SUPPLEMENTAL DATA

S1.1 Excluded subjects

From the initial set of 45 medication-free OCD patients, 39 healthy comparison subjects and 17 unaffected siblings that participated, four patients and two comparison subjects were excluded. Reasons for exclusion were the following: excessive head movement during scanning (>3mm; N=2 patients), behavioral outlier removal (SSRT > 3 SD above group mean, N=1 patient), data-loss due to technical problems (N=1 comparison subject), and brain pathology accidentally discovered on the structural scan (N=2, one comparison subject and one patient). Twenty-eight patients gave permission for contacting their sibling(s), which resulted in the inclusion of 17 patient-sibling pairs (four siblings did not meet the inclusion criteria and seven siblings declined).

S1.2 Stop-signal task and data acquisition and analysis

The horse-race model of response inhibition states that performance on stop trials is decided by the race between an excitatory Go-process and an inhibitory Stop-process. The fastest process will determine the outcome (i.e. Stop-Error or Stop-Success). Subjects indicated the direction of an arrow with a button-press of their right or left index finger respectively, as fast and accurate as possible. The stop-signal delay started at 250ms and was updated online by a tracking algorithm which subtracted 50ms from the delay after a Stop-Success-trial or added 50ms after a Stop-Error-trial. The subject-specific duration of the Stop-process (stop-signal reaction time; SSRT) was then calculated by subtracting the critical stop-signal delay (the mean delay when stop success is 50%) (4) from the median reaction time on Go-trials. Since the stop-signal delay had a fixed starting point, delay values of the last 75% of stop trials were averaged to give a stable stop-signal delay estimate for each subject. Trials were presented pseudo-randomly with the restriction that the first 12 trials were Go-trials and that Stop-trials did not succeed each other. Go-trials started with a fixation cross (500ms) followed by an arrow (1000ms). Stop-trials were identical to Go-trials, except that the arrow was superimposed by the stop-signal, a cross, after the stop-signal delay. The inter-trial interval jittered randomly between 1500-2500ms. Each subject

performed 252 trials. Task duration was around 16 minutes. The task was programmed in E-Prime 1.2 (Psychology Software Tools, Pittsburgh, PA, USA). To familiarize participants with the procedure, subjects performed a practice run of the task prior to scanning.

Stimuli were presented on a beamer screen visible through a mirror mounted on the 8-channel head coil. An MRI-compatible response box (Current Designs, Philadelphia, PA, USA) was used to collect the button-presses. To reduce motion artifacts in the imaging data, the subject's head was immobilized with foam pads. To ensure steady-state magnetization equilibrium, 3 dummy scans were made before data-acquisition (1). Coordinates of selected *inhibition*-related and *error*-related regions-of-interest are similar to previous reports (2;3)

S2.1 Co-morbid diagnoses

Twenty-two OCD patients (54%) met criteria for one or more current axis-I diagnosis aside from their primary diagnosis of OCD: specific phobia (N=10), mood disorder (N=9), social phobia (N=5), panic disorder (N=3), eating disorder (N=2), agoraphobia (N=1), somatoform disorder (N=1) and Tourette's Syndrome (N=1).

Siblings had no current axis 1 psychiatric diagnosis apart from one sibling meeting criteria for an anxiety disorder not otherwise specified and one having moderate claustrophobia that did not interfere with the scanning session.

S2.2 Demographic, clinical and behavioral results of the subjects in the analysis with 17 patient-sibling pairs and 17 matched comparison subjects.

The three groups included in the fMRI three-group ANOVA (N=51) did not differ from each other on demographic or behavioral data (see Supplemental Table S1), except from gender showing a near-trend effect. Post-hoc tests showed that the percentage males in the sibling group was significantly higher as compared to patients [χ^2=4.25, p=.039, two-tailed], while comparison subjects did not differ from patients and siblings in gender ratio [χ^2=.48, p=.486, two-tailed; and χ^2=1.94, p=.16, two-tailed, respectively]. As in the analysis including the complete samples, post-hoc tests showed that patients had significantly higher scores on the Yale-Brown Obsessive-Compulsive Scale, Obsessive-Compulsive Inventory-Revised and

Montgomery Åsberg Depression Rating Scale compared with both comparison subjects and siblings (all p<.05), while there was no difference between siblings and comparison subjects on these clinical variables (all p>.60).

The subsets of OCD patients and comparison subjects included in the three-group comparison also did not differ from the complete samples of OCD patients and comparison subjects in demographic, clinical or behavioral measures (all p>.17).

Table S1. Demographic, clinical and behavioral measures from 17 patient-sibling pairs and 17 matched healthy comparison subjects included in the fMRI three-group comparison

	OCD patients (N=17)		Siblings (N=17)		Comparison subjects (N=17)		Statistical analysis	
	Mean	SD	Mean	SD	Mean	SD	F (df=2, 48)	p-value
Demographic measures								
Age (years)	37.9	10.7	38.3	13.4	38.9	12.4	0.03	0.972
Gender (men:women, (% men))	6:11	(35%)	12:5	(71%)	8:9	(47%)	χ^2=4.4	0.111
Handedness (right:left, (% right))	16:1	(94%)	13:4	(77%)	13:4	(77%)	χ^2=2.4	0.297
Educational level (years)[a]	5.7	1.4	5.7	1.3	5.8	2.4	0.2 [b]	0.891
Clinical measures								
Yale-Brown Obsessive-Compulsive Scale (points)	21.4	6.4	0.1	0.2	0.0	0	45.8 [b]	<.001
Obsessive-Compulsive Inventory-Revised, total score (points)	25.0	12.7	4.1	1.1	4.4	6.1	28.7 [b]	<.001
Obsessive-Compulsive Inventory-Revised, washing score (points)	3.8	4.5	0.2	0.4	0.4	0.8	11.7 [b]	.003
Obsessive-Compulsive Inventory-Revised, checking score (points)	6.2	3.5	0.6	0.8	0.8	1.1	26.9 [b]	<.001
Obsessive-Compulsive Inventory-Revised, symmetry score (points)	4.8	4.1	0.8	1.3	1.2	2.0	13.1 [b]	.001
MADRS score (points)	11.2	8.4	1.9	3.5	0.9	1.6	23.4 [b]	<.001
Behavioral measures								
SSRT (ms)	200.4	47.0	198.4	37.2	196.0	34.5	0.07	0.933
Mean Go-trial reaction time (ms)	679.4	125.2	738.9	160.0	679.8	152.2	0.9	0.403
Errors on Go-trials (%)	1.5	1.7	1.8	2.4	0.9	1.2	1.6 [b]	0.444

SD, standard deviation; χ^2, Chi-square test (df=2); MADRS, Montgomery Åsberg Depression Rating Scale.
[a] Educational level was recorded in 9 levels ranging from 1 (no finished education) to 9 (university training).
[b] Kruskal-Wallis test; H(df=2, 48).

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Table S2A. Main effect of *inhibition* over all subjects in whole-brain analysis (N=95)

Region	BA	Side	k_e	Region-of-interest*	Coordinates[a]			Z	p_{FWE}
					x	y	z		
Occipital, parietal, temporal cortex	19	R	3036	N	39	-85	-5	>8	.000
	37			N	42	-61	-17	>8	.000
	39			N	48	-73	-8	>8	.000
	40			Y	42	-55	43	>8	.000
Occipital, parietal, temporal cortex	19	L	2354	N	-36	-88	-5	>8	.000
	37			N	-42	-64	-17	>8	.000
	19			N	-42	-79	-5	>8	.000
	40			Y	-51	-55	43	>8	.000
Prefrontal cortex, subcortical areas (including sub-thalamic nucleus)	47	R / L	3387	Y	33	23	-11	>8	.000
	9			N	45	11	37	>8	.000
	46			N	51	17	19	>8	.000
	6			Y	9	17	67	>8	.000
	NA			Y	3	-15	-2	5.34	.000
Frontal cortex, subcortical areas	47	L	1153	Y	-33	23	-8	>8	.000
	9			N	-42	17	-8	>8	.000
	NA			N	-39	23	40	7.58	.000
Caudate nucleus	NA	L	123	N	-9	11	1	>8	.000
Mid-cingular cortex	23	R	74	N	3	-28	31	6.07	.000
Hippocampus	NA	R	37	N	24	-28	-8	5.97	.000
Hippocampus	NA	L	4	N	-24	-28	-8	4.96	.006
Brainstem	NA	R	3	N	3	-22	-20	4.75	.014
Mid-cingular cortex	24	R	5	N	3	-4	34	4.71	.017
Pre-supplementary motor area	6	L	1	Y	-15	14	67	4.58	.029

Table S2B. Main effect of *error* over all subjects in whole-brain analysis (N=95)

Region	BA	Side	k_e	Region-of-interest*	Coordinates			Z	p_{FWE}
					x	y	z		
Cerebellum	NA	L / R	1992	N	-24	-61	-26	7.60	.000
				N	-15	-58	-17	7.55	.000
				N	18	-58	-20	7.37	.000
Insula, postcentral gyrus, superior and middle temporal gyrus	13	L	534	N	-51	-22	16	6.82	.000
	22			N	-51	-1	4	6.71	.000
	21			N	-45	-28	-19	6.53	.000
Postcentral gyrus, insula, superior temporal gyrus	43	R	291	N	60	-16	16	6.06	.000
	13			N	51	8	1	5.85	.000
	22			N	45	-28	19	5.59	.000
Anterior cingulate cortex	32	R/L	104	Y	0	20	34	5.99	.000
Pre-supplementary motor area	6	R	13	N	9	8	70	5.60	.000
Precentral gyrus	4	R	35	N	54	-16	43	5.32	.001
					45	-19	43	4.97	.005
Precentral gyrus	4	L	10	N	-54	-22	43	5.01	.001
Thalamus	NA	L	4	N	-15	-22	4	4.66	.039

BA, Brodmann Area; k_e, cluster size; Z, Z-score; p_{FWE}, Family-Wise Error corrected p-value for search volume; R, right; L, left; *Peak used for Region-of-Interest analysis; Y, yes, N, No. Coordinates are in MNI space. *Inhibition*-contrast: Stop-Success-trials>Go-trials; *Erro*r-contrast: Stop-Error-trials>Stop-Success-trials.

Table S3. Main effect of *inhibition* and *error* per study group per region-of-interest.

Region-of-interest	Side	OCD patients (N=41) Coordinates			k_e	Z	p_{FWE}	Siblings (N=17) Coordinates [a]			k_e	Z	p_{FWE}	Comparison subjects (N=37) Coordinates [a]			k_e	Z	p_{FWE}
		x	y	z				x	y	z				x	y	z			
Inhibition																			
Inferior frontal gyrus	R	33	23	-11	132	6.87	.000	36	20	-8	119	6.89	.000	36	23	-14	131	7.46	.000
	L	-30	20	1	123	6.24	.000	-33	23	-8	137	5.45	.000	-33	23	-8	151	7.17	.000
		-30	23	-11		6.12	.000												
		-39	17	-8		6.05	.000												
Pre-supplementary motor area	R	9	17	67	85	5.34	.000	6	17	64	112	4.75	.000	6	20	58	76	4.63	.000
		6	17	58		5.29	.000	18	14	67		4.45	.000	9	17	57		4.31	.001
	L	-9	20	64	39	4.05	.001	-12	23	64	42	3.79	.003	-					
								-15	8	70		3.58	.012						
Inferior parietal cortex	R	39	-55	43	162	6.18	.000	51	-58	46	169	5.41	.000	45	-55	40	171	7.02	.000
		48	-55	37		5.72	.000	33	-58	46		5.38	.000	45	-58	52		6.44	.000
	L	-51	-55	43	90	6.05	.000	-54	-52	37	80	3.91	.004	-51	-58	49	159	6.96	.000
														-57	-61	37		6.28	.000
Sub-thalamic nucleus	R/L	0	-16	-2	35	3.62	.006	6	-10	7	1	3.00	.050	9	-10	4	71	4.14	.005
		9	-10	4	1	3.07	.032							3	-19	1		3.49	.011
Error																			
Anterior cingulate cortex	R/L	-3	20	34	46	3.59	.007	0	23	25	7	3.29	.020	3	20	34	117	4.31	.001
								3	29	31	1	3.08	.036						

BA, Brodmann Area; k_e, cluster size; Z, Z-score; FWE, Family-Wise Error corrected for search volume; R, right; L, left. Coordinates are in MNI space. *Inhibition*-contrast: Stop-Success-trials>Go-trials; *Error*-contrast: Stop-Error-trials>Stop-Success-trials.

Supplemental References

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