Data supplement for Sequeira et al., Association of Neural Reward Circuitry Function With Response to Psychotherapy in Youths With Anxiety Disorders. Am J Psychiatry (doi: 10.1176/appi.ajp.2020.20010094)

SUPPLEMENTAL METHODS

Participants

Ninety-two youths with anxiety completed the pre-treatment monetary reward task in the magnetic resonance imaging (MRI) scanner. Data from 11 youths were excluded because of issues with scanner alignment (*n*=2), excessive motion in the scanner (*n*=2), and study withdrawal (*n*=7). Of the 81 patients with usable fMRI pre-treatment data, 72 had completed post-treatment clinical assessments. Post-treatment data were missing either because of study withdrawal/treatment dropout (*n*=5) or missing/incomplete diagnostician-rated forms (*n*=4).

All patients were required to meet DSM-IV criteria for either generalized anxiety disorder (GAD), separation anxiety disorder (SAD), and/or social phobia (SoPh). Of the 81 anxious youths with usable pre-treatment fMRI data, 48 patients were diagnosed with GAD only, eight patients were diagnosed with SoPh only, and 15 patients were diagnosed with SAD only. Further, eight patients were diagnosed with GAD and SoPh, one patient was diagnosed with GAD and SAD, and one patient was diagnosed with GAD, SoPh, and SAD. Other comorbid diagnoses included specific phobia (*n*=10), attention-deficit hyperactivity disorder- not otherwise specified (*n*=1), attention-deficit hyperactivity disorder- inattentive type (*n*=1), enuresis (*n*=2), tic disorder (*n*=3), oppositional defiant disorder (*n*=2), and panic disorder (*n*=1).

Sensitivity Analysis: Therapy Type

Interactions between therapy type (CBT, CCT) and neural activation/connectivity (centered) on treatment response at post-treatment were examined using logistic regression in SPSS v25. A model was run for each cluster resulting from the BOLD or gPPI analyses using Benjamini-Hochberg correction procedures[45] with a false discovery rate of 0.05. Significance was evaluated using the change in $\chi 2$ when the interaction term was added to the model. Additional analyses were also performed in SPM12 to examine interactions between treatment response and therapy type on neural activation across the whole brain.

SUPPLEMENTAL RESULTS

Sensitivity Analysis: Sample Variance

Given unequal group sizes, post-hoc analyses were performed to verify that unequal sample variance was not driving findings from planned comparisons examining whether 1) treatment responders differed from non-responders and 2) treatment responders and healthy youth as a combined group differed from non-responders. First, we calculated Welch's t-tests, and examined Levene's statistics testing homogeneity of variance, to examine group differences in extracted parameter estimates. Findings suggest that group differences in magnitude, rather than variance, drive present findings (Welch's t= -3.34 and -3.60, *p*s = 001, Levene's test *p*s > .33). Second, we randomly selected 24 responders to include in responder>non-responder *t*-test analysis and found a similar pattern of results, suggesting that unequal cell sizes are not contributing unduly to the present findings.

TABLE S1. Results from exploratory whole-brain one-way ANOVA for the win>loss contrast (voxel-wise threshold of $p<.005$ uncorrected; extent threshold of 20 voxels, or 160 mm^3).

Region	Brodmann area	cluster size (mm^3)	peak MNI [x,y,z]	peak voxel-level *Z*	cluster-level $p_{FWE\text{-}corrected}$
Differences between 3 groups					
R medial PFC	10	1792	2, 52, 20	3.14	.503
R primary motor cortex	4	544	62, -6, 24	3.42	.918
L medial PFC	10	464	-22, 52, 18	3.05	.938
R angular gyrus	39	328	30, -80, 32	2.93	.966
L medial PFC	10	256	-18, 42, -2	2.97	.977
L inferior frontal gyrus	44	176	-44, 12, 28	3.04	.987
Responders>Non-Responders					
R primary motor cortex	4	1384	60, -6, 24	3.51	.683
sgACC/NAcc	25	1072	4, 16, -6	3.16	.607
L medial PFC	10	776	-18, 40, -4	3.43	.840
L primary motor cortex	4	232	-42, -6, 16	3.11	.958
L insula	13	288	-28, 10, 12	2.99	.948
R inferior frontal gyrus	44	272	46, 14, 18	2.78	.951
R premotor cortex	6	224	50, -6, 38	2.84	.960
Non-Responders>Responders					
No suprathreshold clusters					
Youth with anxiety>Healthy youth					
R medial PFC	10	10776	0, 52, 18	3.72	.016
R angular gyrus	39	2784	30, -80, 30	3.55	.383
L inferior frontal gyrus	44	1072	-42, 12, 26	3.44	.764
R supramarginal gyrus	40	576	56, -22, 16	3.10	.888
L inferior frontal gyrus	45	296	-42, 28, 12	2.98	.947
R medial PFC	10	272	42, 48, 16	3.16	.951
R superior temporal gyrus	22	184	54, 8, -6	2.94	.966
L medial PFC	10	160	-28, 62, 8	2.79	.970
Healthy youth>Youth with anxiety					
No suprathreshold clusters					

FIGURE S1. Region-of-interest (ROI) mask of the medial prefrontal cortex and striatum, used in primary BOLD analyses.

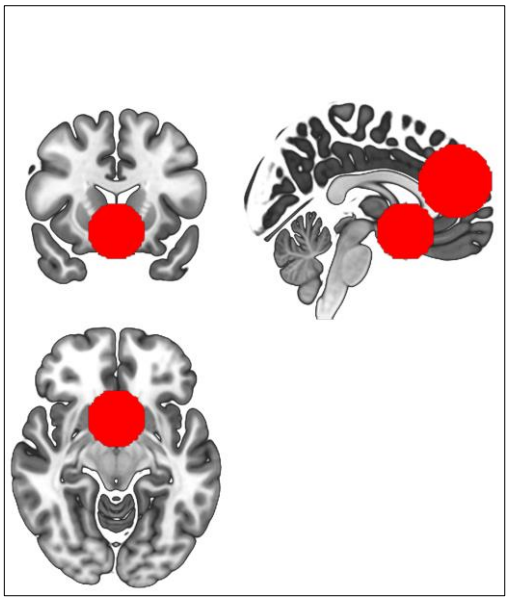

FIGURE S2. Parameter estimates from the mPFC cluster during win relative to control (win>control) and loss relative to control (loss>control) were extracted using the MarsBar toolbox in SPM12. This cluster was derived from the original win>loss analysis. Mean parameter estimates for win>control and loss>control are depicted below.

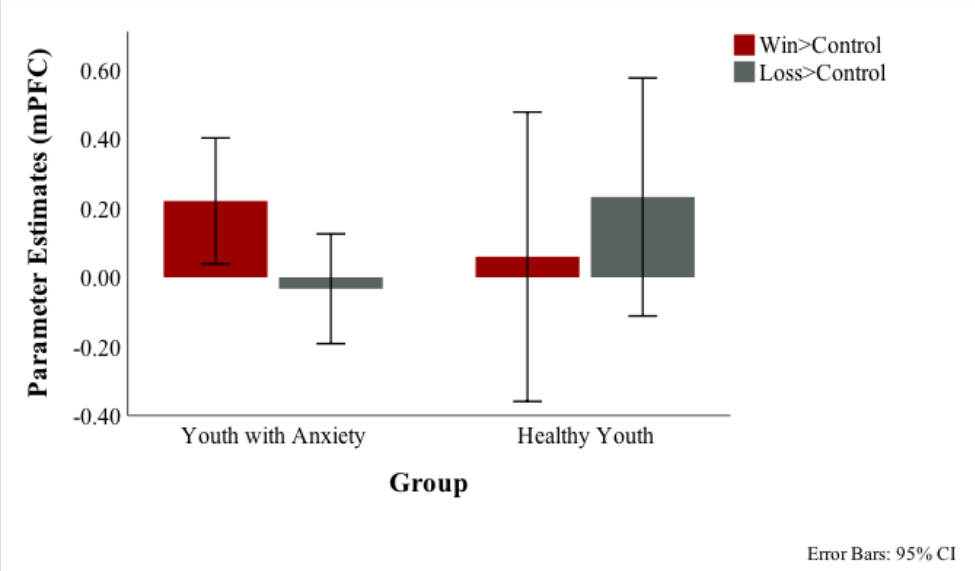

FIGURE S3. Parameter estimates from the sgACC/NAcc cluster during win relative to control (win>control) and loss relative to control (loss>control) were extracted using the MarsBar toolbox in SPM12. This cluster was derived from the original win>loss analysis. Mean parameter estimates for win>control and loss>control are depicted below. Differences between groups were probed using *t*-tests, with Hedges' *g* measures of effect size.

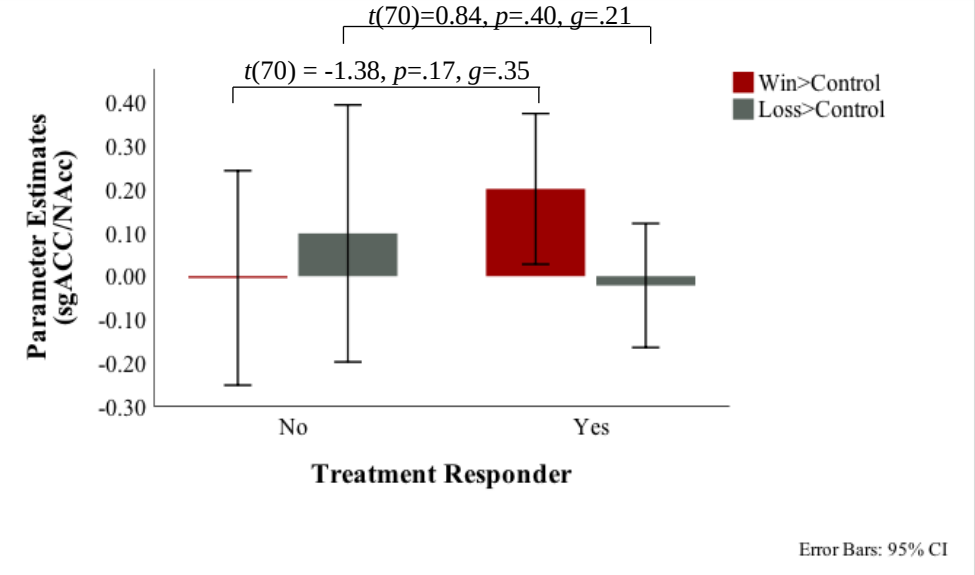

FIGURE S4. Parameter estimates (betas) from the sgACC/NAcc cluster during win only and loss only were extracted using the MarsBar toolbox in SPM12. This cluster was derived from the original win>loss analysis. Mean parameter estimates are depicted below. Differences between groups were probed using *t*-tests, with Hedges' *g* measures of effect size.