

SUPPLEMENTARY DATA

Supplementary eTable 1. Demographics: Control and BD groups

Characteristic	Control (n=156)	BD (N=412)	p
Migraine, n(%)	10 (6)	127 (31)	<1x10 <sup>-3</sup>
Female, n(%)	86 (55)	270 (66)	.03
Female with migraine (n,% of migraine)	9 (90)	105 (83)	1x10 <sup>-6</sup>
Age, mean (SD)	33 (14)	40 (13)	<1x10 <sup>-3</sup>
BMI, mean (SD)	25.5 (5.7)	29.1 (6.7)	1x10 <sup>-6</sup>
Migraine AAO <sup>a</sup> , mean (SD)	18.20 (10.7)	22.35 (12.2)	.30

<sup>a</sup>AAO: Age at onset

Supplementary eTable 2. Medication use in BD group: Comparing Those With And Without Migraine

Medication	No migraine (n=285)	Migraine (n=127)	p
Valproic Acid, n(%)	120 (24)	55 (37)	$2 \times 10^{-3}$
Topiramate, n(%)	23 (5)	23 (16)	$6 \times 10^{-6}$
Gabapentin, n(%)	37 (8)	26 (18)	$2.5 \times 10^{-4}$
SSRI, n(%)	178 (63)	94 (74)	0.02
SNRI <sup>a</sup> , n(%)	68 (24)	44 (35)	0.02
TCA, n(%)	40 (14)	38 (30)	$< 1 \times 10^{-3}$
MAOI, n(%)	4 (1)	1 (1)	0.51 (exact)

<sup>a</sup>AD tested for associated with RC: SNRI associated with RC in both groups ( $p < 3 \times 10^{-3}$ ), TCA and SSRI are not ( $p > .36$ ).

Supplementary eTable 3a. Clinical Characteristics in BD Group by Gender and BD diagnosis: Comparing BPI women With And Without Migraine

Characteristic	No migraine (n=123 )	Migraine (n= 69)	p <sup>a</sup>
Rapid cycling, n(%)	47 (38)	25 (36)	0.79
Mixed Symptoms, n(%)	53 (46)	34 (56)	0.22
Mixed Episodes, n(%)	38 (33)	26 (43)	0.21
Psychosis, n(%)	78 (68)	40 (61)	0.33
Suicide attempts, n(%)	52 (43)	36 (52)	0.22
Anxiety disorder, n(%)	50 (41)	27 (39)	0.84
Alcohol use disorder, n(%)	49 (40)	31 (45)	0.49
Drug use disorder, n(%)	8 (7)	12 (17)	0.02
Manic episodes, median (IQR)	3 (5)	3 (12)	0.27
Depressive episodes, median (IQR)	5 (16)	10 (27)	<0.01
Hypomanic episodes, median (IQR)	4 (20)	6 (24)	0.47
	(n=67)	n=(37)	p
AAO, mean (SD)	17.61 (6.57)	15.92 (7.55)	0.24
BMI, mean (SD)	28.63 (7.59)	31.45 (9.31)	0.11
Baseline depression, mean (SD)	12.73 (11.11)	17.81 (14.26)	0.06
Baseline mania, mean (SD)	2.75 (3.84)	3.03 (3.99)	0.73
CTQ emotional abuse, mean (SD)	12.61 (6.13)	14.11 (6.22)	0.24
CTQ physical abuse, mean (SD)	8.24 (4.75)	9.08 (4.93)	0.40
CTQ sexual abuse, median (IQR)	5 (4)	7 (14)	0.05
CTQ emotional neglect, mean (SD)	12.43 (5.94)	14.38 (5.89)	0.11
CTQ physical neglect, mean (SD)	8.84 (2.79)	8.76 (2.73)	0.89
FACES II cohesion, mean (SD)	3.97 (2.15)	3.32 (1.99)	0.14
FACES II adaptability, mean (SD)	3.81 (2.16)	3.19 (2.00)	0.16
LEOS Undesirable events, mean (SD)	2.27 (2.45)	2.14 (2.04)	0.78
LEC life events scale, mean (SD)	4.06 (3.09)	4.38 (2.92)	0.61
Neuroticism, mean (SD)	60.18 (14.65)	62.81 (12.74)	0.36
Extraversion, mean (SD)	50.18 (11.49)	46.86 (12.66)	0.18
Openness, mean (SD)	58.25 (12.27)	56.51 (14.68)	0.52
Agreeableness, mean (SD)	49.58 (12.29)	44.78 (12.14)	0.06
Conscientiousness, mean (SD)	43.03 (14.43)	41.70 (11.52)	0.63

Abbreviations: Childhood Trauma Questionnaire (CTQ); Life Events Occurrence Survey (LEOS); Life Events Checklist (LEC); Family Adaptability and Cohesion Evaluation Scale II (FACES II); Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness from the Five Factor model NEO-Personality Index – Revised (NEO-PI-R). Baseline depression symptoms were measured with the Hamilton Depression Rating Scale (HDRS-29), baseline manic symptoms were measured with the Young Mania Rating Scale (YMRS).

<sup>a</sup> comparisons between groups done using independent sample t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous

variables (manic, depressive, and hypomanic episodes, CTQ sexual abuse); Pearson Chi-square used for categorical variables.

Supplementary eTable 3b. Clinical Characteristics in BD Group by Gender and BD diagnosis: Comparing BPI Men With And Without Migraine

BPI MEN: Characteristic	(n=100)	(n=14)	p <sup>a</sup>
Rapid Cycling, n(%)	26 (26)	9 (64)	<0.01
Mixed Symptoms, n(%)	32 (36)	8 (62)	0.07
Mixed Episodes, n(%)	25 (28)	5 (39)	0.52
Psychosis, n(%)	67 (71)	11 (79)	0.75
Suicide Attempts, n(%)	25 (25)	4 (29)	0.76
Anxiety Disorder, n(%)	27 (27)	5 (36)	0.53
Alcohol Use Disorder, n(%)	56 (56)	5 (36)	0.15
Drug Use Disorder, n(%)	26 (26)	3 (21)	0.71
Manic episodes, median (IQR)	3 (5)	4 (11)	0.56
Depressive episodes, median (IQR)	4 (12)	6.5 (50)	0.20
Hypomanic episodes, median (IQR)	1 (22)	17.5 (48)	0.08
	(n=45)	n=(9)	p
AAO, mean (SD)	21.07 (11.05)	14.44 (3.81)	0.08
BMI, mean (SD)	30.19 (5.73)	29.89 (8.44)	0.90
Baseline depression, mean (SD)	9.29 (8.73)	16.89 (11.63)	0.30
Baseline mania, mean (SD)	3.62 (6.73)	3.89 (4.22)	0.91
CTQ emotional abuse, mean (SD)	9.67 (4.59)	10.89 (6.13)	0.49
CTQ physical abuse, mean (SD)	7.82 (3.30)	8.67 (5.75)	0.54
CTQ sexual abuse, median (IQR)	5 (5)	5 (10)	0.90
CTQ emotional neglect, mean (SD)	11.00 (5.01)	11.89 (6.37)	0.65
CTQ physical neglect, mean (SD)	8.67 (2.31)	8.89 (3.89)	0.82
FACES II cohesion, mean (SD)	4.20 (2.07)	3.67 (1.66)	0.47
FACES II adaptability, mean (SD)	4.29 (1.87)	3.22 (1.30)	0.11
LEOS Undesirable events, mean (SD)	1.87 (2.28)	2.00 (2.50)	0.88
LEC life events scale, mean (SD)	4.51 (3.27)	6.33 (4.21)	0.15
Neuroticism, mean (SD)	59.18 (12.68)	67.89 (11.71)	0.06
Extraversion, mean (SD)	50.96 (11.52)	43.78 (12.14)	0.10
Openness, mean (SD)	54.49 (11.39)	58.11 (8.18)	0.37
Agreeableness, mean (SD)	50.82 (11.89)	49.33 (13.23)	0.74
Conscientiousness, mean (SD)	44.91 (13.52)	47.67 (19.29)	0.61

Abbreviations: Childhood Trauma Questionnaire (CTQ); Life Events Occurrence Survey (LEOS); Life Events Checklist (LEC); Family Adaptability and Cohesion Evaluation Scale II (FACES II); Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness from the Five Factor model NEO-Personality Index – Revised (NEO-PI-R). Baseline depression symptoms were measured with the Hamilton Depression Rating Scale (HDRS-29), baseline manic symptoms were measured with the Young Mania Rating Scale (YMRS).

<sup>a</sup> comparisons between groups done using independent sample t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous variables (manic, depressive, and hypomanic episodes, CTQ sexual abuse); Pearson Chi-square used for categorical variables.

Supplementary eTable 3c. Clinical Characteristics in BD Group by Gender and BD diagnosis: Comparing BPII Women With And Without Migraine

	No migraine	Migraine	
Characteristic	(n=25)	(n=22)	p <sup>a</sup>
Rapid cycling, n(%)	7 (28)	11 (50)	0.12
Mixed Symptoms, n(%)	9 (38)	9 (47)	0.52
Mixed Episodes, n(%)	2 (8)	2 (11)	0.81
Psychosis, n(%)	3 (13)	5 (25)	0.28
Suicide attempts, n(%)	12 (50)	8 (38)	0.42
Anxiety disorder, n(%)	17 (68)	10 (46)	0.12
Alcohol use disorder, n(%)	8 (32)	9 (41)	0.53
Drug use disorder, n(%)	4 (16)	5(23)	0.56
Depressive episodes, median (IQR)	9 (45)	10 (21)	
Hypomanic episodes, median (IQR)	8 (28)	20 (38)	
	(n=16)	n=(15)	p
AAO, mean (SD)	17.19 (7.14)	14.53 (6.24)	0.28
BMI, mean (SD)	28.16 (6.99)	28.97 (2.86)	0.67
Baseline depression, mean (SD)	12.50 (8.66)	18.93 (10.64)	0.79
Baseline mania, mean (SD)	1.25 (2.08)	4.20 (4.54)	0.03
CTQ emotional abuse, mean (SD)	10.81 (6.73)	13.53 (5.34)	0.22
CTQ physical abuse, mean (SD)	7.63 (4.52)	7.27 (3.56)	0.81
CTQ sexual abuse, median (IQR)	5.5 (6)	6 (7)	0.68
CTQ emotional neglect, mean (SD)	10.44 (5.75)	15.13 (6.44)	0.04
CTQ physical neglect, mean (SD)	8.00 (1.75)	8.80 (2.51)	0.31
FACES II cohesion, mean (SD)	3.25 (1.92)	4.00 (2.10)	0.31
FACES II adaptability, mean (SD)	3.25 (1.95)	3.53 (1.96)	0.69
LEOS Undesirable events, mean (SD)	0.94 (0.93)	1.60 (1.50)	0.16
LEC life events scale, mean (SD)	5.00 (3.83)	4.60 (4.10)	0.78
Neuroticism, mean (SD)	62.38 (12.64)	71.73 (11.13)	0.04
Extraversion, mean (SD)	47.13 (10.60)	44.47 (9.87)	0.48
Openness, mean (SD)	54.38 (11.46)	59.13 (11.08)	0.25
Agreeableness, mean (SD)	45.63 (14.31)	55.33 (12.78)	0.06
Conscientiousness, mean (SD)	41.00 (12.14)	43.07 (15.57)	0.68

Abbreviations: Childhood Trauma Questionnaire (CTQ); Life Events Occurrence Survey (LEOS); Life Events Checklist (LEC); Family Adaptability and Cohesion Evaluation Scale II (FACES II); Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness from the Five Factor model NEO-Personality Index – Revised (NEO-PI-R). Baseline depression symptoms were measured with the Hamilton Depression Rating Scale (HDRS-29), baseline manic symptoms were measured with the Young Mania Rating Scale (YMRS).

<sup>a</sup> comparisons between groups done using independent sample t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous

variables (depressive, and hypomanic episodes, CTQ sexual abuse); Pearson Chi-square used for categorical variables.

Supplementary eTable 3d. Clinical Characteristics in BD Group by Gender and BD diagnosis: Comparing BPII Men With And Without Migraine

Characteristic	(n=12)	(n=7)	p <sup>a</sup>
Rapid Cycling, n(%)	4 (33)	3 (43)	1.00
Mixed Symptoms, n(%)	3 (27)	2 (29)	1.00
Mixed Episodes, n(%)	2 (18)	2 (29)	0.61
Psychosis, n(%)	2 (18)	0	0.50
Suicide Attempts, n(%)	4 (36)	2 (29)	0.73
Anxiety Disorder, n(%)	3 (25)	4 (57)	0.16
Alcohol Use Disorder, n(%)	3 (25)	4 (57)	0.16
Drug Use Disorder, n(%)	1 (8)	1 (14)	1.00
Depressive episodes, median (IQR)	5 (27)	20 (37)	0.10
Hypomanic episodes, median (IQR)	20 (37)	20 (24)	0.53
	<u>(n=5)</u>	<u>n=(3)</u>	<u>p</u>
AAO, mean (SD)	16.40 (5.13)	20.00 (4.00)	0.34
BMI, mean (SD)	27.42 (3.19)	25.47 (0.67)	0.35
Baseline depression, mean (SD)	6.60 (5.86)	18.00 (13.00)	0.13
Baseline mania, mean (SD)	3.80 (5.85)	1.67 (1.53)	0.57
CTQ emotional abuse, mean (SD)	8.20 (2.78)	10.00 (2.65)	0.40
CTQ physical abuse, mean (SD)	5.60 (0.89)	6.33 (1.53)	0.41
CTQ sexual abuse, median (IQR)	0 (0)	7 (0)	0.14
CTQ emotional neglect, mean (SD)	10.40 (4.04)	11.33 (7.10)	0.82
CTQ physical neglect, mean (SD)	7.80 (1.10)	8.33 (1.53)	0.58
FACES II cohesion, mean (SD)	5.60 (2.30)	3.67 (2.31)	0.29
FACES II adaptability, mean (SD)	5.20 (2.05)	3.67 (2.31)	0.36
LEOS Undesirable events, mean (SD)	1.00 (1.00)	1.33 (1.53)	0.72
LEC life events scale, mean (SD)	3.80 (2.39)	7.67 (6.43)	0.25
Neuroticism, mean (SD)	58.20 (14.41)	74.33 (5.51)	0.12
Extraversion, mean (SD)	59.00 (13.77)	50.33 (2.52)	0.34
Openness, mean (SD)	62.40 (15.24)	60.67 (19.09)	0.89
Agreeableness, mean (SD)	43.00 (20.68)	44.33 (9.24)	0.92
<u>Conscientiousness, mean (SD)</u>	<u>46.00 (16.75)</u>	<u>41.67 (7.51)</u>	<u>0.69</u>

Abbreviations: Childhood Trauma Questionnaire (CTQ); Life Events Occurrence Survey (LEOS); Life Events Checklist (LEC); Family Adaptability and Cohesion Evaluation Scale II (FACES II); Neuroticism, Extraversion, Openness, Agreeableness and Conscientiousness from the Five Factor model NEO-Personality Index – Revised (NEO-PI-R). Baseline depression symptoms were measured with the Hamilton Depression Rating Scale (HDRS-29), baseline manic symptoms were measured with the Young Mania Rating Scale (YMRS).

<sup>a</sup> comparisons between groups done using independent sample t-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous



variables (depressive, and hypomanic episodes, CTQ sexual abuse); Pearson Chi-square used for categorical variables.