

Supplementary Table 1 Univariate logistic regression analyses of demographic and clinical features for patients with BD and comorbid anxiety disorders versus non-comorbid anxiety disorders

Features	Comorbid anxiety group (N=58*)	Non-comorbid anxiety group (N=51*)	Odds ratio (95% CI)	P-value
Sex (male), N (%)	23 (39.7)	22 (43.1)	0.87 (0.40–1.86)	.713
History of marriage, N (%)	27 (47.4)	33 (64.7)	0.49 (0.23–1.07)	.072
History of divorce, N (%)	12 (20.7)	12 (23.5)	0.85 (0.34–2.10)	.721
History of spouse's death, N (%)	3 (5.2)	1 (2.0)	2.73 (0.27–27.08)	.392
Presence of spouse, N (%)	15 (25.9)	25 (49.0)	0.36 (0.16–0.81)	.013
Presence of child, N (%)	17 (29.3)	26 (51.0)	0.40 (0.18–0.88)	.022
Presence of housemate, N (%)	41 (70.7)	43 (84.3)	0.45 (0.17–1.15)	.096
Currently employed, N (%)	22 (37.9)	25 (49.0)	0.64 (0.30–1.36)	.245
History of job turnover, N (%)	40 (69.0)	30 (60.0)	1.48 (0.67–3.28)	.332
History of smoking, N (%)	26 (44.8)	19 (37.3)	1.37 (0.63–2.95)	.424
Family history of BD in first-degree relatives, N (%)	16 (28.1)	10 (19.6)	1.60 (0.65–3.94)	.307
Family history of MDD in first-degree relatives, N (%)	5 (8.6)	3 (5.9)	1.51 (0.34–6.66)	.587
Family history of schizophrenia in first-degree relatives, N (%)	0 (0.0)	0 (0.0)	–	–
Family history of suicide in first-degree relatives, N (%)	3 (5.2)	0 (0.0)	n.c.	.984
Family history of alcohol abuse in first-degree relatives, N (%)	4 (6.9)	5 (9.8)	0.68 (0.17–2.69)	.584
Early age at onset of MDE (<25 years), N (%)	26 (44.8)	19 (37.3)	1.37 (0.63–2.95)	.424
Early age at onset of mood episode (<25 years), N (%)	35 (60.3)	23 (45.1)	1.85 (0.86–3.97)	.113
History of psychotic symptoms, N (%)	7 (12.1)	5 (9.8)	1.26 (0.37–4.26)	.707
Early age at onset of psychotic symptoms (<30 years), N (%)	4 (57.1)	1 (25.0)	4.00 (0.27–60.32)	.317
History of suicide attempt, N (%)	27 (46.6)	17 (33.3)	1.74 (0.80–3.79)	.162
History of psychiatric hospitalization, N (%)	9 (15.5)	8 (15.7)	0.99 (0.35–2.78)	.981
Seasonal mood episodes, N (%)	9 (15.5)	6 (11.8)	1.38 (0.45–4.18)	.571
Two or more previous mood episodes, N (%)	38 (69.1)	37 (75.5)	0.72 (0.30–1.72)	.467
Five or more previous mood episodes, N (%)	18 (32.7)	14 (28.6)	1.22 (0.53–2.81)	.647
Two or more previous mood episodes within the past year, N (%)	9 (16.1)	10 (20.4)	0.75 (0.28–2.02)	.565
Five or more previous mood episodes within the past year, N (%)	2 (3.6)	2 (4.1)	0.87 (0.12–6.42)	.891

Mood stabilizer therapy in present use, N (%)	39 (67.2)	33 (64.7)	1.12 (0.51–2.48)	.780
Antidepressant therapy in present use, N (%)	38 (65.5)	33 (64.7)	1.04 (0.47–2.28)	.929
Antipsychotics therapy in present use, N (%)	22 (37.9)	20 (39.2)	0.95 (0.44–2.05)	.891
Anxiolytic therapy in present use, N (%)	37 (63.8)	23 (45.1)	2.14 (0.99–4.63)	.052
Mood lability with antidepressants, N (%)	23 (41.8)	13 (29.5)	1.71 (0.74–3.97)	.209
Antidepressant-related switch to mania/hypomania, N (%)	17 (30.9)	13 (28.9)	1.10 (0.47–2.61)	.827
Mood reactivity, N (%)	27 (46.6)	28 (54.9)	0.72 (0.34–1.52)	.385
Significant weight gain or increase in appetite, N (%)	18 (31.0)	9 (17.6)	2.10 (0.85–5.22)	.110
Hypersomnia, N (%)	13 (22.4)	12 (23.5)	0.94 (0.38–2.30)	.890
Lead paralysis, N (%)	12 (20.7)	9 (17.6)	1.22 (0.47–3.18)	.688
Interpersonal rejection sensitivity, N (%)	37 (63.8)	18 (35.3)	3.23 (1.47–7.08)	.003
Atypical depression, N (%)	11 (19.0)	6 (11.8)	1.76 (0.60–5.15)	.305
Pathological guilt feelings, N (%)	34 (58.6)	17 (33.3)	2.83 (1.30–6.19)	.009
Duration of MDE period (≤ 1 month), N (%)	14 (25.0)	10 (20.8)	1.27 (0.50–3.19)	.616
Duration of MDE period (< 6 months), N (%)	31 (55.4)	29 (60.4)	0.81 (0.37–1.78)	.603
Current psychotic symptoms, N (%)	4 (6.9)	0 (0.0)	n.c.	.981
History of parent's bereavement, N (%)	9 (16.4)	8 (16.3)	1.00 (0.35–2.84)	.996
History of nurture except parents, N (%)	4 (7.1)	5 (10.2)	0.68 (0.17–2.68)	.578
Comorbid substance-related disorder, N (%)	7 (12.3)	4 (8.0)	1.61 (0.44–5.86)	.470
Comorbid personality disorder, N (%)	2 (3.6)	0 (0.0)	n.c.	.980
Mixed features of MDE, N (%)	17 (29.3)	14 (27.5)	1.10 (0.48–2.53)	.830
Age (years), mean \pm SD	36.2 \pm 9.0	39.5 \pm 11.5	0.97 (0.93–1.01)	.092
Duration of education (years), mean \pm SD	13.5 \pm 2.7	14.0 \pm 2.2	0.93 (0.79–1.08)	.330
Amount of alcohol intake (g/week), mean \pm SD	139.4 \pm 153.9	101.8 \pm 126.3	1.00 (1.00–1.01)	.379
Age at onset of (hypo) manic episode (years), mean \pm SD	25.9 \pm 10.8	29.1 \pm 11.3	0.97 (0.94–1.01)	.157
Age at onset of MDE (years), mean \pm SD	27.8 \pm 9.8	30.2 \pm 10.8	0.98 (0.94–1.01)	.216
Age at onset of mood episode (years), mean \pm SD	24.9 \pm 10.3	28.1 \pm 11.0	0.97 (0.94–1.01)	.124
Age at onset of psychotic symptoms (years), mean \pm SD	27.1 \pm 6.8	34.8 \pm 12.6	0.90 (0.77–1.06)	.206
Previous mood episodes, mean \pm SD	8.9 \pm 32.4	5.2 \pm 6.9	1.01 (0.98–1.03)	.500
Previous mood episodes within the past year, mean \pm SD	0.9 \pm 1.8	1.0 \pm 1.4	0.96 (0.76–1.23)	.762
Duration of MDE period (month), mean \pm SD	12.7 \pm 19.6	7.3 \pm 9.0	1.03 (1.00–1.06)	.099
GAF score, mean \pm SD	54.3 \pm 10.4	54.8 \pm 11.7	1.00 (0.96–1.03)	.838
SF-36, Physical functioning, mean \pm SD	68.1 \pm 18.3	73.2 \pm 23.6	0.99 (0.97–1.01)	.204
SF-36, Role physical, mean \pm SD	40.0 \pm 27.6	44.4 \pm 30.8	0.99 (0.98–1.01)	.440
SF-36, Bodily pain, mean \pm SD	52.1 \pm 26.8	55.9 \pm 27.3	0.99 (0.98–1.01)	.464

SF-36, General health perception, mean ± SD	29.5 ± 14.7	34.7 ± 18.4	0.98 (0.96–1.00)	.108
SF-36, Vitality, mean ± SD	17.3 ± 14.3	22.3 ± 17.3	0.98 (0.96–1.00)	.100
SF-36, Social functioning, mean ± SD	37.3 ± 26.6	49.8 ± 25.7	0.98 (0.97–1.00)	.017
SF-36, Role emotional, mean ± SD	29.0 ± 22.7	33.5 ± 27.3	0.99 (0.98–1.01)	.355
SF-36, Mental health, mean ± SD	23.3 ± 15.0	30.6 ± 19.0	0.97 (0.95–1.00)	.031
SF-36, Physical component summary, mean ± SD	37.6 ± 11.0	40.5 ± 13.5	0.98 (0.95–1.01)	.239
SF-36, Mental component summary, mean ± SD	20.3 ± 8.9	23.9 ± 8.9	0.95 (0.91–1.00)	.044
QIDS-J score, mean ± SD	17.7 ± 3.7	15.9 ± 5.0	1.10 (1.01–1.20)	.037
CATS, Total score, mean ± SD	1.53 ± 0.76	1.29 ± 0.69	1.58 (0.93–2.69)	.093
CATS, Neglect score, mean ± SD	1.80 ± 0.90	1.43 ± 0.84	1.62 (1.04–2.52)	.035
CATS, Sexual abuse score, mean ± SD	0.37 ± 0.67	0.12 ± 0.28	3.54 (1.13–11.15)	.031
CATS, Punishment score, mean ± SD	1.93 ± 0.80	1.93 ± 0.89	1.00 (0.63–1.57)	.991

Notes: *Subject with missing data was excluded.

Abbreviations: BD, bipolar disorder; CATS, Child Abuse and Trauma Scale; CI, confidence interval; GAF, Global Assessment of Functioning; MDD, major depressive disorder; MDE, major depressive episode; n.c., not calculated; QIDS-J, Quick Inventory of Depressive Symptomatology-Self Report, Japanese version; SD, standard deviation; SF-36, 36-item Short-form Health Survey.

Supplementary Table 2 Univariate logistic regression analyses of demographic and clinical features for patients with MDD and comorbid anxiety disorders versus non-comorbid anxiety disorders

Features	Comorbid anxiety group (N=118*)	Non-comorbid anxiety group (N=199*)	Odds ratio (95% CI)	P-value
Sex (male), N (%)	43 (36.4)	88 (44.4)	0.72 (0.45–1.14)	.163
History of marriage, N (%)	65 (55.1)	98 (49.7)	1.24 (0.78–1.96)	.359
History of divorce, N (%)	29 (24.8)	32 (16.2)	1.71 (0.97–3.01)	.063
History of spouse's death, N (%)	1 (0.9)	7 (3.5)	0.24 (0.03–1.94)	.179
Presence of spouse, N (%)	41 (34.7)	67 (33.8)	1.04 (0.64–1.68)	.869
Presence of child, N (%)	55 (46.6)	83 (41.9)	1.21 (0.76–1.91)	.416
Presence of housemate, N (%)	79 (66.9)	147 (74.6)	0.69 (0.42–1.14)	.144
Currently employed, N (%)	50 (42.4)	118 (59.6)	0.50 (0.31–0.79)	.003
History of job turnover, N (%)	82 (69.5)	112 (57.4)	1.69 (1.04–2.74)	.034
History of smoking, N (%)	49 (41.5)	69 (34.8)	1.33 (0.83–2.12)	.236
Family history of BD in first-degree relatives, N (%)	9 (7.7)	8 (4.0)	1.98 (0.74–5.28)	.173
Family history of MDD in first-degree relatives, N (%)	21 (17.9)	25 (12.7)	1.51 (0.80–2.83)	.205
Family history of schizophrenia in first-degree relatives, N (%)	4 (3.4)	4 (2.0)	1.72 (0.42–7.00)	.451
Family history of suicide in first-degree relatives, N (%)	3 (2.5)	5 (2.5)	1.01 (0.24–4.29)	.993
Family history of alcohol abuse in first-degree relatives, N (%)	10 (8.5)	4 (2.0)	4.49 (1.38–14.66)	.013
Early age at onset of MDE (<25 years), N (%)	21 (18.4)	39 (20.3)	0.89 (0.49–1.60)	.687
Early age at onset of mood episode (<25 years), N (%)	21 (18.4)	39 (20.3)	0.89 (0.49–1.60)	.687
History of psychotic symptoms, N (%)	15 (12.9)	9 (4.6)	3.08 (1.30–7.30)	.010
Early age at onset of psychotic symptoms (<30 years), N (%)	6 (40.0)	4 (44.4)	0.83 (0.16–4.44)	.831
History of suicide attempt, N (%)	26 (22.2)	22 (11.1)	2.29 (1.23–4.26)	.009
History of psychiatric hospitalization, N (%)	16 (13.6)	16 (8.1)	1.78 (0.86–3.72)	.122
Seasonal mood episodes, N (%)	7 (6.0)	10 (5.1)	1.21 (0.45–3.26)	.710
Two or more previous mood episodes, N (%)	40 (36.4)	63 (33.0)	1.16 (0.71–1.90)	.552
Five or more previous mood episodes, N (%)	6 (5.5)	19 (9.9)	0.52 (0.20–1.35)	.180
Two or more previous mood episodes within the past year, N (%)	2 (1.8)	5 (2.6)	0.68 (0.13–3.55)	.645
Five or more previous mood episodes within the past year, N (%)	0 (0.0)	1 (0.5)	n.c.	.987

Mood stabilizer therapy in present use, N (%)	27 (22.9)	35 (17.7)	1.38 (0.79–2.43)	.261
Antidepressant therapy in present use, N (%)	101 (85.6)	176 (88.9)	0.74 (0.38–1.46)	.390
Antipsychotics therapy in present use, N (%)	20 (16.9)	29 (14.6)	1.19 (0.64–2.21)	.585
Anxiolytic therapy in present use, N (%)	79 (66.9)	121 (61.1)	1.29 (0.80–2.08)	.298
Mood lability with antidepressants, N (%)	4 (3.5)	4 (2.0)	1.76 (0.43–7.18)	.430
Antidepressant-related switch to mania/hypomania, N (%)	1 (0.9)	2 (1.0)	0.86 (0.08–9.62)	.905
Mood reactivity, N (%)	41 (35.0)	77 (38.9)	0.85 (0.53–1.36)	.496
Significant weight gain or increase in appetite, N (%)	19 (16.2)	16 (8.1)	2.21 (1.09–4.48)	.029
Hypersomnia, N (%)	22 (18.8)	15 (7.6)	2.82 (1.40–5.70)	.004
Lead paralysis, N (%)	20 (17.1)	37 (18.7)	0.90 (0.49–1.63)	.723
Interpersonal rejection sensitivity, N (%)	45 (38.5)	52 (26.3)	1.75 (1.08–2.86)	.024
Atypical depression, N (%)	12 (10.3)	17 (8.6)	1.22 (0.56–2.65)	.621
Pathological guilt feelings, N (%)	51 (43.6)	28 (14.1)	4.69 (2.73–8.06)	<.001
Duration of MDE period (≤ 1 month), N (%)	14 (12.0)	20 (10.3)	1.19 (0.58–2.46)	.639
Duration of MDE period (<6 months), N (%)	54 (46.2)	81 (41.5)	1.21 (0.76–1.91)	.426
Current psychotic symptoms, N (%)	2 (1.7)	3 (1.5)	1.12 (0.18–6.81)	.901
History of parent's bereavement, N (%)	27 (25.2)	50 (26.0)	0.96 (0.56–1.65)	.879
History of nurture except parents, N (%)	8 (7.5)	10 (5.2)	1.48 (0.57–3.87)	.425
Comorbid substance-related disorder, N (%)	11 (9.5)	3 (1.5)	6.73 (1.84–24.67)	.004
Comorbid personality disorder, N (%)	0 (0.0)	0 (0.0)	–	–
Mixed features of MDE, N (%)	5 (4.2)	5 (2.5)	1.72 (0.49–6.06)	.401
Age (years), mean \pm SD	40.0 \pm 9.1	39.9 \pm 11.0	1.00 (0.98–1.02)	.918
Duration of education (years), mean \pm SD	12.9 \pm 2.5	13.8 \pm 2.2	0.86 (0.77–0.94)	.002
Amount of alcohol intake (g/week), mean \pm SD	192.1 \pm 320.4	113.3 \pm 165.2	1.00 (1.00–1.00)	.091
Age at onset of (hypo) manic episode (years), mean \pm SD	–	–	–	–
Age at onset of MDE (years), mean \pm SD	34.0 \pm 10.0	34.2 \pm 10.4	1.00 (0.98–1.02)	.868
Age at onset of mood episode (years), mean \pm SD	34.0 \pm 10.0	34.2 \pm 10.4	1.00 (0.98–1.02)	.868
Age at onset of psychotic symptoms (years), mean \pm SD	36.1 \pm 10.0	29.6 \pm 7.4	1.09 (0.98–1.22)	.109
Previous mood episodes, mean \pm SD	1.6 \pm 2.8	1.7 \pm 3.5	0.99 (0.92–1.07)	.834
Previous mood episodes within the past year, mean \pm SD	0.3 \pm 0.5	0.2 \pm 0.6	1.29 (0.84–1.99)	.242
Duration of MDE period (month), mean \pm SD	20.2 \pm 33.0	17.2 \pm 28.0	1.00 (1.00–1.01)	.390
GAF score, mean \pm SD	56.8 \pm 9.4	53.8 \pm 10.3	1.03 (1.01–1.06)	.013
SF-36, Physical functioning, mean \pm SD	72.3 \pm 22.4	80.7 \pm 15.7	0.98 (0.96–0.99)	<.001
SF-36, Role physical, mean \pm SD	45.1 \pm 27.6	55.4 \pm 29.1	0.99 (0.98–1.00)	.003

SF-36, Bodily pain, mean ± SD	53.0 ± 27.3	63.5 ± 27.4	0.99 (0.98–0.99)	.001
SF-36, General health perception, mean ± SD	32.7 ± 15.4	38.9 ± 16.4	0.98 (0.96–0.99)	.001
SF-36, Vitality, mean ± SD	18.7 ± 16.1	28.2 ± 19.1	0.97 (0.96–0.98)	<.001
SF-36, Social functioning, mean ± SD	48.6 ± 28.2	49.9 ± 26.3	1.00 (0.99–1.01)	.691
SF-36, Role emotional, mean ± SD	34.5 ± 25.4	44.7 ± 26.2	0.98 (0.98–0.99)	.001
SF-36, Mental health, mean ± SD	28.5 ± 17.5	36.9 ± 19.9	0.98 (0.96–0.99)	<.001
SF-36, Physical component summary, mean ± SD	39.4 ± 12.4	44.4 ± 10.2	0.96 (0.94–0.98)	<.001
SF-36, Mental component summary, mean ± SD	23.5 ± 10.9	26.7 ± 11.3	0.97 (0.95–0.99)	.015
QIDS-J score, mean ± SD	15.9 ± 4.4	13.1 ± 5.0	1.13 (1.07–1.19)	<.001
CATS, Total score, mean ± SD	1.34 ± 0.69	1.04 ± 0.69	1.83 (1.32–2.56)	<.001
CATS, Neglect score, mean ± SD	1.55 ± 0.92	1.15 ± 0.92	1.58 (1.23–2.03)	<.001
CATS, Sexual abuse score, mean ± SD	0.20 ± 0.59	0.12 ± 0.28	1.55 (0.89–2.69)	.120
CATS, Punishment score, mean ± SD	1.94 ± 0.79	1.59 ± 0.77	1.81 (1.33–2.46)	<.001

Notes: *Subject with missing data was excluded.

Abbreviations: BD, bipolar disorder; CATS, Child Abuse and Trauma Scale; CI, confidence interval; GAF, Global Assessment of Functioning; MDD, major depressive disorder; MDE, major depressive episode; n.c., not calculated; QIDS-J, Quick Inventory of Depressive Symptomatology-Self Report, Japanese version; SD, standard deviation; SF-36, 36-item Short-Form Health Survey.

Supplementary text

List of participating institutions (alphabetical order).

Aozora Clinic, Aratama-Kokoro Clinic, Fukushima Clinic, Hannan Hospital, Hitsuji Clinic, Hokkaido University Hospital, Inada Clinic, J Clinic, JCHO Tokyo Shinjuku Medical Center, Kawamura-Mental Clinic, Kindai University Hospital, Kouseiren Takaoka Hospital, Maruyama-park Mental Clinic, MikuniHill Hospital, Nishio Clinic, Nonami-Shinryo Clinic, Sapporo City General Hospital, Sapporo Kobushi Clinic, Seishinkai Fujita Mental Care Satellite, Seishinkai Okehazama Hospital Fujita Kokoro Care Center, Shinagawa-Shinryo Naika, Urban Life Clinic, Yashima Mental Clinic.