SI Table 1

Classification of mice as responders or non-responders to SSRIs on the TST. $TPH2^{+/+}$ or $TPH2^{-/-}$ mice were classified as drug responders if their immobility times were 2 standard deviations lower than the mean of their respective non-treated controls. A significant Fisher's exact p value indicates that the proportion of responders and non-responders is different in $TPH2^{+/+}$ versus $TPH2^{-/-}$ mice. The number of male (M) and female (F) drug responders and non-responders for all groups is also specified within brackets in the format [#M,#F]. The number of controls (not drug treated) used for drug treated mice were as follows: fluoxetine (TPH2+/+: 6M,6F; TPH2-/-: 7M,6F), paroxetine (TPH2+/+: 5M,5F; TPH2-/-: 5M,6F) and citalopram (TPH2+/+: 5M,6F; TPH2-/-: 6M,5F).

	Responders (%)		**Non-responders (%)**		**Fisher's exact**
SSRI	***TPH2*$^{+/+}$**	***TPH2*$^{-/-}$**	***TPH2*$^{+/+}$**	***TPH2*$^{-/-}$**	***p value***
Fluoxetine	33.3 (5[3M,2F]/15)	18.8 (3[2M,1F]/16)	66.7 (10[5M,5F]/15)	81.2 (13[7M,6F]/16)	ns
Paroxetine	92.3 (12[5M,7F]/13)	38.5 (5[2M,3F]/13)	7.7 (1[1M,0F]/13)	61.5 (8[3M,5F]/13)	0.0112
Citalopram	81.2 (13[7M,6F]/16)	31.2 (5[3M,2F]/16)	18.8 (3[2M,1F]/16)	68.8 (11[5M,6F]/16)	0.0113

SI Table 2

Cut off values for classification into responders or non-responders. Immobility times lower than mean-2SD were considered responders. Mice that had the same immobility (mean + 2SD) or higher times than non-treated controls were classified as non-responders.

	Fluoxetine		**Paroxetine**		**Citalopram**	
	***TPH2*$^{+/+}$**	***TPH2*$^{-/-}$**	***TPH2*$^{+/+}$**	***TPH2*$^{-/-}$**	***TPH2*$^{+/+}$**	***TPH2*$^{-/-}$**
Mean	152.9	150.9	108.8	147.4	111.0	129.4
SD	33.8	45.2	26.3	25.4	25.4	31.4
2SD	67.6	90.4	52.6	50.8	50.8	62.7
Mean - 2SD	85.3	60.5	56.2	96.6	60.1	66.7
Mean + 2SD	220.4	241.3	161.4	198.2	161.8	192.1

Abbreviations: SD= standard deviation.

SI Table 3

Unpredictable chronic mild stress- The unpredictable chronic mild stress (UCMS) procedure is based on those designed for rats (Willner, 1997, Psychopharmacolgy, 134, 319-329) and mice (Mutlu et al., 2012, Life Sciences, 91, 1252-1262) and is generally accepted as the most effective and valid test for inducing depressive-like behaviors in rodents. In this test, mice are exposed to a series of mild stressors over a 6 week period. Mice are generally exposed to 3 stressors per day, Monday through Friday. Mice are not exposed to stressors on Saturdays and Sundays. The 3 stressors given on any given day (morning [am], midday [md] and afternoon [pm]) are shown in the matrix below. The nature of those stressors that are not obvious is explained below the matrix.

		Monday	**Tuesday**	**Wednesday**	**Thursday**	**Friday**
Week 1	am	H_2O depr 30’	social stress 15’	cage tilt 1.5h	forced swim 15’	lights off 30’
	md	handling 5-10’	lights off 1h	social stress 15’	bed remove 2h	cage tilt 1,5h
	pm	bed remove 1h	sucrose on coat	lights off 1h	lights off 15’	wheeling 10’
Week 2	am	lights off 1h	cage tilt 1.5h	social stress 5’	bed remove 1h	lights off 2h
	md	handling 5-10’	sucrose on coat	lights off 1h	social stress 5’	H_2O remove 1h
	pm	cage tilt 90’	bed remove 1h	forced swim 10’	cage tilt 1h	wheeling 15’
Week 3	am	lights off 2h	lights off 2h	H_2O depr 2h	cage tilt 2.5h	social stress 5’
	md	handling 5-10’	social stress 15’	social stress 5’	forced swim 10’	wheeling 15’
	pm	sucrose on coat	cage tilt 2.5h	bed remove 3h	dryer 10’	lights off 2h
Week 4	am	lights on O/N	social stress 15’	bed remove 3.5h	bed removal 3.5h	wheeling 10’
	md	handing 5-10 min	saline inj	social stress 15’	forced swim 15’	H_2O remove 2h
	pm	sucrose on coat	lights off 2h	cage exchng 1h	dryer 10’	confinement 15’
Week 5	am	wheeling 10’	cage tilt 1.5h	lights off 2h	forced swim 10’	lights off 2h
	md	H_2O remove 2h	saline inj	cage exchng 2h	dryer	H_2O remove 1.5h
	pm	sucrose on coat	cage exchng 1h	confinement 15’	cage exchng 3h	wheeling 15 min
Week 6	am	lights off 4h	cage tilt 2h	confinement 15’	forced swim 15’	social stress 5’
	md	sucrose on coat	bed remove 2h	cage exchng O/N	dryer 5’	wheeling 10’
	pm	water depr 3h	social stress 30’	saline injection	cage exchng 3h	H_2O remove 2h

Abbreviations: H_2O depr= water deprivation; exchng= exchange; O/N= overnight

Stressor explanations:

1) handling- mice are handled in a gloved hand for indicated times
2) bed remove- bedding removed from cage for indicated time, then replaced
3) lights off- lights are turned off in the test room during the light phase for the indicated times
4) cage tilt- cage placed on surface at a 45º angle for indicated times
5) sucrose on coat- sucrose (10% solution) sprayed on dorsal coat to induced grooming
6) wheeling- mouse cages placed on wheeled lab cart and cart pushed from experimental room to room for indicated times
7) H_2O removal- water AND food removed from cages for indicated times then replaced
8) social stress- mice (2-3) put into cage with “stranger mice” (2-3) of same genotype and sex for indicated times, then returned to home cage
9) saline injection- single ip injection of sterile saline (1 ml/kg)
10) cage exchange (exchng)- mice taken from home cage and put into an empty cage of a male mouse (removed for test)
11) forced swim- 5 mice of same sex and genotype placed in water at room temperature as in forced swim test for indicated times. Mice then removed, dried with a hair dryer, and returned to home cage
12) confinement- placed into a DecapiCone for indicated times as a mode of acute restraint stress
13) dryer- mice exposed to sound of hair dryer used in forced swim test near cage for indicated times

Body weight and coat status are assessed before initiation of the UCMS protocol and weekly throughout the entire procedure. Coat status from 8 body parts (head, neck, dorsal coat, ventral coat, tail, forepaws and hind paws) is scored as 0 for well groomed and 1 for unkempt by 2-3 observers blind to mouse genotype. The total score per test was derived by summing the individual scores for each body part.