

TABLE S1. Biological Information on *SLC6A4*, *HTR3B*, and *HTR3A* Polymorphisms Examined in This Study^a

Gene	SNP No.	dbSNP ID	Location Within the Gene	Chromosomal Location	Alleles	Minor Allele Frequency (Minor Allele) ^b	p values for Deviation from Hardy-Weinberg Equilibrium ^c		Primers and Probe Sequences / Context Sequence ID of ABI Primers and Probes
							OND Group	Placebo Group	
<i>SLC6A4</i>	1	5'-HTTLPR	promoter	25,588,443 to 25,588,485 ^d	L/S	0.450 (S)	1.000	0.779	Forward: TCCTCCGCTTTGGCGCCTCTTCC Reverse: TGGGGGTTGCAGGGGAGATCCTG
	2	rs1042173	3'-UTR	25,549,137	T/G	0.425 (G)	0.790	0.930	C_7473190_10
<i>HTR3A</i>	3	rs1150226	5'-near gene	113,350,751	G/A	0.058 (A)	0.545	0.675	C__7488474_10
	4	rs1062613	5'-UTR	113,351,216	C/T	0.214 (T)	0.989	0.258	C__7488465_10
	5	rs33940208	Exon 1(L168L)	113,351,287	C/T	not reported (T=0.017 ^e)	1.000	1.000	C__22275584_10
	6	rs1176722	Intron 1	113,353,684	A/G	0.159 (A)	0.793	0.645	C__7488431_10
	7	rs1176720	Intron 2	113,354,963	C/G	0.186 (G)	0.678	1.000	C__1646939_10
	8	rs2276302	Intron 3	113,355,350	A/G	0.319 (G)	1.000	0.061	C__1646938_1_
	9	rs1176719	Intron 4	113,357,397	A/G	not reported (A=0.258 ^e)	0.365	0.878	C__1372135_1_
	10	rs10160548	Intron 5	113,361,891	G/T	0.341 (G)	0.356	0.255	C__1372126_10
	11	rs1150220	Intron 7	113,363,096	C/T	not reported (T=0.233 ^e)	1.000	0.525	C__7488415_1_
	12	rs1176713	Exon 8 (L459L)	113,365,635	G/A	0.257 (G)	1.000	0.835	C__1372122_10
<i>HTR3B</i>	13	rs3758987	5'-near gene	113,280,485	T/C	0.252 (C)	0.746	0.452	C__27512451_10
	14	rs11606194	Intron 2	113,286,191	T/C	0.097 (C)	0.766	1.000	C__26324626_10
	15	rs4938056	Intron 2	113,291,749	C/T	0.376 (T)	0.615	0.240	C__3053567_10
	16	rs12270070	Intron 2	113,304,257	G/C	0.226 (C)	0.325	0.587	C__3053563_10
	17	rs1176746	Intron 4	113,307,811	G/A	0.425 (A)	0.154	0.354	C__7488605_10

18	rs1176744	Exon 5 (Y129S)	113,308,238	A/C	0.292 (C)	0.972	0.437	C__7488596_1_
19	rs2276307	Intron 6	113,309,097	A/G	0.226 (G)	0.821	0.870	C__1646949_1_
20	rs1672717	Intron 6	113,317,943	A/G	0.425 (G)	1.000	1.000	C__3053558_10
21	rs17614942	Intron 8	113,321,587	C/A	0.049 (A)	0.987	1.000	C__32983576_10

^a All chromosomal locations are in reference to: NC_000017.9 for *SLC6A4*, NM_006028.3 for *HTR3B*, and NM_213621.1 for *HTR3A*.

SNP=single-nucleotide polymorphism; ABI=Applied Biosystems (Foster City, CA); OND=ondansetron.

^b From HapMap CEU (European ancestry) sample.

^c Data from this study.

^d Reference citation: Garcia LF, Aluja A, Fibla J, Cuevas L, Garcia O: Incremental effect for antisocial personality disorder genetic risk combining 5-HTTLPR and 5-HTTVNTR polymorphisms. *Psychiatry Res* 2010; 177:161–166.

^e pilot_1_CEU_low_coverage_panel.

TABLE S2. Mean Drinks per Drinking Day Estimates in All Examined Genotype Groups^a

Gene	SNP	Genotype	DDD in Ondansetron Group				DDD in Placebo Group				Ondansetron vs. Placebo Comparison					
			Estimate	95% CI		N	Estimate	95% CI		N	Estimate	95% CI		p-Value for DDD Difference	FDR ^b	p-Value for Genotype Frequency Difference
				Lower	Upper			Lower	Upper			Lower	Upper			
<i>HTR3A</i>	rs1150226	AG	4.18	2.91	5.44	20	6.00	4.84	7.16	24	-1.82	-3.53	-0.12	0.036	0.311	0.968
		GG	6.11	5.53	6.69	113	6.04	5.49	6.6	115	0.07	-0.68	0.81	0.859		0.970
	rs1062613	CC	3.70	1.37	6.04	6	4.47	1.62	7.32	4	-0.76	-4.44	2.91	0.682		0.474
		TC	5.21	4.36	6.05	48	6.29	5.5	7.07	54	-1.08	-2.21	0.05	0.061		0.416
	rs33940208	TT	6.27	5.61	6.92	81	5.9	5.25	6.56	82	0.36	-0.51	1.24	0.417		0.675
		CC	5.76	5.19	6.34	123	6.01	5.47	6.55	126	-0.24	-0.97	0.47	0.498		0.754
	rs1176722	CT	6.06	4.09	8.04	12	6.12	4.34	7.9	14	-0.06	-2.30	2.19	0.962		0.754
		AA	2.25	-2	6.51	2	4.69	1.78	7.6	4	-2.43	-7.59	2.72	0.355		0.408
	rs1176720	AG	5.93	4.93	6.93	36	6.51	5.49	7.54	32	-0.58	-1.98	0.82	0.415		0.329
		GG	5.88	5.25	6.5	94	6.01	5.4	6.62	99	-0.13	-0.95	0.68	0.749		0.618
		CC	2.21	-2.02	6.45	2	7.55	4.2	10.91	3	-5.34	-10.76	0.08	0.053		0.663
	rs2276302	CG	5.85	4.88	6.82	38	6.08	5.12	7.04	36	-0.23	-1.57	1.09	0.730		0.578
		GG	5.83	5.22	6.44	95	5.94	5.34	6.54	101	-0.11	-0.92	0.7	0.788		0.861
		AA	6.13	5.42	6.85	67	6.13	5.35	6.9	57	0.01	-1.01	1.02	0.989		0.423
	rs1176719	AG	5.77	4.97	6.57	57	5.97	5.28	6.66	73	-0.20	-1.20	0.8	0.695		0.203
		GG	3.82	2.05	5.59	11	5.94	4.12	7.76	10	-2.12	-4.65	0.4	0.099		0.761
	rs10160548	AA	4.33	2.50	6.16	11	7.65	5.92	9.38	11	-3.32	-5.78	-0.86	0.008	0.172	0.872
		AG	5.94	5.08	6.81	46	5.22	4.45	5.98	60	0.73	-0.38	1.83	0.197		0.278
		GG	5.88	5.21	6.54	78	6.46	5.76	7.15	69	-0.58	-1.49	0.34	0.215		0.373
		GG	4.69	3.11	6.26	14	5.73	4.52	6.93	24	-1.04	-2.97	0.89	0.289		0.119
		GT	5.82	5.08	6.55	68	6.25	5.48	7.02	59	-0.44	-1.45	0.58	0.400		0.088
rs1150220	TT	6.01	5.21	6.81	53	5.88	5.1	6.66	57	0.13	-0.95	1.21	0.811		0.641	
	AA	2.69	-0.46	5.84	4	6.79	4.25	9.33	5	-4.10	-8.15	-0.06	0.047		0.833	
		AG	5.60	4.66	6.53	40	5.91	5.1	6.71	52	-0.31	-1.5	0.87	0.610		0.615

TABLE S2. Continued

Gene	SNP	Genotype	DDD in Ondansetron Group				DDD in Placebo Group				Ondansetron vs. Placebo Comparison					
			Estimate	95% CI		N	Estimate	95% CI		N	Estimate	95% CI		p-Value for DDD Difference	FDR ^b	p-Value for Genotype Frequency Difference
				Lower	Upper			Lower	Upper			Lower	Upper			
		GG	5.96	5.34	6.58	91	5.95	5.3	6.6	82	0.01	-0.85	0.86	0.983		0.365
	rs1176713	GG	4.43	1.94	6.93	6	8.34	6.45	10.23	9	-3.91	-6.99	-0.82	0.013	0.172	0.511
		AG	5.45	4.58	6.32	46	5.58	4.79	6.36	57	-0.13	-1.25	0.99	0.824		0.837
		AA	6.05	5.4	6.7	82	6.06	5.38	6.74	73	-0.01	-0.91	0.89	0.982		0.189
<i>HTR3B</i>	rs3758987	CC	6.52	4.81	8.22	11	4.92	3.00	6.83	9	1.60	-0.96	4.16	0.220		0.533
		CT	5.76	4.9	6.62	51	6.32	5.57	7.08	62	-0.57	-1.65	0.52	0.306		0.322
		TT	5.73	5.02	6.43	70	5.85	5.14	6.56	69	-0.13	-1.1	0.85	0.801		0.969
	rs11606194	CC	0.08	-5.83	5.99	1	2.14	-3.45	7.74	1	-2.07	-10.23	6.09	0.620		0.846
		CT	6.66	5.13	8.18	14	5.66	4.50	6.82	25	0.995	-0.90	2.89	0.302		0.450
		TT	5.71	5.14	6.29	117	6.14	5.58	6.7	114	-0.43	-1.17	0.32	0.261		0.669
	rs4938056	CC	6.56	5.63	7.48	40	5.86	5	6.71	47	0.70	-0.51	1.91	0.259		0.566
		CT	5.36	4.61	6.1	62	6.23	5.48	6.97	61	-0.88	-1.9	0.15	0.095		0.645
		TT	5.86	4.78	6.94	30	5.98	4.94	7.02	31	-0.12	-1.58	1.34	0.870		0.892
	rs12270070	CC	3.3	-0.05	6.65	3	6.18	4.07	8.3	7	-2.88	-6.83	1.07	0.153		0.213
		CG	6.2	5.34	7.06	48	5.83	4.93	6.74	42	0.37	-0.83	1.57	0.548		0.147
		GG	5.64	4.99	6.29	84	6.09	5.47	6.71	91	-0.45	-1.31	0.41	0.302		0.480
	rs1176746	AA	5.44	4.22	6.67	22	6.16	5.01	7.31	25	-0.72	-2.38	0.94	0.394		0.729
		AG	6.08	5.27	6.9	54	5.87	5.11	6.62	61	0.22	-0.85	1.28	0.696		0.690
		GG	5.65	4.87	6.44	59	6.12	5.31	6.92	54	-0.47	-1.54	0.61	0.398		0.405
	rs1176744	AA	6.14	5.4	6.87	65	6.08	5.37	6.78	70	0.05	-0.92	1.04	0.909		0.939
		AC	5.37	4.56	6.18	56	6.01	5.20	6.82	54	-0.64	-1.72	0.45	0.249		0.608
		CC	5.38	3.77	6.98	13	5.36	3.88	6.84	15	0.02	-2.15	2.19	0.986		0.757
	rs2276307	AA	5.65	4.98	6.32	80	6.09	5.39	6.78	77	-0.44	-1.34	0.47	0.343		0.684
		AG	6.32	5.44	7.19	46	5.9	5.12	6.67	55	0.42	-0.72	1.56	0.473		0.549
		GG	4.35	2.25	6.46	8	6.64	4.65	8.64	8	-2.29	-5.19	0.62	0.122		0.892

TABLE S2. Continued

Gene	SNP	Genotype	DDD in Ondansetron Group				DDD in Placebo Group				Ondansetron vs. Placebo Comparison					
			Estimate	95% CI		N	Estimate	95% CI		N	Estimate	95% CI		p-Value for DDD Difference	FDR ^b	p-Value for Genotype Frequency Difference
				Lower	Upper			Lower	Upper			Lower	Upper			
	rs1672717	AA	5.54	4.75	6.33	57	6.19	5.39	7	53	-0.65	-1.73	0.43	0.236		0.414
		AG	5.54	4.78	6.29	62	5.76	5.05	6.48	66	-0.23	-1.22	0.77	0.655		0.813
		GG	7.4	6.03	8.76	17	6.37	5.15	7.60	21	1.03	-0.79	2.84	0.269		0.640
	rs17614942	AC	3.86	2.49	5.22	17	6.59	5.31	7.88	19	-2.73	-4.6	-0.87	0.004	0.156	0.896
		AA	5.58	0.03	11.13	1	4.04	-1.65	9.73	1	1.54	-6.38	9.47	0.703		0.964
		CC	6.09	5.52	6.66	117	5.97	5.42	6.53	119	0.12	-0.61	0.84	0.757		0.958

^a Genetic polymorphisms that were associated with more than 1.5 drinks/drinking day difference between the ondansetron and placebo groups, and that had more than five subjects within each treatment group, are enclosed within boxes. SNP=single-nucleotide polymorphism; DDD=drinks per drinking day; CI=confidence interval; FDR=false discovery rate.

^bAs mentioned in the Method section, FDR values were assessed only for the variants that survived the “screening process”.

TABLE S3. Combinations of Genotypes Significantly Associated with the Primary Outcome Measure, Drinks per Drinking Day^a

Combination	Genotype Combination	Population Carrying the Genotype Combination	Estimated Mean Difference for DDD (95% CI) and p-Value
1	<i>SLC6A4</i> -LL/TT + <i>HTR3A</i> -rs1176713-GG	O=3 P=3 (2%)	-7.64 (-12.65 to -2.63) 0.003
2	<i>SLC6A4</i> -LL/TT + <i>HTR3B</i> -rs17614942-AC	O=6 P=4 (4%)	-4.25 (-7.87 to -0.63) 0.021
3	<i>SLC6A4</i> -LL/TT + <i>HTR3A</i> -rs1150226-AG + <i>HTR3B</i> -rs17614942-AC	O=4 P=3 (3%)	-4.05 (-8.41 to 0.31) 0.069
4	<i>SLC6A4</i> -LL/TT + <i>HTR3A</i> -rs1150226-AG	O=5 P=3 (3%)	-3.92 (-8.09 to 0.26) 0.066

^a All comparisons are between the ondansetron and placebo groups and are listed in descending order of magnitude of their drinks per drinking day reductions; mean differences for DDD are in standard drinks; negative values indicate improvement from baseline. DDD=drinks per drinking day; CI=confidence interval; O=ondansetron; P=placebo.