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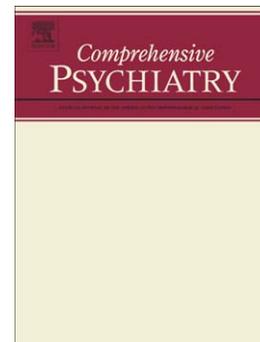
Comorbid atypical depression in borderline personality disorder is common and correlated with anxiety related psychopathology

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**Comorbid atypical depression in borderline personality disorder is
common and correlated with anxiety related psychopathology**

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Abstract

Background: The core features of borderline personality disorder (BPD) are affective instability, unstable relationships and identity disturbance. Axis I-comorbidities are frequent, in particular affective disorders. The concept of atypical depression is complex and often underestimated. The purpose of the study was to investigate the comorbidity of atypical depression in borderline patients regarding anxiety related psychopathology and interpersonal problems.

Methods: 60 patients with BPD were assessed with the Structured Clinical Interviews for DSM-IV Axis I and II Disorders (SCID I, SCID II) as well as the Atypical Depression Diagnostic Scale (ADDS). Additionally, patients completed a questionnaire (SCL-90-R, BDI, STAI, STAXI, IIP-C).

Results: Forty-five BPD patients (81.8%) had a comorbid affective disorder of which 15 (27.3%) were diagnosed with an atypical depression.

In comparison to patients with major depressive disorder or no comorbid depression, patients with atypical depression showed significant higher scores in psychopathological symptoms regarding anxiety and global severity as well as interpersonal problems.

Conclusions: The presence of atypical depression in borderline patients is correlated with psychopathology, anxiety, and interpersonal problems and seems to be of clinical importance for personalized treatment decisions.

Keywords: borderline personality disorder, atypical depression, anxiety, interpersonal problems, rejection sensitivity, comorbidity

Introduction

Borderline is one of the most common personality disorders that affects about 1 to 2% of the general population, around 10% psychiatric outpatients and 20% psychiatric inpatients. The diagnosis is more common in women (75%) than in men [1,2].

BPD was included in 1980 in the DSM-III Classification [3]. The main characteristics include affective instability, unstable relationship patterns, disturbed identity as well as impulsivity. DSM-IV-TR defines affective instability as intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days, due to a marked reactivity of mood [4].

BPD is considered both psychologically [5] and biologically [6] as a heterogeneous disorder and is associated with high comorbidity [7]. Biological vulnerability and developmental insults combined determine the presentation of BPD. The diagnostic criteria of BPD can be organised in to four sectors of psychopathology: affective, cognitive, behavioural and interpersonal criteria [8]. Patients vary widely in their severity of manifestation of these factors and even don't need to be impaired in all four factors. There are 126 different possibilities (clusters) to fulfil the diagnostic criteria for BPD (at least 5 of 9 different criteria) [9]. These dissimilarities can lead to alternate courses of the disorder [10] as well as different treatment responses.

The disorder of affectivity in Borderline disorder is conceptualized in different ways. Psychiatrists emphasize either the disorder of affect regulation with difficulty of personality-conditioned affect control [11,12], or the emotional dysregulation due to elevated biological vulnerability [13].

Gunderson and Phillips [14] point out that depressive disorder in Borderline disorders shows a qualitatively different characteristic than in major depression being more developmentally and interpersonally based.

Comorbidities are very common in patients with BPD and seem to predict the characteristic as well as the course of the disorder. Several studies have found that borderline patients are often diagnosed with an Axis I Disorder (e.g. anxiety disorders and substance abuse) [8,15]. However the most frequent comorbidities are affective disorders, especially major depression, which occurs in 70 to 90% of all borderline patients [16,17]. Zanarini et al. [17] reported that 80% had experienced a major depression episode at some point in their medical history. It seems that a specific depressive subtype is often connected with BPD; Posternak and

Zimmermann [18] found that 27% of their borderline patients had a comorbid atypical depression (AD). The international BRIDGE-Study [19] examined 2658 patients with an MDD regarding BPD and Bipolar Disorder. A bipolar diagnosis was more frequent in the non-borderline group whereas borderline patients reported significantly more atypical features.

Atypical depression (AD) was introduced to specify major depressive episodes in DSM-IV following a series of antidepressant trials showing that such patients responded preferentially to monoamine oxidase inhibitors (MAOIs) [20]. This depressive form is characterized by depressive mood, emotional reactivity, increased sleep, eating disorders as well as somatic impairment and affects about 30% of unipolar depressive patients, mostly women. Biological studies [21] as well as statistical classifications [22] support the hypothesis of a distinct depressive subtype. Compared to melancholia and other depression, atypical depression shows an earlier age of onset and a more chronic course of illness [23]. The quality of the depressive experience in borderline personality disorder has always been perceived to be different from the depression experienced in major depression (MDD) [24].

Perugi and colleagues [25] compared patients who met DSM-IV criteria for major depressive episode with atypical features in terms of a comorbid BPD. The group with a comorbid borderline disorder had significant higher lifetime comorbidity for bulimia nervosa, cyclothymia as well as Axis II disorders of the anxious and dramatic cluster (narcissistic, dependent and avoidant). This group also scored higher on multiple Atypical Depression Diagnostic Scale items (mood reactivity, interpersonal sensitivity, functional impairment, avoidance of relationships and other rejection avoidance). Most interestingly, heightened rejection sensitivity seems to be a feature in both AD and BPD [26].

Deliberate self-harm is correlated with heightened sensitivity to interpersonal rejection [27]. High Rejection Sensitivity is also associated with increased Borderline Personality features among people low in self-reported Executive Control and among those high in self-reported Executive Control, the relationship between Rejection Sensitivity and Borderline Personality features is attenuated [28]. Patients with BPD may be more sensitive to rejection, and these fears of rejection may result in increased emotion dysregulation and subsequent behavioral problems [29] or rage [30].

Anxiety disorders seem to be rather common in Borderline Personality Disorder [31,32]. Silverman et al. [33] studied the comorbidity of patients with an Axis II disorder and found

rates of 89% anxiety disorders in BPD patients. A national epidemiologic survey with over 34'000 adults [34] also showed a high co-occurrence of anxiety disorder with BPD.

However, AD is also reported to be connected to anxiety disorders. Gili and colleagues [35] compared AD, melancholic and non-melancholic depression in non-borderline patients and found that AD patients had higher rates of comorbid anxiety disorders. More specific studies showed a correlation of AD with social phobia and panic disorder [36-38].

Given that anxiety and rejection sensitivity are common in both AD and BPD the question arises how the co-occurrence of the both disorders is affecting the patient? From our point of view until now there hasn't been a study investigating BPD and comorbid AD in reference to anxiety.

Aims of the study

Since BPD and Depression are rather common in co-occurrence the aim of our study was to more closely examine a specific group of depression - atypical depression- in association with BPD. We expected patients with comorbid AD to show a more severe psychopathology compared to other BPD patients with either a different type of depression or no depression at all.

Another hypothesis was whether this co-occurrence of AD leads to more interpersonal problems in BPD patients.

Methods

Study Design and Participants

All Patients were inpatients at the Psychiatric Hospital of the University of Basel and were diagnosed with a borderline personality disorder (BPD) according the DSM-IV-TR criteria. Patients participated in a matched-controlled inpatient study for BPD patients (Basel Borderline Inpatient Study (BABIS)). Aims of this study were to compare the effects of transference focused psychotherapy (TFP)-based disorder specific inpatient treatment versus treatment as usual and to identify the possible influence of subgroups within the heterogeneous group of BPD patients. Detailed descriptions of the aims, methods and sample characteristics of the Basel Borderline Inpatient Study (BABIS) supported by a research grant from the Swiss National Science Foundation have been reported separately [39].

Exclusion criteria were schizophrenia, schizoaffective disorder, active psychosis or acute manic episode.

Written informed consent was obtained from each patient. The study was approved by the local Ethics Committee (EKBB).

Interviews

Clinically experienced interviewers attended a special education of the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I/P) [40] and for DSM-IV Axis II Disorders (SCID-II) [41] and were trained to pay particular attention to distinguishing Axis I mental state conditions from Axis II personality trait phenomena. The SCID I and II are semi-structured interviews for assessing clinical and personality disorders. High interrater reliability has been shown for both interviews [42,43].

Additionally the Atypical Depression Diagnostic Scale (ADDS) [44,45] was used to examine atypical depression more detailed. The ADDS is a semistructured interview designed to investigate the presence and severity of atypical features during current depressive episodes.

Questionnaire data

To measure the general psychiatric symptoms and subjective complaints, we administered the SCL-90-R [46], the Beck Depression Inventory [47], the Spielberger State and Trait Inventory [48], and the Spielberger State and Trait Anger Inventory [49].

For evaluation of interpersonal criteria we used the Inventory of Interpersonal Problems [50], a 64-item self-report instrument designed to measure interpersonal deficiencies and excesses in 8 subscales (e.g. too responsible, too controlling). External validity of the IIP-C scales has been demonstrated.

Statistical Analyses

All statistical analyses were conducted with SPSS/20.0. Assumption of homoscedasticity and normality distribution was checked prior to the analysis. χ^2 -tests were used for testing intergroup differences. Multivariate Analysis, Oneway Anova parametric method were performed for group comparison as well as Student's *t*-Test. All statistical tests were considered significant at a two-sided level of $p < 0.05$.

Results

60 patients diagnosed with borderline personality disorder (BPD) were included in the study and interviewed. 5 patients didn't complete the questionnaire and were therefore excluded. Of the 55 patients included in the study, 44 (80%) were female, 11 (20%) male. The mean age was 28.9 years (SD = 8.7).

53 patients (96.4%) were diagnosed with a comorbid Axis I Disorder, most frequently with an affective disorder ($n=45$, 81.8%). 35 patients (63.6%) showed a comorbid Axis II disorder, predominant a Cluster C disorder ($n=28$, 50.9%). An anxiety disorder was diagnosed in 29 patients (52.7%). 15 patients (27.3%) were given the diagnosis of an Atypical Depression. All patients with comorbid atypical depression met the BPD criterion of affective instability.

Insert Table 1 (Demographic and Clinical Characteristics)

To further analyze our results we sub-divided our patients in the following three groups: (1) patients with Atypical Depression, (2) patients with a depression other than AD and (3) patients with no depression.

Oneway-ANOVA found significances in depression (BDI, $p=0.002$), anxiety (STAI, state anxiety $p=0.002$; trait anxiety $p=0.001$), scales regarding general psychopathology (SCL-90-R, GSI $p=0.011$), as well as interpersonal problems (IIP-C, $p=0.003$).

Furthermore the AD group was diagnosed significantly more often with a comorbid anxiety disorder ($\chi^2=0.002$) than the other two groups.

However there were no differences in the three groups regarding anger or aggression.

Insert Table 2 (Intergroup Differences)

As table 2 displays, group 1 (AD) showed the highest scores in the significant data. Independent-measures t -Test between the three groups showed that the AD group can be distinguished from the others groups in Trait anxiety (STAI), Anxiety, Obsessive-Compulsion, Phobia and GSI (SCL-90-R) as well as Overly Accommodating (IIP-C).

Discussion

Our major finding was that patients with an atypical depression showed the highest scores in all psychopathological data. A possible explanation of our result could be summative effects since both conditions BPD and AD are associated with anxiety and interpersonal sensitivity

This finding is consistent with a study of McGinn et al. [51] which compared major depressive disorder patients with and without atypical depression (AD). AD predicted the presence of comorbid Axis I (100% AD vs. 33% NonAD), Axis II (90% vs. 35%), and both Axis I and II (65% vs. 8.14%) disorders. The high prevalence of Axis I and II comorbidity in major depression might be explained, at least in part, by the presence of atypical depression. Significant differences between the 3 groups in our study (atypical depression, other depression, no depression) were found in results on depression, general psychopathology, anxiety and interpersonal sensitivity.

Affective disturbances in borderline personality disorder are yet not clearly understood so further studies should continue to deepen our knowledge on different affective disorders in BPD patients (depression, dysthymia, dysphoria, and other form of affective pain). 25 dysphoric states (mostly affects) were found to be significantly more common among borderline patients than controls in the study of Zanarini et al. [31] but nonspecific to borderline personality disorder. Equally important, overall mean Dysphoric Affect Scale scores correctly distinguished borderline personality disorder from other personality disorders in 84% of the subjects. The results of the Zanarini study [31] suggest that the subjective affective pain of borderline patients may be both more pervasive and more multifaceted than previously recognized, and that the overall “amplitude“ of this pain may be a particularly good marker for the borderline diagnosis. Consistent with our results (see table 2: BDI score of AD and other depression) Levy et al. [52] could not find differences between depressed, depressed borderline, and borderline non-depressed inpatients in overall level of impairment or severity of depression. Phenomenologically, however, depressive experiences were quite different in this study. Subjects with borderline personality disorder, with and without a diagnosed depressive disorder, scored higher than subjects with depression only on the measure of anaclitic neediness (severe emotional dependence on another person, especially relating to the dependence of an infant on a mother or surrogate mother), correlated with interpersonal distress, self-destructive behaviors, and impulsivity.

Mood lability and interpersonal sensitivity traits could be related by a “cyclothymic temperamental diathesis” or “borderline-affective” cluster. [25,53]. This cluster, in turn, seems to underlie the complex pattern of anxiety, sensitivity, mood and impulsive disorders which is clinically shared by atypical depression, some bipolar II, few bulimia nervosa [54] and several borderline patients. Cyclothymic reactivity and neurotic features (i.e., atypicality and panic attacks) or structural problems may appear (in line with the description by the French psychiatrist Pierre Kahn [55] relevant to the definition of what today is considered

bipolar II disorder [56].

In sum our findings could also be suitable with Kernberg's model [57] differentiating biological and characterological depression. In the case of characterological depression, often associated with chronic suicidal tendencies, depressive affect like other affects experienced by the patient, corresponds to the underlying internalized object relations.

A distinct subgroup of borderline patients could be characterized by co-occurrence of AD associated with high phobic and general anxiety, higher general psychopathology and interpersonal problems but no differences concerning psychoticism and paranoid ideation. A possible connecting mechanism for both borderline personality disorder and atypical depression related pathology could be increased rejection sensitivity giving rise to interpersonal problems.

Possible methodological limitations of this study are the small sample size and the fact that all BPD patients (in all of the three groups) were severely disturbed (high psychopathological scores (see table 2), had fewer partners and high comorbidity (see table 1). It remains unclear if a comorbid atypical depression would also be associated with more severe psychopathology, anxiety and interpersonal problems in other personality disorders than BPD.

In summary the fundamental pattern of atypical depression is represented by chronic mild depressions, which are characterized by a younger age at onset, female predominance, interpersonal rejection sensitivity, and mood lability, which are difficult to distinguish from characterological pathology. Patients who present with such patterns are frequently diagnosed with borderline, histrionic, or avoidant personality disorders. Congruent with our results the New South Wales University group (see [58,59]) asserts the structural priority of anxiety symptoms over mood symptoms and the significance of interpersonal rejection sensitivity in atypical depression. This concept overlaps considerably with that of "hysteroid dysphoria", which was proposed by Klein and Liebowitz [60], and was one precursor of Columbia group's later concept of atypical depression.

Differential treatment response of subtypes of patients with borderline personality have been identified [61-63]. A careful phenomenological analysis of early clinical phenotypes, a clinical staging (with valid severity indexes), and strategic biomarker research are the building blocks for a future personalized psychiatry [64]. Current therapies are limited because they do not recognize or accommodate the extensive heterogeneity of borderline personality disorder and its complex etiology [65]. Currently, insufficient evidence is available supporting most personalizing variables for Borderline Personality Disorder or Depression (an important exception is cytochrome p450 activity). "Some of the features that

have potential as personalizing variables that can help predict response to particular treatments, pending replication studies, include sex, hormonal status, atypical depression, childhood trauma, family history of mental illness, and certain biomarkers and genetic polymorphisms” [66,pp1].

Unfortunately the concept of atypical depression has become overextended and gradually lost its construct validity. Therefore, the diagnostic criteria for atypical depression should be reconsidered in reference to various definitions and concepts and refined through accumulated clinical research (see [67]). “A fuller appreciation of the BPD patient's interpersonal relationships and the person's reactions and affects to and within those relationships holds the key to understanding the nature of the quality of the depression of BPD.” [24,pp25].

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Table 1: Demographic and Clinical Characteristics of the Patients

	<i>Borderline Patients (n=55)</i>
Age (mean, SD)	28.86 (8.74)
Gender (n, %)	
Female	44 (80)
Male	11 (20)
Marital status (n, %)	
Living alone	43 (78.2)
Living with a partner	12 (21.8)
Current employment (n, %)	
Employed (full/part time)	28 (50.9)
Unemployed	27 (49.1)
Years of education (n, %)	
None	1 (1.8)
< 9	23 (41.8)
9-12	21 (38.2)
> 12	10 (18.2)
Duration of illness (n, %)	
<1 year	4 (7.3)
1 year to 5 years	18 (32.7)
5 to 10 years	9 (16.4)
10 to 20 years	18 (32.7)
>20 years	6 (10.9)
Comorbid Axis I Disorder (n, %)	
None	2 (3.3)
Affective disorder	45 (81.8)
Anxiety disorder	29 (52.7)
Substance related disorder	34 (61.8)
Eating disorder	19 (34.5)
Comorbid Axis II Disorder (n, %)	
None	19 (34.5)
Cluster A	10 (18.2)
Cluster B	6 (10.9)
Cluster C	28 (50.9)
n/a	1 (1.8)

Note. SD= Standard Deviation

Table 2: Intergroup Differences regarding Psychopathology

	<i>Group 1 Atypical Depression (n=15)</i>	<i>Group 2 Other Depression (n=30)</i>	<i>Group 3 No Depression (n=10)</i>	<i>F-value (p)</i>
SCL-90-R, mean (SD)				
Global severity index (GSI)	1.7 (0.6)	1.3 (0.7)	1.1 (0.6)	4.936 (.011)*
Somatization	16.2 (11.4)	11.0 (7.8)	10.0 (5.8)	2.658 (.080) ^{n.s.}
Obsessive-Compulsive	18.7 (8.4)	13.7 (7.6)	10.1 (4.6)	6.910 (.002)**
Interpersonal Sensitivity	18.1 (7.1)	14.1 (8.4)	11.3 (6.2)	3.890 (.027)*
Depression	31.0 (10.1)	24.9 (12.4)	18.1 (7.8)	7.092 (.002)**
Anxiety	18.4 (7.5)	12.1 (7.9)	12.5 (7.4)	3.874 (.027)*
Hostility	9.1 (5.5)	7.5 (5.4)	6.6 (5.3)	1.022 (.367) ^{n.s.}
Phobic Anxiety	13.2 (7.5)	7.3 (6.9)	5.7 (5.5)	6.269 (.004)**
Paranoid Ideation	8.7 (4.0)	6.6 (5.3)	6.2 (5.6)	1.342 (.270) ^{n.s.}
Psychoticism	11.5 (8.3)	9.5 (7.5)	8.5 (7.1)	0.704 (.499) ^{n.s.}
BDI, mean (SD)				
Sum	30.3 (8.5)	25.7 (11.5)	17.5 (9.9)	7.151 (.002)**
STAI, mean (SD)				
State Anxiety	59.9 (11.1)	51.1 (13.9)	48.5 (12.3)	6.961 (.002)**
Trait Anxiety	62.4 (6.9)	55.2 (11.4)	50.5 (11.8)	8.501 (.001)**
STAXI, mean (SD)				
State Anger	20.7 (9.3)	16.0 (5.9)	15.1 (7.1)	2.804 (.070) ^{n.s.}
Trait Anger	21.9 (6.9)	21.8 (7.7)	19.4 (5.9)	0.773 (.467) ^{n.s.}
IIP, mean (SD)				
Sum	2.0 (0.4)	1.8 (0.6)	1.3 (0.6)	6.548 (.003)**
Domineering/Controlling	5.5 (3.8)	7.6 (4.8)	6.1 (4.9)	0.955 (.392) ^{n.s.}
Vindictive/Self-Centered	11.2 (3.7)	11.5 (5.6)	10.1 (5.5)	0.380 (.686) ^{n.s.}
Cold/Distant	12.5(5.1)	13.3 (6.3)	11.3 (5.3)	0.562 (.574) ^{n.s.}
Socially Inhibited	20.1(6.5)	16.8 (7.1)	12.4 (5.8)	6.440 (.003)**
Nonassertive	21.5 (8.2)	16.4 (7.1)	9.9 (8.2)	9.924 (.000)**
Overly Accommodating	20.0 (5.9)	15.2 (7.9)	11.5 (5.2)	8.160 (.001)**
Self-Sacrificing	21.8 (5.4)	18.8 (7.7)	14.3 (5.8)	6.476 (.003)**
Intrusive/Needy	12.5 (4.3)	12.6 (6.6)	9.6 (6.3)	1.537 (.225) ^{n.s.}

Notes. SD= standard deviation, n.s.: non significant, * $p < 0.05$, ** $p < 0.01$