

Supplementary Table 1. 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	
SLC6A4	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
HTR3A	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
HTR3B	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

^aAll 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.

^bFrom HapMap CEU (European ancestry) sample.

^cData from this study.

^dReference 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.

^epilot_1_CEU_low_coverage_panel.

Supplementary Table 2. 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	
		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	
	rs33940208	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	
		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	
	rs1176722	AA	2.25	-2	6.51	2	4.69	1.78	7.6	4	-2.43	-7.59	2.72	0.355		0.408	
		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	
	rs1176720	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	
		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	
	rs2276302	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	
		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	
		rs1176719	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
	rs10160548	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		
	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		
rs1150220	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		
	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	
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	

^aGenetic 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".

Supplementary Table 3. 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

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.