



Supporting Information

for *Adv. Sci.*, DOI: 10.1002/advs.201900752

Gut Microbiota Changes in Patients with Bipolar Depression

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SUPPLEMENTARY FIGURES

Figure S1: Principle coordinates of microbial communities by principal coordinate analysis (PCoA) among three cohorts. (A-F) PCoA of unweighted UniFrac, weighted UniFrac, Hellinger, JSD, Pearson and Spearman distances at the OTU level showing significant differences in the first three principal coordinates between BD patients and healthy controls.

Figure S2: Taxonomy resolution of gut microbiota among healthy controls, untreated and treated BD patients. (A) Taxonomy resolution in all samples; each bar represents ratio of reads annotated at that level. (B) Relative abundance levels of the phyla present in samples from healthy controls, untreated and treated BD patients. *Bacteroidetes*, *Firmicutes*, *Proteobacteria*, and *Actinobacteria* were the most abundant in the gut microbiota. (C) Relative abundance levels of genera present in samples from healthy controls, untreated and treated BD patients. The *Bacteroides*, *Prevotella*, *Faecalibacterium*, *Roseburia* and *Lachnospiracea incertae sedis* genera dominate the gut microbiota.

Figure S3: Differences of gut microbiota between BD-I and BD-II subgroups.

(A) Principle coordinates of microbial communities by principal coordinate analysis (PCoA) between BD-I and BD-II patients, indicating no difference between BD-I and BD-II patients. (B) LDA scores showed significant bacterial differences between BD-I (red) and BD-II (green) subgroups. (C) A cladogram of different taxonomic compositions between BD-I (red) and BD-II (green) subgroups.

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Figure S1: Principle coordinates of microbial communities by principal coordinate analysis (PCoA) among three cohorts.

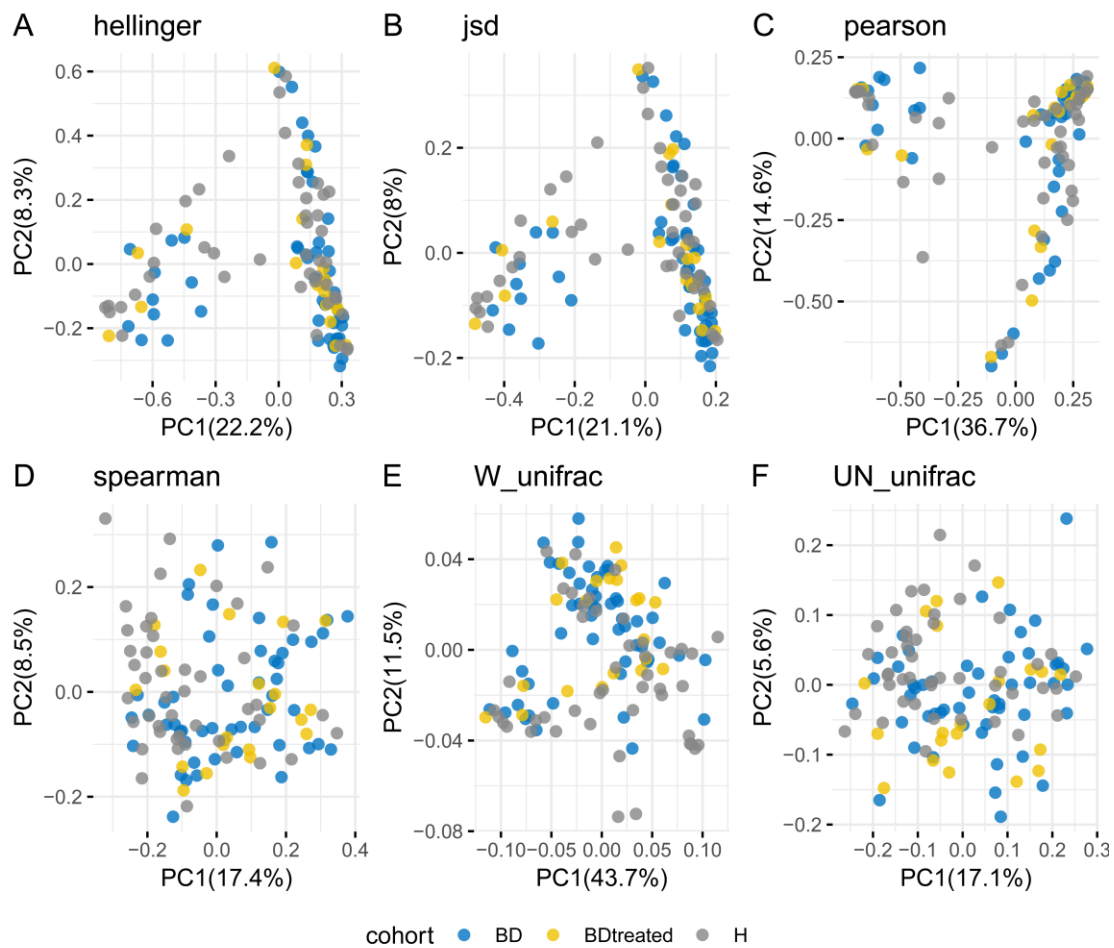


Figure S2: Taxonomy resolution of gut microbiota among healthy controls, untreated and treated BD patients.

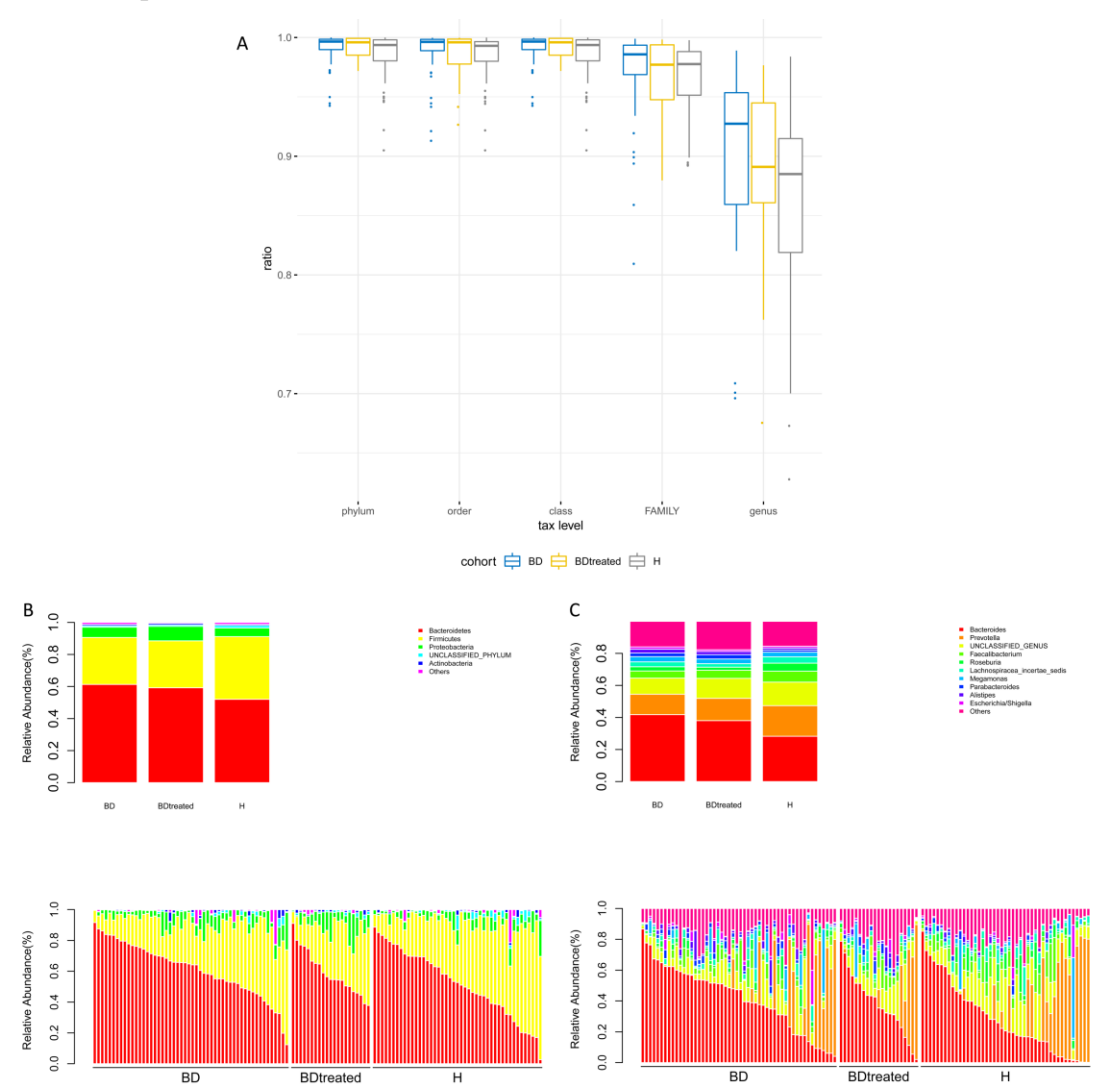


Figure S3: Differences of gut microbiota between BD-I and BD-II subgroups.

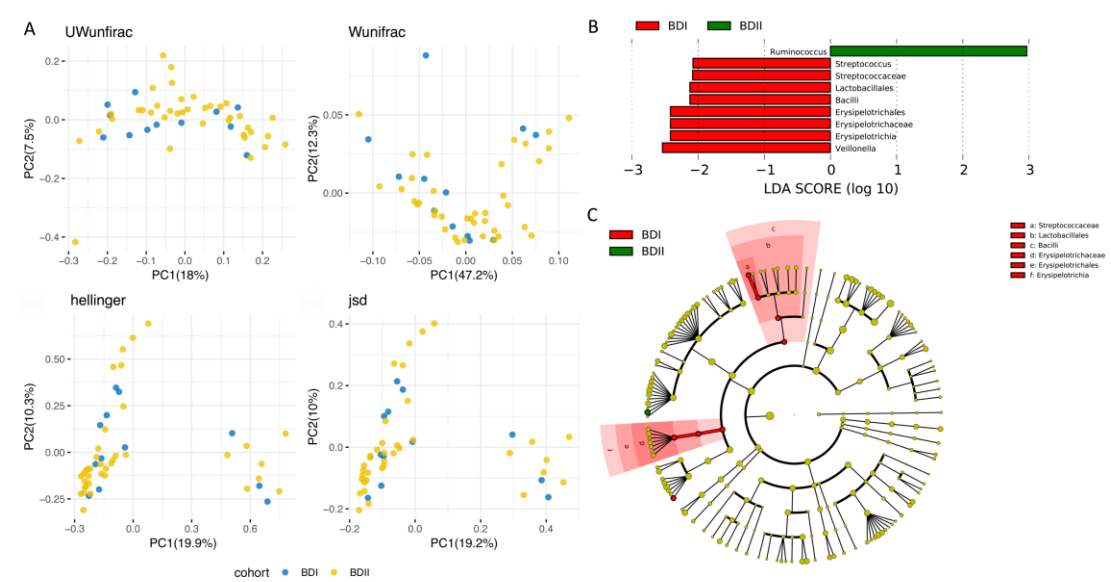


Table S1. Detailed characteristics of the recruited subjects

Num ber	Gro up	Gen der	Age (ye ar)	B MI	Fam ily histo ry	Ons et age (ye ar)	Durat ion of illness	Bipol ar diagn osis	MAD RS	HDRS -17	YM RS	
1	BD	Fem ale	40	25. 59	Y	21	19	I	35	39	0	
2	BD	Male	40	21. 47	N	34	6	II	25	27	3	
3	BD	Male	41	23. 88	N	41	0.5	II	23	29	2	
4	BD	Male	16	17. 72	N	14	1.5	II	37	36	2	

5	BD	Female	14	26.37	N	12	2	I	32	34	2	
6	BD	Female	NA	NA	NA	NA	NA	NA	NA	NA	NA	Discard
7	BD	Male	22	23.15	N	16	6	II	25	43	1	
8	BD	Male	16	28.73	Y	15	1	II	26	24	2	
9	BD	Male	34	22.91	Y	33	1	II	23	31	3	
10	BD	Female	19	22.84	N	12	7	NA	14	15	1	
11	BD	Female	26	17.58	N	24	2	I	33	31	4	
12	BD	Male	15	17.92	N	15	0.75	I	32	37	4	
13	BD	Male	NA	NA	NA	NA	NA	NA	NA	NA	NA	Discard
14	BD	Male	27	28.08	N	18	9	II	25	33	3	
15	BD	Female	58	22.58	N	48	10	I	46	50	0	
16	BD	Male	28	NA	N	NA	NA	I	23	30	1	
17	BD	Female	NA	NA	NA	NA	NA	NA	NA	NA	NA	Discard
18	BD	Female	21	16.82	N	16	5	I	21	24	3	
19	BD	Female	43	25.81	N	26	17	II	22	26	3	
20	BD	Male	23	22.49	N	16	7	II	25	28	3	
21	BD	Male	15	16.71	N	NA	NA	II	51	39	2	
22	BD	Male	16	16.36	N	12	4	II	30	40	1	
23	BD	Female	38	21.37	Y	23	15	I	20	18	1	
24	BD	Male	18	24.21	N	12	6	I	26	20	3	
25	BD	Female	17	20.58	N	14	3	II	35	25	4	
26	BD	Male	16	22.23	N	14	1.5	II	17	22	1	

27	BD	Male	16	30. 45	N	16	0.25	NA	27	30	4	
28	BD	Male	22	19. 53	N	19	3	II	41	35	3	
29	BD	Male	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
30	BD	Male	19	22. 1	Y	16	3	II	15	15	2	
31	BD	Fem ale	40	20. 31	Y	29	11	II	28	33	2	
32	BD	Male	19	19	N	17	2	II	17	13	0	Disc ard
33	BD	Fem ale	16	24. 22	Y	14	2	II	16	18	2	
34	BD	Fem ale	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
35	BD	Fem ale	25	16. 8	N	23	2	II	32	34	2	
36	BD	Fem ale	18	18. 44	N	15	3	II	30	29	0	
37	BD	Fem ale	17	16. 41	N	15	2	II	27	24	0	
38	BD	Male	17	21. 22	Y	15	2	II	38	40	0	
39	BD	Male	30	23. 84	N	16	14	I	22	22	2	
40	BD	Male	27	23. 3	N	16	11	II	26	38	5	
41	BD	Male	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
42	BD	Fem ale	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
43	BD	Male	17	19. 75	N	15	2	II	11	8	4	Disc ard
44	BD	Fem ale	24	21. 37	Y	16	8	II	44	39	1	
45	BD	Fem ale	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
46	BD	Male	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
47	BD	Fem ale	20	19. 78	N	19	1	II	7	5	0	Disc ard
48	BD	Male	34	23. 67	Y	7	30	I	4	7	0	Disc ard

49	BD	Fem ale	30	21. 5	N	29	1	II	15	19	0	
50	BD	Fem ale	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
51	BD	Male	31	27. 04	Y	21	10	I	28	35	4	
52	BD	Fem ale	NA	NA	NA	NA	NA	NA	NA	NA	NA	Disc ard
53	BD	Fem ale	22	17. 96	N	21	1	II	28	30	3	
54	BD	Male	16	17. 3	N	NA	NA	II	30	36	0	
55	BD	Male	21	18. 43	N	15	3	II	32	35	0	
56	BD	Fem ale	21	23. 44	N	NA	NA	II	38	37	3	
57	BD	Fem ale	22	21. 77	N	20	2	II	6	6	0	Disc ard
58	BD	Male	17	20. 05	N	15	2	II	16	13	0	Disc ard
59	BD	Fem ale	29	17. 53	N	22	7	II	45	36	0	
60	BD	Fem ale	14	20. 43	N	13	0.25	II	19	22	4	
61	BD	Male	20	21. 78	N	15	5	II	48	46	0	
62	BD	Male	20	17. 43	N	19	1	II	20	24	3	
63	BD	Male	41	13. 86	NA	NA	NA	NA	NA	NA	NA	Disc ard
64	BD	Male	21	18. 94	Y	21	0.5	II	NA	NA	NA	Disc ard
65	BD	Fem ale	20	18. 2	Y	15	5	II	21	29	0	
66	BD	Male	39	27. 73	Y	34	5	II	28	26	0	
67	BD	Male	27	25. 86	N	24	3	II	16	12	3	Disc ard
68	BD	Fem ale	26	25. 95	N	25	1	I	26	40	2	
69	BD	Male	17	18. 94	Y	17	0.25	II	17	18	3	
70	BD	Fem ale	17	21. 45	N	14	3	II	34	37	1	

71	BD	Fem ale	17	22. 21	N	17	0.25	II	21	20	0	
72	BD	Fem ale	22	20. 03	Y	NA	NA	II	20	22	0	
73	H	Fem ale	35	19. 31	N	/	/	/	/	/	/	
74	H	Fem ale	49	23. 24	N	/	/	/	/	/	/	
75	H	Fem ale	43	NA	N	/	/	/	/	/	/	
76	H	Male	32	23. 94	N	/	/	/	/	/	/	
77	H	Fem ale	28	21. 99	N	/	/	/	/	/	/	
78	H	Fem ale	38	21. 26	N	/	/	/	/	/	/	
79	H	Male	49	18. 86	N	/	/	/	/	/	/	
80	H	Male	54	27. 28	N	/	/	/	/	/	/	
81	H	Male	50	NA	N	/	/	/	/	/	/	
82	H	Fem ale	36	19. 25	N	/	/	/	/	/	/	
83	H	Male	38	NA	N	/	/	/	/	/	/	
84	H	Fem ale	38	19. 39	N	/	/	/	/	/	/	
85	H	Male	31	21. 29	N	/	/	/	/	/	/	
86	H	Male	59	26. 73	N	/	/	/	/	/	/	
87	H	Fem ale	61	22. 29	N	/	/	/	/	/	/	
88	H	Fem ale	28	18. 76	N	/	/	/	/	/	/	
89	H	Fem ale	22	20. 28	N	/	/	/	/	/	/	
90	H	Male	24	24. 22	N	/	/	/	/	/	/	
91	H	Fem ale	24	17. 78	N	/	/	/	/	/	/	
92	H	Male	34	20. 38	N	/	/	/	/	/	/	
93	H	Fem	24	20.	N	/	/	/	/	/	/	

		ale		31								
94	H	Fem ale	46	24. 65	N	/	/	/	/	/	/	
95	H	Fem ale	24	20. 81	N	/	/	/	/	/	/	
96	H	Male	17	20. 42	N	/	/	/	/	/	/	
97	H	Male	18	20. 28	N	/	/	/	/	/	/	
98	H	Male	17	27. 68	N	/	/	/	/	/	/	
99	H	Male	17	21. 79	N	/	/	/	/	/	/	
100	H	Male	18	20. 16	N	/	/	/	/	/	/	
101	H	Male	38	25. 35	N	/	/	/	/	/	/	
102	H	Male	30	29. 41	N	/	/	/	/	/	/	
103	H	Male	42	25. 69	N	/	/	/	/	/	/	
104	H	Fem ale	37	23. 05	N	/	/	/	/	/	/	
105	H	Male	25	20. 76	N	/	/	/	/	/	/	
106	H	Fem ale	60	20. 03	N	/	/	/	/	/	/	
107	H	Fem ale	47	26. 04	N	/	/	/	/	/	/	
108	H	Male	40	21. 63	N	/	/	/	/	/	/	
109	H	Fem ale	31	20. 31	N	/	/	/	/	/	/	
110	H	Fem ale	26	19. 48	N	/	/	/	/	/	/	
111	H	Male	54	25. 16	N	/	/	/	/	/	/	
112	H	Male	46	22. 73	N	/	/	/	/	/	/	
113	H	Fem ale	45	24. 6	N	/	/	/	/	/	/	
114	H	Male	38	27. 66	N	/	/	/	/	/	/	

115	H	Male	34	22. 75	N	/	/	/	/	/	/	
116	H	Fem ale	49	20. 13	N	/	/	/	/	/	/	
117	H	Fem ale	37	NA	N	/	/	/	/	/	/	

Table S2. PERMANOVA results by using distances and characteristics of recruited individuals					
	Cohort (P)	Age (P)	BMI (P)	Gender (P)	Residual (R ²)
Weighted Unifrac	0.0252	0.2349	0.1615	0.0024	0.88386
Unweighted Unifrac	0.0003	0.04015	0.1947	0.1054	0.92159
Spearman	1e-4	0.0025	0.1107	0.0233	0.88351
Hellinger	0.011899	0.078592	0.023598	0.006	0.91146
JSD	0.012	0.088291	0.02	0.006	0.91465
Pearson	0.059194	0.1225	0.011	0.006	0.87986

Table S3. Demographic and clinical details of BD patients following quetiapine treatment			
Demographic and Clinical Indexes		BD patients following quetiapine treatment	
		N=20	%
Sex	Female	11	55
	Male	9	45
Bipolar diagnosis	I	3	15
	II	17	85
Age (year, mean $\pm$ SD)		23.95 $\pm$ 7.44	
BMI (kg/m ² , mean $\pm$ SD)		21.91 $\pm$ 3.56	
Onset age (year, mean $\pm$ SD)		19.75 $\pm$ 6.75	
Duration of illness (year, mean $\pm$ SD)		4.25 $\pm$ 3.71	
		Pre-treatment	Post-treatment
			P
MADRS score (mean $\pm$ SD)		25.75 $\pm$ 7.87	11.29 $\pm$ 8.35
HDRS-17 score (mean $\pm$ SD)		28.25 $\pm$ 7.27	11.65 $\pm$ 8.76
YMRS score (mean $\pm$ SD)		2.10 $\pm$ 1.52	1.47 $\pm$ 1.77
			0.33
Abbreviations: SD, standard deviation.			

Table S4. 16S rRNA Sequencing Data from the Recruited Subjects										
Group	Available_reads	Random_chosen_reads	Observed	Shannon	Simpson	Inverse Simpson	Observed	Chao1	Ice	
BD	46240	20000	212	3.02	0.88	8.45	181	203.13	189.73	
BD	32679	20000	192	2.27	0.76	4.08	163	217.38	179.85	
BD	58880	20000	58	1.4	0.6	2.51	36	56.17	52.31	
BD	65496	20000	184	3.32	0.93	14.29	143	173.38	152.39	
BD	39391	20000	113	1.96	0.72	3.6	92	144.56	105.66	
BD	59076	20000	178	2.16	0.73	3.72	127	165.23	137.1	Discard
BD	44069	20000	164	3.13	0.93	13.51	140	166.28	150.28	
BD	40081	20000	128	2.18	0.8	4.94	106	129.06	116.72	
BD	37355	20000	106	2.26	0.83	5.91	89	125	96.43	
BD	33767	20000	172	3.06	0.9	9.59	144	173.39	150.75	
BD	29266	20000	163	2.78	0.88	8.21	138	179.29	151.84	
BD	33406	20000	193	3.12	0.91	11.26	165	190.29	176.49	
BD	41989	20000	104	1.91	0.68	3.08	80	104.08	85.98	Discard
BD	52315	20000	204	1.35	0.38	1.62	158	188.86	170.86	
BD	49139	20000	125	1.39	0.48	1.93	93	122.39	101.18	
BD	38368	20000	127	1.97	0.64	2.8	112	153.14	120.55	
BD	37256	20000	157	2.64	0.84	6.12	138	168.73	146.92	Discard
BD	84800	20000	226	2.82	0.88	8.17	156	171.16	163.54	
BD	63966	20000	106	1.31	0.46	1.85	75	93.05	82.7	
BD	32100	20000	24	2.8	0.79	4.71	21	257.	233.	

			5				5	88	89	
BD	35515	20000	21 3	3.24	0.91	10.84	18 7	254. 5	204. 51	
BD	25650	20000	12 7	2.99	0.9	10.46	10 7	149. 67	111. 86	
BD	34465	20000	23 6	3.45	0.93	13.53	20 2	231. 17	212. 37	
BD	44085	20000	12 5	2.46	0.84	6.27	99	113. 45	104. 78	
BD	37447	20000	12 6	2.61	0.87	7.56	10 5	195	119. 59	
BD	38963	20000	20 6	2.3	0.68	3.12	17 0	200. 12	181. 68	
BD	30276	20000	11 6	2.35	0.8	4.88	10 0	109. 5	107. 6	
BD	30471	20000	19 8	2.13	0.65	2.88	16 7	201	180. 66	
BD	38880	20000	17 0	2.85	0.85	6.82	15 0	182. 67	159. 37	Disca rd
BD	50290	20000	16 3	3	0.88	8.16	12 9	149. 83	139. 16	
BD	31294	20000	15 7	3.03	0.91	10.87	13 7	150. 33	143. 47	
BD	78146	20000	22 0	3.05	0.91	11.51	16 4	186. 5	173. 42	Disca rd
BD	35979	20000	15 6	3.05	0.92	12.83	13 3	161. 04	144. 18	
BD	46205	20000	28 4	2.95	0.8	5	22 5	262. 5	240. 08	Disca rd
BD	43377	20000	15 9	2.76	0.87	7.92	12 6	168. 25	134. 58	
BD	44736	20000	16 4	3.04	0.91	10.86	11 9	143. 5	126. 5	
BD	37227	20000	14 5	2.96	0.9	9.6	12 4	173	134	
BD	30284	20000	17 5	3.24	0.92	12.52	15 6	210	170. 95	
BD	39846	20000	11 8	2.64	0.87	7.79	98	131. 06	106. 03	
BD	40227	20000	23 7	3.55	0.94	16.52	20 4	254. 7	216. 44	
BD	31440	20000	16 4	2.91	0.85	6.69	14 9	207. 91	163. 07	Disca rd

BD	50906	20000	20 7	2.89	0.86	7.03	14 9	185. 13	162. 35	Disca rd
BD	33110	20000	17 9	3.34	0.93	13.86	15 6	202. 72	165. 41	Disca rd
BD	27298	20000	13 3	2.64	0.85	6.82	11 9	137. 38	126. 6	
BD	23899	20000	18 7	3.21	0.93	14.85	17 5	245. 23	197. 89	Disca rd
BD	43997	20000	31 2	3.74	0.94	17.69	25 0	280. 42	262. 08	Disca rd
BD	24871	20000	12 9	2.26	0.74	3.78	11 7	131. 24	124. 81	Disca rd
BD	29935	20000	15 5	2.8	0.88	8.11	13 9	191. 07	147. 71	Disca rd
BD	32283	20000	19 8	3.46	0.95	18.36	17 1	202. 11	184. 8	
BD	54836	20000	14 9	2.11	0.71	3.45	10 8	237. 6	124. 62	Disca rd
BD	22415	20000	12 3	2.09	0.76	4.25	11 4	144. 15	125. 51	
BD	39952	20000	17 8	2.7	0.81	5.32	14 6	194. 05	156. 51	Disca rd
BD	38105	20000	18 2	3.05	0.91	11	15 2	196. 46	164. 34	
BD	50314	20000	11 5	1.65	0.59	2.42	85	115. 73	99.3 8	
BD	51022	20000	22 1	2.95	0.87	7.79	17 9	229	193. 8	
BD	71955	20000	20 9	3.08	0.88	8.31	16 8	180. 25	173. 55	
BD	32870	20000	18 3	2.27	0.78	4.47	15 3	185. 4	166. 5	Disca rd
BD	26400	20000	14 4	2.79	0.88	8.38	12 5	155. 73	133. 8	Disca rd
BD	36953	20000	19 7	3.77	0.96	25.43	16 4	186. 53	173. 98	
BD	42349	20000	13 9	2.63	0.87	7.43	11 9	158. 06	126. 94	
BD	56395	20000	18 2	2.58	0.8	4.96	14 3	173	153. 21	
BD	49871	20000	24 4	2.95	0.88	8.39	20 0	257. 78	214. 18	
BD	41342	20000	17 7	2.32	0.82	5.71	12 5	182. 14	141. 38	Disca rd

BD	55649	20000	24 3	3.48	0.94	16.41	17 6	221. 38	187. 85	Disca rd
BD	69218	20000	21 6	2.75	0.84	6.19	15 4	192	167. 44	
BD	50903	20000	13 2	1.37	0.49	1.97	89	118. 39	96.4 9	
BD	55015	20000	18 6	2.72	0.87	7.87	14 4	180. 3	156. 86	Disca rd
BD	36867	20000	12 5	3.04	0.91	11.06	11 4	136	121. 95	
BD	11735	11735	63	2.14	0.8	5.01	57	75	60.7 1	
BD	298358	20000	29 7	3.46	0.94	17.02	18 0	253. 5	197. 07	
BD	34784	20000	14 6	2.94	0.91	10.68	12 9	155. 89	135. 52	
BD	23110	20000	15 6	2.93	0.9	9.54	14 3	192. 85	156. 81	
BD Treat ed	27221	20000	18 8	2.58	0.79	4.67	17 3	209. 03	186. 18	
BD Treat ed	29797	20000	10 8	2.14	0.8	4.98	93	105. 97	102. 07	
BD Treat ed	38709	20000	16 0	0.75	0.21	1.26	12 8	229. 25	147. 51	
BD Treat ed	43087	20000	26 9	3.18	0.92	12.67	20 5	251. 23	219. 11	
BD Treat ed	35602	20000	14 4	2.84	0.88	8.2	11 8	129. 64	122. 84	
BD Treat ed	17999	17999	16 6	3.18	0.89	9.38	15 4	202. 05	164. 56	
BD Treat ed	13503	13503	19 1	1.98	0.55	2.21	18 0	200. 64	190. 65	
BD Treat ed	13910	13910	15 5	3.63	0.95	20.72	15 8	178. 25	168. 13	
BD Treat	63322	20000	12 2	1.98	0.78	4.58	87	113. 18	96.2 3	

ed										
BD Treat ed	10991	10991	14 7	3.2	0.91	11.25	14 0	215	149. 01	
BD Treat ed	64447	20000	17 6	3.02	0.9	10.19	12 3	158. 04	134. 74	
BD Treat ed	43105	20000	12 5	1.81	0.64	2.77	10 2	126. 04	110. 9	
BD Treat ed	45896	20000	17 9	2.63	0.77	4.43	14 1	155. 29	147. 37	Disca rd
BD Treat ed	19944	19944	16 0	2.77	0.85	6.59	15 1	183. 03	163. 43	Disca rd
BD Treat ed	25638	20000	16 1	3.16	0.93	13.71	14 7	208. 25	159. 93	
BD Treat ed	19409	19409	21 0	3.39	0.93	14.07	20 1	283. 29	217. 42	
BD Treat ed	12567	12567	73	2.39	0.82	5.49	69	125. 25	74.7 3	
BD Treat ed	23198	20000	17 7	3.16	0.91	10.79	16 5	197. 24	178. 84	Disca rd
BD Treat ed	24480	20000	12 3	3.01	0.9	10.21	12 2	150. 17	130. 76	
BD Treat ed	64904	20000	16 8	2.61	0.87	7.83	12 6	177. 57	142. 53	
BD Treat ed	22179	20000	20 5	3.52	0.94	17.2	19 4	254. 5	211. 84	
BD Treat ed	24581	20000	16 0	3.37	0.94	15.85	14 2	170. 8	148. 75	
BD Treat ed	22480	20000	12 1	2.62	0.84	6.28	10 8	139. 25	118. 8	
H	39285	20000	14	2.83	0.87	7.83	12	171.	136.	

			9				9	25	75	
H	48572	20000	20 0	3.1	0.88	8.43	16 9	188. 6	178. 61	
H	51033	20000	20 0	3.33	0.92	12.35	17 2	195. 36	182. 63	
H	66009	20000	24 4	3.6	0.95	18.6	19 4	220. 69	203. 8	
H	47241	20000	27 0	3.79	0.95	21.13	22 9	281. 36	246. 35	
H	47266	20000	18 0	3.15	0.92	12.15	15 4	184. 73	162. 9	
H	40216	20000	19 7	3.19	0.91	11.19	16 8	187. 53	175. 41	
H	35014	20000	15 3	2.4	0.74	3.9	13 8	164	148. 52	
H	37721	20000	10 9	1.19	0.39	1.63	86	161	100. 46	
H	59331	20000	18 3	2.67	0.85	6.61	15 5	201. 29	166. 74	
H	24844	20000	19 1	3.3	0.92	13.21	17 4	212. 03	192. 56	
H	34017	20000	12 3	2.56	0.85	6.62	10 3	119. 9	106. 71	
H	54677	20000	13 0	1.72	0.69	3.21	97	130. 8	106. 62	
H	33348	20000	22 6	3	0.86	7.21	19 3	240. 12	204. 12	
H	34162	20000	70	1.54	0.6	2.48	55	71.6 7	58.0 2	
H	32607	20000	11 6	2.32	0.81	5.19	10 3	119. 2	108. 31	
H	35866	20000	29 5	3.67	0.95	19.42	21 9	267. 40	233. 09	
H	31549	20000	14 9	3.10	0.93	13.64	11 3	153. 00	119. 84	
H	33795	20000	35 5	4.00	0.96	25.92	27 5	337. 50	291. 45	
H	42037	20000	18 6	2.04	0.73	3.66	13 8	202. 65	156. 08	
H	39993	20000	27 7	3.07	0.86	6.90	20 2	263. 54	214. 82	
H	52848	20000	21 1	2.94	0.88	8.57	14 6	186. 04	158. 65	

H	45582	20000	22 4	2.20	0.71	3.49	16 4	218. 86	182. 90	
H	37284	20000	27 5	2.51	0.72	3.55	20 9	230. 03	217. 83	
H	46038	20000	20 7	2.24	0.81	5.26	15 4	186. 40	165. 74	
H	33097	20000	23 5	2.69	0.84	6.41	18 6	234. 09	203. 32	
H	32272	20000	24 3	2.06	0.64	2.77	18 2	213. 13	196. 46	
H	13237	13237	24 0	2.49	0.70	3.29	20 8	246. 35	221. 56	
H	39505	20000	28 6	3.27	0.90	10.07	21 8	258. 02	231. 70	
H	28654	20000	29 4	3.89	0.96	27.62	22 8	266. 03	240. 44	
H	32853	20000	27 3	3.69	0.96	23.12	21 2	240. 44	221. 66	
H	40727	20000	25 8	2.85	0.87	7.46	19 0	218. 66	199. 37	
H	31731	20000	28 0	3.57	0.94	16.57	22 4	308. 96	239. 75	
H	32322	20000	20 5	2.87	0.86	7.08	15 4	182. 04	163. 50	
H	31055	20000	26 6	3.13	0.90	9.79	21 1	267. 25	227. 98	
H	30930	20000	21 6	3.68	0.96	23.32	16 5	189. 00	172. 66	
H	28741	20000	25 5	3.27	0.91	10.90	20 0	248. 66	215. 06	
H	22257	20000	26 4	3.82	0.95	21.58	21 2	293. 00	222. 76	
H	42029	20000	28 6	3.16	0.92	12.73	19 5	237. 47	206. 12	
H	24712	20000	29 9	3.41	0.92	12.00	23 6	280. 08	252. 19	
H	31451	20000	37 3	3.92	0.96	22.84	29 4	372. 77	316. 62	
H	27428	20000	12 2	2.53	0.88	8.07	92	124. 40	97.9 2	
H	63668	20000	41 7	3.11	0.85	6.56	27 3	327. 39	291. 72	
H	37556	20000	25 1	2.03	0.64	2.79	19 1	239. 02	208. 02	

H	38333	20000	35 4	3.48	0.92	12.38	26 2	311. 47	283. 31	
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Table S5. Wicoxon rank sum test of principle coordinates in BD patients and healthy controls

PC	Cohort	P value
Unweighted_Unifrac_PC1	BD_H	0.004010234
Unweighted_Unifrac_PC2	BD_H	0.006613568
Unweighted_Unifrac_PC3	BD_H	0.000234761
Unweighted_Unifrac_PC4	BD_H	0.015413256
Unweighted_Unifrac_PC5	BD_H	0.00808057
Unweighted_Unifrac_PC1	BDtreated_H	0.037808237
Unweighted_Unifrac_PC2	BDtreated_H	0.005476419
Unweighted_Unifrac_PC3	BDtreated_H	0.000253896
Weighted_Unifrac_PC2	BD_H	8.56E-05
Weighted_Unifrac_PC2	BDtreated_H	0.000918378
Weighted_Unifrac_PC4	BDtreated_H	0.009204282
Weighted_Unifrac_PC5	BDtreated_H	0.025863306
Weighted_Unifrac_PC4	BD_ BDtreated_	0.00752612
Hellinger_PC1	BD_H	0.023938492
Hellinger_PC2	BD_H	0.024349082
Hellinger_PC3	BD_H	0.002706114
Hellinger_PC4	BD_H	0.000968565
Hellinger_PC4	BDtreated_H	0.023421163
JSD_PC1	BD_H	0.016570556
JSD_PC2	BD_H	0.015135017
JSD_PC3	BD_H	0.0038417
JSD_PC4	BD_H	0.00211161
JSD_PC4	BDtreated_H	0.021901476
Spearman_PC1	BD_H	0.00010472
Spearman_PC3	BD_H	3.20E-08
Spearman_PC4	BD_H	0.002017219
Spearman_PC1	BDtreated_H	0.00199482
Spearman_PC3	BDtreated_H	0.000226506
Spearman_PC4	BDtreated_H	2.90E-05

Pearson_PC1	BD_H	0.024765569
Pearson_PC2	BD_H	0.023938492
Pearson_PC3	BD_H	0.000667811
Pearson_PC5	BD_H	0.049912618
Pearson_PC4	BDtreated_H	0.036668288
Pearson_PC5	BDtreated_H	0.042655116

Table S6. Genera to construct random forest models to distinguish BD and healthy controls

Genus	Mean (BD)	Mean (H)	P value	Enrich
Anaerofilum	0	1.78E-05	0.001712543	H
Brucella	4.81E-06	0	0.030089686	BD
Bacteroides	0.417235558	0.282727841	0.001526887	BD
Helicobacter	0	4.44E-06	0.03078809	H
Halomonas	0.000103962	4.44E-05	0.000905155	BD
Gemmiger	0.006697115	0.011019461	0.009419587	H
Roseburia	0.026004924	0.049788418	0.016124731	H
Parabacteroides	0.022587608	0.01294098	0.000405006	BD
Porphyromonas	2.21E-05	1.00E-05	0.015499423	BD
Escherichia/Shigella	0.014265587	0.010825604	0.046620251	BD
Delftia	5.77E-06	0	0.030089686	BD
Parasutterella	0.009427885	0.013315036	0.011611481	H
Leptotrichia	9.62E-07	5.56E-06	0.031797739	H
Coproccoccus	0.002905769	0.007006443	0.004615631	H
UNCLASSIFIED_GENUS	0.100295728	0.146505452	0.001456654	H
Klebsiella	0.00168677	0.00239279	0.040163271	H
Slackia	4.81E-06	2.00E-05	0.013171202	H
Microcella	6.73E-06	1.11E-06	0.039323546	BD
Ruminococcus	0.007025	0.013781164	0.01223063	H
Rothia	6.73E-06	3.11E-05	0.021262243	H
Turicibacter	0.000516694	7.39E-05	0.006286757	BD
Anaerofustis	5.77E-06	0	0.017217234	BD
Peptoniphilus	1.54E-05	3.33E-06	0.041360185	BD
Sporobacter	4.81E-06	1.33E-05	0.022840678	H
Neisseria	5.77E-06	1.83E-05	0.004260251	H
Weissella	6.06E-05	0	0.009885673	BD
Erysipelotrichaceae_incertae_sedis	0.001177502	0.001184444	0.040369485	BD
Lachnospira	1.77E-05	7.78E-06	0.034717402	BD
Lactobacillus	0.000204808	1.00E-05	0.000291309	BD

Faecalibacterium	0.044677559	0.068554216	0.021408432	H
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Table S7. HDRS-17 and MADRS score changes following quetiapine treatment in BD patients

Number	HDRS-17 scores			MADRS scores		
	Untreated	Treated	Reductive ratio	Untreated	Treated	
1	29	7	0.76	23	9	
2	24	13	0.46	26	14	
3	33	34	-0.03	25	26	
4	24	5	0.79	21	2	
5	28	5	0.82	25	5	
6	25	13	0.48	35	16	
7	35	12	0.66	41	7	
8	33	13	0.61	28	12	
9	18	8	0.56	16	9	
10	38	NA	NA	26	NA	
11	19	13	0.32	15	12	
12	35	10	0.71	28	9	
13	6	4	0.33	6	4	Discard
14	13	10	0.23	16	11	Discard
15	36	32	0.11	45	35	
16	24	10	0.58	20	8	
17	29	5	0.83	21	6	
18	22	18	0.18	26	19	Discard
19	40	NA	NA	26	NA	
20	18	9	0.50	17	11	
21	37	NA	NA	34	NA	
22	20	8	0.60	21	10	
23	20	1	0.95	22	1	

Table S8. Genera to construct random forest models to distinguish quetiapine treatment response in BD patients

Genus	Mean (Respond)	Mean (Nonrespond)	P value	Enrich
Acinetobacter	0	4.00E-05	0.015061822	Nonrespond
Asaccharobacter	0	6.00E-05	0.015223682	Nonrespond
Eubacterium	4.17E-06	0.00015	0.002262979	Nonrespond
Paraprevotella	0.003254669	0	0.007173648	Respond
Lactococcus	0	3.00E-05	0.015223682	Nonrespond
Lachnospira	3.90E-05	0	0.035646108	Respond
Lactobacillus	1.25E-05	0.00017	0.03624997	Nonrespond
TM7_genera_incertae_sedis	6.25E-05	0	0.036612569	Respond
Achromobacter	0	2.00E-05	0.015061822	Nonrespond
Bifidobacterium	0.0014375	0.01763	0.035603193	Nonrespond