

**Appendix 1** to Kwon, JS, Kim, T, Kwak, S et al. The Neural Bases of Clinical and Neurocognitive Differences between Early- and Late-Onset Obsessive-Compulsive Disorder. *J Psychiatry Neurosci* 2019.

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## **Supplementary Results**

### *Demographic and clinical characteristics in the subset analysis*

In the subset analysis that matched patients on the duration of illness rather than age, early-onset patients were younger ( $F(2, 165) = 11.95, p < .001$ ) than late-onset patients and healthy controls (HCs) (Table S1). They also had an earlier age at onset ( $t(45) = -10.84, p < .001$ ) than late-onset patients. Other demographic and clinical variables were not significantly different between groups.

### *Neurocognitive differences in the subset analysis*

In the subset analysis comparing neurocognitive functions, there were significant group effects for the COWA letter ( $F(2, 145) = 3.43, p < .05$ ), WAIS BD ( $F(2, 164) = 5.92, p < .01$ ), RCFT organization ( $F(2, 145) = 5.29, p < .01$ ), and IED ( $F(2, 125) = 5.01, p < .01$ ). In post hoc results, worse performances in the WAIS BD and IED were replicated in late-onset patients compared to HCs. The WAIS BD performance in late-onset patients ( $M = 12.30, SD = 2.64$ ) was significantly worse than early-onset patients ( $M = 14.00, SD = 2.55$ ). In addition, the RCFT organization score ( $M = 5.26, SD = 1.84$ ) was lower in late-onset patients compared to HCs ( $M = 6.39, SD = 1.54$ ). However, early-onset patients no more showed worse RCFT copy & IR, and IED (Table S2).

### *Whole brain volumetric comparisons in the subset analysis*

As shown in Table S4, the ANOVA group effects were similar to the results of total dataset. In the post hoc comparison between the two OCD subgroups, larger volumes of the right medial OFG (peak at (15, 26, -27),  $T = 5.15$ , corrected  $p < .001$ , cluster size = 903) and left MFG (peak at (-42, 9, 56),  $T = 4.31$ , corrected  $p < .05$ , cluster size = 188) were replicated in early-onset patients. They also had larger right precentral gyrus volume (peak at (54, 12, 33),  $T = 4.68$ , corrected  $p < .001$ , cluster size = 515) compared to late-onset patients.

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Table S1. Demographic and clinical characteristics of the subset

Variables	Early-onset OCD (N=34)	Late-onset OCD (N=31)	HCs (N=103)	Statistics	
	N			X <sup>2</sup> (df)	p
Sex (Male/Female)	22/12	16/15	64/39	1.39 (2)	0.499
Handedness (Left/Right)	3/31	3/28	7/96	0.35 (2)	0.841
Medication exposure (Drug-naïve/Unmedicated)	9/25	13/18		1.73 (1)	0.188
Symptom dimensions <sup>a</sup>					
Aggressive/checking	12 (35 %)	17 (55 %)		2.61 (1)	0.106
Contamination/cleaning	11 (32 %)	12 (39 %)		0.30 (1)	0.583
Symmetry/ordering	14 (41 %)	7 (23 %)		2.58 (1)	0.108
Sexual/religious	4 (12 %)	3 (10 %)		0.07 (1)	0.789
Hoarding	1 (3 %)	0 (0 %)		0.92 (1)	0.336
Miscellaneous	15 (44 %)	11 (35 %)		0.50 (1)	0.48
		<b>Mean (SD)</b>		<b>F (df)</b>	<b>p</b>
Age (years)	20.50 (2.90)	27.13 (4.19)	25.24 (6.86)	11.95 (2, 165)	< .001
IQ <sup>b</sup>	110.74 (9.25)	109.87 (12.46)	113.13 (12.62)	1.12 (2, 164)	0.330
TIV (L)	1.54 (0.14)	1.47 (0.11)	1.49 (0.15)	2.30 (2, 165)	0.103
				<b>T (df)</b>	<b>p</b>

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Age at onset (years)	13.79 (1.92)	21.58 (3.56)	-10.84 (45)	< .001
Duration of illness (years)	6.74 (3.16)	5.55 (2.95)	1.57 (63)	0.121
Y-BOCS				
Total	26.44 (6.12)	27.52 (4.86)	-0.78 (63)	0.439
Obsessions	13.76 (3.50)	14.32 (2.21)	-0.78 (56)	0.442
Compulsions	12.68 (3.53)	13.19 (3.89)	-0.56 (63)	0.576
HAM-D	10.79 (7.08)	11.97 (5.36)	-0.75 (63)	0.457
HAM-A	9.41 (6.40)	10.55 (4.76)	-0.81 (63)	0.423

Abbreviations – HAM-D: Hamilton Depression Rating Scale; HAM-A: Hamilton Anxiety Rating Scale; HCs: healthy controls; IQ: intelligence quotient; OCD: obsessive-compulsive disorder; TIV: total intracranial volume; Y-BOCS: Yale-Brown Obsessive Compulsive Scale

<sup>a</sup>: As measured with the Y-BOCS symptom checklist.

<sup>b</sup>: IQ was assessed using the short form of the Wechsler Adult Intelligence Scale, which consists of the vocabulary, arithmetic, block design, and picture arrangement subtests.

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Table S2. Neurocognitive differences in the subset analysis

Variables	Early-onset OCD (N=34)	Late-onset OCD (N=31)	HCs (N=103)	Statistics		
		Mean (SD)		F (df)	p	Post hoc
<i>Visuospatial ability: construction &amp; memory</i>						
RCFT Copy	17.88 (1.12)	18.42 (1.03)	18.39 (1.17)	2.71 (2, 145)	0.070	n.s.
RCFT IR	12.18 (3.49)	12.74 (2.89)	13.51 (2.73)	2.65 (2, 145)	0.074	n.s.
RCFT DR	12.68 (3.12)	12.23 (3.01)	13.11 (2.98)	1.02 (2, 145)	0.364	n.s.
<i>Verbal fluency</i>						
COWA Letter	41.74 (8.57)	39.90 (14.85)	45.42 (9.96)	3.43 (2, 145)	< .05	LO < HCs <sup>†</sup>
COWA Category	38.47 (7.47)	39.48 (9.48)	42.02 (8.72)	2.43 (2, 145)	0.092	n.s.
<i>Executive function: organization</i>						
WAIS PA	11.29 (1.45)	11.57 (2.13)	11.34 (1.93)	0.21 (2, 164)	0.815	n.s.
WAIS BD	14.00 (2.55)	12.30 (2.64)	14.03 (2.42)	5.92 (2, 164)	< .01	LO < EO <sup>*</sup> ; LO < HCs <sup>**</sup>
RCFT Organization	6.00 (1.74)	5.26 (1.84)	6.39 (1.54)	5.29 (2, 145)	< .01	LO < HCs <sup>**</sup>
<i>Executive function: cognitive flexibility</i>						
IED Errors	16.56 (9.11)	19.45 (11.08)	13.07 (8.70)	5.01 (2, 125)	< .01	LO > HCs <sup>**</sup>
<i>Decision-making</i>						
CGT Decision-making	0.90 (0.11)	0.90 (0.10)	0.92 (0.09)	0.63 (2, 109)	0.537	n.s.

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CGT Risk-taking	0.54 (0.14)	0.54 (0.14)	0.58 (0.14)	0.85 (2, 109)	0.432	n.s.
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Abbreviations – BD: Block design; CGT: Cambridge Gambling Task; COWA: Controlled Oral Word Association; DR: delayed recall; EO: early-onset OCD; HCs: healthy controls; IED: Intra-Extra Dimensional Set Shift; IR: immediate recall; LO: late-onset OCD; n.s.: not significant; OCD: obsessive-compulsive disorder; PA: Picture arrangement; RCFT: Rey-Osterrieth Complex Figure Test; WAIS: Wechsler Adult Intelligence Scale

\* < .05, \*\* < .01, \*\*\* < .001

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Table S3. Whole brain morphometry analyses among EO, LO, and HCs in the full dataset

Region	Cluster size ( <i>k</i> )	MNI coordinate (mm)			<i>F</i>	Corrected <i>p</i>
		x	y	z		
<i>ANOVA group effects</i>						
EO						
L Precentral gyrus	325	-58	9	28	22.47	< .001
L MFG	638	-36	9	54	21.63	< .001
R medial OFG	641	18	30	-22	21.47	< .001
R anterior OFG	486	22	58	-18	18.48	< .001
L Cerebellar lobule III	185	-4	-42	-12	16.83	< .05
R Thalamus	238	6	-9	-10	16.70	< .01
L MTG	309	-54	-42	4	14.76	< .001
LO						
NA <sup>a</sup>	-	-	-	-	-	-
HCs						
R anterior OFG	329	38	36	-21	20.89	< .001
R Lingual gyrus	908	12	-33	-4	16.63	< .001
R Cerebellar lobule VIII	403	28	-42	-56	15.38	< .001
R STG	255	70	-22	0	14.73	< .01
L posterior OFG	200	-27	18	-22	13.98	< .05
<i>Post hoc: EO versus HCs</i>						
EO > HCs						
R anterior OFG	3419	34	38	-21	4.61	< .001
L Precentral gyrus	292	-58	9	28	4.39	< .01
L Cerebellar lobule III	899	-4	-40	-14	4.34	< .001
R Cerebellar lobule VIII	2834	28	-44	-57	4.20	< .001
L MFG	582	-36	9	54	4.19	< .001
R STG	945	70	-24	2	4.16	< .001
L Cerebellar lobule IX	278	-18	-45	-60	4.09	< .01
L medial OFG	883	-16	15	-27	4.08	< .001

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R MTG	170	58	-10	-22	3.89	< .01
L STG	179	-50	-3	-10	3.59	< .01
L Caudate	272	-9	6	15	3.58	< .01
EO < HCs						
NA <sup>a</sup>	-	-	-	-	-	-
<i>Post hoc: LO versus HCs</i>						
					<i>T</i>	Uncorrected <i>p</i>
LO > HCs						
R Lingual gyrus	23	12	-32	-3	3.28	0.76
L superior TP	10	-33	20	-26	3.27	0.86
L Angular gyrus	5	-38	-58	40	3.26	0.91
R Cerebellar lobule IX	8	4	-50	-60	3.20	0.88
LO < HCs						
NA <sup>a</sup>	-	-	-	-	-	-

Abbreviations – EO: early-onset OCD; HCs: healthy controls; L: left hemispheric; LO: late-onset OCD; MFG: middle frontal gyrus; MTG: middle temporal gyrus; OFG: orbitofrontal gyrus; R: right hemispheric; STG: superior temporal gyrus; TP: temporal pole

<sup>a</sup>: not survived under a voxel-level threshold of  $p < .001$

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Table S4. Whole brain morphometry analyses among EO, LO, and HCs in the subset

Region	Cluster size (k)	MNI coordinate (mm)			F	Corrected p
		x	Y	z		
<i>ANOVA group effects</i>						
EO						
R medial OFG	8099	16	24	-26	36.14	< .001
L MFG	1198	-40	8	54	27.48	< .001
R Precentral gyrus	1021	51	-2	39	23.36	< .001
L superior TP	1122	-51	9	-21	21.93	< .001
R medial SFG	233	4	68	8	21.64	< .01
R MTG	1074	63	-28	-8	20.67	< .001
L SFG	372	-24	42	36	20.45	< .001
L posterior OFG	878	-21	9	-18	19.17	< .001
L Caudate	382	-9	10	15	18.34	< .001
R Caudate	369	12	6	20	17.94	< .001
L MTG	668	-60	-46	6	17.26	< .001
R SFG	188	24	52	36	17.17	< .05
L MFG	193	-32	51	8	15.99	< .05
R MCG	269	2	-22	44	15.62	< .01
R IPL	241	48	-51	48	15.51	< .01
LO						
NA <sup>a</sup>	-	-	-	-	-	-
HCs						
NA <sup>a</sup>	-	-	-	-	-	-
<i>Post hoc: EO versus LO</i>						
EO > LO						
R medial OFG	903	15	26	-27	5.15	< .001
R Precentral gyrus	515	54	12	33	4.68	< .001
L MFG	188	-42	9	56	4.31	< .05



EO < LO							
NA <sup>a</sup>							
<i>Post hoc: EO versus HCs</i>							
					<i>T</i>	<i>Corrected p</i>	
EO > HCs							
R medial OFG	1190	16	21	-27	4.73	< .001	
R Thalamus	2332	6	-9	-10	4.49	< .001	
R anterior OFG	825	39	36	-18	4.26	< .001	
L superior TP	503	-51	9	-20	4.19	< .001	
R STG	585	70	-28	2	4.12	< .001	
L posterior OFG	454	-21	12	-21	4.09	< .001	
R Precentral gyrus	366	57	0	39	4.09	< .001	
L Precentral gyrus	226	-57	6	30	4.02	< .05	
R Caudate	230	12	4	21	4.00	< .01	
L Caudate	257	-9	10	15	4.00	< .01	
L MFG	323	-39	8	54	3.96	< .001	
EO < HCs							
NA <sup>a</sup>							
<i>Post hoc: LO versus HCs</i>							
					<i>T</i>	<i>Uncorrected p</i>	
LO > HCs							
R SPL	147	22	-51	58	4.22	0.30	
R Fusiform gyrus	108	28	-87	-3	4.18	0.38	
L STG	15	-54	-45	18	3.50	0.77	
R Heschl's gyrus	87	45	-18	10	3.45	0.43	
LO < HCs							
R rectus	21	9	27	-28	3.96	0.72	

Abbreviations – EO: early-onset OCD; HCs: healthy controls; IPL: inferior parietal lobe; L: left hemispheric; LO: late-onset OCD; MCG: middle cingulate gyrus; MFG: middle frontal gyrus; MTG: middle temporal gyrus; OFG: orbitofrontal gyrus; R: right hemispheric; SFG:

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superior frontal gyrus; SPL: superior parietal lobe; STG: superior temporal gyrus; TP: temporal pole

<sup>a</sup>: not survived under a voxel-level threshold of  $p < .001$

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Table S5. Volumetric comparisons between drug-naïve and unmedicated OCD patients

Region	Cluster size ( <i>k</i> )	MNI coordinate (mm)			<i>T</i>	Uncorrected <i>p</i>
		x	y	z		
DNO > UMO						
NA <sup>a</sup>	-	-	-	-	-	-
DNO < UMO						
R Cerebellar lobule IX	24	6	-56	-64	3.47	0.72
L MTG	18	-48	-66	4	3.39	0.76
R Cerebellar lobule IX	19	4	-62	-44	3.36	0.75
L MOG	1	-38	-72	30	3.20	0.96

Abbreviations – DNO: drug-naïve obsessive-compulsive disorder; MOG: middle occipital gyrus; MTG: middle temporal gyrus; UMO: unmedicated obsessive-compulsive disorder

<sup>a</sup>: not survived under a voxel-level threshold of  $p < .001$

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Table S6. VBM results from analysis of covariance controlling for total intracranial volume

Region	Cluster size ( <i>k</i> )	MNI coordinate (mm)			<i>F</i>	Corrected <i>p</i>
		x	y	z		
<i>ANOVA group effects</i>						
EO						
R medial OFG	583	18	30	-22	23.93	< .001
L Precentral gyrus	277	-58	9	28	21.04	< .01
L MFG	500	-38	9	54	19.97	< .001
R Thalamus	337	6	-9	-10	19.71	< .001
R anterior OFG	376	33	56	-16	18.68	< .001
R Parahippocampal gyrus	333	24	-34	-8	16.26	< .001
R Parahippocampal gyrus	163	16	4	-18	14.58	< .05
L MTG	205	-57	-46	6	13.77	< .05
LO						
NA <sup>a</sup>	-	-	-	-	-	-
HCs						
NA <sup>a</sup>	-	-	-	-	-	-
<i>Post hoc: EO versus LO</i>						
EO > LO						
L Precentral gyrus	88	-58	8	33	3.70	0.374
R medial OFG	67	18	30	-22	3.66	0.440
R anterior OFG	55	32	56	-18	3.43	0.487
L MFG	72	-38	9	56	3.42	0.423
EO < LO						
L Lingual	46	-16	-74	-4	3.80	0.528
<i>Post hoc: EO versus HCs</i>						
EO > HCs						
R medial OFG	162	18	32	-20	3.43	< .05

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EO < HCs						
NA <sup>a</sup>	-	-	-	-	-	-
<i>Post hoc: LO versus HCs</i>						
					<i>T</i>	<i>Uncorrected p</i>
LO > HCs						
R posterior OFG	44	39	34	-21	3.57	0.567
R Lingual gyrus	57	12	-32	-3	3.42	0.510
LO < HCs						
NA <sup>a</sup>	-	-	-	-	-	-

Abbreviations – EO: early-onset OCD; HCs: healthy controls; L: left hemispheric; LO: late-onset OCD; MFG: middle frontal gyrus; MTG: middle temporal gyrus; OFG: orbitofrontal gyrus; R: right hemispheric

<sup>a</sup>: not survived under a voxel-level threshold of  $p < .001$