

Supplemental Table S1: Long range PCR primers for *CYP2D6* copy number assay

Primer	Sequence	Position	Strand
2D6dupl-F^a	CCTGGGAAGGCCCATGGAAG	chr22:42,522,003-42,522,023	negative
2D6dupl-R^a	CAGTTACGGCAGTGGTCAGCT	chr22:42,530,646-42,530,666	positive
5-2D6del^b	CACCAGGCACCTGTACTCCTC	chr22:42,534,666-42,534,686	negative
3-2D6del^b	CAGGCATGAGCTAAGGCACCCAGAC	chr22:42,519,025-42,519,049	positive
DPKup^{ab}	GTTATCCCAGAAGGCTTTGCAGGCTTCA	chr22:42,527,113-42,527,140	negative
DPKlow^{ab}	GCCGACTGAGCCCTGGGAGGTAGGTA	chr22:42,522,040-42,522,065	Positive
^a PCR amplification with these primers results in 5.1kb product if no duplication is present, and 5.1 and 3.5 kb products if a duplication is present. ^b PCR amplification with these primers results in 5.1 kb product if no deletion present, and 5.1 and 3.5 kb products if a deletion is present.			

Supplemental Table S2: Variants used to identify *CYP2D6* star alleles

rsID	rs7692 58	rs28371 696	rs1065 852	rs5030 862	rs72549 357	rs50308 63	rs28371 706	rs5030 655	rs1135 824	rs5030 865	rs3892 097	rs28371 717	rs35742 686	rs5030 656	rs1694 7	rs5030 867	rs28371 725	rs59421 388	rs1135 840
Updated rsID					rs77467 1100	rs20137 7835													
HG19 chr22 Locus	42526 763	425267 17	42526 694	42526 670	4252665 6	4252591 2	425257 72	42525 085	42525 044	42525 035	42524 947	425243 10	425242 43	42524 175	42523 943	42523 858	425238 05	425236 10	42522 613
Reference	C	C	G	C	C	C	G	CA	T	C	C	C	CT	CCTT	A	T	C	C	G
*1															G				C
*2																			
*3													C		G				C
*3B									C				C		G				C
*4			A								T				G				
*5	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅	∅
*6								C							G				C
*6C								C							G				
*7															G	G			C
*8										A									
*9														C	G				C
*10			A												G				
*11						G													
*12				T															
*14A			A								T								
*14B											T								
*15					CA										G				C
*17							A												
*29																		T	
*33												A			G				C
*35	T																		
*41																	T		
*46		T																	

∅ - No alleles, as *5 is deletion of the *CYP2D6* gene

Supplemental Table S3: Genotype and phenotype characteristics of study cohort

Diplotype	Number of Individuals	Frequency (%)	Phenotype
CYP2D6 *1/*2xN	4	1.6	UM
CYP2D6 *1/*1xN	1	0.4	UM
CYP2D6 *1xN/*2	1	0.4	UM
CYP2D6 *1/*1	39	15.2	NM
CYP2D6 *1/*2	37	14.4	NM
CYP2D6 *1/*4	34	13.2	NM
CYP2D6 *2/*4	17	6.6	NM
CYP2D6 *1/*41	14	5.4	NM
CYP2D6 *1/*35	10	3.9	NM
CYP2D6 *2/*41	9	3.5	NM
CYP2D6 *1/*9	8	3.1	NM
CYP2D6 *1/*17	6	2.3	NM
CYP2D6 *1/*5	6	2.3	NM
CYP2D6 *1/*3	4	1.6	NM
CYP2D6 *2/*2	4	1.6	NM
CYP2D6 *1/*29	3	1.2	NM
CYP2D6 *2/*6	3	1.2	NM
CYP2D6 *35/*41	3	1.2	NM
CYP2D6 *2/*17	2	0.8	NM
CYP2D6 *2/*35	2	0.8	NM
CYP2D6 *2/*5	2	0.8	NM
CYP2D6 *3/*35	2	0.8	NM
CYP2D6 *4/*35	2	0.8	NM
CYP2D6 *1/*10	1	0.4	NM
CYP2D6 *1/*33	1	0.4	NM
CYP2D6 *1/*6	1	0.4	NM
CYP2D6 *10/*35	1	0.4	NM
CYP2D6 *10/*46	1	0.4	NM
CYP2D6 *1xN/*4	1	0.4	NM
CYP2D6 *2/*10	1	0.4	NM
CYP2D6 *2/*29	1	0.4	NM
CYP2D6 *2/*3	1	0.4	NM
CYP2D6 *2/*9	1	0.4	NM
CYP2D6 *35/*35	1	0.4	NM
CYP2D6 *17/*5	3	1.2	IM
CYP2D6 *4/*10	3	1.2	IM
CYP2D6 *4/*41	3	1.2	IM
CYP2D6 *4/*9	3	1.2	IM
CYP2D6 *3/*41	2	0.8	IM
CYP2D6 *10/*5	1	0.4	IM

CYP2D6 *4/*17	1	0.4	IM
CYP2D6 *4/*29	1	0.4	IM
CYP2D6 *41/*5	1	0.4	IM
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CYP2D6 *4/*4	7	2.7	PM
CYP2D6 *3/*4	5	1.9	PM
CYP2D6 *3/*5	1	0.4	PM
CYP2D6 *4/*4xN	1	0.4	PM
CYP2D6 *4/*6	1	0.4	PM
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Supplemental Table S4: Adverse event characteristics and frequencies by metabolizer status

Adverse Event (AE)	Individuals with AE <i>n=104</i> (%)	Poor Metabolizers with AE, <i>n=15</i> (%)	Intermediate Metabolizers with AE, <i>n=18</i> (%)	Normal Metabolizers with AE, <i>n=218</i> (%)	Ultrarapid Metabolizers with AE, <i>n=6</i> (%)
Weight change	23 (8.9)	0	5 (27.8)	17 (7.8)	1 (16.7)
Extrapyramidal symptoms	16 (6.2)	1 (6.7)	0	14 (6.4)	1 (16.7)
Hypersomnia or sedation	15 (5.8)	2 (13.3)	2 (11.1)	11 (5)	0
Hyperphagia or increased appetite	11 (4.3)	0	1 (5.6)	10 (4.6)	0
Elevation of blood glucose	5 (1.9)	0	1 (5.6)	4 (1.8)	0
Abnormal thyroid function test	5 (1.9)	0	2 (11.1)	3 (1.4)	0
Hyperprolactinemia or gynecomastia	4 (1.6)	0	2 (11.1)	2 (0.9)	0
Hyper salivation	4 (1.6)	0	1 (5.6)	3 (1.4)	0
Elevation of serum lipids	3 (1.2)	0	1 (5.6)	2 (0.9)	0
QTc prolongation	3 (1.2)	0	1 (5.6)	2 (0.9)	0
Behavioral concerns	3 (1.2)	0	1 (5.6)	2 (0.9)	0
Anxiety or nervousness	2 (0.8)	0	0	2 (0.9)	0
Constipation	2 (0.8)	0	0	2 (0.9)	0
Precocious puberty	2 (0.8)	0	0	2 (0.9)	0
Muscle cramps	1 (0.4)	1 (6.7)	0	0	0
Headache	1 (0.4)	0	0	1 (0.5)	0
Hot flashes	1 (0.4)	0	0	0	1 (16.7)
Fainting episode	1 (0.4)	0	0	0	1 (16.7)
Bruising	1 (0.4)	0	1 (5.6)	0	0
Oculogyric crisis	1 (0.4)	1 (6.7)	0	0	0

Supplemental Table S5: Cohort characteristics by adverse event presence

Characteristics	Adverse Event (Frequency (%) or median (IQR))	No Adverse Event (Frequency (%) or median (IQR))	<i>P</i> value*
Age	8.4 (6.3-10.7)	8.3 (6.3-10.3)	0.8
Male sex	57 (75)	131 (72.4)	0.8
Race			0.04
White	64 (84.2)	153 (84.5)	
African-American	6 (7.9)	23 (12.7)	
Asian/Pacific islander	1 (1.3)	4 (2.2)	
Unknown	4 (5.3)	1 (0.6)	
Native American	1 (1.3)	0	
Ethnicity			0.3
Hispanic	1 (1.3)	5 (2.8)	
Non-Hispanic	72 (94.7)	174 (96.1)	
Unknown	3 (4)	2 (1.1)	
Specific indication for risperidone			
Aggression	45 (59.2)	80 (44.2)	0.03
Behavioral problems	20 (26.3)	59 (32.6)	0.4
Agitation	16 (21.1)	26 (14.4)	0.2
Irritability	25 (32.9)	38 (21)	0.06
Self-injurious behaviors	25 (32.9)	20 (11.1)	<0.001
Baseline dosing regimen of risperidone (mg/day)	0.5 (0.4-1)	0.5 (0.5-1)	0.6

**P* values from Kruskal-Wallis test for continuous variables and Fisher's exact for categorical variables. IQR – Interquartile Range