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FAMILY HISTORY STUDY OF THE FAMILIAL COAGGREGATION OF BORDERLINE PERSONALITY DISORDER WITH AXIS I AND NON-BORDERLINE DRAMATIC CLUSTER AXIS II DISORDERS

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Abstract

The purpose of this study was to assess the familial coaggregation of borderline personality disorder (BPD) with a full array of axis I disorders and four axis II disorders (antisocial personality disorder, histrionic personality disorder, narcissistic personality disorder, and sadistic personality disorder) in the first-degree relatives of borderline probands and axis II comparison subjects. Four hundred and forty-five inpatients were interviewed about familial psychopathology using the Revised Family History Questionnaire—a semistructured interview of demonstrated reliability. Of these 445 subjects, 341 met both DIB-R and DSM-III-R criteria for BPD and 104 met DSM-III-R criteria for another type of personality disorder (and neither criteria set for BPD). The psychopathology of 1580 first-degree relatives of borderline probands and 472 relatives of axis II comparison subjects was assessed. Using structural models for familial coaggregation, it was found that BPD coaggregates with major depression, dysthymic disorder, bipolar I disorder, alcohol abuse/dependence, drug abuse/dependence, panic disorder, social phobia, obsessive-compulsive disorder, generalized anxiety disorder, posttraumatic stress disorder, somatoform pain disorder, and all four axis II disorders studied. Taken together, the results of this study suggest that common familial factors, particularly in the areas of affective disturbance and impulsivity, contribute to borderline personality disorder.

The degree to which borderline personality disorder (BPD) may coaggregate with axis I and axis II psychiatric disorders in families, and thus may share familial factors with these conditions, has been incompletely studied. Previous research has found a low lifetime prevalence of schizophrenia and bipolar I disorder (Baron, Gruen, Asnis & Lord, 1985; Links, Steiner & Huxley, 1988; Loranger, Oldham & Tulis 1982; Loranger & Tulis 1985; Pope, Jonas, Hudson, Cohen & Gunderson 1983; Schulz et al., 1989; Silverman et al., 1991; Soloff & Millward, 1983; Zanarini, Gunderson, Marino, Schwartz & Frankenburg, 1988) but an elevated lifetime prevalence of major depression (Baron et al., 1985; Links et al., 1988; Loranger et al., 1982; Pope et al., 1983; Schulz et al., 1986; Schulz et al., 1989; Silverman et al., 1991; Soloff & Millward, 1983; Zanarini et al., 1988), substance use disorders (Links et al., 1988; Loranger & Tulis 1985; Pope et al., 1983; Schulz et al., 1986; Schulz et al., 1989; Silverman et al., 1991; Zanarini et al., 1988), and antisocial personality disorder (Links et al., 1988; Pope et al. 1983; Schulz et al., 1989; Silverman et al. 1991; Soloff & Millward 1983; Zanarini et al., 1988) in the first-degree relatives of probands with BPD. However, previous studies have been limited by an incomplete assessment of axis I disorders and a failure to assess axis II disorders other than BPD and APD. Previous studies

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have also been limited by small samples and at times, assessment of relatives that is not blinded to proband status.

We conducted a family history study, with assessments of relatives based on proband's report that was blinded to proband status, that examined a wide range of axis I disorders and four axis II disorders in the first-degree relatives of probands with BPD vs. probands with other personality disorders (OPD).

Methods

Participants

All probands were inpatients at McLean Hospital in Belmont, Massachusetts admitted and interviewed between 1991–1995. Each proband was initially screened to determine that he or she: 1) was between the ages of 18–50, 2) had a known or estimated IQ of 71 or higher, 3) had no history or current symptomatology of a serious organic condition, schizophrenia, schizoaffective disorder, or bipolar I disorder, and 4) was fluent in English.

Three semistructured diagnostic interviews were administered to each proband blinded to his or her clinical diagnoses. These instruments were: 1) the Structured Clinical Interview for DSM-III-R Axis I Disorders (SCID I) (Williams et al., 1992), 2) the Revised Diagnostic Interview for Borderlines (DIB-R) (Zanarini, Gunderson, Frankenburg, & Chauncey, 1989), and 3) the Diagnostic Interview for DSM-III-R Personality Disorders (DIPD-R) (Zanarini, Frankenburg, Chauncey, & Gunderson, 1987). Good-excellent levels of inter-rater and test-retest reliability were established for all axis I and II disorders diagnosed with enough frequency for a kappa statistic to be computed (Zanarini & Frankenburg, 2001; Zanarini, Frankenburg, & Vujanovic, 2002).

Probands were interviewed about the psychopathology of their first-degree relatives by a second team of interviewers, who were blinded to their diagnostic status, using the Revised Family History Questionnaire (FHQ-R) (Zanarini, 1990). This semistuctured interview assesses the presence of a full array of lifetime axis I disorders according to DSM-III-R criteria as well as all five dramatic cluster axis II disorders. Axis I disorders were initially assessed for each relative using a probe and then if the probe was endorsed, each criterion for that disorder was assessed. For axis II disorders, each criterion was assessed in a systematic fashion. (Results pertaining to borderline personality disorder have been presented elsewhere [Zanarini et al., 2004]).

The psychometric properties of this measure have been described elsewhere (Zanarini et al., 1988). For this particular study, the inter-rater reliability of axis I and II disorders was assessed in a subsample of 98 first-degree relatives of 20 probands. Conjoint interviews using two separate raters were conducted. As Table 1 shows, 19 kappas were in the excellent range (>.75) and two were in the good range (.40–.75) (Fleiss, 1981).

This study was approved by the McLean Hospital Institutional Review Board, and written informed consent was obtained from each participant before any study procedures were administered.

Statistical analysis

To evaluate the familial coaggregation of BPD with axis I and II disorders, we used logistic regression models based on a structural approach to the analysis of familial coaggregation, defined as the association induced by the presence of common familial factors for two disorders (Hudson et al., 2008). For the first model (basic model), the outcome was the presence of a given axis I or II disorder in a relative, and the predictor was BPD in the

corresponding proband (e.g., lifetime major depression in a relative predicted by BPD in proband). This model produces a valid estimate of coaggregation under the assumption of that neither of the two disorders is a cause of the other (i.e., no “direct effects”). This model also underestimates coaggregation when there are direct effects. For the second model (adjusted for proband/relative comorbidity), we added terms for BPD in the relative and the axis I or axis II disorder in the proband (e.g., major depression in relative predicted by BPD in proband, adjusted for major depression in proband and BPD in relative). This model underestimates coaggregation, both in the presence or absence of direct effects. Thus, these two models provide upper- and lower-bound estimates for coaggregation in the setting where direct effects might be present. Further details of these models are presented elsewhere (Hudson et al., 2008). We consider the plausibility for direct effects of BPD with various axis I and II disorders in the discussion.

In all models for outcomes in probands, we adjusted for sex and age, using five age categories based on quintiles of the distribution. In models for outcomes in relatives, we adjusted for the relative's age, sex, and relationship to the proband (parent, sibling, or child). In the case of relatives, because observations within families are correlated, we used generalized estimating equations (Liang and Zeger, 1986) to estimate standard errors, with independence as the working covariance structure.

To compare demographic characteristics between probands with BPD and with OPD, and between relatives of probands with BPD and with OPD, we used Student’s t-test for continuous variables and Fisher’s exact test for binary variables.

We did not correct the results of our analyses for multiple comparisons due to the difficulty of determining an appropriate and not overly conservative correction for correlated outcomes. Therefore, the reader should bear in mind when viewing the results that some findings, especially those of marginal significance ($0.01 < p < 0.05$), may represent Type I error.

All analyses were performed using Stata 9.2 software (StataCorp, College Station, Texas).

Results

All told, our battery of diagnostic interviews was administered to 520 consecutive inpatients at McLean Hospital who met our inclusion/exclusion criteria. Three hundred and seventy-nine patients met both DIB-R and DSM-III-R criteria for BPD and 125 met DSM-III-R criteria for at least one nonborderline axis II disorder (and neither criteria set for BPD). Sixteen others were excluded from further study because they either met criteria for schizophrenia (N=2) or bipolar I disorder (N=2) or failed to meet DSM-III-R criteria for any axis II disorder (N=12).

Of the 504 remaining patients, 37 were discharged from the hospital before the FHQ-R could be administered. An additional 22 knew too little about their first-degree relatives to make informed judgments about their psychopathology. Of the 445 remaining patients, 341 met study criteria for BPD and 104 met study criteria for another type of personality disorder and neither criteria set for BPD.

Demographic characteristics of probands and relatives are shown in Table 2. BPD probands were significantly more likely to be female than OPD probands ($p<0.001$). They were also slightly but significantly younger than OPD subjects ($p=0.048$). Roughly equal percentages of the relatives in each group were female ($p=0.43$) and roughly equal percentages were also parents ($p=0.75$), siblings ($p=0.40$), and children ($p=0.12$). In addition, the mean age of the relatives of BPD probands was quite similar to that of OPD probands ($p=0.12$).

The lifetime prevalence of axis I and II disorders in the original sample of BPD and OPD probands has been presented elsewhere (Zanarini et al., 1998a; Zanarini et al., 1998b). Table 3 presents the lifetime prevalence of the slightly smaller sample used in the current study.

The lifetime prevalence of axis I disorders in relatives of BPD and OPD probands is presented in Table 4. Using the main model, we found a statistically significant odds ratio for the coaggregation between BPD and a large number of individual disorders (major depressive disorder, dysthymic disorder, bipolar I disorder, alcohol abuse/ dependence, drug abuse/dependence, panic disorder, social phobia, obsessive-compulsive disorder, generalized anxiety disorder, posttraumatic stress disorder, somatoform pain disorder), as well as with the category of at least one disorder within a class of disorders for almost all classes (mood disorders, substance use disorders, anxiety disorders, somatoform disorders, and eating disorders).

Using the model adjusted for proband and relative comorbidity, we found a statistically significant odds ratio for the coaggregation between BPD and the following disorders or classes of disorders: major depressive disorder, dysthymic disorder, bipolar I disorder, alcohol abuse/dependence, drug abuse/dependence, panic disorder, obsessive-compulsive disorder, generalized anxiety disorder, any mood disorder, and any substance use disorder.

For several disorders for which the coaggregation odds ratio from the main model was statistically significant and the odds ratio from the model adjusted for proband/relative comorbidity was not (social phobia, posttraumatic stress disorder, and any eating disorder), we also performed an analysis of direct effects in a single direction. These models made the following assumptions about lack of direct effects: BPD is not a direct cause of posttraumatic stress disorder and BPD is not directly caused by social phobia or eating disorders; the models allowed that direct effects could be present in the opposite direction (e.g., posttraumatic stress disorder could be a cause of BPD). The odds ratio (95% CI) for coaggregation were as follows: social phobia, 1.7 (0.83, 3.5), $p=0.14$; posttraumatic stress disorder, 1.4 (0.75, 2.63), $p=0.28$; and any eating disorder, 1.8 (1.3, 2.5), $p<0.001$.

The lifetime prevalence of non-BPD dramatic cluster axis II disorders in relatives of BPD and OPD probands is presented in Table 5. Using the main model, we found a statistically significant odds ratio for the coaggregation between BPD and each of the axis II disorders studied. Only antisocial personality disorder was insignificant in our second model. However, as we were unable to exclude a bidirectional relationship between APD and BPD, we did not evaluate a unidirectional direct effects model.

As our sample contained a significantly higher percentage of female probands with BPD than female probands with other axis II disorders, we reran all analyses pertaining to relative diagnoses with proband gender added as another covariate. Our results were basically the same as our findings described above that did not control for proband gender.

Non-significant odds ratios for coaggregation from all models were almost always above one, and the upper limit of the 95% confidence intervals almost always included values that would be considered scientifically important. Thus, we could not exclude the possibility of coaggregation of BPD with any disorder or with any class of disorders.

Discussion

We found that the BPD coaggregates with a broad range of axis I and non-BPD dramatic cluster disorders within families, including mood disorders, substance use disorders, anxiety disorders, and eating disorders. These results suggest that BPD shares familial factors with these other conditions. These findings are consistent with the results of other family studies

that have found coaggregation with major depressive disorder (Baron et al., 1985; Links et al., 1988; Loranger et al., 1982; Pope et al., 1983; Schulz et al., 1986; Schulz et al., 1989; Silverman et al., 1991; Soloff & Millward, 1983; Zanarini et al., 1988), with substance use disorders (Links et al., 1988; Loranger & Tulis 1985; Pope et al., 1983; Schulz et al., 1986; Schulz et al., 1989; Silverman et al., 1991; Zanarini et al., 1988), and APD (Links et al., 1988; Pope et al. 1983; Schulz et al., 1989; Silverman et al. 1991; Soloff & Millward 1983; Zanarini et al., 1988). As with previous studies (Baron et al., 1985; Links et al., 1988; Loranger et al., 1982; Loranger & Tulis 1985; Pope et al., 1983; Schulz et al., 1989; Silverman et al., 1991; Soloff & Millward, 1983; Zanarini et al., 1988), we failed to find significant coaggregation with schizophrenia but because of the low prevalence of schizophrenia among relatives, our study and others have had little power to detect coaggregation with this disorder.

Our findings concerning significant familial coaggregation with anxiety and eating disorders are new. The only other study to assess these disorders in the first-degree relatives of borderline patients, which involved a relatively small sample of outpatients meeting criteria for BPD or other axis II disorders, failed to find significant between-group differences (Zanarini et al., 1988). Although no previous study has found significant familial coaggregation with bipolar I disorder (Links et al., 1988; Loranger et al., 1982; Pope et al., 1983; Schulz et al., 1989; Silverman et al., 1991; Zanarini et al., 1988), previous studies have employed small sample sizes and hence may have lacked sufficient power to detect this type of coaggregation. However, it is important to note that this finding should be regarded with caution given the large confidence interval we found. Such a large confidence interval suggests that the estimate of the magnitude of coaggregation is unstable due to the relatively small number of relatives in each study group found to have this disorder. It should also be noted that this significant difference seems to be related more to the low prevalence of bipolar I disorder in the relatives of OPD probands than to a high prevalence of bipolar I disorder in the relatives of probands with BPD. In fact, major depression is nine times as common among these relatives as bipolar I disorder—a finding that is consistent with the findings of prior studies. Finally, our results pertaining to histrionic, narcissistic, and sadistic personality disorders represent new findings as the prevalence of these disorders in first-degree relatives has not been assessed before, while our results concerning APD are equivocal as our basic model found a significant between-group difference, while our model controlling for proband and relative comorbidity did not.

In order to understand the statistical analysis in this and other family studies, it is important to address the handling of possible direct effects; specifically, the extent to which BPD may be a cause of an axis I or II disorder, or an axis I or II disorder may be a cause of BPD. In the literature, some family studies have reported analyses similar to our main model, which did not attempt to control for these effects, whereas other studies used analyses that purported to control for them. However, as discussed elsewhere (Hudson et al., 2008), none of these previous analyses has been based on an explicit causal model of coaggregation, so that the validity of the conclusions drawn from these analyses has not been clear. The major conceptual difficulty is that unadjusted models, similar to our basic model, are valid estimates of coaggregation in the absence of direct effects but underestimate coaggregation in the presence of direct effects (Hudson et al., 2008). Conversely, models that attempt to adjust for direct effects will always underestimate the coaggregation effect to some degree, regardless of the magnitude of direct effects, and can seriously underestimate the coaggregation effect when direct effects are absent. Because the importance of direct effects is unclear and because adjusting for them underestimates coaggregation, we chose the unadjusted model as our primary analysis.

Notably, in our secondary analysis -- which used the more conservative model that allowed for direct effects of BPD on other disorders and another disorder on BPD – the overall findings of the study changed only slightly. There were four disorders (social phobia, posttraumatic stress disorder, eating disorders, and APD) for which the coaggregation odds ratio was statistically significant in the main model and not significant in the model adjusted for proband and relative comorbidity. For these disorders (with the exception of APD described above), we used an analysis that allowed for direct effects in one direction but not the other (i.e., BPD could cause social phobia- or eating disorders, and posttraumatic stress disorder could cause BPD; but social phobia or eating disorders are not a direct cause for BPD, and BPD is not a direct cause of posttraumatic stress disorder). We found that the coaggregation odds ratio for eating disorders was similar to that of the main model and was statistically significant, and that the coaggregation odds ratios for social phobia and posttraumatic stress disorder were similar to the model adjusted for proband and relative comorbidity and were not statistically significant. Thus, the weight of the evidence suggests that BPD coaggregates with eating disorders, but it is unclear whether BPD coaggregates with social phobia or posttraumatic stress disorder.

The disorders with which BPD coaggregates in families are much the same as those that co-occur with BPD in individuals (Zanarini et al., 1989; Zanarini et al., 1998a; Zanarini et al., 1998b)—disorders of affect (mood disorders, anxiety disorders) and impulse spectrum disorders (substance use disorders, eating disorders, and other dramatic cluster personality disorders). These disorders span a broad range and even include larger groupings of disorders, such as externalizing and internalizing disorders (Krueger et al., 1999) and “affective spectrum disorder” (Hudson et al., 2003). This observation raises the question of whether the shared familial factors have much specificity, or rather are more general non-specific factors predisposing to psychiatric illness.

The results of this study and other family history studies do not permit conclusions regarding the nature of the common familial factors that may underlie BPD and certain axis I and II disorders. These factors may be either genetic factors or common family environmental factors. Evidence for genetic factors includes results of twin studies; Torgersen and colleagues (2000) finding a high degree of heritability in dramatic cluster axis II disorders. These common genetic factors might operate through endophenotypes such as the intersecting dimensions of impulsivity and emotional lability suggested by Siever and Davis (1991). There is probably less reason to suspect common familial environmental factors, because twin studies have failed to identify an important role for these factors in most axis I and II disorders but such factors could include subtle failures in parenting or frank experiences of abuse or neglect (Zanarini et al., 1998).

Several limitations of the study that might bias the results should be considered. First, if BPD probands were more likely to report axis I and II disorders in relatives (e.g., because of their comorbidity or for reasons intrinsic to having BPD, such as their hyperbolic temperament [Zanarini & Frankenburg, 1994]), the estimated odds ratios for coaggregation would be biased upward. There is some evidence of such positive bias in family history studies, in that there is a tendency for individuals with a given disorder versus an individual without that condition to report that disorder present in a relative (Kendler et al., 1991; Roy, Walsh, & Kendler, 1996). Second, if the personality disorders comprising the OPD grouping have some familial coaggregation with axis I and non-BPD axis II disorders, the estimated odds ratios for coaggregation with BPD would be biased downward. Third, the probands sampled probably include individuals with more severe illness and greater axis I and II comorbidity than present in a sample drawn from the general population. The effect of this sampling would likely be to bias the coaggregation odds ratios upwards. Fourth, although our level of inter-rater reliability was relatively good, it is likely that indirect diagnoses are

less reliable than direct interviews; poorer reliability, in turn, would be expected to bias the results towards the null. These limitations, which are intrinsic to family history studies from clinical samples, underscore the need to confirm of these results in a family interview study in which relatives are interviewed directly while the rater is blinded to proband status and in which probands are ascertained not only from clinic samples but also from community-based samples.

In conclusion, the results of this study suggest that common familial factors, particularly in the areas of affective disturbance and impulsivity, contribute to borderline personality disorder. If confirmed by studies using the family interview method, genetic studies, studies of candidate endophenotypes, and studies of family environment should be conducted to explore the nature of these common factors.

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References

Baron M, Gruen R, Asnis L, Lord S. Familial transmission of schizotypal and borderline personality disorders. American Journal of Psychiatry. 1985; 142:927–933. [PubMed: 4025588]

Fleiss, JL. Statistical methods for rates and proportions. 2. New York: John Wiley; 1981. p. 38-46.

Hudson JI, Javaras KN, Laird NM, VanderWeele TJ, Pope HG Jr, Hernan MA. A structural approach to the familial aggregation of disorders. Epidemiology. 2008; 19:431–439. [PubMed: 18379420]

Hudson JI, Mangweth B, Pope HG Jr, De Col C, Hausmann A, Gutweniger S, Laird NM, Biebl W, Tsuang MT. Family study of affective spectrum disorder. Archives of General Psychiatry. 2003; 60:170–177. [PubMed: 12578434]

Kendler KS, Silberg JL, Neale MC, Kessler RC, Heath AC, Eaves LJ. The family history method: Whose psychiatric history is measured? American Journal of Psychiatry. 1991; 148:1501–1504. [PubMed: 1928463]

Krueger RF. The structure of common mental disorders. Archives of General Psychiatry. 1999; 56:921–926. [PubMed: 10530634]

Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. Biometrika. 1986; 73:13–22.

Links P, Steiner M, Huxley G. The occurrence of borderline personality disorder in the families of borderline patients. Journal of Personality Disorders. 1988; 2:14–20.

Loranger A, Oldham J, Tulis E. Familial transmission of DSM-III borderline personality disorder. Archives of General Psychiatry. 1982; 39:795–799. [PubMed: 7165479]

Loranger A, Tulis E. Family history of alcoholism in borderline personality disorder. Archives of General Psychiatry. 1985; 42:153–157. [PubMed: 3977541]

Pope HG Jr, Jonas JM, Hudson JI, Cohen BM, Gunderson JG. The validity of DSM-III borderline personality disorder: A phenomenologic, family history, treatment response, and long-term follow-up study. Archives of General Psychiatry. 1983; 40:23–30. [PubMed: 6849616]

Roy MA, Walsh D, Kendler KS. Accuracies and inaccuracies of the family history method: a multivariate approach. Acta Psychiatrica Scandanavica. 1996; 93:224–234.

Schulz P, Schulz S, Goldberg S, Ettigi P, Resnick R, Friedel R. Diagnoses of the relatives of schizotypal outpatients. Journal of Nervous Mental Disorders. 1986; 174:475–463.

Schulz P, Soloff P, Kelly T, Morgenstern M, Franco D, Schulz S. A family history study of borderline subtypes. Journal of Personality Disorders. 1989; 3:217–229.

Silverman J, Pinkham L, Horvath T, Coccaro E, Klar H, Schear S, Apter M, Davidson M, Mohs R, Siever L. Affective and impulsive personality disorder traits in the relatives of patients with borderline personality disorder. American Journal of Psychiatry. 1991; 48:1378–1385. [PubMed: 1897620]

Soloff P, Millward J. Psychiatric disorders in the families of borderline patients. Archives of General Psychiatry. 1983; 40:37–44. [PubMed: 6849617]

Williams JBW, Gibbon M, First MB, Spitzer RL, Davies M, Borus J, Howes M, Kane J, Pope HG, Rounsaville B, Wittchen H. The Structured Clinical Interview for DSM-III-R (SCID). II Multi-site test-retest reliability. Archives of General Psychiatry. 1992; 49:624–629. [PubMed: 1637252]

Zanarini MC, Frankenburg FR. Attainment and maintenance of reliability of axis I and II disorders over the course of a longitudinal study. Comprehensive Psychiatry. 2001; 42:369–374. [PubMed: 11559863]

Zanarini MC, Frankenburg FR, Chauncey DL, Gunderson JG. The Diagnostic Interview for Personality Disorders: Interrater and test-retest reliability. Comprehensive Psychiatry. 1987; 28:467–480. [PubMed: 3691072]

Zanarini MC, Frankenburg FR, Dubo ED, Sickel AE, Trikha A, Levin A, Reynolds V. The axis I comorbidity of borderline personality disorder. American Journal of Psychiatry. 1998a; 155:1733–39. [PubMed: 9842784]

Zanarini MC, Frankenburg FR, Dubo ED, Sickel AE, Trikha A, Levin A, Reynolds V. The axis II comorbidity of borderline personality disorder. Comprehensive Psychiatry. 1998b; 39:296–302. [PubMed: 9777282]

Zanarini MC, Frankenburg FR, Vujanovic AA. The interrater and test-retest reliability of the Revised Diagnostic Interview for Borderlines (DIB-R). Journal of Personality Disorders. 2002; 16:270–276. [PubMed: 12136682]

Zanarini MC, Frankenburg FR, Yong L, Raviola G, Reich DB, Hennen J, Hudson JI, Gunderson JG. Borderline psychopathology in the first-degree relatives of borderline and axis II comparison probands. Journal of Personality Disorders. 2004; 18:439–447. [PubMed: 15519954]

Zanarini MC, Gunderson JG, Frankenburg FR, Chauncey DL. Discriminating borderline personality disorder from other Axis II disorders. American Journal of Psychiatry. 1990; 147:161–167. [PubMed: 2301653]

Zanarini MC, Gunderson JG, Frankenburg FR. Axis I phenomenology of borderline personality disorder. Comprehensive Psychiatry. 1989; 30:149–156. [PubMed: 2920550]

Zanarini MC, Gunderson JG, Frankenburg FR, Chauncey DL. The revised diagnostic interview for borderlines: Discriminating BPD from other axis II disorders. Journal of Personality Disorders. 1989; 3:10–18.

Zanarini MC, Gunderson JG, Frankenburg FR, Chauncey DL. Discriminating borderline personality disorder from other Axis II disorders. American Journal of Psychiatry. 1990; 147:161–167. [PubMed: 2301653]

Zanarini MC, Gunderson JG, Marino MF, Schwartz EO, Frankenburg FR. DSM-III disorders in the families of borderline outpatients. Journal of Personality Disorders. 1988; 2:292–302.

Table 1

Interrater Reliability of Axis I and II Disorders as Assessed by FHQ-R

Disorder	Interrater Kappa (N=98 relatives of 20 probands)
Mood Disorders	
Major Depression	.85
Dsythymia	.91
Bipolar I Disorder	1.0
Cyclothymia	---
Bipolar II Disorder	1.0
Substance Use Disorders	
Alcohol Abuse/Dependence	.94
Drug Abuse/Dependence	.91
Psychotic Disorders	
Schizophrenia	
Other Psychotic Disorder	.66
Anxiety Disorders	
Panic Disorder	.83
Agoraphobia	---
Social Phobia	1.0
Simple Phobia	.92
Obsessive-Compulsive Disorder	1.0
Generalized Anxiety Disorder	.88
PTSD	1.0
Somatoform Disorders	
Hypochondriasis	1.0
Somatization Disorder	---
Somatoform Pain Disorder	1.0
Eating Disorders	
Anorexia Nervosa	1.0
Bulimia Nervosa	.88
Non-Borderline Axis II Disorders	
Histrionic Personality Disorder	.86
Narcissistic Personality Disorder	.84
Sadistic Personality Disorder	.95
Antisocial Personality Disorder	.64

Table 2

Characteristics of Probands and Relatives, by Proband Group

	BPD	OPD
Probands		
Total, N	341	104
Age ± SD —yr	27.7 (6.9)	29.4 (9.1)
Female sex —N (%)	268 (78.6)	60 (57.7)
Relatives		
Total, N	1580	472
Age ± SD —yr	41.5 (15.0)	42.7 (16.3)
Range	15 – 83	15 – 91
Female sex —N (%)	796 (50.4)	228 (48.3)
Mothers, N	340	104
Fathers, N	335	102
Sisters, N	442	113
Brothers, N	431	137
Daughters, N	14	11
Sons, N	18	5

Table 3

Lifetime Prevalence of Axis I and Axis II Disorders among Probands

	N (%)	
	Probands with BPD (N=341)	**Probands with OPD (N=104)**
Mood Disorders		
Major Depressive Disorder	283 (83.0)	73 (70.2)
Dysthymic Disorder	132 (38.7)	28 (26.9)
Bipolar I Disorder	0 (0.0)	0 (0.0)
Bipolar II Disorder	31 (9.1)	1 (1.0)
Cyclothymic Disorder	0 (0.0)	0 (0.0)
Any Mood Disorder	328 (96.2)	77 (74.0)
Substance Use Disorders		
Alcohol Abuse/Dependence	182 (53.4)	45 (43.3)
Drug Abuse/Dependence	158 (46.3)	37 (35.6)
Any Substance Use Disorder	221 (64.8)	52 (50.0)
Psychotic Disorders		
Any Psychotic Disorder	3 (0.9)	0 (0.0)
Anxiety Disorders		
Panic Disorder	164 (48.1)	19 (18.3)
Agoraphobia	43 (12.6)	4 (3.9)
Social Phobia	158 (46.3)	19 (18.3)
Simple Phobia	109 (32.0)	16 (15.4)
Obsessive Compulsive Disorder	55 (16.1)	5 (4.8)
Generalized Anxiety Disorder	45 (13.2)	3 (2.9)
Posttraumatic Stress Disorder	186 (54.6)	22 (21.2)
Any Anxiety Disorder	299 (87.7)	53 (51.1)
Somatoform Disorders		
Hypochondriasis	16 (4.7)	2 (1.9)
Somatization Disorder	16 (4.7)	0 (0.0)
Somatoform Pain Disorder	16 (4.7)	1 (1.0)
Any Somatoform Disorder	37 (10.9)	3 (2.9)
Eating Disorders		
Anorexia Nervosa	74 (21.7)	12 (11.5)
Bulimia Nervosa	88 (25.8)	16 (15.4)
Eating Disorder NOS	90 (26.4)	10 (9.6)
Any Eating Disorder	183 (53.7)	30 (28.9)
Axis II Disorders		
Histrionic	53 (15.5)	8 (7.7)
Narcissistic	52 (15.3)	14 (13.5)

	N (%)	
	Probands with BPD (N=341)	**Probands with OPD (N=104)**
Antisocial	77 (22.6)	19 (18.3)
Sadistic	20 (5.9)	5 (4.8)
Any Non-borderline Dramatic Cluster Personality Disorder	137 (40.2)	32 (30.8)

Table 4

Lifetime Prevalence of Axis I Disorders in Relatives of Probands with BPD and OPD, and Odds Ratios for Coaggregation of BPD with Axis I Disorders.

	Prevalence (%)		Main Model			Model Adjusted for Proband/Relative Comorbidity		
			Odds Ratio[a]			Odds Ratio[b]		
Disorder	BPD N=1580	OPD N=472	Estimate	95% CI	P	Estimate	95% CI	P
Mood Disorders								
Major Depressive Disorder	18.3	11.9	1.7	1.2, 2.3	<0.001	1.4	1.04, 2.0	0.030
Dysthymic Disorder	11.9	6.4	2.0	1.3, 3.0	0.001	1.8	1.2, 2.8	0.004
Bipolar I Disorder	2.1	0.4	5.1	1.23, 21.6	0.025	4.5	1.07, 19.1	0.040
Bipolar II Disorder	1.2	1.1	1.1	0.41, 3.0	0.820	0.9	0.33, 2.5	0.863
Cyclothymic Disorder	0.4	0.9	.53	0.15, 1.8	0.32	.40	0.11, 1.4	0.15
Any Mood Disorder	27.9	17.6	1.8	1.4, 2.4	<0.001	1.4	1.08, 1.9	0.014
Substance Use Disorders								
Alcohol Abuse/Dependence	29.6	17.8	2.0	1.6, 2.6	<0.001	1.9	1.4, 2.5	<0.001
Drug Abuse/Dependence	17.2	8.1	2.4	1.7, 3.5	<0.001	2.1	1.4, 3.1	<0.001
Any Substance Use Disorder	35.8	20.8	2.2	1.7, 2.8	<0.001	1.9	1.5, 2.5	<0.001
Psychotic Disorders								
Any Psychotic Disorder	1.1	0.6	2.0	0.57, 6.7	0.29	1.6	0.45, 5.6	0.47
Anxiety Disorders								
Panic Disorder	9.4	2.8	3.7	2.1, 6.6	<0.001	2.9	1.6, 5.2	0.001
Agoraphobia	1.8	1.3	1.5	0.60, 3.6	0.394	1.3	0.54, 3.3	0.52
Social Phobia	4.1	1.9	2.1	1.04, 4.3	0.038	1.6	0.75, 3.3	0.23
Simple Phobia	7.8	5.5	1.4	0.92, 2.2	0.11	1.1	0.71, 1.8	0.63
Obsessive Compulsive Disorder	4.6	1.5	3.2	1.5, 7.0	0.004	2.5	1.1, 5.6	0.022
Generalized Anxiety Disorder	2.8	0.2	14	1.9, 104	0.009	12	1.7, 90	0.014
Posttraumatic Stress Disorder	6.9	2.8	2.5	1.4, 4.6	0.002	1.4	0.74, 2.7	0.30
Any Anxiety Disorder	22.8	12.9	2.0	1.5, 2.7	<0.001	1.4	0.98, 1.9	0.069
Somatoform Disorders								
Hypochondriasis	1.5	0.6	2.4	0.70, 7.9	0.17	1.9	0.55, 6.4	0.32

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Disorder	Prevalence (%)		Main Model			Model Adjusted for Proband/Relative Comorbidity		
			Odds Ratio[a]			Odds Ratio[b]		
	BPD N=1580	OPD N=472	Estimate	95% CI	P	Estimate	95% CI	P
Somatization Disorder	0.7	0.2	3.6	0.43, 26	0.25	2.4	0.30, 19	0.42
Somatoform Pain Disorder	2.3	0.4	5.6	1.3, 23	0.019	4.2	0.99, 18	0.052
Any Somatoform Disorder	3.8	1.3	3.1	1.3, 7.4	0.008	2.5	1.04, 5.8	0.042
Eating Disorders								
Anorexia Nervosa	3.1	1.3	2.3	0.98, 5.5	0.056	1.4	0.57, 3.5	0.46
Bulimia Nervosa	3.5	2.5	1.4	0.72, 2.6	0.34	1.1	0.55, 2.0	0.88
EDNOS	1.8	1.1	1.7	0.64, 4.4	0.29	1.4	0.52, 3.7	0.52
Any Eating Disorder	18.0	10.2	1.9	1.4, 2.6	<0.001	1.0	0.60, 1.7	0.98

[a] Odds ratio for disorder in a relative of a proband with BPD vs. disorder in a relative of a proband with OPD, adjusted for relative's age, sex, and relationship to proband (parent, sibling, child)

[b] Odds ratio for disorder in a relative of a proband with BPD vs. disorder in a relative of a proband with OPD, adjusted for disorder in the proband (proband comorbidity), BPD in a relative (relative comorbidity), and relative's age, sex, and relationship to proband (parent, sibling, child)

Table 5

Lifetime Prevalence of Axis II Disorders in Relatives of Probands with BPD and OPD, and Odds Ratios for Coaggregation of BPD with Non-borderline Axis II Disorders.

	Prevalence (%)		Main Model			Model Adjusted for Proband/Relative Comorbidity		
			Odds Ratio[a]			Odds Ratio[b]		
Disorder	BPD N=1580	OPD N=472	Estimate	95% CI	P	Estimate	95% CI	P
Histrionic	10.5	5.1	2.2	1.40, 3.4	0.001	1.8	1.14, 2.9	0.012
Narcissistic	9.8	4.9	2.1	1.36, 3.4	0.001	2.0	1.21, 3.2	0.007
Antisocial	9.1	6.1	1.6	1.03, 2.4	0.036	1.4	0.92, 2.3	0.113
Sadistic	15.2	9.5	1.8	1.28, 2.5	0.001	1.8	1.21, 2.5	0.003

[a] Odds ratio for disorder in a relative of a proband with BPD vs. disorder in a relative of a proband with OPD, adjusted for relative's age, sex, and relationship to proband (parent, sibling, child)

[b] Odds ratio for disorder in a relative of a proband with BPD vs. disorder in a relative of a proband with OPD, adjusted for disorder in the proband (proband comorbidity), BPD in a relative (relative comorbidity), and relative's age, sex, and relationship to proband (parent, sibling, child)