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Familial Aggregation of Candidate Phenotypes for Borderline Personality Disorder

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Abstract

Borderline personality disorder (BPD) and its core DSM factor-analytically derived phenotypes aggregate in families. To potentially inform future conceptualizations of BPD, this study examined the familial aggregation and coaggregation with BPD of three additional candidate phenotypes for BPD psychopathology: anxiousness, aggressiveness and cognitive dysregulation. Participants included 347 probands (126 with BPD, 128 without BPD, and 93 with major depressive disorder) and 814 parents and siblings of probands. All participants completed diagnostic assessments and scales assessing the candidate phenotypes. The familial aggregation of phenotypes (correlation of level of phenotype between family members), the familial coaggregation of phenotypes with BPD (correlation of phenotype with BPD between family members), and the within-individual correlation of phenotypes with BPD were assessed. All three candidate phenotypes showed high levels of familial aggregation (r's = .14 – .53, p's < .001), the magnitudes of which were comparable to DSM-based core sectors of psychopathology. Anxiousness and cognitive dysregulation showed strong within-individual associations with BPD (r's = .55 and .46, respectively; p's < .001) and substantial familial coaggregation with BPD (r's = .12 and .13, respectively; p's ≤ .002). In contrast, aggressiveness showed a weak within-individual association with BPD (r = .11, p = .12) and little familial coaggregation with BPD (r = .05, p = .21). These findings suggest that anxiousness and cognitive dysregulation are promising phenotypes for BPD psychopathology that move beyond factor-analytically based conceptualizations. In contrast, aggressiveness was only weakly related to BPD, suggesting that this phenotype may not represent an essential feature of this disorder.

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Keywords

Aggression; anxiety; borderline personality disorder; cognitive dysregulation; family study; psychiatric genetics

Defining the essential characteristics of borderline personality disorder (BPD) is a challenge that has faced researchers and clinicians for decades (Grinker, Werble, & Drye, 1968; Gunderson & Singer, 1975; Kernberg, 1967; Knight, 1953; Perry & Klerman, 1978). The validity of the core sectors of BPD psychopathology (i.e., affective, interpersonal, behavioral and cognitive) reflected in the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM) is supported not only by factor analytic studies, but also by family and twin studies, which demonstrate high levels of familial aggregation for BPD and for each of the core sectors (Gunderson, Zanarini, et al., 2011), and heritability estimates of BPD ranging from 35%–67% (Bornovalova, Hicks, Iacono, & McGue, 2009; Distel et al., 2008; Kendler et al., 2008; Torgersen et al., 2000). The construct of BPD is additionally supported by behavioral genetics research (Amad, Ramoz, Thomas, Jardri, & Gorwood, 2014; Distel et al., 2008) and studies on its temporal stability and course (Bornovalova et al., 2009; Gunderson, Stout, et al., 2011). Furthermore, the relationship of BPD to its core sectors of psychopathology is best explained by a model whereby the sectors are manifestations of a unitary liability to BPD (Distel et al., 2010; Kendler, Myers, & Reichborn-Kjennerud, 2011; Merikangas & Swendsen, 1997).

In addition to previously established core sectors of BPD psychopathology (Gunderson, Zanarini, et al., 2011), more narrowly defined “phenotypes” (used here to indicate a collection of related traits that is a manifestation of underlying BPD liability) may also hold promise as key features of BPD. *Aggressivity*, though partly reflected in the affective, behavioral, and interpersonal factors, has not been adequately represented in prior research despite its central role in Kernberg’s seminal theory-based conceptualization of BPD (Kernberg, 1967). The criterion of inappropriate and intense anger in the DSM is more closely tied to an affective instability phenotype for BPD rather than aggression (Chabrol, Montovany, Callahan, Chouicha, & Duconge, 2002; Sanislow et al., 2002). Anxiety is pervasive in BPD (Zanarini, Frankenburg, & Fitzmaurice, in press) and while it is not specific to this disorder (Zanarini et al., 1998), anxiety symptoms are elevated in relatives of individuals with BPD (Bandelow et al., 2005). Still, the familial aggregation of *anxiousness* and its familial coaggregation with BPD has not been studied. *Cognitive dysregulation* represents the tendency for thinking to become disorganized, especially during times of stress, and to experience unusual perceptions and ideas. This phenotype overlaps with the factor-analytically established cognitive core sector of BPD psychopathology. However, a broader phenotype of cognitive dysregulation that encompasses quasi-psychotic thought and hallucination-like experiences, symptoms that may be distinguishing characteristics of BPD (Zanarini, Frankenburg, Wedig, & Fitzmaurice, 2013; Zanarini, Gunderson, & Frankenburg, 1990), may be useful for detecting subtle variations in this domain that may aggregate in families.

The present study reports on data from a family study to examine whether aggressivity, anxiousness and cognitive dysregulation represent possible additional important phenotypes of BPD psychopathology that may inform diagnostic conceptualizations of this study. The primary aims of this study were to determine the familial aggregation of these candidate phenotypes, and the familial coaggregation of these phenotypes with BPD.

Method

Participants

Three groups of probands were recruited: 1) individuals with BPD, 2) individuals without a lifetime diagnosis of BPD, and 3) individuals with a lifetime diagnosis of major depressive disorder (MDD), with or without a lifetime diagnosis of BPD. Probands were eligible to participate if they were female, 18 to 35 years old, had no physical or neurological condition that could cause serious psychiatric symptoms or intellectual disability, and had at least two parents or siblings who were willing to participate who did not have a lifetime diagnosis of schizophrenia, schizoaffective disorder, or bipolar I disorder. Some of the probands with BPD or with MDD were recruited from McLean Hospital inpatient units and partial hospital program, while members of all three diagnostic groups were recruited using advertisements on posters, radio, and the internet. Individuals were first screened by telephone to determine whether they presumptively met criteria for the study, and their diagnoses were subsequently confirmed by interview.

Procedures

This study was approved by the McLean Hospital Institutional Review Board. Written informed consent was obtained from the participants after all aspects of the study were explained thoroughly and before the administration of any study procedures.

All participants (probands and relatives) completed four semi-structured interviews that were administered by clinically experienced raters: 1) the Background Information Schedule (Zanarini, Frankenburg, Khera, & Bleichmar, 2001), which assesses demographic information, psychosocial functioning, and history of psychiatric treatment; 2) the Structured Clinical Interview for DSM-IV Axis I Disorders (First, Spitzer, Gibbon, & Williams, 2002); 3) the Diagnostic Interview for DSM-IV Personality Disorders (DIPD-IV) (Zanarini, Frankenburg, Sickel, & Yong, 1996), which assesses each criterion for all DSM-IV personality disorders using a three-point scale (0, not present; 1, present but of uncertain clinical significance; and 2, present and clinically significant); and 4) the Revised Diagnostic Interview for Borderlines (DIB-R) (Zanarini, Gunderson, Frankenburg, & Chauncey, 1989), which assesses the four core sectors of BPD psychopathology (affective, interpersonal, behavioral and cognitive). Interviewers for relatives were unaware of information about probands. Interrater reliability for BPD on the DIPD-IV and DIB-R was κ=1.0. Interrater reliability (as assessed by the intra-class correlation coefficient) for dimensional DIPD-IV ratings ranged from .76 (behavioral) to 1.00 (interpersonal) and for the DIB-R from .93 (cognitive) to .99 (affective) (Gunderson, Zanarini, et al., 2011).

For the candidate phenotypes, the following measures were used: 1) Buss-Perry Aggression Questionnaire (Buss & Perry, 1992) scales for hostility, physical aggression and verbal aggression, which have internal consistency reliabilities ranging from .72_.85, and 2) Dimensional Assessment of Personality Pathology_Basic Questionnaire (DAPP_BQ) (Livesley & Jackson, 2009) scales for anxiousness and cognitive dysregulation, with internal consistency reliabilities of .94 and .90, respectively. Cognitive dysregulation on the DAPP_BQ contains items that partly overlap with the DSM criterion-based cognitive phenotype (e.g., stress-related cognitive disturbances and quasi-psychotic thought, dissociative symptoms) but also assesses perceptual distortions (e.g., bodily illusions, auditory hallucination-like experiences). Both forms of cognitive dysregulation are highly prevalent in patients with BPD (Zanarini et al., 2013) and they were jointly examined in statistical analyses under the broader cognitive dysregulation scale from the DAPP-BQ.

Statistical Analysis

Demographic characteristics of probands and relatives were compared using linear regression for continuous variables and the Fisher's exact test for categorical variables.

Familial aggregation of candidate phenotypes was examined by estimating the correlation of the level of a given phenotype in a relative with the level of that phenotype in the corresponding proband using the Pearson product-moment correlation coefficient. Within-individual associations of the phenotypes with BPD were examined by estimating the tetrachoric correlation coefficient. The familial coaggregation of candidate phenotypes with BPD was examined by estimating the correlation of the level of a given phenotype in a relative with the presence of BPD in the corresponding proband using the tetrachoric correlation coefficient.

For comparison purposes, we also estimated the above correlation coefficients corresponding to the familial aggregation, within-person association with BPD, and the familial coaggregation of the four established factor-analytically derived core sectors, as assessed by the DIB-R (with the findings for familial aggregation previously reported (Gunderson, Zanarini, et al., 2011).

For all analyses except for characteristics of the sample, we corrected for the effects of over-sampling probands with BPD and MDD compared with their representation in the source population by weighting participants proportionally to the inverse probability of their selection.

Calculation of the selection probabilities requires knowing the prevalence of BPD from the source population from which our sample was drawn. To calculate the prevalence of BPD, we used a method developed for estimating prevalence from relatives of case and control probands (Javaras, Laird, Hudson, & Ripley, 2010), and employed previously in studies using this sample and others (Hudson, Zanarini, Mitchell, Choi-Kain, & Gunderson, 2014; Waller & Ross, 1997). To calculate the prevalence of MDD, we used the prevalence of MDD from the weighted sample of probands and relatives from the BPD and non-BPD proband groups. The effect of these procedures was to create a pseudo-sample that is representative of families from the underlying source population.

Statistical analyses were carried out using Stata 9.2 (StataCorp, 2006) and Mplus, version 6 (Muthén & Muthén, 2010). All analyses (except for demographic characteristics) adjusted standard errors for the correlation of observations within families. The 2-tailed α level was set at .05.

Results

Characteristics of Participants

A total of 347 probands were interviewed: 126 individuals with BPD (of which 59 were patients and 67 were from the community, 128 individuals without BPD (of which all were from the community), and 93 individuals with MDD (12 of whom also had BPD; 6 were patients and 87 were from the community). Of the 814 parents and siblings of these probands, 294 were in the BPD group, 315 in the non-BPD group, and 205 in the MDD group. Note that because of missing data on some of the measures of the candidate phenotypes, the number of participants presented in this report is slightly less than that reported in previous studies using this sample (Gunderson, Zanarini, et al., 2011; Hudson et al., 2014).

Demographic characteristics of probands and relatives are presented in Table 1. A small and statistically significant, but scientifically inconsequential, difference in mean age was observed between proband groups (mean age of BPD probands was 1.8 years less than MDD probands and 3.1 years less than non-BPD probands).

Familial Aggregation of Candidate Phenotypes

All three of the candidate phenotypes showed statistically significant levels of familial aggregation, with correlations ranging from .14 (cognitive dysregulation) to .53 (aggressiveness) (Table 2). The component traits of aggressiveness (including hostility, physical aggression and verbal aggression) showed similar levels of familial aggregation and all were statistically significant (p's < .001) (Table 2).

Associations of Phenotypes with BPD within Individuals

Anxiousness and cognitive dysregulation were moderately associated with BPD within individuals (r's = .55 and .46, respectively; p's < .001) (Table 2). Whereas aggressiveness and its component traits were highly familial, these phenotypes were not significantly correlated with BPD within individuals (r's ranged from .05 to .12) and notably weaker than those found for the four core BPD sectors (Table 2).

Coaggregation of Phenotypes with BPD between Family Members

Anxiousness and cognitive dysregulation displayed a significant familial coaggregation with BPD (r's = .12 and 13, respectively; p's < .002), and at a level commensurate to the four core sectors of BPD psychopathology (r's ranged from .10 to .18). Aggressiveness and its component traits (hostility, physical aggression, and verbal aggression), however, exhibited low and statistically non-significant levels of familial coaggregation with BPD (r's < .05, p's > .18).

Discussion

The present study provided strong evidence supporting the familial aggregation of three candidate phenotypes for BPD—anxiousness, aggressiveness and cognitive dysregulation. Aggressiveness showed a somewhat higher level of familial aggregation as compared to anxiousness and cognitive dysregulation. These findings are consistent with known levels of familiality for aggressive (Meyer et al., 2000) and anxiety (Skre, Onstad, Edvardsen, Torgersen, & Kringlen, 1994) disorders, and for disorders characterized by cognitive disturbance or dissociation (Hill et al., 2013; Waller & Ross, 1997). All of the candidate phenotypes also showed magnitudes of familial aggregation roughly similar to those of the factor-analytically based core sectors for BPD reported previously (Gunderson, Zanarini, et al., 2011).

In addition to being highly familial, anxiousness and cognitive dysregulation also shared robust associations with BPD, both within individuals and between family members, similar to those of the DSM factor-analytically based core sectors (8). These patterns indicate that anxiousness and cognitive dysregulation are not only linked to a diagnosis of BPD within individuals, but also that BPD coaggregates with these phenotypes in families. Therefore, higher levels of these sectors may reflect familial risk for BPD, suggesting that anxiousness and cognitive dysregulation may form essential features of BPD.

In striking contrast to anxiousness and cognitive dysregulation, aggressiveness showed only a very weak and non-significant relationship with BPD based on analyses of its association with BPD within individuals and between family members (coaggregation). Aggressiveness is a multifaceted phenotype that includes such symptom dimensions as hostility and both verbal and physical aggression. Whereas verbal aggression showed perhaps a modest (albeit not statistically significant) association with BPD within individuals, neither this trait nor the other component phenotypes of aggressiveness showed a significant association with BPD between family members. These results challenge the notion that aggressiveness may be a central feature of BPD (McCloskey et al., 2009).

These findings may inform future diagnostic conceptualizations of BPD by highlighting candidate phenotypes that may represent important features of the disorder, potentially aiding with clinical diagnosis and possibly with differentiation from other related disorders. Based on the current findings and prior work on the DAPP-BQ (Pukrop et al., 2009), it may be reasonable to speculate, for example, that anxiousness is less specifically associated with BPD as compared to cognitive dysregulation. Future research on these candidate phenotypes for BPD should evaluate their overlap with and distinctiveness from phenotypes for other personality disorders. In addition, treatment approaches may address these symptoms as well as the more recognized features of BPD, including among family members who may be at an increased risk for psychopathology.

There are several limitations of this study that should be considered. First, probands were not sampled randomly from a defined source population, which may have led to an ascertainment bias if recruited probands were not representative of individuals with these disorders in the source population. As previously discussed (Gunderson, Zanarini, et al.,

2011), however, there is no evidence in this dataset for a significant interaction between source of proband recruitment (hospital versus community) and measures of familial aggregation of BPD, suggesting that the recruitment sources yielded similarly representative probands. Additionally, aside from disorders excluded by design, probands were recruited without knowledge of whether they had other comorbid mental disorders. Second, we had insufficient power to evaluate the potential effects of sex, age, or other covariates. However, no evidence for effects of age and sex was found with this dataset in our previous analyses of familial aggregation of BPD (Gunderson, Zanarini, et al., 2011), nor have twin studies found evidence of sex effects for the heritability of BPD (Distel et al., 2010). Nevertheless, it is possible that the patterns of associations observed in the current study, particularly the minimal relationship of aggressiveness with BPD, may be related to the recruitment of female probands, limiting generalizability of these findings to males with BPD. Third, we used weighting based on the inverse probability of selection using a novel estimator of the prevalence of BPD derived from the data on relatives, rather than a direct assessment of prevalence. Any additional uncertainty attributable to use of this method is not reflected in the standard errors, but any such uncertainty would, in any event, be expected to be small relative to other sources. Fourth, not all eligible parents and siblings chose to participate, and thus this missing data could have introduced bias if the characteristics of the non-interviewed relatives were substantially different from those of the interviewed relatives.

In conclusion, on the basis of within-individual associations with BPD and familial coaggregation with BPD, anxiousness and cognitive dysregulation appear closely related to BPD and, like the factor-analytically based sectors in the DSM, these phenotypes might represent further manifestations of the spectrum of symptoms that stems from an underlying BPD liability. By contrast, aggressiveness is a highly familial entity, but one that appears only very weakly associated with BPD, and thus is unlikely to be an essential component of BPD.

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References

Amad A, Ramoz N, Thomas P, Jardri R, Gorwood P. Genetics of borderline personality disorder: systematic review and proposal of an integrative model. Neuroscience and Biobehavioral Reviews. 2014; 40:6–19.10.1016/j.neubiorev.2014.01.003 [PubMed: 24456942]

Bandelow B, Krause J, Wedekind D, Broocks A, Hajak G, Ruther E. Early traumatic life events, parental attitudes, family history, and birth risk factors in patients with borderline personality disorder and healthy controls. Psychiatry Research. 2005; 134(2):169–179.10.1016/j.psychres.2003.07.008 [PubMed: 15840418]

Bornovalova MA, Hicks BM, Iacono WG, McGue M. Stability, change, and heritability of borderline personality disorder traits from adolescence to adulthood: a longitudinal twin study. Development and Psychopathology. 2009; 21(4):1335–1353.10.1017/S0954579409990186 [PubMed: 19825271]

Buss AH, Perry M. The aggression questionnaire. Journal of Personality and Social Psychology. 1992; 63(3):452.10.1037/0022-3514.63.3.452 [PubMed: 1403624]

Chabrol H, Montovany A, Callahan S, Chouicha K, Duconge E. Factor analyses of the DIB-R in adolescents. Journal of Personality Disorders. 2002; 16(4):374–384.10.1521/pedi.16.4.374.24123 [PubMed: 12224129]

Distel MA, Willemsen G, Ligthart L, Derom CA, Martin NG, Neale MC, Boomsma DI. Genetic covariance structure of the four main features of borderline personality disorder. Journal of Personality Disorders. 2010; 24(4):427–444.10.1521/pedi.2010.24.4.427 [PubMed: 20695804]

Distel MA, Trull TJ, Derom CA, Thiery EW, Grimmer MA, Martin NG, Boomsma DI. Heritability of borderline personality disorder features is similar across three countries. Psychological Medicine. 2008; 38(09):1219–1229.10.1017/S0033291707002024 [PubMed: 17988414]

First, MB.; Spitzer, RL.; Gibbon, M.; Williams, J. Structured clinical interview for DSM-IV axis I disorders — patient edition (SCID-I/P, 11/2002 revision). New York, NY: Biometrics Research Department, New York State Psychiatric Institute; 2002.

Grinker, Roy Richard; Werble, Beatrice; Drye, Robert C. The borderline syndrome: A behavioral study of ego-functions. Basic books; New York: 1968.

Gunderson JG, Singer MT. Defining borderline patients: an overview. American Journal of Psychiatry. 1975; 132(1):1–10. [PubMed: 802958]

Gunderson JG, Stout RL, McGlashan TH, Shea MT, Morey LC, Grilo CM, Skodol AE. Ten-year course of borderline personality disorder: psychopathology and function from the Collaborative Longitudinal Personality Disorders study. Archives of General Psychiatry. 2011; 68(8):827–837.10.1001/archgenpsychiatry.2011.37 [PubMed: 21464343]

Gunderson JG, Zanarini MC, Choi-Kain LW, Mitchell KS, Jang KL, Hudson JI. Family study of borderline personality disorder and its sectors of psychopathology. Archives of General Psychiatry. 2011; 68(7):753–762.10.1001/archgenpsychiatry.2011.65 [PubMed: 21727257]

Hill SK, Reilly JL, Keefe RS, Gold JM, Bishop JR, Gershon ES, Sweeney JA. Neuropsychological impairments in schizophrenia and psychotic bipolar disorder: Findings from the Bipolar-Schizophrenia Network on Intermediate Phenotypes (B-SNIP) study. American Journal of Psychiatry. 2013; 170(11):1275–1284.10.1176/appi.ajp.2013.12101298 [PubMed: 23771174]

Hudson JI, Zanarini MC, Mitchell KS, Choi-Kain LW, Gunderson JG. The contribution of familial internalizing and externalizing liability factors to borderline personality disorder. Psychological Medicine. 2014:1–11.10.1017/S0033291713003140 [PubMed: 24406267]

Javaras KN, Laird NM, Hudson JI, Ripley BD. Estimating disease prevalence using relatives of case and control probands. Biometrics. 2010; 66(1):214–221.10.1111/j.1541-0420.2009.01272.x [PubMed: 19459833]

Kendler KS, Aggen SH, Czajkowski N, Roysamb E, Tambs K, Torgersen S, Reichborn-Kjennerud T. The structure of genetic and environmental risk factors for DSM-IV personality disorders: a multivariate twin study. Archives of General Psychiatry. 2008; 65(12):1438–1446.10.1001/archpsyc.65.12.1438 [PubMed: 19047531]

Kendler KS, Myers J, Reichborn-Kjennerud T. Borderline personality disorder traits and their relationship with dimensions of normative personality: a web-based cohort and twin study. Acta Psychiatrica Scandinavica. 2011; 123(5):349–359.10.1111/j.1600-0447.2010.01653.x [PubMed: 21198457]

Kernberg O. Borderline personality organization. Journal of the American Psychoanalytic Association. 1967; 15(3):641–685. [PubMed: 4861171]

Knight RP. Borderline states. Bulletin of the Menninger Clinic. 1953; 17(1):1–12. [PubMed: 13009379]

Livesley, WJ.; Jackson, D. Manual for the Dimensional Assessment of Personality Pathology—Basic Questionnaire. Port Huron, MI: Sigma; 2009.

McCloskey MS, New AS, Siever LJ, Goodman M, Koenigsberg HW, Flory JD, Coccaro EF. Evaluation of behavioral impulsivity and aggression tasks as endophenotypes for borderline personality disorder. Journal of Psychiatric Research. 2009; 43(12):1036–1048.10.1016/j.jpsychires.2009.01.002 [PubMed: 19232640]

Merikangas KR, Swendsen JD. Genetic epidemiology of psychiatric disorders. Epidemiologic Reviews. 1997; 19(1):144–155. [PubMed: 9360911]

Meyer JM, Rutter M, Silberg JL, Maes HH, Simonoff E, Shillady LL, Eaves LJ. Familial aggregation for conduct disorder symptomatology: the role of genes, marital discord and family adaptability. Psychological Medicine. 2000; 30(4):759–774. [PubMed: 11037084]

Muthén, Linda K.; Muthén, Bengt O. Mplus: Statistical analysis with latent variables: User's guide. Muthén & Muthén; 2010.

Perry JC, Klerman GL. The borderline patient. A comparative analysis of four sets of diagnostic criteria. Archives of General Psychiatry. 1978; 35(2):141–150. [PubMed: 623500]

Pukrop, Ralf; Steinbring, Iris; Gentil, Iris; Schulte, Caspar; Larstone, Roseann; Livesley, John W. Clinical Validity of the "Dimensional Assessment of Personality Pathology (DAPP)" for Psychiatric Patients With and Without a Personality Disorder Diagnosis. Journal of Personality Disorders. 2009; 23(6):572–586.10.1521/pedi.2009.23.6.572 [PubMed: 20001176]

Sanislow CA, Grilo CM, Morey LC, Bender DS, Skodol AE, Gunderson JG, McGlashan TH. Confirmatory factor analysis of DSM-IV criteria for borderline personality disorder: findings from the collaborative longitudinal personality disorders study. American Journal of Psychiatry. 2002; 159(2):284–290.10.1176/appi.ajp.159.2.284 [PubMed: 11823272]

Skre I, Onstad S, Edvardsen J, Torgersen S, Kringlen E. A family study of anxiety disorders: familial transmission and relationship to mood disorder and psychoactive substance use disorder. Acta Psychiatrica Scandinavica. 1994; 90(5):366–374.10.1111/j.1600-0447.1994.tb01608.x [PubMed: 7872042]

StataCorp, LP. Stata/SE 9.2 for Windows. StataCorp LP; College Station, TX, USA: 2006.

Torgersen S, Lygren S, Oien PA, Skre I, Onstad S, Edvardsen J, Kringlen E. A twin study of personality disorders. Comprehensive Psychiatry. 2000; 41(6):416–425.10.1053/comp.2000.16560 [PubMed: 11086146]

Waller NG, Ross CA. The prevalence and biometric structure of pathological dissociation in the general population: taxometric and behavior genetic findings. Journal of Abnormal Psychology. 1997; 106(4):499–510.10.1037/0021-843X.106.4.499 [PubMed: 9358680]

Zanarini MC, Frankenburg FR, DeLuca CJ, Hennen J, Khera GS, Gunderson JG. The pain of being borderline: dysphoric states specific to borderline personality disorder. Harvard Review of Psychiatry. 1998; 6(4):201–207.10.3109/10673229809000330 [PubMed: 10370445]

Zanarini MC, Frankenburg FR, Fitzmaurice GM. Severity of anxiety symptoms reported by borderline patients and axis II comparison subjects: description and prediction over 16 years of prospective follow-up. Journal of Personality Disorders. (in press). 10.1521/pedi_2014_28_141

Zanarini MC, Frankenburg FR, Khera GS, Bleichmar J. Treatment histories of borderline inpatients. Comprehensive Psychiatry. 2001; 42(2):144–150.10.1053/comp.2001.19749 [PubMed: 11244151]

Zanarini MC, Frankenburg FR, Wedig MM, Fitzmaurice GM. Cognitive experiences reported by patients with borderline personality disorder and axis II comparison subjects: a 16-year prospective follow-up study. American Journal of Psychiatry. 2013; 170(6):671–679.10.1176/appi.ajp.2013.13010055 [PubMed: 23558452]

Zanarini MC, Gunderson JG, Frankenburg FR. Cognitive features of borderline personality disorder. American Journal of Psychiatry. 1990; 147(1):57–63. [PubMed: 2293789]

Zanarini, Mary C.; Gunderson, John G.; Frankenburg, Frances R.; Chauncey, Deborah L. The revised diagnostic interview for borderlines: discriminating BPD from other axis II disorders. Journal of Personality Disorders. 1989; 3(1):10–18.10.1521/pedi.1989.3.1.10

Zanarini, MC.; Frankenburg, FR.; Sickel, AE.; Yong, L. The diagnostic interview for DSM-IV personality disorders (DIPD-IV). Belmont, MA: McLean Hospital; 1996.

Table 1

Demographic characteristics of proband and relative groups with borderline personality disorder, without borderline personality disorder, and with major depressive disorder.

	BPD	Non-BPD	Major Depressive Disorder
Probands			
Total, No.	126	128	93
Age, y, mean (SD)	23.9 (4.7)	25.8 (4.8)	27.1 (5.1)
Female sex, No. (%)	126 (100)	128 (100)	93 (100)
Race/Ethnicity, No. (%)			
White	90 (71)	84 (66)	61 (66)
African-American	14 (11)	22 (17)	16 (17)
Hispanic	19 (15)	20 (16)	12 (13)
Other	3 (2)	2 (2)	4 (4)
Socioeconomic Status, mean (SD)	2.6 (1.2)	2.6 (1.0)	2.6 (1.2)
Relatives			
Total, No.	294	315	205
Age, y, mean (SD)	41.8 (14.8)	40.8 (15.5)	42.3 (16.2)
Relationship to proband, No. (%)			
Mother	107 (36)	103 (33)	73 (36)
Father	69 (23)	53 (17)	37 (18)
Sister	70 (24)	101 (32)	65 (32)
Brother	48 (16)	58 (18)	30 (15)

Abbreviation: BPD, borderline personality disorder.

Note: There were no significant differences in characteristics between proband or relative groups except that the mean age of BPD probands was significantly lower than non-BPD probands (P =.002) and MDD probands (P <.001).

Table 2

Familial aggregation of candidate phenotypes and their coaggregation with borderline personality disorder.

	Familial Aggregation			Relationship of Phenotype to BPD					
				Co-occurrence with BPD within individuals			Coaggregation with BPD between family members		
	r^a	SE	*P*	r^b	SE	*P*	r^c	SE	*P*
Candidate Phenotype									
Anxiousness	.21	.04	<.001	.55	.09	<.001	.12	.04	.001
Cognitive dysregulation	.14	.05	.002	.46	.05	<.001	.13	.04	.002
Aggressiveness									
Hostility	.48	.03	<.001	.12	.07	.076	.05	.04	.20
Physical	.56	.03	<.001	.05	.07	.47	.05	.04	.18
Verbal	.43	.03	<.001	.10	.06	.094	.00	.04	1.0
Total	.53	.03	<.001	.11	.17	.12	.05	.04	.21
Core Sectors (DIB-R)									
Affective	.25	.05	<.001	.89	.02	<.001	.16	.04	<.001
Interpersonal	.25	.04	<.001	.67	.03	<.001	.18	.04	<.001
Behavioral	.18	.03	<.001	.72	.03	<.001	.18	.04	<.001
Cognitive	.16	.04	<.001	.54	.04	<.001	.10	.04	.014

[a] Correlation of phenotype in relative with phenotype in proband.

[b] Correlation of phenotype with BPD within individuals (regardless of status as proband or relative)

[c] Correlation of phenotype in relative with BPD in proband

Note: Based on 814 relatives and 347 probands with complete data on all variables.