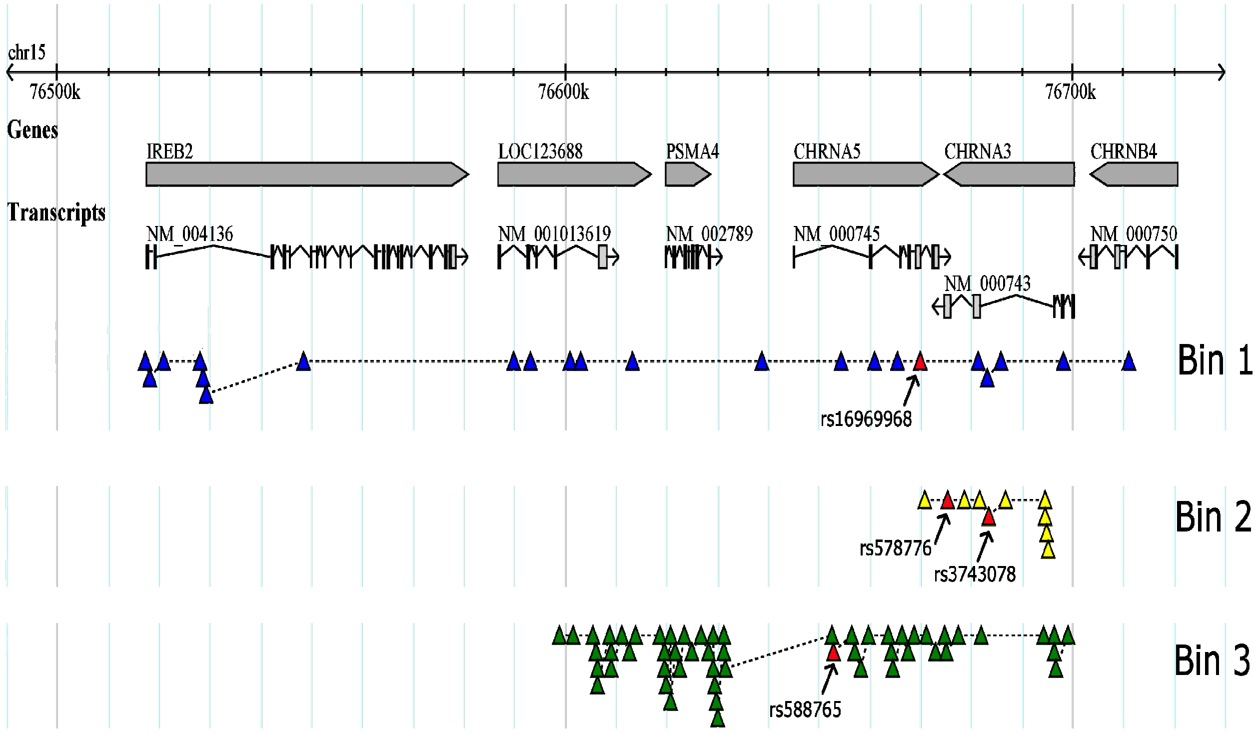
Supplementary Figure 1. Three major linkage disequilibrium bins across the *CHRNA5-CHRNA3-CHRNB4* gene cluster. These bins are defined by pair-wise linkage disequilibrium with $r^2 \geq 0.8$ among polymorphisms in subjects of European origin. Arrows indicate representative variant in each bin.

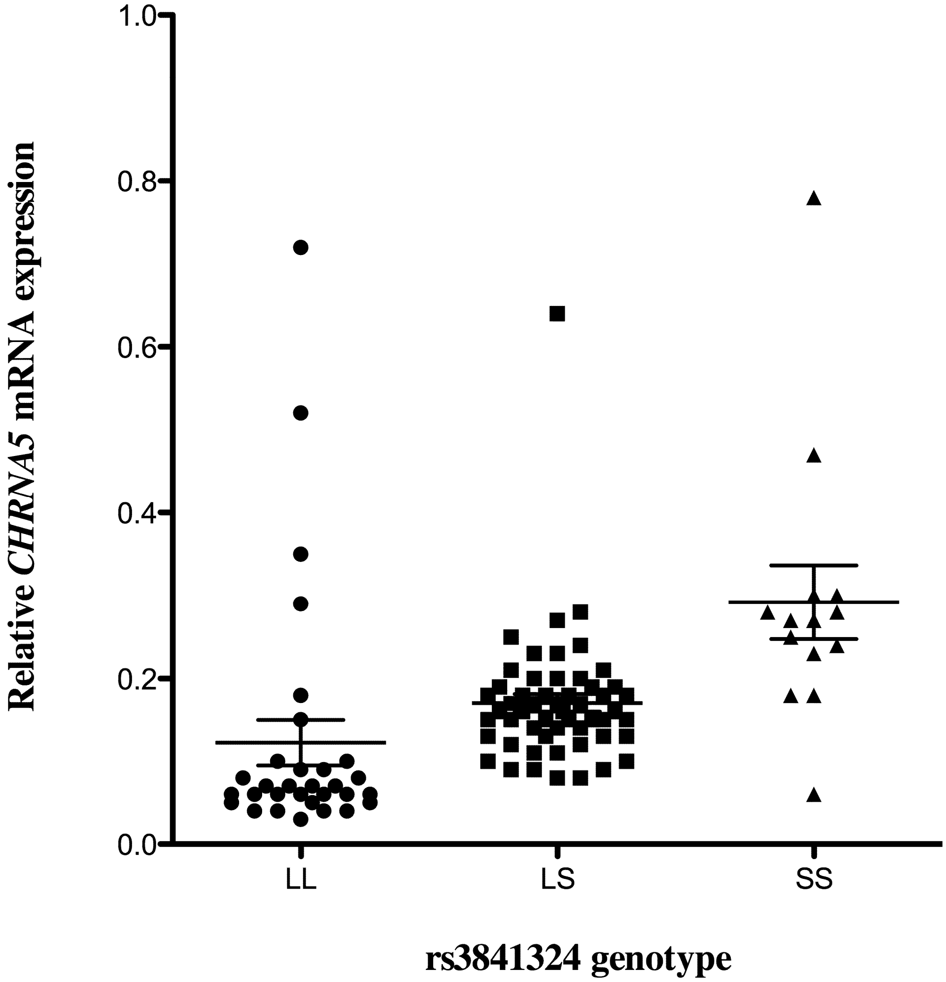
Supplementary Figure 2. Minor allele of rs3841324 is associated with increased mRNA expression of *CHRNA5* in human frontal cortex ($p=1.11x10^{-9}$)

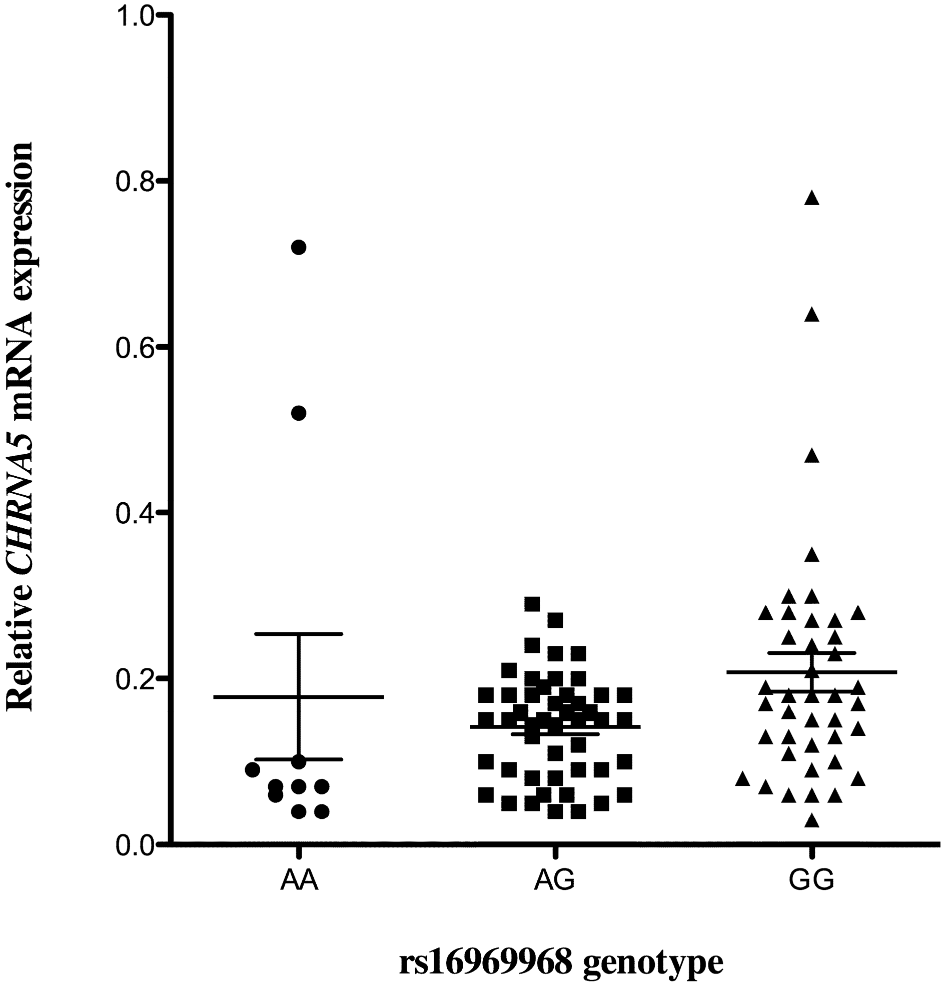
The bars represent mean ± SD of *CHRNA5* mRNA expression.

Supplementary Figure 3. Minor allele of rs16969968 is weakly associated with increased mRNA expression of *CHRNA5* in human frontal cortex ($p=1.26x10^{-2}$)

The bars represent mean ± SD of *CHRNA5* mRNA expression.


chr15
76500k
76600k
76700k
Genes
IREB2
LOC123688
PSMA4
CHRNA5
CHRNA3
CHRNB4
Transcripts
NM_004136
NM_001013619
NM_002789
NM_000745
NM_000743
NM_000750
Bin 1
rs16969968
Bin 2
rs578776
rs3743078
Bin 3
rs588765


1.0
0.8
0.6
0.4
0.2
0.0
Relative *CHRNA5* mRNA expression
LL
LS
SS
rs3841324 genotype


1.0
0.8
0.6
0.4
0.2
0.0
Relative *CHRNA5* mRNA expression
AA
AG
GG
rs16969968 genotype

Supplementary Table 1. The effect of covariates on *CHRNA5*, *CHRNA3*, and *CHRNB4* mRNA expression.

Each cell indicates the p values.

Covariate	log(A5)	log(A3)	log(B4)
Postmortem Interval	0.02	0.43	0.28
Age	0.40	1.76E-07	0.29
Sex	0.57	0.03	0.01
Site of Brain Bank	0.09	2.81E-06	0.04
Smoking history	0.82	0.26	0.03

Supplemental Table 2. Association of *CHRNA3* and *CHRNB4* mRNA expression in human brain with variants in the *CHRNA5-CHRNA3-CHRNB4* gene cluster. The data shown here are from a linear regression. Blue, yellow and green colors represent highly correlated (r^2 0.6) variants in bins 1, 2, and 3, respectively. MAF=minor allele frequency. *indicates a synonymous coding SNP; **indicates a non-synonymous coding SNP.

					CHRNA3				***CHRNB4***			
Variant	**Gene**	**Allele 1 (Minor)**	**Allele 2 (Major)**	**Minor allele frequency**	**N**	**Regression coefficient**	**95% Confidence interval**	P value	**N**	**Regression coefficient**	**95% Confidence interval**	P value
🟩 rs880395	*upstream of CHRNA5 transcription*	A	G	0.44	94	-0.22	-0.47, 0.02	0.08	73	-0.16	-0.37, 0.05	0.13
🟩 rs7164030		G	A	0.46	90	-0.26	-0.50, -0.01	0.05	69	-0.13	-0.34, 0.08	0.24
🟨 rs905739		G	A	0.24	93	0.30	0.02, 0.58	0.04	72	0.10	-0.15, 0.35	0.43
🟦 rs2036527		A	G	0.33	93	-0.01	-0.28, 0.26	0.92	72	0.17	-0.06, 0.40	0.16
🟩 rs3841324		S	L	0.41	94	-0.22	-0.48, 0.04	0.11	73	-0.14	-0.36, 0.08	0.22
🟨 rs684513	*CHRNA5*	G	C	0.22	90	0.31	0.01, 0.60	0.05	69	0.04	-0.22, 0.30	0.77
🟨 rs667282		C	T	0.25	93	0.30	0.03, 0.57	0.03	72	0.06	-0.17, 0.30	0.59
🟩 rs588765		T	C	0.42	93	-0.24	-0.48, 0.01	0.06	72	-0.19	-0.40, 0.01	0.06
🟦 rs17486278		C	A	0.33	93	0.01	-0.26, 0.28	0.92	72	0.19	-0.04, 0.42	0.11
🟩 rs601079		A	T	0.45	91	-0.26	-0.51, -0.02	0.04	71	-0.20	-0.41, 0.01	0.07
🟩 rs680244		T	C	0.4	88	-0.29	-0.55, -0.03	0.03	68	-0.16	-0.37, 0.06	0.15
🟩 rs621849		G	A	0.41	89	-0.30	-0.55, -0.05	0.02	68	-0.17	-0.38, 0.04	0.12
🟨 rs569207		T	C	0.23	93	0.31	0.03, 0.58	0.03	72	0.06	-0.18, 0.29	0.65
🟨 rs637137		A	T	0.23	93	0.30	0.03, 0.58	0.03	72	0.08	-0.16, 0.31	0.53
🟩 rs692780		G	C	0.35	93	-0.26	-0.50, -0.02	0.04	72	-0.24	-0.44, -0.04	0.02
🟩 rs11637635		A	G	0.32	86	-0.28	-0.54, -0.02	0.04	65	-0.24	-0.46, -0.01	0.04
🟦 rs951266		A	G	0.34	93	0.00	-0.26, 0.26	1.00	72	0.17	-0.05, 0.40	0.13
🟩 rs555018		G	A	0.41	91	-0.26	-0.51, -0.02	0.04	70	-0.14	-0.34, 0.06	0.16
🟦 rs16969968**		A	G	0.36	93	0.01	-0.25, 0.28	0.92	72	0.19	-0.04, 0.42	0.11
🟩 rs514743		T	A	0.34	93	-0.24	-0.48, 0.00	0.06	72	-0.27	-0.47, -0.07	0.01
🟩 rs615470		T	C	0.32	82	-0.27	-0.54, 0.00	0.05	64	-0.28	-0.51, -0.06	0.01
🟨 rs578776	*CHRNA3*	A	G	0.29	92	0.28	0.02, 0.55	0.04	71	0.13	-0.09, 0.35	0.26
🟨 rs12910984		G	A	0.26	91	0.30	0.04, 0.57	0.03	70	0.01	-0.21, 0.24	0.91
🟦 rs1051730*		A	G	0.32	92	0.01	-0.26, 0.28	0.94	71	0.19	-0.04, 0.42	0.11
🟨 rs3743078		G	C	0.24	91	0.31	0.03, 0.58	0.03	71	0.05	-0.19, 0.29	0.66
🟦 rs1317286		G	A	0.33	84	0.03	-0.25, 0.31	0.84	65	0.18	-0.06, 0.42	0.14
🟨 rs938682		G	A	0.26	91	0.31	0.04, 0.58	0.03	70	0.03	-0.21, 0.27	0.78
🟨 rs11637630		G	A	0.23	92	0.30	0.03, 0.58	0.03	71	0.08	-0.16, 0.31	0.53
🟨 rs6495308		C	T	0.24	93	0.32	0.05, 0.59	0.02	72	0.06	-0.18, 0.30	0.63
rs8192479		T	C	0.01	91	0.70	-0.25, 1.66	0.15	70	1.19	-0.01, 2.39	0.06
🟩 rs3743075*		T	C	0.33	93	-0.24	-0.48, 0.00	0.06	72	-0.27	-0.46, -0.07	0.01
🟩 rs3743074		G	A	0.35	90	-0.26	-0.51, -0.02	0.03	69	-0.22	-0.42, -0.02	0.04
🟦 rs8040868*		C	T	0.4	93	0.00	-0.25, 0.25	0.98	72	0.25	0.04, 0.47	0.03
rs8192475**		T	C	0.08	94	-0.02	-0.57, 0.53	0.94	73	0.35	-0.09, 0.79	0.13
🟩 rs1878399		G	C	0.44	93	-0.24	-0.48, 0.01	0.06	72	-0.21	-0.42, -0.01	0.05
rs12914008**	*CHRNB4*	A	G	0.06	93	-0.08	-0.69, 0.52	0.79	72	0.46	-0.03, 0.95	0.07
🟦 rs17487223		T	C	0.34	92	0.02	-0.24, 0.28	0.87	71	0.21	0.00, 0.42	0.05
rs950776		C	T	0.35	93	-0.21	-0.47, 0.05	0.11	72	-0.34	-0.55, -0.13	0.00
rs12440014		G	C	0.26	92	0.27	0.00, 0.55	0.05	71	0.04	-0.21, 0.29	0.77
rs11636605		A	G	0.23	94	0.28	0.00, 0.56	0.05	73	-0.01	-0.27, 0.24	0.91
rs3813567	*upstream of CHRNB4 transcription*	G	A	0.21	93	0.30	0.00, 0.59	0.05	72	0.00	-0.25, 0.26	0.97
rs4887075		C	T	0.06	92	-0.08	-0.60, 0.43	0.76	71	-0.15	-0.58, 0.28	0.49
rs1996371		C	T	0.41	94	0.03	-0.21, 0.27	0.82	73	0.29	0.09, 0.49	0.01
rs16970006		C	T	0.07	91	0.01	-0.52, 0.53	0.98	70	-0.19	-0.65, 0.27	0.41

Supplementary Table 3. ***CHRNA5*** **mRNA expression (normalized with endogenous** ***GAPDH*** **gene) of different rs16969968-rs588765 diplotype.**
The mean expression is calculated without outliers.

	rs588765					
	CC		**CT**		**TT**	
rs16969968	# of subjects	Mean (Std.D)	# of subjects	Mean (Std.D)	# of subjects	Mean (Std.D)
GG	5	0.074 (0.045)	17	0.139 (0.044)	16	0.251 (0.083)
AG	16	0.086 (0.045)	31	0.166 (0.047)		
AA	8	0.068 (0.021)				