

Table S1. Studies excluded in secondary screening (with reasons).

Ref	Authors (Year)	Reason for exclusion
S1	Chatterjee B et al. (2014)	Did not include control group
S2	Chatterjee B et al. (2014)	Did not include control group
S3	Chen B et al. (2001)	Post mortem study
S4	Chen SL et al. (2014)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S5	Chou YH et al. (2012)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S6	da Graca Cantarelli M et al. (2014)	Did not include control group
S7	da Silva PV (2012)	Overlapping data
S8	Del Debbio A et al. (2008)	Data unavailable
S9	Dell'Osso L et al. (2011)	Overlapping data
S10	Duffy A et al. (2014)	Not bipolar disorder; subjects are offspring of bipolar patients
S11	Dunham JS et al. (2009)	Postmortem study
S12	Ferenzstajn E et al. (2014)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S13	Ferenzstajn E et al. (2014)	Not bipolar disorder; subjects are offspring of bipolar patients
S14	Fernandes BS et al. (2010)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S15	Filus J et al. (2010)	Did not include control group
S16	Gama CS et al. (2007)	Overlapping data
S17	Goldstein BI et al. (2011)	Included patients < 18 years
S18	Gomes FA et al. (2010)	Not an original article
S19	Grande I et al. (2011)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S20	Grande I et al. (2012)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S21	Grande I et al. (2013)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S22	Grande I et al. (2012)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S23	Grande I et al. (2014)	Control group included first degree relatives of bipolar patients
S24	Grande I et al. (2014)	Duplicated article
S25	Gronli O et al. (2009)	Data unavailable
S26	Hashimoto K (2014)	Not an original article
S27	Hashimoto K (2015)	Not an original article
S28	Kapczinski F et al. (2009)	Not an original article
S29	Kapczinski F et al. (2008)	Overlapping data
S30	Kauer-Sant'Anna M et al. (2010)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S31	Kauer-Sant'Anna M (2007)	Did not include a control group

S32	Knorr U et al. (2012)	Not bipolar disorder
S33	Kunz M et al. (2010)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S34	Lahera G et al. (2014)	Insufficient data for meta-analysis
S35	Lee SY et al. (2015)	Duplicated article
S36	Licinio J et al. (2002)	Not an original article
S37	Licinio J et al. (2010)	Not an original article
S38	Machado-Vieira R et al. (2009)	Not bipolar disorder
S39	Mesman E et al. (2015)	Not bipolar disorder; subjects are offspring of bipolar patients
S40	Moreira L et al. (2011)	Not an original article
S41	Munkholm K et al. (2014)	Double-counting of patients (Multiple blood samples)
S42	Nair A et al. (2006)	Not an original article
S43	Permoda-Osip A et al. (2011)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S44	Piccinni A et al. (2009)	Not bipolar disorder; data unavailable
S45	Post RM (2007)	Not an original article
S46	Rakofsky JJ et al. (2012)	Not an original article
S47	Rybakowski JK (2014)	Not an original article
S48	Scola G et al. (2015)	Not an original article
S49	Sousa RT et al. (2011)	Duplicated article
S50	Suwalska A et al. (2008)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S51	Teixeira AL et al. (2010)	Not an original article
S52	Teixeira AL et al. (2011)	Meeting abstract; data included in meta-analysis (full-manuscript available)
S53	Terao T (2008)	Not an original article
S54	Trajkovska V et al. (2008)	Did not include a control group
S55	Tsai SJ (2004)	Not an original article
S56	Vasconcelos-Moreno MP et al. (2012)	Not bipolar disorder; subjects are offspring of bipolar patients
S57	Videira Dias V et al. (2009)	Data unavailable
S58	Vinberg M et al. (2009)	Did not include a control group
S59	Yalcin Arslan Y et al. (2013)	Overlapping data
S60	Yatham LN et al. (2009)	Overlapping data
S61	Yuan TF (2008)	Not an original article
S62	Zhang C et al. (2014)	Meeting abstract; data included in meta-analysis (full-manuscript available)

Table S2. Characteristics of studies included in between-group meta-analyses of peripheral BDNF levels in bipolar disorder, across different mood states.

A) Bipolar Depression

Ref	Author (Year)	Sample Size (Patients/Controls)	Age (mean \pm SD)		BDNF Unit	BDNF (mean \pm SD)		Baseline Depression Scores	Sample Source (Type of Assay)	Manufacturer of the Test
			Patients	Controls		Patients	Controls			
S63	Ceylan (2012)	8 / 37	45.5 \pm 10.8 37.5	35.2 \pm 11.7 64.9	pg/mL	3984.3 \pm 606.1	7050.7 \pm 2644.3	26.5 \pm 2.6	Serum (ELISA)	Chemikine
S64	Cunha (2006)	21 / 32	40.7 \pm 9.2 71.4	40.7 \pm 12.1 65.6	pg/ μ g	0.15 \pm 0.13	0.20 \pm 0.07	22.8 \pm 4.4	Serum (ELISA)	Chemicon
S65	de Oliveira (2009)	20 / 22	35.0 \pm 11.2 90.0	35.2 \pm 8.1 90.0	pg/ μ L	0.22 \pm 0.17	0.40 \pm 0.12	21.4 \pm 7.7	Serum (ELISA)	Chemicon
S66	Dell'Osso (2010)	16 / 15	46.7 \pm 17.7 50.0	46.9 \pm 9.2 80.0	pg/mL	2119.0 \pm 1339.8	5400.0 \pm 2.3	27.8 \pm 5.3	Plasma (ELISA)	Promega
S67	Fernandes (2009)	40 / 30	41.3 \pm 8.4 55.0	41.0 \pm 12.0 60.0	pg/ μ g	0.15 \pm 0.08	0.38 \pm 0.12	23.4 \pm 7.5	Serum (ELISA)	Chemicon
S68	Grande (2014)	27 / 62	36.3 \pm 11.3 74.1	34.2 \pm 9.4 81.3	ng/mL	42.9 \pm 25.5	36.4 \pm 21.2	22.1 \pm 6.6	Serum (ELISA)	Millipore
S69	Kapczinski (2011)	20 / 80	46.1 \pm 9.3 80.0	40.7 \pm 12.5 60.0	pg/ μ g	0.12 \pm 0.05	0.13 \pm 0.09	24.3 \pm 8.2	Serum (ELISA)	Chemicon
S70	Li (2014)	21 / 167	32.2 \pm 4.1 71.4	30.9 \pm 4.5 79.0	pg/mL	2.7 \pm 0.5	3.0 \pm 0.4	22.2 \pm 1.7	Plasma (ELISA)	R&D Systems
S71	Mackin (2007)	20 / 14	48.6 \pm 10.8 5.0	43.7 \pm 12.9 14.3	pg/mL	13755.2 \pm 7932.2	13800.4 \pm 9107.0	18.1 \pm 9.9	Serum (ELISA)	Promega
S72	Magalhaes (2012)	31 / 92	21.7 \pm 2.4 74.2	22.4 \pm 2.7 57.4	pg/ μ g	0.24 \pm 0.11	0.27 \pm 0.15	N/A	N/A (N/A)	N/A
S73	Panizzutti (2013)	54 / 54	50 75.9	48 72.0	ng/mL	25.9 \pm 8.5	25.1 \pm 7.7	21.0	Serum (ELISA)	N/A
S74	Rabie (2014)	25 / 15	32.1 \pm 8.3 60.0	30.5 \pm 5.0 46.7	pg/mL	23.3 \pm 11.1	42.2 \pm 12.9	21 \pm 5.6	Serum (ELISA)	Quantikine
S75	Su (2011)	10 / 21	22.7 \pm 2.9 0.0	25.0 \pm 3.0 0.0	ng/mL	5.4 \pm 4.7	12.5 \pm 3.0	N/A	Plasma (Other)	Biomedicines
S76	Tunca (2014)	26 / 61	42.5 \pm 10.5 32.1	38.3 \pm 11.6 56.7	pg/mL	3639.6 \pm 1395.1	5646.2 \pm 2587.0	24.0 \pm 5.7	Serum (ELISA)	Chemikine

S77	Yoshimura (2006)	6 / 20	N/A N/A	30.0 ± 11.0 55.0	pg/mL	16.0 ± 8.1	26.2 ± 11.0	24.0 ± 6.0	Serum (ELISA)	Promega
B) Euthymia										
Ref	Author (Year)	Sample Size (Patients/Controls)	Age (mean ± SD) % Females		BDNF Unit	BDNF (mean ± SD)		Sample Source (Type of Assay)	Manufacturer of the Test	
			Patients	Controls		Patients	Controls			
S78	Andreazza (2014)	76 / 118	64.0 ± 9.7 N/A	65.9 ± 9.6 N/A	pg/μg	8.95 ± 6.22	12.29 ± 8.81	N/A	N/A	
S79	Barbosa (2010)	19 / 38	44.5 ± 10.9 57.9	42.9 ± 9.7 52.6	pg/mL	2695.8 ± 1570.1	1211.0 ± 1043.4	Plasma (ELISA)	DuoSet, R&D Systems	
S80	Barbosa (2012)	25 / 25	50.9 ± 9.1 68.0	48.0 ± 7.1 56.0	pg/mL	3901.0 ± 2357.1	1754.4 ± 1354.9	Plasma (ELISA)	DuoSet, R&D Systems	
S81	Barbosa (2013)	48 / 58	47.8 ± 10.4 74.3	46.8 ± 9.4 72.4	pg/mL	2649.1 ± 1861.0	1615.8 ± 1144.0	Plasma (ELISA)	DuoSet, R&D Systems	
S63	Ceylan (2012)	30 / 37	37.3 ± 10.8 60.0	35.2 ± 11.7 64.9	pg/mL	8041.5 ± 2205.6	7050.7 ± 2644.3	Serum (ELISA)	Chemikine	
S82	Chen (2014)	367 / 126	31.7 ± 11.2 48.8	32.4 ± 7.5 38.8	ng/mL	14.9 ± 10.00	17.3 ± 9.1	Plasma (ELISA)	Quantikine	
S83	Chou (2012)	23 / 33	36.5 ± 8.9 73.9	37.6 ± 7.8 63.6	pg/mL	328.0 ± 242.4	334.5 ± 343.6	Plasma (ELISA)	Promega	
S64	Cunha (2006)	32 / 32	40.3 ± 12.0 62.5	40.7 ± 12.1 65.6	pg/μg	0.19 ± 0.08	0.20 ± 0.07	Serum (ELISA)	Chemicon	
S84	Dias (2009)	65 / 50	37.8 ± 10.5 63.1	33.6 ± 9.7 72.0	pg/μg	0.28 ± 0.21	0.24 ± 0.21	Serum (RIA)	Promega	
S85	Hsieh (2014)	28 / 28	36.6 ± 8.1 67.9	36.6 ± 7.9 67.9	pg/mL	586.0 ± 758.2	445.4 ± 408.0	Serum (ELISA)	N/A	
S69	Kapczinski (2011)	20 / 80	46.6 ± 12.7 60.0	40.7 ± 12.5 60.0	pg/μg	0.11 ± 0.01	0.13 ± 0.01	Serum (ELISA)	Chemicon	
S86	Kauer-Sant'Anna (2009)	60 / 60	31.9 ± 11.6 63.3	32.6 ± 11.8 65.0	pg/mL	0.6 ± 0.3	0.6 ± 0.3	Serum (ELISA)	Chemicon	
S87	Kenna (2014)	26 / 47	32.9 ± 6.4 100.0	31.8 ± 6.4 100.0	ng/mL	53.8 ± 52.6	43.5 ± 40.8	Plasma (ELISA)	Promega	

S88	Langan (2009)	24 / 22	40.7 ± 9.0 41.6	40.4 ± 7.9 54.5	ng/mL	35.9 ± 8.2	33.5 ± 11.9	Serum (N/A)	N/A
S89	Lotrich (2013)	21/26	64.8 ± 9.1 53.9	65.5 ± 8.4 61.9	N/A	21.3 ± 5.4	21.6 ± 7.1	Serum (ELISA)	R&D Systems
S72	Magalhaes (2012)	11 / 92	21.8 ± 2.4 72.7	22.4 ± 2.7 57.4	pg/μg	0.19 ± 0.07	0.27 ± 0.15	N/A	N/A
S90	Monteleone (2008)	28 / 22	45.1 ± 11.2 60.7	40.1 ± 16.4 63.6	pg/mL	27.8 ± 14.7	42.6 ± 12.7	Serum (RIA)	Promega
S91	Panizzutti (2014)	31/27	46.4 ± 12.9 74.2	45.9 ± 6.8 74.1	ng/mL	27.9 ± 7.8	26.5 ± 7.3	Serum (ELISA)	Chemicon
S92	Rosa (2014)	50 / 50	41.3 ± 13.4 56.0	41.6 ± 13.6 56.0	ng/mL	1.6 ± 0.8	1.6 ± 0.8	Plasma (ELISA)	R&D Systems
S93	Rybakowski (2010)	60/60	52.6 ± 10.2 58.3	52.1 ± 13.6 58.3	ng/mL	23.6 ± 13.3	28.9 ± 10.9	Plasma (ELISA)	Quantikine
S94	Sodersten (2014)	262 / 155	39.0 ± 12.6 63.1	37.8 ± 14.6 56.8	ng/mL	29.8 ± 7.9	25.3 ± 8.6	Serum (ELISA)	Adipo Bioscience
S95	Suwalska (2010)	141 / 75	53.7 ± 12.7 63.8	55.7 ± 11.7 69.3	ng/mL	24.2 ± 17.0	27.4 ± 10.4	Serum (ELISA)	Quantikine
S96	Tramontina (2007)	114/137	42.5 ± 11.5 71.9	44.1 ± 13.8 67.1	pg/μg	0.14 ± 0.08	0.16 ± 0.08	Serum (ELISA)	Chemicon
S76	Tunca (2014)	37 / 61	36.2 ± 10.0 62.2	38.3 ± 11.6 56.7	pg/mL	6851.0 ± 3275.9	5646.2 ± 2587.0	Serum (ELISA)	Chemikine

C) (Hypo)mania

Ref	Author (Year)	Sample Size (Patients/Controls)	Age (mean ± SD) % of Females		BDNF Unit	BDNF (mean ± SD)		Baseline YMRS Scores	Sample Source (Type of Assay)	Manufacturer of the Test
			Patients	Controls		Patients	Controls			
S79	Barbosa (2010)	34 / 38	49.6 ± 14.2 61.8	42.9 ± 9.7 52.6	pg/mL	3161.1 ± 1409.3	1211.0 ± 1043.4	28.5 ± 6.2	Plasma (ELISA)	DuoSet, R&D Systems
S81	Barbosa (2013)	48 / 58	51.0 ± 13.7 62.5	46.8 ± 9.4 72.4	pg/mL	3075.3 ± 1592.6	1615.8 ± 1144.0	25.2 ± 7.9	Plasma (ELISA)	DuoSet, R&D Systems
S63	Ceylan	15 / 37	37.7 ± 11.1	35.2 ± 11.7	pg/mL	4422.7 ±	7050.7 ±	30.1 ± 11.8	Serum	Chemikine

	(2012)		66.7	64.9		1279.7	2644.3		(ELISA)	
S64	Cunha (2006)	32 / 32	40.1 ± 12.6 43.8	40.7 ± 12.1 65.6	pg/μg	0.14 ± 0.04	0.20 ± 0.07	34.5 ± 7.1	Serum (ELISA)	Chemicon
S65	de Oliveira (2009)	24 / 22	41.8 ± 13.5 66.6	35.2 ± 8.1 66.6	pg/μL	0.28 ± 0.11	0.40 ± 0.12	32.2 ± 10.1	Serum (ELISA)	Chemicon
S97	Goka (2009)	29 / 29	32.6 ± 8.3 48.3	33.8 ± 6.6 48.3	pg/mL	14.3 ± 5.8	40.2 ± 9.7	35.9 ± 9.4	Serum (ELISA)	Quantikine
S68	Grande (2014)	19 / 62	36.3 ± 13.2 36.8	36.7 ± 13.3 22.2	ng/mL	36.4 ± 30.5	36.4 ± 21.2	26.0 ± 9.4	Serum (ELISA)	Millipore
S98	Huang (2012)	26 / 56	33.2 ± 11.7 53.8	32.5 ± 5.7 64.3	ng/mL	4.2 ± 4.0	6.7 ± 10.1	42.1 ± 7.5	Serum (RIA)	Promega
S69	Kapczinski (2011)	20 / 80	37.9 ± 12.1 60.0	40.7 ± 12.5 60.0	pg/μg	0.13 ± 0.01	0.13 ± 0.01	30.1 ± 6.9	Serum (ELISA)	Chemicon
S99	Karamustafalio-glu (2015)	68/30	34.7 ± 10.6 0	30.9 ± 7.6 0	ng/ml	2.4 ± 2.3	4.9 ± 4.4	45.1 ± 7.7	Plasma (ELISA)	N/A
S100	Kim (2013)	116 / 123	35.9 ± 11.7 63.8	35.4 ± 10.4 54.6	pg/mL	976.9 ± 904.8	927.6 ± 609.4	34.0 ± 9.6	Whole Blood (ELISA)	DuoSet, R&D Systems
S101	Laske (2005)	8/30	50.9 ± N/A 33.3	58.1 ± N/A 73.3	ng/ml	15.7 ± 3.0	21.3 ± 5.4		Serum (ELISA)	DuoSet, R&D Systems
S102	Machado-Vieira (2007)	30 / 30	26.0 ± 4.0 76.7	26.5 ± 5.2 76.7	pg/mL	224.8 ± 76.5	318.5 ± 114.2	36.9 ± 0.5	Plasma (ELISA)	Chemicon
S103	Palomino (2006)	14 / 12	23.7 ± 6.9 N/A	25.5 ± 5.2 N/A	ng/mL	3.8 ± 2.0	7.9 ± 3.7	N/A	Plasma (ELISA)	Chemicon
S74	Rabie (2014)	25 / 15	29.7 ± 6.7 36.0	30.5 ± 5.0 46.7	pg/mL	19000 ± 5657.0	42200 ± 1298	48 ± 3.86	Serum (ELISA)	Quantikine
S104	Tramontina (2009)	10 / 10	34.9 ± 13.8 50.0	34.3 ± 4.0 50.0	pg/μg	0.26 ± 0.10	0.31 ± 0.05	26.2 ± 9.5	Serum (ELISA)	Chemicon
S76	Tunca (2014)	33 / 61	36.8 ± 12.0 65.7	38.3 ± 11.6 56.7	pg/mL	4129.2 ± 1704.0	5646.2 ± 2587.0	30.4 ± 11.1	Serum (ELISA)	Chemikine
S105	Tunca (2015)	39 / 78	36.6 ± 11.7 66.7	38.2 ± 11.5 51.3	pg/mL	3743.9 ± 2113.6	5457.2 ± 2734.3	31.6 ± 11.1	Serum (ELISA)	ChemiKine
S106	Wang (2011)	28 / 30	37.5 ± 13.6 60.7	36.9 ± 6.3 56.6	pg/mL	1194.9 ± 2214.6	639.9 ± 257.4	31.2 ± 5.0	Whole Blood (ELISA)	N/A

S77	Yoshimura (2006)	12 / 20	34.1 ± 15.0 N/A	30.0 ± 11.0 55.0	pg/mL	26.2 ± 11.0	24.2 ± 7.9	22.0 ± 5.0	Plasma (ELISA)	Promega
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D) Mixed Episode

Ref	Author (Year)	Sample Size (Patients/Controls)	Age (mean ± SD) % Females		BDNF Unit	BDNF (mean ± SD)		Baseline YMRS (HDRS) Scores	Sample Source (Type of Assay)	Manufacturer of the Test
			Patients	Controls		Patients	Controls			
S68	Grande (2014)	15 / 62	40.3 ± 10.4 75.0	37.2 ± 10.6 73.3	ng/mL	44.2 ± 34.9	36.4 ± 21.2	19.9 ± 8.3 (18.3 ± 8.9)	Serum (ELISA)	Millipore
S72	Magalhaes (2012)	10 / 92	21.6 ± 2.0 70.0	22.4 ± 2.7 57.4	pg/μg	0.30 ± 0.11	0.27 ± 0.15	N/A	N/A	N/A
S107	Piccini (2015) [†]	19 / 15	38.2 ± 10.0 47.4	36.9 ± 9.2 80.0	ng/mL	3.3 ± 2.6	5.4 ± 2.3	N/A (6.0 ± 0.2 [†])	Plasma (ELISA)	Promega

[†] Applied CGI-S, instead of HDRS

Table S3. Characteristics of studies included in within-group meta-analyses of peripheral BDNF levels in bipolar disorder across different mood states.

A) Bipolar Depression

Ref	Author (Year)	Sample Size (Baseline/Final)	Age (mean ± SD) % Females	BDNF Unit	BDNF (mean ± SD)		Baseline HDRS Scores (Change)	Intervention (Length of follow-up)	Source, Manufacturer of the Test
					Baseline	Post-Treatment			
S108	Grande (2012)	17 / 17	38.7 ± 11.7 77.0	ng/mL	49.3 ± 11.6	57.0 ± 17.6	21.6 ± 5.6 (-9.3)	Quetiapine ER (16 weeks)	Serum, Millipore
S68	Grande (2014)	27 / 26	36.3 ± 11.3 74.1	ng/mL	42.9 ± 25.5	39.4 ± 16.1	22.1 ± 6.6 (-14.2)	Quetiapine ER or TAU (16 weeks)	Serum, Millipore
S109	Lee (2015)	117 / 76	30.7 ± 11.1 44.4	ng/mL	17.6 ± 8.5	16.8 ± 9.7	19.2 ± 5.4 (-9.8)	Valproate (12 weeks)	Plasma, Quantikine
S71	Mackin (2007)	20 / 20	48.6 ± 10.8 5.0	pg/mL	13755.2 ± 7932.2	9001.7 ± 4511.5	18.1 (N/A)	Mifepristone (1 week)	Serum, Promega
S110	Rybakowski (2013) Responders	13 / 13	49.0 ± 11.0 84.0	ng/mL	38071 ± 9711	40402 ± 9038	21.0 ± 5.0 (-17.0)	Ketamine (2 weeks)	Serum, R&D Systems
S110	Rybakowski (2013) Non-responders	12 / 12	49.0 ± 11.0 84.0	ng/mL	42387 ± 7414	38904 ± 6024	21.0 ± 5.0 (-2.0)	Ketamine (2 weeks)	Serum, R&D Systems
S77	Yoshimura (2006)	6 / 6	N/A	ng/mL	16.0 ± 8.1	17.0 ± 7.0	24.0 ± 6.0 (-5.0)	Risperidone (4 weeks)	Plasma, Promega
S111	Yoshimura (2010)	14/14	N/A	ng/mL	1.1 ± 0.8	2.1 ± 0.6	19.0 ± 2.5 (-8.6)	Atypical antipsychotics (4 weeks)	Plasma, Promega

Abbreviation: TAU = treatment as usual; ER = extended-release.

B) (Hypo)mania

Ref	Author (Year)	Sample Size (Baseline/ Final)	Age (mean \pm SD) % Females	BDNF Unit	BDNF (mean \pm SD)		Baseline YMRS Scores (Change)	Intervention (Length of follow-up)	Manufacturer of the Test
					Baseline	Post-Treatment			
S82	Chen (2014)	309/198	31.4 \pm 11.2 47.2	ng/mL	15.0 \pm 10.7	17.9 \pm 9.4	11.3 \pm 6.0 (-6.1)	Valproate + Dextromethorphan (12 weeks)	Plasma, Quantikine
S112	de Sousa (2011)	10 / 10	25.4 \pm 7.5 40.0	pg/mL	406.3 \pm 69.5	510.9 \pm 127.1	37.3 \pm 9.5 (-26.6)	Lithium (4 weeks)	Plasma, Chemicon
S97	Goka (2009)	29 / 29	32.6 \pm 8.3 48.3	pg/mL	14.3 \pm 5.8	20.5 \pm 7.3	35.9 \pm 9.4 (-30.7)	Multiple drugs (4 weeks)	Serum, Quantikine
S68	Grande (2014)	19 / 19	36.3 \pm 13.2 36.8	ng/mL	36.4 \pm 30.5	27.8 \pm 11.7	26.0 \pm 9.4 (-21.7)	Quetiapine ER or TAU (16 weeks)	Serum, Millipore
S98	Huang (2012)	26 / 21	31.7 \pm 10.6 61.9	ng/mL	4.0 \pm 4.0	4.6 \pm 3.7	42.1 \pm 7.5 (-36.2)	Lithium, valproate, various antipsychotics (4 weeks)	Serum Promega
S99	Karamustafalioglu (2015)	46 / 46	N/A 0.0	ng/mL	2.2 \pm 1.8	2.1 \pm 1.7	43.7 \pm 5.8 (-40.7)	Haloperidol + quetiapine (4 weeks)	Plasma, N/A
S100	Kim (2013)	116 / 102	36.0 \pm 11.7 62.7	pg/mL	976.9 \pm 904.8	983.1 \pm 770.3	34.0 \pm 9.6 (-28.7)	Multiple drugs (6 weeks)	Whole blood, DuoSet
S113	Kurita (2014)	24/24	54.5 \pm 16.0 45.8	pg/mL	5493 \pm 4905	6619 \pm 4709	32.5 \pm 8.3 (-22.5)	Lithium, valproate, various antipsychotics (6 weeks)	Plasma, N/A
S103	Palomino (2006)	14 / 14	N/A	ng/mL	3.8 \pm 2.0	5.7 \pm 2.5	N/A	Lithium, mood stabilizers, atypical antipsychotics (12 weeks)	Plasma, Chemicon
S104	Tramontina (2009)	10 / 10	34.9 \pm 13.8 50.0	pg/ μ g	0.26 \pm 0.10	0.38 \pm 0.14	26.2 \pm 9.5 (-20.3)	Lithium, valproate, various antipsychotics (8 weeks)	Serum, Chemicon

S106	Wang (2011)	28 / 28	N/A 60.7	pg/mL	1194.9 ± 2214.6	1252.7 ± 1629.7	31.2 ± 5.0 (-26.0)	Lithium and Quetiapine (8 weeks)	Plasma, N/A
S114	Ye (2010)	58 / 43	38.4 ± 14.6 55.2	ng/mL	20.3 ± 8.1	24.7 ± 10.8	35.4 ± 5.4 (-18.1)	N/A (4 weeks)	Serum, Transhold
S77	Yoshimura (2006)	12 / 12	N/A	ng/mL	26.2 ± 11.0	26.1 ± 11.0	22.0 ± 5.0 (-17.0)	Risperidone (4 weeks)	Plasma, Promega

Abbreviation: TAU = treatment as usual; ER = extended release.

C) Mixed Episode

Ref	Author (Year)	Sample Size (Baseline/Final)	Age (mean \pm SD) % Females	BDNF Unit	BDNF (mean \pm SD)		Baseline YMRS Scores (Change)	Intervention	Manufacturer of the Test
					Baseline	Post-Treatment			
S68	Grande (2014)	15 / 15	40.3 \pm 10.4 75.0	ng/mL	44.2 \pm 34.9	36.9 \pm 13.0	19.9 \pm 8.3 (-18.2)	Quetiapine ER or TAU	Millipore

Abbreviation: TAU = treatment as usual; ER = extended release.

Table S4. Characteristics of meta-analyses of peripheral BDNF in bipolar disorder.

Mood State	Study Data Sets, N	Cases/Controls, N	Meta-analysis ES (95% CI)	95 % Prediction Interval	P Value ^a	Largest Study ES (95% CI)	I ² , %	Egger's Test P Value
Between-group MA								
Bipolar depression	15	345 / 722	-0.94 (-1.38 – -0.50)	-2.73 – 0.86	< 0.001	-0.77 (-1.23 – -0.31)	89	0.002
Euthymia	24	1598 / 1459	0.05 (-0.13 – 0.23)	-0.79 – 0.90	0.569	-0.24 (-0.44 – -3.95)	81	0.632
Mania	19	605 / 792	-0.56 (-0.99 – -0.13)	-2.53 – 1.40	0.010	0.06 (-0.19 – 0.32)	92	0.038
<i>Serum</i>	11	255 / 451	-1.01 (-1.50 – -0.51)	-2.85 – 0.84	< 0.001	-0.67 (-1.06 – -0.28)	88	0.040
<i>Plasma</i>	6	206 / 188	-0.03 (-0.98 – 0.92)	-3.51 – 3.45	0.951	1.06 (0.66 – 1.47)	95	0.527
<i>Plasma (without Barbosa)</i>	4	124 / 92	-0.72 (-1.27 – -0.17)	-3.06 – 1.61	0.010	-0.80 (-1.24 – -0.36)	70	0.885
Within-group MA								
Bipolar depression	8	184	0.05 (-0.28 – 0.38)	-1.02 – 1.13	0.754	-0.09 (-0.74 – -0.36)	77	0.423
Mania	13	556	0.26 (0.09 – 0.44)	-0.32 – 0.84	0.003	0.29 (-0.17 – 0.19)	69	0.369

Abbreviations: CI = confidence interval; ES = effect size; MA = meta-analysis

^a P value in test for overall effect (z).

Table S5. Assessment of bias across meta-analyses of peripheral BDNF in bipolar disorder.

Mood State	Significance threshold reached	Observed Positive Data Sets, N	Expected positive data sets ^a		Estimate of heterogeneity ^c	Small-study effects rule ^d	Prediction interval rule ^e
			N	P value ^b			
Between-group meta-analysis							
Bipolar depression	< 0.01	9	11.0	0.251	Very large	Yes	Yes
Euthymia	> 0.05	10	5.8	0.048	Very large	No	Yes
Mania	< 0.01	12	1.1	< 0.001	Very large	Yes	Yes
<i>Serum</i>	< 0.01	7	7.1	0.975	Very large	Yes	Yes
<i>Plasma</i>	> 0.05	5	5.5	0.447	Very large	No	Yes
<i>Plasma (without Barbosa)</i>	> 0.01 but < 0.05	3	2.9	0.896	Large	No	Yes
Within-group meta-analysis							
Bipolar depression	> 0.05	2	0.5	0.042	Very large	No	Yes
Mania	< 0.01	6	4.6	0.431	Large	No	Yes

^a Expected is the sum of the power of all studies to detect a difference equal to the effect size of the largest study with $\alpha = 5\%$.

^b P value in χ^2 -based excess significance test.

^c Large: $50\% \leq I^2 < 75\%$; Very Large: $I^2 \geq 75\%$

^d $P < 0.1$ in Egger's test of publication bias and effect size of the largest study more conservative than the effect size of the meta-analysis

^e 95% prediction interval includes the null value (zero)

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