Functional connectivity alterations between the DMN and occipital cortex in patients with OCD

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Introduction

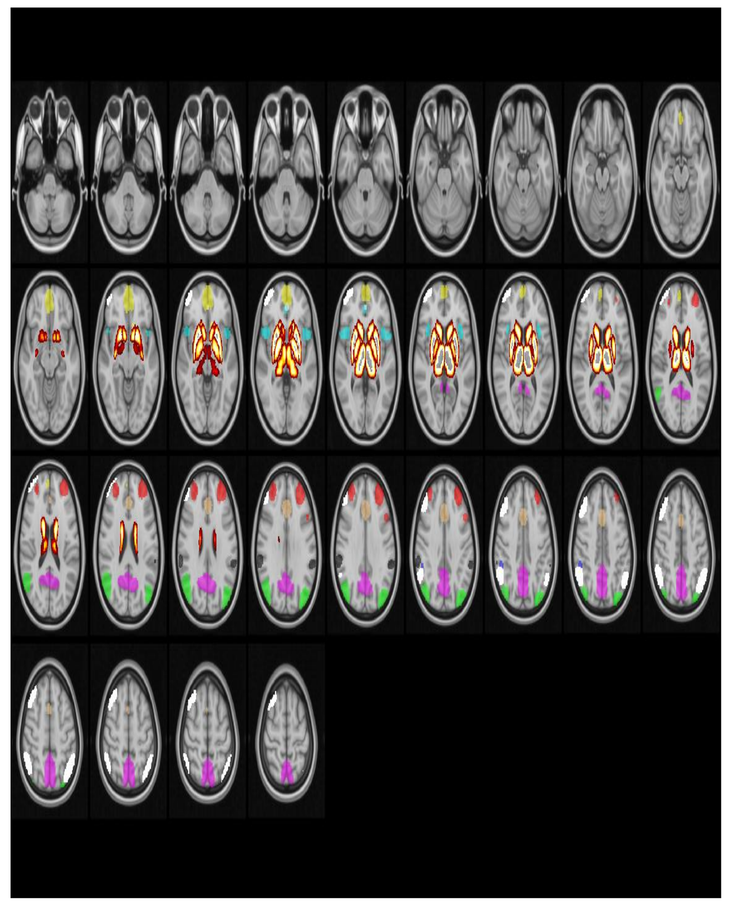
OCD (Obsessive Compulsive Disorder) is disabling psychiatric conditioning, with a prevalence of 2%-3% in the general population. OCD is characterized by obsessions (persistent and intrusive thoughts) and compulsions (rituals or repetitive behaviour performed to reduce the anxiety caused by obsessions). The pathophysiology of OCD was often conceptualized via the cotrico-striato-thalamo-cortical model (Milad and Rauch, 2012); many studies presented volumetric and connectivity changes in those regions among OCD patients. A meta-analysis focusing on resting-state functional MRI (rs-fMRI) seed analysis (Gürsel et al., 2018) found altered connectivity inside the Default Mode Network (DMN), Salience (SN), and Frontoparietal (FPN) networks as well as hypoconnectivity between these three networks. Additionally, the Fronto-Striatal-Circuitry presented general dysconnectivity (no specific direction of connectivity change).

We aimed to test the replicability of the meta-analysis findings in OCD patients.

Methods

A total of 64 participants completed 13 minutes of resting-state fMRI 3T with eyes open (27 OCD patients and 37 age, sex, and education matched healthy controls, HC). Seed to voxel (whole brain) analyses were conducted for 30 seeds based on the reported findings in Gürsel's meta-analysis (figure 1, table 1). Five seeds were created with five-diameter spheres based on the coordinates of the significant group-difference clusters. In addition, 15 seeds were constructed to represent FPN, DMN, SN from the CONN ICA network (Whitfield-Gabrieli et al., 2012), and ten seeds to represent the thalamus and the striatum based on the Harvard-Oxford Atlas sub-Cortical Structural Atlas (Caviness et al., 1996). For each seed-to-voxel analysis, we performed separate second-level GLMs to compare OCD with controls, including maximum motion as a covariate via the CONN toolbox v.19c. We considered findings significant at FWE-corrected p-values ≤ 0.05 at cluster and voxel level. Moreover, we probed the robustness of our findings using two different parcellation approaches 1) utilizing the DiFuMo functional atlas (Dadi et al., 2020) and 2) using Independent Component Analysis (ICA) as data-driven network parcellation to use as seeds.

Figure 1 & Table 1: 30 seeds for the seed to voxel analyses



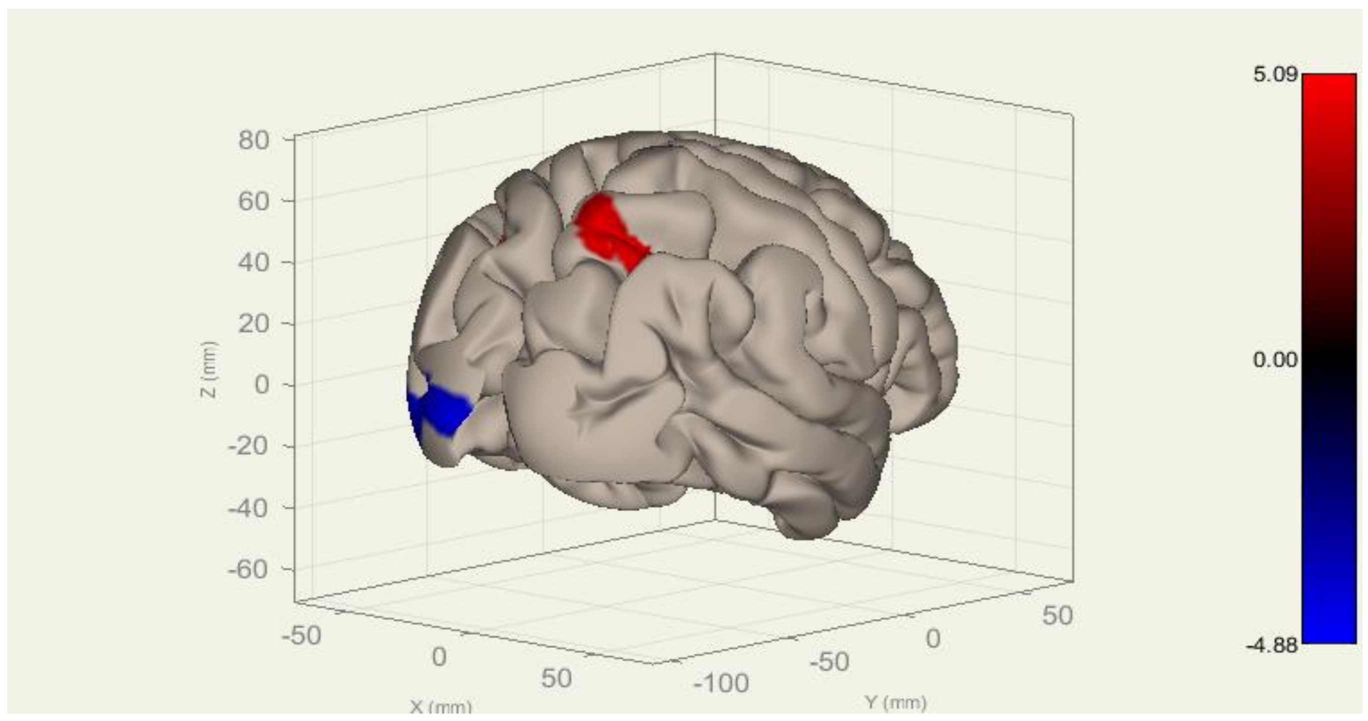
	seed	K	source
1	Thalamus r	24,274	Harvard-Oxford
2	Thalamus l	24,134	Harvard-Oxford
	Striatum related seeds		
3	Caudate r	17126	Harvard-Oxford
4	Caudate l	16087	Harvard-Oxford
5	Putamen r	20057	Harvard-Oxford
6	Putamen l	19805	Harvard-Oxford
7	Pallidum r	9932	Harvard-Oxford
8	Pallidum l	9565	Harvard-Oxford
9	Accumbens r	4431	Harvard-Oxford
10	Accumbens l	4699	Harvard-Oxford
	Default Mode Network (DMN) related seeds		
11	Medial Pre-Frontal Cortex (MPFC)	1346	ICA_CONN
12	Lateral Parietal (l) (LPl)	1041	ICA_CONN
13	Lateral Parietal (r)	1326	ICA_CONN
14	Posterior Cingulate Cortex (PCC)	4833	ICA_CONN
	Salience Network related seeds		
15	Anterior Cingulate Cortex (ACC)	1063	ICA_CONN
16	Insula l	446	ICA_CONN
17	Insula r	338	ICA_CONN
18	Rostral Pre-Frontal Cortex l (RPFC l)	1166	ICA_CONN
19	Rostral Pre-Frontal Cortex r (RPFC r)	581	ICA_CONN
20	supramarginal gyrus l (SMG l)	233	ICA_CONN
21	supramarginal gyrus r (SMG r)	284	ICA_CONN
	Frontal Parietal Network (FPN) related seeds		
22	Lateral Pre-Frontal Cortex l (LPFC l)	1703	ICA_CONN
23	Lateral Pre-Frontal Cortex r (LPFC r)	1758	ICA_CONN
24	Posterior Parietal Cortex (PPC l)	832	ICA_CONN
25	Posterior Parietal Cortex (PPC r)	837	ICA_CONN
	A meta-analysis (Gürsel et al., 2018) related seeds		
26	Anterior Cingulate Cortex (ACC as part of DMN)	81	Meta-analysis
27	Medial Pre-Frontal Cortex (MPFC as part of DMN)	81	Meta-analysis
28	Limbic (as part of FPN)	81	Meta-analysis
29	middle frontal gyrus (as part of FPN)	81	Meta-analysis
30	Right Supramarginal Gyrus (as part of SN)	81	Meta-analysis

Functional connectivity group differences

Seed	Peak cluster (x, y, z)	K	size pFWE	pFWE* 30 seeds	Cluster location	T -value
DMN					-	
Lateral Parietal Left (LP_l)	(-32 -94 -2)	677	0.000	**0.000**	OP l (Occipital Pole Left); iLOC l (Lateral Occipital Cortex, inferior division Left)	-5.28
	(+26 -60 +50)	195	0.035	NS	sLOC r (Lateral Occipital Cortex, superior division Right); Precuneous (Precuneous Cortex)	4.66
Lateral Parietal Right (LP_r)	(-34 -94 -04)	486	0.000	**0.006**	OP l (Occipital Pole Left); iLOC l (Lateral Occipital Cortex, inferior division Left)	-4.88
	(+24 -54 +40)	450	0.000	**0.01**	sLOC r (Lateral Occipital Cortex, superior division Right); Precuneous (Precuneous Cortex)	5.09
	(-28 -36 +42)	203	0.028	NS	SPL l (Superior Parietal Lobule Left); sLOC l (Lateral Occipital Cortex, superior division Left)	4.92
Posterior Cingulate Cortex (PCC)	(+02 -82 +34)	181	0.041	NS	Cuneal r (Cuneal Cortex Right); Cuneal l (Cuneal Cortex Left); OP l (Occipital Pole Left)	-4.76
SN						
Anterior Cingulate Cortex (ACC)	(+40 -86 -12)	353	0.002	NS	iLOC r (Lateral Occipital Cortex, inferior division Right); OP r (Occipital Pole Right)	4.9
Insula_l	(+50 -74 -06)	265	0.007	NS	iLOC r (Lateral Occipital Cortex, inferior division Right)	4.80
Insula_r	(+22 -54 +20)	291	0.005	NS	Precuneous (Precuneous Cortex)	-5.02

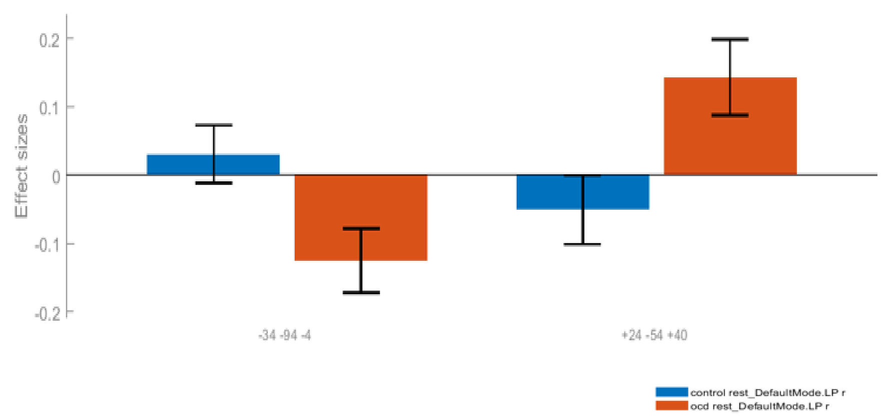
MNI coordinates; Significant = p <0.05 size pFWE corrected. Nine clusters presented significant group differences (OCD vs. HC) for seed regions of the DMN and the SN. After additional correction for the number of seed-to-voxel analyses, three clusters based on DMN seeds remained significant: (LP_r/l) to the left occipital pole and LP_r to a cluster comprised the right superior Lateral Occipital Cortex (sLOC_r) and the precuneus.

Highly significant connectivity alterations in OCD



Significant connectivity alterations in OCD: Significant connected clusters to LP_r (OCD>control) after correction for multiplied comparisons and number of ROIs (p_{FWE}*30 ROIs<0.05): [+24 -54 +40] (sLOC_r, PREC) hyperconnectivity indicated a pattern of stronger positive connectivity in the OCD group ; [-34 -94 -04] (OP_l, iLOC_l) hypoconnectivity indicated a pattern of stronger negative (i.e., inverse) connectivity in the OCD group. MNI Coordinates (results were similar to bilateral seed LP_l).

Group effect size for the highly significant clusters



The effect size for OCD and HC: connectivity measures between LP_r to [-34 -94 -04] left occipital pole and [+24-54 +40] occipital lateral right.

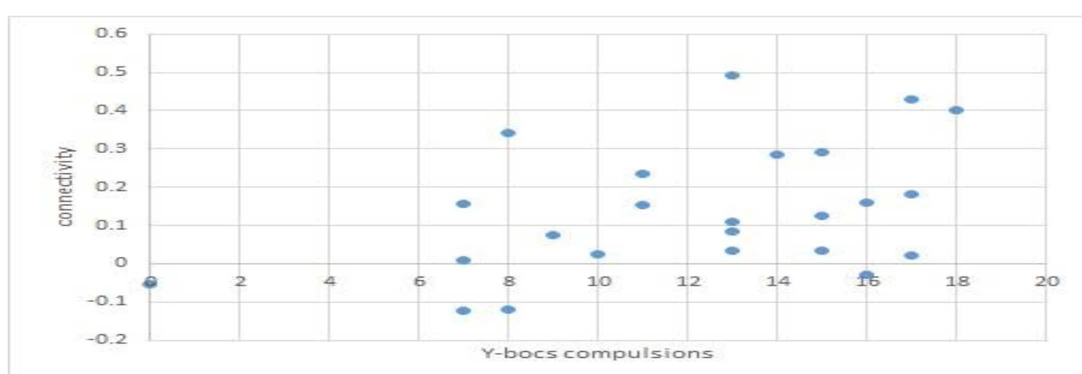
Participant's psychopathology and demographic measures

Demographic	Mean ± SD HC	OCD	*p-value*
N	33	24	
Age	35.7 ± 11.5	37.2 ± 11.9	0.61
Gender (M/F)	15/18	13/11	0.52
Education level	3	3	0.64
BDI	2.6±3	19.2±13.5	0.00
STAI	32.1±5.9	47.2±12.8	0.00
OCI	10.3 ± 9.8	29 ±13.1	0.00
IQ_WST	107 ± 8.4	106 ± 9.5	0.68
Y-BOCS	-	22.42 ± 7.6	-

After default pre-processing seven participants were excluded due to quality assurance reports.

Mean (standard deviation) of demographic variables and questionnaires scores for OCD and control groups. BDI: Beck Depression Inventory; STAI: The State-Trait Anxiety Inventory; OCI: Obsessive-Compulsive Inventory; IQ_WST: Verbal IQ; Y-BOCS: Yale-Brown Obsessive-Compulsive Scale. Significant=p<0.05

Correlation between hyperconnectivity to OCD compulsion severity



Among OCD patients: positive Pearson correlation between connectivity measures between LP_r and of [+24 -54 +40] to Y-BOCS compulsions scale (r = 0.43, p<0.05, N = 24).

Discussion

Our findings replicated partly the meta-analysis findings of Gürsel et al., specifically SN and DMN hypoconnectivity, by using seeds based on the meta-analysis. We identified aberration between the SN and, in particular, the DMN to the visual network. This raises the question about the visual system's involvement in OCD symptoms and the abnormal connectivity of a unimodal region as the visual network to the multimodal DMN. Previous studies found evidence for decreased metabolic activities, abnormal connectivity, and volumetric changes in the left inferior parietal and parietal-occipital junction, suggesting the possible existence of visual processing deficits in OCD (Gonçalves et al., 2010). Our findings support those previous discoveries. Several studies (Ravindran et al., 2020; Stern et al., 2016) presented significant hyperconnectivity among OCD patients between DMN-related seeds and the visual cortex primary regions V1 and V2 after viewing or imagining an OCD related stimuli to evoke stress. Since the regions in which we found abnormal connectivity in our study during resting-state are similar, this raises the question of whether the abnormal emotion-related visual-to-DMN connectivity might point towards cognitive occupation with symptoms, also during our rest measure, in the absent of OCD threatening stimuli.

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