD. In contrast, traumatic events were experienced and, at the time of the study, still recalled as severely traumatic. These events were reported as still evoking a serious emotional reaction, and patients had not been able to cope with them until today. All traumatic events met criterion A. Modifying the script-driven technique (i.e., listening to a record of the interview) patients were asked to define three key words for each of the four events.

CASE REPORT. Patient 2 was sexually abused by her teacher in the hall of the residence. The key words (cues) for this traumatic episode were teacher, hall of residence, and touch. She also reported a severe sunburn with medical consequences for 2 days during a hiking tour on the island of Malta. The key words (cues) for this nontraumatic episode were sun, Malta, and hiking.

The key words were agreed upon with the patients as cue stimuli for the active recall of the episode during fMRI (cue-driven method). According to the experiences with our clinically unstable BPD patients during a pilot study, this approach has the advantage of giving patients the chance to control their emotional...
arousal to prevent major movement artifacts and dissociation, as far as possible (Lanius et al. 2002).

Stimulus Presentation and Design

Structural scanning was obtained in the days before fMRI to exclude brain damage, and all technical and study details were explained. On the day of fMRI acquisition, we started the protocol with a self-rating scale (see below) before patients entered the tomograph. We chose a boxcar design with presentation of two activation conditions (trauma condition and non-trauma condition) in a between-subjects randomly balanced order and with the presentation of a baseline condition (BC). The protocol consisted of 12 activation blocks, with each preceded and followed by a BC. Each block was introduced by the key words (cues) using the scanner’s intercom. The key words were presented with the task either to recall the associated autobiographical episode in a previous pilot study with six subjects, each condition lasted 30 seconds and was presented six times. Baseline condition also lasted 30 seconds to ensure that the image contrast sufficiently returned to baseline (a diagram is available on request). During each condition, 10 sets of 16 axial T2*-weighted MR slices were obtained.

Before the MRI acquisition, patients completed a self-rating scale for obtaining the intensity of mood (current anger, sadness, anxiety, helplessness, security) by a 5-point Likert scale (0 = not at all to 4 = extreme). After the fMRI acquisition, patients completed this scale with regard to the feelings experienced during the TCs and the NTCs, separately. In addition, we obtained the intensity of sensory qualities of TC and NTC recalls, as well as the global impressions of vividness and unreality (Table 1).

MRI Acquisition

Magnetic resonance imaging scanning was performed on a 1.5 Tesla scanner (Siemens Magnetom Symphony, Erlangen, Germany) equipped with a standard head coil. On the day of fMRI, scout images were obtained. Sagittal T1-weighted images were obtained in each subject, scanning to position the axial T2*-weighted images along the anterior commissure-posterior commissure (AC-PC) line. For fMRI, 16 contiguous axial T2*-weighted images were obtained using a standard echo-planar imaging (EPI) sequence (time of repetition [TR] = 2500 milliseconds, time of inversion [TI] = 9000 milliseconds, field of view [FOV] = 192 mm, matrix 64 × 64). Two hundred forty scans were acquired over a 12-minute period. For anatomical reference and to exclude gross brain pathology, a T1-weighted three-dimensional [3D]-sequence (MPRAGE) (TR = 11.1 milliseconds, TE = 4.3 milliseconds, slice thickness 1.5 mm, FOV 201 × 230 mm, matrix 224 × 256) and an axial fluid-attenuated inversion recovery (FLAIR) data set (TR = 9000 milliseconds, TE = 110 milliseconds, time of inversion [TI] = 2500 milliseconds, slice thickness 5 mm, FOV 201 × 230, matrix 220 × 256) were obtained for each patient.

Table 1. Intensity of Affective Qualities a Before fMRI Acquisition, and Intensity of Affective Sensory Qualities, b and Global Impressions, c During Recalls of the Traumatic and Nontraumatic Episodes Under fMRI

<table>
<thead>
<tr>
<th></th>
<th>Before fMRI</th>
<th>Traumatic Condition (TC)</th>
<th>Nontraumatic Condition (NTC)</th>
<th>Z-values d</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affective Qualities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anger</td>
<td>.25 ± .45</td>
<td>1.25 ± 1.22</td>
<td>1.08 ± 1.31</td>
<td>.32, ns</td>
</tr>
<tr>
<td>Sadness</td>
<td>1.25 ± .97</td>
<td>1.92 ± 1.24</td>
<td>.83 ± 1.19</td>
<td>2.10, p = .036</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1.50 ± .90</td>
<td>2.75 ± 1.06</td>
<td>1.17 ± .94</td>
<td>2.62, p = .009</td>
</tr>
<tr>
<td>Helplessness</td>
<td>1.17 ± .83</td>
<td>3.00 ± 1.13</td>
<td>1.25 ± 1.29</td>
<td>2.69, p = .007</td>
</tr>
<tr>
<td>Security</td>
<td>1.17 ± .83</td>
<td>.33 ± .89</td>
<td>1.08 ± 1.00</td>
<td>1.71, ns</td>
</tr>
<tr>
<td>Sensory Qualities</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual</td>
<td>–</td>
<td>2.58 ± .79</td>
<td>2.75 ± .45</td>
<td>.63, ns</td>
</tr>
<tr>
<td>Visual-colored</td>
<td>–</td>
<td>1.92 ± 1.68</td>
<td>1.42 ± 1.31</td>
<td>1.67, ns</td>
</tr>
<tr>
<td>Visual-scenic</td>
<td>–</td>
<td>2.50 ± .90</td>
<td>2.25 ± .62</td>
<td>1.00, ns</td>
</tr>
<tr>
<td>Olfactory</td>
<td>–</td>
<td>.50 ± 1.00</td>
<td>.25 ± .62</td>
<td>1.73, ns</td>
</tr>
<tr>
<td>Acoustic</td>
<td>–</td>
<td>2.25 ± .87</td>
<td>1.50 ± 1.09</td>
<td>1.85, ns</td>
</tr>
<tr>
<td>Tactile</td>
<td>–</td>
<td>1.67 ± .98</td>
<td>.67 ± .78</td>
<td>2.49, p = .013</td>
</tr>
<tr>
<td>Global Impressions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vivid</td>
<td>–</td>
<td>2.42 ± .79</td>
<td>2.42 ± .51</td>
<td>0, ns</td>
</tr>
<tr>
<td>Unreal</td>
<td>–</td>
<td>1.33 ± 1.23</td>
<td>.33 ± .65</td>
<td>2.59, p = .010</td>
</tr>
</tbody>
</table>

Mean ± SD, n = 12.
a fMRI, functional magnetic resonance imaging; TC, traumatic condition; NTC, nontraumatic condition.
b 0 = not at all; 1 = low, 2 = moderate; 3 = intense; 4 = extreme.
c Wilcoxon test between retrospective scores in traumatic and nontraumatic conditions.
d Z-values for obtaining the intensity of mood (current anger, sadness, anxiety, helplessness, security) by a 5-point Likert scale (0 = not at all to 4 = extreme). After the fMRI acquisition, patients completed this scale with regard to the feelings experienced during the TCs and the NTCs, separately. In addition, we obtained the intensity of sensory qualities of TC and NTC recalls, as well as the global impressions of vividness and unreality (Table 1).
Revised (Maercker and Schuckers; Beck Depression Inventory (Beck and Steer 1994); CTQ indicates Childhood Trauma Questionnaire (Bernstein and Fink 1998); IES-R indicates Impact of Event Scale, Revised; ns, not significant.

Dissociative Experience Scale; CTQ, Childhood Trauma Questionnaire; IES-R, Impact of Event Scale, Revised; fMRI, functional magnetic resonance imaging; WMS-R, Wechsler Memory Scale, Revised; ns, not significant.

Image and Statistical Analyses

Functional MRI data were analyzed using SPM99 (Wellcome Department of Imaging Neuroscience, London, United Kingdom; http://www.fil.ion.ucl.ac.uk/spm99, accessed September 26, 2003) for all image preprocessing and voxel-based statistical analyses within the context of the general linear model. Image realignment corrected for head movement using the SPM99 default algorithm. Spatial normalization reduced anatomical differences before group comparisons, again using default settings and the standard stereotactic space of SPM99, the MNI brain (Montreal Neurologic Institute). Spatial smoothing followed with a Gaussian kernel of 10 mm full width at half maximum (FWHM) to increase both signal and anatomical conformity. Using fixed-effect statistical analysis on a voxel-by-voxel basis, differences between conditions were assessed over the total group and over the subgroups. For the contrasts (NTC > TC), maps of the t-statistic were corrected for multiple comparisons at p < .05 (T > 4.49). For the results of the fixed-effect analysis, MNI coordinates of the major activations were transformed to the Talairach space (Talairach and Tournoux 1988) using a correction procedure (Brett 1999) and then fed into the Talairach Daemon (Lancaster et al. 2000) to obtain anatomical projections of maximum activation automatically (i.e., without any observer interaction). Hemispherical asymmetry indices (AI) were calculated as the ratio \( [V_R - V_L]/[V_R + V_L] \) with \( V_R \) and \( V_L \) being activation volumes of the right and left hemispheres. Derived from the determination of highly lateralized brain functions like language dominance, this approach yielded AIs ranging from -1 to +1.
analyses are two-tailed with applied for the basic analyses of group differences. Statistical between +1 and −1 (i.e., strong right and left asymmetry, respectively) (Binder et al 1996).

Statistical analyses of data apart from fMRI were performed using SPSS versions 10.0 (SPSS Inc., Chicago, Illinois). The χ²-test, the Wilcoxon test, and the Mann–Whitney U-test were applied for the basic analyses of group differences. Statistical analyses are two-tailed with α levels of significance, \( p < .05 \).

### Results

#### Sample Characteristics and Traumatization History

The mean age of our sample was 32.7 ± 9.3 years, and five patients (41.7%) lived in a partnership. The mean time of education was 11.2 ± 1.6 years with five patients (41.7%) between +1 and −1 (i.e., strong right and left asymmetry, respectively) (Binder et al 1996).

Statical analyses of data apart from fMRI were performed using SPSS versions 10.0 (SPSS Inc., Chicago, Illinois). The χ²-test, the Wilcoxon test, and the Mann–Whitney U-test were applied for the basic analyses of group differences. Statistical analyses are two-tailed with \( p \) levels of significance, \( p < .05 \).

#### Table 3. Brain Regions Showing Increased Activity Associated with the Recall of Traumatic Autobiographical Episodes Compared with Negative but Nontraumatic Episodes in Female Patients with BPD

<table>
<thead>
<tr>
<th>Region</th>
<th>Hemisphere</th>
<th>Talairach Coordinates*</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>k</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Orbital and Middle Frontal Gyrus</td>
<td>R</td>
<td>36 40 −12 145 5.74</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior Frontal Gyrus (BA 47)</td>
<td>R</td>
<td>45 23 −14 7 4.81</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior Frontal Gyrus (BA 45)</td>
<td>R</td>
<td>42 21 15 11 4.73</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral Orbital and Middle Frontal Gyrus</td>
<td>L</td>
<td>−33 52 −8 120 6.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Frontal Gyrus (BA 46)</td>
<td>L</td>
<td>−45 42 14 1 4.51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Temporal Gyrus (BA 38)</td>
<td>R</td>
<td>42 19 −31 75 5.64</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Temporal Gyrus (BA 38)</td>
<td>L</td>
<td>−48 13 −26 7 4.81</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital Lingual Gyrus (BA 18)</td>
<td>L</td>
<td>−15 −87 −18 44 5.92</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital Lingual Gyrus and Cuneus (BA 17, 18)</td>
<td>R</td>
<td>6 −85 −9 106 5.54</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital Lingual Gyrus (BA 18)</td>
<td>R</td>
<td>21 −79 −9 2 4.55</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital Lingual Gyrus (BA 18)</td>
<td>R</td>
<td>27 −76 −9 1 4.48</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occipital Fusiform Gyrus (BA 19)</td>
<td>R</td>
<td>39 −74 −14 5 4.93</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebellum, Anterior Lobe</td>
<td>L</td>
<td>−27 −38 −29 29 5.63</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( n = 12 \)

Height threshold \( T = 4.49, p \) corrected \( < .05 \).

Data from fixed effects analysis (\( p = .05 \) corrected, k, number of activated voxels in cluster; Z, highest Z-statistic within an area of activation; BA, Brodmann area, partly included by the activated cluster; x, distance \[ \text{mm} \] to right \( [+\] \) or left \( [-] \) of the midsagittal line; y, distance anterior \( [+] \) or posterior \( [-] \) to vertical plane through the anterior commissure; z, distance above \( [+] \) or below \( [-] \) the intercommissural (AC-PC) line).

BPD, borderline personality disorder; PTSD, posttraumatic stress disorder; BA, Brodmann area; R, right; L, left; AC-PC, anterior commissure-posterior commissure.

*Coordinates represent single voxels with maximum activity projections within clusters of activation covering areas of differing size (k).

#### Table 4. Brain Regions Showing Increased Activity Associated with the Recall of Traumatic Autobiographical Episodes Compared with Negative but Nontraumatic Episodes in Female Patients with BPD but without PTSD

<table>
<thead>
<tr>
<th>Region</th>
<th>Hemisphere</th>
<th>Talairach Coordinates*</th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>k</th>
<th>Z</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral Orbital and Middle and Superior Frontal Gyrus (BA 10, 11)</td>
<td>L</td>
<td>−33 52 −8 86 6.52</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior Frontal Gyrus (BA 44)</td>
<td>R</td>
<td>45 15 16 42 5.69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior Frontal Gyrus (BA 11)</td>
<td>R</td>
<td>33 49 −13 23 5.09</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior Frontal Gyrus (BA 47)</td>
<td>R</td>
<td>36 35 −2 5 4.88</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inferior Frontal Gyrus (BA 46)</td>
<td>R</td>
<td>33 33 12 1 4.51</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle Frontal Gyrus (BA 47)</td>
<td>R</td>
<td>33 40 7 1 4.49</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\( n = 6 \)

Height threshold \( T = 4.49, p \) corrected \( < .05 \).

Data from fixed effects analysis (\( p = .05 \) corrected, k, number of activated voxels in cluster; Z, highest Z-statistic within an area of activation; BA, Brodmann area, partly included by the activated cluster; x, distance \[ \text{mm} \] to right \( [+\] \) or left \( [-] \) of the midsagittal line; y, distance anterior \( [+] \) or posterior \( [-] \) to vertical plane through the anterior commissure; z, distance above \( [+] \) or below \( [-] \) the intercommissural (AC-PC) line).

BPD, borderline personality disorder; PTSD, posttraumatic stress disorder; BA, Brodmann area; R, right; L, left; AC-PC, anterior commissure-posterior commissure.

*Coordinates represent single voxels with maximum activity projections within clusters of activation covering areas of differing size (k).
having reached a high school degree (the German “Abitur”).

All patients were right-handed. There were no significant differences between the patients with and without additional current PTSD (each subgroup n = 6) with regard to comorbid psychiatric diagnoses, psychopathology, traumatization history, and prescribed medication until 7 days before assessments (Table 2). Declarative memory measures did not differ either, and the memory performance of both subgroups was within the normal range (z = -1 to +1).

**Affective States and Sensory Qualities During Memory Tasks**

Patients experienced significantly higher levels of anxiety and helplessness and a moderately higher level of sadness but not anger during the recall of traumatic events compared with the recall of nontraumatic events (Table 1). Vice versa, they experienced a significantly lower feeling of security. Visual memory qualities were moderate to intense in both conditions but did not differ between them. Only the tactile sensations were significantly stronger in the TC than in the NTC, and the olfactory and the acoustic sensations showed a trend to be more intense in the TC. Although patients reported rather vivid memories under both conditions, a substantial impression of unreality was only experienced while recalling the traumatic episodes. Dissociative states were neither observed by the staff nor reported by any subject. The six BPD patients without PTSD reported the traumatic (U = .5; p = .002) and the nontraumatic visual memories (U = 3.0, p < .02) to be more colored than the six BPD patients with additional PTSD. All other sensory and affective qualities as well as global impressions did not differ between the two subgroups.

**fMRI-Activations in Traumatic Compared with Nontraumatic Memory Conditions**

Contrasting TC > NTC in all subjects revealed a widespread, bilateral cortical and subcortical pattern of activation during TC (Table 3). This pattern included orbitofrontal cortex (OFC) areas in both hemispheres, left frontal areas (Brodmann areas [BA] 45–47) including Broca area, as well as right more than left occipital-mesial and temporal-anterior areas. Activation of the left anterior lobe of the cerebellum was also observed. Separate analyses of TC > NTC in the two subgroups explained different parts of the localization of fMRI activation.

In the subgroup without additional PTSD, we found an exclusively OFC activation pattern on both sides, including the inferior, middle, and superior frontal gyrus (Table 4), as well as Broca’s area (Figure 1, thresholded for display at T ≥ 3.0). The hemispheric asymmetry index was −.12 (derived from the values in Table 4), indicating modestly more activation in the left hemisphere.
Contrasting TC > NTC in the subgroup with additional PTSD, we observed a substantially different pattern with only a minor activation of the OFC. Instead, we found major right-sided activation of the anterior temporal lobe, including parahippocampal gyrus and amygdala, as well as a relatively minor anterior temporal activation on the left side (Table 5, Figure 2). Consequently, the hemispheric asymmetry index was .56 (derived from values in Table 5), indicating a substantially larger activation of the right side of the brain. Furthermore, we found a larger left-sided than right-sided activation of the posterior cingulate gyrus, as well as of medial occipital areas and the cerebellum.

**Discussion**

In this fMRI study of severely traumatized women with BPD, we compared the autobiographical memory of traumatic episodes (TC) with that of aversive but nontraumatic episodes (NTC). Patients reported higher levels of anxiety, helplessness, and tactile sensations, as well as stronger feelings of unreality, in the TC compared with the NTC. Although we did not measure additional physiologic parameters (like heart rate and blood pressure), these results indicate the subjects’ actual engagement in the experimental tasks.

Contrasting TC > NTC in all subjects revealed a widespread, bilateral cortical and subcortical pattern of activation during TC, including the orbitofrontal cortex (OFC) and Broca’s area, as well as occipital-mesial and temporal-anterior areas. This pattern includes most of the activated areas found by Fink et al (1996) and Piefke et al (2003) in two PET studies when contrasting autobiographical memory conditions with baseline conditions. The central finding of this study, however, was the different fMRI activation patterns when contrasting TC versus NTC in the two traumatized BPD subgroups with and without additional current PTSD. In BPD patients without current PTSD, we observed a widespread activation of the OFC in both hemispheres, as well as activation of the Broca area. Neuroimaging studies showed the OFC to be activated in the encoding and retrieval of information in healthy volunteers (Henson et al 1999; Iidaka et al 2000; McDermott et al 1999), in aversive but nontraumatic stimulus-presentation in PTSD (Lanius et al 2001; Rauch et al 1996; Shin et al 1999), in the presentation of aversive versus neutral pictures in BPD (Herpertz et al 2001), and in script-driven memory presentation of abandonment in BPD patients (Schmahl et al 2003).

Noteworthy, structural (Taylor et al 2003) and functional disturbances of the OFC were also observed in major depression (overviews by Drevets 1998 and Davidson et al 2002), and it cannot be excluded that the activation of the OFC by the recall of traumatic memories in our study is influenced by the depressive psychopathology in the BPD patients without PTSD.

On the other side, in BPD patients with additional PTSD (but with a similar level of depressive psychopathology)
and autobiographical memory tasks (Iidaka et al. 2000; &cerebellum was activated in neutral word-specific episodic retrieval tasks in healthy volunteers (Nyberg et al. 1996). On the other hand, parts of the network were deactivated in a PET study using personal past (Markowitsch et al. 1997). On the other hand, this sensomotor and temporolimbic pattern included parts of the visual system (right more than left temporal association cortex and bilateral primary/secondary visual cortex areas), parts of the limbic system (left more than right posterior cingulate gyrus, right parahippocampal gyrus, right amygdala), parts of the sensorimotor cortex (precentral more than postcentral gyrus, right more than left), and the left cerebellum. A case report of a female patient with trauma-related autobiographical amnesia from her youth also demonstrated a strong right anterior temporal activation in relation to unsuccessful retrieval attempts of her personal past (Markowitsch et al. 1997). On the other hand, parts of the network were deactivated in a PET study using neutral retrieval tasks in healthy volunteers (Nyberg et al. 1996). In two further studies, the right instead of the left cerebellum was activated in neutral word-specific episodic and autobiographical memory tasks (Iidaka et al. 2000; Piefke et al. 2003). Although activation of the left posterior cingulate gyrus was also found in an autobiographical memory task of real-life experiences (Maddock et al. 2001), the lateralization of (temporal and frontal) activation in episodic memory has been controversially discussed (Cabeza et al. 1997).

In the present study, we found no activation of the hippocampal region and of the amygdala in the BPD without PTSD subgroup because we analyzed a contrast of two relatively remote and emotionally negative autobiographical memories (TC > NTC). On the other side we saw right-sided activation of the parahippocampal region and of the amygdala in the BPD plus PTSD subgroup. These findings again underline that traumatic memories in subjects with trauma-associated mental disorders like PTSD activate different neural networks and/or lead to stronger activation of the relevant regions of the limbic system.

The two substantially different patterns of neural activation found in this study when comparing BPD patients with and without PTSD are in line with the dual representation model of traumatic memories as previously proposed by several authors (Brewin et al. 1996; Brewin 2001; Metcalfe and Jacobs 1996; Wessa and Flor 2002). Brewin et al. (1996) characterized a situationally accessible memory system
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(SAM) as cue-dependent, unconscious, and uncontrollable. On the other side, the verbally accessible memory system (VAM) was characterized as more independent from cues and situations and as verbally and consciously accessible. According to this model, the process of resolving and overcoming a traumatic experience includes the transfer of trauma-relevant information from the SAM to the VAM. It was hypothesized that in PTSD this transfer is disturbed. In the brain, emotional memories of the SAM system, with its fast fear-conditioning circuits (including the primary sensory cortices, thalamus, and amygdala), are thought to be predominant and/or cannot sufficiently be (top-down) inhibited by projections of higher order areas (prefrontal, cingulate, hippocampal, and language areas). In our study of traumatized BPD patients, we may have observed neural correlates of the VAM system in the subgroup without additional PTSD and predominant neural correlates of an insufficiently inhibited SAM system in the subgroup with additional PTSD.

In the light of these neurobiological findings and considering that all of our patients were severely traumatized, the presence or absence of comorbid PTSD might indicate relevant subgroups of BPD with therapeutic implications. Further studies are needed to clarify this distinction in greater samples and on different levels (e.g., clinical outcome and response to trauma-specific interventions). Although many traumatized patients are able to grossly remember the traumatic event, patients with PTSD are known to frequently recall traumatic events as flashbacks (i.e., detailed dissociated sensory and affective imprints associated with a high emotional arousal). On the other hand, they have difficulties in verbally communicating their experiences and the associated feelings. They are, as van der Kolk et al (1997) and van der Kolk and Fisler (1995) noted, not able to tell a story (i.e., a personal narrative is not available). Thus, previous research, clinical observations, and the present study point to a therapeutic approach, which includes the direct treatment of traumatic memories at least in the subgroup of patients with BPD and with additional PTSD. The goal would be to reorganize traumatic memories on a “higher” cortical level, verbally accessible for the patient. Such an approach might also lead to the suppression of lower level fear-conditioning circuits.

The main limitation of this study is the small sample size, which does not allow generalization of the findings. Further studies in patients with BPD with and without PTSD and with PTSD only and follow-up studies focusing on therapeutic interventions, as well as investigations of traumatized healthy persons, are needed to strengthen the above-mentioned conclusions. Furthermore, the “cue-driven” recall of traumatic memories under fMRI conditions by using key words instead of complete scripts is a new modification, which may lead to different results than the latter one. Although there are some advantages (e.g., more control on emotional arousal by the patients), both methodological approaches should be compared to be sure that the same networks are activated.

Summarizing our main result, when comparing traumatic memories and negative but nontraumatic memories in an fMRI task, BPD patients without comorbid PTSD show primarily activation of the prefrontal cortex, including the Broca area, whereas in patients with additional PTSD, activation of somatomotor and temporolimbic areas, including the amygdala, dominated. These results indicate that different neural networks are involved in the recall of traumatic memories in BPD patients with and without PTSD.

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