

Table S1

Breakdown of alcohol abuse, alcohol dependence, drug abuse and drug dependence in the externalizing group of BPI Subjects in the entire Discovery and Validation sample.

Externalizing disorder	DSM-III-R diagnosis (BPI subjects in Waves 1-2, N=456)		DSM-IV diagnosis (BPI subjects in Waves 3-5, N=4465)	
	N	%	N	%
Alcohol abuse	30	6.6	539	12.1
Alcohol dependence	177	38.8	1354	30.3
Cannabis abuse	1	0.2	409	9.2
Cannabis dependence	89	19.5	717	16.1
Cocaine abuse	0	0.0	137	3.1
Cocaine dependence	29	6.4	480	10.8
Sedative abuse	2	0.4	89	2.0
Sedative dependence	13	2.9	146	3.3
Stimulant abuse	0	0.0	167	3.7
Stimulant dependence	32	7.0	283	6.3
Opioid abuse	1	0.2	74	1.7
Opioid dependence	16	3.5	173	3.9
Hallucinogen abuse	0	0.0	73	1.6
Hallucinogen dependence	0	0.0	55	1.2
Phencyclidine abuse	0	0.0	25	0.6
Phencyclidine dependence	0	0.0	26	0.6
Polysubstance dependence	0	0.0	19	0.4
Other substance abuse	0	0.0	25	0.6

Other substance dependence	0	0.0	26	0.6
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Table S2

Clinical features in Discovery sample European Americans BPI subjects grouped by externalizing disorders (categorical parameters).

Non-Externalizing Group vs. Externalizing Group									
Parameter	Non-Externalizing		Externalizing		χ^2 (1 df)	<i>P</i> (two-sided)	Odds Ratio: Value	Odds Ratio: 95% CI	
	N	%	N	%				Lower	Upper
Gender									
Male	164	42.6	302	53.4	10.615	0.001	0.649	0.500	0.842
Female	221	57.4	264	46.6					
Disabled									
Yes	64	16.9	138	24.9	8.343	0.004	0.616	0.443	0.857
No	314	83.1	417	75.1					
Self harm									
Yes	20	10.4	89	26.6	19.548	<0.001	0.320	0.190	0.540
No	172	89.6	245	73.4					
Rapid switching									
Yes	169	47.2	336	63.0	21.863	<0.001	0.524	0.399	0.688

No	189	52.8	197	37.0					
Rapid cycling									
Yes	152	43.9	314	60.2	22.024	<0.001	0.519	0.394	0.683
No	194	56.1	208	39.8					
Number of clean depressive episodes^a									
1 to 8	222	65.5	271	52.0	15.235	<0.001	1.750	1.320	2.321
>8	117	34.5	250	48.0					
Number of clean depressive episodes per year^a									
0 to 0.4	191	57.4	238	46.8	9.049	0.003	1.532	1.159	2.023
>0.4	142	42.6	271	53.2					
Number of clean manic episodes^b									
1 to 4	211	58.6	230	44.0	18.266	<0.001	1.804	1.375	2.367
>4	149	41.4	293	56.0					

Number of clean manic episodes per year^b									
0 to 0.4	199	56.9	248	49.6	4.349	0.037	1.339	1.017	1.763
>0.4	151	43.1	252	50.4					

Non-Externalizing Group vs. Early-Onset Subgroup									
Parameter	Non-Externalizing		Early-Onset		χ^2 (1 df)	P (two-sided)	Odds Ratio: Value	Odds Ratio: 95% CI	
	N	%	N	%				Lower	Upper
Gender									
Male	164	42.6	137	58.1	13.989	<0.001	0.536	0.386	0.744
Female	221	57.4	99	41.9					
Disabled									
Yes	64	16.9	64	27.8	10.212	0.001	0.529	0.356	0.784
No	314	83.1	166	72.2					
Self harm									
Yes	20	10.4	52	34.9	30.191	<0.001	0.217	0.122	0.385

No	172	89.6	97	65.1					
Rapid switching									
Yes	169	47.2	160	72.1	34.513	<0.001	0.346	0.242	0.496
No	189	52.8	62	27.9					
Rapid cycling									
Yes	152	43.9	149	69.0	33.551	<0.001	0.352	0.246	0.504
No	194	56.1	67	31.0					
Number of clean depressive episodes^a									
1 to 8	222	65.5	96	44.2	24.397	<0.001	2.392	1.687	3.391
>8	117	34.5	121	55.8					
Number of clean depressive episodes per year^a									
0 to 0.4	191	57.4	96	45.1	7.865	0.005	1.639	1.159	2.318
>0.4	142	42.6	117	54.9					
Number of clean									

manic episodes^b									
1 to 4	211	58.6	88	41.1	16.451	<0.001	2.028	1.438	2.859
>4	149	41.4	126	58.9					
Number of clean manic episodes per year^b									
0 to 0.4	199	56.9	103	49.3	3.023	0.082	1.356	0.962	1.913
>0.4	151	43.1	106	50.7					

a. According to the DSM-IV, a clean depressive episode is a depressive episode without prior physical illness, drug or alcohol abuse, organic precipitants, or bereavement.

b. According to the DSM-IV, a clean manic episode is a manic episode without prior physical illness, drug or alcohol abuse, or organic precipitants.

Table S3

Clinical features in Discovery sample European Americans BPI subjects grouped by externalizing disorders (continuous parameters).

Non-Externalizing Group vs. Externalizing Group

Parameter	Non-Externalizing		Externalizing		<i>t</i>	<i>df</i>	<i>P</i> (two-sided) ^b
	Mean	SD	Mean	SD			
Age	44.07	13.81	41.08	12.09	3.427	744.401	0.001
	(N=382)		(N=561)				
Years of school	15.37	2.80	14.45	2.85	4.911	934	<0.001
	(N=379)		(N=557)				
Age at onset of illness	21.38	10.13	17.91	7.82	5.498	632.854	<0.001
	(N=360)		(N=544)				
Age at onset of depression	22.06	11.00	18.96	9.44	4.318	661.793	<0.001
	(N=348)		(N=531)				
Age at onset of mania	26.53	11.67	22.99	9.56	4.805	685.743	<0.001
	(N=368)		(N=528)				
Age of first drink	16.60	4.47	13.96	4.69	5.369	390	<0.001
	(N=136)		(N=256)				
Age of first tobacco use	16.04	5.21	14.64	4.73	3.353	631	0.001

	(N=197)		(N=436)				
Number of suicide attempts	2.52	2.39	3.10	3.84	-1.848	353.024	0.065
	(N=122)		(N=277)				
Age of first suicide attempt	24.49	10.49	21.48	8.43	2.217	221	0.028
	(N=61)		(N=162)				
Interepisode GAS ^a	75.32	14.98	70.85	14.11	3.081	403	0.002
	(N=179)		(N=226)				
Non-Externalizing Group vs. Early-Onset Subgroup							
Parameter	Non-Externalizing		Early-Onset		<i>t</i>	<i>df</i>	<i>P</i> (two-sided) ^b
	Mean	SD	Mean	SD			
Age	44.07	13.81	39.97	11.44	3.991	563.516	<0.001
	(N=382)		(N=235)				
Years of school	15.37	2.80	13.79	2.87	6.742	609	<0.001
	(N=379)		(N=232)				
Age at onset of illness	21.38	10.13	16.28	7.24	7.115	579.210	<0.001
	(N=360)		(N=229)				
Age at onset of depression	22.06	11.00	17.03	8.91	5.994	538.732	<0.001

	(N=348)		(N=223)				
Age at onset of mania	26.53	11.67	20.92	8.66	6.644	557.345	<0.001
	(N=368)		(N=219)				
Age of first drink	16.60	4.47	12.76	3.92	7.172	249	<0.001
	(N=136)		(N=115)				
Age of first tobacco use	16.04	5.21	13.39	4.42	5.379	385	<0.001
	(N=197)		(N=190)				
Number of suicide attempts	2.52	2.39	3.43	4.33	-2.061	197.795	0.041
	(N=122)		(N=127)				
Age of first suicide attempt	24.49	10.49	20.89	8.57	2.209	135	0.029
	(N=61)		(N=76)				
Interepisode GAS ^a	75.32	14.98	69.85	14.21	2.853	265	0.005
	(N=179)		(N=88)				

a. GAS, Global Assessment Scale.

b. *P*-values were determined after performing Levene's Test for Equality of Variances to check equality of variances assumption.

Table S4

Clinical features in Discovery sample African Americans BPI subjects grouped by externalizing disorders (categorical parameters).

Non-Externalizing Group vs. Externalizing Group									
Parameter	Non-Externalizing		Externalizing		χ^2 (1 df)	<i>P</i> (two-sided)	Odds Ratio: Value	Odds Ratio: 95% CI	
	N	%	N	%				Lower	Upper
Gender									
Male	21	24.1	79	34.3	3.047	0.081	0.608	0.347	1.066
Female	66	75.9	151	65.7					
Disabled									
Yes	28	38.9	70	33.3	0.730	0.393	1.273	0.731	2.215
No	44	61.1	140	66.7					
Self harm									
Yes	5	8.5	33	24.3	6.539	0.011	0.289	0.107	0.783
No	54	91.5	103	75.7					
Rapid switching									
Yes	36	56.2	98	62.0	0.635	0.426	0.787	0.437	1.419

No	28	43.8	60	38.0					
Rapid cycling									
Yes	30	48.4	89	61.4	3.000	0.083	0.590	0.324	1.075
No	32	51.6	56	38.6					
Number of clean depressive episodes^a									
1 to 8	45	60.0	93	46.5	3.976	0.046	1.726	1.007	2.959
>8	30	40.0	107	53.5					
Number of clean depressive episodes per year^a									
0 to 0.4	33	45.8	79	42.2	0.273	0.602	1.157	0.669	1.999
>0.4	39	54.2	108	57.8					
Number of clean manic episodes^b									
1 to 4	43	51.2	113	52.8	0.063	0.802	0.937	0.566	1.563
>4	41	48.8	101	47.2					

Number of clean manic episodes per year^b									
0 to 0.4	41	50.6	97	49.0	0.061	0.805	1.067	0.636	1.790
>0.4	40	49.4	101	51.0					

Non-Externalizing Group vs. Early-Onset Subgroup									
Parameter	Non-Externalizing		Early-Onset		χ^2 (1 df)	P (two-sided)	Odds Ratio: Value	Odds Ratio: 95% CI	
	N	%	N	%				Lower	Upper
Gender									
Male	21	24.1	35	37.6	3.820	0.051	0.527	0.276	1.006
Female	66	75.9	58	62.4					
Disabled									
Yes	28	38.9	33	35.5	0.202	0.653	1.157	0.612	2.186
No	44	61.1	60	64.5					
Self harm									
Yes	5	8.5	21	26.6	7.243	0.007	0.256	0.090	0.726

No	54	91.5	58	73.4					
Rapid switching									
Yes	36	56.2	58	66.7	1.703	0.192	0.643	0.331	1.250
No	28	43.8	29	33.3					
Rapid cycling									
Yes	30	48.4	52	65.8	4.340	0.037	0.487	0.246	0.962
No	32	51.6	27	34.2					
Number of clean depressive episodes^a									
1 to 8	45	60.0	34	41.0	5.711	0.017	2.162	1.144	4.084
>8	30	40.0	49	59.0					
Number of clean depressive episodes per year^a									
0 to 0.4	33	45.8	34	43.0	0.119	0.730	1.120	0.589	2.130
>0.4	39	54.2	45	57.0					
Number of clean									

manic episodes^b									
1 to 4	43	51.2	48	53.9	0.130	0.718	0.896	0.493	1.628
>4	41	48.8	41	46.1					
Number of clean manic episodes per year^b									
0 to 0.4	41	50.6	41	50.0	0.006	0.937	1.025	0.555	1.894
>0.4	40	49.4	41	50.0					

a. According to the DSM-IV, a clean depressive episode is a depressive episode without prior physical illness, drug or alcohol abuse, organic precipitants, or bereavement.

b. According to the DSM-IV, a clean manic episode is a manic episode without prior physical illness, drug or alcohol abuse, or organic precipitants.

Table S5

Clinical features in Discovery sample African Americans BPI subjects grouped by externalizing disorders (continuous parameters).

Non-Externalizing Group vs. Externalizing Group

Parameter	Non-Externalizing		Externalizing		<i>t</i>	<i>df</i>	<i>P</i> (two-sided) ^b
	Mean	SD	Mean	SD			
Age	43.78 (N=85)	12.02	41.00 (N=221)	9.93	1.895	130.464	0.060
Years of school	14.16 (N=73)	2.70	13.01 (N=210)	2.53	3.289	281	0.001
Age at onset of illness	21.29 (N=87)	9.02	16.12 (N=230)	8.11	4.905	315	<0.001
Age at onset of depression	21.34 (N=77)	9.25	17.28 (N=215)	9.44	3.251	290	0.001
Age at onset of mania	26.95 (N=84)	10.89	22.46 (N=222)	10.49	3.305	304	0.001
Age of first drink	17.00 (N=61)	5.13	14.22 (N=166)	5.17	3.603	225	<0.001
Age of first tobacco use	16.00	5.96	15.65	6.48	0.327	188	0.744

	(N=47)		(N=143)				
Number of suicide attempts	3.18	3.33	4.61	7.14	-0.916	123	0.361
	(N=22)		(N=103)				
Age of first suicide attempt	24.31	9.86	20.73	8.52	1.351	78	0.181
	(N=13)		(N=67)				
Interepisode GAS ^a	75.11	14.98	66.50	16.78	2.184	69	0.032
	(N=27)		(N=44)				
Non-Externalizing Group vs. Early-Onset Subgroup							
Parameter	Non-Externalizing		Early-Onset		<i>t</i>	<i>df</i>	<i>P</i> (two-sided) ^b
	Mean	SD	Mean	SD			
Age	43.78	12.02	39.38	9.80	2.645	162.209	0.009
	(N=85)		(N=90)				
Years of school	14.16	2.70	12.59	2.52	3.869	164	<0.001
	(N=73)		(N=93)				
Age at onset of illness	21.29	9.02	15.42	8.28	4.550	178	<0.001
	(N=87)		(N=93)				
Age at onset of depression	21.34	9.25	16.66	9.61	3.179	164	0.002

	(N=77)		(N=89)				
Age at onset of mania	26.95	10.89	22.19	11.18	2.843	172	0.005
	(N=84)		(N=90)				
Age of first drink	17.00	5.13	13.26	4.79	4.580	150	<0.001
	(N=61)		(N=91)				
Age of first tobacco use	16.00	5.96	15.52	7.24	0.385	124	0.701
	(N=47)		(N=79)				
Number of suicide attempts	3.18	3.33	4.13	4.14	-0.955	74	0.343
	(N=22)		(N=54)				
Age of first suicide attempt	24.31	9.86	19.13	8.47	1.833	50	0.073
	(N=13)		(N=39)				
Interepisode GAS ^a	75.11	14.98	66.80	17.78	1.737	45	0.089
	(N=27)		(N=20)				

a. GAS, Global Assessment Scale.

b. *P*-values were determined after performing Levene's Test for Equality of Variances to check equality of variances assumption.

Table S6

Clinical features in Validation sample BPI subjects grouped by externalizing disorders (categorical parameters).

Non-Externalizing Group vs. Externalizing Group									
Parameter	Non-Externalizing		Externalizing		χ^2 (1 df)	<i>P</i> (two-sided)	Odds Ratio: Value	Odds Ratio: 95% CI	
	N	%	N	%				Lower	Upper
Gender									
Male	120	27.5	303	37.8	13.323	<0.001	0.624	0.484	0.805
Female	316	72.5	498	62.2					
Disabled									
Yes	123	28.7	282	35.8	6.334	0.012	0.721	0.559	0.931
No	306	71.3	506	64.2					
Self harm									
Yes	53	21.3	159	35.4	15.115	<0.001	0.493	0.344	0.707
No	196	78.7	290	64.6					
Rapid switching									
Yes	222	53.9	526	68.2	23.748	<0.001	0.544	0.426	0.696

No	190	46.1	245	31.8					
Rapid cycling									
Yes	219	54.5	495	66.4	15.670	<0.001	0.607	0.473	0.778
No	183	45.5	251	33.6					
Number of clean depressive episodes^a									
1 to 8	214	55.9	331	45.0	11.844	0.001	1.546	1.205	1.982
>8	169	44.1	404	55.0					
Number of clean depressive episodes per year^a									
0 to 0.4	192	51.3	307	42.8	7.188	0.007	1.409	1.096	1.811
>0.4	182	48.7	410	57.2					
Number of clean manic episodes^b									
1 to 4	227	54.4	282	37.6	30.891	<0.001	1.983	1.555	2.528
>4	190	45.6	468	62.4					

Number of clean manic episodes per year^b									
0 to 0.4	219	53.2	348	47.5	3.324	0.068	1.252	0.983	1.595
>0.4	193	46.8	384	52.5					

Non-Externalizing Group vs. Early-Onset Subgroup									
Parameter	Non-Externalizing		Early-Onset		χ^2 (1 df)	P (two-sided)	Odds Ratio: Value	Odds Ratio: 95% CI	
	N	%	N	%				Lower	Upper
Gender									
Male	120	27.5	127	41.4	15.561	<0.001	0.538	0.395	0.733
Female	316	72.5	180	58.6					
Disabled									
Yes	123	28.7	114	37.5	6.339	0.012	0.670	0.490	0.916
No	306	71.3	190	62.5					
Self harm									
Yes	53	21.3	79	45.1	27.284	<0.001	0.329	0.215	0.503

No	196	78.7	96	54.9					
Rapid switching									
Yes	222	53.9	227	74.9	33.064	<0.001	0.391	0.283	0.541
No	190	46.1	76	25.1					
Rapid cycling									
Yes	219	54.5	206	70.1	17.360	<0.001	0.511	0.372	0.702
No	183	45.5	88	29.9					
Number of clean depressive episodes^a									
1 to 8	214	55.9	112	40.0	16.309	<0.001	1.899	1.389	2.597
>8	169	44.1	168	60.0					
Number of clean depressive episodes per year^a									
0 to 0.4	192	51.3	102	37.5	12.158	<0.001	1.758	1.279	2.417
>0.4	182	48.7	170	62.5					
Number of clean									

manic episodes^b									
1 to 4	227	54.4	104	35.6	24.439	<0.001	2.160	1.588	2.937
>4	190	45.6	188	64.4					
Number of clean manic episodes per year^b									
0 to 0.4	219	53.2	131	45.2	4.339	0.037	1.377	1.019	1.862
>0.4	193	46.8	159	54.8					

a. According to the DSM-IV, a clean depressive episode is a depressive episode without prior physical illness, drug or alcohol abuse, organic precipitants, or bereavement.

b. According to the DSM-IV, a clean manic episode is a manic episode without prior physical illness, drug or alcohol abuse, or organic precipitants.

Table S7

Clinical features in Validation sample BPI subjects grouped by externalizing disorders (continuous parameters).

Non-Externalizing Group vs. Externalizing Group

Parameter	Non-Externalizing		Externalizing		<i>t</i>	<i>df</i>	<i>P</i> (two-sided) ^b
	Mean	SD	Mean	SD			
Age	44.77 (N=433)	13.50	42.07 (N=793)	11.92	3.484	799.036	0.001
Years of school	15.56 (N=427)	2.62	14.61 (N=780)	2.62	6.038	1205	<0.001
Age at onset of illness	20.36 (N=434)	9.18	16.96 (N=801)	8.42	6.382	824.447	<0.001
Age at onset of depression	21.38 (N=402)	10.99	18.09 (N=777)	9.67	5.071	726.566	<0.001
Age at onset of mania	26.18 (N=428)	11.33	22.97 (N=786)	9.55	4.974	759.830	<0.001
Age of first drink	16.12 (N=398)	5.30	14.36 (N=773)	4.35	5.719	677.399	<0.001
Age of first tobacco use	16.29	4.81	15.23	5.45	2.874	976	0.004

	(N=288)		(N=690)				
Number of suicide attempts	2.33	2.40	3.32	5.07	-3.148	558.586	0.002
	(N=166)		(N=406)				
Age of first suicide attempt	24.57	12.09	21.80	9.63	1.886	117.298	0.062
	(N=82)		(N=245)				
Interepisode GAS ^a	73.40	13.32	69.82	13.77	2.875	491	0.004
	(N=203)		(N=290)				
Non-Externalizing Group vs. Early-Onset Subgroup							
Parameter	Non-Externalizing		Early-Onset		<i>t</i>	<i>df</i>	<i>P</i> (two-sided) ^b
	Mean	SD	Mean	SD			
Age	44.77	13.50	40.74	11.43	4.381	713.448	<0.001
	(N=433)		(N=306)				
Years of school	15.56	2.62	14.00	2.61	7.897	723	<0.001
	(N=427)		(N=298)				
Age at onset of illness	20.36	9.18	15.43	8.02	7.748	706.946	<0.001
	(N=434)		(N=307)				
Age at onset of depression	21.38	10.99	16.67	9.54	6.049	677.437	<0.001

	(N=402)		(N=296)				
Age at onset of mania	26.18	11.33	21.37	9.35	6.293	717.083	<0.001
	(N=428)		(N=306)				
Age of first drink	16.12	5.30	13.49	4.18	7.144	701	<0.001
	(N=398)		(N=305)				
Age of first tobacco use	16.29	4.81	13.81	4.94	6.025	560	<0.001
	(N=288)		(N=274)				
Number of suicide attempts	2.33	2.40	4.25	7.15	-3.350	214.744	0.001
	(N=166)		(N=175)				
Age of first suicide attempt	24.57	12.09	20.01	9.17	2.886	143.221	0.005
	(N=82)		(N=117)				
Interepisode GAS ^a	73.40	13.32	69.01	13.36	2.756	308	0.006
	(N=203)		(N=107)				

a. GAS, Global Assessment Scale.

b. *P*-values were determined after performing Levene's Test for Equality of Variances to check equality of variances assumption.