

University of Freiburg/Germany

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Summary

Based on a study on the efficacy of DBT-inpatient treatment, we could install the Borderline Research Unit. The aim of this unit is to study treatment as well as basic neurophysiological, neuropsychological and epidemiological features of Borderline Personality Disorder. Currently, the Unit is funded by the German Research Foundation (1996-2002) and (2000-2002), the Ministry of Science of Baden Württemberg (2000-2002), and the BPDRF. Within the last year, we could finish 11 projects, covering a broad field of research. From a clinical perspective, the most important findings are the data of the inpatient DBT-study, which show very good treatment response to 3 months inpatient treatment compared to a wait list. Detailed analysis however suggest that about 55% of the included patients show very strong effect-sizes in contrast to a group of 45 % of patients, who do not benefit from the treatment at all. Questions regarding variables (both neurobiological als well as psychological) predicting treatment response require to be answered. This will be the task of the next research period.

We are happy to report, that a proposal, based on our data, to install a multi-center-research cooperation between 4 German universities (Aachen, Lübeck, Kiel and Freiburg) under the leadership of the Freiburg Borderline Research Unit has been aproved by the German Research Foundation in Nov. 2001. The project is planned for 10 years. It focusses the interplay between psychotherapy and neurobiological patterns in BPD, depression and OCD. The first three years are funded with 2.5 Million Euros. Thus, we are proud to report, that the support of the BPDRF has been productive already.

With regard to the next period we are taking into account the advise of the advisory board and are focussing on neurophysiological and psychological subtype differentiation. In cooperation with Maria Karayiorgou and Svenn Torgersen, we are collecting DNA from a sample of about 300 patients with BPD and healthy controls. This project is reported seperately by the PI of this project, M. Karayiorgou.

1. Finished Projects

1.1. Evaluation of the Borderline Symptom List (BSL)

We have developed a self-report procedure to quantitatively assess specific complaints, respectively subjective impairments of female patients with BPD (Borderline Symptom List, BSL). The construction of the scale has since been published in German (Bohus et al., 2001). Within the last year we have proceeded the process of validation. The paper is submitted.

The analyses to construct the scale as well as to determine values of reliability and validity were carried out in six different samples.

- 1.) Analysis of the scale structure is based on a sample of 308 female subjects between the ages of 17 and 56 years (mean = 30 years) who fulfilled the DSM-IV criteria for BPD. Diagnosis was assessed by means of the BPD-segments of the IPDE . 76% of the subjects were inpatients, 24% were in outpatient treatment. 24.6% met 5 DSM-IV criteria, 35.3% met 6 criteria, 23.5% met 7 criteria, 11.8% met 8 criteria and 4.8% met 9 criteria.

- 2.) To test the influence of gender, we additionally administered the scale to 72 male subjects who fulfilled the DSM-IV criteria for BPD (mean age: 31 years; range from 18 to 58 years). 35% of the male BPD patients met 5 DSM-IV criteria, 38% met 6, 17% met 7, 8% met 8, and 2% met 9 criteria. Analyses of the 380 male and female BPD patients reveal that the correlations between gender and the individual scales of the BSL are all slight. There were also no indications of any age-dependence of the scales ($|r| < .07$). Correlations between level of education were also slight ($|r| .02 - -.16$).
- 3.) The questionnaire was administered to 204 healthy controls (HC: 119 females; mean age = 30 years; range from 19 to 45 years; 85 males; mean age: 31 years; range from 19 to 44 years). The healthy controls were recruited at random from the resident register of the City of Freiburg, Germany. Exclusion criteria were any lifetime axis-I diagnosis, current psychotherapy, psychopharmacotherapy or first-degree relatives with mental disorders.
- 4.) To test the specificity of the BSL, we administered the scale to 283 patients with different Axis-I diagnoses (Clinical based diagnoses according to the criteria of the DSM-IV). (Schizophrenia: $n = 51$, mean age: 35 years, range from 20 -65 years; Major Depression: $n = 86$, mean age = 46 years, range from 18-77 years; Anxiety Disorder: $n = 19$, mean age = 43 years, range from 20-63 years; Obsessive-Compulsive Disorder: $n = 29$, mean age: = 41 years, range from 23-60 years). The scores for each BSL scale were higher among the patients with borderline personality disorders. Furthermore, the BSL discriminates significantly between healthy controls and patients of the different Axis-I diagnostic groups, an exception being the subscale "dysphoria". On this particular scale the female borderline patients differ significantly only from healthy controls ($p < .001$) and patients with schizophrenia ($p < .001$). A comparison of patients with different Axis-I disorders among themselves yielded only a small number of significant differences. Thus depressive patients score significantly higher than schizophrenic patients on the subscales "self image" ($p = 0.28$) and "dysphoria" ($p < .001$).
- 5.) To determine test-retest reliability the BSL was administered twice after an interval of 7 days to 35 female subjects experiencing BPD. Test-retest reliability of the total scale after one week was $r = .80$. Values for the subscales ranged from $r = .72$ ("Intrusions") to $r = .85$ ("Self image"). The subscale "Hostility" was an exception with a value of $r = .50$. As expected these values are less than those for internal consistency since no temporally stable variables were to be assessed.
- 6.) To determine convergent, respectively divergent validity, the correlation between the BSL and established self- and external report procedures for recording individual syndromes and problem behaviors (e.g. depression, aggression, self-injury) were calculated on the basis of a sample of 21 BPD patients. Positive correlations resulted at first for self- (BDI) and external evaluation (HAMD) procedures for assessment of depression. Thus the BDI correlates with the individual subscales "self-destruction" ($r = .51$), "dysphoria" ($r = .56$) and isolation ($r = .71$), as well as with the total score of the BSL ($r = .53$). Furthermore positive correlations are observed between the BSL and a self-report procedure for assessment of dissociations (FDS); the German version of the DES, Berstein and Putnam. Positive correlations also result among others for the total score on the FDS and diverse BSL subscales. Only low to moderate correlations result between the BSL and procedures for assessment of anxiety (STAI) and aggression (STAXI). Calculations of the correlation between the BSL and the mental symptom load (SCL-90-R) yield particularly high correlations between the GSI (global severity index) score of the SCL-90-R and the total score of the BSL ($r = .78$). The subscale "self-destruction" correlates further with $r = .54$ to the number of self-injuries within the past four weeks.
- 7.) To measure the scale's sensitivity to change, the BSL was administered twice to 63 female borderline patients before and after a 3-month DBT-treatment. The BPD patients were treated over the course of 12 weeks as either in- or outpatients according to the disorder-specific concept of Dialectical Behavior Therapy a (DBT according to Marsha Linehan). With the exception of the

subscales "loneliness" and "hostility" the patients improved significantly on the total scale and the remaining 5 subscales.

One paper is published (Bohus et al., 2001), a second paper is submitted

1.2 Development and psychometric properties of the Dissociation – Tension Scale (DSS)

The Dissociation - Tension-Scale (DSS) is conducted as a self-rating instrument to assess present-time dissociative features. In addition, the level of current experienced aversive inner tension is assessed. The study validates the psychometric quality of the DSS. The sample included 195 female probands. Internal consistency is high (Cronbachs $\alpha = .94$). The same is true for split-half reliability according to Gutman ($r = .93$). DSS correlates highly with scales assessing life-time dissociative features or similar constructs but differs from global scales. The DSS discriminates well between different diagnostic groups and seems to be sensitive to assess changing symptomatology.

The DSS is a reliable and valid instrument to assess present-time dissociative experiences as well as aversive inner tension.

The paper is under review

1.3 Experience of aversive tension and dissociation in female patients with Borderline Personality Disorder – a controlled study

The aim of the study was to operationalize the experience, duration and intensity of aversive tension within patients with BPD under natural conditions. In addition we studied the relationship between aversive tension and the experience of dissociative features. Seventy-two female patients with BPD together with 55 healthy controls, completed a self-rating questionnaire covering the previous 24 h. Substantial and highly significant differences with regard to the duration and intensity of the subjectively perceived states of aversive tension were found. Amongst patients with BPD there was a strong correlation between duration and intensity of tension, and experience of dissociative features, both somatoform and psychological. The findings underline the clinical importance of states of aversive tension in BPD particularly with regard to stress-related induction of dissociative features.

The paper is published (Stiglmayr et al., 2001)

1.4 Aversive tension in patients with borderline-personality disorder: A computer-based controlled open field study

Typical dysfunctional behavioral patterns of individuals meeting criteria for borderline personality disorder (BPD), for example, self mutilation, are often intended to terminate intense states of tension that are subjectively described as extremely aversive. This study aims to operationalize the subjective appraisal of frequency, intensity and course of these states of aversive internal tension under conditions of daily life. A sample of 63 female subjects meeting criteria for BPD and 40 mentally healthy controls were each given a **hand-held PC**. For two consecutive days, participants were prompted at hourly intervals to record their present state of aversive tension and prompting events. The MONITOR software was used.

Hypothesis I postulated that BPD patients will report a generally higher level of internal aversive tension than will mentally healthy controls. The results demonstrate the expected direction: compared to healthy controls, patients reported a higher average level of tension ($t=13.97$, $df=101$, $p<0.001$). The average level of tension among patients was 4.45 ($SD=2.15$, $range=0-8.55$), while that reported by controls was 0.55 ($SD=.55$, $range=0-1.83$).

Hypothesis II postulated that aversive internal tension is triggered more frequently in BPD patients than in healthy controls. The respective percentage of newly triggered states of tension was calculated controlling for the number of total entries made. For 9.6% of the entries patients listed an increase of

tension (SD=7.8%, range=0%-30.8%), while controls listed an increase for only 3.6% (SD=4.8%, range=0%-17.7%). This difference is statistically significant ($t=4.76$, $df=98$, $p<0.001$).

Hypothesis III postulated that subjectively experienced aversive tension increases more rapidly in patients with BPD than in mentally healthy controls. The speed of the tension increase was assessed by means of an additional question automatically asked by the hand-held PC in the event of increased tension. A total of 48 patients experienced 121 episodes of tension increase, as opposed to 18 controls who experienced 29 such increases. Patients experienced these increases in tension as markedly more rapid and more sudden than did the controls ($t=3.94$, $df=64$, $p<0.001$). On a scale of 0 to 9 the mean among patients was 6.81 (SD=1.66, range=1.00-9.00; $N_{pat}=48$), while among controls it was 4.40 (SD=2.39, range=0.50-9.00; $N_{con}=18$).

Hypothesis IV postulated that aversive tension persists longer in patients with BPD than in mentally healthy controls. The average tension interval among patients covers 1.98 data entry timepoints (SD=1.06, range=1.00-5.00; $N_{pat}=48$), that of the controls 1.10 (SD=0.26, range=1.00-2.00; $N_{con}=18$). This difference is statistically significant ($t=5.30$, $df=64$, $p<0.001$).

Events preceding a state of tension

Patients list "being alone" as well as the experience of subjective failure significantly more often as the event preceding a state of tension ($p<0.05$), while controls list a subjectively experienced rejection as well as other events significantly more often ($p<0.05$). Patients listed rejection significantly less often than "failure" ($\chi^2=9.35$, $df=1$, $p<0.01$) or "being alone" ($\chi^2=17.93$, $df=1$, $p<0.001$) which did not differ from each other. Also following an alpha correction according to Bonferroni these events remain significant.

Events preceding a decrease in tension

In comparison to the controls, patients report the application of a skill significantly more often as the reason for a reduction of tension ($\chi^2=6.69$, $df=1$, $p<0.05$), controls significantly more often report no specific event ("nothing particular") ($\chi^2=7.93$, $df=1$, $p<0.001$).

The study confirms the importance of states of aversive tension as a subjective marker for affect dysregulation for patients meeting criteria for BPD. Computer-assisted assessment is a method of high validity and economy which can be used to study the interplay of events, appraisal, behavior and triggered emotions under daily life conditions.

The paper is under review

1.5 HPA-axis dysregulation in female patients with Borderline Personality Disorder

Hypocortisolism and supersuppression to dexamethasone are well established findings in chronic posttraumatic stress disorder (PTSD). Patients with borderline personality disorder (BPD) often report early traumatization and suffer from comorbid PTSD. We therefore hypothesized that patients with BPD show similar dysfunctions in the hypothalamic-pituitary-adrenal axis as patients with PTSD. We studied 23 female patients with BPD and 24 matched healthy controls. All patients were free of a current major depressive disorder, 11 patients suffered from comorbid PTSD. Saliva cortisol levels were determined during natural (non-laboratory) conditions under the control of portable minicomputers on 3 consecutive days every 2 h between awakening and 22.00 h. In addition, cortisol in response to awakening was determined in four 15 min-intervals on day 1 and 2. In the evening of day 2, 0.5 mg dexamethasone was given in order to assess cortisol suppression on day 3 (dexamethasone suppression test, DST). In contrast to our hypothesis, patients with BPD showed higher cortisol levels than the healthy controls as demonstrated by higher total cortisol in response to awakening and higher total daily cortisol. There were significantly more non-suppressors of cortisol in the DST in the patient group than in the control group. No differences were found between patients with and without concurrent PTSD.

The results suggest that female patients with BPD show hypercortisolism and non-suppression to dexamethasone under ambulatory conditions. These findings do not support the concept of BPD as a chronic PTSD.

The paper is in preparation

1.6 Startle Response in Female Patients with Borderline Personality Disorder: Examination of the Impact of Dissociative Experiences

We used a startle response paradigm to investigate sensitivity and reactivity to acoustic stressors as an indicator for dysregulation of emotional response of patients with BPD. We hypothesized that patients with BPD would reveal enhanced responses to startling tones and that this would be influenced by present state dissociative experiences. Twenty one unmedicated female patients with BPD and 21 healthy female controls listened to 15 startling tones (95-dB, 500-ms, 1000-Hz) while heart rate, skin conductance and orbicularis oculi electromyogram responses were measured. Present-state dissociative experiences and anxiety were assessed by self rating scales. Covariance analysis showed that the BPD group had a significantly higher startle response in the electromyogram as compared to controls. In this group, present-state dissociative experiences significantly influenced the startle response as well as the habituation of the startle response, i.e. only patients with low present-state dissociative experiences had enhanced startle responses whereas patients with high present-state dissociative experiences had responses similar to those of the healthy controls.

This study showed for the first time an influence of present-state dissociative experiences on physiological parameters. Our data suggest that present-state dissociative experiences may compensate an enhanced startle response. This finding may explain negative results of previous studies investigating the startle response during affective stimulation in patients with BPD and may have important research and clinical implications.

The paper is under review

1.7 Subtle Prefrontal Neuropathology in A Pilot Magnetic Resonance Spectroscopy Study in Patients with Borderline Personality Disorder

Previously published functional brain imaging studies using [¹⁸F]- deoxyglucose-PET provided evidence of frontal hypometabolism within patients with BPD. In this study we used absolute quantitative proton magnetic resonance spectroscopy (MRS) to find a possible neurochemical correlate of this functional disturbance. We studied 12 unmedicated female patients with BPD and 14 healthy matched controls. Short echo time (TE = 30ms) single voxel spectroscopy was obtained from the left dorsolateral prefrontal cortex and the left striatum. Absolute concentrations of the neurometabolites were calculated. We found a significant 19 % reduction of absolute N-acetyl aspartate concentrations in the dorsolateral prefrontal cortex in BPD (T = 2.554; p = 0.01) compared to control subjects. This is the first study demonstrating neurochemical frontal brain pathology in patients with BPD, supporting the hypothesis that a disturbed frontal neurotransmission may contribute to the pathogenesis of this disorder.

The paper is published (Tebartz van Elst et al., 2001)

1.8 Positron emission tomography in female patients with Borderline Personality Disorder

One functional brain imaging study of DeLaFuente et al using [¹⁸F]Deoxyglucose-PET previously reported frontal and prefrontal hypometabolism of patients meeting criteria for PBD. In order to replicate these findings we studied brain metabolism at baseline in 12 medication-free female patients with BPD without current substance abuse or depression and 12 healthy female controls by [¹⁸F]Deoxyglucose-PET and statistical parametric mapping.

We found significant frontal and prefrontal hypermetabolism in patients with BPD relative to controls as well as significant hypometabolism in the hippocampus and cuneus. This study demonstrated limbic and prefrontal dysfunction under resting conditions in patients with BPD by FDG-PET. Dysfunction in this network of brain regions, which has been implicated in the regulation of emotion, may underlie symptoms of BPD.

1.9 Subgroup differentiation of patients with borderline personality disorder by the interpersonal circumplex

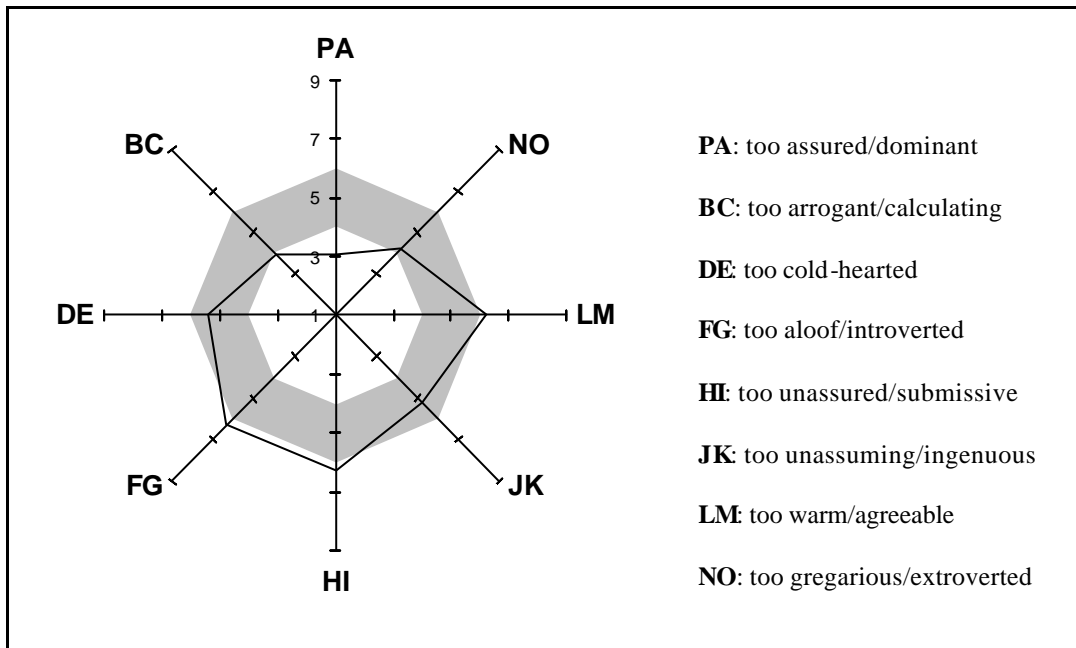
Although the categorical diagnosis of BPD is currently considered to be sufficiently reliable and valid (e.g. International Personality Disorder Examination, IPDE (Loranger et al. 1994), there is considerable heterogeneity of symptomatology across individuals with BPD. For example, some individuals with the BPD diagnosis are fairly high-functioning, while others may be unemployed for extended periods, are socially isolated or in and out of chaotic relationships, are chronically suicidal, and require multiple psychiatric hospitalizations (cited in Wagner, 1998). Currently, there is no consensus on valid means of subtyping individuals with BPD, despite the widely recognized heterogeneity of the disorder.

The heterogeneity of BPD may impede both basic and clinical research in BPD. For example, while there is an increasing interest in research aimed at understanding the underlying genetic or neurobiological mechanisms of BPD (e.g., NIH, 2001) these factors remain poorly understood. The heterogeneity of BPD suggests that there may be several different biological pathways to the disorder, which may in part explain the slow progress in these areas of research. Identification of valid subtypes of BPD may facilitate the study of the underlying genetic or neurobiological mechanisms of BPD. Similarly, valid subtypings may facilitate the development and evaluation of effective treatment interventions.

Disturbance of interpersonal behavior is one of the core features of BPD. The most established model today for the systematic categorization of interactive behavior is the circumplex model developed by Horowitz. However, for borderline personality disorder (as opposed to other personality disorders) no data have been published to date that would permit a valid categorization within this approach. It could be the case that subtypes of interpersonal problems exist for BPD (subtypes that could be located in various octants of the circumplex), which make a unitary categorization not possible. The current study is therefore an examination of subtypes of BPD using the circumplex model. The specific hypotheses were the following: 1) Individuals with BPD will show different interpersonal problems using the circumplex model (as measure by the Inventory of Interpersonal Problems (IIP; citation), described below), compared to a non-clinical sample; 2) Subgroups of individuals with BPD will be identifiable using the IIP; 3) Temporal stability will exist in subgroups of BPD, evidenced by consistency in profiles over a 4-month period. A total of 95 female patients were recruited consecutively for the study, i.e. without any preliminary selection. The average age of the patients was 27.1 years (max. 45; min. 17). They fulfilled an average of 6.7 of the 9 possible DSM-IV criteria (9 = 11; 8 = 14 ; 7 = 26; 6 = 28; 5 = 16;) and scored an average of 9.3 of 10 possible points on the DIB-R (10 = 51; 9 = 23; 8 = 16; 7 = 3; 6 = 2).

According to the first hypothesis, the average total IIP profile for all patients within the sample differed from the mean Stanine scores (between 4 to 6) of a healthy normal population on 5 scales (see fig. 1) .

Figure 1

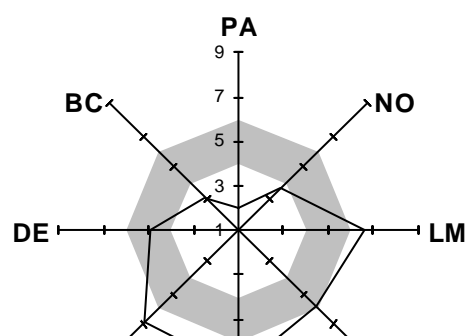
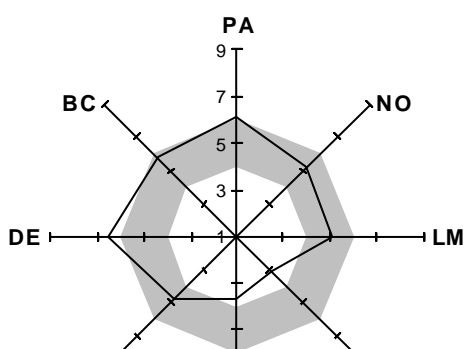


According to the second hypothesis, distinguishable subgroups could be found in the population studied. The hierarchical cluster analysis yields two clusters of different sizes (see Fig. 2), which can be described as follows and are distinguishable from one another:

Cluster 1 contains the average of the profiles for 26 patients and deviates on the Scales DE (mean = 6.5), JK (mean = 3.1) and HI (mean = 3.6) from the normal range (between 4 to 6). With regard to content this means that patients in this cluster are more likely to describe themselves as aloof and cold, finding it difficult to feel close to anyone or to show affection (higher score on DE), at the same time portraying themselves as not being complaisant enough or not being submissive enough as well as too concerned with keeping a limit to others (low scores on JK and HI). We refer to this subgroup as the *autonomous type*. **Cluster 2** (n = 69) deviates from the normal range on a total of six scales and is characterized above all by the most extreme scores on the scales PA (mean = 2.0), BC (mean = 3.1) and HI (mean = 7.3). This means that patients in this group describe themselves as being not autocratic and dominant enough and as having too little influence on and control over others (lower score on PA). They find it difficult to inform others of their needs and portray themselves as having too little self-confidence and being too submissive (higher score on HI), as well as too strongly avoiding competition and conflict (lower score on BC). Furthermore the Stanine means for this group of patients on the scales LM, FG and NO (indicate too much friendliness, complaisance and a subjective feeling of obtrusiveness above the normal range). They rate their interactive behavior in comparison to that of the autonomous types as being more deviant from the norm, and thus as more pathological on many more scales (ratio 6:3). We refer to this subgroup as the *dependent type*. A statistical comparison of the means reveals that the respective scale scores for both clusters differ significantly in all 8 octants.

Figure 2

autonomous Type (Cluster 1, n = 26) *Dependent Type* (Cluster 2, n = 69)



PA: too assured/dominant; **BC** too arrogant/calculating; **DE:** too cold-hearted; **FG:** too aloof/introverted; **HI:** too unassured/submissive; **JK:** too unassuming/ingenuous; **LM:** too warm/agreeable; **NO:** too gregarious/extroverted

The categorization of both subgroups as an *autonomous* or *dependent* type is supported by the comparison of both with regard to their mean number of hospital stays, attempts at suicide, and comorbidity. With regard to all three variables the dependent type (Cluster 2) exhibits the respectively higher mean (in view of the expected small to average effect sizes). This corresponds to the expectation that the patients in this subgroup not only see themselves as depending too much upon others but generally actually demand, respectively need more outside support.

With regard to the diagnosed rates of comorbidity, the variable *substance dependency* represents a trend towards a relationship pointing towards an increased number of comorbid disorders in the dependent type. At the same time, this exception confirms the clinical observation that patients with drug problems are frequently more anxious about their independence and autonomy.

The self-estimated profiles of interpersonal problems typical for both subgroups remained stable over a period of four months with regard to the strength of their mean Stanine scores, i.e. the average dimensional extent within the circumplex model was not reduced. This result points to the assumption that a longer observation period is required to make any statements on the development, respectively the improvement in interpersonal problems in personality disorders.

Paper is submitted

1.10. Laser-evoked potentials in patients with borderline personality disorder

Approximately 60% of females experiencing borderline personality disorder (BPD) and self injurious behaviour report attenuated pain perception or analgesia during self-mutilation. The aim of this study was to use laser evoked brain potentials (LEPs) to gain insight into the factors that lead to this hypoalgesic state. For this purpose, 10 female patients with BPD (according to DSM-IV) and 14 healthy female control subjects were investigated using brief radiant heat pulses generated by a Thulium laser and a 7-channel EEG recording. Heat pulses were applied in a spatial discrimination task and during a mental arithmetic task. BPD patients tended to have higher heat pain thresholds and pain ratings were reduced to 25% of controls. There was no difference in task performance between patients and controls. Latencies and amplitudes of the vertex potential of LEPs did not differ between patients and controls. Likewise, there was no difference in P3 results. The vertex potential and the P3 amplitudes, however, were significantly reduced during distraction by mental arithmetic in both groups. In addition, P3 amplitudes reflected task difficulty. This study confirms previous findings of

attenuated pain perception in BPD patients. Normal LEPs and normal discrimination task performance indicate that this attenuation is not related to the sensory-discriminative component of pain. Normal P3 potentials suggests that attention deficits also do not play a role. These findings suggest that the most likely cause of hypoalgesia in BPD is an alteration of the affective-motivational or cognitive-evaluative pain components.

The paper is under review

1.11 Effectiveness of Inpatient Dialectical Behavioral Therapy for Borderline Personality Disorder: a Controlled Trial

Dialectical Behavioral Therapy (DBT) was developed by M. Linehan as a comprehensive principle-driven outpatient treatment program for chronically suicidal individuals meeting criteria for (BPD). In a controlled randomized study Linehan could demonstrate that standard outpatient DBT is superior to unspecific treatment programs regarding reduction of parasuicidal behaviors, length and frequency of hospitalizations, treatment drop out, anger regulation and interpersonal functioning. Despite of these promising results, the number of controlled research studies on DBT is still limited. In addition to standard outpatient DBT, the model has been modified to treat patients with substance abuse and BPD, eating disorders and depression. In addition, DBT has been adapted to family and adolescent treatments, forensic settings, case management as well as to inpatient and day-treatment settings.

Inpatient DBT treatment was initially developed by Charles Swenson at New York Hospital, White Plains, and has been described in detail previously. In summary, the three-month period of treatment encompasses the following goals: Theoretical training of the patient regarding the neurobehavioral basis of BPD, acquisition of specific skills, contingency management of reinforcers following self-injurious behavior or suicidal communication, and management of discharge.

We have previously published the pre-post data of 24 female patients who had finished a three-month inpatient-DBT treatment. Comparing the month prior to hospitalization and the month after discharge the authors had found significant improvements in ratings of depression, dissociation, anxiety and global stress as well a highly significant decrease in the number of self-mutilating acts. Despite of these promising results (mean effect sizes at 1.04), the interpretation of the data was hampered by the lack of a control group, the limited number of patients and the heterogeneity of the participants: due to geographical circumstances, about half of the patients had the opportunity to continue DBT as outpatient treatment after discharge, while the others had to go back to nonspecific treatment as usual. Post hoc analysis of the data revealed significant differences between this two groups regarding inpatient treatment effectiveness.

In this study we collected data of a more homogenous group of patients and compared the treatment outcome with a natural wait list. In addition we examined predictor variables for therapy response.

Until recently, the Borderline Research Unit at the University of Freiburg has been the only ward in Germany providing DBT inpatient treatment; thus, a waiting list inevitably grew. Patients who had to wait for treatment usually had some kind of alternative treatment or were encouraged to find some. Entry into the treated group followed in consecutive order. With this procedure we followed a previously applied design by Meares and Stevenson (21) (22). Between October 96 and October 2000, 80 patients met the inclusion criteria. After complete description of the study, 20 patients refused to participate (most of them because of uncertainty about coming back for the post-assessment). Sixty patients were enrolled in the study; 9 of those admitted to the inpatient unit dropped out of treatment before regular termination (22,0%), and one could not be reached for the post-assessment. This resulted in a final sample of 31 in the DBT group and 19 in the waiting list (WL) group . Thirteen patients on the waiting list have been treated subsequently.

Measurements

For measuring the broad range of symptoms in patients with BPD we used self-rating questionnaires as well as expert ratings. Table 1 shows the instruments for assessment.

Table 1 Assessment instruments

BPD Diagnostic	Structured Clinical Interview for DSM-IV, axis II	SCID-II	First et al (23)
Comorbidity	Structured Clinical Interview for DSM-IV, axis I	SCID-I	First et al (23)
Parasuicidal Behavior	Lifetime Parasuicide Count	LPC	Linehan (24)
Treatment History	Treatment History Interview	THI	Linehan (25)
Symptoms	Symptom-Checklist	SCL-90-R	Derogatis (26)
	Hamilton Anxiety Scale	HAMA	Hamilton (27)
	State-Trait-Anxiety Inventory	STAI	Spielberger et al (28)
	Beck Depression Inventory	BDI	Beck et al (29)
	Hamilton Depression Scale	HAMD	Hamilton (30)
	State-Trait- Anger Inventory	STAXI	Spielberger et al (31)
	Dissociations Experiences Scale	DES	Bernstein & Putnam (32)
Social Functioning	Global Assessment of Functioning Scale	GAF	Endicott et al (33)
	Inventory of Interpersonal Problems	IIP	Horowitz et al (34)

Timing Assessment points were at the initial interview for the waiting list participants and at inpatient admittance for the DBT group. Post-testing was conducted four months after the initial assessment (i.e. four weeks after discharge for the DBT group). Research assessors were blind for group assignment of the patients. The interrater reliability of the assessors for the expert rating instruments ranged between .83 and .95.

Results The DBT and waiting list groups did not differ significantly at the first assessment point on any measures. Nonetheless the results for the pre-post-tests are shown separately for both groups before results for multiple regression analysis for the total sample are presented. Pre-post tests: Table 2 shows the results for the t-tests for dependent samples for both the DBT group and the waiting list group. The degrees of freedom are 30 for the first and 18 for the latter. The table lists the mean values and standard deviations for each group, pre and post, as well as the t-value, its probability p, and the corresponding effect size d.

Tab. 2 Pre-Post-Tests (T-Tests), n=31 (DBT) and n=19 (WL)

Variable	M _{pre}	SD _{pre}	M _{post}	SD _{post}	T	P	D
DES - DBT	26.1	14.6	18.3	15.0	3.29	.003**	.53
DES - WL	32.1	14.4	30.1	13.7	1.06	.306	.14
GAF - DBT	48.5	8.4	59.9	10.3	-5.76	<.001**	1.21
GAF - WL	48.1	11.1	49.4	9.9	-0.46	.652	.12
HAMA - DBT	24.0	8.8	18.7	11.5	2.91	.007**	.52
HAMA - WL	25.2	9.0	24.6	8.9	0.36	.722	.007
STAI - DBT	73.1	5.6	64.9	9.9	4.23	.000***	1.02
STAI - WL	74.4	8.0	75.5	6.3	-0.93	.363	.15

BDI - DBT	31.3	9.4	20.9	13.4	4.31	<.001**	.90
BDI - WL	35.9	11.2	36.7	11.7	-0.61	.550	.07
HAMD - DBT	17.1	5.9	12.5	7.6	3.02	.005**	.68
HAMD - WL	18.6	6.1	19.2	6.1	-0.42	.676	.10
IIP - DBT	7.61	1.43	6.61	1.87	3.02	.005**	.60
IIP - WL	7.89	1.05	7.89	1.00	0.00	1.00	.00
STAXI - DBT	6.43	2.6	6.13	2.6	0.69	.495	.12
STAXI - WL	7.11	2.2	6.84	2.3	0.93	.367	.12
SCL-90-R							
Global Severity – DBT	1.74	0.48	1.18	0.81	3.76	<.001**	.84
Global Severity – WL	1.92	0.68	1.99	0.71	-0.72	.484	.10
Symptom Distress – DBT	2.36	0.43	1.88	0.64	3.70	<.001**	.88
Symptom Distress – WL	2.58	0.46	2.59	0.47	-0.16	.876	.02
Symptom Total – DBT	65.4	11.6	50.7	22.6	3.51	.002**	.82
Symptom Total – WL	64.9	16.6	66.8	15.7	-0.84	.410	.12

For the DBT group there are significant changes in all variables but anger. Even when applying the Bonferroni-correction with $p=.0045$ there are still seven of 11 variables significant. The wait list group did not show any significant changes at the 4-month point.

Since the variable “frequency of self-injuries during the last month” failed to meet normality assumptions we conducted a rank sign test for pre-post-differences. Table 6 shows the results.

Table 6 Sign rank test for change in frequency of self-injuries

	<i>N</i>	Mean _{-ranks}	Mean _{+ranks}	Z	P	g
DBT	31	12.9	9.3	-2.51	.012*	.24
WL	19	6.1	10.1	-0.13	.900	.14

Participants in the DBT group showed significant reductions in self-injurious behavior while the wait list group did not change. More detailed analysis of the subgroup of patients who engaged in self-mutilating behavior during the four weeks immediately before the study admission point (DBT: 21 out of 31; wait list: 13 out of 19) revealed that 13 of 21 patients in the DBT group (62%) reported no more self-injuries at post-assessment compared to 4 of 13 patients on the wait list (31%).

Group-by-time comparisons

Multiple regression analyses were conducted to compare pre-post changes of the two groups. The four-month scores on each outcome variable were subtracted from the corresponding initial score and these change scores were then entered into the regression equations. Number of DSM-IV-criteria and whether participants started antidepressant medication, neuroleptic medication or Naltrexone were entered into the regression first. Pre-values and group membership were entered next as independent variables.

Table 3 Multiple Regressions with pre-values and group membership, $n=50$

Variablen	Beta	T-value	P	R ² _{group(cor r)}	f ²
BDI	.450	3.12	.003**	.166	.20
GAF	-0.360	-3.10	.003**	.110	.12
SCL-GSI	0.395	2.95	.005**	.130	.15
HAMA	.333	2.29	.027*	.087	.10
HAMD	.373	2.66	.011*	.110	.12
IIP	.302	2.23	.030*	.069	.07
STAI	.473	3.49	.001**	.201	.25

Participants who received DBT inpatient treatment improved significantly more than participants without DBT on seven of the nine variables analyzed. When using the Bonferroni-correction (which is not always recommended because of the loss of power of the analysis) there were significant between group differences ($p < .006$) on four of the nine outcome variables. Effect sizes for amount of variance due to group membership varied between .07 and .25 which signifies a medium to high effect. There were no between-group differences on the DES and the STAXI. In addition, for seven outcome variables (global adjustment, global symptoms, dissociation, depression, interpersonal functioning, anxiety, anger) GAF, GSI, DES, HAMD, IIP, STAI, STAXI) the degree of change over the 4-month period was predicted by initial score on the respective variables. In these cases poor initial pre-values correlated with high improvements suggesting that some of the pre-post changes were most likely due to a return to baseline functioning. None of the changes in clinical outcomes were significantly related to number of DSM-IV-criteria nor was there a significant influence of starting medications on any change in outcome variables.

Differences between the two groups regarding the frequency of self-injuries were analyzed using logistic regression analysis. The frequency of self-injuries was dichotomized at the median value. Overall, this model was significant ($\chi^2=13,1$, $df=1$, $p=.006$). Only the pre-value of the variable contributed significantly as a predictor variable ($\chi^2=7,61$, $df=1$, $p=.006$). The groups did not differ significantly.

Clinically significant change within the DBT group

The DBT group showed an overall treatment effect for the inpatient DBT treatment. Additionally, we wanted to know whether patients not only showed change but recovered in a clinical sense. We followed the suggestions of Jacobson (Jacobson, 1988, Jacobson et Truax, 1991, Jacobson et al, 1999) to determine the degree of so-called clinically significant change. As an outcome variable we chose the global symptom score of the SCL-90-R (GSI), since it is widely used and provides information about a great range of psychopathology. We examined the intercorrelation matrix of the post-scores and found correlations between the GSI and the other variables presented in Table 5 ranging from .459 at the lowest (trait-anger) to .834 at the highest (BDI). The GSI as a representative of the symptom variables appears to be a fair choice. One aspect of clinically significant change concerns the post-test-scores of the sample. As

a cutoff point we used the criterion that the post-test score should fall within the range of two standard deviations of the normal population. Seventeen of 31 (54.8%) patients fulfilled that criterion. The second aspect of clinically significant change has to do with the reliability of the change from pre-test to post-test. Jacobson suggested an index, called the RCI (Reliable Change Index) that represents an standardized amount of change for each patient in the sample. An RCI larger than 1.96 is unlikely to occur by chance ($p < .05$) and, thus, is an indicator of reliable clinical change.

We computed the RCI's in our DBT sample for GSI scores. Each of the 17 participants who had clinically significant change had improved. Since the data overlapped with the normal population we combined the two aspects (distance from normal and RCI) to guarantee that participants considered as responders had post-test-scores in the normal range and changed from the dysfunctional into the functional population. Using this criterion, 14 patients (45.2%) could be considered recovered in a clinically relevant way. Those responders showed a mean reduction in the SCL-90-GSI from the pre-score of 1.75 ($sd=0.38$) to a post-score of .49 ($sd=0.27$) which represents an effect size of 3.19. The non-responders showed no difference in their pre- and post-scores (mean=1.74, $sd=0.57$ pre and mean=1.79, $sd=0.61$ post).

2. Projects in progress

2.1 Monitoring of additional heart rate and distress of female patients with borderline personality disorder under open field conditions

As described previously in details (see „Research Report April 15- December 31, 2000), we have used portable mini-computers to assess psychological and physiological data under open field conditions. We had created an innovative method which is able to separate out the portion of measured heart rate which has physical causes. This method is based on the evidence that physiological arousal is an additive combination of physical and emotional stressors. The coherence between heart rate and physical activity is proved to be linear. The remaining non-metabolic heart rate, so called **additional heart rate**, is highly correlated with emotional arousal. We are currently testing the following hypotheses:

- 1.) States of aversive tension in patients with BPD correspond with states of additional heart rate.
- 2.) Patients with BPD, as compared to healthy controls, are less frequently able to assign distinct, categorical emotions to physiological arousal, operationalized via additional heart rate.

In order to examine these hypotheses we have now collected data of 24 female patients with BPD and 34 sex- and age matched controls. Within the next research period we have to include further 20 patients.

2.2 Evaluation of DBT – inpatient treatment - a controlled randomized study

In order to evaluate the 3-month DBT-inpatient treatment as an additional DBT component, we have conducted a randomized controlled study. The design was to compare two treatment arms:

- 1.) Three months DBT inpatient treatment followed by 21 months DBT outpatient treatment
- 1.) Twenty four months DBT outpatient treatment.

We have now included 80 female patients meeting criteria for BPD, the last patient will finish the treatment phase within the next month. We are currently starting the data analysis.

2.3 fMRI- study on heat induced pain perception within patients with BPD

As mentioned above, we could demonstrate reduced pain sensitivity but normal somato-sensory potentials with borderline-patients to laser-induced pain. Pain perception consists of a sensory-discriminative and an affective-motivational component and both are influenced by attention as a general cognitive-evaluative component. Our findings of an intact correlation between LEP amplitudes and subjective pain ratings as well as unaltered nociceptive discrimination in patients with BPD indicate that the sensory-discriminative pain component in this population is normal. P3 components of LEPs in BPD patients had the same amplitude as those of control subjects and were altered by a distraction task (mental arithmetic) to a similar extent in patients and control subjects. These findings rule out the possibility that attention deficits contribute to lower pain ratings in patients with BPD.

Thus the most likely cause of analgesia in BPD is an alteration of the affective-motivational pain component.

From a neuroanatomical point of view, the sensory-discriminative pathway has been localized in the lateral nociceptive system (lateral thalamic nuclei, primary and secondary somatosensory cortex). The affective-motivational component of pain can anatomically be connected with the medial nociceptive system (medial thalamic nuclei, insula, and anterior cingulate). The anterior cingulate cortex (ACC) appears to play a decisive role in processing the affective-motivational component of pain. Imaging studies using functional magnetic resonance or positron emission tomography identified ACC as part of the neural circuitry of pain. Consistent with the idea of reduced affective pain processing in BPD patients, De La Fuente and coworkers found decreased metabolism in ACC measured by FDG-PET.

In order to study the role of the anterior cingulate we now have conducted a study using a fMRI-compatible thermode and fMRI. 25 female patients with BPD and healthy controls will be included. We have just started the study and enrolled five subjects.

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