Reduced amygdala and hippocampus size in trauma-exposed women with borderline personality disorder and without posttraumatic stress disorder

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Background: Individuals with posttraumatic stress disorder (PTSD) display reduced hippocampus size and impaired cognition. However, studies on individuals with borderline personality disorder (BPD) are rare, and studies on trauma-exposed patients with BPD but without PTSD are lacking. **Methods:** Twenty-four trauma-exposed women with BPD (10 with PTSD and 14 without) and 25 healthy controls underwent 3-dimensional structural magnetic resonance imaging of the amygdala and hippocampus and a clinical and neuropsychological investigation. **Results:** Compared with controls, patients with BPD and PTSD displayed significantly reduced amygdala (34%) and hippocampus (12%) size and significantly impaired cognition. Trauma-exposed patients with BPD but without PTSD also showed significantly reduced amygdala (22%) and hippocampus (11%) size but normal cognition. Amygdala and hippocampus size did not differ significantly between patients with and without PTSD. **Limitations:** The sample sizes of trauma-exposed groups are relatively small. A larger sample size may have revealed statistically significant differences in amygdala size between those with and without PTSD. **Conclusion:** Our results demonstrate strong amygdala size reduction in trauma-exposed patients with BPD with or without PTSD, much exceeding that reported for trauma-exposed individuals without BPD. Our data suggest that BPD is associated with small amygdala size. Furthermore, evidence is increasing that amygdala and hippocampus size reduction is not only due to PTSD, but also to traumatic exposure.

Introduction

Previous studies have suggested that posttraumatic stress disorder (PTSD) is associated with small hippocampus size[1,2] and reduced cognitive functions.[3–7] Meta-analysis[2] has revealed minor size reductions of the left amygdala in patients with PTSD and no amygdala size reduction in trauma-exposed patients without PTSD. Hippocampus size reductions covary with PTSD severity[2] and cognitive deficits,[3–5,7] suggesting that hippocampal damage may be a powerful predictor for the severity and chronic character of PTSD.

Studies concerning amygdala or hippocampus size reduction in patients with borderline personality disorder (BPD) are rare. So far, studies have used mixed samples, including patients with and without traumatic exposure and with and without PTSD.[8–13] A recent study[14] reported strong amygdala and hippocampus size reduction in individuals with BPD and PTSD. However, detailed comparisons of trauma-exposed patients with BPD with and without PTSD are lacking.

The present study examined amygdala and hippocampus volumes and cognitive functions in patients with BPD with and without PTSD and healthy controls. The goals of our study were to investigate whether trauma-exposed patients with BPD but without PTSD display amygdala and hippocampus size reduction and impaired cognition and to analyze how cognitive deficits are related to amygdala and hippocampus size in trauma-exposed individuals. We expected that trauma-exposed patients with BPD but without PTSD would show reduced amygdala and hippocampus size and impaired cognition. We supposed that cognitive deficits of trauma-exposed individuals would be related to small hippocampus size.

Methods

Participants

The sample comprised young female in-patients admitted to the Asklepios Psychiatric Hospital, Göttingen, Germany. The patients had BPD and had been exposed to severe childhood sexual and physical abuse. We assessed patients within 3 weeks

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J Psychiatry Neurosci 2009;34(5):383-8.

Submitted Aug. 19, 2008; Revised Nov. 8, 2008, Jan. 25, 2009; Accepted Jan. 26, 2009

after admission to the hospital when they were in a clinically stable phase.

We assessed all patients using a routine physical and neurologic examination, magnetic resonance imaging (MRI) and laboratory testing. We excluded patients with a history of neurologic disease, electroencephalographic abnormalities or pathological MRI signal (visual inspection of T_1, T_2 and fluid-attenuated inversion recovery sequences), being indicative for vascular or inflammatory diseases. We also excluded patients with psychotic disorders, bipolar disorder, current substance use disorders (Structured Clinical Interview for DSM-IV [SCID-I]),[15] or dissociative disorders (Structured Clinical Interview for DSM-IV Dissociative Disorders [SCID-D]).[16]

We compared trauma-exposed patients with healthy controls matched for sex, age, height and years of education. We recruited controls through an advertisement in a local newspaper and leaflets distributed in the Hospital of the University of Göttingen and in town. We included only individuals without a history of neurologic or psychiatric (as assessed by the SCID-I)[15] disorders.

We obtained written informed consent from all participents after providing them with a complete description of the study. The ethical committee of the medical faculty of the University of Göttingen approved the study design.

Clinical and neuropsychological assessment

We investigated trauma-exposed patients using the SCID-I and II[15] and the SCID-D interviews.[16] We used the Traumatic Antecedent Questionnaire (TAQ)[17] to assess neglect as well as physical and sexual abuse experiences during childhood and adolescence (ages 7–18 yr). We used the Impact of Events Scale — Revised (IES-R)[18] to assess PTSD symptoms. We evaluated a broad range of clinical symptoms using the Symptom Checklist-90-Revised (SCL-90-R).[19] We assessed depressive symptoms using the Beck Depression Inventory (BDI).[20] We assessed alcohol consumption and alcohol-related clinical symptoms using the Münchner Alkoholismus Test (MALT).[21]

We assessed intellectual, mnemonic and attentional function using the Wechsler Adult Intelligence Scale-Revised (WAIS-R),[22] the Wechsler Memory Scale-Revised (WMS-R),[23] the Trail Making Test (TMT)[24] and the subtest Attentional Shift of the Testbatterie zur Aufmerksamkeitsprüfung (TAP).[25]

All diagnoses were established by consensus among at least 2 psychiatrists (U.S. and the psychiatrist in charge) using the DSM-IV criteria and information obtained from the SCID interviews. The diagnostic procedures have been shown to be highly reliable.[12] Among the trauma-exposed participants with BPD, comorbid disorders included recurrent major depression, alcohol-related disorders and eating disorders. Patients were on a stable dose of medication for at least 3 weeks before the study; some were on antidepressants and some occasionally received sedatives.

MRI assessment

We obtained MRI scans with a 1.5 T Philips Gyroscan machine in all participants using previously described techniques.[12,14] We performed volumetric analysis on the basis of 3-dimentional (3-D) MRI scans. We transferred the images to a computer workstation and processed them using CURRY software, version 4.5 (Neurosoft Inc.). We reformatted the images into continuous 1 mm–thick slices.

We calculated intracranial volume and total brain volume with automated multistep algorithms and 3-D region growing methods limited by grey value thresholds. Simultaneous 3-D visualization of brain structures and manual tracing allowed a precise identification and delineation of regions of interest (ROIs). We separately disarticulated the amygdala and hippocampus from surrounding tissue on coronal slices by means of manual tracing according to a standardized protocol.[26] We separated the amygdala and hippocampus by 3-D visualization of the alveus and the inferior horn of the lateral ventricle. A single rater (C.L.), blind to the diagnosis, did the assessment. To define intrarater reliability, the analyst reassessed 1 hemisphere of 10 randomly chosen patients. The intraclass correlation coefficients for this procedure were $r = 0.94$ for the amygdala and $r = 0.95$ for the hippocampus. Inter-rater reliabilities, including that of this rater, have been published previously (hippocampus, $r = 0.96$; amygdale, $r = 0.96$).[12,27]

Statistical analysis

We applied analyses of variance (ANOVA) and post-hoc tests to compare differences between groups on demographic, clinical and cognitive variables and on intracranial volume and brain:skull ratio. We corrected the ANOVA testing subscales of neuropsychological and clinical instruments for multiple testing (Bonferroni correction: α levels, TAQ and IES-R = 0.016, SCL-R and WAIS-R = 0.025, WMS-R = 0.0125). We assessed subgroups of trauma-exposed patients using the Mann–Whitney U test. We compared amygdala and hippocampus volumes of trauma-exposed groups and the control group using analyses of covariance (ANCOVA) with group as the between-subject factor and hemisphere as the within-subject factor and with adjustment for total brain volume. We also computed the ANCOVA with IQ as a further covariate. We compared total brain volumes of all groups using ANCOVA with adjustment for intracranial volume. We used multiple stepwise regression analyses with a significance level for selecting variables of $\alpha = 0.05$ to examine the relations between amygdala and hippocampus volumes and neuropsychological variables. We used left- and right-sided amygdala and hippocampus volumes and total brain volume as explanatory variables and neuropsychological test results as dependent variables. All analyses were 2-tailed; we set the level of statistical significance at $p < 0.05$. We performed statistical analyses using the Statistical Package for the Social Sciences (SPSS for Windows, version 14.0).

Results

Participants

Our sample comprised 24 young female in-patients with BPD who had been exposed to severe childhood sexual and

physical abuse and 25 healthy matched controls. Participant characteristics are provided in Table 1.

Trauma-exposed subgroups

Ten trauma-exposed patients met criteria for chronic PTSD according to the DSM-IV. These patients were also included in a previous report.[14] The remaining 14 trauma-exposed patients confirmed criterion A, but did not meet criteria B–D of the DSM-IV. Among these patients, few clinical symptoms relating to criteria B–D were also present (Table 1, IES-R). However, they were unable to determine whether these symptoms developed as a result of a specific traumatic exposure or whether they were also present before the trauma.

All trauma-exposed patients met criteria for BPD (SCID-II); all had received the diagnosis of BPD based on clinical judgment at the time of the assessment and at an earlier time. Nineteen patients met criteria for recurrent major depression; of these, 7 had PTSD. Seven patients had alcohol-related disorders (lifetime abuse, $n = 3$; lifetime dependence, $n = 4$); of these, 3 had PTSD. Ten patients had eating disorders (lifetime anorexia, $n = 3$; lifetime bulimia, $n = 3$; current bulimia, $n = 4$); of these, 4 had PTSD. Seven patients were on antidepressant medications; 4 of them had PTSD). Five patients occasionally received sedatives (diazepam or lorazepam); 3 of them had PTSD.

The trauma-exposed groups did not differ with respect to age, height, education, disorder duration, depression severity, global psychological distress (SCL-90-R) and alcohol consumption (Table 1). However, patients with PTSD reported significantly more sexual abuse (TAQ) and stronger intrusions (IES-R) than those without PTSD. The amount of

Table 1: Clinical and neuropsychological characteristics of trauma-exposed patients with borderline personality disorder with or without posttraumatic stress disorder and healthy controls

	Group; mean (SD)*				
Variable	BPD with PTSD ($n = 10$)	BPD without PTSD ($n = 14$)	Controls ($n = 25$)	Statistical test	p value
Age, [range] yr	32 (7) [21–43]	32 (5) [26–39]	33 (7) [21–45]	$F_{2,46} = 0.2$	0.85
Education, y	14 (2)	16 (3)	14 (2)	$F_{2,46} = 2.4$	0.10
Handedness, left:right	0:10	2:12	0:25	Fisher exact test	0.12
Duration of disorder, yr	16 (7)	14 (9)		$t_{20} = 0.4$	0.67
TAQ					
Neglect	5.7 (1.6)¶	5.1 (1.4)¶	2.9 (0.9)	$F_{2,43} = 24.7$	< 0.001
Physical abuse	5.4 (1.6)¶	4.7 (2.1)¶	2.3 (1.1)	$F_{2,41} = 16.9$	< 0.001
Sexual abuse	6.0 (2.0)¶**	4.1 (2.3)¶	2.0 (0.1)	$F_{2,42} = 24.0$	< 0.001
IES-R					
Intrusions	3.8 (0.8)	2.4 (0.9)		$t_{19} = 3.6$	0.002
Avoidance	3.8 (1.5)	3.5 (0.8)		$t_{19} = 0.5$	0.62
Hyperarousal	3.9 (0.9)	2.9 (1.1)		$t_{19} = 2.2$	0.040
SCL-90-R					
Global severity index	1.8 (0.6)¶	1.6 (0.5)¶	0.3 (0.3)	$F_{2,46} = 59.7$	< 0.001
Positive symptom distress index	2.4 (0.6)¶	2.4 (0.5)¶	1.3 (0.4)	$F_{2,46} = 35.8$	< 0.001
Beck Depression Inventory[20]	29 (11)	27 (8)		$t_{22} = 0.3$	0.75
Münchner Alkoholismus Test[21]†	6 (7)	6 (6)		$t_{22} = 0.3$	0.98
WAIS-R‡					
Verbal IQ	94 (11)**	105 (14)	111 (13)	$F_{2,46} = 6.7$	0.003
Performance IQ	94 (16)††	104 (17)	116 (16)	$F_{2,46} = 7.0$	0.002
WMS-R					
Verbal memory	106 (10)	110 (10)	112 (14)	$F_{2,46} = 1.0$	0.36
Visual memory	88 (14)¶**	109 (15)	118 (17)	$F_{2,46} = 12.2$	< 0.001
Delayed recall	103 (15)‡‡	116 (16)	119 (14)	$F_{2,46} = 4.1$	0.023
Attention/concentration	80 (11) ¶§§	100 (18)	102 (12)	$F_{2,46} = 9.9$	< 0.001
Trail Making Test[24]					
Part A, s	35 (10)¶**	24 (12)	21 (5)	$F_{2,46} = 9.2$	< 0.001
Part B, s	65 (36)	49 (17)	45 (13)	$F_{2,46} = 3.1$	0.06
TAP, attentional shift, ms§	1304 (782)**††	848 (217)	779 (125)	$F_{2,46} = 7.2$	0.002

BPD = borderline personality disorder; IES-R = Impact of Events Scale — Revised;[18] IQ = intelligence quotient; PTSD = posttraumatic stress disorder; SCL-90-R = Symptom Checklist-90-Revised;[19] SD = standard deviation; TAP = Testbatterie zur Aufmerksamkeitsprüfung;[25] TAQ = Traumatic Antecedent Questionnaire;[17] WAIS-R = Wechsler Adult Intelligence Scale — Revised;[22] WMS-R = Wechsler Memory Scale — Revised.[23]

*Unless otherwise indicated.

†The Münchner Alkoholismus Test is a clinician-administered rating scale: 0–5 = normal alcohol consumption, 6–10 = likely alcohol abuse, 11–52 = alcohol abuse or dependence.

‡IQ estimates on the Wechsler Adult Intelligence Scale — Revised were derived from Information, Similarities, Picture Completion and Block Design scores.

§The Testbatterie zur Aufmerksamkeitsprüfung involves 1-figure numbers and letters presented simultaneously on the left and right of a computer screen with the position of these stimuli varying across trials. Participants have to press a left- or right-hand button corresponding to the position of the target stimulus (number or letter), which alternates between trials.

¶Significantly different from controls ($p < 0.001$; post-hoc test).

**Significantly different from trauma-exposed patients with BPD but without PTSD ($p < 0.05$; post-hoc test).

††Significantly different from controls ($p < 0.01$; post-hoc test).

‡‡Significantly different from controls ($p < 0.05$; post-hoc test).

§§Significantly different from trauma-exposed patients with BPD but without PTSD ($p < 0.01$; post-hoc test).

reported neglect and physical abuse (TAQ) did not differ between the 2 groups. Trauma-exposed patients taking antidepressants ($n = 7$) did not differ from those not taking antidepressants ($n = 17$) with respect to brain measures or any clinical or neuropsychological variables (Mann–Whitney U tests, $p > 0.10$). The same was true for patients who occasionally took sedatives ($n = 5$) and those who did not ($n = 19$) ($p > 0.12$).

Brain measures

Patients with PTSD had significantly smaller total brain volumes and increased global atrophy (brain:skull ratio) when compared with controls (Table 2). An overall 3×2 (group × hemisphere) ANCOVA comparing the amygdala volumes of patients with and without PTSD and controls and adjusting for total brain volume yielded a significant effect of group, indicating smaller amygdala volumes of trauma-exposed patients (Table 2). The post-hoc 2×2 (group × hemisphere) ANCOVA for each trauma-exposed group and the control group confirmed these results (PTSD v. controls: $F_{1,32} = 46.2$, $p < 0.001$; non–PTSD v. controls: $F_{1,36} = 15.2$, $p < 0.001$). Patients with and without PTSD did not differ significantly ($F_{1,21} = 1.3$, $p = 0.28$).

The overall 3×2 (group × hemisphere) ANCOVA comparing the hippocampus volumes of patients with and without PTSD and controls and adjusting for total brain volume also yielded a significant effect of group, indicating smaller hippocampus volumes of trauma-exposed patients (Table 2). The post-hoc 2×2 (group × hemisphere) ANCOVA for each trauma-exposed group and the control group confirmed these results (PTSD v. controls: $F_{1,32} = 9.3$, $p = 0.005$; non-PTSD v. controls: $F_{1,36} = 9.0$, $p = 0.005$). Patients with and without PTSD did not differ significantly ($F_{1,21} = 0.0$, $p = 0.97$).

We repeated ANCOVA testing amygdala and hippocampus volumes while introducing IQ (WAIS-R) as a further covariate. The results of all analyses remained the same, except for the comparison of hippocampus volumes across the group with PTSD and controls, which did not yield a significant effect of group ($F_{1,31} = 2.4$, $p = 0.14$). Results of our 1-way ANCOVA across these 2 groups were also not significant (left hippocampus: $F_{1,31} = 0.6$, $p = 0.44$; right hippocampus: $F_{1,31} = 3.3$, $p = 0.08$).

Neuropsychological results

Compared with controls, patients with PTSD were significantly impaired on all intellectual and mnemonic measures

Table 2: Morphometric measures of trauma-exposed patients with borderline personality disorder with or without posttraumatic stress disorder and healthy controls

Variable	Group; mean (SD)*			Statistical test	*p* value
	BPD with PTSD ($n = 10$)	BPD without PTSD ($n = 14$)	Controls ($n = 25$)		
Height, cm	168 (5)	166 (6)	169 (6)	$F_{2,46} = 1.1$	0.35
Intracranial volume, mL	1326 (115)	1419 (76)	1384 (88)	$F_{2,46} = 2.9$	0.07
Total brain volume, mL†	1027 (94)¶	1121 (69)	1106 (81)	$F_{2,45} = 6.3$	0.004
Brain:skull ratio, %	77 (2)**	79 (2)	80 (2)	$F_{2,46} = 7.6$	0.001
Amygdala‡					
Left, mL	0.72 (0.19)††	0.90 (0.27)‡‡	1.12 (0.15)	$F_{2,45} = 13.1$	< 0.001
ANCOVA adjusted means (% difference in regional volume relative to controls)	0.74 (–33.6)	0.89 (–22.2)	1.11		
Right, mL	0.77 (0.14)††	0.89 (0.24)††	1.15 (0.16)	$F_{2,45} = 17.9$	< 0.001
ANCOVA adjusted means (% difference in regional volume relative to controls)	0.76 (–34.2)	0.89 (–22.3)	1.15		
Hippocampus§					
Left, mL	2.49 (0.41)	2.68 (0.37)§§	2.95 (0.43)	$F_{2,45} = 4.0$	0.025
ANCOVA adjusted means (% difference in regional volume relative to controls)	2.65 (–9.5)	2.61 (–10.7)	2.93		
Right, mL	2.54 (0.46)‡‡	2.84 (0.43)‡‡	3.16 (0.35)	$F_{2,45} = 7.5$	0.002
ANCOVA adjusted means (% difference in regional volume relative to controls)	2.68 (–14.5)	2.78 (–11.1)	3.13		

ANCOVA = analysis of covariance; BPD = borderline personality disorder; PTSD = posttraumatic stress disorder; SD = standard deviation.
*Unless otherwise indicated.
†One-way ANCOVA controlling for intracranial volume.
‡The overall 3×2 (group × hemisphere) ANCOVA using total brain volume as covariate had the following F values: group, $F_{2,45} = 18.0$, $p < 0.001$; hemisphere, $F_{2,45} = 3.0$, $p = 0.09$; group × hemisphere, $F_{2,45} = 0.3$, $p = 0.754$.
§The overall 3×2 (group × hemisphere) ANCOVA using total brain volume as covariate had the following F values: group, $F_{2,45} = 7.4$, $p = 0.002$; hemisphere, $F_{2,45} = 0.5$, $p = 0.50$; group × hemisphere, $F_{2,45} = 0.7$, $p = 0.497$.
¶Significantly different from controls ($p < 0.001$; 1-way ANCOVA controlling for intracranial volume).
**Significantly different from controls ($p < 0.001$; post-hoc test).
††Significantly different from controls ($p < 0.001$; 1-way ANCOVA controlling for total brain volume).
‡‡Significantly different from controls ($p < 0.01$; 1-way ANCOVA controlling for total brain volume).
§§Significantly different from controls ($p < 0.05$; 1-way ANCOVA controlling for total brain volume).

applied except verbal memory and delayed recall (WMS-R) and TMT part B (Table 1). In contrast, trauma-exposed patients without PTSD were unimpaired. Accordingly, patients with PTSD had lower test scores than those without PTSD, reaching statistical significance for most mnemonic and attentional measures applied (Table 1).

We entered the left- and right-sided amygdala and hippocampus volumes and total brain volumes of trauma-exposed patients into multiple regression analyses. Performance IQ ($R^2 = 0.261$, $p = 0.011$), attention/concentration (WMS-R; $R^2 = 0.319$, $p = 0.004$) and part B of the TMT ($R^2 = 0.217$, $p = 0.022$) were significantly predicted by right hippocampus volume, indicating better test performance in patients with larger hippocampus volumes. All other predictors did not reach the inclusion criterion of $\alpha = 0.05$.

Discussion

We found 12% hippocampus size reduction in patients with BPD and PTSD and an 11% reduction in those without PTSD. Our results are well matched to those of previous studies,[8–12] reporting about 10%–20% hippocampus size reduction in patients with BPD compared with healthy controls. Our results further indicate that hippocampus size of trauma-exposed patients with BPD but without PTSD was significantly reduced compared with healthy controls. So far, one previous study[8] applied a similar test design to ours and reached similar results.

Results concerning amygdala size reduction in patients with BPD are equivocal. We found an enormous amygdala size reduction in patients with BPD and PTSD (34%) and, to a somewhat lesser degree, in those without PTSD (22%). To our knowledge, 5 previous studies investigated amygdala size in patients with BPD, with 2 studies reporting only minor or no amygdala size reduction[8,28] and 3 studies[9–11] reporting strong amygdala size reduction (about 15%–25%). We suppose that differing sample characteristics are responsible for the heterogeneous results. All studies so far used mixed samples, including patients with and without traumatic exposure and with and without PTSD.

Studies on amygdala size in patients with PTSD but without BPD are also rare. A recent meta-analysis[2] demonstrated minor amygdala size reduction in patients with PTSD and no amygdala size reduction in trauma-exposed patients without PTSD. Thus, from the presently available data, it may be speculated that BPD, irrespective of traumatic exposure or subsequent development of PTSD, has a negative impact on amygdala size. However, studies investigating patients with BPD but without trauma exposure are needed to firmly test this assumption.

It also seems likely that the traumatic stress itself exerted some adverse effects on the brains of our patients with BPD. Previous studies have already found significant relations between severity of traumatic exposure and severity of hippocampus size reduction.[4,6,8] Accordingly, recent meta-analyses on PTSD[1,2] found that hippocampus size differences across studies were smaller when comparing patients with PTSD and trauma-exposed controls and larger when comparing patients with PTSD and healthy controls.

So far, cognitive deficits have been repeatedly reported for patients with PTSD.[3–7] Studies comparing trauma-exposed patients with and without PTSD yielded better cognitive performance of patients without PTSD; however, these differences mostly failed to reach statistical significance.[4,6,7,29] The same is true for the present study. Across participants, worse cognitive performance was significantly related to smaller right hippocampus size. Previous studies have already demonstrated relations between hippocampus size reduction and cognitive deficits among individuals who had been exposed to traumatic stress,[3–5,7,12] suggesting that hippocampal damage may be a powerful predictor of cognitive deficits in patients having been exposed to traumatic stress.

Total brain volumes of our trauma-exposed patients with PTSD were decreased, and the amount of global atrophy (brain:skull ratio) increased. Individuals with BPD or PTSD have been reported to have an increased prevalence of subtle neurologic impairment and brain insults.[30,31] Head trauma may be associated with physical abuse and might be responsible for the behavioural and brain abnormalities of patients with BPD and PTSD rather than the disease itself. However, ANCOVA controlling for total brain volume indicated significant differences in regional brain volumes between patients with PTSD and controls. Furthermore, we excluded patients with a history of neurologic disease. Nevertheless, future studies should make any effort to gather information on the nature of physical abuse that participants experienced.

Limitations

A limitation of our study is that sample sizes of trauma-exposed groups were relatively small. Larger sample sizes may have revealed statistically significant differences of amygdala size between patients with and without PTSD.

Our trauma-exposed patients had lower IQs than controls. Present evidence suggests that hippocampus size accounts for a modest proportion of the variance in human intelligence,[32] leaving open the possibility that the small hippocampus size of our patients with PTSD was related to preexisting low intelligence rather than to PTSD or BPD. This assumption is supported by the finding of low precombat intelligence as a risk factor for PTSD developing in combat veterans.[33] Performance IQ of our trauma-exposed patients was significantly predicted by right hippocampus volumes, and our ANCOVA comparing hippocampus volumes across our patients with PTSD and controls and adjusting for total brain volume and IQ failed to reveal a significant effect of group. Nevertheless, our study design does not allow deciding whether hippocampus size reduction in our trauma-exposed patients was the cause or result of their lower IQs.

Acknowledgements: We express our appreciation to the participants of this study. We further wish to thank E. Kohlhase for assistance in participants' assessments. Research was supported by grant IR 15/8 from the Deutsche Forschungsgemeinschaft.

Competing interests: None declared.

Contributors: Drs. Weniger, Sachsse and Irle designed the study. Drs. Weniger and Lange acquired the data, which Drs. Weniger, Lange and Irle analyzed. Dr. Irle wrote the article, and, together with all authors, revised it. All authors gave final approval for the article to be published.

References

1. Smith ME. Bilateral hippocampal volume reduction in adults with post-traumatic stress disorder: a meta-analysis of structural MRI studies. *Hippocampus* 2005;15:798-807.
2. Karl A, Schaefer M, Malta LS, et al. A meta-analysis of structural brain abnormalities in PTSD. *Neurosci Biobehav Rev* 2006;30:1004-31.
3. Bremner JD, Randall PR, Scott TM, et al. MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder. *Am J Psychiatry* 1995;152:973-81.
4. Gurvits TV, Shenton ME, Hokama H, et al. Magnetic resonance imaging study of hippocampal volume in chronic, combat-related posttraumatic stress disorder. *Biol Psychiatry* 1996;40:1091-9.
5. Bremner JD, Randall PR, Vermetten E, et al. Magnetic resonance imaging-based measurement of hippocampal volume in posttraumatic stress disorder related to childhood physical and sexual abuse — a preliminary report. *Biol Psychiatry* 1997;41:23-32.
6. Winter H, Irle E. Hippocampal volume in adult burn patients with and without posttraumatic stress disorder. *Am J Psychiatry* 2004; 161:2194-200.
7. Vythilingam M, Luckenbaugh DA, Lam T, et al. Smaller head of the hippocampus in Gulf War-related posttraumatic stress disorder. *Psychiatry Res* 2005;139:89-99.
8. Driessen M, Herrmann J, Stahl K, et al. Magnetic resonance imaging volumes of the hippocampus and the amygdala in women with borderline personality disorder and early traumatization. *Arch Gen Psychiatry* 2000;57:1115-22.
9. Tebartz van Elst L, Hesslinger B, Thiel T, et al. Frontolimbic brain abnormalities in patients with borderline personality disorder: a volumetric magnetic resonance imaging study. *Biol Psychiatry* 2003;54:163-71.
10. Schmahl CG, Vermetten E, Elzinga BM, et al. Magnetic resonance imaging of hippocampal and amygdala volume in women with childhood abuse and borderline personality disorder. *Psychiatry Res* 2003;122:193-8.
11. Brambilla P, Soloff PH, Sala M, et al. Anatomical MRI study of borderline personality disorder patients. *Psychiatry Res* 2004;131:125-33.
12. Irle E, Lange C, Sachsse U. Reduced size and abnormal asymmetry of parietal cortex in women with borderline personality disorder. *Biol Psychiatry* 2005;57:173-82.
13. Zetzsche T, Preuss UW, Frodl T, et al. Hippocampal volume reduction and history of aggressive behaviour in patients with borderline personality disorder. *Psychiatry Res* 2007;154:157-70.
14. Weniger G, Lange C, Sachsse U, et al. Amygdala and hippocampal volumes and cognition in adult survivors of childhood abuse with dissociative disorders. *Acta Psychiatr Scand* 2008;118:281-90.
15. Wittchen HU, Zaudig M., Frydrich T. *Strukturiertes Klinisches Interview für DSM-IV. Achse I und II*. Göttingen (Germany): Hogrefe; 1997.
16. Gast U, Oswald T, Zündorf F, et al. *Strukturiertes Klinisches Interview für DSM-IV. Dissoziative Störungen*. Göttingen (Germany): Hogrefe; 2000.
17. Herman JL, Perry JC, Van der Kolk BA. Childhood trauma in borderline personality disorder. *Am J Psychiatry* 1989;146:490-5.
18. Maercker A, Schützwohl M. Erfassung von psychischen Belastungsfolgen: die impact of events skala — revidierte version (IES-R). *Diagnostica* 1998;44:130-41.
19. Derogatis LR. *SCL-90-R: Administration, scoring and procedures manual-I for the revised version*. Baltimore (MD): John Hopkins University School of Medicine; 1977.
20. Hautzinger M, Bailer M, Worall H, et al. *Beck Depressions Inventar (BDI)*. Bern (Switzerland): Huber; 1995.
21. Feuerlein W, Küfner H, Ringer C, et al. *Münchner Alkoholismus Test (MALT)*. Weinheim (Germany): Beltz; 1979.
22. Tewes U. *HAWIE-R. Hamburg-Wechsler-Intelligenztest für Erwachsene. Revision 1991*. Bern (Switzerland): Huber; 1991.
23. Wechsler D. *Wechsler Memory Scale-Revised (WMS-R)*. San Antonio (TX): Psychological Corporation; 1987.
24. Reitan RM. *Trail Making Test. Manual for Administration and Scoring*. South Tucson (AZ): Reitan Neuropsychological Laboratory; 1992.
25. Zimmermann P, Fimm B. *Testbatterie zur Aufmerksamkeitsprüfung (TAP), version 1.02*. Freiburg (Germany): Psytest; 1993.
26. Pruessner JC, Li LM, Serles W, et al. Volumetry of hippocampus and amygdala with high-resolution MRI and three-dimensional analysis software: minimizing the discrepancies between laboratories. *Cereb Cortex* 2000;10:433-42.
27. Weniger G, Lange C, Irle E. Abnormal size of the amygdala predicts impaired emotional memory in major depressive disorder. *J Affect Disord* 2006;94:219-29.
28. Zetzsche T, Frodl T, Preuss UW, et al. Amygdala volume and depressive symptoms in patients with borderline personality disorder. *Biol Psychiatry* 2006;60:302-10.
29. Shin LM, Shin PS, Heckers S, et al. Hippocampal function in posttraumatic stress disorder. *Hippocampus* 2004;14:292-300.
30. Van Reekum R, Links PS, Finlayson MA, et al. Repeat neurobehavioral study of borderline personality disorder. *J Psychiatry Neurosci* 1996;21:13-20.
31. Gurvits TV, Gilbertson MW, Lasko NB, et al. Neurological soft signs in chronic posttraumatic stress disorder. *Arch Gen Psychiatry* 2000;57:181-6.
32. Andreasen NC, Flaum M, Swayze V II, et al. Intelligence and brain structure in normal individuals. *Am J Psychiatry* 1993;150:130-4.
33. Macklin ML, Metzger LJ, Litz BT, et al. Lower precombat intelligence is a risk factor for posttraumatic stress disorder. *J Consult Clin Psychol* 1998;66:323-6.