Beucke et al. Default mode network subsystem alterations in obsessive–compulsive disorder. *Br J Psychiatry* doi: 10.1192/bjp.bp.113.137380

Online supplement DS1

Method

Averaged DMN subsystem (voxel-based ROI-to-ROI) analyses. Since seed-based functional connectivity analyses exclusively consider one seed region (thus, only one component of a subsystem) at a time, voxel-based ROI-to-ROI analyses were carried out in order to derive values (i.e. one per subsystem) exclusively characterizing the averaged connectivity in each subsystem. Pearson's correlation coefficient (r) matrices including the correlation of each voxel to every other voxel time course that were used for a separate analysis of this dataset (1) were used. After subsampling the voxel size to 4×4×4 mm, cells of the correlation matrix representing the correlation between the voxels constituting components of the subsystems were identified based on the voxel coordinates of spheres used for seed-to-voxel fcMRI analyses (online Table DS2). Subsequently, correlation coefficients representing the connections between subsystem components (midline core: one connection; dMPFC self system: six connections, MTL memory system: ten connections, Fig. DS2(d) were z transformed and averaged subsequently, resulting in one z value indexing the averaged connectivity in midline core, dMPFC self, and MTL memory subsystems separately. These values were subsequently compared between OCD patients and healthy controls using one-way analyses of variance (ANOVAs) in SPSS (Version 19). A statistical threshold of $P < 0.017$ (representing a Bonferroni corrected P value adjusted for three comparisons) was considered significant.

Confirmatory functional connectivity (seed-to-voxel) analyses for DAN, SN and ECN. Additional seed-to-voxel rs-fcMRI analyses comparing connectivity in DAN, ECN and SN were conducted following the observation of higher (OCD > HC) connectivity of DMN seeds with areas approaching coordinates that were previously shown to be part of the DAN (2, 3), the SN (4, 5) and the ECN (2, 5), and also in order to relate to previous studies suggesting abnormal functional interactions among networks in OCD (6, 7). Additional seed-to-voxel analyses were carried out for the following left-lateralized seed region coordinates previously used in rs-fcMRI studies to identify the SN, the DAN and the ECN (3-5): superior parietal lobule (DAN, MNI_{xyz} = -25, -53, 52), anterior insula (SN, MNI_{xyz} = -31, 11, 8) and dorsolateral prefrontal cortex (ECN, MNI_{xyz} = -42, 34, 20), followed by comparisons (two-sample t tests) between OCD patients and healthy controls using a statistical threshold of $P < 0.017$ (Bonferroni corrected P value adjusted for three comparisons after cluster-level correction).

Correlational analyses with OCD symptom severity. After observing significantly reduced connectivity in the dMPFC self system, we sought to explore potential associations between dMPFC and obsessive-compulsive symptoms. Using a voxelwise approach, we computed correlations between dMPFC whole-brain connectivity maps and symptom severity by including Y-BOCS total scores as a covariate in a random effects model containing dMPFC connectivity maps of the entire group OCD patients ($N = 46$). In addition, this analysis was repeated twice after splitting the patient group in half (i.e. voxelwise correlations in unmedicated OCD patients only ($N = 23$), and medicated patients ($N = 23$), respectively). As for group comparisons, the significance threshold for these voxelwise correlational analyses was set at $P < 0.0045$ (cluster-corrected P value adjusted for 11 measurements). Kolmogorov-Smirnov tests (SPSS, Version 19) were applied to ensure that the peak of clusters surviving this threshold and Y-BOCS scores were normally distributed.

Online supplement DS2

Results

Averaged DMN subsystem (voxel-based ROI-to-ROI) analyses. Comparing the averaged correlation between single voxels representing components of each subsystem (*midline core, self system, memory system*) between OCD patients and healthy controls revealed reduced connectivity in the *midline core* ($F_{1,90} = 4.46$, $P = 0.038$) and significantly ($P < 0.017$, corrected for three comparisons) reduced connectivity in the dMPFC *self system* ($F_{1,90} = 7.14$, $P = 0.009$, Fig. DS2(d)). There were no significant group differences regarding MTL *memory subsystem* connectivity ($F_{1,90} = 0.04$, $P = 0.84$). Potential medication effects were addressed by comparing midline core and connectivity of the two subsystems between *unmedicated* OCD patients ($N = 23$) as compared to healthy controls ($N = 23$), and between *unmedicated* ($N = 23$) and *medicated* ($N = 23$) OCD patients. This revealed reduced connectivity in the dMPFC *self system* in *unmedicated* OCD patients ($F_{1,44} = 6.13$, $P = 0.017$), but no significant differences in the midline core ($F_{1,44} = 3.31$, $P = 0.076$) and the MTL *memory system* ($F_{1,44} = 0.01$, $P = 0.92$) as compared to healthy controls, further no significant differences in the *midline core* ($F_{1,44} = 1.34$, $P = 0.25$), dMPFC *self* ($F_{1,44} = 2.20$, $P = 0.15$) and MTL *memory* ($F_{1,44} = 0.16$, $P = 0.69$) *subsystems* in *medicated* patients compared to healthy controls, and no differences between *unmedicated* and *medicated* OCD patients in the *midline core* ($F_{1,90} = 0.18$, $P = 0.67$), dMPFC *self system* ($F_{1,90} = 1.51$, $P = 0.23$) and MTL *memory subsystem* ($F_{1,90} = 0.20$, $P = 0.66$). Comparisons of OCD patients without lifetime history of affective disorders ($N = 18$) to matched healthy controls ($N = 18$) revealed non-significant trends for reduced connectivity in the dMPFC *self system* ($F_{1,34} = 3.54$, $P = 0.07$), and no differences regarding connectivity of the *midline core* ($F_{1,34} = 2.18$, $P = 0.15$) or the *MTL memory system* ($F_{1,34} = 0.01$, $P = 0.92$).

Table DS1 Coordinates of the eleven default mode network seed regions of interest**.** Coordinates are based on Montreal Neurological Institute (MNI) coordinate space. Seed regions are identical to the previous study by Andrews-Hanna and colleagues (8) identifying subsystems of the default network, except for the Temporal pole seed, where the coordinate was slightly modified from MNI_{xyz} = -50, 14, -40 to MNI_{xyz} = -50, 10, -40 to fit the present preprocessed fMRI data. In accordance with the previous Default Network subsystem study (8) seed regions are 8mm spheres, and thus Brodmann areas list approximate locations for reference.

DMN subsystem	Seed region	Abbreviation	Brodmann Areas	MNI_{xyz}
midline core	Anterior medial prefrontal cortex	aMPFC	10, 32	-6, 52, -2
	Posterior cingulate cortex	PCC	23,31	-8, -56, 26
dMPFC self system	Dorsal medial prefrontal cortex	dMPFC	9, 32	0, 52, 26
	Temporal parietal junction	TPJ	40, 39	-54, -54, 28
	Lateral temporal cortex	LTC	21, 22	-60, -24, -18
	Temporal pole	TempP	21,38	-50, 10, -40
MTL memory system	Ventral medial prefrontal cortex	vMPFC	11, 24, 25, 32	0, 26, -18
	Posterior inferior parietal lobule	pIPL	39	-44, -74, 32
	Retrosplenial cortex	Rsp	29, 30, 19	-14, -52, 8
	Parahippocampal cortex	PHC	20, 36, 19	-28, -40, -12
	Hippocampal formation	HF	20, 36	-22, -20, -26

Abbreviations: MTL, medial temporal lobe; MNI, Montreal Neurological Institute.

Table DS2 Confirmatory functional connectivity results. Seed-to-voxel analyses for previously used seed region for dorsal attention (3), salience/ventral attention (4, 5) and control (3, 5) networks: Between-group effects for OCD patients and healthy controls. Peaks of connectivity difference coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. Between-group effects are thresholded at $P<.017$ (Bonferroni-corrected *P* value to adjust for multiple comparisons, given that three additional seeds were compared between OCD patients and controls).

Network	Seed region	Group difference region	Direction	MNI_{xyz}	*z* Score	CS	*P* value	BA
Dorsal Attention	left SPL	Temporal pole	OCD > HC	2, 48, -6	4.36	93	.008	21
		Posterior cingulate cortex	OCD > HC	-8, -56, 28	3.82	159	< .001	31
		Anterior medial prefrontal cortex	OCD > HC	2, 64, -10	3.82	99	.006	10
		Precentral gyrus	HC > OCD	40, -20, 60	3.71	143	< .001	4, 6
Salience / Ventral attention	left anterior insula	Parahippocampal gyrus / culmen	OCD > HC	-26, -50, 10	4.52	435	< .001	19, 37
		Middle temporal gyrus	OCD > HC	-62, -16, -12	4.49	170	< .001	21
		Inferior parietal lobule	HC > OCD	52, -40, 40	3.54	89	.01	40
Executive Control	left DLPFC	Superior temporal gyrus	OCD > HC	-64, -18, -2	4.08	226	< .001	22
		Inferior frontal gyrus	HC > OCD	-48, 8, 26	3.64	87	.01	9

Abbreviations: HC, healthy controls; OCD, obsessive-compulsive disorder; SPL, superior parietal lobule; DLPFC, dorsolateral prefrontal cortex; CS, cluster size; BA, Brodmann area.

Table DS3 (a–k) Within-group (i.e. main) effects for all seed-to-voxel analyses in both groups.

Table DS3(a) Regions correlating with the aMPFC seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
aMPFC seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Medial prefrontal gyrus (cluster including aMPFC, dMPFC, vMPFC)	-6, 52, -4	> 8	10	-6, 52, -4	> 8	10
Posterior cingulate cortex/Precuneus (clusters including PCC, Rsp)	-4, -56, 28	> 8	31	-2, -56, 28	> 8	31
Middle, Inferior & Superior temporal gyrus (clusters including LTC, TempP[§])	-62, -18, -18	> 8	21	-62, -16, -18	6.53	21
	64, -4, -22	7.80	21	58, -6, -26	6.76	21
				-42, 8, -38	5.18	38
Superior temporal gyrus (including TPJ)*	-50, -60, 30	5.10	39	-50, -60, 30	5.64	39
Middle temporal gyrus, Inferior parietal lobe & Precuneus (clusters including pIPL)	-46, -70, 38	7.73	39	-46, -66, 28	7.17	39
	50, -68, 38	5.94	39	54, -60, 28	5.60	39
Parahippocampal gyrus (cluster including PHC[§], HF)	-22, -28, -20	6.27	28	-20, -16, -28	5.68	28
				24, -18, -20	5.68	28
Inferior frontal gyrus	-32, 16, -20	6.89	47			
Insula	32, 18, -18	5.99	13			
Thalamus	2, -10, 10	6.34				
Posterior cerebellum	40, -76, -38	6.53		42, -74, -44	5.17	

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. * Significant main effects identified by a region of interest search using a corrected threshold of P_{FWE} <.05 in both groups. § Significant main effects identified by a region of interest search in patients (P_{FWE} <.05, corrected).

Table DS3(b) Regions correlating with the PCC seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
PCC seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Posterior cingulate cortex (cluster including PCC, Rsp)	-8, -56, 26	> 8	31	-8, -56, 26	> 8	31
Anterior cingulate cortex/Medial frontal gyrus (cluster including aMPFC, dMPFC, vMPFC)	2, 50, -8	> 8	32	-4, 52, -8	> 8	32
Inferior parietal lobe/Middle temporal gyrus (clusters including pIPL, TPJ)	-42, -70, 34	> 8	39	-44, -66, 30	> 8	39
	48, -64, 32	> 8	39	48, -62, 30	7.82	39
Inferior/Superior/medial temporal gyrus (clusters including LTC, TempP)	-60, -12, -22	> 8	21	-38, 18, -38	6.55	38
	62, -10, -20	6.86	21	-60, -10, -22	6.51	21
				54, 2, -36	6.43	21
				-60, -42, -8	5.51	20
Superior frontal gyrus				22, 32, 54	6.90	6
Inferior frontal gyrus	-34, 20, -22	5.40	47			
Parahippocampal gyrus (cluster including HF)	-22, -16, -24	6.17	28	-24, -16, -26	7.03	35
Anterior Cerebellum / Parahippocampal gyrus (cluster including PHC§)	-22, -36, -14	6.03	36	24, -16, -22	5.45	28

Anterior Cerebellum	20, -32, -14	6.77				
Posterior Cerebellum	8, -56, -42	6.17		28, -84, -34	5.42	
	46, -74, -38	5.63				
	-26, -82, -36	5.12				

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. [§] Significant main effects identified by a region of interest search in patients using a corrected threshold of P_{FWE} <.05.

Table DS3(c) Regions correlating with the dMPFC seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
dMPFC seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Medial frontal gyrus (cluster including aMPFC, dMPFC, vMPFC)	0, 52, 26	> 8	9	0, 52, 26	> 8	9
Posterior cingulate cortex (cluster including PCC)	-4, -52, 30	> 8	31	4, -54, 32	> 8	31
	2, -22, 40	7.32	31			
Inferior frontal gyrus	-36, 20, -20	> 8	47	-40, 22, -18	6.97	47
	44, 32, -16	6.25	47	40, 34, -14	5.56	47
Middle frontal gyrus				-40, 20, 50	5.12	6
Inferior parietal lobe/Middle temporal gyrus (clusters including pIPL, TPJ, LTC and TempP)	-50, -62, 34	> 8	39	-52, -66, 28	> 8	39

	60, -8, -24	7.69	21	56, 0, -28	6.80	21
	56, -62, 36	7.43	39	56, -58, 30	6.99	39
				-54, 0, -34	6.55	21
Posterior Cerebellum	30, -84, -38	6.87		-30, -86, -36	6.77	
	-26, -82, -36	6.55		30, -84, -36	5.80	

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels.

Table DS3(d) Regions correlating with the TPJ seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
TPJ seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Superior/Middle temporal gyrus (cluster including TPJ, LTC, TempP and pIPL)	-54, -54, 28	> 8	39	-54, -54, 28	> 8	39
Superior/Middle/Inferior frontal gyrus (clusters including dMPFC)	-6, 46, 46	> 8	8	-8, 46, 46	7.41	8
	-42, 14, 48	7.68	6	-50, 28, -10	7.61	47
	48, 36, -12	5.63	47	-40, 22, 50	5.50	6
Inferior parietal lobe/Middle temporal gyrus	56, -54, 36	6.88	40	56, -50, 36	7.84	40
	44, 14, -40	6.38	38	-58, -32, -6	7.11	21
	56, -32, -4	5.72	21			
Inferior temporal gyrus				-52, -8, -36	5.88	20

Posterior cingulate cortex/Midcingulate cortex/Precuneus (clusters including PCC)	-10, -52, 36	6.47	31	-2, -22, 42	5.67	31
	-2, -20, 42	6.21	31	-8, -52, 38	5.53	31
Posterior Cerebellum	20, -80, -32	6.96		20, -80, -34	6.73	

Abbreviations: BA, Brodmann area. [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels.

Table DS3(e) Regions correlating with the LTC seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
LTC seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Superior/Middle temporal gyrus, Medial/Superior/Inferior frontal gyrus & Inferior parietal lobe (clusters including TPJ, LTC, TempP, dMPFC, aMPFC, vMPFC and pIPL)	-60, -24, -18	> 8	21	-58, -24, -18	> 8	21
	-48, -64, 38	> 8	39	-48, -68, 40	> 8	39
				46, 16, -40	6.28	38
	60, -14, -18	> 8	21	60, -14, -18	7.84	21
	54, -62, 38	7.09	39	-12, 42, 54	6.85	6
				42, 36, -14	6.04	47
				-4, 52, -16	5.96	10
				-36, 50, -4	5.35	10
				16, 30, 56	5.20	6
				52, -58, 34	5.19	39

Posterior cingulate cortex/Precuneus (clusters including PCC)	-2, -44, 34	> 8	31	-4, -48, 36	6.58	31
				-2, -24, 40	5.43	31
Posterior cerebellum	26, -86, -34	> 8		44, -72, -42	7.09	
	-26, -86, -34	6.18				

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels.

Table DS3(f) Regions correlating with the TempP seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
TempP seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Superior/Middle temporal gyrus & Fusiform gyrus (clusters including TempP and LTC)	-50, 10, -40	> 8	38	-50, 10, -40	> 8	38
	54, 4, -34	> 8	21	52, -6, -32	> 8	20
Medial / Superior frontal gyrus (cluster including aMPFC, dMPFC, vMPFC§)	-2, 42, -20	> 8	11	-8, 48, 46	7.67	8
				14, 56, 42	5.20	8
Inferior parietal lobe/Middle temporal gyrus (clusters including pIPL and TPJ)	-48, -60, 30	7.19	39	-56, -64, 24	6.58	39
				58, -60, 28	5.37	39
Posterior cingulate cortex/Precuneus (clusters including PCC)	-2, -52, 34	6.65	31	-2, -54, 32	6.40	31
Anterior cingulate cortex	2, 4, -10	5.47	25			
Posterior Cerebellum	32, -88, -36	6.42		22, -80, -38	7.33	
	-32, -86, -36	5.34		-24, -84, -34	5.53	

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. [§] Significant main effects identified by a region of interest search in patients using a corrected threshold of P_{FWE} <.05.

Table DS3(g) Regions correlating with the vMPFC seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
vMPFC seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Anterior cingulate/Medial frontal cortex (clusters including aMPFC, vMPFC, dMPFC)	0, 26, -18	> 8	32	0, 26, -18	> 8	32
Parahippocampal gyrus/Amygdala (clusters including PHC[§], HF)	-24, -16, -20	7.34	28	-22, -16,-22	6.27	28
	20, -8, -18	7.19				
Posterior cingulate cortex (cluster including PCC, Rsp)	-2, -54, 24	7.33	23	-6, -56, 26	7.49	31
Inferior/Superior frontal gyrus	-20, 32, 52	7.04	6	40, 32, -20	6.15	47
	38, 36, -18	6.64	47	-14, 38, 50	5.70	6
	20, 36, 50	5.61	6			
Middle temporal gyrus/Inferior parietal lobe (clusters including pIPL)	-46, -74, 36	6.73	39	52, -64, 28	7.29	39
	48, -66, 34	5.71	39	-46, -70, 28	5.69	39
Inferior/Superior/Middle temporal gyrus (clusters including LTC, TempP)	-60, -18, -18	6.88	21	58, -8, -24	7.09	21
	62, -10, -20	6.72	21	-58, -18,-24	5.86	21
	-38, 14, -40	5.83	38	38, 16, -42	5.79	38
	-66, -42, -10	5.58	21	-42, 6, -44	5.60	38

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. * Significant within-group main effects

identified by a region of interest search using a corrected threshold of P_{FWE} <.05 in both groups. § Significant main effects identified by a region of interest search in patients using a corrected threshold of P_{FWE} <.05.

Table DS3(h) Regions correlating with the pIPL seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
pIPL seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Inferior parietal lobe/Middle temporal gyrus (cluster including pIPL)	-44, -74, 32	> 8	39	-44, -76, 32	> 8	39
Posterior cingulate cortex/Precuneus (cluster including PCC, Rsp)	-4, -62, 24	> 8	31	2, -62, 28	> 8	31
Inferior parietal lobe/Middle temporal gyrus	50, -64, 30	> 8	39	52, -66, 28	> 8	39
Superior/Medial frontal gyrus (cluster including aMPFC, vMPFC, dMPFC)	24, 32, 52	> 8	6	-28, 24, 58	7.25	6
	-6, 60, -4	7.56	10			
Middle frontal gyrus	-26, 26, 54	7.35	6			
Inferior temporal gyrus (cluster including LTC)	-60, -10, -16	6.35	21			
Middle temporal gyrus	58, -8, -20	5.93	21	-66, -20, -16		21
	-64, -36, -14	5.10	21	52, -4, -28		21
Parahippocampal gyrus (cluster including PHC*, HF*)	-28, -40, -12	5.66	36	-26, -38, -14	5.70	36
	-22, -14, -26	4.50	28	-26, -18, -26	5.42	36
Fusiform gyrus	-28, -40, -14	5.65	37			
Anterior cerebellum	18, -32, -14	5.71				
Posterior cerebellum				12, -90, -36	6.07	
				48, -64, -42	5.40	

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. * Significant within-group main effects identified by a region of interest search using a corrected threshold of P_{FWE} <.05 in both groups.

Table DS3(i) Regions correlating with the Rsp seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
Rsp seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Posterior cingulate cortex (cluster including Rsp, PCC, PHC, HF)	-14, -52, 8	> 8	30	-14, -52, 8	> 8	30
Anterior cingulate/Medial prefrontal gyrus (cluster including aMPFC, vMPFC)	6, 48, -10	> 8	32	-6, 54, -2	7.66	10
Inferior parietal lobe/Superior occipital gyrus (cluster including pIPL)	-34, -84, 30	6.28	19	-46, -74, 28	5.43	39

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e., main) effects are thresholded at P_{FWE} <.05, corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. * Significant within-group (main) effects identified by a region of interest search using a corrected threshold of P_{FWE} <.05 in both groups.

Table DS3(j) Regions correlating with the PHC seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
PHC seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Parahippocampal gyrus (cluster including HF, PHC, Rsp, PCC)	-28, -40, -10	> 8	36	-28, -40, -10	> 8	36
				22, -20, -18	> 8	35

Inferior parietal lobe/Superior occipital gyrus (cluster including pIPL)	-36, -80, 34	6.98	19	-40, -76, 30	6.61	19
Anterior cingulate/Medial prefrontal cortex (cluster including aMPFC§, vMPFC)	0, 14, -8	6.47	25	-4, 26, -14	6.16	24
				-4, 58, -6	4.57	10
Inferior parietal lobe/Superior occipital gyrus	44, -76, 34	6.47	19			
Precuneus	-4, -60, 48	5.50	7			

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. * Significant within-group (main) effects are identified by a small volume search using a corrected threshold of P_{FWE} <.05 in both groups. § Significant main effects identified by a region of interest search in patients using a corrected threshold of P_{FWE} <.05.

Table DS3(k) Regions correlating with the HF seed in OCD patients and healthy controls. Within-group (i.e. main) effects were derived from two-sample t-tests used to perform comparisons between groups (displayed in Table 1 of the main article). Effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. In the case of effect clusters including spheres of DMN seed regions used in this study, the name of the seed regions are indicated in brackets.

	Controls			**Patients**		
	Anatomy[a]	**Statistic[b]**		**Anatomy**	**Statistic**	
HF seed correlated region	**x, y, z**	***z* Score**	**BA**	**x, y, z**	***z* Score**	**BA**
Parahippocampal gyrus (cluster including HF, PHC)	-24, -20, -26	> 8	28	-24, -20, -26	> 8	28
	20, -14, -26	> 8	28	20, -14, -28	> 8	28
Posterior cingulate cortex (including PCC and Rsp)	-6, -54, 12	7.10	30	-4, -52, 14	7.08	29
Anterior cingulate/Medial prefrontal gyrus (clusters including aMPFC and vMPFC)	0, 20, -8	6.24	25		6.08	32
				-4, 22, -14	5.89	32
Inferior frontal gyrus				-32, 8, -22	6.39	47

Inferior parietal lobe (including IPL*)	48, -68, 30	5.47	39	-44, 70, 26	5.24	39
	-38, -72, 36	4.56	39			

Abbreviations: BA, Brodmann area; [a] Peaks of effect coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. [b] Magnitude statistics for within-group (i.e. main) effects are thresholded at P_{FWE} <.05, whole-brain corrected for multiple comparisons, using a minimum cluster extent (K_E) of 50 contiguous voxels. * Significant within-group (main) effects identified by a region of interest search using a corrected threshold of P_{FWE} <.05 in both groups.

Table DS4(a) Comparison of *unmedicated* OCD patients (*N*=23) and healthy controls (*N*=23) with respect to seed-based functional connectivity for the eleven default mode network regions of the left hemisphere. Peaks of connectivity difference coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. Between-group effects are thresholded at *P*<.0045 (cluster-corrected for multiple comparisons).

DMN subsystem	Seed region	Group difference region	Direction	MNI_{xyz}	*z* Score	CS	*P* value	BA
midline core	aMPFC	Posterior cerebellum (tonsil)	HC > OCDU	10, -58, -46	4.39	115	.002	
	PCC	n.s.						
dMPFC self system	dMPFC	Insula / Precentral gyrus	OCDU > HC	52, 4, 6	4.65	196	< .001	44, 13
		Anterior cerebellum (culmen) / retrosplenial cortex	HC > OCDU	-4, -50, -2	4.24	111	.002	
		Anterior cingulate cortex	HC > OCDU	-2, 44, -2	3.84	109	.003	32, 24
	TPJ	Precuneus	OCDU > HC	10, -80, 48	4.35	206	< .001	19
	LTC	Dorsal medial prefrontal cortex	HC > OCDU	-10, 48, 26	4.17	729	< .001	9, 10
	TempP	n.s.						
MTL memory system	vMPFC	n.s.						
	pIPL	n.s.						
	Rsp	Postcentral gyrus	HC > OCDU	-60, -14, 20	5.07	189	< .001	3, 43
		Posterior cerebellum	HC > OCDU	-18, -78, -10	3.73	113	.002	
	PHC	Middle occipital gyrus	HC > OCDU	-30, -86, 22	3.92	111	.002	19
		Precuneus	HC > OCDU	32, -70, 48	3.73	161	< .001	19
	HF	n.s.		-				

Abbreviations: HC, healthy controls; OCDU, obsessive-compulsive disorder, unmedicated; aMPFC, anterior medial prefrontal cortex; PCC, posterior cingulate cortex; dMPFC, dorsal medial prefrontal cortex; TPJ, temporal parietal junction; LTC, lateral temporal cortex; TempP, temporal pole; vMPFC, ventral medial prefrontal cortex; pIPL, posterior inferior parietal lobule; Rsp, retrosplenial cortex; PHC, parahippocampal cortex; HF=hippocampal formation; MTL, medial temporal lobe; CS, cluster size; BA, Brodmann area; DMN, Default mode network.

Table DS4(b) Comparison of *medicated* OCD patients (*N*=23) and healthy controls (*N*=23) with respect to seed-based functional connectivity for the eleven default mode network regions of the left hemisphere. Peaks of connectivity difference coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. Between-group effects are thresholded at *P*<.0045 (cluster-corrected for multiple comparisons).

DMN subsystem	Seed region	Group difference region	Direction	MNI_{xyz}	*z* Score	CS	*P* value	BA
midline core	aMPFC	n.s.						
	PCC	Fusiform gyrus	OCDM > HC	-48, -58, -14	3.96	165	< .001	37
dMPFC self system	dMPFC	n.s.						
	TPJ	n.s.						
	LTC	Middle temporal gyrus	OCDM > HC	60, -62, -2	3.91	139	< .001	37
	TempP	n.s.						
MTL memory system	vMPFC	Middle frontal gyrus	HC > OCDM	-44, 52, -14	4.63	142	< .001	10
		Postcentral / Precentral gyrus	OCDM > HC	-6, -28, 76	4.60	140	< .001	3, 4
	pIPL	n.s.						
	Rsp	Inferior frontal gyrus	OCDM > HC	-44, 28, 6	5.59	251	< .001	13
	PHC	n.s.						
	HF	n.s.						

Abbreviations: HC, healthy controls; OCDM, obsessive-compulsive disorder, medicated; aMPFC, anterior medial prefrontal cortex; PCC, posterior cingulate cortex; dMPFC, dorsal medial prefrontal cortex; TPJ, temporal parietal junction; LTC, lateral temporal cortex; TempP, temporal pole; vMPFC, ventral medial prefrontal cortex; pIPL, posterior inferior parietal lobule; Rsp, retrosplenial cortex; PHC, parahippocampal cortex; HF=hippocampal formation; MTL, medial temporal lobe; CS, cluster size; BA, Brodmann area; DMN, Default mode network.

Table DS4(c) Comparison of *unmedicated* OCD patients (*N*=23) and *medicated* OCD patients (*N*=23) with respect to seed-based functional connectivity for the eleven default mode network regions of the left hemisphere. Peaks of connectivity difference coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. Between-group effects are thresholded at *P*<.0045 (cluster-corrected for multiple comparisons).

DMN subsystem	Seed region	Group difference region	Direction	MNI_{xyz}	*z* Score	CS	*P* value	BA
midline core	aMPFC	n.s.						
	PCC	n.s.						
dMPFC self system	dMPFC	n.s.						
	TPJ	Posterior cerebellum (tonsil)	OCDU > OCDM	-26, -60, -50	4.03	242	< .001	
	LTC	n.s.						
	TempP	n.s.						
MTL memory system	vMPFC	n.s.						
	pIPL	n.s.						
	Rsp	Medial frontal / cingulate gyrus	OCDU > OCDM	6, 10, 48	3.85	157	< .001	6, 24
	PHC	n.s.						
	HF	Middle frontal gyrus	OCDM > OCDU	-34, 10, 50	4.35	192	< .001	6, 8

Abbreviations: HC, healthy controls; OCDU, obsessive-compulsive disorder, unmedicated; OCDM, obsessive-compulsive disorder, medicated; aMPFC, anterior medial prefrontal cortex; PCC, posterior cingulate cortex; dMPFC, dorsal medial prefrontal cortex; TPJ, temporal parietal junction; LTC, lateral temporal cortex; TempP, temporal pole; vMPFC, ventral medial prefrontal cortex; pIPL, posterior inferior parietal lobule; Rsp, retrosplenial cortex; PHC, parahippocampal cortex; HF=hippocampal formation; MTL, medial temporal lobe; CS, cluster size; BA, Brodmann area; DMN, Default mode network.

Table DS5 Comparison of *OCD patients without history of affective disorders* (*N*=18) and *matched* healthy control participants (*N*=18) with respect to seed-based functional connectivity for the eleven default mode network regions. Peaks of connectivity difference coordinates (x, y, z) are given in Montreal Neurological Institute (MNI) space. Between-group effects are thresholded at *P*<.0045 (cluster-corrected for multiple comparisons).

DMN subsystem	Seed region	Group difference region	Direction	MNI_{xyz}	*z* Score	CS	*P* value	BA
midline core	aMPFC	Anterior Cingulate/Anterior medial prefrontal cortex	HC > OCD	8, 34, -8	3.76	111	.002	24, 32
	PCC	n.s.						
dMPFC self system	dMPFC	Middle frontal/Dorsal medial prefrontal cortex	HC > OCD	-22, 38, 30	4.54	111	.002	8, 9
		Dorsal medial prefrontal cortex	HC > OCD	-6, 54, 16	4.35	129	< .001	9
	TPJ	n.s.						
	LTC	Anterior Cingulate/Dorsal medial prefrontal cortex	HC > OCD	-10, 36, 20	4.30	222	< .001	32, 9
	TempP	Anterior Cingulate/Dorsal medial prefrontal cortex	HC > OCD	-2, 42, 20	4.18	207	< .001	32, 9
		Caudate	HC > OCD	8, 10, 8	4.05	175	< .001	
MTL memory system	vMPFC	n.s.						
	pIPL	n.s.						
	Rsp	n.s.						
	PHC	n.s.						
	HF	Putamen	HC > OCD	32, 8, -2	4.15	117	.002	

Abbreviations: HC, healthy controls; OCD, obsessive-compulsive disorder, unmedicated; aMPFC, anterior medial prefrontal cortex; PCC, posterior cingulate cortex; dMPFC, dorsal medial prefrontal cortex; TPJ, temporal parietal junction; LTC, lateral temporal cortex; TempP, temporal pole; vMPFC, ventral medial prefrontal cortex; pIPL, posterior inferior parietal lobule; Rsp, retrosplenial cortex; PHC, parahippocampal cortex; HF=hippocampal formation; MTL, medial temporal lobe; CS, cluster size; BA, Brodmann area; DMN, Default mode network.

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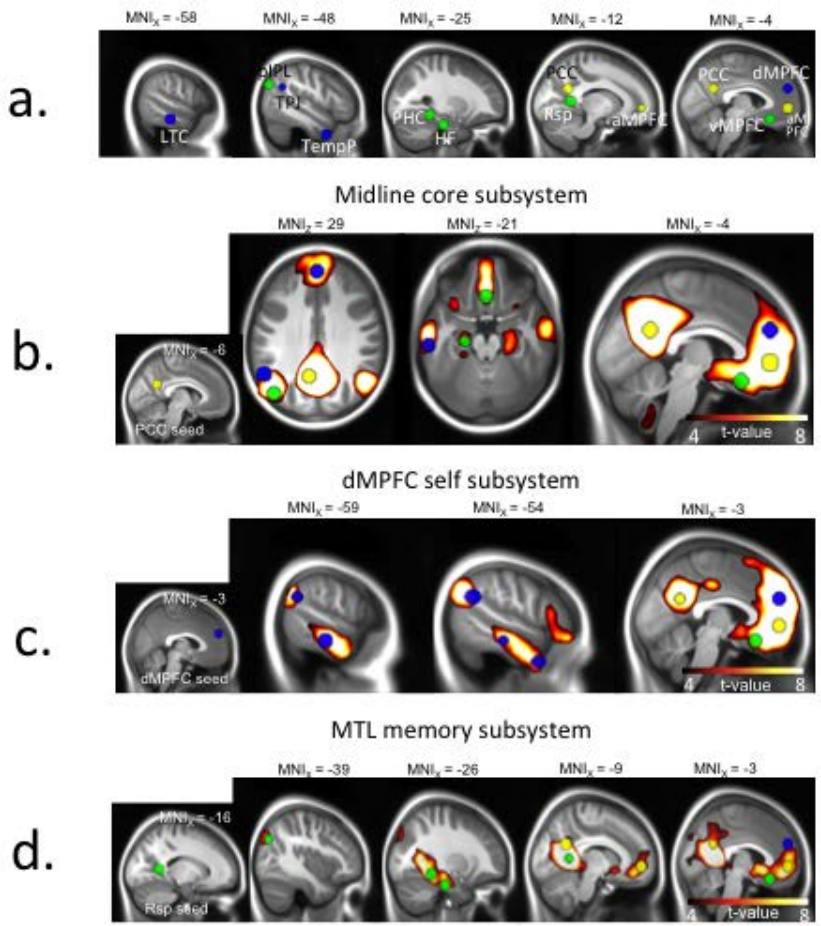

Fig. DS1 Identification of default mode network (DMN) subsystems using resting-state functional connectivity MRI in 46 healthy controls. (a) Eleven 8mm sphere DMN seed regions were used to identify subsystems (see online Table DS2 for MNI coordinates). Midline core regions are displayed in yellow, dMPFC self regions in blue, and medial temporal lobe (MTL) memory regions in green colour. (b) Functional connectivity within the midline core as revealed by the posterior cingulate cortex (PCC) seed, correlating with anterior medial prefrontal cortex (aMPFC) as the second midline core component and both dorsomedial prefrontal cortex (dMPFC) self and MTL memory subsystems. (c) Functional connectivity within the dMPFC self subsystem as revealed by the dMPFC seed, correlating with the remaining dMPFC self subsystem components (lateral temporal cortex (LTC) temporal pole (TempP) and temporal parietal junction (TPJ)) and the midline core. (d) Functional connectivity within the MTL memory subsystem as revealed by the retrosplenial (Rsp) seed, correlating with the remaining MTL memory subsystem components (parahippocampal cortex (PHC), hippocampal formation (HF), posterior inferior parietal lobule (pIPL) and ventral medial prefrontal cortex (vMPFC)) and the midline core.

Figure DS2

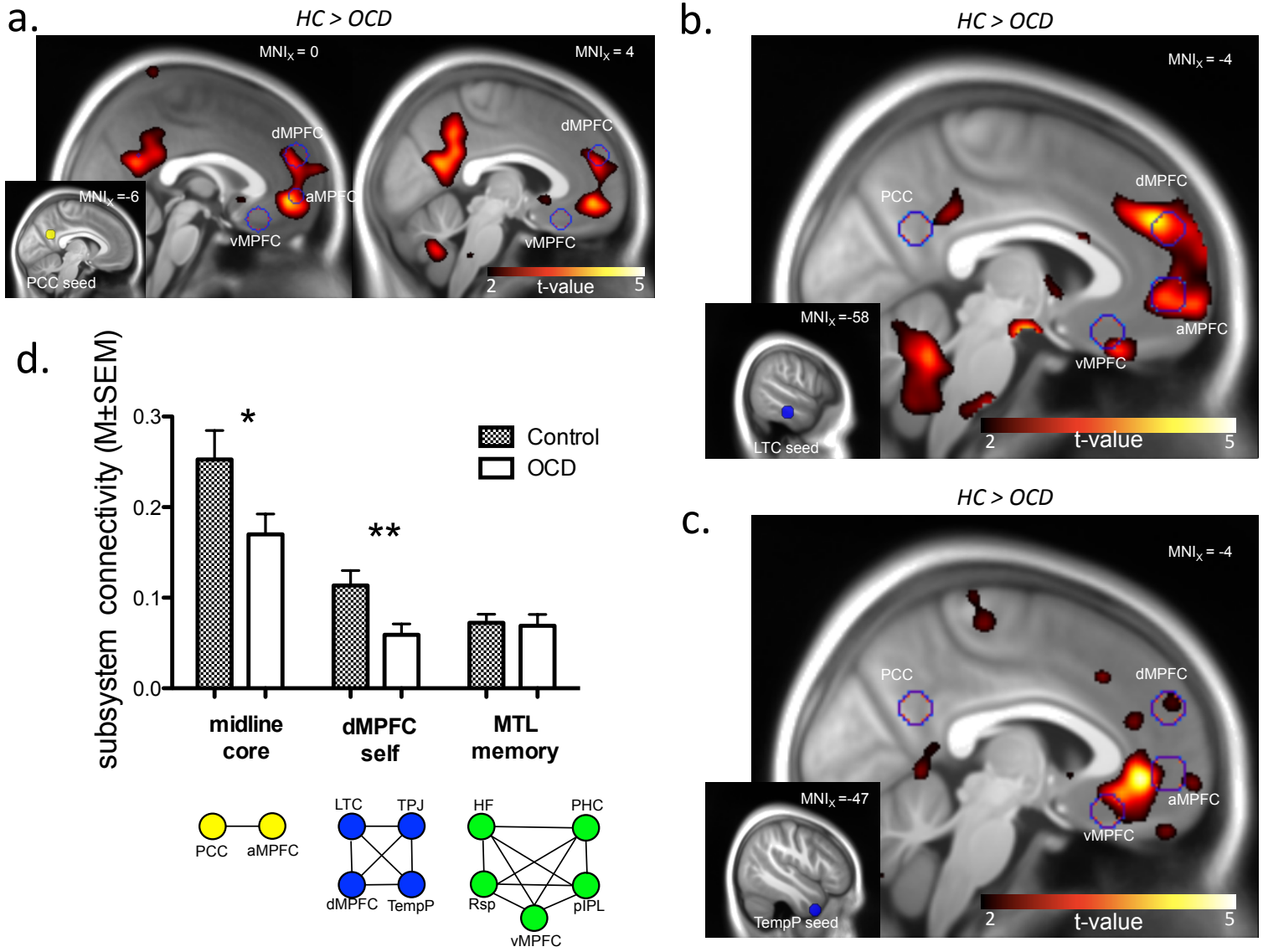
a.
HC > OCD
MNIx = 0
MNIx = 4
dMPFC
aMPFC
vMPFC
MNIx =-6
PCC seed
2
t-value
5
b.
HC > OCD
MNIx = -4
PCC
dMPFC
aMPFC
vMPFC
MNIx =-58
LTC seed
2
t-value
5
c.
HC > OCD
MNIx = -4
PCC
dMPFC
aMPFC
vMPFC
MNIx =-47
TempP seed
2
t-value
5
d.
subsystem connectivity (M±SEM)
0.3
0.2
0.1
0.0
*
**
Control
OCD
midline core
dMPFC self
MTL memory
PCC
aMPFC
LTC
TPJ
dMPFC
TempP
HF
PHC
Rsp
pIPL
vMPFC

Fig. DS2 Reduced within default mode network subsystem connectivity in patients with obsessive–compulsive disorder (OCD) as compared with healthy controls (control group (HC) > OCD group). (a) Reduced connectivity between posterior cingulate cortex (PCC) seed and anterior medial prefrontal cortex (aMPFC) and contralateral PCC, indicating reduced connectivity within the midline core in the OCD group. (b) Reduced connectivity between lateral temporal cortex (LTC) seed and the dorsomedial prefrontal cortex (dMPFC), indicating reduced connectivity in the dMPFC self system in the OCD group. (c) Reduced connectivity between temporal pole (TempP) seed and anterior cingulate/medial prefrontal cortex in the OCD group compared with the control group. Blue circles indicate locations of default mode network seed regions used to study default mode network functional connectivity in the present study. (d) Results from voxel-based region of interest (ROI)-to-ROI analyses (online supplement DS1), revealing reduced connectivity in midline core and dMPFC self system when exclusively considering the correlation among single voxels representing components of the three subsystems. The schematic figures of the three subsystems illustrate the connections (i.e. correlation coefficients) that were considered to derive an index for the averaged connectivity within the subsystems (i.e. one connection for the midline core, six connections for the dMPFC self system, ten connections for the medial temporal lobe (MTL) memory system). * indicates significance at $P<0.05$, ** corresponds to the corrected threshold of $P<0.017$. MNI, Montreal Neurological Institute; vMPFC, ventral medial prefrontal cortex; SEM, standard error of the mean; TPJ, temporal parietal junction; HF, hippocampal formation; PHC, parahippocampal cortex; Rsp, retrosplenial cortex; pIPL, posterior inferior parietal lobule.

Figure DS3

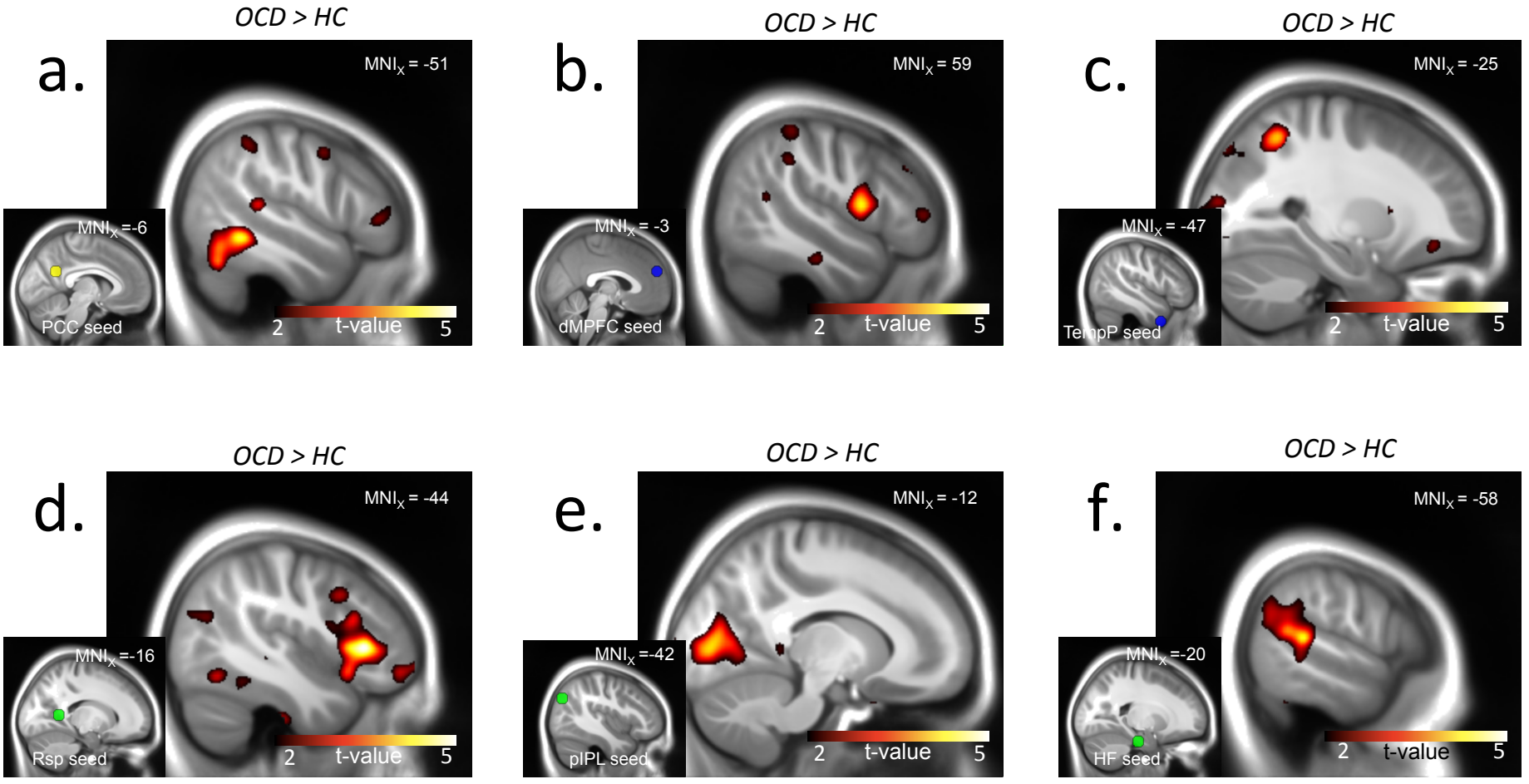
a.
OCD > HC
MNI$_X$ = -51
MNI$_X$ =-6
PCC seed
2
t-value
5
b.
OCD > HC
MNI$_X$ = 59
MNI$_X$ = -3
dMPFC seed
2
t-value
5
c.
OCD > HC
MNI$_X$ = -25
MNI$_X$ = -47
TempP seed
2
t-value
5
d.
OCD > HC
MNI$_X$ = -44
MNI$_X$ =-16
Rsp seed
2
t-value
5
e.
OCD > HC
MNI$_X$ = -12
MNI$_X$ =-42
pIPL seed
2
t-value
5
f.
OCD > HC
MNI$_X$ = -58
MNI$_X$ =-20
HF seed
2
t-value
5

Fig. DS3 Higher connectivity between default mode network and other cortical regions in patients with obsessive–compulsive disorder (OCD) as compared with the healthy control group (OCD group > control (HC) group).Brain areas showing significantly (P<0.0045, cluster-corrected for multiple comparisons) higher connectivity with default mode network seeds in the OCD group compared with the control group. (a) The fusiform gyrus with the posterior cingulate cortex (PCC) seed; (b) the anterior insula with the dorsomedial prefrontal cortex (dMPFC) seed; (c) the superior parietal lobule with the temporal pole (TempP) seed; (d) the inferior frontal gyrus with the retrosplenial (Rsp) seed; (e) the lingual gyrus with the posterior inferior parietal lobule (pIPL) seed; (f) the superior temporal gyrus with the hippocampal formation (HF) seed.

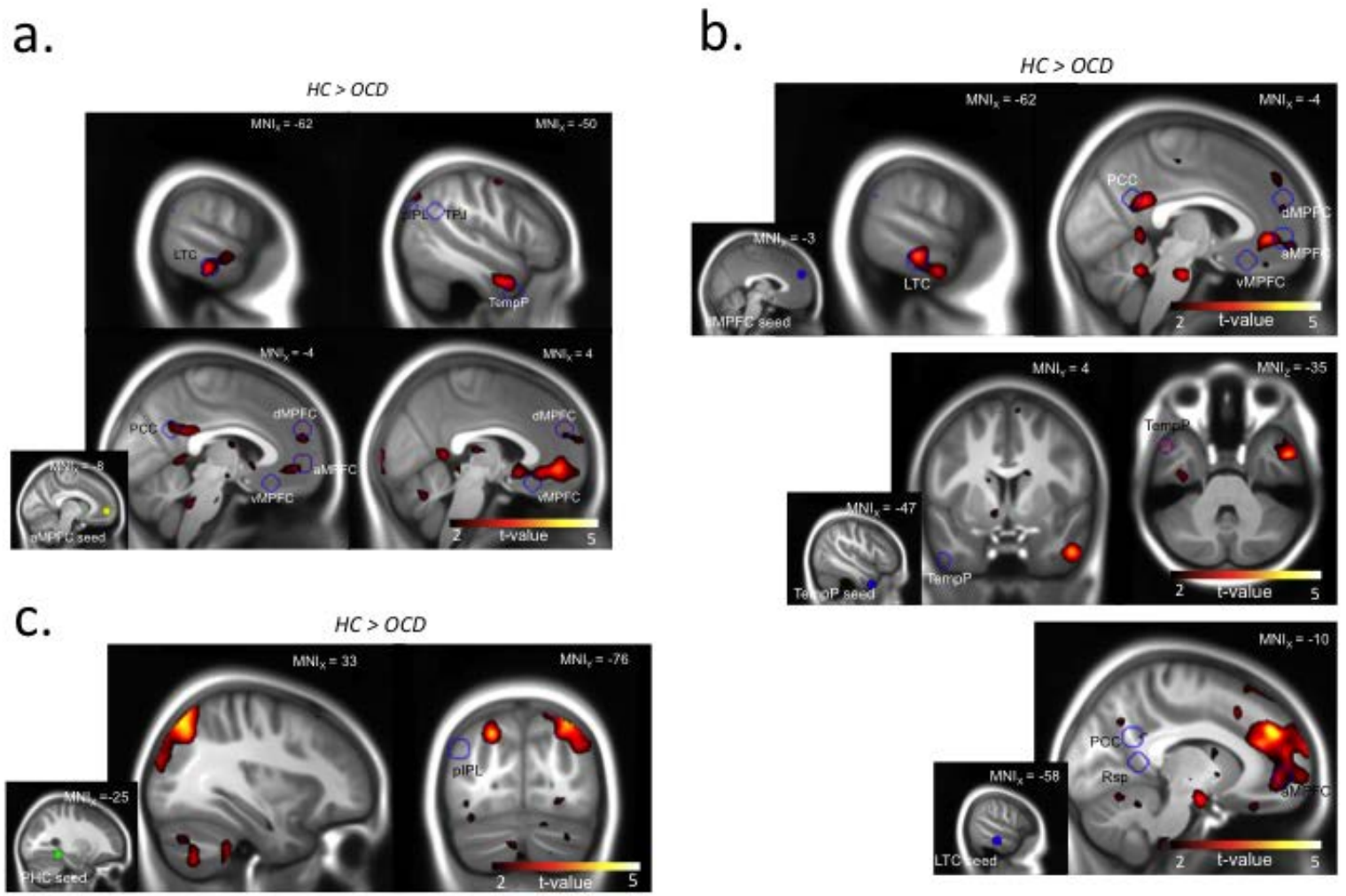

Fig. DS4 Additional slices revealing reduced connectivity with DMN seed regions in OCD group compared with healthy controls (HC) (HC > OCD, *n*=46 *v.* *n*=46). (a) trends (*P*<0.001, uncorrected) for reduced connectivity of the anterior medial prefrontal cortex (aMPFC) seed with temporal pole (TempP), temporal parietal junction (TPJ) and dorsomedial prefrontal cortex (dMPFC); (b) trends (*P*<0.001, uncorrected) for reduced connectivity of the dMPFC seed with LTC and midline core, and for the TempP seed with the contralateral temporal pole, and additional slices showing significant differences with respect to connectivity of the lateral temporal cortex (LTC) seed in addition to Fig. DS2(b); (c) significantly reduced connectivity of the superior parietal lobule with the parahippocampal cortex (PHC) seed in the OCD group compared with the control group.

Fig. DS5 Confirmatory seed-to-voxel results for (a) dorsal attention, (b) salience and (c) executive control networks (obsessive–compulsive disorder (OCD) group >control (HC) group). Higher connectivity of the superior parietal lobule (SPL) seed with midline core and temporal pole (TempP) (a), between the anterior insula seed and anterior medial prefrontal cortex (aMPFC), parahippocampal cortex (PHC), TempP and lateral temporal cortex (LTC) (b), and between the dorsolateral prefrontal cortex (DLPFC) seed and the midline core and lateral temporal regions. dMPFC, dorsomedial prefrontal cortex; vMPFC, ventral medial prefrontal cortex; PCC, posterior cingulate cortex; Rsp, retrosplenial cortex; pIPL, posterior inferior parietal lobule; TPJ, temporal parietal junction; HF, hippocampal formation; LTC, lateral temporal cortex.

Figure DS6

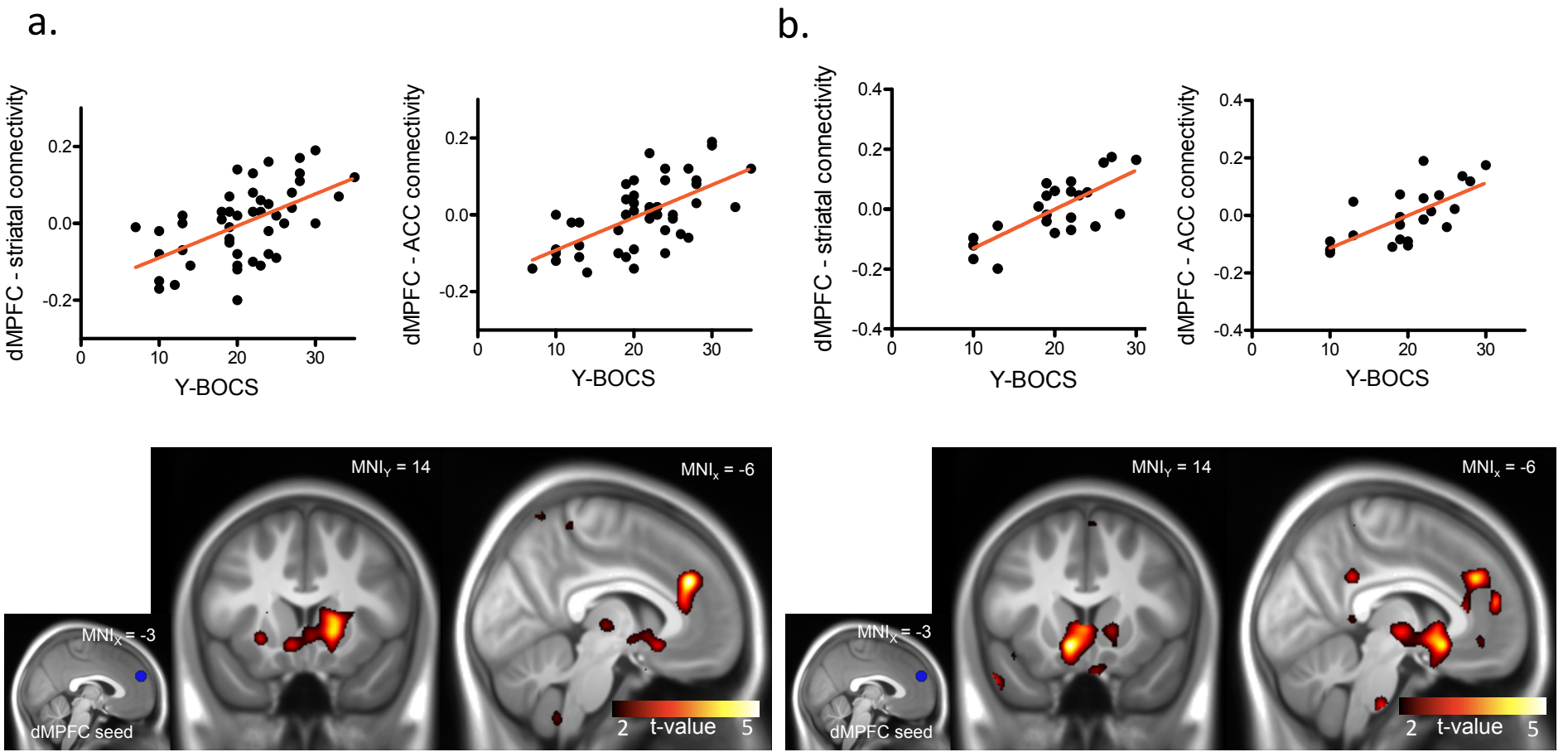
a.
b.
dMPFC - striatal connectivity
dMPFC - ACC connectivity
Y-BOCS
0.2
0.0
-0.2
0.4
-0.4
0
10
20
30
MNI$_Y$ = 14
MNI$_x$ = -6
MNI$_x$ = -3
dMPFC seed
2
t-value
5

Fig. DS6 Correlation between dorsomedial prefrontal cortex (dMPFC) connectivity and global obsessive–compulsive disorder (OCD) symptom severity. Positive relationships were evident between dMPFC connectivity with the ventral striatum and also the anterior cingulate cortex and total Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores. (a) Effects in the entire OCD group (n=46); (b) effects in unmedicated patients in the OCD group only (n=23). ACC, anterior cingulate cortex.