Error Processing and Inhibitory Control in Obsessive-Compulsive Disorder: A Meta-Analysis Using Statistical Parametric Maps

Supplementary Information

Literature search methods

There were no restrictions on the date of publication or language. Authors of foreign language papers were contacted for further details of their studies. Contacted authors were also welcomed to provide additional unpublished data, and searches included data published as conference abstracts in addition to data published in peer-reviewed journals, thus ensuring access to the largest possible selection of datasets. After removal of duplicates from the original search results, the titles were screened independently against the inclusion/exclusion criteria by two reviewers (L.J.N. and Y.L.). The full text was reviewed for remaining studies by L.J.N. and Y.L. against the inclusion/exclusion criteria, and data (sample sizes, % OCD medicated, symptom severity, gender ratio, age, task type, comorbidities, methods for assessing comorbidity, IQ, performance differences) were extracted from included studies independently by both reviewers. L.J.N. and Y.L. assessed all articles and achieved 100% agreement. Both L.J.N. and Y.L. are educated to PhD level.

Random-effects meta-analysis of behavioral performance

For the analysis of task performance, 8 datasets provided RT measures of inhibitory control (1–8). This included conflict RT data (defined as incongruent RT - congruent RT) from 5 datasets (1–3, 5, 8), stop-signal reaction time (SSRT) data from two datasets (4, 6), and anti-saccade reaction time data for one dataset (7). In addition, inhibitory control error rates were available from 9 datasets (1–9), while congruent/go error rates were available from 6 datasets

(1–5, 8). The Go No/Go task does not provide a relevant RT measure of inhibitory control, and therefore the Hough dataset was excluded from this analysis (9). One dataset did not report separate error rates for incongruent and congruent trials. Moreover, in this study reported mean RT was collapsed across both trial types, which prevented the calculation of conflict RT or similar RT measures of inhibitory control (10). It was therefore excluded from these analyses.

Anisotropic effect-size version of the seed-based *d* mapping (AES-SDM)

Unthresholded whole-brain t-maps were converted into a common Montreal Neurological Institute (MNI) stereotaxic space (voxel size: 2x2x2 mm^3), and converted subsequently into effect-size and effect-size variance maps. For within-group maps, effect sizes were calculated for each voxel using the following formula, where *y* is the effect size, *J* is the exact form of the Hedge correction factor (see (11)), *df* is the degrees of freedom, *n* is sample size and *t* is the t-score at each voxel.

$$y_i = J(df_i) \times \sqrt{\frac{1}{n_i}} \times t_i$$

For between-group maps, effect sizes were calculated using the following formula, where n_1 is sample size of the patient group and n_2 is sample size of the control group.

$$y_i = J(df_i) \times \sqrt{\frac{1}{n_{i,1}} + \frac{1}{n_{i,2}}} \times t_i$$

Including original t-maps rather than data extracted from peak coordinates substantially increases the sensitivity of voxel-based fMRI meta-analyses (12). Where original statistical maps were unavailable, cluster peak coordinates and t-scores were used to recreate effect-size and effect-size variance maps where the effect-size of non-peak voxels was estimated

using an anisotropic unnormalized Gaussian kernel in which voxels more correlated with the peak were assigned higher effect sizes (13). Positive and negative effect sizes were included in the same map, in order to correctly take into account between-study heterogeneity (e.g., opposing directional findings) in overlapping regions (14). Following this, a mean map was created by performing a voxel-wise calculation of the random-effects mean of the study maps, with each study weighted by the inverse of the sum of its variance plus the between-study variance meaning that studies with larger sample sizes or lower variability were more highly weighted. Effect-sizes at each voxel were converted into SDM-Z values. Assessment of statistical significance was performed using standard permutation testing, against the null hypothesis that BOLD response/group differences are the same throughout the brain. Specifically, null distributions were obtained by randomly permuting the location of voxels within the individual studies. We conducted 50 whole-brain permutations, corresponding to roughly 4,000,000 permuted meta-analytic voxel effect-sizes. We used the default voxel *p*-value threshold of $p<0.005$. In addition, a cluster extent threshold of 80 voxels and a peak SDM-Z value threshold of >2 were used to reduce the false positive rate. For meta-regressions, we used the recommended threshold of $p<.0005$, and with only regions found in the main analysis included (14–16).

The effect size SDM method has been empirically validated by comparing its results with a mega-analysis of the individual data of the studies included in a meta-analysis (12). This validation showed ES-SDM to have a good overlap with the mega-analysis, with an adequate sensitivity and an excellent control of false positives. Moreover, AES-SDM has been used in 100 studies to date, and a number of previous studies have used this method to perform t-map based meta-analyses (17–20).

Example syntax for PubMed database

(ocd AND error AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND error AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND error AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND error AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND errors AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND errors AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND errors AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND errors AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND inhibition AND fmri [Title/Abstract]) OR (ocd AND stop AND fmri [Title/Abstract]) OR (ocd "go no/go" AND fmri [Title/Abstract]) OR (ocd AND stroop AND fmri [Title/Abstract]) OR (ocd AND simon AND fmri [Title/Abstract]) OR (ocd AND flanker AND fmri [Title/Abstract]) OR (ocd AND "multi source interference " AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND inhibition AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND stop AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND "go no/go" AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND stroop AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND simon AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND flanker AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND "multi source interference" AND fmri [Title/Abstract]) OR (ocd AND inhibition "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND stop AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd "go no/go" AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND stroop AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND simon AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND flanker AND "functional magnetic resonance imaging"[Title/Abstract]) OR (ocd AND "multi source interference" AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND inhibition AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND stop AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND "go no/go" AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND stroop AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND simon AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND flanker AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND "multi source interference" AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND stop AND fmri [Title/Abstract]) OR (ocd "go no/go" AND fmri [Title/Abstract]) OR (ocd AND stroop AND fmri [Title/Abstract]) OR (ocd AND simon AND fmri [Title/Abstract]) OR (ocd AND flanker AND fmri [Title/Abstract]) OR (ocd AND "multi source interference " AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND inhibition AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND stop AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND "go no/go" AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND stroop AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND simon AND fmri [Title/Abstract]) OR ("obsessive compulsive disorder" AND flanker AND fmri

[Title/Abstract]) OR ("obsessive compulsive disorder" AND "multi source interference" AND fmri [Title/Abstract]) OR (ocd AND inhibition "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND stop AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd "go no/go" AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND stroop AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND simon AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND flanker AND "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND "multi source interference" AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND inhibition AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND stop AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND "go no/go" AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND stroop AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND flanker AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND "multi source interference" AND "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND inhibition "functional magnetic resonance imaging" [Title/Abstract]) OR ("obsessive compulsive disorder" AND inhibition "functional magnetic resonance imaging" [Title/Abstract]) OR (ocd AND inhibition AND fmri [Title/Abstract])

Literature search results

Following duplicate removal, the initial search included a total of 268 papers and abstracts. Of these, 181 were excluded based on title and abstract review. Of the remaining studies, 72 were excluded following a full text review. Reasons included not using task-based fMRI (21–36), using a non-relevant fMRI task (37–48), papers were reviews or meta-analyses (16, 49–60), due to patient overlap with included studies (61–65), use of scanning parameters with very limited brain coverage (66, 67), or including no OCD-HC comparisons (68–70). One dataset was excluded as it examined patients who had undergone deep-brain stimulation (71). It was determined via correspondence with the authors as part of an earlier project (15, 16) that the studies by Nakao and colleagues (72–75) used substantially overlapping patient and control samples, and moreover that t-map data for these studies were not available.

Moreover, the accuracy rates were very high (98% in HC) and error trials were not modeled in the original analyses. Therefore, we did not re-contact these authors regarding this data for the present study. For one foreign language study (76), we did not receive a response to our correspondence regarding further details on the publication such as error rates and the potential availability of t-map data.

As the primary focus of the meta-analysis was on the error contrast, datasets with very few errors were also excluded (77–81). Specifically, studies which did not report an error contrast and which had high accuracy rates (e.g., > 95%) were examined closely on a case-by-case basis by YL and LJN, before a decision was made as to whether the authors should be contacted for unpublished data. In the study by Marsh et al (77), patients on average made less than one incongruent error and less than one congruent error. In Go/No-Go studies by Pena-Garijo (78) and Roth (79), patients made on average less than one Go error and less than one No-Go error. In a Stroop study by Schlosser (80), patients on average made less than one congruent error as well as an average of only one incongruent error. One 2005 study by Viard (81) and colleagues did not report error rates, and did not model errors as regressors in the original fMRI analysis. Moreover, given that the task contained only relatively few trials (32 incongruent, 32 congruent), that accuracy rates on this task are usually very high (82), and that the authors do not consider errors in their behavioral or fMRI analysis in the original manuscript (suggesting that their number may be trivial), we decided that this dataset would be unlikely to provide enough error trials to produce a viable error contrast.

Some datasets met our initial inclusion criteria, but were determined subsequently to be unavailable from the authors for inclusion in the current meta-analysis (83–87). For these

datasets, we provide full details on the sample demographics and fMRI findings below.

For one study containing a Simon task dataset and a go/no-go task dataset, errors were not modeled at the first-level in the analyses contained in the original paper. Instead errors were pooled the into the implicit baseline (83). T-map data were not available. This study by Page and colleagues examined brain activation to correct incongruent trials versus correct congruent trials as well as correct no-go versus go trials in ten unmedicated male adults with OCD (mean age = 39.1 years, mean Y-BOCS = 23.5) and 11 male controls (mean age = 34.1). The authors found hypoactivation within temporo-parietal and cerebellar regions during the Simon task in patients with OCD. During the go/no-go task, patients showed hyperactivation in vmOFC, PCC and temporal lobe, but hypoactivation in rACC, basal ganglia, thalamus and cerebellum.

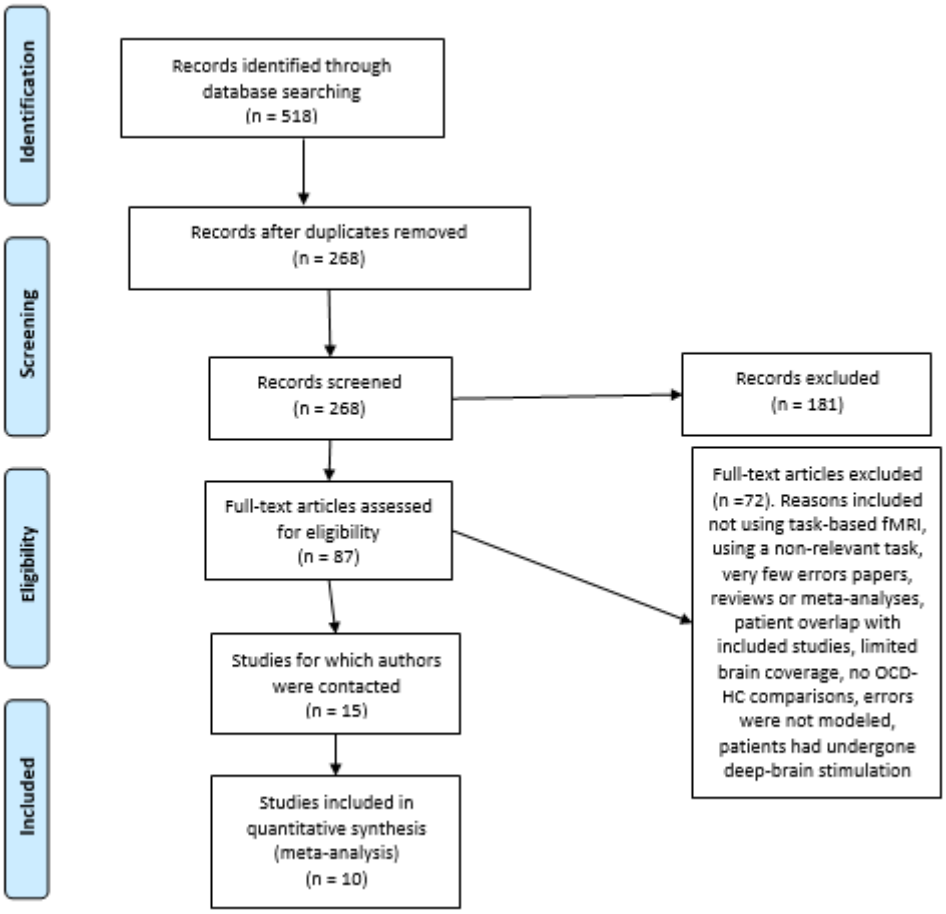
In one study by Morein-Zamir and colleagues (84), in which the authors examined brain activation abnormalities in 19 patients with OCD (14 males, 14 medicated, mean age = 37.8, Y-BOCS = 19.95) and 19 HC (14 males, mean age = 36.2) during a combined switch-go/no-go task, it was reported that patients showed hyperactivation in left occipital lobe and left caudate during correct response inhibition. It was determined after contacting the authors that the majority of subjects included in the original paper made no errors or else very few errors during this task, and that inclusion in the current analysis was therefore not feasible.

The paper by Kang and colleagues (85) used a stop task to study brain activation during successful stopping in 18 unmedicated adult patients with OCD (12 male, mean age = 24.9, mean Y-BOCS = 22.1) and 18 HC (12 male, mean age = 24.7). This study reports hypoactivation

in patients in rACC, pMFC, basal ganglia, temporal lobe and cerebellum, and hyperactivation in parietal lobe, parahippocampal gyrus and cerebellum, relative to HC.

In the paper by Maltby and colleagues, 14 adult patients with OCD (9 male, mean age = 39.36, mean Y-BOCS = 24.64) and 14 HC (mean age = 36.55) completed a go/no-go task. During errors, patients with OCD showed hyperactivation relative to HC within aI/fO, rACC, dACC, PCC and basal ganglia. During inhibitory control, patients showed relative hyperactivation in rACC, pMFC, PCC, dlPFC, basal ganglia and cerebellum.

In a stop task paper by Tolin and colleagues (87), 24 patients with OCD (18 males, 19 medicated, mean age = 33.54) showed hyperactivation in right fO and left aI/fO during errors, but hypoactivation in rACC during correct inhibitory control, relative to 24 HC (4 males, mean age = 51.29).



Supplementary Figure S1. PRISMA flow diagram summarizing the literature search.

Supplementary Table S1. Current comorbid diagnoses in patients from 10 OCD fMRI datasets.

Study	Clinical assessment	Anxiety disorders	Mood disorders	Additional information
Agam (7)	SCID	Generalized Anxiety Disorder: N=1 (4.8%), Panic Disorder: N=1 (4.8%), Posttraumatic Stress Disorder: N=1 (4.8%), Social Phobia: N=4 (19.0%), Specific Phobia: N=8 (38.1%).	Major Depressive Disorder: N=1 (4.8%), Dysthymia: N=4 (19.0%).	Patients were excluded if they met diagnostic criteria for any comorbid psychiatric disorders except for anxiety and mood disorders.
de Wit (4)	SCID	Panic Disorder: N=3 (7.31%), Social Anxiety: N=5 (12.2%), Specific Phobia: N=10 (24.39%).	Mood Disorders: N=9 (21.95%).	Agoraphobia: N=1 (2.44%), Eating Disorder: N=2 (4.88%), Somatoform Disorder: N=1 (2.44%), Tourette's Syndrome: N=1 (2.44%). Patients were excluded if they had current or past diagnoses of psychosis
Fitzgerald (8)	K-SADS-PL	Generalized Anxiety Disorder: N=12 (17.4%), Panic Disorder: N=3 (4.4%), Separation Anxiety Disorder: N=5 (7.2%), Social Anxiety: N=5 (7.2%), Specific Phobia: N=6 (8.7%).	None	Attention Deficit Hyperactivity Disorder: N=9 (13.0%), Developmental Coordination Disorder: N=1 (1.5%), Impulse Control Disorder: N4 (5.8%), Tics: N=12 (17.4%), Tourettes Syndrome: N=7 (10.1%). Patients were excluded if they met diagnostic criteria for a major depressive disorder or if they had current or past diagnoses of autism spectrum, psychotic or substance use disorders.
Fitzgerald (2)	SCID	None	None	Patients were excluded if they met diagnostic criteria for any comorbid psychiatric disorders.
Grutzmann (10)	SCID	Anxiety Disorders: N=9 (45%).	Mood Disorders: N=2 (10%).	Somatoform Disorder: N= 1 (5%) Patients were excluded if they met diagnostic criteria for substance use disorder or if they had a current or past diagnosis of psychosis.
Hough (9)	SCID	Generalized Anxiety Disorder: N=2 (11.76%), Panic Disorder: N=2 (11.76%), Social Anxiety: N=4 (23.53%).	None	Obsessive-Compulsive Personality Disorder: N=3 (17.65%).

Study	Clinical assessment	Anxiety disorders	Mood disorders	Additional information
				Patients were excluded if they met diagnostic criteria for substance use disorder or if they had a current or past diagnosis of psychosis.
Huyser (3)	ADIS-C/P	Anxiety Disorders: N=12 (48%)	Mood Disorders: N=3 (12%)	Externalizing Disorders: N=3 (12%) Tics: 2 (8%)
Rubia (6)	MDI	None	None	Patients were excluded if they met diagnostic criteria for any comorbid psychiatric disorders.
Stern (1)	SCID	Panic Disorder: N = 5 (12.82%), Social Anxiety: N =1 (2.56%), Specific Phobia: N=5 (12.82%).	Depressive disorder not otherwise specified: N=6 (15.38%), Dysthymia: N=1 (2.56%).	Patients were excluded if they met diagnostic criteria for current or past psychosis, bipolar spectrum mood disorders, or developmental disorders.
Yücel (5)	SCID	None	None	Patients were excluded if they met diagnostic criteria for any comorbid psychiatric disorders.

Abbreviations: ADIS-C/P, Anxiety Disorders Interview Schedule for Children for DSM-IV - Child and Parent Versions (88)*; K-SADS-PL, Kiddie-Schedule for Affective Disorders-Present and Lifetime Version* (89)*; MDI, Maudsley Diagnostic Interview* (90)*; SCID, Structured Clinical Interview for DSM-IV Axis-I Disorders* (91).

Within-group findings

HC errors. HC showed significant activation to errors within bilateral aI/fO/STL, pMFC sub-regions including dACC, SMA and pre-SMA, SMG/angular gyrus/STL, thalamus/brainstem and occipital lobe. Significant deactivation to errors was found in bilateral aLPFC/mOFC/frontal pole, caudate/thalamus, putamen (extending into PI in the right hemisphere), PCC/precuneus, postcentral/premotor cortex, DLPFC, MTL/STL and occipital lobe (Supplementary Table S1).

OCD errors. Patients with OCD showed significant activation to errors within bilateral aI/fO/STL, dACC, SMA and pre-SMA, SMG/angular gyrus, thalamus/brainstem and occipital lobe, as well as right-lateralized DLPFC. Significant deactivation to errors was found in bilateral mOFC/frontal pole, caudate/thalamus, putamen, PCC/precuneus, premotor cortex/postcentral gyrus/SPL, DLPFC, left MTL/STL, left hippocampus/amygdala and right angular gyrus and occipital lobe (Supplementary Table S2).

HC inhibitory control. During inhibitory control, HC showed significant activation in bilateral aI/fO/STL, dACC, SMA and pre-SMA, occipital lobe/SPL/precuneus/SMG/angular gyrus, premotor cortex, thalamus/caudate/brainstem, cerebellum and right DLPFC. Significant deactivation was observed in bilateral mOFC/frontal pole, precuneus/PCC, premotor cortex/postcentral gyrus/SMA, PI/STL, hippocampus and occipital lobe, as well as left DLPFC (Supplementary Table S3).

OCD inhibitory control. Patients with OCD had significant activation in bilateral aI/fO/STL, DLPFC, dACC, SMA and pre-SMA, occipital lobe/precuneus/SPL/SMG, (ITL, premotor cortex, thalamus/brainstem and right caudate. Significant deactivation was found in mOFC/rACC/frontal pole, precuneus/PCC, and PI extending into STL on the right side (Supplementary Table S4).

Supplementary Table S2. Meta-analysis results for fMRI studies of error-processing in HC.

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
HC errors activation							
L aI/fO/STL	-48,16,-2	7.815	0.6	0.35	<0.0000001	1995	45/44/47/38
L & R dACC/SMA/pre-SMA	0,34,32	6.413	0.48	0.31	<0.0000001	1912	32/24/8/9
L & R occipital lobe	0,-82,18	4.707	0.39	0.29	<0.00001	2052	17/18/19
R aI/fO/STL	44,14,2	6.392	0.47	0.33	<0.0000001	1436	45/44/47/38
R SMG/angular gyrus/STL	66,-40,28	4.830	0.35	0.26	<0.000005	639	40/22/42
L & R thalamus/brainstem	4,-20,-10	3.895	0.30	0.27	<0.0001	651	
L SMG/angular gyrus/STL	-58,-46,30	4.628	0.35	0.24	<0.00001	506	40/22/42
L aI/fO/STL	-40,-8,-12	4.120	0.29	0.23	<0.00005	95	
HC errors deactivation							
R postcentral/premotor cortex	26,-22,54	-4.207	-0.31	-0.22	<0.000005	579	4/3/2/6
R caudate/thalamus	20,-20,26	-3.799	-0.39	-0.21	<0.00005	493	
L postcentral gyrus/premotor cortex	-28,-38,54	-3.937	-0.25	-0.21	<0.00005	481	4/3/2/6/7
R MTL/occipital lobe	44,-70,-2	-3.583	-0.25	-0.2	<0.0001	441	37/18/19
L DLPFC	-20,22,44	-4.866	-0.33	-0.25	<0.0000005	411	9/8/46
R putamen/PI	30,-10,4	-4.599	-0.35	-0.26	<0.000001	358	
L & R alPFC/mOFC/frontal pole	-12,66,10	-3.623	-0.27	-0.21	<0.0001	417	10/11

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
L & R paracentral lobule/premotor cortex	-4,-32,54	-3.678	-0.26	-0.22	<0.00005	289	4/5
L caudate/thalamus	-18,8,22	-4.795	-0.35	-0.23	<0.0000005	190	
L & R PCC/precuneus	16,-46,36	-3.761	-0.27	-0.23	<0.00005	168	
R DLPFC	24,32,52	-3.52	-0.34	-0.27	<0.0001	174	8/9
R STL/MTL	60,0,-8	-3.296	-0.24	-0.22	<0.0005	166	22/21
L occipital lobe	-30,-90,6	-3.19	-0.22	-0.19	<0.0005	141	18/19
L putamen	-28,-2,6	-3.809	-0.28	-0.23	<0.00005	107	
L MTL/STL	-62,-14,-8	-2.997	-0.22	-0.2	<0.001	105	22/21

Abbreviations: aI, anterior insula; aLPFC, anterior lateral prefrontal cortex; dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; fO, frontal operculum; HC, healthy controls; MNI, Montreal Neurological Institute; mOFC, medial orbitofrontal cortex; MTL, middle temporal lobe; PCC, posterior cingulate cortex; pre-SMA; pre-supplementary motor area; PI, posterior insula; SDM, Seed-based d Mapping; SMA, supplementary motor area; SMD, standardized mean difference (Hedges' g); SMG, supramarginal gyrus; STL, superior temporal lobe.

Supplementary Table S3. Meta-analysis results for fMRI studies of error-processing in OCD.

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
OCD errors activation							
L & R dACC/pre-SMA/SMA, R DLPFC	2,26,30	9.402	0.72	0.41	<0.0000001	2692	24,32,6,8,9
L aI/fO/STL	-38,24,-4	7.609	0.62	0.4	<0.0000001	1706	47,45,44,38
R aI/fO/STL	48,10,-2	7.004	0.51	0.36	<0.0000001	1534	45,44,47,38
L & R occipital lobe	-20,-72,6	5.678	0.4	0.34	<0.0000001	1379	17,18,19
L & R thalamus/brainstem	4,-26,0	4.988	0.34	0.26	<0.00001	684	
R SMG/angular gyrus	60,-38,30	5.224	0.36	0.28	<0.0000001	568	40,42,22
L SMG/angular gyrus	-58,-46,30	5.733	0.43	0.28	<0.0000001	567	40,42,22
OCD errors deactivation							
L & R premotor cortex/postcentral gyrus/SPL	24,-22,56	-4.819	-0.3	-0.22	<0.000005	1585	6,4,3
L precuneus/PCC	-12,-52,36	-4.374	-0.3	-0.26	<0.00001	353	23
L caudate/thalamus	-22,-26,24	-4.898	-0.37	-0.25	<0.000001	306	
R DLPFC	24,32,42	-3.758	-0.28	-0.22	<0.0001	328	9,8
L DLPFC	-28,22,48	-4.519	-0.34	-0.26	<0.000005	287	8.9
R putamen	24,8,4	-4.857	-0.34	-0.25	<0.000005	239	
L putamen	-24,6,4	-4.64	-0.32	-0.25	<0.000005	228	

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
R caudate	18,8,22	-4.59	-0.32	-0.23	<0.000005	163	
L MTL/STL	-56,-8,-8	-4.543	-0.31	-0.22	<0.000005	163	22,21
L hippocampus/amygdala	-26,-10,-22	-3.602	-0.25	-0.19	<0.0005	144	
L & R mOFC/frontal pole	6,52,-10	-3.735	-0.27	-0.25	<0.0001	137	11,10
R occipital lobe	36,-84,14	-3.2	-0.22	-0.2	<0.001	104	19,18

Abbreviations: aI, anterior insula; dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; *fO, frontal operculum; MNI, Montreal Neurological Institute; MTL, middle temporal lobe; mOFC, medial orbitofrontal cortex; PCC, posterior cingulate cortex; pre-SMA, pre-supplementary motor area; OCD, obsessive-compulsive disorder; SDM, Seed-based d Mapping; SMA, supplementary motor area; SMD, standardized mean difference (Hedges' g); SMG, supramarginal gyrus; SPL, superior parietal lobe; STL, superior temporal lobe.*

Supplementary Table S4. Meta-analysis results for fMRI studies of inhibitory control in HC.

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
HC inhibitory control activation							
L & R thalamus/caudate/ brainstem	-8,-8,10	6.657	0.46	0.32	<0.0000001	2085	
R aI/fO/STL	34,18,8	7.258	0.51	0.36	<0.0000001	1031	44,45,47,38
L & R SMA/pre-SMA/dACC	-4,14,58	5.121	0.36	0.38	<0.0000001	1108	6,32,24,8
R SPL/SMG/angular gyrus/occipital lobe	42,-44,58	5.535	0.39	0.4	<0.0000001	950	2,7,40,19
L occipital lobe/SPL/precuneus/ SMG/angular gyrus	-28,-72,36	4.761	0.42	0.45	<0.0001	787	19,7,40
L aI/fO/STL	-40,10,2	5.962	0.4	0.39	<0.0000001	590	45,47,38
L premotor cortex	-48,2,24	4.985	0.42	0.39	<0.00005	607	6
R premotor cortex	38,-8,62	4.361	0.34	0.34	<0.0005	374	6
R DLPFC	34,44,34	5.129	0.34	0.29	<0.0000001	81	46,9
HC inhibitory control deactivation							
L & R premotor cortex/postcentral gyrus/SMA/PCC	28,-26,50	-4.089	-0.27	-0.18	0.000005	1174	6,4,23
L & R mOFC/frontal pole	-2,56,-8	-4.118	-0.28	-0.17	0.000005	1223	10/11
L & R precuneus/PCC	-6,-52,20	-3.453	-0.29	-0.21	0.00005	432	30/29/23
R PI/STL	40,-18,4	-3.035	-0.22	-0.21	0.0005	386	41/42

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
L PI/STL	-36,-18,8	-3.343	-0.22	-0.21	0.0001	239	41/42
L hippocampus	-24,-14,-20	-3.778	-0.25	-0.17	0.00005	160	
R STL	54,-26,8	-3.454	-0.23	-0.17	0.00005	176	22
R hippocampus	26,-16,-20	-3.064	-0.2	-0.15	0.0005	113	
L DLPFC	-26,30,48	-3.061	-0.2	-0.19	0.0005	117	8,9
R occipital lobe	46,-74,28	-2.659	-0.23	-0.18	0.0001	94	19
L occipital lobe	-40,-80,36	-3.481	-0.26	-0.23	0.00005	80	19

Abbreviations: aI, anterior insula; dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; fO, frontal operculum; HC, healthy controls; MNI, Montreal Neurological Institute; PCC, posterior cingulate cortex; pre-SMA, pre-supplementary motor area; PI, posterior insula; SDM, Seed-based d Mapping; SMA, supplementary motor area; SMD, standardized mean difference (Hedges' g); SMG, supramarginal gyrus; STL, superior temporal lobe.

Supplementary Table S5. Meta-analysis results for fMRI studies of inhibitory control in OCD.

Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
OCD inhibitory control activation							
L aI/fO/premotor cortex/DLPFC	-42,8,26	7.224	0.5	0.37	<0.0000001	1928	44,47,6,8
R premotor cortex/IFG/DLPFC	38,2,40	6.294	0.55	0.38	<0.0000001	1684	6,44,45,8,
R occipital lobe/precuneus/SPL/SMG	30,-60,38	5.455	0.45	0.34	<0.0000001	1666	19,7,2,40
L occipital lobe/precuneus/SPL/SMG	-26,-60,36	4.075	0.46	0.4	<0.0001	1254	19,7,2,40
R aI/fO/STL	38,16,-2	4.485	0.32	0.26	<0.00005	740	45,47,38
L & R thalamus/brainstem, R caudate	-6,-28,-4	4.594	0.48	0.35	<0.00005	721	
L & R SMA/pre-SMA/dACC	8,24,38	5.442	0.44	0.34	<0.0000001	632	32,6,8,24
R ITL/occipital lobe	52,-62,-18	4.326	0.29	0.39	<0.00005	635	37,19,20
L occipital lobe/ITL	-50,-68,-16	4.31	0.3	0.3	<0.00005	235	37,19
R caudate/thalamus	12,-2,12	4.273	0.3	0.27	<0.00005	191	
OCD inhibitory control deactivation							
L & R mOFC/rACC/frontal pole	-2,56,-6	-5.33	-0.35	-0.24	<0.0000001	1860	10,11,32,25
L & R precuneus/PCC	-4,-54,20	-5.404	-0.35	-0.25	<0.0000001	1533	23,30
R PI/STL	48,-10,18	-4.403	-0.34	-0.28	<0.00005	1144	42,22
L DLPFC	-24,24,42	-5.648	-0.37	-0.25	<0.0000001	321	9,8
R DLPFC	24,28,44	-4.516	-0.32	-0.21	<0.00005	301	9,8

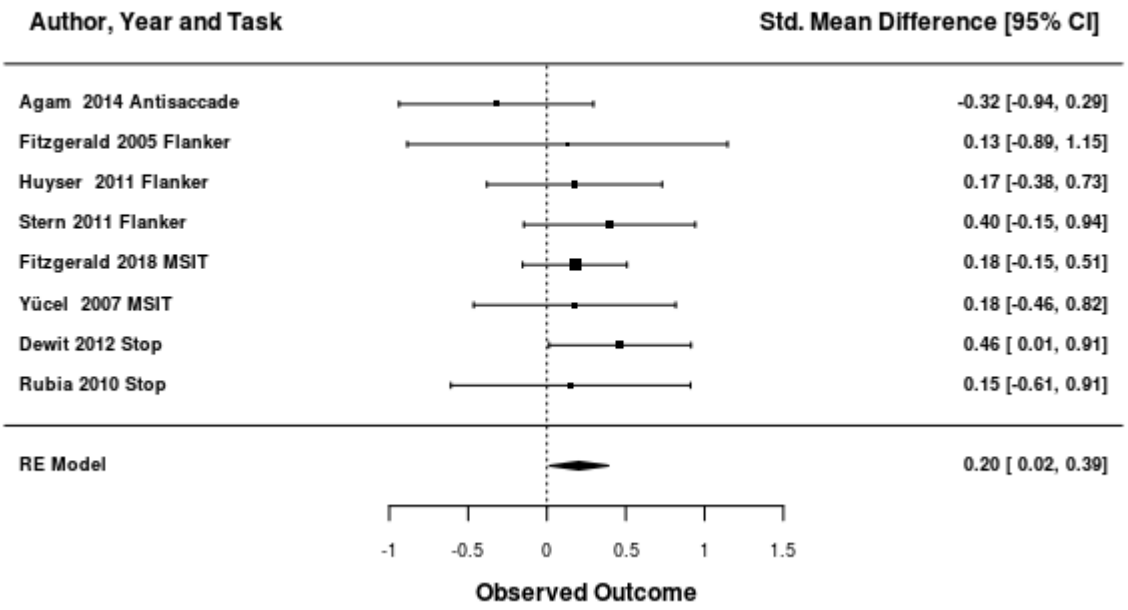
Contrast	MNI x, y, z Coordinates	Peak SDM-Z	Peak SMD	Mean SMD	P Value	No. of Voxels	Brodmann areas
R premotor cortex/postcentral gyrus	28,-28,60	-3.91	-0.25	-0.2	<0.0005	229	6,4
R angular gyrus/occipital lobe	54,-66,30	-4.174	-0.28	-0.22	<0.0001	184	39,19
L PI	-36,-16,6	-3.792	-0.26	-0.24	<0.0005	125	
L angular gyrus/occipital lobe	-46,-74,30	-3.524	-0.31	-0.24	<0.0005	95	39,19

Abbreviations: aI, anterior insula; dACC, dorsal anterior cingulate cortex; DLPFC, dorsolateral prefrontal cortex; fO, frontal operculum; ITL, inferior temporal lobe; MNI, Montreal Neurological Institute; mOFC, medial orbitofrontal cortex; OCD, obsessive-compulsive disorder; PCC, posterior cingulate cortex; pre-SMA, pre-supplementary motor area; PI, posterior insula; SDM, Seed-based d Mapping; SMA, supplementary motor area; SMD, standardized mean difference (Hedges' g); SMG, supramarginal gyrus; SPL, superior parietal lobe; STL, superior temporal lobe.

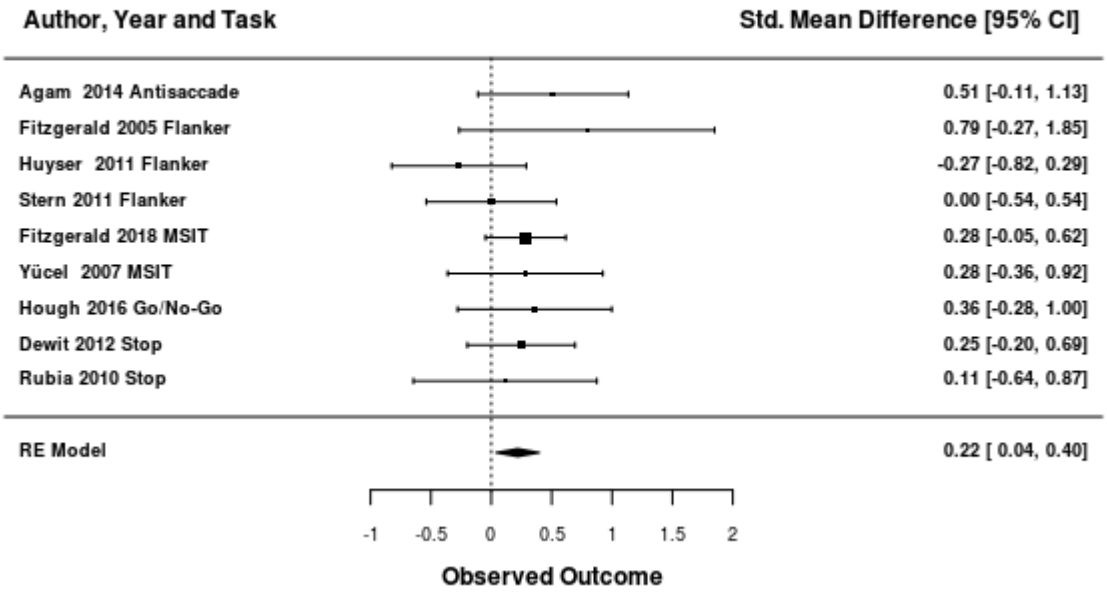
Adult subgroup analysis

During errors, increased activation in right aI/fO (MNI x,y,z = 52,20,18, SDM-Z= 2.934, p<0.001, voxels = 350) and aLPFC (MNI x,y,z = 24,52,12, SDM-Z= 3.384, p<0.001, voxels = 87) remained significant in adult patients with OCD relative to controls. In addition, left fO hyperactivation was found in adult patients with OCD relative to HC (MNI x,y,z = -44,32,16, SDM-Z= 2.686, p=0.0001, voxels = 141). Increased activation in SMA (MNI x,y,z = 0,8,46, SDM-Z= 1.944, p=0.003, voxels = 13) and pre-SMA (MNI x,y,z = -6,34,60, SDM-Z= 2.274, p<0.001, voxels = 16) in patients relative to HC remained but only at relaxed thresholds, most likely due to the reduced power in this sensitivity analysis relative to the primary analysis.

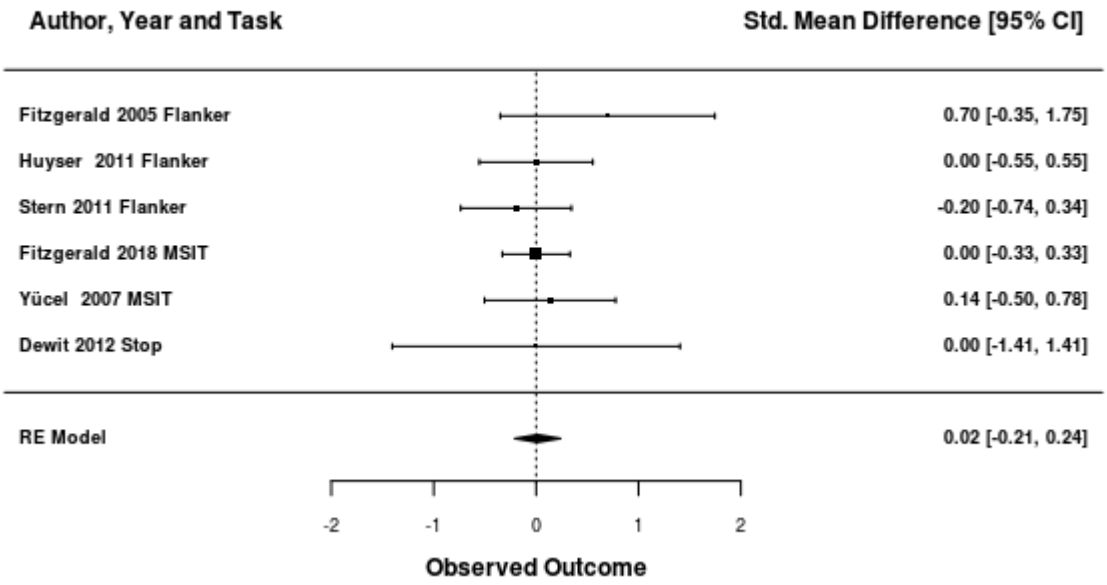
During inhibitory control, hyperactivation in left premotor cortex (MNI x,y,z = -26,2,60, SDM-Z= 2.211, p<0.001, voxels = 224) as well as hypoactivation in right AI/fO/STL (MNI x,y,z = 54,4,-4, SDM-Z= 3.010, p<0.001, voxels = 141) and bilateral thalamus (MNI x,y,z = 4,-10,14, SDM-Z=3.083, p<0.0003, voxels = 182) remained significant in adults with OCD relative to HC. Additional regions of hypoactivation in adult patients were found in right postcentral gyrus (MNI x,y,z = 40,-24,60, SDM-Z= 3.136, p<0.001, voxels = 96), left postcentral gyrus (MNI x,y,z = -54,-16,20, SDM-Z= 3.041, p<0.001, voxels = 100) and left cerebellum (MNI x,y,z = -6,-64,-22, SDM-Z= 3.306, p<0.001, voxels = 139). Underactivation in rACC/vACC (MNI x,y,z = 14,40,18, SDM-Z= 3.424, p<0.001, voxels = 67) and left caudate (MNI x,y,z = -16,6,22, SDM-Z = 3.054, p<0.001, voxels = 24) remained significant in adult patients relative to controls only at a relaxed threshold.



Supplementary Figure S2. Forest plot with standardized mean differences in reaction time measures of inhibitory control between patients with OCD and HC. CI, confidence interval; MSIT, multisource interference task; Std., standardized.



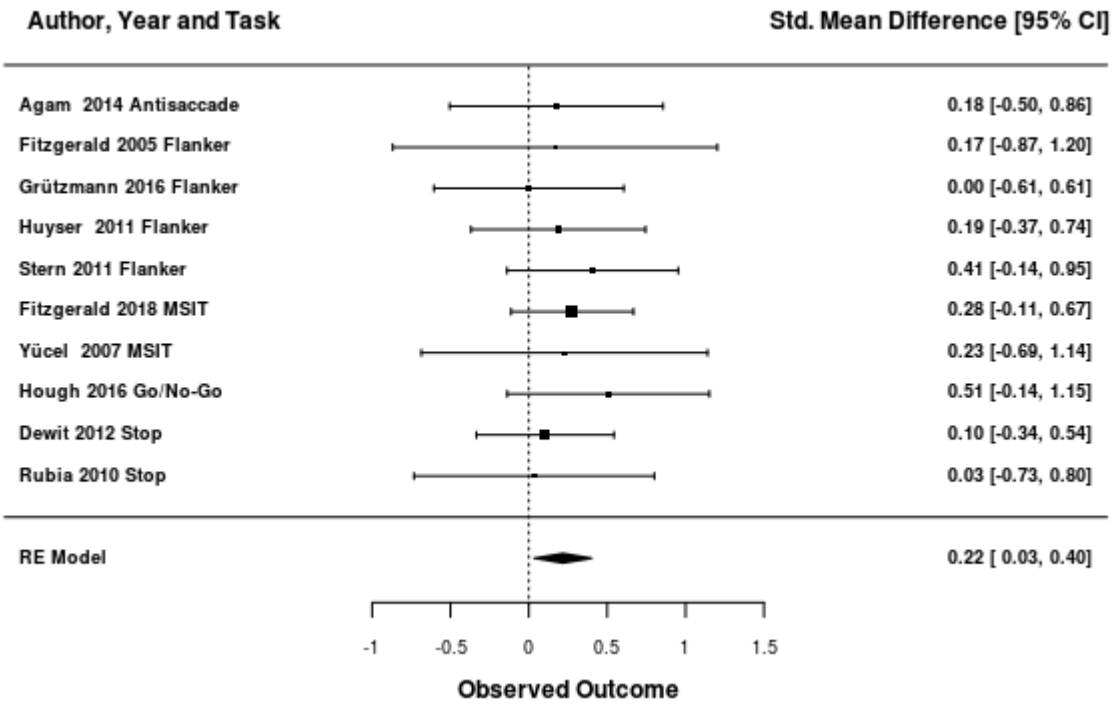
Supplementary Figure S3. Forest plot with standardized mean differences in inhibitory control error rates between patients with OCD and HC. CI, confidence interval; MSIT, multisource interference task; Std., standardized.



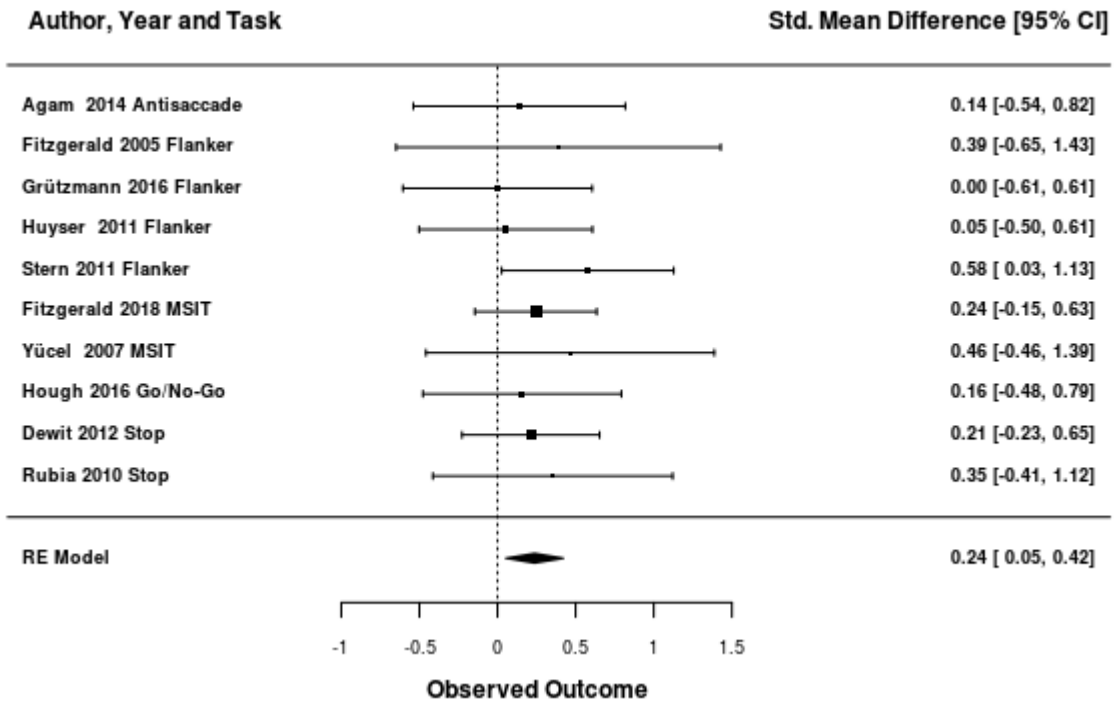
Supplementary Figure S4. Forest plot with standardized mean differences in congruent/go error rates between patients with OCD and HC. CI, confidence interval; MSIT, multisource interference task; Std., standardized.

Forest plots for between-group brain findings

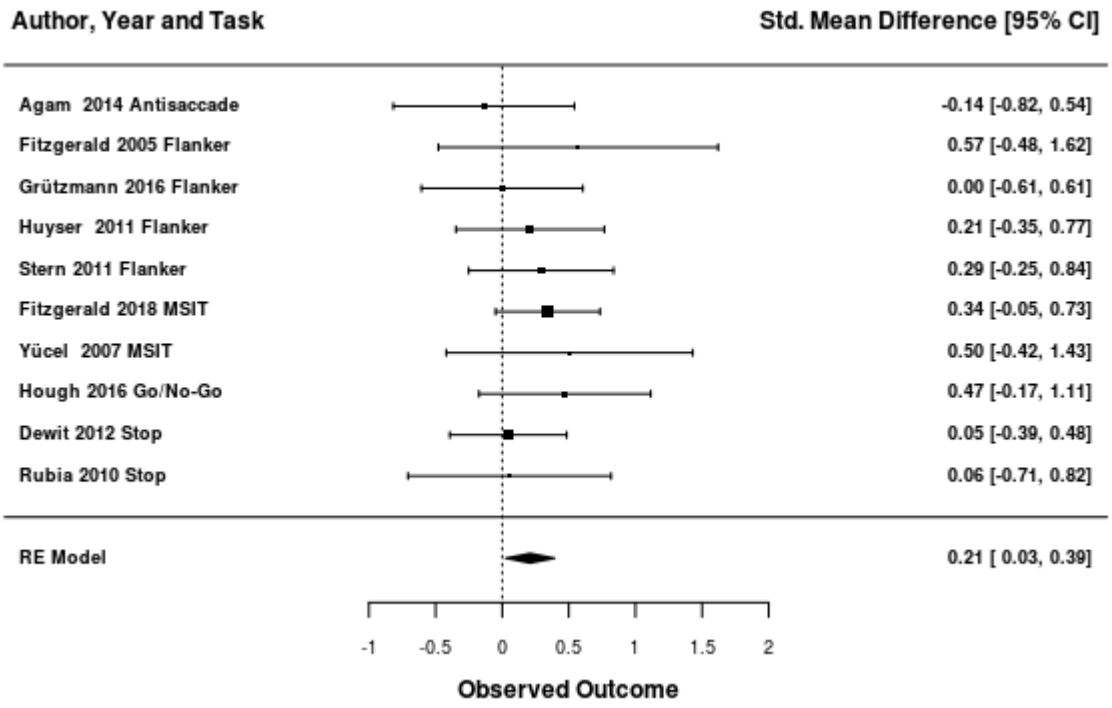
Cluster effect sizes and variances were extracted using the 'extract' function in AES-SDM (www.sdmproject.com), and plotted in forest plots. Importantly, the data contained in the plots were extracted from clusters that were already found to be significant in the whole-brain analyses. In addition, the plots are of average cluster effect sizes whereas AES-SDM performs separate analyses at each voxel. Therefore, these plots were produced only to illustrate the relative influence of each dataset in driving the significant between-group findings and do not themselves represent formal tests or exact representations of the tests performed in AES-SDM.



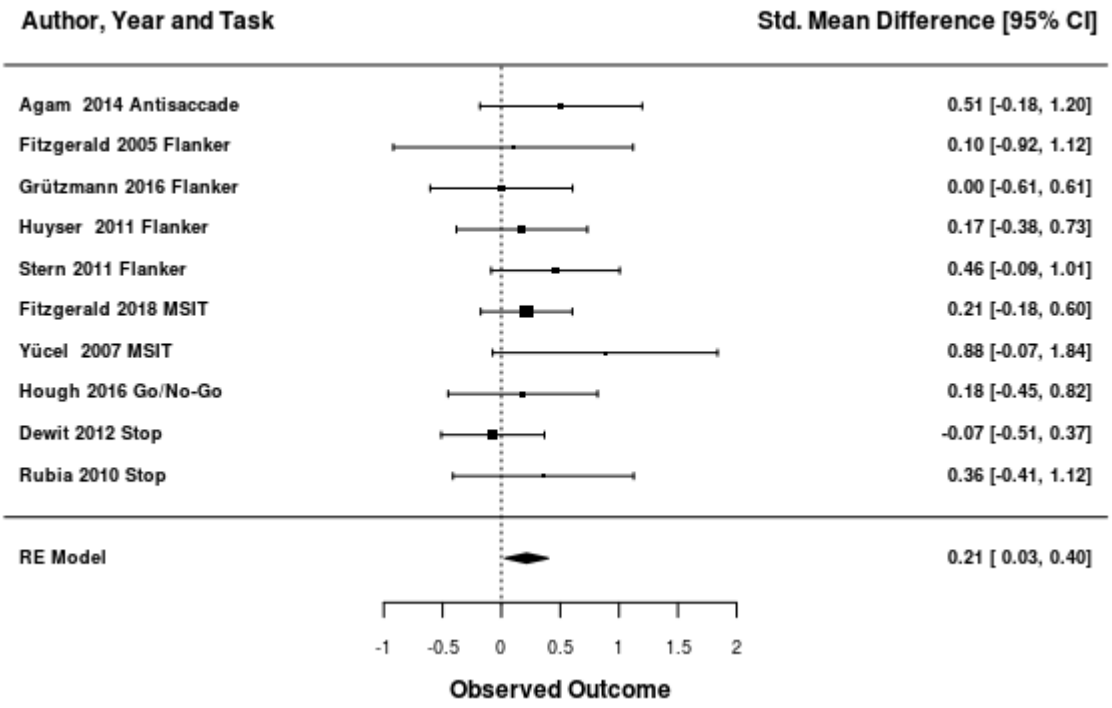
Supplementary Figure S5. Forest plot with standardized mean differences in brain activation during errors in right aI/fO (MNI x,y,z = 44,42,18) between patients with OCD and HC. CI, confidence interval; Std., Standardized.



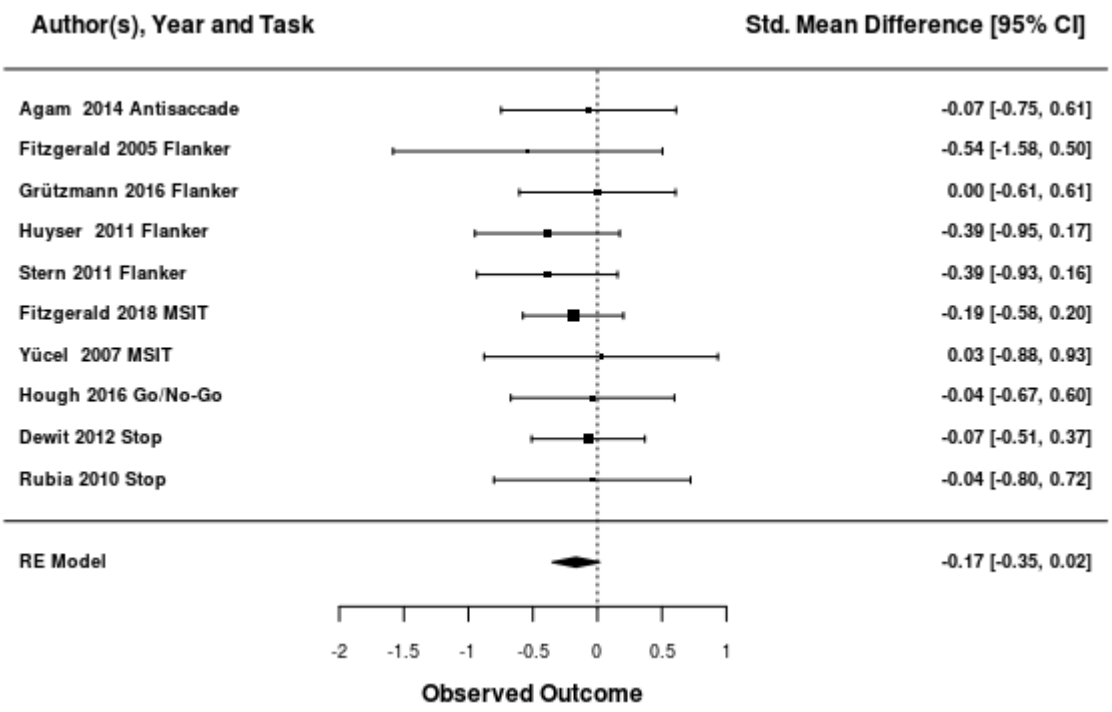
Supplementary Figure S6. Forest plot with standardized mean differences in brain activation during errors in right aLPFC (MNI x,y,z = 24,50,12) between patients with OCD and HC. CI, confidence interval; Std., Standardized.



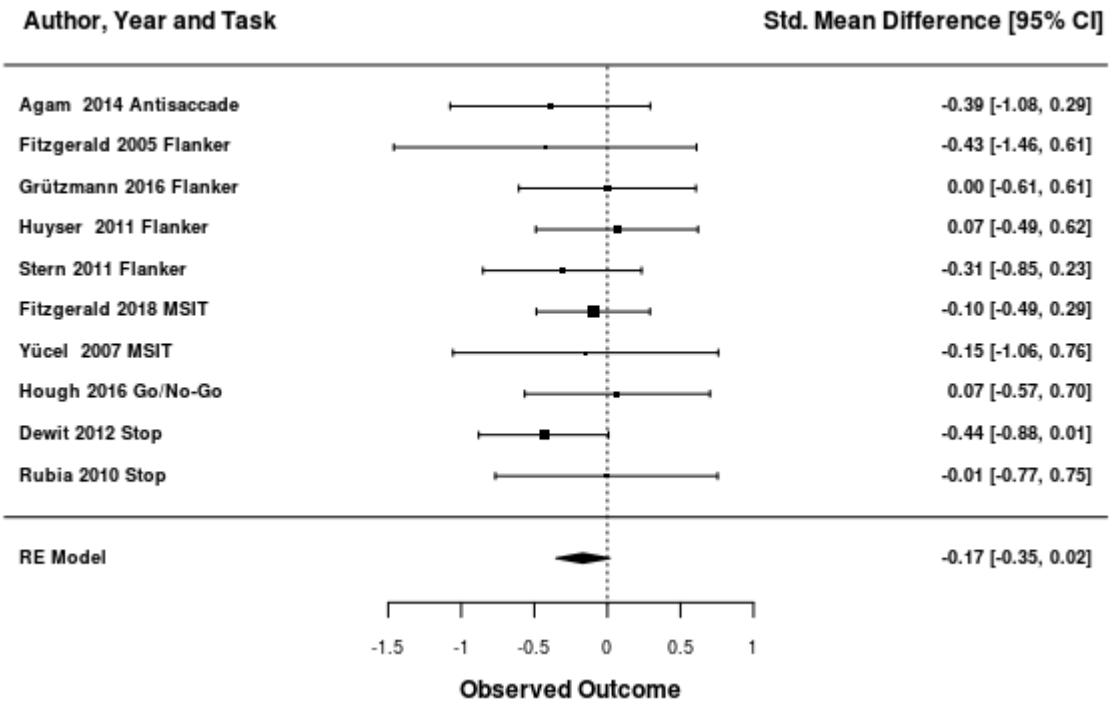
Supplementary Figure S7. Forest plot with standardized mean differences in brain activation during errors in bilateral pre-SMA/right premotor cortex (MNI x,y,z = 20,12,48) between patients with OCD and HC. CI, confidence interval; Std., Standardized.



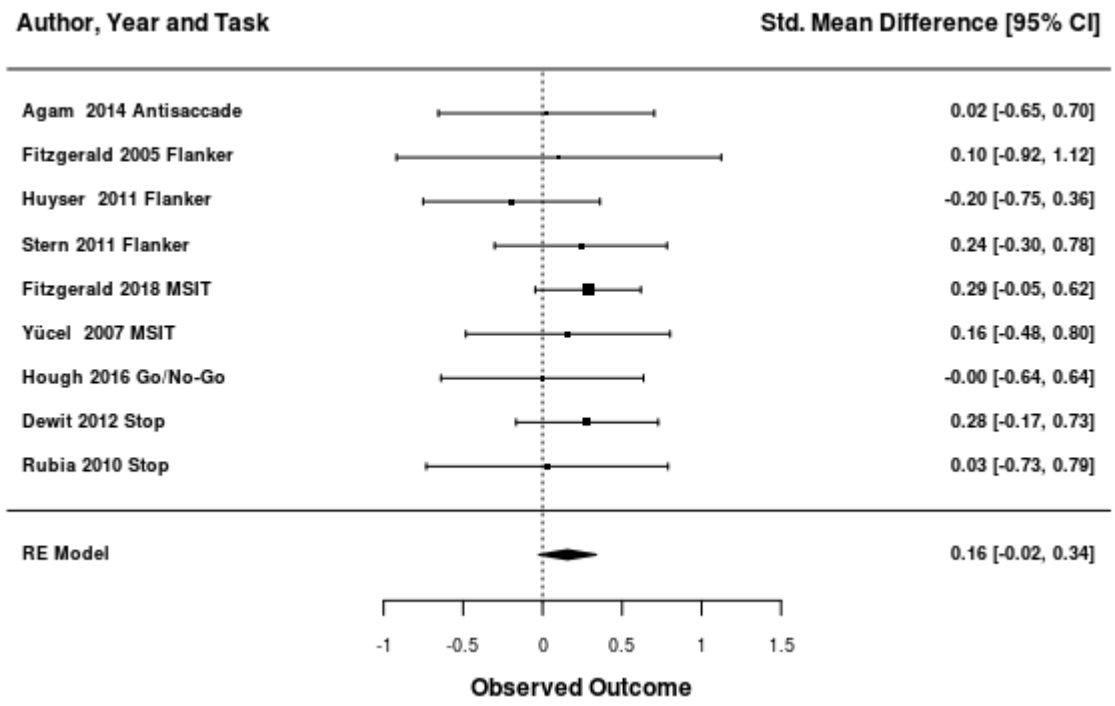
Supplementary Figure S8. Forest plot with standardized mean differences in brain activation during errors in dACC/SMA (MNI x,y,z =4,10,46) between patients with OCD and HC. CI, confidence interval; Std., Standardized.



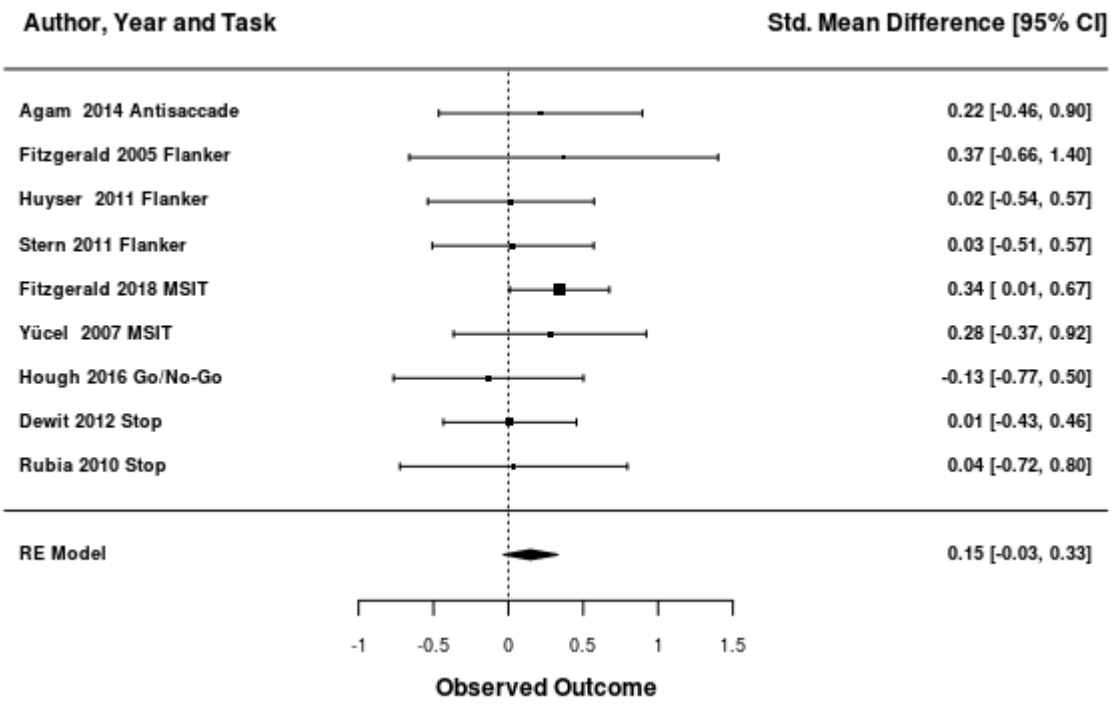
Supplementary Figure S9. Forest plot with standardized mean differences in brain activation during errors in L & R occipital lobe (MNI x,y,z =10,-82,16) between patients with OCD and HC. CI, confidence interval; Std., Standardized.



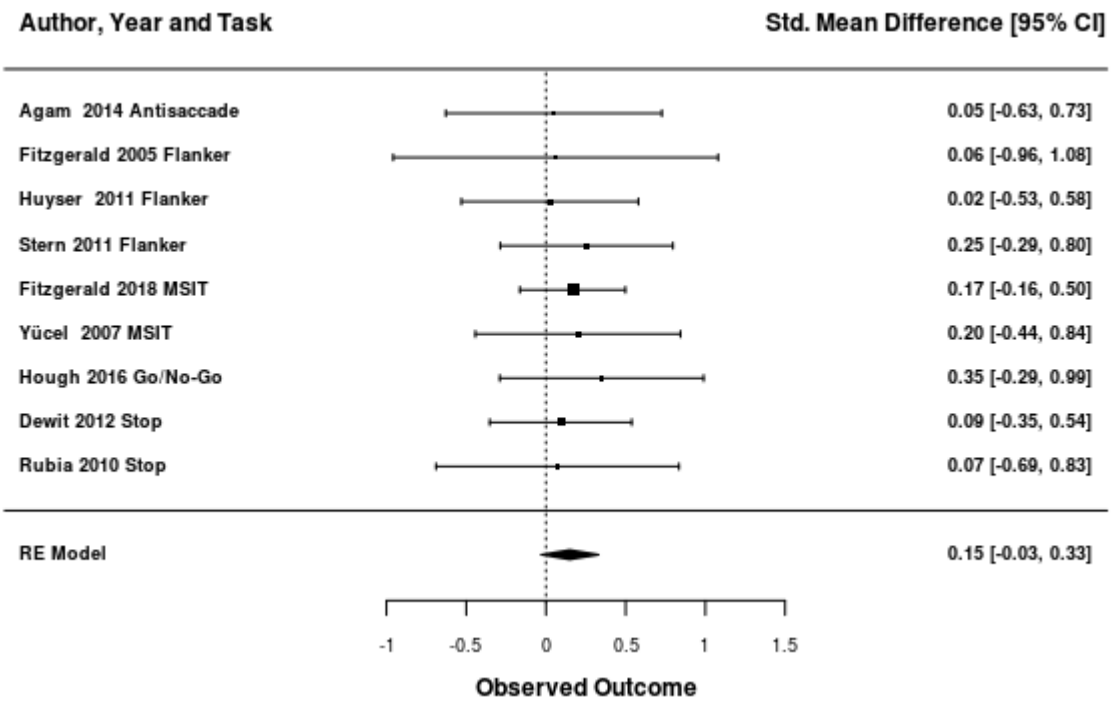
Supplementary Figure S10. Forest plot with standardized mean differences in brain activation during errors in R MTL (MNI x,y,z = 50,-4,-20) between patients with OCD and HC. CI, confidence interval; Std., Standardized.



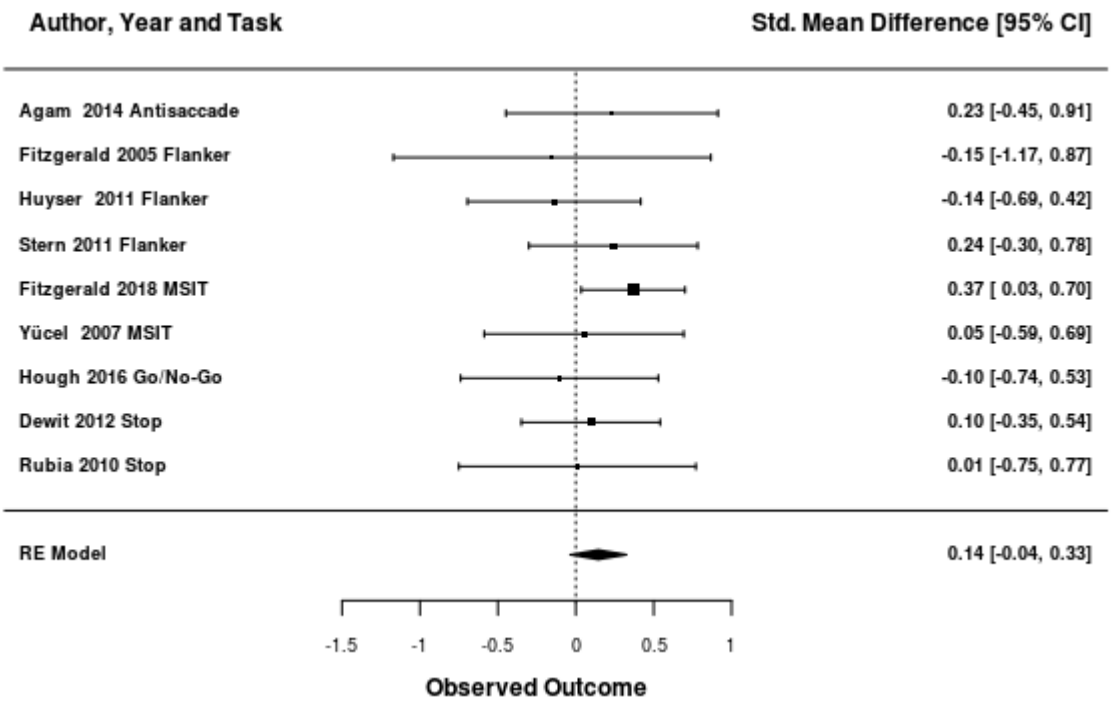
Supplementary Figure S11. Forest plot with standardized mean differences in brain activation during inhibitory control in left premotor cortex (MNI x,y,z = -26,0,60) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



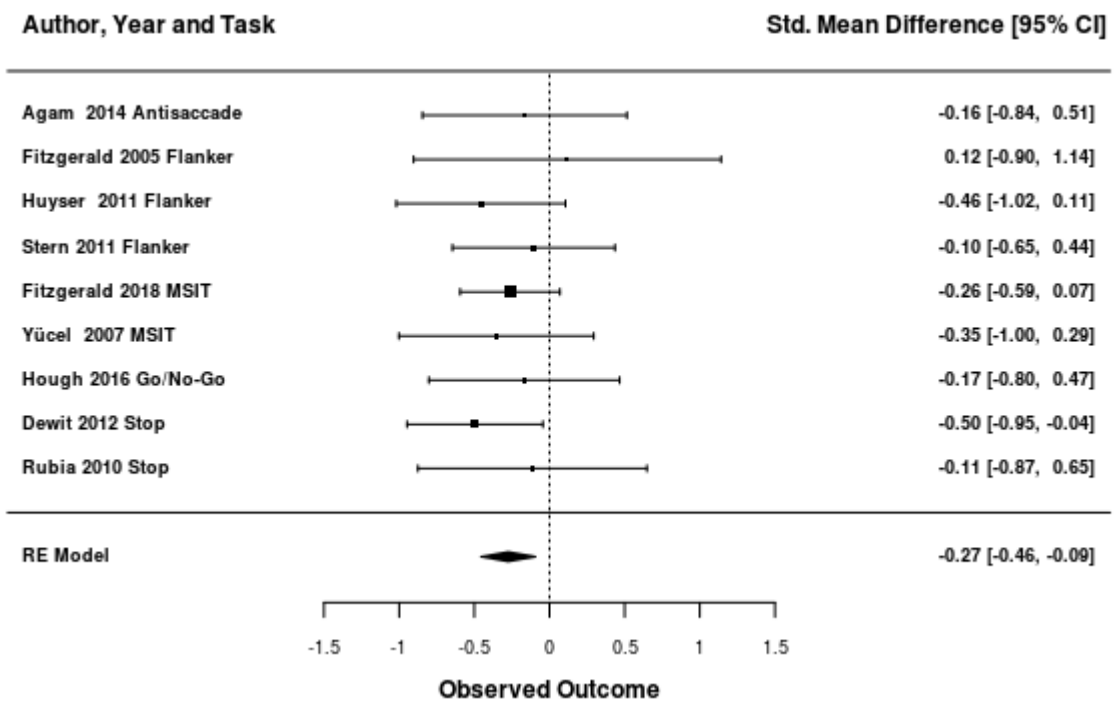
Supplementary Figure S12. Forest plot with standardized mean differences in brain activation during inhibitory control in right premotor cortex (MNI x,y,z = 30,-6,52) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



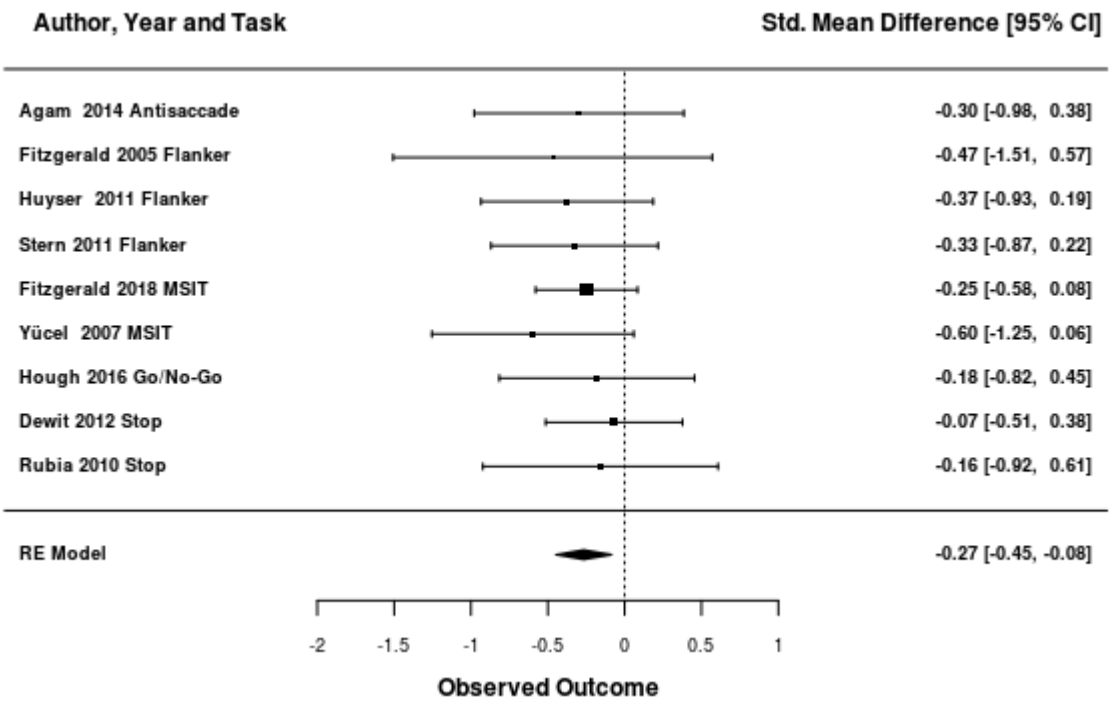
Supplementary Figure S13. Forest plot with standardized mean differences in brain activation during inhibitory control in right ITL/occipital lobe (MNI x,y,z = 48,-54,-10) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



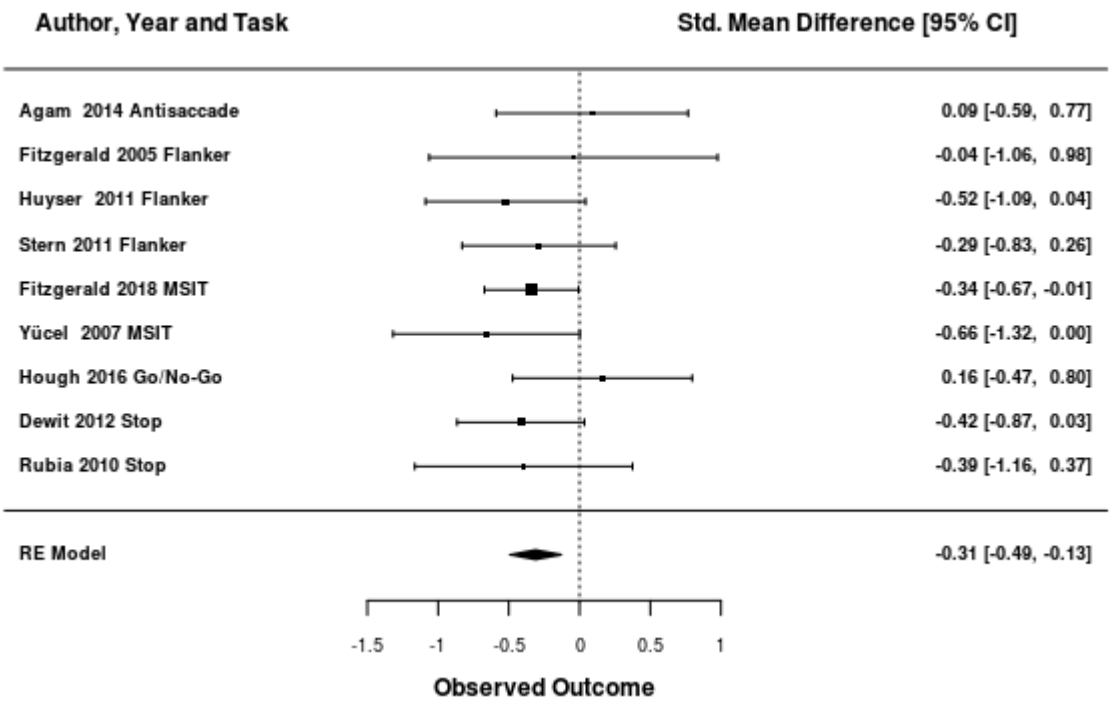
Supplementary Figure S14. Forest plot with standardized mean differences in brain activation during inhibitory control in right SPL (MNI x,y,z = 28,-52,56) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



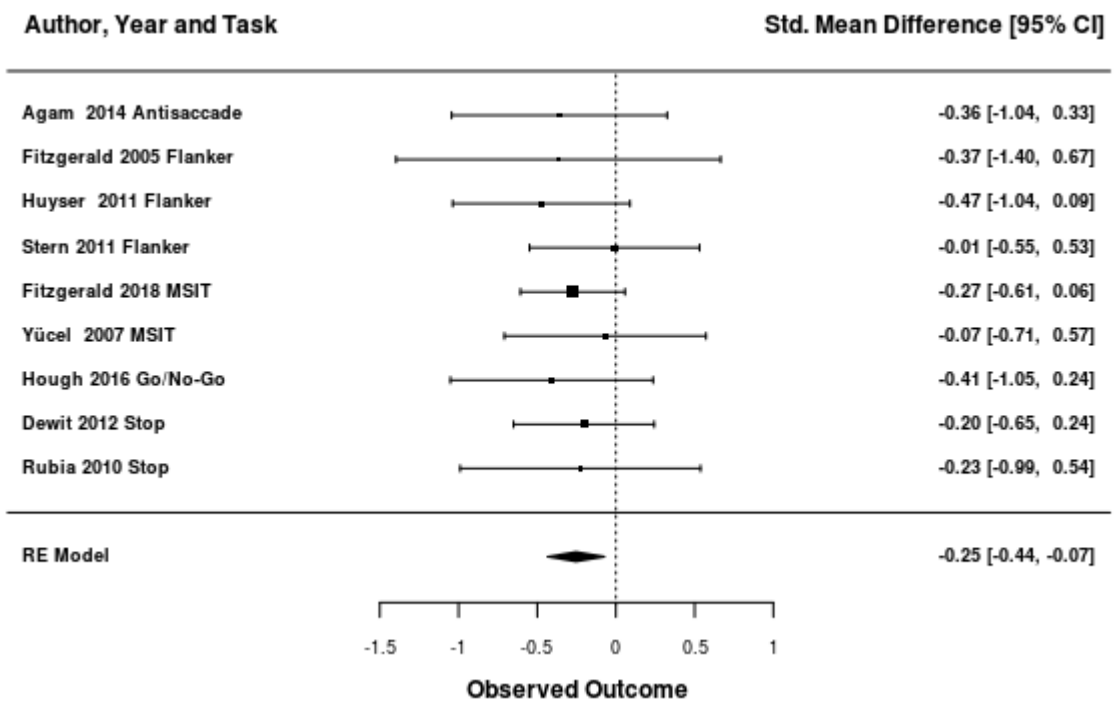
Supplementary Figure S15. Forest plot with standardized mean differences in brain activation during inhibitory control in left and right thalamus, left caudate (MNI x,y,z = -16,6,22) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



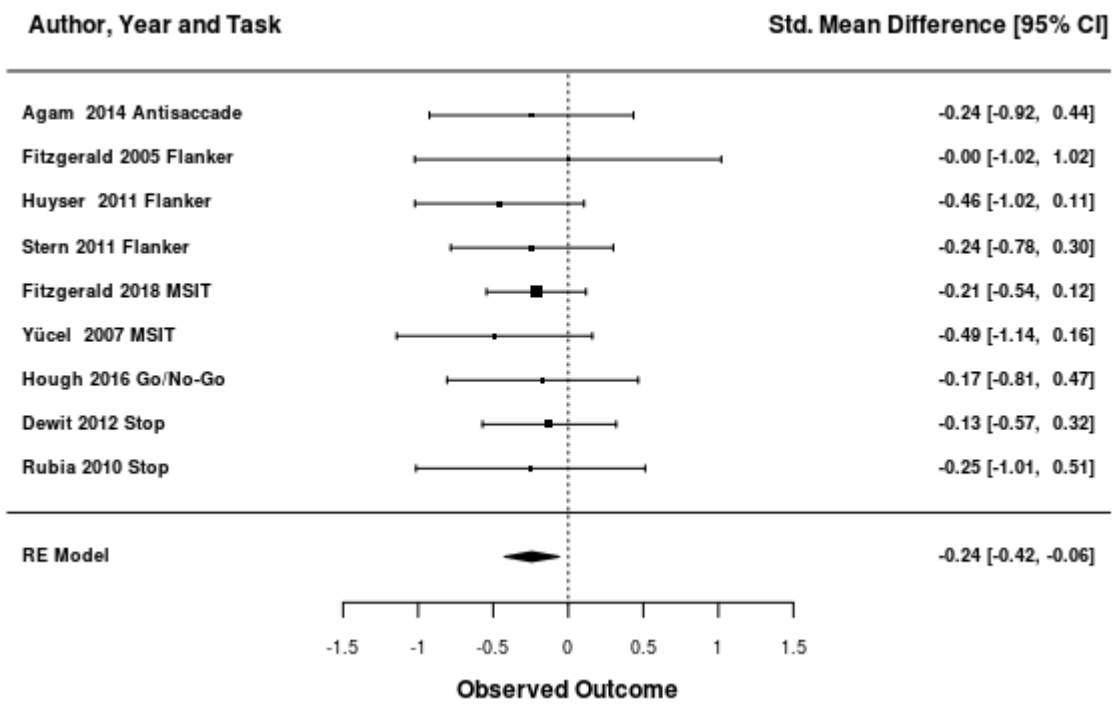
Supplementary Figure S16. Forest plot with standardized mean differences in brain activation during inhibitory control in left and right ACC/rACC/vACC (MNI x,y,z = 14,42,12) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



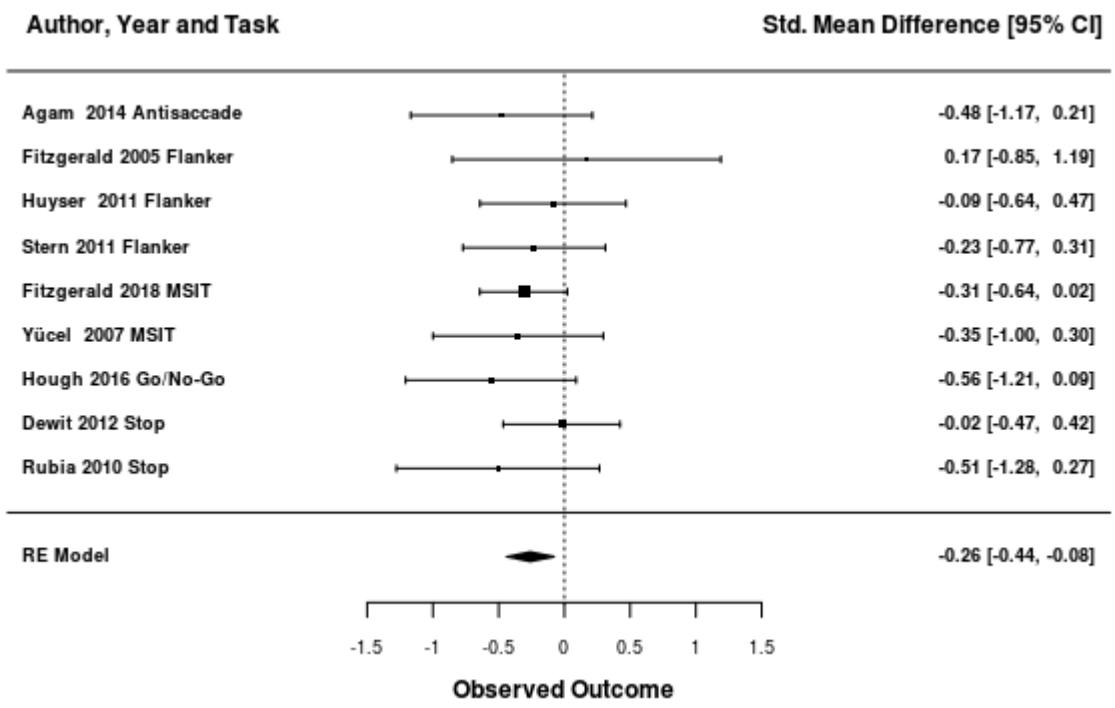
Supplementary Figure S17. Forest plot with standardized mean differences in brain activation during inhibitory control in right occipital lobe (MNI x,y,z = 26,-54,2) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



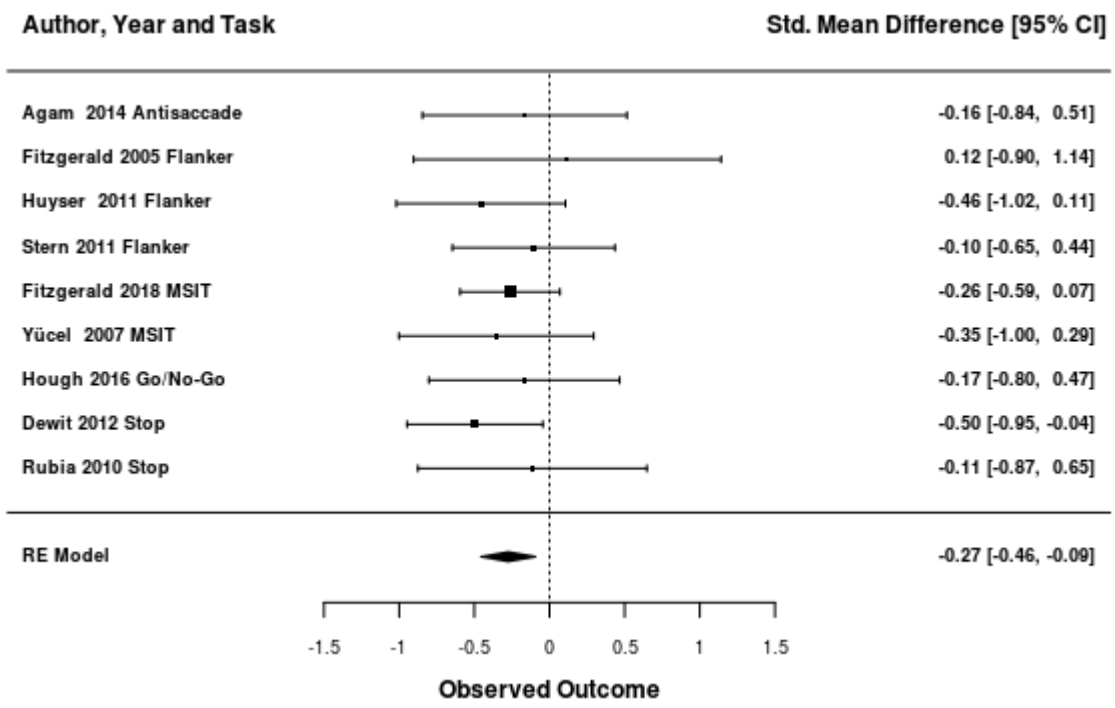
Supplementary Figure S18. Forest plot with standardized mean differences in brain activation during inhibitory control in right SMG/angular gyrus (MNI x,y,z = 56,-44,30) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



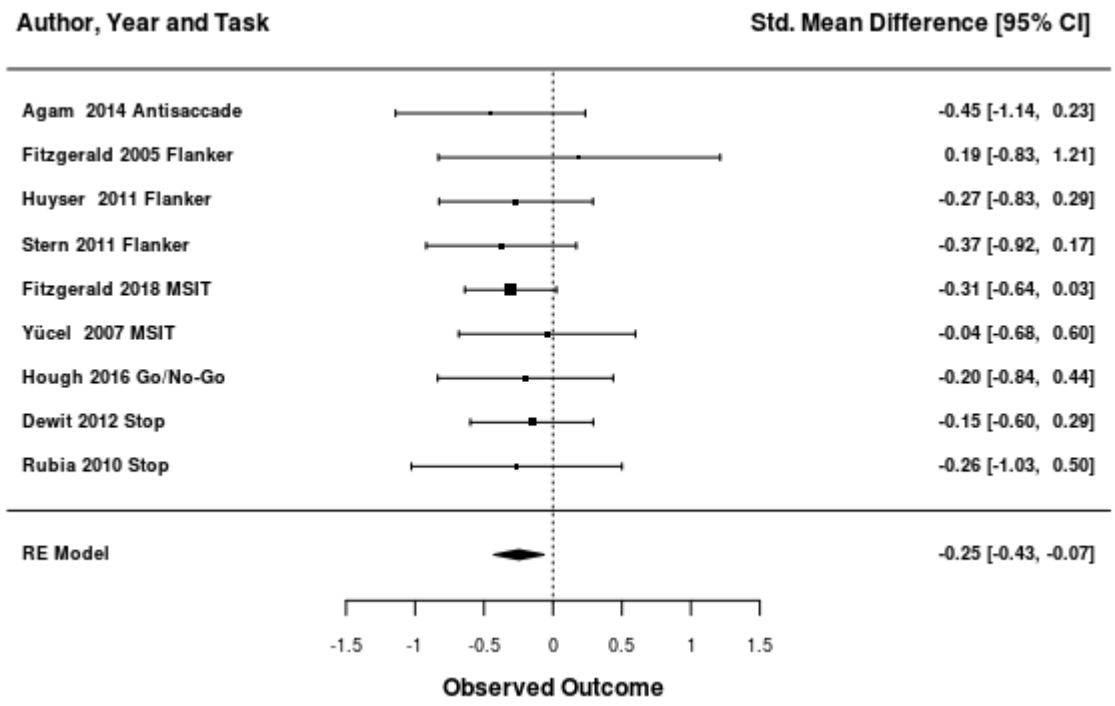
Supplementary Figure S19. Forest plot with standardized mean differences in brain activation during inhibitory control in left occipital lobe/cerebellum (MNI x,y,z = -28,-46, -8) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



Supplementary Figure S20. Forest plot with standardized mean differences in brain activation during inhibitory control in right mOFC (MNI x,y,z = 20,36,-18) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



Supplementary Figure S21. Forest plot with standardized mean differences in brain activation during inhibitory control in right caudate (MNI x,y,z = 18,-12,22) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.



Supplementary Figure S22. Forest plot with standardized mean differences in brain activation during inhibitory control in R aI/fO/STL (MNI x,y,z = 48,18,4) between patients with OCD and HC. CI, confidence interval; Std., Standardized. Positive effect sizes indicate greater activation in OCD relative to HC.

Supplementary Table S6. Results of the reliability (jackknife) analyses for areas showing increased activation in patients with OCD relative to HC during error processing.

	R aI/fO	R aLPFC	L & R pre-SMA	L & R dACC/SMA
Study				
Agam	y	y	y	y
de Wit	y	y	y	y
Fitzgerald	y	y	n	y
Fitzgerald	y	y	n	y
Grutzmann	y	y	y	y
Hough	y	y	n	y
Huyser	y	y	y	y
Rubia	y	y	y	y
Stern	y	y	n	y
Yücel	y	y	n	y

y = brain region remains significant in the analysis; n = brain region is no longer significant in this analysis.

Abbreviations: aI, anterior insula; aLPFC, anterior lateral prefrontal cortex; dACC, dorsal anterior cingulate cortex; fO, frontal operculum; MNI, Montreal Neurological Institute; pre-SMA, pre-supplementary motor area; SMA, supplementary motor area.

Supplementary Table S7. Results of the reliability (jackknife) analyses for areas showing decreased activation in patients with OCD relative to HC during error processing.

	L & R occipital lobe	R MTL
Study		
Agam	y	y
de Wit	y	n
Fitzgerald	y	y
Fitzgerald	y	y
Grutzmann	y	y
Hough	y	y
Huyser	y	y
Rubia	y	y
Stern	y	n
Yücel	y	y

y = brain region remains significant in the analysis; n = brain region is no longer significant in this analysis.

Abbreviations; MTL, middle temporal lobe.

Supplementary Table S8. Results of the reliability (jackknife) analyses for areas showing increased activation in patients with OCD relative to HC during inhibitory control.

	L premotor cortex	R premotor cortex	R ITL/ occipital lobe	R SPL
Study				
Agam	y	y	y	n
de Wit	y	y	y	y
Fitzgerald	n	n	n	n
Fitzgerald	y	y	y	y
Hough	y	y	n	y
Huyser	y	y	y	y
Rubia	y	y	y	y
Stern	y	y	n	n
Yücel	y	y	y	y

y = brain region remains significant in the analysis; n = brain region is no longer significant in this analysis.

Abbreviations: ITL, inferior temporal lobe; SPL, superior parietal lobe.

Supplementary Table S9. Results of the reliability (jackknife) analyses for areas showing decreased activation in patients with OCD relative to HC during inhibitory control.

	L & R thalamus, R caudate	L & R rACC /vACC	R occipital lobe	R SMG/ angular gyrus	L occipital lobe/ cerebellum	R mOFC	R caudate	R aI/fO/ STL
Study								
Agam	y	y	y	y	y	y	y	n
de Wit	y	y	y	y	y	y	n	y
Fitzgerald	y	y	y	y	n	n	n	n
Fitzgerald	y	y	y	y	y	y	y	y
Hough	y	y	y	y	y	n	y	y
Huyser	y	y	y	y	y	y	y	y
Rubia	y	y	y	y	y	y	y	y
Stern	y	y	y	y	y	n	y	n
Yücel	y	y	y	y	n	y	y	y

y = brain region remains significant in the analysis; n = brain region is no longer significant in this analysis.

Abbreviations: aI, anterior insula; fO, frontal operculum; mOFC, medial orbitofrontal cortex; rACC, rostral anterior cingulate cortex; SMG, supramarginal gyrus; STL, superior temporal lobe; vACC, ventral anterior cingulate cortex.

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