Reduced Size and Abnormal Asymmetry of Parietal Cortex in Women with Borderline Personality Disorder

Eva Irle, Claudia Lange, and Ulrich Sachsse

Background: Evidence is accumulating that suggests borderline personality disorder (BPD) and posttraumatic stress disorder (PTSD) are related to small hippocampal size. Psychotic symptoms are frequent in both disorders. Psychotic spectrum disorders are known to be related to abnormalities of temporoparietal cortices.

Methods: Using structural magnetic resonance imaging (3D-MRI), parietal cortex and hippocampal volumes were assessed in 30 young women with BDP who had been exposed to severe childhood sexual and physical abuse and in 25 healthy control subjects.

Results: Compared with control subjects, BPD subjects had significantly smaller right parietal cortex (~11%) and hippocampal (~17%) volumes. The parietal cortex of borderline subjects showed a significantly stronger leftward asymmetry when compared with control subjects. Stronger psychotic symptoms and schizoid personality traits in borderline subjects were significantly related to reduced leftward asymmetry. Stronger trauma-related clinical symptoms and neuropsychologic deficits were significantly related to smaller hippocampal size.

Conclusions: Our results are consistent with previous findings of small hippocampal size in BPD and PTSD. Reduced right parietal cortex size in individuals with BPD may reflect a neurodevelopmental deficit of the right hemisphere.

Key Words: Hippocampus, parietal asymmetry, posttraumatic stress disorder, psychotic symptoms, structural magnetic resonance imaging (3D-MRI), trauma

Borderline personality disorder (BPD) is defined as an intermediate level of personality organization that is considered to occupy a borderline area between neurosis and psychosis (Kernberg 1967; Kernberg et al 2000). Stress-related dissociative and psychotic symptoms occur in about 75% of individuals with BPD (Skodol et al 2002) and in about 40% of individuals with posttraumatic stress disorder (PTSD; David et al 1999; Hamner et al 1999). Psychotic symptoms in BPD and PTSD usually involve nonbizarre hallucinations or delusions and are not associated with formal thought disorder or flat or inappropriate affect. They tend to be transient (lasting minutes or hours), and reality testing is usually impaired for only a short time. Psychotic symptoms in PTSD may cause substantial psychologic distress (Hamner 1997) and are associated with higher levels of psychopathology (Kernberg et al 2000). The subanesthetic application of the N-methyl-D-aspartate (NMDA) antagonist ketamine in humans is known to produce psychotic and dissociative symptoms (Krystal et al 1994). It has been proposed that NMDA receptor hypofunction might cause excitotoxic limbic (i.e., hippocampal) and temporoparietal cortical neurodegeneration in schizophrenia (Olney and Farber 1995).

Research thus far has focused on size reductions of the amygdala and hippocampus in individuals with BPD who were exposed to childhood physical or sexual abuse (Driessen et al 2000; Rüsche et al 2003; Schmahl et al 2003a; Tebartz van Elst et al 2003). Functional imaging studies show that persons with BPD display pronounced prefrontal dysfunction (de la Fuente et al 1997; Juengling et al 2003; Soloff et al 2000, 2003) and enhanced prefrontal and amygdala activation in response to emotional stimuli (Donegan et al 2003; Herpetz et al 2001; Schmahl et al 2003b). Dysfunction in prefrontal regions (Brodmann areas 9–11) is suggested to be implicated in the deficits of persons with BPD to regulate emotional behavior (Soloff et al 2003).

Studies investigating the structural and functional neural correlates of psychotic features in BPD and PTSD are lacking. However, research on individuals with schizophrenia has repeatedly pointed to abnormalities of temporoparietal cortices. Individuals with schizophrenia were shown to have a reduced leftward asymmetry, size reduction, or both (Frederikse et al 2000; Shenton et al 1992). A recent study demonstrated that transcranial magnetic stimulation of the left temporo-parietal cortex improves auditory hallucinations in schizophrenia (Hoffman et al 2003). Evidence is increasing that stress-related hyperglutamatergic states may also contribute to dissociative symptoms and neural toxicity (i.e., hippocampal degeneration) in individuals with schizophrenia, indicating more severe symptoms in individuals with more pronounced size reductions (Barta et al 1990; Gaser et al 2004; Kwon et al 1999; Shenton et al 1992). A recent study demonstrated that transcranial magnetic stimulation of the left temporo-parietal cortex improves auditory hallucinations in schizophrenia (Hoffman et al 2003).

Increasing evidence suggests that glutamatergic dysfunction represents an important part of the pathophysiology of psychotic states. The subanesthetic application of the N-methyl-D-aspartate (NMDA) antagonist ketamine in humans is known to produce psychotic and dissociative symptoms (Krystal et al 1994). It has been proposed that NMDA receptor hypofunction might cause excitotoxic limbic (i.e., hippocampal) and temporoparietal cortical neurodegeneration in schizophrenia (Olney and Farber 1995). Evidence is increasing that stress-related hyperglutamatergic states may also contribute to dissociative symptoms and neural toxicity (i.e., hippocampal degeneration) in individuals who have been exposed to traumatic stress (Chambers et al 1999). A recent study found that burn victims with enduring ketamine application in the posttraumatic state showed significantly stronger PTSD symptoms than burn victims without such treatment (Winter and Irle 2004). More severe PTSD symptoms were related to smaller hippocampal size, as previous investigations have shown (Bremner et al 1997, 2003; Gilbertson et al 2002; Gurvits et al 1996; Villarreal et al 2002).
Table 1. Demographic and Clinical Characteristics of Borderline and Control Subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Borderline Subjects</th>
<th>Control Subjects</th>
<th>Statistic</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>31 ± 6</td>
<td>33 ± 7</td>
<td>t(53) = −.89</td>
<td>.373</td>
</tr>
<tr>
<td>Education (years)</td>
<td>11 ± 2</td>
<td>11 ± 2</td>
<td>t(53) = .23</td>
<td>.822</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>168 ± 6</td>
<td>169 ± 6</td>
<td>t(53) = −.21</td>
<td>.836</td>
</tr>
<tr>
<td>Handedness (left/right)</td>
<td>2.28</td>
<td>0.25</td>
<td></td>
<td>.495</td>
</tr>
<tr>
<td>Duration of Trauma-Related Clinical Symptoms (years)</td>
<td>14 ± 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic Antecedent Questionnaire</td>
<td>4.8 ± 1.2</td>
<td>2.4 ± 0.5</td>
<td>t(29.1) = 8.90</td>
<td>.000</td>
</tr>
<tr>
<td>Dissociative Experiences Scale (total score)</td>
<td>24.7 ± 12.3</td>
<td>2.1 ± 4</td>
<td>t(50) = 8.17</td>
<td>.000</td>
</tr>
<tr>
<td>Diagnostic Interview for Borderlines, Psychotic Symptoms</td>
<td>5.5 ± 3.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCID-I, Psychotic Symptoms</td>
<td>1.7 ± 2.3</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>SCID-II, Schizoid Traits</td>
<td>1.5 ± 2.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCID-II, Schizotypal Traits</td>
<td>1.7 ± 1.6</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Impact of Events Scale-Revised</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrusions</td>
<td>3.0 ± 1.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoidance</td>
<td>3.7 ± 1.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperarousal</td>
<td>3.1 ± 1.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beck Depression Inventory</td>
<td>27 ± 9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Münchner Alkoholismustest</td>
<td>6 ± 7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SCID, Structured Clinical Interview for DSM-IV.

*Table values are given as mean ± SD unless otherwise indicated.

*Fisher’s Exact Test.

*Neglect and physical and sexual abuse experiences during childhood and adolescence (7–18 years). Six borderline subjects were unable to complete parts or all of the questionnaire.

*Clinician-administered rating scale; 0–5 = normal alcohol consumption, 6–10 = likely alcohol abuse, 11–52 = alcohol abuse or dependence.

In this investigation, the volumes of the parietal cortex and the hippocampus of 30 women with borderline personality disorder (BPD) who had been exposed to severe childhood sexual and physical abuse were compared with those of a healthy matched control group (n = 25). The goals of our study were 1) to investigate whether parietal cortex size is reduced in a sample of BPD subjects, 2) to investigate whether the parietal cortex of BPD subjects has an abnormal asymmetry, 3) to analyze how psychotic symptoms and psychosis-related personality traits are associated with parietal cortex size and asymmetry, and 4) to verify whether hippocampal size is reduced in BPD subjects and is associated with trauma-related symptoms.

Methods and Materials

Subjects

The sample comprised 30 young female inpatients with the diagnosis of borderline personality disorder (BPD) according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association 1994) admitted to the Psychiatric State Hospital of Lower Saxony, Göttingen, Germany (Table 1). The hospital has a specialized therapeutic unit for women who have experienced severe childhood sexual and physical abuse.

All subjects were assessed with a routine physical and neuroligic examination, magnetic resonance imaging, and laboratory testing. Subjects with a history of neurologic disease (multiple sclerosis; n = 1) or electroencephalograph abnormalities being indicative for temporal lobe epilepsy (n = 2) or hyperintense magnetic resonance imaging (MRI) signals (n = 2) were excluded beforehand. Subjects with psychotropic disorders (DSM-IV Axis I) were also excluded. Eight subjects were on antidepressant medication. Some subjects were occasionally treated with benzodiazepines (n = 5) or mild neuroleptics (n = 6).

All borderline subjects were investigated with the Structured Clinical Interview for DSM-IV (SCID-I and SCID-II; First et al 1995, 1997; Wittchen et al 1997) and the Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D; Gast et al 2000; Steinberg 1994) conducted by a master’s-level psychologist. Seven subjects received a second SCID-I interview conducted by another clinician. Both interviewers were blind to each other but had access to clinical information. Agreement between interviewers (expressed as kappa, a statistic that corrects for chance agreement) was 1.0 (p = .008) for the current or lifetime diagnosis of major depression and PTSD, respectively. All borderline subjects met DSM-IV criteria for BPD. All subjects but one had received the diagnosis of BPD by clinical judgment at an earlier time. Four subjects met DSM-IV criteria for schizoid personality disorder, five for paranoid personality disorder and two for schizotypal personality disorder.

Eleven borderline subjects (37%) met criteria for lifetime or current PTSD. Three (10%) subjects met criteria for lifetime panic disorder with agoraphobia, eight (27%) for current panic disorder with agoraphobia, one subject (3%) for lifetime agoraphobia without panic disorder, and three (10%) for current agoraphobia without panic disorder. Three (10%) subjects met criteria for current generalized anxiety disorder, two (7%) for lifetime social phobia, six (20%) for current social phobia, and six (20%) for current obsessive-compulsive disorder. Thirteen (43%) subjects met criteria for lifetime major depression and 18 (60%) for current major depression. Three (10%) subjects met criteria for current somatization disorder and three (10%) for current pain disorder. Six (20%) subjects met criteria for lifetime anorexia, three (10%) for current anorexia, three (10%) for lifetime bulimia, and seven (23%) for current bulimia. Six (20%) subjects met criteria for lifetime alcohol abuse, 2 (7%) for current alcohol abuse, three (10%) for lifetime alcohol dependence, and two (7%) for lifetime sedative abuse. Four (14%) subjects met criteria for lifetime depersonalization disorder and 23 (77%) for current depersonalization disorder. One (3%) subject met criteria for lifetime dissociative amnesia, six (20%) for current dissociative amnesia, and four (13%) for current dissociative identity disorder.

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Borderline subjects were compared with 25 healthy female control subjects comparable with regard to age, height, and years of education. Control subjects were recruited for the study by an advertisement in a local newspaper and leaflets distributed in the Hospital of the University of Göttingen and in town. Only subjects without a history of neurologic or psychiatric (as assessed by the SCID-I) disorder were studied.

After a complete description of the study was given to the subjects, written informed consent was obtained. The study design was approved by the Ethical Committee of the Medical Faculty of the University of Göttingen.

Clinical and Neuropsychologic Assessment

The Traumatic Antecedent Questionnaire (TAQ; Herman et al 1989) was used to assess neglect as well as physical and sexual abuse experiences during childhood and adolescence (7–18 years). The Impact of Events Scale-Revised (IES-R; Maercker and Schützwohl 1998; Weiss and Marmar 1996) was used to assess PTSD symptoms. Duration of trauma-related clinical symptoms was defined as the number of years since PTSD symptoms or other trauma-related clinical symptoms appeared. Delusions and hallucinations were assessed by aid of the SCID-I (screening module for psychotic symptoms; score: 0–15). The Diagnostic Interview for Borderline Patients (DIB; Gunderson and Kolb 1981; Pütterich 1990) was used to assess borderline personality traits (i.e., fulfilled criteria of paranoid, schizoid and schizotypal personality disorder, respectively) were assessed by the SCID-II. The Dissociative Experiences Scale (DES; Bernstein and Putnam 1986; Frewberger et al 1999) was applied as a measure of dissociative symptom severity. Depressive symptoms were assessed by the Beck Depression Inventory (BDI; Beck et al 1961; Beck et al 1960; Hautzinger et al 1995). The amount of alcohol consumption and alcohol-related clinical symptoms were assessed by the Münchner Alkoholischem-Test (MALT) (Feuerlein et al 1979). Intellectual, mnemonic, and attentional functions were assessed by the Wechsler Adult Intelligence Scale—Revised (WAIS-R; Tewes 1991; Wechsler 1981), the Wechsler Memory Scale—Revised (WMS-R; Wechsler 1987), and a computer-driven working memory test (Testbatterie zur Aufmerksamkeitsprüfung [TAP]; Zimmermann and Fimm 1993).

MRI Acquisition and Analysis

All subjects received an MRI scan using a 1.5-T Philips Gyroscan machine. Scanning parameters of the T1-weighted three-dimensional sequence were as follows: echo time = 6.0 msec; repetition time = 24.0 ms; flip angle = 30°; field of view = 256; slice plane = sagittal; matrix = 256 × 256; slice thickness = 1.3 mm; slice number = 130; acquisition mode = three-dimensional (3D). Volumetric analysis was done on the basis of 3D MRIs. The images were transferred to a computer workstation and processed using the CURRY software (version 4.5; Compumedics, Melbourne, Australia). Images were reformatted into continuous 1-mm-thick slices. Intracranial volume and total brain volume was calculated with automated multistep algorithms and 3D region growing methods that are limited by gray-value thresholds. Simultaneous 3D visualization of brain structures and manual tracing allowed a precise identification and delineation of regions of interest. We used sulcal landmarks for the delineation of the parietal cortex because they have the advantage of directly modeling the substantial interindividual morphologic variability of the human cerebral cortex (Radmacher et al 1992).

Parietal Cortex. The anterior border of the parietal cortex was defined by the central sulcus. On the medial surface, a vertical line was drawn between central and cingulate sulci. The posterior border was defined by the parietooccipital sulcus. The ventrolateral border was defined by the sylvian fissure. A line passing through the sylvian fissure was extended posteriorly and served as postsylvian ventrolateral boundary. The inferior medial boundary was defined by a line passing through the cingulate sulcus, which was extended into the parietooccipital sulcus. Manual markings were made on coronal slices by drawing a straight line between sylvian fissure and central sulcus and between the posterior extension of the sylvian fissure and the cingulate sulcus. The resulting volume (Figure 1) includes gray and white matter of the postcentral, supramarginal, and angular gyrus; the superior parietal lobe; and the precuneus (Brodmann areas 1–3, 5, 7, 39, and 40).

Parietal cortex asymmetry was calculated as follows: (left volume – right volume) / (left volume + right volume). Positive values indicate left-greater-than-right asymmetry, and negative values indicate right-greater-than-left asymmetry.

Hippocampus. The hippocampus was disarticulated from surrounding tissue on coronal slices by means of manual tracing according to a standardized protocol (Pruessner et al 2000) and
with the aid of the serial sections provided by Duvernoy (1998). The anterior border of the hippocampus was found on the coronal slice showing the alveus, the uncal recess of the inferior horn of the lateral ventricle, or both, and the posterior border was found on the slice where an ovoid mass of gray matter appeared inferiomedially to the trigone of the lateral ventricle.

All analyses were done blind to subjects’ test performance. For defining the intrarater and interrater reliability (the raters were blind to the diagnosis), each hemisphere of 10 randomly chosen cases were reassessed, respectively. The intraclass correlation coefficients for this procedure were \( r = .98 \) (intrarater) and \( r = .98 \) (interrater) for the parietal cortex and \( r = .95 \) (intrarater) and \( r = .96 \) (interrater) for the hippocampus.

### Statistical Analysis

Student \( t \) tests (or Mann–Whitney \( U \) tests in case of small subject numbers) were applied to compare differences between groups on demographic, clinical, and neuropsychologic variables and on intracranial and total brain volume. Frequencies were compared using Fisher’s Exact Test. Partial correlation coefficients controlling for total brain volume and multiple regression analyses were used to examine the relationship between regional brain volumes and clinical and neuropsychologic variables. The alpha of correlation and regression analyses was not adjusted because the data are considered exploratory.

We used nonparametric tests to analyze regional brain volumes because of deviations of left and right parietal cortex volumes from normal distribution in both groups of subjects (Kolmogorov–Smirnov test; \( D \) values between .155 and .186, \( p \) values between .01 and .09). The parietal cortex and the hippocampus of borderline and control subjects was compared by nonparametric \( 2 \times 2 \) analyses of covariance (ANCOVA; Brunner et al 2002) controlling for total brain volume with the between-subjects factor of Group (borderline, control subjects) and the within-subjects factors of Hemisphere (left, right).

All analyses were two-tailed, and alpha was defined as \( p < .05 \). Statistical computations were performed using the Statistical Package for the Social Sciences (SPSS for Windows, version 10.0) and the Statistical Analysis System (SAS for Windows, version 8.01; nonparametric ANCOVAs: http://www.ams.med.uni-goettingen.de/Projekte/LD/Makros_LD.html).

### Results

#### Brain Measures: Group Comparisons

The groups did not differ with respect to intracranial volume and total brain volume (Table 2). The \( 2 \) (Group) \( \times 2 \) (Hemisphere) \( \text{ANCOVA} \) comparing the parietal cortex of borderline and control subjects yielded a significant effect of Group (\( p = .035 \)) and Hemisphere (\( p = .000 \)), indicating larger parietal cortex volumes of control subjects and larger left compared with right parietal cortex volumes (Figure 2). The interaction of Group and Hemisphere was also significant (\( p = .026 \)). The follow-up regional ANCOVA models revealed that borderline subjects had significantly smaller right parietal cortices (\( p = .005 \)) compared with control subjects.

#### Table 2. Brain Measures of Borderline and Control Subjects

<table>
<thead>
<tr>
<th>Volume (mL)</th>
<th>Borderline Subjects ((n = 30))</th>
<th>Control Subjects ((n = 25))</th>
<th>Difference (%) and Effect Size</th>
<th>Statistic</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial Volume</td>
<td>1363 ± 97</td>
<td>1384 ± 88</td>
<td>-1.5 (-.23)</td>
<td>( t(53) = -0.79 )</td>
<td>.432</td>
</tr>
<tr>
<td>Total Brain</td>
<td>1074 ± 99</td>
<td>1106 ± 81</td>
<td>-2.9 (-.36)</td>
<td>( t(53) = -1.27 )</td>
<td>.209</td>
</tr>
<tr>
<td>Parietal Cortex*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>130 ± 20</td>
<td>142 ± 19</td>
<td>-9.2 (-.62)</td>
<td>( T = 4.43 )</td>
<td>.035</td>
</tr>
<tr>
<td>Left*</td>
<td>68 ± 10</td>
<td>72 ± 10</td>
<td>-5.9 (-.40)</td>
<td>( T = 1.09 )</td>
<td>.296</td>
</tr>
<tr>
<td>Right*</td>
<td>63 ± 10</td>
<td>70 ± 9</td>
<td>-11.1 (-.74)</td>
<td>( T = 7.92 )</td>
<td>.005</td>
</tr>
<tr>
<td>Asymmetry Index*</td>
<td>.069 ± .081</td>
<td>.024 ± .082</td>
<td></td>
<td>( t(53) = 2.07 )</td>
<td>.043</td>
</tr>
<tr>
<td>Hippocampus*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5.3 ± 0.8</td>
<td>6.2 ± 0.7</td>
<td>-17.0 (-1.20)</td>
<td>( T = 18.92 )</td>
<td>.000</td>
</tr>
<tr>
<td>Left*</td>
<td>2.6 ± 0.5</td>
<td>3.0 ± 0.4</td>
<td>-15.4 (-.89)</td>
<td>( T = 11.07 )</td>
<td>.008</td>
</tr>
<tr>
<td>Right*</td>
<td>2.7 ± 0.4</td>
<td>3.2 ± 0.3</td>
<td>-18.5 (-1.43)</td>
<td>( T = 19.67 )</td>
<td>.000</td>
</tr>
</tbody>
</table>

*Table values are given as mean ± SD.

*Percentage of difference in regional volumes is relative to control subjects. Effect sizes (in parentheses) are group mean differences divided by pooled SD.

*The hypothesis-driven group \( \times \) hemisphere \((2 \times 2)\) analysis of covariance (ANCOVA)-type statistic using total brain volume as covariate had the following \( T \) values: group, \( T(1) = 4.43, p = .035 \); hemisphere, \( T(1) = 14.27, p = .000 \); group \( \times \) hemisphere, \( T(1) = 4.93, p = .026 \).

*The hypothesis-driven group \( \times \) hemisphere \((2 \times 2)\) ANCOVA-type statistic using total brain volume as covariate had the following. \( T \) values: group, \( T(1) = 18.92, p = .000 \); hemisphere, \( T(1) = 15.16, p = .000 \); group \( \times \) hemisphere, \( T(1) = 1.03, p = .310 \).

*One-way ANCOVA-type statistic controlling for total brain volume with the between-subjects factor of Group (borderline, control subjects) and the within-subjects factors of Hemisphere (left, right).

\( \text{Difference} \% = (\text{Right} - \text{Left}) / \text{Right} \times 100\% \). Positive values indicate left-greater-than-right asymmetry.
Parietal cortex asymmetry was significantly different ($p = .043$) between borderline and control subjects, indicating a more pronounced left-greater-than-right asymmetry in borderline compared with control subjects (Figure 3). Parietal cortex asymmetry values of two left-handed borderline subjects (see Table 1) were within .5 SD of those of the whole BPD sample.

The 2 (Group) × 2 (Hemisphere) ANCOVA comparing the hippocampus of borderline and control subjects yielded a significant effect of Group ($p = .000$) and Hemisphere ($p = .000$), indicating smaller hippocampal volumes of borderline compared with control subjects and larger right compared with left hippocampal volumes (Figure 4). For detailed results of all statistical comparisons, see Table 2.

Relationship Between Psychotic Symptoms and Parietal Cortex Measures

All borderline subjects reported frequent episodes of depersonalization and derealization (DIB). Nineteen borderline subjects experienced nonbizarre hallucinations or delusions as assessed by the screening module for psychotic symptoms (SCID-I). The content of delusions included referential, persecutory, somatic, or grandiose themes. Hallucinations occurred in all sensory modalities (i.e., auditory, visual, tactile, olfactory, or gustatory). In three subjects, auditory hallucinations included hearing voices; two of these subjects met criteria for current dissociative identity disorder. None of the subjects experienced disorganized or catatonic behavior. Subjects with psychotic symptoms according to the SCID-I ($n = 19$) did not differ significantly from subjects without psychotic symptoms ($n = 11$) on any clinical or neuropsychologic variable or on brain measures except for parietal cortex asymmetry ($U$ test; $p = .023$), for which subjects with psychotic symptoms showed a weaker leftward asymmetry (.046 ± .077) than subjects without psychotic symptoms (.109 ± .076).

Accordingly, the amount of psychotic symptoms (screening module for psychotic symptoms, SCID-I) was significantly related to parietal cortex asymmetry of borderline subjects ($n = 30$; $r_s = -.41; p = .026$), indicating a reduced leftward asymmetry in subjects with more psychotic symptoms (Figure 5). A very similar relationship was obtained for the amount of psychotic symptoms as assessed by the DIB ($r_s = -.37; p = .050$; Figure 6). Borderline subjects with a reduced leftward asymmetry displayed also more schizoid personality traits (SCID-II; $r_s = -.59; p = .001$) (Figure 7).

Nonparametric partial correlations controlling for total brain volume revealed a positive relationship between right parietal cortex volume and psychotic symptoms (DIB; $r = .43; p = .024$), indicating larger right parietal cortex volumes in subjects with stronger psychotic symptoms. The relationship between right parietal cortex volume and schizotypal personality traits (SCID-II) closely approached conventional levels of significance ($r = .36; p = .053$).

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Figure 3. Scatter plot of parietal cortex asymmetry values of subjects with borderline personality disorder and healthy control subjects. Group means are indicated by horizontal lines. Positive values indicate left-greater-than-right asymmetry; and negative values indicate right-greater-than-left asymmetry.

Figure 4. Scatter plot of left and right hippocampal volumes (mL) for subjects with borderline personality disorder and healthy control subjects. Group means are indicated by horizontal lines.

Figure 5. Relationship between parietal cortex asymmetry and number of psychotic symptoms as assessed by the screening module for psychotic symptoms (Structured Clinical Interview for DSM-IV—$I$; see Clinical and Neuropsychological Assessment in Methods and Materials; $r_s = -.41; p = .026$). The best-fitting line has an exponential function ($R^2 = .15; p = .036$). Positive values on the x axis indicate left-greater-than-right asymmetry; negative values indicate right-greater-than-left asymmetry. Asymmetry values of two subjects coincided exactly in two cases. For comparison, 15 female subjects with schizophrenia from the study of Frederikse et al (2000) presented with an inferior parietal cortex asymmetry of $-1.1 ± .28$. 

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values $< .05$), indicating better performance of subjects with larger parietal cortex volumes. For detailed results, see Table 3.

**Influence of Comorbid Disorders and Medication**

Comparing borderline subjects fulfilling DSM-IV criteria for current or lifetime PTSD ($n = 11$) with borderline subjects not fulfilling PTSD criteria ($n = 19$) revealed smaller intracranial (1314 $\pm$ 74 vs. 1389 $\pm$ 99; $U$ test, $p = .027$) and total brain (1021 $\pm$ 68 vs. 1105 $\pm$ 103; $p = .011$) volumes of subjects with PTSD. One-way ANCOVAs controlling for total brain volume revealed that subjects with and without PTSD did not differ with regard to left (2.4 $\pm$ .4 vs. 2.7 $\pm$ .5) and right (2.5 $\pm$ .4 vs. 2.8 $\pm$ .5) hippocampal volume and left (67 $\pm$ 11 vs. 69 $\pm$ 10) and right (62 $\pm$ 11 vs. 64 $\pm$ 10) parietal cortex volume ($p$ values $>.60$). Parietal cortex asymmetry also did not differ significantly (.064 $\pm$ .077 vs. .072 $\pm$ .086; $p = .767$). Subjects with PTSD performed worse than subjects without PTSD on neuropsychologic measures (Verbal IQ, Verbal Memory, Visual Memory, Delayed Recall, Attention/Concentration; $p$ values $< .05$) and reported more intrusions (IES-R; $p = .001$), more hyperarousal (IES-R; $p = .003$), and more severe sexual abuse (TAQ; $p = .023$) than subjects without PTSD.

Borderline subjects with current or lifetime anorexia ($n = 8$) did not differ from subjects without anorexia ($n = 22$) with regard to intracranial volume (1329 $\pm$ 95 vs. 1376 $\pm$ 97), total brain volume (1024 $\pm$ 112 vs. 1092 $\pm$ 90), or parietal cortex asymmetry ($r_{10.24} = .084$ vs. $.079$; $U$ tests; $p > .15$), or with regard to left (2.5 $\pm$ .6 vs. 2.6 $\pm$ .4) and right (2.7 $\pm$ .4 vs. 2.7 $\pm$ .5) hippocampal volume or left (68 $\pm$ 13 vs. 68 $\pm$ 10) and right (61 $\pm$ 11 vs. 64 $\pm$ 10) parietal cortex volume (one-way ANCOVAs controlling for total brain volume; $p > .50$). Subjects with anorexia did not differ from subjects without anorexia on neuropsychologic measures ($p > .20$ except Working Memory (TAP), for which subjects with anorexia reacted slower than subjects without anorexia (795 $\pm$ 144 vs. 623 $\pm$ 157; $p = .017$).

Borderline subjects with current or lifetime alcohol abuse or dependence ($n = 10$) did not differ from subjects without these disorders ($n = 20$) on brain volume measures or on parietal

![Figure 6](https://www.elsevier.com/locate/biopsy)

**Figure 6.** Relationship between parietal cortex asymmetry and number of psychotic symptoms as assessed by the Diagnostic Interview for Borderline Patients (see Clinical and Neuropsychologic Assessment in Methods and Materials; $r_1 = -.37$; $p = .050$). Positive values on the x axis indicate left-greater-than-right asymmetry; negative values indicate right-greater-than-left asymmetry.

**Relationship Between Trauma-Related Symptoms and Hippocampal Volume**

Partial correlations controlling for total brain volume yielded a significant relationship between intrusions (IES-R) and right hippocampal volume ($r = -.56$; $p = .003$), and between hyperarousal (IES-R) and left ($r = -.39$; $p = .047$) and right ($r = -.44$; $p = .026$) hippocampal volume, indicating more intrusions and stronger hyperarousal in subjects with smaller hippocampal volumes. The duration of trauma-related clinical symptoms was significantly related to left hippocampal volume ($r = -.54$; $p = .002$), indicating smaller left hippocampal volumes in subjects with longer duration of symptoms.

Stronger neglect (TAQ) during childhood and adolescence was significantly related to smaller left ($r_1 = -.57$; $p = .002$) and right ($r_1 = -.43$; $p = .024$) hippocampal volumes. There was also a significant negative relationship between the amount of neglect and total brain volume ($r_1 = -.46$; $p = .015$). Partial correlations controlling for total brain volume between neglect and hippocampal volume were marginally significant for the left hippocampus ($r = -.38$; $p = .052$) and insignificant for the right hippocampus.

**Neuropsychological Performance and Brain Measures**

Compared with control subjects, borderline subjects showed significantly reduced intellectual functions (WAIS-R). Borderline subjects were also impaired on tests of memory and attention (WMS-R; Table 3). The volumes of left and right hippocampus and left and right parietal cortex were entered into multiple regression analyses (method: stepwise; significance level for selecting variables: $\alpha = .05$). Total brain volume was entered as a further predictor to control for the influence of brain size. Considering borderline subjects, only right hippocampal volume significantly predicted intellectual, mnemonic, and attentional performance (proportion of explained variance ($R^2$) between .15 and .30; $p$ values $< .05$), and the addition of the other variables did not significantly improve the prediction. Larger right hippocampal volumes were related to better test performance. Considering control subjects, parietal cortex volume significantly predicted attentional test performance ($R^2$ between .19 and .28; $p$

![Figure 7](https://www.elsevier.com/locate/biopsy)

**Figure 7.** Relationship between parietal cortex asymmetry and number of schizoid personality traits (criteria for schizoid personality disorder as assessed by the Structured Clinical Interview for DSM-IV—II; $r_1 = -.59$; $p = .001$). The best-fitting line has an exponential function ($R^2 = .30$; $p = .002$). Positive values on the x axis indicate left-greater-than-right asymmetry; and negative values indicate right-greater-than-left asymmetry. Asymmetry values of two subjects coincided exactly in one case.
cortex asymmetry ($U$ tests or ANCOVAs controlling for total brain volume; $p > .30$). Relationships between alcohol consumption and alcohol-related clinical symptoms (MALT) and any brain measure were not significant for the whole BPD sample or BPD subjects with alcohol disorders, respectively (Spearman correlations; $p > .10$).

Depressive symptom severity (BDD) was not related to intracranial or total brain volume, left or right hippocampal volume, left or right parietal cortex volume, or parietal cortex asymmetry (Spearman correlations; $p > .40$). Depressive symptom severity was also not related to any neuropsychologic measure ($p > .10$).

Brain measures did not differ between borderline subjects taking antidepressant drugs ($n = 8$) and those who did not ($n = 22$; $p > .30$). Subjects taking benzodiazepines ($n = 5$) did not differ from those who did not ($n = 25$; $p > .30$), and subjects taking mild neuroleptics ($n = 6$) did not differ from those who did not ($n = 24$) ($p$-values $>.40$). Brain measures of subjects taking antidepressants, benzodiazepines or neuroleptics were within .5 SD of the brain measures of unmedicated subjects, respectively.

Discussion

Reduced Size and Abnormal Asymmetry of the Parietal Cortex in BPD

Our results demonstrate reduced size of the right parietal cortex in borderline subjects (Table 2, Figure 2). Accordingly, our data revealed a stronger parietal leftward asymmetry of borderline compared with control subjects (Figure 3). Psychotic symptoms and schizoid personality traits of borderline subjects were significantly related to parietal cortex asymmetry, indicating a reduced leftward asymmetry in subjects with stronger psychotic symptoms and more schizoid personality traits (Figures 5–7). Parietal cortex asymmetry of borderline subjects with pronounced psychotic symptoms was similar to that reported for women with schizophrenia (Frederikse et al 2000; Figure 5).

Research on individuals with schizophrenia has demonstrated size reduction of the left temporoparietal cortices, reduced leftward asymmetry of these cortices when compared with control subjects, or both (Frederikse et al 2000; Niznikiewicz et al 2000; Shapleske et al 1999; Sommer et al 2001). The subgroup of our borderline subjects with pronounced psychotic and schizoid symptoms also presented with a reduced leftward asymmetry (see Figures 5–7). It might be speculated that a reduction of the normal left-greater-than-right asymmetry of temporoparietal cortices increases the likelihood for developing psychotic symptoms. Nevertheless, the majority of our borderline subjects had an increased leftward asymmetry due to reduced right parietal cortex size. Possibly, increased leftward parietal cortex asymmetry protects the majority of individuals with BPD from developing more pronounced and disabling psychotic symptoms.

Currently, reduced leftward or even reversed temporoparietal asymmetry in schizophrenia is considered a neurodevelopmental deficit of the left hemisphere (Pearlson et al 1996; Shenton et al 2001). The pattern of parietal cortex abnormality we found in our borderline subjects may be considered a neurodevelopmental deficit of the right hemisphere. Individuals with BPD and PTSD were reported to have a considerably increased prevalence of subtle neurologic impairment (Gurvits et al 2000; Reekum et al 1996). Weintraub and Mesulam (1983) described a behavioral syndrome characterized by emotional and interpersonal difficulties, shyness, visuospatial disturbances, and inadequate paralinguistic communicative abilities related to neurologic signs of right hemisphere dysfunction.

The BPD subjects in our study displayed marked deficits in the domain of attention, visual memory, and visuospatial cognition (Table 3). Similar neuropsychologic findings have been obtained earlier in individuals with BPD (O’Leary et al 1991).
Currently, the role of the right parietal cortex is modeled as an epicenter for the mental representation and attentional targeting of salient extrapersonal events (Mesulam 1999). Visuospatial and attentional functions are most likely compromised after lesions of the right posterior parietal cortex (Mesulam 1998). Accordingly, the attentional performance of our control subjects was significantly related to parietal cortex size (Table 3), which may serve as a kind of validation of the parietal cortex measure used in this study. Attentional deficits as well as visuospatial and memory deficits of borderline subjects, however, were related to small right hippocampal size instead (Table 3). These results support earlier studies demonstrating a strong relationship between hippocampal size and cognitive functioning of individuals who had been exposed to traumatic stress (Bremner et al 1995a, 1997; Gurvits et al 1996).

The mechanism for developing small right parietal cortices could also be sought in the traumatic life history of our borderline subjects. It could be speculated that early and repeated interpersonal traumatic events lead to a pervasive pattern of detachment from social relationships and thus to an understimulation of the right parietal cortex. Recent evidence suggests that maturation of parietal and frontal cortices continues into adulthood (Sowell et al 2003), rendering them likely candidates for environmental plasticity. An exploratory analysis of our data, however, did not reveal any relationships among the severity of traumatic experiences (TAQ), trauma-related clinical symptoms (IES-R), or dissociative symptoms (DES) and right parietal cortex volume or parietal cortex asymmetry, respectively.

**Hippocampal Size Reduction in BPD**

Our results complement earlier findings on reduced hippocampal size in adult survivors of childhood abuse with BPD (Driessen et al 2000; Rüscher et al 2003; Schmahel et al 2003a; Tebarzt van Elst et al 2003) or without BPD (Bremner et al 1997, 2003; Stein et al 1997; Villarreal et al 2002; Vythilingam et al 2002). We found smaller hippocampal volumes in borderline subjects with stronger trauma-related clinical symptoms. Similar relationships between PTSD symptom severity and reduced hippocampal size were reported for adult survivors of childhood abuse (Bremner et al 1997, 2003; Villarreal et al 2002), combat veterans (Gilbertson et al 2002; Gurvits et al 1996), and adult burn survivors (Winter and Irlé 2004).

Our results might argue for a detrimental influence of prolonged trauma-related distress on hippocampal size. Preclinical evidence suggests that stress-related hyperglutamatergic states may induce hippocampal degeneration in individuals with traumatic exposure (Chambers et al 1999). Evidence also suggests that small hippocampal size is a risk factor for developing PTSD in Vietnam combat veterans (Gilbertson et al 2002) and that lower precombat intelligence predicts exposure to more severe combat (Macklin et al 1998).

Our borderline subjects with the additional diagnosis of PTSD presented with more neuropsychologic deficits and smaller brain size than subjects without PTSD and reported more childhood sexual abuse. Early childhood sexual abuse in women was shown to be a significant predictor of both BPD and PTSD (McLean and Gallop 2003). Others have reported neuropsychologic deficits in individuals with childhood abuse (Bremner et al 1995b). Future studies are needed to elucidate the specific role of early sexual abuse on brain size and development.

**Methodologic Considerations**

BPD subjects with the diagnosis of any current or lifetime psychotic disorder were rigorously excluded. Further exclusion criteria were a history of neurologic disorders, electroencephalograph abnormalities, or hyperintensive MRI signals. As a consequence, the spectrum and variability of psychotic symptoms and DSM-IV cluster A personality traits and the severity of brain abnormalities may have been reduced in our sample. Nevertheless, we found a significant right parietal cortex size reduction (Figure 2) and a relationship between parietal cortex asymmetry and psychotropic symptoms and schizoid personality traits (Figures 5–7).

Our BPD sample presented with a high DSM-IV Axis I comorbidity. Therefore, the findings of our study must be considered with caution. Concurrent Axis I disorders are found in the vast majority of individuals with BPD (Zanarini et al 1998), leading to the conclusion that any BPD sample being limited to subjects with the sole diagnosis of BPD cannot be considered representative (Skodol et al 2002). Our results do not give evidence for an influence of comorbid disorders on the size of the parietal cortex or the hippocampus of our BPD subjects. We cannot completely rule out that comorbid depressive disorder had an influence on our findings, however. Twenty-six of our BPD subjects met criteria for current or lifetime major depression, thus preventing a more rigorous test of subgroups (i.e., subjects with and without major depression).

Our findings may not be valid for men with BPD. Previous research has demonstrated considerable gender differences in the temporoparietal cortex asymmetry of normal individuals and individuals with schizophrenia or schizotypal personality disorder (Dickey et al 2002, 2003; Frederikse et al 2000; Niznikiewicz et al 2000; Shapleske et al 1999).

**Conclusions and Directions for Future Research**

Our results demonstrate reduced size and abnormal asymmetry of the parietal cortex in BPD. Reduced right parietal cortex size in BPD may reflect a neurodevelopmental deficit of the right hemisphere. It might be speculated that a reduced leftward asymmetry of temporoparietal cortices increases the likeliness for developing psychotic symptoms, whereas increased leftward parietal cortex asymmetry may protect individuals with BPD and PTSD from developing more pronounced and disabling psychotic symptoms.

Studies are currently being done in our department to determine whether specific posterior cortical areas, especially the precuneus and posterior cingulate cortex, have a reduced size in subjects with BPD. A current positron emission tomography study (Lange et al, unpublished data) has revealed reduced resting glucose metabolism in the precuneus and posterior cingulate cortex of a subgroup of 17 borderline subjects who are also included in this report.

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