Relationships Between Altered Functional Magnetic Resonance Imaging Activation and Cortical Thickness in Euthymic Bipolar I Disorder

Supplementary Information

Supplemental Methods and Materials

fMRI Paradigm

Participants were instructed to respond via button box as quickly and accurately as possible with their right index finger to a total of 14 pictures shown during Go or NoGo conditions. In the Go condition (Block A), participants viewed a 2-sec instruction screen “Push for every picture,” followed by the presentation of Spiderman. The Go condition included only the target pictures, Spiderman, presented for 2-sec without an interstimulus interval. In the NoGo condition (Block B), participants were presented with the visual 2-sec instruction “Push only when you see Spiderman,” whereby a non-target non-Spiderman picture (2-sec) was shown seven times, and a Spiderman picture (2-sec) was shown seven times in a pseudorandom sequence. The task included 4 30-sec “Go” blocks and 4 30-sec “No-Go” blocks, which were composed of a total of 112 trials (84 Go trials, 28 NoGo trials). Prior to scanning, participants completed a brief practice session to ensure understanding of the task.

Supplemental Results

Table S1. P-values (uncorrected) showing cortical ROI thickness differences between healthy controls and bipolar patients for the left hemisphere when controlling for age. The ROIs with significant p-values (uncorrected) are shown in red.

No.	Cortical ROI	Thickness P-value
1	Bank of the Superior Temporal Sulcus	0.06857
2	Caudate Anterior Cingulate	0.4438
3	Caudal Middle Frontal	0.0239
4	Cuneus	0.02881
5	Entorhinal	0.5437
6	Fusiform	0.07268
7	Inferior Parietal	0.6136
8	Inferior Temporal	0.5844
9	Isthmus Cingulate	0.1238
10	Lateral Occipital	0.05613
11	Lateral Orbitofrontal	0.7359
12	Lingual	0.035
13	Medial Orbitofrontal	0.5387
14	Middle Temporal	0.236
15	Parahippocampal	0.8357
16	Paracentral	0.04455
17	Pars Opercularis	0.02876
18	Pars Orbitalis	0.7301
19	Pars Triangularis	0.03759
20	Pericalcarine	0.1053
21	Postcentral	0.00583
22	Posterior Cingulate	0.6543
23	Precentral	0.00248
24	Precuneus	0.06995
25	Rostral Anterior Cingulate	0.4606
26	Rostral Middle Frontal	0.2034

27	Superior Frontal	0.1604
28	Superior Parietal	0.6056
29	Superior Temporal	0.004507
30	Supra Marginal	0.1298
31	Frontal Pole	0.2353
32	Temporal Pole	0.8414
33	Transverse Temporal	0.08992
34	Insula	0.7857

Table S2. P-values (uncorrected) showing cortical ROI thickness differences between healthy controls and bipolar patients for the right hemisphere when controlling for age. The ROIs with significant p-values (uncorrected) are shown in red.

No.	**Cortical ROI**	**Thickness P-value**
1	Bank of the Superior Temporal Sulcus	0.02907
2	Caudate Anterior Cingulate	0.03157
3	Caudal Middle Frontal	0.0354
4	Cuneus	0.01898
5	Entorhinal	0.6141
6	Fusiform	0.005265
7	Inferior Parietal	0.3378
8	Inferior Temporal	0.4768
9	Isthmus Cingulate	0.02333
10	Lateral Occipital	0.05964
11	Lateral Orbitofrontal	0.5576
12	Lingual	0.001276
13	Medial Orbitofrontal	0.6034
14	Middle Temporal	0.1724
15	Parahippocampal	0.1738
16	Paracentral	0.02553
17	Pars Opercularis	0.775
18	Pars Orbitalis	0.9076
19	Pars Triangularis	0.1581

20	Pericalcarine	0.04414
21	Postcentral	0.008169
22	Posterior Cingulate	0.08203
23	Precentral	0.02762
24	Precuneus	0.02941
25	Rostral Anterior Cingulate	0.634
26	Rostral Middle Frontal	0.1372
27	Superior Frontal	0.009544
28	Superior Parietal	0.274
29	Superior Temporal	0.03733
30	Supra Marginal	0.05579
31	Frontal Pole	0.2676
32	Temporal Pole	0.6076
33	Transverse Temporal	0.1167
34	Insula	0.2864

We tested for interaction effects of disease state on functional activations as a predictor for the cortical ROI thickness. Functional activations were resampled after cortical surface registration to the Desikan atlas. For the purpose of statistical analysis, the ROI activations were obtained after averaging their contribution for each cortical ROI from the Desikan atlas. Cortical thickness was also averaged for all the cortical ROIs from the Desikan atlas. The full interaction model included ROI cortical thickness as outcome, and additive effects of functional activations, disease state and age along with activation by state interaction as predictors. The null model was the same but excluded the interaction term. Significance of the interaction effect was determined by a F-test between the full model and the null model that was identical to the full model, but excluded the interaction term.

Table S3. P-values (uncorrected) for significant interaction effects of disease state by ROI wise functional activations as predictors of ROI wise cortical thickness.

No.	Cortical ROI	P-value of Interaction
1	Left Isthmus Cingulate	0.043
2	Left Medial Orbitofrontal	0.042
3	Left Rostral Middle Frontal	0.045
4	Right Pars Triangularis	0.046
5	Left Frontal Lobe	0.018

Table S4. P-values (uncorrected) for significant correlations of ROI thickness with illness duration or period in euthymic state when controlling for age.

No.	Cortical ROI	Clinical Variable	Correlation (P-value)
1	Left Middle Temporal	Illness Duration	0.3085456 (0.03919)
2	Right Transverse Temporal	Illness Duration	-0.3075999 (0.03983)
3	Right Parahippocampal	Euthymic Duration	0.3067155 (0.04043)
4	Right Posterior Cingulate	Euthymic Duration	0.3248553 (0.02946)

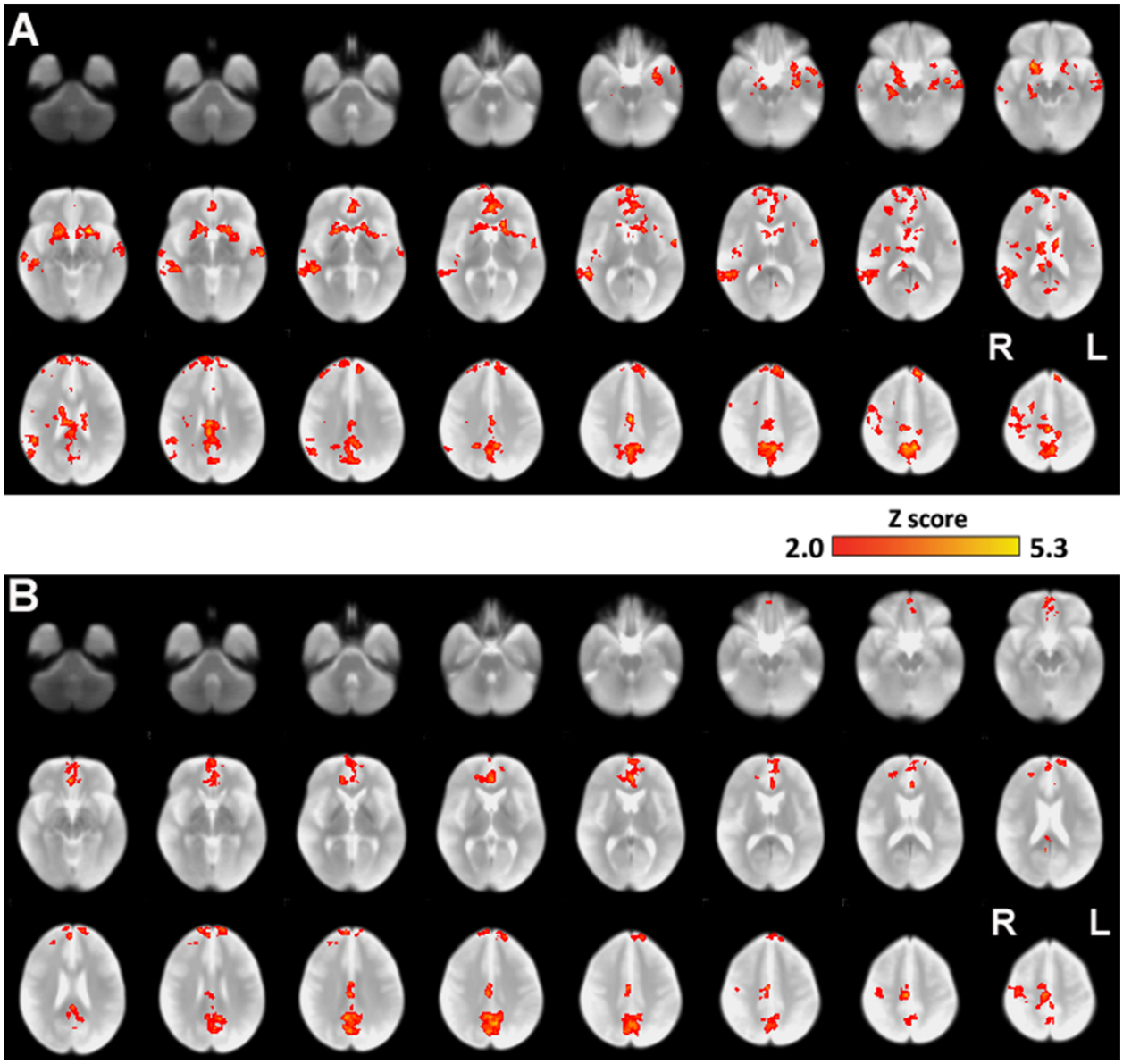

Figure S1. Within-group whole-brain results for control (A) and bipolar subjects (B) during response inhibition (NoGo minus Go) contrast of Go-NoGo fMRI paradigm (Z>2.0, p<0.05 corrected). R= Right; L = Left.

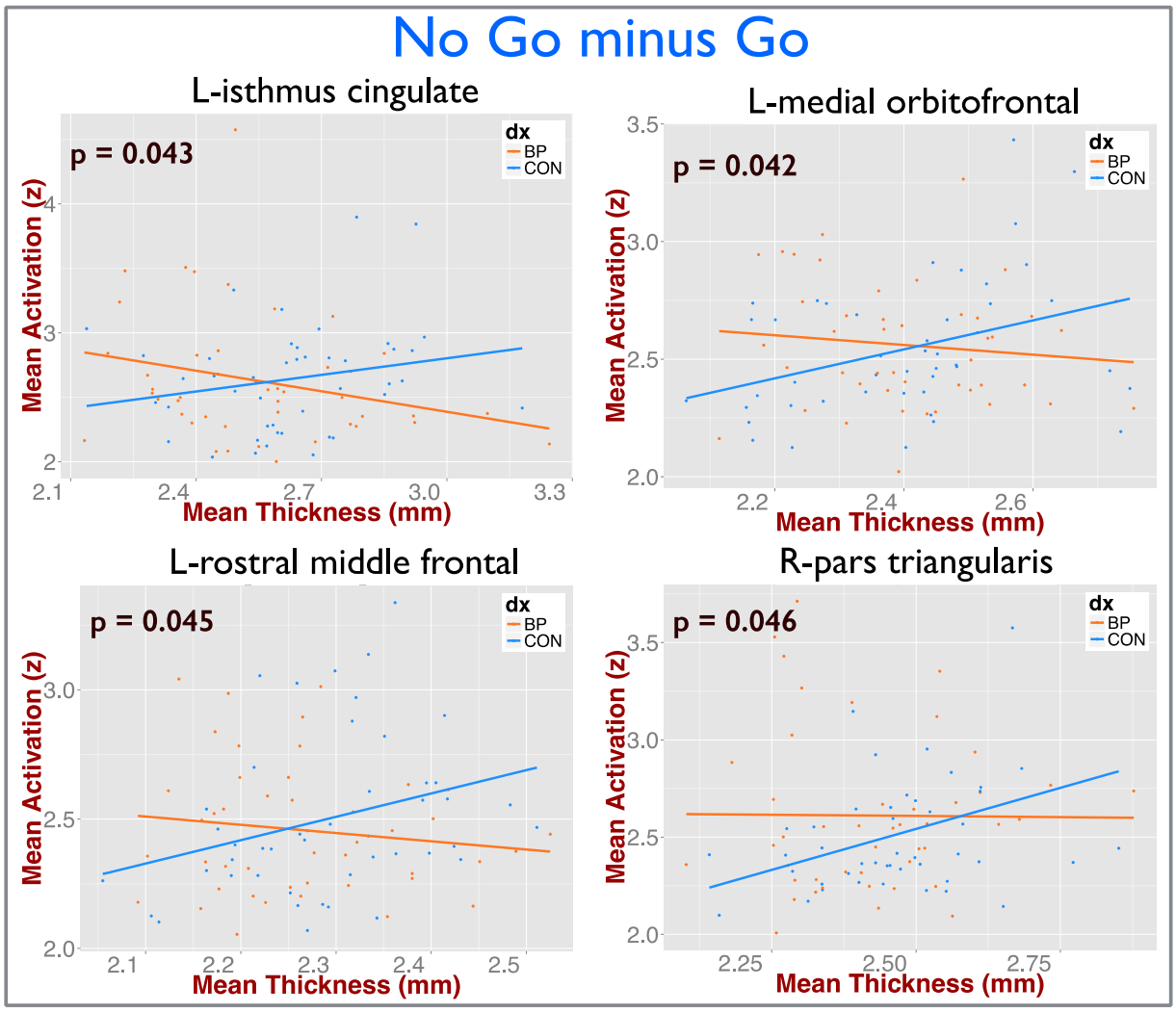

Figure S2. Interaction plots for fMRI activations by disease state as predictors for cortical thickness. Significant interaction effects were found in the left isthmus cingulate, left medial orbitofrontal cortex, left rostral middle frontal cortex and the right pars triangularis. L=Left; R=Right; BP=Bipolar; CON=Controls.

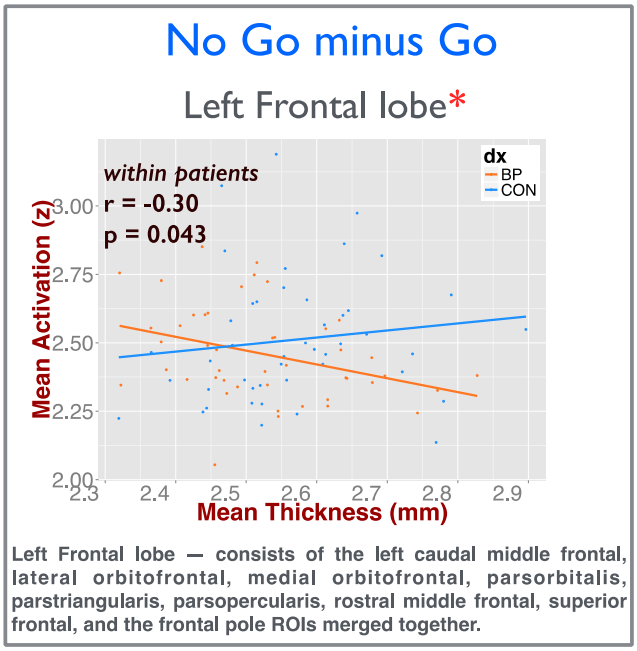

Figure S3. Interaction plot for fMRI activation by disease state as a predictor for cortical thickness in the left frontal lobe. Significant interaction effects were observed in the left frontal lobe that consists of the left caudal middle frontal, lateral orbitofrontal, medial orbitofrontal, pars orbitalis, pars triangularis, pars opercularis, rostral middle frontal, superior frontal, and the frontal pole ROIs merged together. It was also observed that the left frontal lobe mean activations were significantly negatively correlated (r = -0.26, p = 0.043) with the respective mean cortical thickness in patients but not in controls.