**Supplementary Materials**

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| Table S1 |
| *Psychiatric Medication History for Proband and Relative Groups with Borderline Personality Disorder, and Healthy Control Groups* |
|   |  |   |  |   |
|  | Proband | Relative | Control | Fisher’s exact test *p*-valued |
|  | (*n* = 99) | (*n* = 74) | (*n* = 99) |  |
| *Drug Usage* | Life-time | Past 3 Weeks | Life-time | Past 3 Weeks | Life-time | Past 3 Weeks | Life-time | Past 3 Weeks |
|
| *Drug Class* | % | % | % | % | % | % |
|  |  |  |  |  |  |  |  |  |
| Sedatives | 64.65 | 27.27 | 22.97 | 8.11 | 2.02 | 0 | .000 | .002 |
| Stimulants | 22.22 | 15.31a | 9.46 | 2.7 | 0 | 0 | .038 | .008 |
| Minor Tranquilizers | 16.16 | 8.08 | 9.46 | 2.7 | 1.01 | 0 | .259 | .192 |
| Neuroleptics/Major Tranquilizers | 12.24a | 7.22b | 1.35 | 0 | 0 | 0 | .008 | .020 |
| Antidepressants | 88.89 | 53.54 | 25.68 | 12.33c | 0 | 0 | .000 | .000 |
| Mood Stabilizer | 28.28 | 9.09 | 2.7 | 1.35 | 0 | 0 | .000 | .045 |
| Antiparkinson Agents | 2.02 | 1.01 | 0 | 0 | 0 | 0 | .508 | 1.000 |
| Antipsychotic Drugs | 41.84a | 24.24 | 2.7 | 0 | 0 | 0 | .000 | .000 |
| *Note.* a Percentage calculated out of 98 participants. b Percentage calculated out of 97 participants. c Percentage calculated out of 73 participants. dTwo-tailed Fisher’s exact tests were used only to compare probands and relatives because controls were recruited without a personal history of psychiatric disorder and therefore infrequently reported a lifetime history of having been prescribed a psychoactive medication. Other prescribed psychoactive drugs (e.g., marijuana) are not included in the table.  |

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| Table S2*Unadjusted Descriptive Statistics for Dimensional Personality Disorder Scales from the Structured Interview for DSM-IV Personality* |
|   |   |   |   | Proband |   | Relative |   | Control |
|  |  |  |  | (n=103) |   | (n=73) |   | (n=99) |
|  | Personality Disorder Scale |   |   | M | SD |   | M | SD |   | M | SD |
|  | Paranoid |  | 35.04 | 21.97 |  | 8.74 | 10.16 |  | 2.26 | 4.37 |
|  | Schizoid | 9.85 | 10.21 |  | 7.11 | 11.39 |  | 2.26 | 4.53 |
|  | Schizotypal |  |  | 19.42 | 12.4 |  | 4.62 | 5.78 |  | 0.82 | 1.87 |
|  | Antisocial |  | 22.1 | 18.47 |  | 4.44 | 7.91 |  | 0.34 | 1.4 |
|  | Borderline |  | 80.94 | 11.68 |  | 12.68 | 14.26 |  | 1.23 | 2.37 |
|  | Histrionic | 21.12 | 18.21 |  | 4.85 | 6.63 |  | 1.77 | 2.98 |
|  | Narcissistic | 24.5 | 21.68 |  | 6.26 | 9.52 |  | 1.35 | 2.81 |
|  | Avoidant |  |  | 38.93 | 25.37 |  | 11.68 | 14.83 |  | 2.21 | 4.63 |
|   | Dependent |   | 33.09 | 21.4 |  | 4.62 | 8.17 |   | 0.63 | 1.82 |
|  | Obsessive-Compulsive |  | 26.82 | 16.16 |   | 13.76 | 11.13 |  | 5.3 | 7.04 |
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*Note. M=*mean*. SD*=standard deviation. Scale scores were calculated based on a percentage of the total possible rating summed across all items for each personality disorder.

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| Table S3*Unadjusted Descriptive Statistics for the First- and Second-Order Factor Scales on the Barrett Impulsiveness Scale-11* |
|  |  |  |  |  |  |  |  |  |  |  |  |
|   |   |   |   | Proband |   | Relative |   | Control |
|  |  |  |  | (n=98) |   | (n=72) |   | (n=96) |
| Subscale |   |   | M | SD |   | M | SD |   | M | SD |
| First order variable |  |  |  |  |  |  |  |  |  |
|  | Attention |  | 2.7291 | 0.6282 |  | 2.0250 | 0.5910 |  | 1.5750 | 0.3863 |
|  | Cognitive Instability | 2.7925 | 0.6250 |  | 1.8704 | 0.6441 |  | 1.4115 | 0.4202 |
|  | Motor |  |  | 2.6142 | 0.5195 |  | 1.9851 | 0.4209 |  | 1.8695 | 0.4074 |
|  | Perseverance |  | 2.4464 | 0.5713 |  | 1.7072 | 0.5087 |  | 1.5200 | 0.4006 |
|  | Self-Control |  | 2.7639 | 0.5959 |  | 1.8009 | 0.5363 |  | 1.5948 | 0.4755 |
|  | Cognitive Complexity | 2.6556 | 0.5573 |  | 2.2431 | 0.5417 |  | 1.9479 | 0.3627 |
| Second order variable |  |  |  |  |  |  |  |  |  |
|  | Attentional Impulsiveness | 2.7526 | 0.5258 |  | 1.9678 | 0.5132 |  | 1.5138 | 0.3452 |
|  | Motor |  |  | 2.5529 | 0.4461 |  | 1.8847 | 0.3743 |  | 1.7411 | 0.3347 |
|   | Non-planning |   | 2.7154 | 0.4806 |   | 2.0011 | 0.4660 |   | 1.7551 | 0.3528 |
| *Note. M=*mean*. SD*=standard deviation. Subscales coded according to factor structure presented in Patton et al. (1995). |

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| Table S4*Unadjusted Descriptive Statistics for Subscales of the Difficulties in Emotion Regulation Scale* |
|  |  |  |  |  |  |  |  |  |  |  |
|   |   |   | Proband |   | Relative |   | Control |
|  |  |  | (n=91) |   | (n=73) |   | (n=96) |
| Subscale |   | M | SD |   | M | SD |   | M | SD |
| Non-acceptance of emotional responses |  | 3.2912 | 1.1226 |  | 2.0046 | 0.9217 |  | 1.4236 | 0.4890 |
| Difficulty engaging in goal-directed behaviour |  | 4.0352 | 0.7880 |  | 2.6384 | 0.8587 |  | 2.0771 | 0.7641 |
| Impulse control difficulties |  | 3.4480 | 0.9487 |  | 1.6484 | 0.6970 |  | 1.2726 | 0.3893 |
| Lack of emotional awareness |  | 2.7674 | 0.9428 |  | 2.2078 | 0.8286 |  | 2.0313 | 0.7304 |
| Limited access to emotion regulation strategies |  | 3.5475 | 0.8346 |  | 1.8946 | 0.8189 |  | 1.3242 | 0.4766 |
| Lack of emotional clarity |   | 3.0615 | 0.9488 |   | 1.8575 | 0.7360 |   | 1.5198 | 0.4665 |

*Note. M=*mean*. SD*=standard deviation. Subscales coded according to factor structure presented in Gratz and Roemer (2004).

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| Table S5*Unadjusted Descriptive Statistics for Subscales of the Big Five Inventory* |
|  |  |  |  |  |  |  |  |  |  |
|   |   | Proband |   | Relative |   | Control |
|  |  | (n=79) |   | (n=64) |   | (n=89) |
| Subscale |   | M | SD |   | M | SD |   | M | SD |
| Extraversion |  | 2.9498 | 0.8690 |  | 3.1328 | 0.9123 |  | 3.5225 | 0.8657 |
| Agreeableness |  | 3.3005 | 0.7412 |  | 4.0642 | 0.5761 |  | 4.3695 | 0.4834 |
| Conscientiousness |  | 2.9752 | 0.7893 |  | 3.9082 | 0.7628 |  | 4.2335 | 0.6468 |
| Neuroticism |  | 4.1994 | 0.5613 |  | 2.6484 | 0.9158 |  | 1.9882 | 0.6800 |
| Openness |   | 3.8274 | 0.6501 |   | 3.6578 | 0.6401 |   | 3.6448 | 0.6032 |

*Note*. M=mean. SD = standard deviation. Subscales coded according to factor structure presented in John and Srivastava (1999).

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| Table S6*Unadjusted Descriptive Statistics for Symptom and Personality Measures for Non-Affected Relatives* |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   |   |  |   | Non-Affected Relatives |   |
|  |  |  |   | (n=32) |   |
|  |   |   | M | SD |   |
| BIS Subscales |  |  |  |  |  |
| Attention |  |  | 1.9688 | 0.5839 |  |
| Cognitive Instability |  |  | 1.8125 | 0.6276 |  |
| Motor |  |  | 1.9531 | 0.3544 |  |
| Perseverance |  |  | 1.7188 | 0.5227 |  |
| Self-Control |  |  | 1.7500 | 0.4937 |  |
| Cognitive Complexity |  |  | 2.1313 | 0.4967 |  |
| DERS Subscales |  |  |  |  |  |
| Non-acceptance of emotional responses |  |  | 1.8594 | 0.7703 |  |
| Difficulty engaging in goal-directed behavior |  |  | 2.4938 | 0.7466 |  |
| Impulse control difficulties |  |  | 1.3958 | 0.4333 |  |
| Lack of emotional awareness |  |  | 2.2083 | 0.8392 |  |
| Limited access to emotion regulation strategies |  |  | 1.5999 | 0.5231 |  |
| Lack of emotional clarity |  |  | 1.6750 | 0.6196 |  |
| BFI Subscales |  |  |  |  |  |
| Extraversion |  |  | 3.2366 | 0.7738 |  |
| Agreeableness |  |  | 4.2302 | 0.5392 |  |
| Conscientiousness |  |  | 4.0481 | 0.7417 |  |
| Neuroticism |  |  | 2.1696 | 0.7114 |  |
| Openness |  |  | 3.6143 | 0.6564 |  |

*Note:* M= mean, SD= Standard Deviation. DERS subscales coded according to factor structure presented in Gratz and Roemer (2004). BFI subscales coded according to factor structure presented in John and Srivastava (1999). BIS subscales coded according to factor structure presented in Patton et al. (1995). For BFI subscales, non-affected relatives *n*= 28.

Table S7

*Odds Ratios for Lifetime Rates of Psychiatric Disorders in Probands with Borderline Personality Disorder (n=103) versus First-Degree Relatives (n=74)*

|  |  |  |
| --- | --- | --- |
| Diagnosis | Odds Ratio  | 95% Confidence Interval |
| Schizoaffective disorder | 0.24 | (0.01 – 5.89)  |
| Bipolar II | 1.08 | (0.18 – 6.63) |
| Major depressive disorder | 14.42  | (6.76 - 30.79)\*\*\* |
| dysthymic disorder | 11.58 | (0.65 – 206.02) |
| Alcohol-Induced mood disorder | 0.24 | (0.01 – 5.89) |
| Substance-Induced mood disorder | 0.24 | (0.01 – 5.89) |
| Alcohol abuse | 1.49 | (0.53 – 4.18) |
| Alcohol dependence | 2.86 | (1.28 – 6.34)\*\* |
| Substance abuse | 6.15 | (0.75 – 50.26) |
| Polysubstance dependence  | 5.19 | (0.26 – 101.99) |
| Panic Disorder without agoraphobia | 1.82 | (0.61 – 5.41) |
| Panic Disorder with agoraphobia  | 8.14 | (1.83 – 36.15)\*\* |
| Agoraphobia without history of panic disorder | 0.96 | (0.21 – 4.41) |
| Social phobia | 4.44 | (1.74 – 11.36)\*\* |
| Specific phobia | 1.99 | (0.51 – 7.78) |
| Obsessive-compulsive disorder | 30.14 | (1.78 – 509.89)\* |
| Posttraumatic stress disorder | 7.74 | (2.87 – 20.88)\*\*\* |
| Generalized anxiety disorder  | 3.46 | (1.11 – 10.75)\* |
| Substance-induced anxiety disorder | 2.18 | (0.09 – 54.28) |
| Anorexia nervosa | 14.98 | (0.86 – 261.56) |
| Bulimia nervosa | 6.99 | (0.87 – 56.43) |
| Binge-Eating disorder | 4.52 | (0.53 – 38.33) |

*\*p* < .05; *\*\*p* <.01;*\*\*\*p* <.0001 (Fisher’s exact test, two-tailed)

Table S8

*Lifetime Psychiatric Disorders in Probands with BPD, First-Degree Relatives, and Controls*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|   |   | Proband | Relative | Control |
| Diagnosis | (n=101) | (n=74) | (n=99) |
|   |   | n | % | n | % | n | % |
| Schizophrenia or Schizoaffective Disorder | 5 | 4.95 | 5 | 6.76 | 0 | 0 |
| Bipolar Disorder | 15 | 14.85 | 13 | 17.57 | 0 | 0 |
| Depressive Disorder | 61 | 60.4 | 70 | 94.59 | 0 | 0 |
| Anxiety Disorder | 50 | 49.5 | 65 | 87.84 | 0 | 0 |
| Alcoholism | 39 | 38.61 | 44 | 59.46 | 0 | 0 |
| Substance Abuse | 17 | 16.83 | 33 | 44.59 | 0 | 0 |
|  |  |  |  |  |  |  |  |
| *Note:* The table presents the first-degree (mothers, fathers, full siblings and children) family history of psychiatric disorder based on a combination of (a) queries about any knowledge of first-degree relatives’ psychiatric diagnoses (including those that did not participate in the present study) and/or treatment of psychiatric conditions, and (b) confirmed psychiatric diagnoses of relatives based on structured clinical interviews conducted in the present study. |

**Supplemental Methods**

Eligibility criteria for all participants included the following: 16-65 years old (18-65 for probands with BPD); English-speaking; capable to provide written informed consent; no major physical or neurological illness (e.g., seizure disorder); no visual, hearing or manual limitations that would affect performance on laboratory procedures; no history of a severe neurodevelopmental disorder (e.g., autism-spectrum disorder, Down syndrome); no history of significant head trauma (≥ 20 min loss of consciousness and/or > 24 hours posttraumatic amnesia); no current (past month) alcohol or non-alcohol substance abuse or dependence; and no extensive history of alcohol or non-alcohol substance dependence. Probands were required to have a current (at least within the past five years) diagnosis of BPD based on the Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV; American Psychiatric Association, 2000); no history of any psychotic disorder or bipolar I disorder; and at least one first-degree biological relative who was willing and eligible to participate in the study.

To assess potential systematic ascertainment biases related to recruiting probands that were in contact with relatives (*n* = 56) and who were agreeable to participating in the study, we also recruited a sample of probands without available relatives (*n* = 47). The groups did not differ in age, *t*(101) = 1.20, *p* = .23, sex, Fisher’s exact test (two-sided), *p* = .73, years of education, *t*(101) = .30, *p* = .77, or Global Assessment of Function (GAF) (Hall, 1995) scale score, *t*(101) = -1.07, *p* = .29, suggesting that probands with relatives in the study were not different in major demographic characteristics or global clinical severity compared to probands who did not have available relatives. Therefore, the two proband groups were combined in subsequent analyses. There were no additional psychiatric exclusions for relatives so that we could examine the risk for a broad spectrum of psychiatric disorders in this group (except for the aforementioned substance use disorder exclusions that could feasibly affect the intermediate phenotype measures). Additional exclusions for non-psychiatric controls included any personal or first-degree familial history of a DSM-IV psychiatric disorder or suicide attempt; substantial number of personality disorder symptoms within any one DSM-IV cluster; and any consultation with a health professional for mental health concerns with or without a history of pharmacological or psychological treatment.

Following semi-structured interviews, narrative case reports were prepared for each participant and reviewed in a “best estimate” style consensus diagnostic meeting (Klein *et al.* 1994) without knowledge of the participant’s status as a proband, relative or control, and in the absence of information about the participant’s prescribed psychiatric medication and family history of psychiatric illness. In rare cases where insufficient symptom data was volunteered by the participant or otherwise was unavailable in order to rate a disorder, the diagnosis was deferred. In addition to arriving at a consensus DSM-IV diagnosis for the aforementioned psychiatric disorders, each personality disorder criterion rated at a minimum by the interviewer as subthreshold was reviewed in the meeting and a consensus rating was assigned. Dimensional scores were computed for each personality disorder from the SIDP item-level ratings to create a percentage score out of the total possible score for each item, which ranged from 0 (*not present or limited to rare isolated examples*) to 3 (*strongly present—criterion is associated with subjective distress or impairment in social or occupational functioning or intimate relationships*). The mean Cronbach’s α for the scales was 0.78 (ranging from .55 for schizoid personality disorder to .96 for BPD). A modified GAF scale score (Hall, 1995) was also agreed upon in the meeting based on all available data from a demographic, medical and job history questionnaire; semi-structured psychiatric diagnostic interviews (SCID and SIDP); and relevant medical records.

**Sampling Procedures.** Participants were recruited between August, 2011, and June, 2016, from psychiatric clinics, community-based family and consumer groups, and online postings (e.g., Craigslist, Kijiji, The Sashbear Foundation, National Education Alliance for BPD website). Individuals responding to the postings completed a phone screen to assess their eligibility for the study, as well as their first-degree relatives. In total, 378 individuals (probands, *n*=137; relatives, *n*=107; and controls, *n*=134) provided their written informed consent to participate in the study. Participants completed a detailed in-person assessment to further evaluate their eligibility for the study, including comprehensive semi-structured diagnostic interviews to assess DSM-IV psychiatric diagnoses, including all 10 personality disorders. The flowchart in Figure 1 details the numbers of participants in each group that were excluded from the study and the reasons for the exclusions.

Participants were tested at the University of Toronto Scarborough campus, which is in a large and ethnically diverse Canadian urban center. Participants were compensated up to $100 depending on the portions of the study they completed (psychiatric interviewing, neurocognitive testing, brain imaging, and providing a saliva sample for extraction of genetic material). The study was approved by the Research Ethics Boards at the University of Toronto and Centre for Addiction and Mental Health.

**Supplemental Results**

**Psychiatric Diagnoses.** Odds ratios based on the prevalence of psychiatric diagnoses in probands and relatives is presented in Supplementary Table 7. Additionally, participants were queried on their knowledge about whether one or more of their first-degree relatives (including those not participating in the present study) were ever diagnosed with or received treatment for specific Axis I psychiatric conditions, the results of which are included in Supplementary Table 8.

 **Personality Disorder Dimensional Scales.** Age and ethnicity were not significant covariates in multivariate analyses, *Vs* ≤ .05, *F*s ≤ 1.67, *p*s ≥ .09, *ηp2*s ≤ .06. However, sex (*V* = .08, *F* (10, 258) = 2.34, *p* = .012, *ηp2* = .08), and family grouping (*V* = .08, *F* (10, 258) = 2.1, *p* = .03, *ηp2* = .08) were significant multivariate covariates, with a main effect of sex on schizoid personality disorder (*b* = -.052, *p* = .001), and a main effect of family grouping on narcissistic personality disorder (*b* = .00, *p* = .006).

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**Symptom Measures.** On the BIS, sex, education, and ethnicity were not significant covariates in multivariate analyses, *Vs* ≤ .05, *F*s ≤ 2.00, *p*s ≥ .07, *ηp2*s ≤ .05. However, age was a significant covariate, *V* = .07, *F* (6, 253) = 3.27, *p* < .01, *ηp2* = .07, on the attention, *b* = -.008, *p* = .002, cognitive instability, *b* = -.009, *p* = .002, motor, *b* = -.006, *p* = .013, and self-control, *b* = -.007, *p* = .014, subscales. On the DERS, sex, education, and ethnicity were not significant covariates in multivariate analyses, *Vs* ≤ .04, *F*s ≤ 1.68, *p*s ≥ .13, *ηp2*s ≤ .04. Age, however, was a significant covariate, *V* = .09, *F* (6, 247) = 4.03, *p* < .01, *ηp2* = .09, specifically, on the difficulty engaging in goal-directed behavior, *b* = -.012, *p* < .002, lack of emotional awareness, *b* = -.008, *p* = .025, and lack of emotional clarity, *b* = -.009, *p* < .013, subscales.

**Personality Dimensions.** Age and sex were significant covariates in the multivariate analyses, *Vs* ≥ .08, *F*s (5, 220) ≥ 3.73, *p*s < .01, *ηp2*s ≥ .08. Specifically, age was a positively associated with conscientiousness *b* = .02, *p* < .01. Sex was significantly associated with openness, *b* = -.27, *p* = .028, where male participants, across all groups, (*Mmale* = 3.83, *SDmale* = .57) reported higher openness as compared to female participants (*Mfemale* = 3.68, *SDfemale* = .65).

**Probands with Versus without Relatives Recruited to the Study.** On the BIS, probands without recruited relatives scored higher on perseverance *p* < .01, 95% CI [-.59, -.12], and cognitive complexity *p* < .01, 95% CL [-.51, -.08], subscales than those with relatives. Probands with recruited relatives scored higher on the BFI agreeableness subscale, *p* < .01., 95% CI [.16, .82].

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