

Supplementary Tables and Figures

TABLE S1. Clinical Characteristics of the 11 Subjects With Major Depressive Disorder Included in PET Study

Clinical Characteristic	Category, Unit	Value
BDI score	Mean (SD), range	25.3 (8.0), 13 to 35
BAI score	Mean (SD), range	18.6 (10.5), 6 to 37
Age at onset	Mean (SD), range, in years	26.1 (13.9), 17 to 42
Episode duration	Mean (SD), range, in months	59.8 (48.1), 9 to 138
Total illness duration	Mean (SD), range, in years	14.73 (11.3), 3 to 42
Course of Major Depression	Single MDE (N)	1
	2 or 3 MDEs (N)	4
	>3 MDEs (N)	4
	Chronic course	2
Time medication-free	Mean (SD), range, in months	15.3 (13.2), 1 to 39
	Never medicated (N)	4
Comorbid diagnoses	Generalized anxiety disorder (N)	1
	Panic disorder (N)	1
	Social phobia (N)	1
History of suicidality	Suicide attempt/s (N)	1
Depression subtypes	Melancholic (N)	1
	Atypical (N)	0
Family history	Major depressive disorder (N)	6
	Bipolar disorders (N)	1
	Anxiety disorders (N)	1
	Alcohol use disorders (N)	6

BDI=Beck Depression Inventory, BAI=Beck Anxiety Inventory, SD=standard deviation

FIGURE S1. Typical tissue time-activity curves after injecting half the activity as a bolus and the other half as a constant infusion until 60 minutes. The activity reaches a steady state at 30 minutes. At equilibrium, the ratio of the tracer concentration in tissue and blood is directly representing the total distribution volume of the tracer, which itself is directly related to receptor density (Blasberg et al., 1989; Carson et al, 1993).

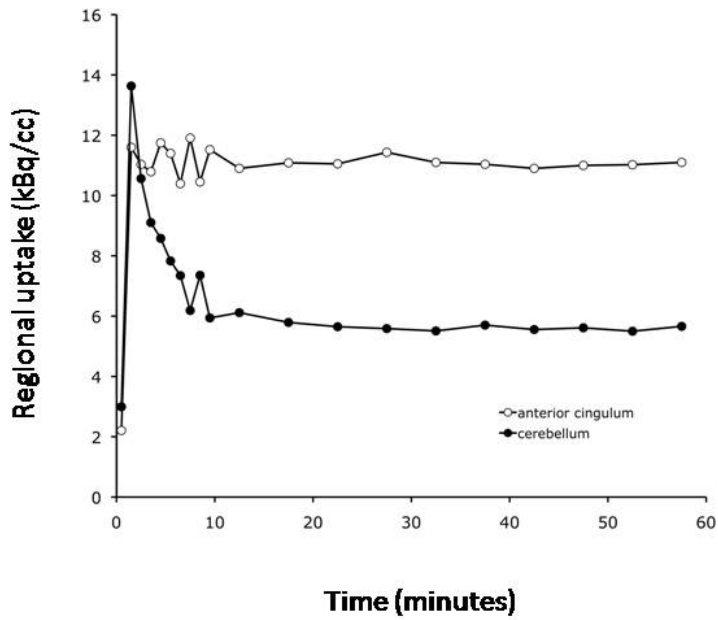


TABLE S2. Summary of Clinical Characteristics of Subjects Included in Postmortem Study

Clinical Characteristic	Healthy Controls (n=15)	Major Depression (n=15)
Age*	49 (14.9) years	52 (14.5) years
Postmortem interval*	17 (5.7) hours	23 (4.8) hours
pH*	6.68 (0.31)	6.52 (0.27)
Gender (female/male)	3/12	3/12
Time in freezer*	141 (24) months	137 (41) months
Medication history ^a	none	n=4 (sertraline, n=2; fluoxetine, n=1; imipramine, n=1)
Comorbid diagnosis	History of alcohol abuse, n=3	Alcohol abuse, n=2; history of alcohol abuse, n=2; dysthymia, n=1
Smoking	Smokers, n=5 History of smoking, n=2	Smokers, n=5
Suicide	none	n=11

* Mean (SD).

^a prescriptions for antidepressants within 4 weeks prior to death; none of the 15 depressed subjects had antidepressants present in their postmortem toxicology screening.

TABLE S3. Clinical Characteristics of Individual Subjects Included in Postmortem Study

Healthy Controls (pair no.)	Age	Sex	PMI	Brain pH	Toxicology	Cause of death
1	30	M	19	6.98	Clean	Heart disease
2	33	M	23	6.86	Clean	Heart disease
3	27	F	15	7.01	Clean	Heart disease
4	37	F	13	5.93	Clean	Viral myocarditis
5	51	F	22	6.30	Clean	Heart disease
6	46	M	11	6.95	Clean	Heart disease
7	54	M	17	6.87	Brompheniramine	Heart disease
8	69	M	26	6.70	Clean	Heart disease
9	70	M	20	6.81	Clean	Heart disease
10	74	M	21	6.62	Clean	Abdominal aortic aneurysm
11	59	M	6	6.79	Lidocaine	Heart disease
12	34	M	24	6.61	Ethanol	Thrombophlebitis
13	54	M	19	6.52	Lidocaine	Heart disease
14*	52	M	17	6.28	Clean	Heart disease
15*	48	M	9	6.98	Clean	Heart disease
Major Depression (pair no.)						
1	41	M	19	6.24	Chlorpheniramine	Heart disease
2	30	M	18	6.91	Ethanol	Suicide (gunshot to chest)
3	34	F	24	6.27	Ethanol, CO, alprazolam	Suicide (CO poisoning)
4	40	F	25	6.32	Morphine, codeine, hydrocodone	Heart disease
5	50	F	28	6.47	Dextromethorphan	Cardiovascular disease
6	46	M	17	6.26	Clean	Homicide
7	54	M	23	6.24	Phenobarbital, phenytoin, CO	Suicide (CO poisoning)
8	64	M	26	6.85	Ethanol	Suicide (gun shot to head)
9	74	M	25	6.67	Diazepam	Suicide (gunshot to head)
10	81	M	33	6.78	Clean	Suicide (drowning)
11	60	M	20	6.31	Ethanol	Suicide (gunshot to chest)
12	42	M	20	6.80	Clean	Suicide (gunshot to chest)
13	52	M	17	6.48	CO	Suicide (CO poisoning)
14*	48	M	21	6.90	Flurazepam	Suicide (gunshot to chest)
15*	65	M	30	6.24	Codeine	Suicide (gunshot to chest)

M, male; F, female; PMI, postmortem interval; CO, carbon monoxide. * subjects not included in mGluR1 study

TABLE S4. Brain Regions With Negative Correlations Between Clinical Symptoms and [¹¹C]ABP688 DVR in Subjects With Major Depressive Disorder (N=11)

Brain Regions	x y z coordinates ^b	t-values
Negative Correlations with Beck Depression Inventory		
R hippocampal formation	22, 38, 7	9.22 ^a
L hippocampal formation	-26, -39, 6	4.41
Negative Correlations with Beck Anxiety Inventory		
R thalamus	14, -13, 3	5.53
L thalamus	-10, -19, 1	5.24
R medial orbital cortex (Brodmann's area 11)	26, 36, -22	4.81
R frontal polar cortex (Brodmann's area 10)	34, 62, -10	4.77
L lateral orbital cortex (Brodmann's area 11/47)	-46, 34, -15	4.58
L mid-cingulate cortex	-22, -31, 44	4.43

All results were significant at $p_{\text{uncorrected}} < 0.001$.

^a Cluster-level, corrected p value = 0.029 after applying the cluster test for multiple testing

^b Coordinates correspond to the stereotaxic array of Talairach and Tournoux (1988)

FIGURE S2. Column scatter graphs displaying mGluR5 DVR in the 11 depressed subjects found in the PET study within the right frontal polar cortex (Brodmann's area 10; see method section). Gray shading indicates that the data was derived from subjects suffering from a comorbid anxiety disorder. Triangles indicate that data were derived from subjects who were drug-naïve at the time of the study.

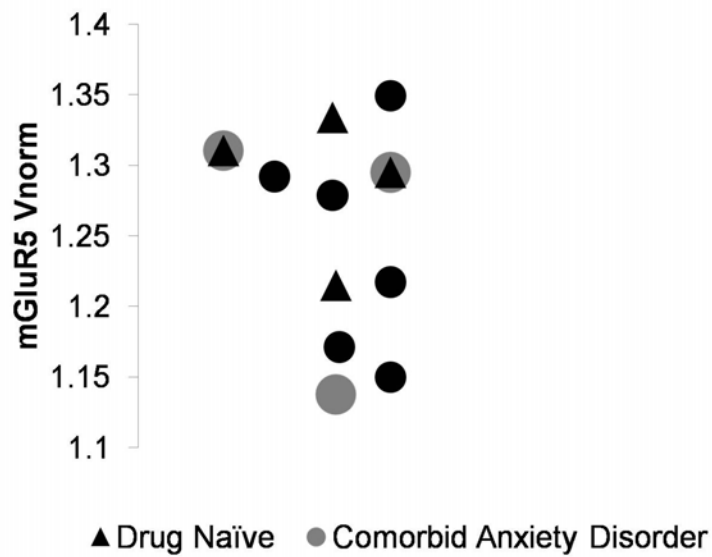


Figure S3. mGluR5 immunoreactivity detected in prefrontal cortex (lanes 1 and 2) and in cerebellum (lanes 3 and 4) from two psychiatrically healthy controls. Each well was loaded with 15µg of total protein. The bottom panel shows immunoreactive actin detected on the same blot as a control for protein loading.

