Supplementary Online Content


eFigure. Plots of Association Between Single Single-Nucleotide Polymorphisms and Bipolar Disorder

eTable 1. List of 124 Candidate Genes

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eFigure. Plots of association between single single-nucleotide polymorphisms (SNPs) and bipolar disorder, by physical position. A, Single SNP odds ratios (ORs) for transmission disequilibrium test (TDT). B, Transmission disequilibrium tests for single SNPs.
### eTable 1. List of 124 Candidate Genes

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| PREP    | Prolyl endopeptidase                                                         | chr6:105827231-105966800 | 140.5 | 22 | 18 | 18 | 117 | 0.88 | 0.80 | 140.5 | 22 | 18 | 18 | 117 | 0.88 | 0.80 |
| PRKCA   | Protein kinase C, α                                                          | chr17:61723869-62235162 | 516.4 | 76 | 71 | 71 | 517 | 0.87 | 0.78 | 516.4 | 76 | 71 | 71 | 517 | 0.87 | 0.78 |
| PTGES   | Prostaglandin E synthase                                                     | chr9:129576171-129604004 | 29.7 | 8 | 5 | 5 | 29 | 0.81 | 0.62 | 29.7 | 8 | 5 | 5 | 29 | 0.81 | 0.62 |
| RAB7    | RAB7, member ras oncogene family                                            | chr3:129924388-130020524 | 103.7 | 6 | 6 | 6 | 28 | 0.96 | 0.96 | 103.7 | 6 | 6 | 6 | 28 | 0.96 | 0.96 |
| RAF1    | V-raf-1 murine leukemia viral oncogene homologue 1                          | chr3:12597623-12684167 | 95.6 | 8 | 7 | 7 | 67 | 0.94 | 0.96 | 95.6 | 8 | 7 | 7 | 67 | 0.94 | 0.96 |
| RGS4    | Regulator of G-protein signaling 4                                          | chr1:159763238-159782959 | 22.2 | 3 | 3 | 3 | 14 | 0.91 | 0.93 | 22.2 | 3 | 3 | 3 | 14 | 0.91 | 0.93 |
| SIAT4A  | ST3 β-galactoside α-2,3-sialyltransferase 1                                   | chr8:134537248-134663109 | 128.0 | 54 | 45 | 45 | 177 | 0.80 | 0.72 | 128.0 | 54 | 45 | 45 | 177 | 0.80 | 0.72 |
| SLC18A1 | Solute carrier family 18 (vesicular monoamine), member 1                    | chr8:20041820-20093804 | 53.4 | 14 | 11 | 11 | 63 | 0.82 | 0.76 | 53.4 | 14 | 11 | 11 | 63 | 0.82 | 0.76 |
| SLC2A2  | Solute carrier family 2 (facilitated glucose transporter), member 2         | chr3:172191895-172237179 | 45.6 | 10 | 9 | 8 | 35 | 0.97 | 1.00 | 45.6 | 10 | 9 | 8 | 35 | 0.97 | 1.00 |
| SLC5A3  | Solute carrier family 5 (inositol transporters), member 3                   | chr21:34381492-34396474 | 17.2 | 3 | 2 | 2 | 11 | 0.88 | 0.91 | 17.2 | 3 | 2 | 2 | 11 | 0.88 | 0.91 |
| SLC6A11 | Solute carrier family 6 (neurotransmitter transporter, GABA), member 11     | chr3:10823410-10956934 | 137.2 | 24 | 17 | 15 | 119 | 0.73 | 0.48 | 137.2 | 24 | 17 | 15 | 119 | 0.73 | 0.48 |
| SLC6A3  | Solute carrier                                                              | chr5:1441625-144366711 | 67.6 | 13 | 11 | 10 | 56 | 0.78 | 0.68 | 67.6 | 13 | 11 | 10 | 56 | 0.78 | 0.68 |

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**Abbreviations:**
cAMP, cyclic adenosine monophosphate; chr, chromosome; CREB, cyclic AMP-responsive element binding; GABA, γ-aminobutyric acid; GTP, glutamyl transpeptidase; HD, heterodimerization; InsP_3, inositol 1,4,5-triphosphate; kb, kilobase; MMTV, mouse mammary tumor virus; PHD, plant homeodomain; SNP, single-nucleotide polymorphism; TNF, tumor necrosis factor.

aInsP_3 and GSK3B/Wnt refer to genes related to the respective signaling pathways; in some cases of convergence, genes are arbitrarily assigned to GSK3B/Wnt.
bIndicates meeting quality control criteria (see text for details).
cIndicates mean R^2 between genotyped SNPs and all HapMap (International HapMap Project) SNPs in the gene region.
dIndicates proportion of HapMap SNPs in the gene region captured with R^2 of 0.8 or greater by the genotyped (tag) SNPs.
eARVCF and COMT lie within 20 kb and were therefore considered a single landmark for tagging purposes.
fBecause of their size, NRG1 and GRIK2 were not assessed using tag SNPs but rather with the inclusion of selected SNPs previously associated with schizophrenia or bipolar disorder.
g+B85
**eTable 2. Summary of SNP Data Cleaning**

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<td>Begin with all genotypes with genotype call score &gt; 0.25, indicating high confidence</td>
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<td>Eliminate SNPs showing &lt; 60% high-confidence genotypes across all genotyped samples (71 SNPs)</td>
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<td>3.</td>
<td>Eliminate individuals with high-confidence genotypes in &lt; 95% of retained SNPs (4 subjects)</td>
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<td>4.</td>
<td>Eliminate SNPs with high-confidence genotypes in &lt; 97.5% of retained individuals (74 SNPs)</td>
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<td>After examination of Mendel errors in all parent-offspring sets, eliminate individuals with suspected pedigree misspecification (&gt; 100 Mendel errors) (2 subjects)</td>
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<td>Eliminate SNPs with high Mendel error rates (&gt; 20 SNPs) (2 markers)</td>
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<td>Eliminate individuals in whom &lt; 1375 of the remaining 1388 SNPs had high-confidence genotype calls (48 individuals) (this accounted for 158 of 324 remaining Mendel errors)</td>
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<td>Eliminate SNPs with &gt; 2 remaining Mendel errors in the data set (15 SNPs)</td>
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<td>Eliminate SNPs with minor allele frequency &lt; 5% and SNPs that failed Hardy-Weinberg equilibrium goodness-of-fit tests in founder individuals (P &lt; .01) (18 SNPs)</td>
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**Abbreviation:** SNP, single-nucleotide polymorphism.
eTable 3. Gene-Based Test for Association With Bipolar Disorder

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**GABA region (no gene)** 5

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| rs426954 | C:T | 184:167 | 1.10 | 0.82 | .36 | .45 |
| rs206949 | A:G | 168:160 | 1.05 | 0.20 | .66 | .75 |
| rs1002067 | A:G | 196:175 | 1.12 | 1.19 | .28 | .30 |
| rs3811995 | C:T | 181:195 | 0.93 | 0.52 | .47 | .58 |
| rs3811991 | T:G | 180:168 | 1.07 | 0.41 | .52 | .50 |

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**GABA region (no gene)**

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**GABRG2**

| rs6886028  | T:A   | GABRG2 | 150:160 | 0.94 | 0.32 | .57 | >.99 |
| rs2268583  | A:G   | GABRG2 | 42:52  | 0.81 | 1.06 | .30 | .37 |
| rs2268582  | A:G   | GABRG2 | 86:86  | 1.00 | 0.00 | >.99 | >.99 |
| rs209353   | C:T   | GABRG2 | 171:185 | 0.92 | 0.55 | .46 | .86 |
| rs209354   | A:C   | GABRG2 | 184:176 | 1.04 | 0.18 | .67 | .65 |
| rs209357   | C:G   | GABRG2 | 196:195 | 1.0  | 0.00 | .96 | >.99 |
| rs211037   | A:G   | GABRG2 | 143:130 | 1.10 | 0.62 | .43 | .65 |
| rs211029   | G:A   | GABRG2 | 151:161 | 0.94 | 0.32 | .57 | .75 |
| rs210985   | A:G   | GABRG2 | 119:112 | 1.06 | 0.21 | .65 | .63 |
| rs365054   | T:C   | GABRG2 | 150:153 | 0.98 | 0.03 | .86 | .86 |
| rs2422106  | C:A   | GABRG2 | 169:165 | 1.02 | 0.05 | .83 | .86 |
| rs721719   | A:G   | GABRG2 | 128:126 | 1.02 | 0.02 | .90 | .86 |
| rs10491328 | A:C   | GABRG2 | 59:70  | 0.84 | 0.94 | .33 | .46 |
| rs211014   | A:C   | GABRG2 | 156:155 | 1.01 | 0.00 | .95 | >.99 |
| rs211013   | G:A   | GABRG2 | 172:180 | 0.96 | 0.18 | .67 | .44 |

**GABRP**

| rs732157   | G:A   | GABRP  | 197:184 | 1.07 | 0.44 | .51 | .50 |
| rs1158443  | G:T   | GABRP  | 182:177 | 1.03 | 0.07 | .79 | >.99 |
| rs7724371  | G:A   | GABRP  | 180:187 | 0.96 | 0.13 | .71 | .86 |
| rs1895409  | A:G   | GABRP  | 111:108 | 1.03 | 0.04 | .84 | >.99 |

**DTNBP1**

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| rs29234 | C:A | 40:41   | 0.98    | 0.01    | .91     | >.99    |         |         |
| rs3130250 | T:C | 109:106 | 1.03    | 0.04    | .84     | >.99    |         |         |
| rs2256266 | A:G | 121:129 | 0.94    | 0.26    | .61     | .86     |         |         |
| rs3130253 | T:C | 60:57   | 1.05    | 0.08    | .78     | .75     |         |         |

FILIP1 6

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| rs6933438 | G:A | 48:52   | 0.92    | 0.16    | .69     | &gt;.99    |         |         |
| rs2951945 | T:G | 146:159 | 0.92    | 0.55    | .46     | .45     |         |         |
| rs13214997 | T:A | 61:59   | 1.034   | 0.03    | .86     | .86     |         |         |
| rs6904580 | G:C | 184:190 | 0.97    | 0.10    | .76     | .86     |         |         |
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**Abbreviations:** Chr, chromosome; GABA, γ-aminobutyric acid; qc, Illumina quality control single-nucleotide polymorphism (SNP); TDT, transmitted to untransmitted.
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**Abbreviations:** chr, chromosome; SNP, single-nucleotide polymorphism.

- Refers to the number of SNPs (eg, SNP 3 indicates the third most significant SNP in the set).
- Adjusted for all single- and multiple-SNP tests.
- The tagging approach was not applied because of gene size.