SUPPLEMENTAL INFORMATION

**Differences in Quantification of the Metabotropic Glutamate
Receptor 5 Across Bipolar Disorder and Major Depressive Disorder**

Holmes *et al.*

Supplemental statistics: power calculations

All power calculations were conducted using G*Power (version 3.1.9.6). After completing

multivariate tests evaluating group differences in V_T for the three prefrontal ROIs, we performed

power calculations to determine achieved power (1-β). Results of these analyses suggest we

were sufficiently powered (1-β>0.8) to detect a main effect of diagnosis between the three

primary diagnostic groups (HC, BD, and MDD):

> Sample size (N)=62
> Groups=3
> Response variables=3
> Observed effect size (f^2)=0.1198
> Error probability (α)=0.05
> **Estimated power (1-β)=0.815**

However, we did not achieve sufficient power to detect a main effect of diagnosis between the

four diagnostic groups (HC, BD-dep, BD-euth, and MDD):

> Sample size (N)=62
> Groups=4
> Response variables=3
> Observed effect size (f^2)=0.0834
> Error probability (α)=0.05
> **Estimated power (1-β)=0.772**

For the exploratory correlation analyses, we used our observed effect sizes (correlation

coefficients, r), to compute required sample sizes that would be required for adequately

powered (1-β>0.8) two-tailed tests:

ROI V_T vs. depression severity (MADRS) in **BD-dep**	ROI V_T vs. depression severity (MADRS) in **MDD**
Observed effect size (r)=0.1*	Observed effect size (r)=0.6*
Error probability (α)=0.05	Error probability (α)=0.05
Actual power (1-β)=0.800	Actual power (1-β)=0.824
Required sample size (*n*)=779	**Required sample size (*n*)=17**
(Actual sample size =27)	(Actual sample size =17)

ROI V_T vs. cognitive function in **BD-dep**	ROI V_T vs. cognitive function in **MDD**
Observed effect size (r)=0.4†	Observed effect size (r)=0.2†
Error probability (α)=0.05	Error probability (α)=0.05
Actual power (1-β)=0.807	Actual power (1-β)=0.801
Required sample size (*n*)=44	**Required sample size (*n*)=191**
(Actual sample size =27)	(Actual sample size =17)

*The lowest ROI with the smallest effect size was used
†The ROI and cognitive domain (psychomotor processing or executive function) combination yielding the smallest effect size was used

Supplemental tables

Table S1. Details of psychiatric medications across subjects. Each row represents the reported medication list for a single subject.

Diagnostic Group	List of current psychiatric medications
BD-euth	Gabapentin, Lithium, Melatonin, Paliperidone,
BD-euth	Amphetamine/dextroamphetamine, Aripiprazole
BD-euth	Quetiapine
BD-dep	Citalopram
BD-dep	Amphetamine/dextroamphetamine, Ziprasidone
BD-dep	Amphetamine/dextroamphetamine
BD-dep	Alprazolam
MDD	Amphetamine/dextroamphetamine, Bupropion, Clonazepam
MDD	Buspirone, Escitalopram, Risperidone
MDD	Amphetamine/dextroamphetamine XR, Vortioxetine
MDD	Buspirone, Duloxetine

Table S2. MANCOVA of [^{18}F]FPEB V_T within PFC subregions across diagnostic groups (HC, MDD, BD), with psychiatric medication status as a covariate.

Multivariate Tests*			
	Effect	**F (DF$_H$, DF$_E$)**	***p*-value**
	Group	2.4 (6, 108.0)	0.033
	Current psych meds	2.7 (3, 54)	0.053
Tests of Between-Subject Effects			
Dependent Variable	**Source**	**F (DF$_H$, DF$_E$)**	***p*-value**
OFC	Group	5.6 (2, 56)	0.006
	Current psych meds	6.6 (1, 56)	0.013
vmPFC	Group	6.1 (2, 56)	0.004
	Current psych meds	6.6 (1, 56)	0.013
dlPFC	Group	7.4 (2, 56)	0.001
	Current psych meds	5.1 (1, 56)	0.028

*Wilks' Lambda, exact statistic

Table S3. MANCOVA of [^{18}F]FPEB V_T within PFC subregions across diagnostic groups (HC, MDD, BD-dep, and BD-euth), with psychiatric medication status as a covariate.

Multivariate Tests*			
	Effect	**F (DF$_H$, DF$_E$)**	***p*-value**
	Group	1.5 (9, 129.1)	0.115
	Current psych meds	2.6 (3, 53)	0.060
Tests of Between-Subject Effects			
Dependent Variable	**Source**	**F (DF$_H$, DF$_E$)**	***p*-value**
OFC	Group	3.7 (3, 55)	0.017
	Current psych meds	6.4 (1,55)	0.014
vmPFC	Group	4.1 (3, 55)	0.011
	Current psych meds	6.4 (1,55)	0.014
dlPFC	Group	4.8 (3, 55)	0.005
	Current psych meds	5.0 (1,55)	0.030

*Wilks' Lambda, exact statistic

Table S4. MANCOVA of [^{18}F]FPEB V_T within PFC subregions across diagnostic groups (HC, MDD, BD), with venous vs. arterial-derived input function as a covariate.

Multivariate Tests*			
	Effect	**F (DF$_H$, DF$_E$)**	***p*-value**
	Group	2.1 (6, 112)	0.055
	Arterial vs. venous	2.5 (3, 56)	0.069
Tests of Between-Subject Effects			
Dependent Variable	**Source**	**F (DF$_H$, DF$_E$)**	***p*-value**
OFC	Group	3.5 (2, 58)	0.037
	Arterial vs. venous	6.8 (1, 58)	0.012
vmPFC	Group	3.9 (2, 58)	0.027
	Arterial vs. venous	6.6 (1, 58)	0.013
dlPFC	Group	5.4 (2, 58)	0.007
	Arterial vs. venous	5.4 (1, 58)	0.023

*Wilks' Lambda, exact statistic

Table S5. MANCOVA of [^{18}F]FPEB V_T within PFC subregions across diagnostic groups (HC, MDD, BD-dep, and BD-euth), with venous vs. arterial-derived input function as a covariate.

Multivariate Tests*			
	Effect	**F (DF$_H$, DF$_E$)**	***p*-value**
	Group	1.4 (9, 134)	0.177
	Arterial vs. venous	2.3 (3, 55)	0.083
Tests of Between-Subject Effects			
Dependent Variable	**Source**	**F (DF$_H$, DF$_E$)**	***p*-value**
OFC	Group	2.3 (3, 57)	0.087
	Arterial vs. venous	6.5 (1,57)	0.014
vmPFC	Group	2.5 (3, 57)	0.066
	Arterial vs. venous	6.3 (1,57)	0.015
dlPFC	Group	3.5 (3, 57)	0.021
	Arterial vs. venous	5.3 (1,57)	0.025

*Wilks' Lambda, exact statistic

Table S6. Mean [^{18}F]FPEB V_T values and ANOVA results for brain regions not included in the primary analysis for HC, BD, and MDD groups.

Brain Region	Group Mean(SD)			Univariate Tests	
	HC (*n*=18)	BP (*n*=27)	MDD (*n*=17)	$F_{2,59}$	*p*-value
Amygdala	30.46(7.68)	26.70(5.11)	30.74(6.45)	2.919	0.062
Caudate	34.74(9.57)	29.15(5.93)	34.25(6.56)	*4.101*	*0.022*
Cerebellum	12.69(2.75)	10.60(2.26)	12.37(4.12)	3.118	0.052
Cingulate, anterior	37.61(7.92)	32.28(6.49)	38.31(7.40)	*4.803*	*0.012*
Cingulate, posterior	27.02(8.23)	22.35(7.04)	25.35(3.78)	2.779	0.07
Hippocampus	27.80(6.24)	24.52(4.75)	28.16(5.55)	3.097	0.053
Insula, anterior	36.86(8.30)	32.28(6.63)	37.32(8.08)	3.044	0.056
Insula, posterior	34.40(8.10)	29.72(5.69)	34.77(7.94)	*3.527*	*0.036*
Occipital cortex	31.96(6.62)	28.18(5.94)	32.02(6.25)	2.843	0.066
Parietal cortex	31.02(10.52)	29.05(5.76)	33.80(6.94)	1.98	0.147
Putamen	33.73(7.76)	28.95(5.51)	33.19(6.13)	*3.809*	*0.028*
Temporal cortex	35.17(8.90)	31.26(6.15)	36.71(7.76)	3.142	0.051
Thalamus	23.63(4.02)	19.78(3.81)	22.21(4.08)	*5.465*	*0.007*

Table S7. Mean [^{18}F]FPEB V_T values and ANOVA results for brain regions not included in the primary analysis for HC, BD-euth, BD-dep, and MDD groups.

Brain Region	Group Mean(SD)				Univariate Tests	
	HC (*n*=18)	BP-euth (*n*=10)	BP-dep (*n*=17)	MDD (*n*=17)	$F_{3,58}$	*p*-value
Amygdala	30.46(7.68)	26.62(4.89)	26.75(5.38)	30.74(6.45)	1.914	0.137
Caudate	34.74(9.57)	29.21(4.85)	29.11(6.63)	34.25(6.56)	2.688	0.055
Cerebellum	12.69(2.75)	11.33(2.03)	10.21(2.34)	12.37(4.12)	2.34	0.083
Cingulate, anterior	37.61(7.92)	32.53(5.18)	32.13(7.30)	38.31(7.40)	*3.156*	*0.031*
Cingulate, posterior	27.02(8.23)	20.97(7.86)	23.16(6.63)	25.35(3.78)	2.062	0.115
Hippocampus	27.80(6.24)	24.60(5.01)	24.48(4.76)	28.16(5.55)	2.031	0.12
Insula, anterior	36.86(8.30)	33.19(5.69)	31.74(7.24)	37.32(8.08)	2.078	0.114
Insula, posterior	34.40(8.10)	30.07(5.14)	29.51(6.14)	34.77(7.94)	2.324	0.085
Occipital cortex	31.96(6.62)	28.53(5.24)	27.98(6.46)	32.02(6.25)	1.881	0.143
Parietal cortex	31.02(10.52)	29.99(5.64)	28.50(5.93)	33.80(6.94)	1.38	0.258
Putamen	33.73(7.76)	29.10(4.84)	28.86(6.01)	33.19(6.13)	2.499	0.069
Temporal cortex	35.17(8.90)	31.83(5.48)	30.93(6.65)	36.71(7.76)	2.093	0.111
Thalamus	23.63(4.02)	20.23(3.97)	19.52(3.80)	22.21(4.08)	*3.66*	*0.018*

Supplemental Figure 1. MANOVA of $[^{18}F]$FPEB V_T within PFC subregions across HC (black), MDD (orange), and BD groups (purple)($F_{6,116}$=2.175, p=0.050). Brackets indicate p-values from independent-sample t-tests. Individual values are depicted with group mean±SD.