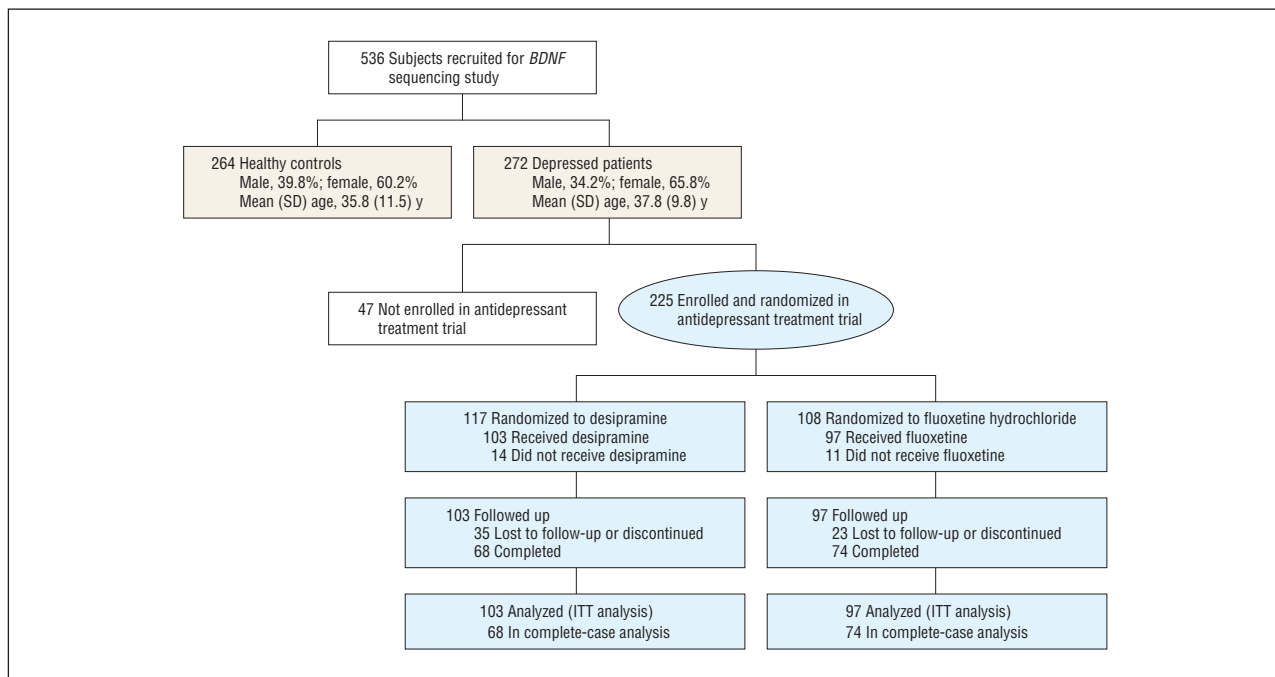


Novel Sequence Variations in the Brain-Derived Neurotrophic Factor Gene and Association With Major Depression and Antidepressant Treatment Response

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eFigure 1. Study flowchart showing the numbers of participants through each stage of the study. Tan boxes represent the sample in the case-control study and blue boxes include the patients with major depressive disorder enrolled in the 1-week placebo lead-in, 8-week double-blind and randomized pharmacogenetic study of antidepressant treatment. *BDNF* indicates brain-derived neurotrophic factor gene; ITT, intention-to-treat sample.

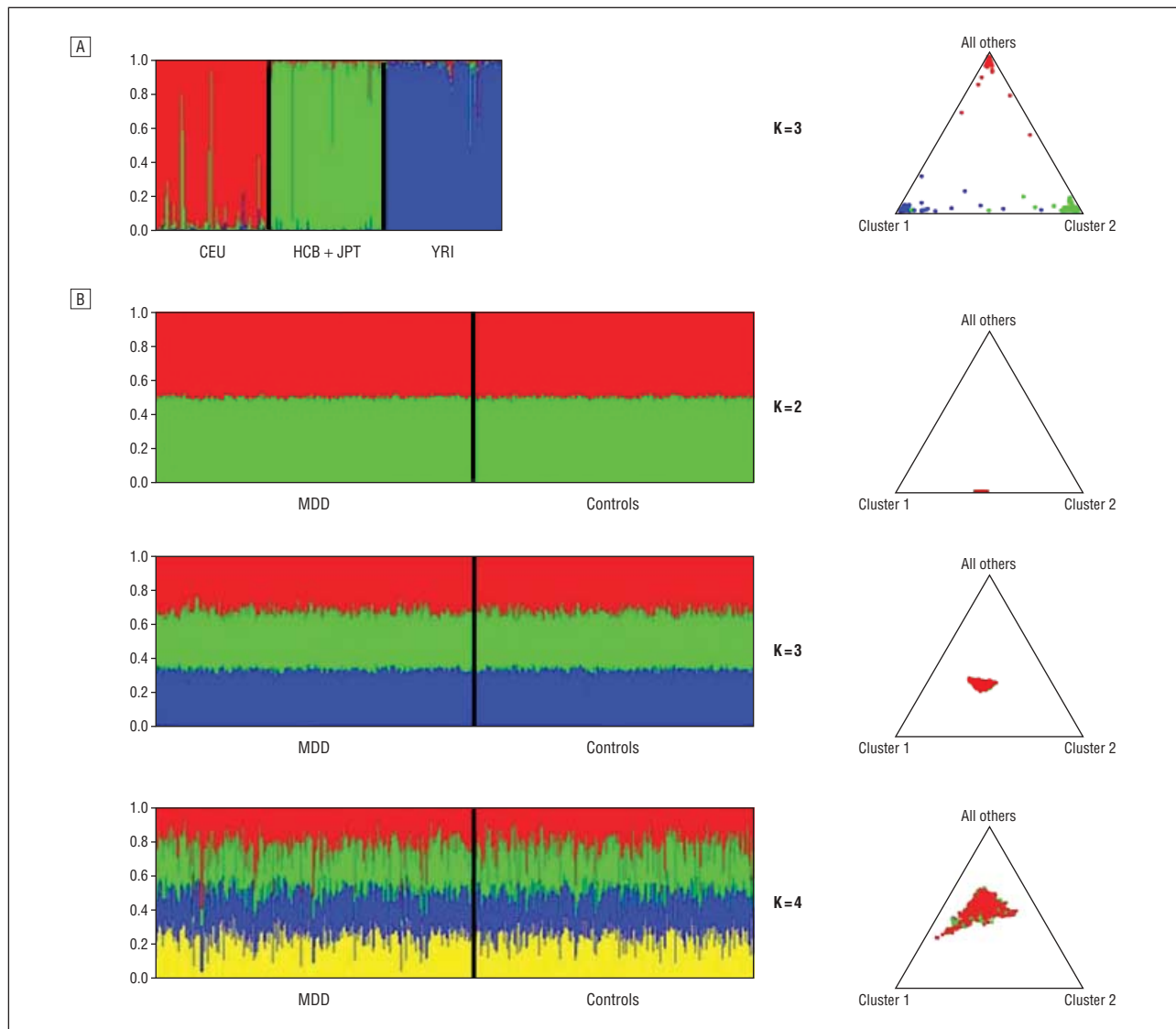


Figure 2. Estimated population structure using 54 unlinked single-nucleotide polymorphisms (SNPs). In the rectangles on the left, each individual is represented by a single vertical line, which is broken into K colored segments, with lengths proportional to each of the K clusters inferred from the STRUCTURE program using the genotype download from the HapMap database (A) and Mexican American patients with major depressive disorder (MDD) and healthy controls in the sample (B) separately. In the triangle plots on the right, each individual is represented by a colored point corresponding to the predefined population. For a given point, the estimate is given by the distance to 1 edge of the triangle. CEU indicates Utah residents with ancestry from northern and western Europe in the United States; HCB, Han Chinese in Beijing; JPT, Japanese in Tokyo; and YRI, Yoruba in Ibadan, Nigeria.

Table 1. Demographic and Clinical Characteristics of Controls and Patients With MDD

Variables	Controls (n=264)	Patients With MDD (n=272)	Desipramine Hydrochloride-Treated Patients (n=103)	Fluoxetine Hydrochloride-Treated Patients (n=97)
Sex, No. (%)				
Female	159 (60.2)	179 (65.8)	68 (66.0)	66 (68.0)
Male	105 (39.8)	93 (34.2)	35 (34.0)	31 (32.0)
Age at recruitment, mean (SD), y	35.8 (11.5)	37.8 (9.8)	38.9 (8.8)	37.8 (10.8)
Baseline HAM-D21 score, mean (SD)	NA	20.9 (4.9)	21.4 (4.0)	21.8 (4.2)
Follow-up, No. (%)				
Completion	NA	142 (71.0) ^a	68 (66.0)	74 (76.3)
Dropout	NA	58 (29.0) ^a	35 (34.0)	23 (23.7)

Abbreviations: HAM-D21, 21-Item Hamilton Depression Rating Scale; MDD, major depressive disorder; NA, not applicable.

^aPatients with MDD who entered the clinical trial and had at least 1 dose of antidepressant medication.

eTable 2. *BDNF* Polymorphisms in Depressed and Healthy Mexican Americans

Polymorphism	Chr Position	Minor/Major Allele	Minor Allele Frequency			SNP Class ^a	Amino Acid Change
			Cases	Controls	All		
NT_009237.17_26463941	27633276	G/A	0.0019	0.0000	0.0010	3' UTR	
NT_009237.17_26464051	27633386	G/A	0.0000	0.0020	0.0010	3' UTR	
NT_009237.17_26464202	27633537	A/T	0.0000	0.0020	0.0010	3' UTR	
rs41282914	27633560	A/G	0.0056	0.0000	0.0029	3' UTR	
rs7124442	27633617	C/T	0.2328	0.2591	0.2456	3' UTR	
NT_009237.17_26464638	27633973	A/G	0.0038	0.0021	0.0030	3' UTR	
NT_009237.17_26464686	27634021	T/C	0.0000	0.0042	0.0020	3' UTR	
rs11030099	27634159	A/C	0.1102	0.1262	0.1176	3' UTR	
rs11030100	27634162	T/G	0.1383	0.1528	0.1450	3' UTR	
NT_009237.17_26465024	27634359	G/A	0.0042	0.0022	0.0032	3' UTR	
NT_009237.17_26465355	27634690	T/C	0.0038	0.0020	0.0030	3' UTR	
NT_009237.17_26465356	27634691	A/G	0.0019	0.0000	0.0010	3' UTR	
rs41282916	27634779	A/G	0.0114	0.0142	0.0128	3' UTR	
NT_009237.17_26465652	27634987	C/T	0.0074	0.0040	0.0058	3' UTR	
NT_009237.17_26465655	27634990	A/G	0.0019	0.0022	0.0020	3' UTR	
NT_009237.17_26465741	27635076	T/G	0.0019	0.0000	0.0010	3' UTR	
NT_009237.17_26465813	27635148	A/G	0.0019	0.0000	0.0010	3' UTR	
NT_009237.17_26465917	27635252	T/C	0.0019	0.0000	0.0011	3' UTR	
rs41282918	27635356	C/A	0.0804	0.1570	0.1202	3' UTR	
rs58597651	27635370	T/C	0.0089	0.0218	0.0150	3' UTR	
NT_009237.17_26466047	27635382	C/A	0.0720	0.0556	0.0643	3' UTR	
rs56820186	27635588	G/T	0.0099	0.0237	0.0165	3' UTR	
NT_009237.17_26466714	27636049	T/C	0.0000	0.0020	0.0010	Synonymous	Ser-Ser
rs2353512	27636238	A/G	0.0037	0.0000	0.0019	Synonymous	Ala-Ala
NT_009237.17_26467094	27636429	T/C	0.0019	0.0019	0.0019	Nonsynonymous	Ala-Thr
rs6265	27636492	A/G	0.0970	0.1513	0.1238	Nonsynonymous	Val-Met
NT_009237.17_26467235	27636570	A/G	0.0000	0.0039	0.0019	Nonsynonymous	His-Tyr
NT_009237.17_26467246	27636581	T/C	0.0000	0.0019	0.0010	Nonsynonymous	Gly-Asp
NT_009237.17_26467608	27636943	T/C	0.0000	0.0022	0.0011	Intronic, 5' UTR	
NT_009237.17_26467647	27636982	A/G	0.0018	0.0019	0.0019	Intronic, 5' UTR	
NT_009237.17_26467777	27637112	C/T	0.0000	0.0019	0.0009	Intronic, 5' UTR	
rs11030101	27637320	T/A	0.2630	0.3276	0.2947	Intronic	
NT_009237.17_26468110	27637445	C/T	0.0000	0.0039	0.0020	Intronic	
rs28722151	27637752	G/C	0.2376	0.3154	0.2759	Intronic	
rs11819808	27637964	T/C	0.0136	0.0040	0.0088	Intronic	
NT_009237.17_26468725	27638060	A/G	0.0000	0.0020	0.0010	Intronic	
rs11030102	27638172	G/C	0.1737	0.1779	0.1758	Intronic	
NT_009237.17_26468885	27638220	A/G	0.0019	0.0057	0.0038	Intronic	
rs57083135	27638432	T/C	0.0093	0.0234	0.0162	Intronic	
NT_009237.17_26469156	27638491	C/T	0.0149	0.0273	0.0210	Intronic	
rs11030103	27638909	G/A	0.2958	0.1895	0.2418	Intronic	
NT_009237.17_26469880	27639215	T/C	0.0022	0.0023	0.0023	Intronic	
NT_009237.17_26470320	27639655	T/C	0.0019	0.0000	0.0010	Intronic	
rs41274436	27639820	T/C	0.0039	0.0042	0.0040	Intronic	
rs12273539	27639887	T/C	0.3471	0.2335	0.2918	Intronic	
rs4923464	27640194	T/C	0.1255	0.1581	0.1416	Intronic	
rs2883196	27640314	A/C	0.0020	0.0021	0.0021	Intronic	
NT_009237.17_26470985	27640320	T/C	0.0000	0.0021	0.0011	Intronic	
rs11030104	27641093	G/A	0.1191	0.1549	0.1370	Intronic	
NT_009237.17_26471969	27641304	G/T	0.0000	0.0020	0.0010	Intronic	
NT_009237.17_26471994	27641329	A/T	0.0000	0.0020	0.0010	Intronic	
NT_009237.17_26472287	27641622	T/C	0.0022	0.0021	0.0021	Intronic	
NT_009237.17_26472415	27641750	A/G	0.0020	0.0000	0.0010	Intronic	
NT_009237.17_26484150	27653485	G/A	0.0019	0.0019	0.0019	Intronic	
NT_009237.17_26484165	27653500	C/T	0.0000	0.0058	0.0029	Intronic	
rs11030109	27653527	A/G	0.0244	0.0292	0.0268	Intronic	
NT_009237.17_26484341	27653676	A/G	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26484374	27653709	A/G	0.0038	0.0019	0.0029	Intronic	
NT_009237.17_26484882	27654217	A/G	0.0000	0.0039	0.0019	Intronic	
NT_009237.17_26485790	27655125	A/G	0.0020	0.0000	0.0010	Intronic	
NT_009237.17_26485814	27655149	C/T	0.0020	0.0000	0.0010	Intronic	
rs55848362	27655172	T/C	0.0100	0.0239	0.0166	Intronic	

(continued)

eTable 2. *BDNF* Polymorphisms in Depressed and Healthy Mexican Americans (continued)

Polymorphism	Chr Position	Minor/Major Allele	Minor Allele Frequency			SNP Class ^a	Amino Acid Change
			Cases	Controls	All		
NT_009237.17_26506355	27675690	T/C	0.0020	0.0000	0.0010	Intronic	
NT_009237.17_26508444	27677559	T/C	0.0020	0.0021	0.0020	Intronic, 5' UTR	
NT_009237.17_26508530	27677865	G/C	0.0023	0.0000	0.0011	Intronic	
NT_009237.17_26508793	27678128	T/A	0.0000	0.0020	0.0010	Intronic	
NT_009237.17_26508807	27678142	T/A	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26508862	27678197	T/C	0.0099	0.0060	0.0080	Intronic	
rs41274438	27678281	C/G	0.0019	0.0020	0.0020	Intronic	
NT_009237.17_26508975	27678310	C/G	0.0000	0.0042	0.0020	Intronic, 5' UTR	
rs56164415	27678311	A/G	0.0252	0.0357	0.0304	Intronic, 5' UTR	
NT_009237.17_26509467	27678802	T/C	0.0060	0.0071	0.0065	Intronic, 5' UTR	
NT_009237.17_26509477	27678812	A/G	0.0020	0.0000	0.0011	Intronic, 5' UTR	
NT_009237.17_26509484	27678819	A/G	0.0000	0.0047	0.0022	Intronic, 5' UTR	
rs61888800	27678854	T/G	0.2419	0.2476	0.2445	Intronic, 5' UTR	
NT_009237.17_26509564	27678899	A/G	0.0020	0.0000	0.0011	Intronic, 5' UTR	
NT_009237.17_26509570	27678905	A/G	0.0020	0.0000	0.0011	Intronic, 5' UTR	
rs41274440	27679214	T/C	0.0094	0.0039	0.0067	Intronic	
rs13306221	27679265	A/G	0.0226	0.0348	0.0286	Intronic	
NT_009237.17_26510057	27679392	A/G	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26510371	27679706	C/G	0.0000	0.0019	0.0009	Intronic, 5' UTR	
NT_009237.17_26510390	27679725	A/C	0.0000	0.0050	0.0024	Intronic, 5' UTR	
rs56133711	27679910	A/G	0.1653	0.1567	0.1611	Intronic	
NT_009237.17_26511192	27680527	C/T	0.0000	0.0066	0.0034	Intronic	
NT_009237.17_26511514	27680849	G/C	0.0037	0.0000	0.0019	Intronic	
NT_009237.17_26511585	27680920	G/T	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26511942	27681277	G/A	0.0000	0.0020	0.0010	Intronic	
rs988748	27681321	C/G	0.1453	0.1641	0.1545	Intronic	
NT_009237.17_26512244	27681579	A/G	0.0000	0.0038	0.0019	Intronic	
rs61666755	27681979	A/G	0.0019	0.0019	0.0019	Intronic	
NT_009237.17_26512732	27682067	A/G	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26512954	27682289	G/A	0.0018	0.0000	0.0009	Intronic	
rs4923468	27682351	A/C	0.0112	0.0233	0.0171	Intronic	
rs10767664	27682562	T/A	0.1399	0.1615	0.1505	Intronic	
NT_009237.17_26513401	27682736	T/C	0.0063	0.0000	0.0032	Intronic	
NT_009237.17_26513479	27682814	G/A	0.0106	0.0044	0.0075	Intronic	
rs7931755	27683077	G/A	0.0132	0.0058	0.0096	Intronic	
NT_009237.17_26513757	27683092	A/T	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26513999	27683334	T/C	0.0019	0.0019	0.0019	Intronic	
rs36211436	27683335	A/G	0.0019	0.0096	0.0057	Intronic	
rs36211437	27683449	T/A	0.0268	0.0298	0.0282	Intronic	
rs2030324	27683491	T/C	0.3689	0.4109	0.3895	Intronic	
NT_009237.17_26514915	27684250	A/G	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26514929	27684264	T/A	0.0019	0.0000	0.0010	Intronic	
NT_009237.17_26529363	27698698	A/C	0.0124	0.0157	0.0139	Intronic, 5' UTR	
NT_009237.17_26529411	27698746	T/C	0.0020	0.0000	0.0011	Intronic, 5' UTR	
NT_009237.17_26530225	27699560	T/C	0.0019	0.0038	0.0028	5' UTR	
NT_009237.17_26530263	27699598	A/G	0.0019	0.0000	0.0010	5' UTR	
NT_009237.17_26531027	27700362	C/T	0.0021	0.0000	0.0012	Upstream	
NT_009237.17_26532034	27701369	A/G	0.0093	0.0078	0.0086	Upstream	
rs12273363	27701435	C/T	0.1541	0.1627	0.1583	Upstream	
NT_009237.17_26532827	27702162	C/T	0.0000	0.0019	0.0010	Upstream	
rs59900890	27702179	G/A	0.0019	0.0000	0.0010	Upstream	
rs55958405	27702259	A/C	0.0209	0.0039	0.0125	Upstream	
NT_009237.17_26532978	27702313	C/T	0.0094	0.0039	0.0067	Upstream	
rs908867	27702340	A/G	0.0380	0.0490	0.0434	Upstream	
NT_009237.17_26533199	27702534	C/G	0.0019	0.0060	0.0039	Upstream	
NT_009237.17_26533563	27702898	G/T	0.0076	0.0040	0.0058	Upstream	
rs10767667	27703125	C/T	0.3636	0.4167	0.3895	Upstream	
NT_009237.17_26533854	27703189	G/A	0.0019	0.0058	0.0038	Upstream	
rs41275150	27703396	C/T	0.0019	0.0000	0.0010	Upstream	
NT_009237.17_26534077	27703412	A/C	0.0000	0.0020	0.0010	Upstream	
rs7931247	27703567	T/C	0.3670	0.4163	0.3909	Upstream	
rs11825814	27703591	T/G	0.0019	0.0020	0.0019	Upstream	

(continued)

eTable 2. *BDNF* Polymorphisms in Depressed and Healthy Mexican Americans (continued)

Polymorphism	Chr Position	Minor/Major Allele	Minor Allele Frequency			SNP Class ^a	Amino Acid Change
			Cases	Controls	All		
NT_009237.17_26534674	27704009	T/G	0.0020	0.0000	0.0010	Upstream	
NT_009237.17_26534904	27704239	T/A	0.0000	0.0024	0.0012	Upstream	
rs12288512	27704247	A/G	0.1410	0.1535	0.1473	Upstream	
NT_009237.17_26535284	27704619	G/A	0.0019	0.0021	0.0020	Upstream	
NT_009237.17_26535457	27704792	T/C	0.0019	0.0000	0.0010	Upstream	
rs11030123	27704861	A/G	0.0428	0.0461	0.0443	Upstream	

Abbreviations: Ala, alanine; Asp, aspartic acid; Chr, chromosome; Gly, glycine; His, histidine; Met, methionine; Ser, serine; SNP, single-nucleotide polymorphism; Thr, threonine; Tyr, tyrosine; UTR, untranslated region; Val, valine.

^aBased on multiple alternative 5' exons in the National Center for Biotechnology Information AceView Database.