

**Pain perception, learning and memory and treatment development in patients with trauma related disorders;**

**Martin Bohus**

**Research Summary**

The overarching aim is to improve the current treatments for patients with trauma related disorders (esp. Posttraumatic Stress Disorder (PTSD), Borderline Personality Disorder (BPD)). Our research team is investigating the gen-environment interaction in the development, the central neuropsychological mechanisms of maintenance and the interaction of psychopharmacology and psychotherapy in its treatment.

**Curriculum Vitae**

- Degrees: 1988 MD University of Freiburg  
2001 Habilitation University of Mannheim
- 1979-1985: Medical School, University of Freiburg
- 1985-1988: Research scientist at the Department of Immunology, University of Freiburg
- 1988-1992: Clinical training (Department of Psychiatry and Neurology of the University of Freiburg)
- 1992: Speciality in Psychiatry and Psychotherapy
- 1992-1996: Director of interdisciplinary priority program: Vulnerability Marker for Major depression
- 2000: Speciality in Psychosomatic medicine
- 2000-2003: Leading scientist of the Freiburg/ Bale Center in the frame of the Borderline personality disorder research foundation
- since 2000: Director of interdisciplinary priority program: Neurobiological aspects of borderline personality disorder
- 2001: Habilitation for Psychiatry and Psychotherapy
- 2001: Full Professorship at the central institute of mental Health, University of Mannheim, Germany (ZI)
- since 2003: Chair in Psychosomatics and Psychotherapy, University of Heidelberg, Director, Dept. of Psychosomatics Psychotherapy, ZI
- since 2003: Associated professorship at the University of Arts, Karlsruhe

**Structure of the Group**

- Group Leader: Martin Bohus
- Senior Scientist: Christian Schmahl
- Postdoctoral fellows: Uli Ebner-Priemer, Nicolaus Kleindienst, Regina Steil
- Scientists: Sonia Kiko, Iris Klossika, Petra Ludaescher, Anna Mall, Jana Mauchnik, Matthias Limberger, Joachim Wiskemann,
- Technicians: Ingar Niedfeldt

Department of Psychosomatic Medicine and Psychotherapy  
Central Institute of Mental Health  
J5, 68161 Mannheim, Germany

+49-621 -1703 4001  
+49-621 - 1703 4005  
martin.bohus@zi-mannheim.de  
http://www.zi-mannheim.de



**Current Research**

**Pain perception assessed by Laser-Evoked Potentials and functional MRI in patients with Borderline Personality Disorder**

Background: Borderline Personality Disorder (BPD) is a frequent psychiatric disorder, and pain perception

was shown to be attenuated in BPD. Our findings from a study using laser-evoked pain potentials suggest that sensory-discriminative pain components seem to be unaffected in this patient population and affective-motivational pain components may be altered in BPD. Studies in healthy subjects have revealed a pain circuit consisting of thalamus, somatosensory cortex, insula, and anterior cingulate cortex (ACC). We used functional MRI and heat pain stimuli to localize alterations in pain processing in BPD.

Method: Patients with Borderline Personality Disorder according to DSM-IV and healthy controls are investigated using brief radiant heat pulses and 7 channel EEG recordings. In addition participants underwent functional MRI during heat pain stimulation. Two stimulus conditions were applied in a randomized fashion: First, a fixed temperature was used. Second, a temperature that was perceived equally painful by all participants was applied.

First results: BPD patients tended to have higher pain thresholds and pain ratings were reduced to 25 % of controls. In contrast, mean amplitudes of LEPs in the BPD group were not reduced compared to those of controls. The ability to spatially discriminate painful stimuli did not differ between both groups. In fMRI, all classical pain regions were activated by stimulation with heat pain in BPD patients as well as controls. Group comparison revealed less activation in Somatosensory Association Cortex (Area 7) in BPD compared to controls under fixed stimulus intensity. During stimulation with equal subjective pain intensities we found more deactivation in ACC (perigenual cingulate) in BPD compared to controls.

Conclusions: Results of our study are consistent with the idea that the anterior cingulate cortex plays a role in altered pain perception in patients with BPD.

**Neuroendocrinological dysregulations in female patients with Borderline Personality Disorder**

Background: Borderline personality disorder (BPD) is characterized by a long lasting, often chronic pattern of dysfunctions in emotional regulation, interpersonal relationships, self-image, and impulse control. The cardinal symptom is a state of aversive tension. Experiencing these symptoms several times a day might lead to a state of chronic stress. Several studies have investigated the physiological consequences of BPD symptoms on neuroendocrine systems.

Dysregulations of the hypothalamic-pituitary-adrenal (HPA) axis, however inconclusive, have been found.

that patients suffering from severe PTSD should benefit from hydrocortisone application during exposure based psychotherapy.

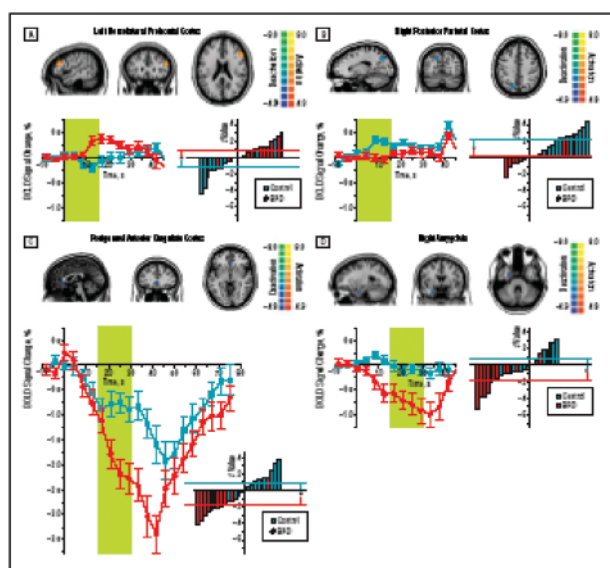


Figure 1. Group comparison of responses to a brief pain stimulus. Individually adjusted pain intensity produced equally perceived pain intensity. Brain activity during individually adjusted painful heat stimulation differed between patients with borderline personality disorder (BPD) and controls in the early-stimulation phase in the left dorsolateral prefrontal cortex (A) and the right posterior parahippocampal cortex (B). In the late phase of individually adjusted heat pain, a subgroup difference in brain activity was seen in the paracentral part of the anterior cingulate cortex (C) and in the right amygdala (D). Each upper row displays the group differences in regional BOLD, control (middle), and contrast (right) activation (P < 0.05), as well as correlation with a mean pain stimulus of 50 mmHg, whole-brain height corrected. In each lower row, line courses of the mean blood oxygen level–dependent (BOLD) signal change for the BPD and control groups are given on the left side; the respective time course is overlaid by the group background. On the right side, displays the region of interest–based reaction–effect analysis, with both time intervals scored by height in the 12 patients and 12 controls. Positive values indicate that the phase-specific predictor explained a net individual signal increase in the mean signal during the contrast coded phase, whereas negative values explain a net signal decrease. The reported BOLD signal changes are averaged with respect to the onset of the pain stimulus, without distinction of possibly multiple phases of the responses. Time courses are indicated by dashed red and blue lines for BPD and control, respectively. Error bars indicate SEM. \*P < 0.05 using a Student's t test.

Methods: In this study, we set out to examine BPD patients in a standardized psychosocial stress paradigm, which is known to lead to substantial increases in HPA axis parameters. Cortisol and catecholamines were measured. A total of 21 female BPD patients and 21 control subjects currently follows the study protocol. All subjects are medication free, have a regular menstrual cycle and are taking part in the study during their luteal phase. Comorbidity with psychiatric disorders like schizophrenia, current depression, current drug abuse, and current severe eating disorders is excluded.

Results: Preliminary results show that patients with a BPD diagnosis showed similar baseline levels in cortisol and catecholamines as in control subjects. However, in the patients group a substantial hyporeactivity in HPA axis function has been found in comparison to the controls as a reaction to the stressor. Furthermore, sympathetic activity as measured by the catecholamines was higher in patients prior to the stressor, but no differences have been observed after the stressor.

Conclusions: The results will be discussed with regard to the effects that borderline-typical psychopathology might have exerted on neuroendocrine function.

### Impact of Hydrocortisone and Psychotherapy on Traumatic Memory Processing in Patients with complex PTSD

Overall aim of this project: to investigate the role of glucocorticoids (GC) in traumatic memory retrieval. Animal and human researches indicate that elevation of central glucocorticoid levels facilitates memory consolidation while impairing delayed memory retrieval. Thus, we postulate

The project is composed of the following parts:

1. A clinical trial investigates both the efficacy of oral hydrocortisone and dialectical cognitive therapy (DCT) and the combination of both in the retrieval of traumatic memories and overall symptomatology in patients suffering from severe chronic PTSD.
2. In order to define neurobiological predictors for (early) treatment response, HPA - axis function will be assessed in all patients prior to treatment.
3. To study the central mechanisms of glucocorticoid-mediated traumatic memory processing, individualized trauma related scripts will be presented during fMRI and modified by either oral hydrocortisone or the glucocorticoid- antagonist mifepristone (misoprostol).

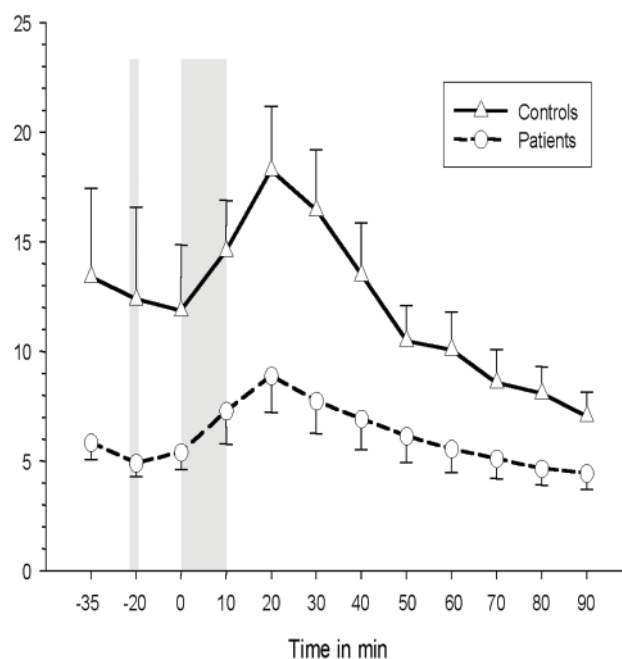


Figure 2. Mean salivary cortisol concentrations during the course of the stress induction study in 15 BPD patients and 17 healthy controls. The social stressor (TSST) is indicated by grey bars (the narrow grey bar indicates the introduction to the TSST). The data shown are the mean plus standard error of mean.