

## Supplemental information

### Tables

**Table S1** Demographic and clinical information of brain samples from the Stanley Medical Research Institute Array Collection

Group	Age	Sex (M/F)	PMI	RI	Brain pH	AAO	Suicide	Total
								Mean (SD)
Bipolar disorder	45.9 (10.0)	13/17	39.1 (18.5)	10.1 (11.0)	6.5 (0.3)	25.1 (9.6)	13	30
Unaffected control	44.7 (7.7)	23/7	28.3 (11.7)	2.9 (2.0)	6.6 (0.3)	na	0	30

F, female; M, male; PMI, postmortem interval; RI, refrigerator interval; na, not applicable

There were 105 samples received for microarray analysis of which 93 passed quality control analysis. Only unaffected subjects (N=30) and individuals with bipolar disorder (N=30) were used in the current analysis.

**Table S2** Polymorphisms detected by direct sequencing of 31 patients with early-onset BD

SNP	Allele	Amino-acid change	Position in the gene	Position in the genomic sequence <sup>c</sup>	MAF	refSNP ID
SNP1	G/T <sup>a</sup>	-	Promoter <sup>b</sup>	-902	0.10	
SNP2	T/C	-	Promoter <sup>b</sup>	-864	0.02	
SNP3	C/A	-	Promoter <sup>b</sup>	-598	0.02	
SNP4	C/A <sup>a</sup>	-	Promoter <sup>b</sup>	-523	0.34	rs6039769
SNP5	G/T	-	Intron 2	56776	0.03	rs362585
SNP6	A/T <sup>a</sup>	-	Intron 3	65704	0.06	rs2076239
SNP7	T/G	-	Intron 4	66121	0.05	
SNP8	A/C <sup>a</sup>	-	Intron 5	77976	0.48	rs362987
SNP9	C/T	D110D	Exon 6	78145	0.06	rs362998
SNP10	G/A	-	Intron 6	80321	0.06	rs363004
SNP11	C/T	-	Intron 6	80354	0.03	rs363005
SNP12	G/A <sup>a</sup>	-	Intron 7	80607	0.16	rs363006
SNP13	T/G	-	Exon 8	87608	0.45	rs3746544
SNP14	T/C <sup>a</sup>	-	Exon 8	87612	0.26	rs1051312
SNP15	C/T <sup>a</sup>	-	Exon 8	88266	0.39	rs8636

MAF: minor allele frequency

<sup>a</sup> tagging SNPs used for association studies<sup>b</sup> the putative promoter region corresponds to a predicted CpG island (<http://genome.ucsc.edu>)<sup>c</sup> The +1 nucleotide corresponds to the transcription start site (NM\_003081 and NM\_130811)

**Table S3. Description of the population used for association studies**

Phenotype	AAO (years)	Number of individuals	Males	Females
Bipolar subjects	≤21	197	87	110
	>21	202	81	121
	ND	10	4	6
Total		409	172	237
Control subjects		136	86	50
<b>Total</b>		<b>545</b>	<b>258</b>	<b>287</b>

AAO: age-at-onset

ND: not-determined

**Table S4** Association study between subjects affected with late-onset bipolar disorder (N=202) and healthy controls (N=136)

SNP	Minor allele	Allele frequency		$\chi^2$	<i>p value</i>	Odds ratio
		in affected individuals	in unaffected controls			
SNP1	T	0.11	0.11	0.00	1	1
SNP4	A	0.35	0.39	1.52	0.22	0.82
SNP6	T	0.05	0.04	0.26	0.61	1.22
SNP8	C	0.44	0.47	0.58	0.45	0.89
SNP12	A	0.15	0.13	0.23	0.63	1.12
SNP14	C	0.25	0.21	1.63	0.20	1.27
SNP15	T	0.35	0.38	0.60	0.44	0.88

**Table S5. Polymorphisms used as genomic control**

NCBI SNP reference	Sequence	Allele frequency						Allele frequency in unaffected individuals	$\chi^2$	p value			
		Chromosome location	Minor allele	in European HapMap population	frequency in affected individuals	Allele frequency in unaffected individuals							
rs3811886	ACCCAACAGCCTCAAGTAGCCTTAT [G/C] TTTTTACCTAACCTGCCTTCTAAA	5	G	0.200	0.220	0.183	1.613	0.204					
rs3751436	TCTTATTAGAAGTACAATACTTCTC [T/C] GCTTGCAAAACTTCCTATTCTACAT	13	T	0.034	0.016	0.008	0.947	0.331					
rs3782578	TCTAGGAAGATTGCTTGCCTTGCA [T/C] GGAGGTGGAGACGGGAGTTAGGGAG	12	T	0.305	0.316	0.285	0.879	0.349					
rs221437	CAGAGTAGCTCCTATAGAAGATTAA [C/T] GTTAAGTTATCTCACTTGGAGAACAA	14	T	0.246	0.268	0.212	3.304	0.069					
rs3786455	ACTTTGAGCTGATGGTTCTCAATTA [T/C] GTCTGATGCCTGAGCTATATAATAG	18	T	0.421	0.451	0.473	0.411	0.521					
rs3781816	GCCTAGACCTGATTGATAACAGGGG [A/G] CCAAGCAAGAAATGAGTGCTGGGAT	11	G	0.217	0.265	0.258	0.051	0.821					
rs3766793	AAAGCAAGCAGGCTACAGATTATT [C/T] TTGTGGAAGATACTTTGGGTTAT	1	T	0.150	0.173	0.133	2.410	0.121					
rs2151512	CTCAGGTGTCCACCTCGAGCGCAGG [C/T] AGAGGTTGAGCGGGAGAGGGGACT	20	T	0.233	0.292	0.267	0.628	0.428					
rs3754749	GCAGATTCCAACGGTATGCTTCA [G/A] AACAAACATAATGTGTGGAGTGTCCA	2	G	0.208	0.177	0.186	0.094	0.759					
rs1921361	TGGGGATATACTTCATCCCTACCT [T/C] AAGAAATTCAATTCTTCTTACTCTCC	X	T	0.483	0.383	0.385	0.316	0.574					
rs2289311	GGGGACAATGCTGGGCAGGGCCATC [G/A] AGACCCCTGCTGCCCTGCCCTCCTG	10	G	0.343	0.340	0.353	0.170	0.680					
rs4782053	AAGAAGAGATGTCTATCTTACACAC [A/G] CACCCCTTTAGGAAAACCTCTGGG	16	G	0.333	0.329	0.275	2.702	0.100					
rs2375801	CCATTCAATTTCAGTTATTCTGTTGA [C/T] TATTTTAAAAGGTGCTAAGGAAGA	4	T	0.350	0.316	0.323	0.045	0.832					
rs4633	CCAAGGAGCAGCGCATCCTGAACCA [C/T] GTGCTGCAGCATGGGAGCCCAGGA	22	T	0.475	0.490	0.444	1.748	0.186					
rs3782219	CTGGGTGCTTATTAGGACTCCAC [C/T] CTACAATTGCAGGCTAAGTTGCAA	12	T	0.192	0.222	0.267	2.249	0.134					

**Table S6** Comparison of allelic and genotypic frequencies of SNP4 between brain sample and French population

Samples	Phenotype	Age at onset	AA (freq.)	AC (freq.)	CC (freq.)	f(A)	f(C)
Brains	Bipolar disorder	Early-onset	1 (.08)	5 (.38)	7 (.54)	0.27	0.73
		Late-onset	0 (.00)	10 (.59)	7 (.41)	0.29	0.71
		Total	1 (.03)	15 (.50)	14 (.47)	0.28	0.72
	Controls		4 (.13)	14 (.47)	12 (.40)	0.37	0.63
French population	Bipolar disorder	Early-onset	17 (.09)	79 (.40)	100 (.51)	0.29	0.71
		Late-onset	28 (.14)	84 (.42)	90 (.45)	0.35	0.65
		Total	46 (.11)	170 (.41)	199 (.48)	0.32	0.68
	Controls		24 (.18)	58 (.43)	54 (.40)	0.39	0.61