Supplemental Material for Marsh et al., **Reward-Based Spatial Learning in Unmedicated Adults with Obsessive-Compulsive Disorder**

SUPPLEMENTAL METHODS

Participants

Unmedicated adults with OCD (n=33) and healthy participants (HC, n=33), group-matched by age, sex, and ethno-racial groups, were recruited through flyers, internet advertisements, and word-of-mouth. Participants with a history of neurological illness, head trauma with loss of consciousness, mental retardation, pervasive developmental disorder, or current Axis I disorders (other than OCD for the OCD participants) were excluded. HCs had no lifetime Axis I disorders. Psychiatric diagnoses were established by a psychiatric evaluation and confirmed with the Structured Clinical Interview for DSM-IV(1). On the MRI scan day, a trained rater assessed OCD severity using the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) (2, 3) and depressive symptoms using the Hamilton Depression Scale(4). The Y-BOCS checklist provided scores for each OCD patient along five symptom dimensions(5, 6). Full-scale IQs were estimated using the Wechsler Abbreviated Scale of Intelligence(7). The Institutional Review Board of the New York State Psychiatric Institute approved this study. Participants provided written informed consent.

Behavioral Analyses

We tested whether the OCD and HC groups differed in their improvement in reward-based spatial learning using linear mixed models with repeated measures over scan runs implemented in SAS version 8.0 (SAS Institute Inc., Cary, NC). Participants who demonstrate learning on the task should be faster at obtaining all 8 rewards during the second compared with the first learning condition (e.g., run 2 versus run 1) (8). To assess whether there were group differences in performance speed, performance speed (defined as time-per-run) was entered as the dependent variable in a model with run (run1, run2) as the within-subjects factor and group (OCD, HC) as the between subjects factor. The same analysis was also conducted using time-per-trial as an alternative way to define performance speed. Because participants who learn should require fewer trials to obtain all 8 rewards over the 2 runs, we also tested whether there were group differences in the total number of trials by entering the total number of trials as the dependent variable in another mixed model with the same within- and between-subjects factors. Group differences in learning (as measured by performance speed and number of trials) were tested by assessing the statistical significance of the group-by-run interaction in these models.

An additional analysis was conducted to assess group differences in performance *across* the learning and control conditions. Performance speed (time taken to obtain the 8 possible rewards in both runs across conditions – i.e., time-per-run) was entered as a dependent variable in a linear mixed model with condition (learning, control) entered as a within-subjects factor, and group entered as a between subjects factor. This analysis yielded statistics for group-by-condition interactions and main effects of group and condition for performance speed (time-per-run) across conditions. Because the total number of trials required in the learning condition determined those values for the control condition for each participant, this variable was not compared statistically across the learning and control conditions.

SUPPLEMENTAL RESULTS

Participants

The majority (n=21) of the OCD participants were treatment-naïve; the rest (n=12) were off of medications for at least 12 weeks (mean (SD) of 109 (127) weeks). Table S1 details what medications they were taking and for how long they had been free of them prior to scanning.

Table S1. Prior Medications

Medications	**Weeks off Medications**	
	Mean (SD)	Range
SRIs (n=10)	126 (133)	18 - 468
Fluoxetine (n=3)	81 (51)	46 - 140
Escitalopram (n=3)	219 (228)	18 - 468
Fluvoxamine (n=2)	67 (52)	30 - 104
Fluoxetine & Escitalopram (n=1)	182	
Sertraline (n=1)	46	
Other (n=2)	25 (9)	18 - 32
Lamotrigine (n=1)	18	
Quetiapine (n=1)	32	

The OCD and healthy groups did not differ in head motion during scanning. Specifically, root mean square motion derived from the six motion parameters was similar across groups (OCD = 1.23 mm; healthy = 1.5 mm, $p = 0.24$).

Behavioral Performance

Both groups demonstrated significant improvement in performance speed in the learning condition from Run 1 to Run 2 in terms of both time-per-run and time-per-trial (main effects of Run, $ps \leq 0.01$, Table S2). As shown in Table S3, a significant main effect of group was found for

the time taken to complete both the learning and control conditions in Run 1 (p = 0.03), deriving from the slower performance speed of OCD participants.

Table S2. Group Differences in Performance Speed Across Runs:

Comparison		**HC**	**OCD**	Main Effect Run F(*p*)
Time-Per-Run (SD)	Run1	125.9 (100)	184.2 (132)	**15.15 (<0.01)**
	Run2	100.5 (59)	85.7 (39.2)	
Test Stat Run 1 v 2 (*p*)		1.35 (0.19)	**4.35 (<0.01)**	
Main Effect Group F(*p*)		0.44 (0.51)		Group x Run 3.61 (0.06)
Time-Per-Trial (SD)	Run1	9.19 (7.82)	9.14 (5.74)	**5.55 (0.02)**
	Run2	7.51 (2.94)	6.73 (3.16)	
Test Stat Run 1 v 2 (*p*)		1.20 (0.24)	1.72 (0.09)	
Main Effect Group F(*p*)		0.67 (0.42)		Group x Run 0.01 (0.9)
				Test Stat HC v OCD (*p*)
Overall Speed (SD)	Per Run	225.8 (120.3)	299.8 (220.6)	1.69 (0.1)
	Per Trial	8.26 (4.37)	8.48 (5.58)	0.22 (0.82)

Table S3. Group Differences in Performance Across the Learning and Control Conditions

Comparison		**HC**	**OCD**	Main Effect[b] Condition F(*p*)
Performance Speed Run 1 (SD)	Learning	125.9 (100)	184.2 (132)	3.48 (0.07)
	Control	118.2 (67.3)	157.8 (85.3)	
T stat Condition Learning v Control (*p*)[a]		0.71 (0.48)	1.80 (0.08)	
Main Effect[b] Group F(*p*)		**4.70 (0.03)**		Group x Condition[b] 1.04 (0.31)
Performance Speed Run 2 (SD)	Learning	100.5 (59)	85.7 (39.2)	2.01 (0.16)
	Control	100.5 (51.2)	100.6 (74.9)	
T stat Condition Learning v Control (*p*)[a]		0.00 (1.00)	-1.55 (0.13)	
Main Effect[b] Group F(*p*)		0.28 (0.60)		Group x Condition[b] 2.01 (0.16)
Total Time (SD)	Learning	225.8 (120.3)	299.8 (220.6)	1.16 (0.29)
	Control	217 (97.2)	279.6 (160.1)	
T stat Condition Learning v Control (*p*)[a]		0.65 (0.52)	0.87 (0.39)	
Main Effect Group F(*p*)		3.57 (0.06)		Group x Condition[b] 0.18 (0.67)

Boldface denotes statistically significant findings.

Exploratory Imaging Analyses

Prior Treatment Effects we conducted an F test (the same omnibus model described in the manuscript) including only the 21 treatment naïve OCD participants. Diagnosis-by-condition-by-event interactions were detected in left hippocampus, amygdala, and ventral putamen (Fig. S1), suggesting that prior treatment did not contribute to our findings for group differences in these areas.

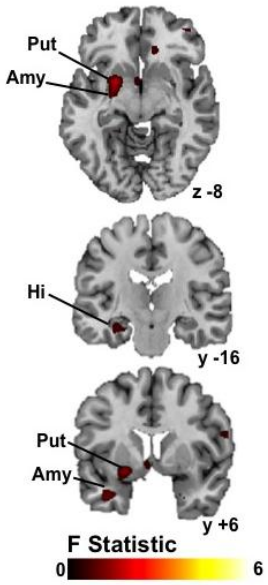

Figure S1. Whole-brain analysis including only the treatment naïve OCD participants (n=17). Interactions (diagnosis-by-condition-by-event) were detected in the left hemisphere cluster comprising ventral putamen, amygdala, and hippocampus (maximum peak –27, -7, –11; 454 voxels (756 mm^3); F=8.74, P<0.05, corrected). Abbreviations: Put, putamen; Amy, amygdala, Hi, hippocampus.

Supplemental References

1. First MB, Spitzer RL, Gibbon M, Williams JBW (2002): *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP).* . New York: Biometrics Research, New York State Psychiatric Institute.
2. Goodman WK, Price LH, Rasmusson SA, Mazure C, Delgado P, Henninger GR, et al. (1989): The Yale-Brown Obsessive Compulsive Scale: I. Development, use, and reliability. *Arch Gen Psychiatry*. 46:1006-1011.
3. Goodman WK, Price LH, Rasmusson SA, Mazure C, Delgado P, Henninger GR, et al. (1989): Yale-Brown Obsessive Compulsive Scale: II. Validity. *Arch Gen Psychiatry*. 46:1012-1018.
4. Hamilton MAX (1967): Development of a Rating Scale For Primary Depressive Illness. *British Journal of Social & Clinical Psychology*. 6:278-296.
5. Pinto A, Eisen JL, Mancebo MC, Greenberg BD, Stout RL, Rasmussen SA (2007): Taboo thoughts and doubt/checking: a refinement of the factor structure for obsessive-compulsive disorder symptoms. *Psychiatry Res*. 151:255-258.
6. Pinto A, Greenberg BD, Grados MA, Bienvenu OJ, 3rd, Samuels JF, Murphy DL, et al. (2008): Further development of YBOCS dimensions in the OCD Collaborative Genetics study: symptoms vs. categories. *Psychiatry Res*. 160:83-93.
7. Wechsler D (1981): *WAIS-R Manual. Wechsler Adult Intelligence Scale-Revised*. San Antonio, TX: The Psychological Corporation. Harcourt Brace Jovanovich, Inc.
8. Marsh R, Hao X, Xu D, Wang Z, Duan Y, Lui J, et al. (2010): A Virtual Reality-Based FMRI Study of Reward-Based Spatial Learning. *Neuropsychologia*. 48:2912-2921.