

Multimodal meta-analysis of white matter abnormalities in obsessive-compulsive disorder

Supplementary Material

eTable 1. White matter volume: data acquisition

WM	Scanner strength (T)	TR / TE (ms / ms)	Flip angle (degrees)	Native resolution (mm ³)
Carmona <i>et al</i> 2007	1.5	13 / 4.2	15	0.9x0.9x2.0
Duran <i>et al</i> 2009	1.5	30 / 9.0	30	0.9x1.2x0.9
Koprivova <i>et al</i> 2009	3.0	2300 / 4.6	10	1.0x1.0x1.0
Lazaro <i>et al</i> 2011	1.5	12 / 5.2	20	0.9x0.9x1.5
Matsumoto <i>et al</i> 2010	1.5	21 / 9.2	30	1.0x1.0x1.0
Pujol <i>et al</i> 2004	1.5	40 / 4.0	30	1.0x1.3x2.5
Riffkin <i>et al</i> 2005	1.5	14 / 3.3	30	0.9x0.9x1.5
Togao <i>et al</i> 2010	1.5	1900 / 3.9	15	0.9x0.9x1.0
van den Heuvel <i>et al</i> 2009	1.5	2700 / 4.0	8	1.0x1.5x1.0
Yoo <i>et al</i> 2008	1.5	14 / 5.5	20	1.5x0.8x0.8

eTable 2. White matter volume: data processing

WM	Final resolution (mm ³)	Modulation	Smoothing kernel	Statistics	Statistical threshold
Carmona <i>et al</i> 2007	0.9x0.9x2.0	Yes	12	Parametric	p < 0.001 uncorrected 40 voxels extent
Duran <i>et al</i> 2009	2.0x2.0x2.0	Yes	12	Parametric	P < 0.05 FWE-corrected
Koprivova <i>et al</i> 2009	NA	Yes	10	Parametric	P < 0.05 FDR-corrected 100 voxels extent
Lazaro <i>et al</i> 2011	1.0x1.0x1.0	Yes	8	Parametric	P < 0.05 FWE-corrected
Matsumoto <i>et al</i> 2010	1.0x1.0x1.0	No	12	Parametric	P < 0.001 uncorrected 400 voxels extent
Pujol <i>et al</i> 2004	1.5	Yes	12	Parametric	p < 0.05 corrected
Riffkin <i>et al</i> 2005	NA	Yes	5	Non parametric	< 1 FP cluster
Togao <i>et al</i> 2010	NA	Yes	12	Parametric	P < 0.05 FDR-corrected 25 voxels extent
van den Heuvel <i>et al</i> 2009	2.0x2.0x2.0	NA	12	Parametric	p < 0.05 corrected
Yoo <i>et al</i> 2008	2.0x2.0x2.0	No	12	Parametric	p < 0.001 20 voxels extent

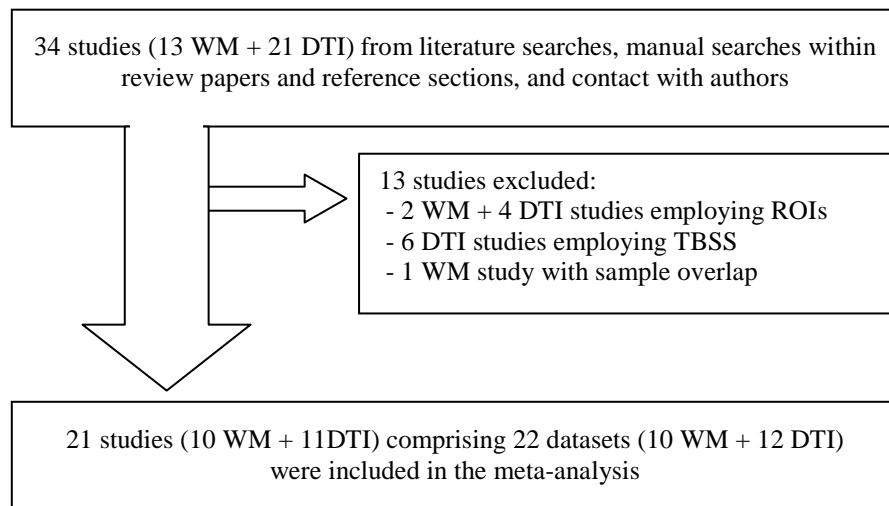
eTable 3. Fractional anisotropy: data acquisition

DTI	Scanner strength (T)	TR / TE (ms / ms)	Native resolution (mm ³)	Number of directions	b-factor (s/mm ²)
Admon <i>et al</i> 2012	1.5	12000 / 97.0	1.6x1.6x3.0	6	1000
Cannistraro <i>et al</i> 2001	1.5	10000 / 67.0	2.0x2.0x2.0	6	600
Fan <i>et al</i> 2012	1.5	9000 / 105.5	1.9x1.9x5.0	25	1000
Garibotto <i>et al</i> 2010	1.5	10804 / 78.0	1.9x1.9x2.3	35	1000
Gruner <i>et al</i> 2010	3.0	14000 / min	1.9x1.9x2.5	31	NA
Ha <i>et al</i> 2009	1.5	9200 / 83.0	2.0x2.0x2.0	12	1000
Li <i>et al</i> 2011	3.0	12000 / 70.8	1.9x1.9x3.0	15	1000
Menzies <i>et al</i> 2008	1.5	12000 / 93.0	2.3x1.9x4.0	25	1000
Nakamae <i>et al</i> 2008	1.5	6000 / 88.0	1.8x2.2x3.0	15	1000
Szeszko <i>et al</i> 2005	1.5	10000 / 86.7	1.7x1.7x5.0	25	1000
Yoo <i>et al</i> 2007	1.5	7390 / 62.0	1.7x1.7x4.0	6	600

eTable 4. Fractional anisotropy: data processing

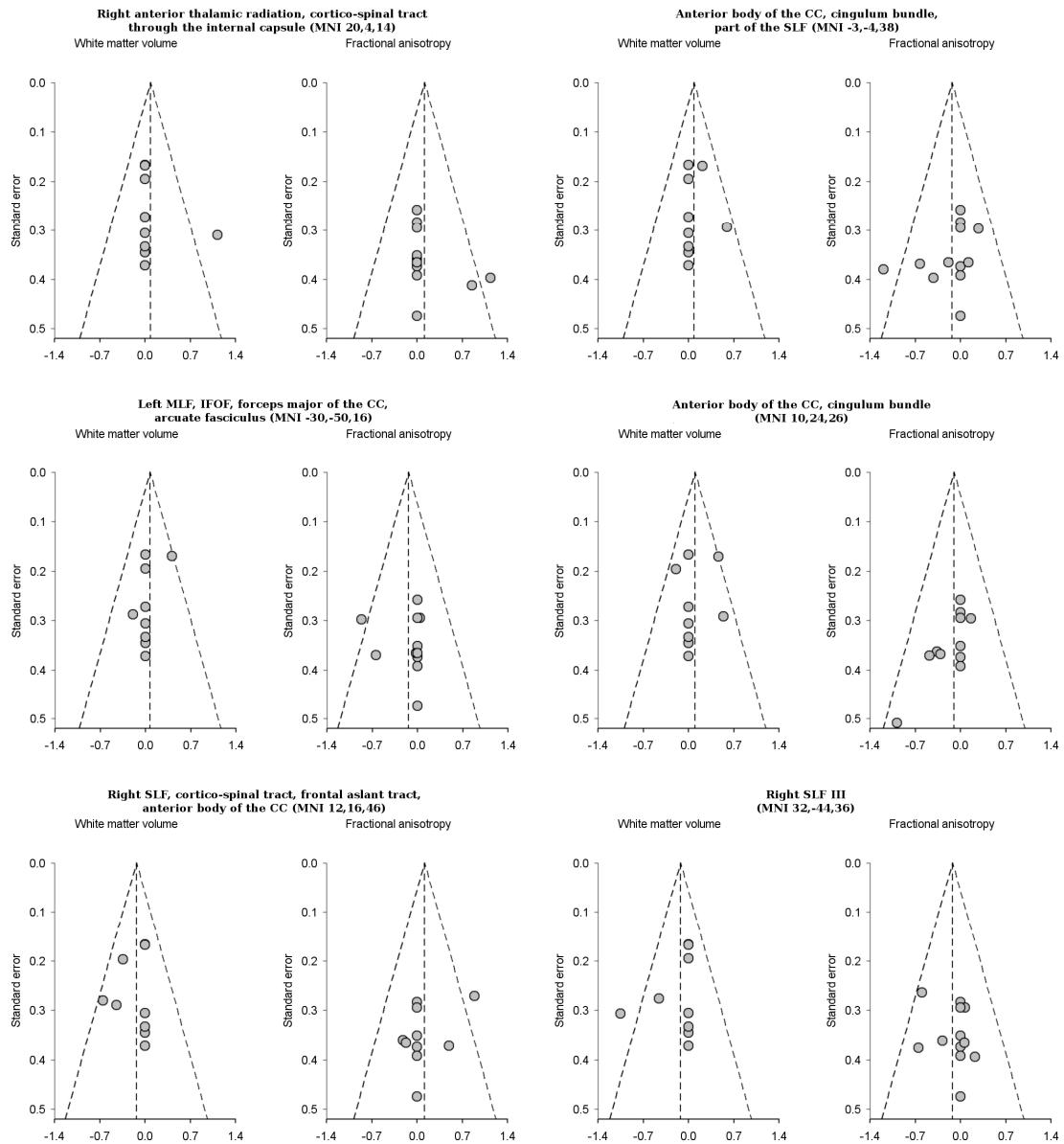
DTI	Motion and Eddy currents correction	Final resolution (mm ³)	Smoothing FWHM (mm)	Statistics	Statistical threshold
Admon <i>et al</i> 2012	DtiTool	3.0x3.0x3.0	8	Parametric	p < 0.005 cluster-corrected
Cannistraro <i>et al</i> 2001	FSL	1.0x1.0x1.0	1.5	Parametric	p < 0.05 uncorrected, 20 voxels extent and p = 0.005 for clusters' means
Fan <i>et al</i> 2012	FSL	2.0x2.0x2.0	6		p < 0.001 uncorrected, 10 voxels extent
Garibotto <i>et al</i> 2010	BrainVISA	NA	NA	Parametric	p < 0.005 uncorrected, 20 voxels extent
Gruner <i>et al</i> 2010	FSL	1.0x1.0x1.0	8	Parametric	p < 0.05 cluster-corrected
Ha <i>et al</i> 2009	FSL	2.0x2.0x2.0	6	Parametric	p < 0.001 uncorrected, 15 voxels extent
Li <i>et al</i> 2011	DtiStudio	3.0x3.0x3.0	8	Parametric	p < 0.05 FDR-corrected, 50 voxels extent
Menzies <i>et al</i> 2008	NA	NA	8	Non parametric	< 1 FP cluster
Nakamae <i>et al</i> 2008	DtiStudio	NA	8	Parametric	p < 0.001 uncorrected, 100 voxels extent
Szeszko <i>et al</i> 2005	In-house	1.0x1.0x1.0	7	Parametric	p < 0.005, 20 voxels extent
Yoo <i>et al</i> 2007	SPM	2.0x2.0x2.0	10	Parametric	p < 0.001, 20 voxels extent

eFigure 1. Inclusion of studies in the meta-analysis.



Note: The search and contact with authors retrieved a total of 34 potentially suitable studies (13 WMV and 21 DTI). Of those, two WMV (Di Paola *et al*, 2012; Huyser *et al*, 2012) and four DTI studies (Chiu *et al*, 2011; Lochner *et al*, 2012; Oh *et al*, 2011; Saito *et al*, 2008) were excluded because they employed a ROI approach, six other DTI studies were excluded because they employed TBSS (Benedetti *et al*, 2012; Bora *et al*, 2011; Fontenelle *et al*, 2011; Jayarajan *et al*, 2012; Nakamae *et al*, 2011; Zarei *et al*, 2011), and one WMV study (Lazaro *et al*, 2009) was excluded because its sample overlapped with the sample from another larger study (Lazaro *et al*, 2011). Thus, 21 studies (providing twenty-two datasets: 10 WMV and 12 DTI) completed before 31st of January 2013 could be included in the meta-analysis (Admon *et al*, 2012; Cannistraro *et al*, 2007; Carmona *et al*, 2007; Duran *et al*, 2009; Fan *et al*, 2012; Garibotto *et al*, 2010; Gruner *et al*, 2012; Ha *et al*, 2009; Koprivova *et al*, 2009; Lazaro *et al*, 2011; Li *et al*, 2011; Matsumoto *et al*, 2010; Menzies *et al*, 2008; Nakamae *et al*, 2008; Pujol *et al*, 2004; Riffkin *et al*, 2005; Szeszko *et al*, 2005; Togao *et al*, 2010; van den Heuvel *et al*, 2009; Yoo *et al*, 2007; Yoo *et al*, 2008).

eFigure 2. Funnel plots of the peaks of white matter multimodal abnormality.



Note: The horizontal axis is the effect size of the difference between patients and healthy controls.

REFERENCES

- Admon R, Bleich-Cohen M, Weizmant R, Poyurovsky M, Faragian S, Hendl T (2012). Functional and structural neural indices of risk aversion in obsessive-compulsive disorder (OCD). *Psychiatry Res* **203**(2-3): 207-213.
- Benedetti F, Giacosa C, Radaelli D, Poletti S, Pozzi E, Dallaspezia S, et al (2012). Widespread changes of white matter microstructure in obsessive-compulsive disorder: effect of drug status. *Eur Neuropsychopharmacol* **23**(7): 581-593.
- Bora E, Harrison BJ, Fornito A, Cocchi L, Pujol J, Fontenelle LF, et al (2011). White matter microstructure in patients with obsessive-compulsive disorder. *J Psychiatry Neurosci* **36**(1): 42-46.
- Cannistraro PA, Makris N, Howard JD, Wedig MM, Hodge SM, Wilhelm S, et al (2007). A diffusion tensor imaging study of white matter in obsessive-compulsive disorder. *Depress Anxiety* **24**(6): 440-446.
- Carmona S, Bassas N, Rovira M, Gispert JD, Soliva JC, Prado M, et al (2007). Pediatric OCD structural brain deficits in conflict monitoring circuits: a voxel-based morphometry study. *Neurosci Lett* **421**(3): 218-223.
- Chiu CH, Lo YC, Tang HS, Liu IC, Chiang WY, Yeh FC, et al (2011). White matter abnormalities of fronto-striato-thalamic circuitry in obsessive-compulsive disorder: A study using diffusion spectrum imaging tractography. *Psychiatry Res* **192**(3): 176-182.
- Di Paola M, Luders E, Rubino IA, Siracusano A, Manfredi G, Girardi P, et al (2012). The structure of the corpus callosum in obsessive compulsive disorder. *Eur Psychiatry*.
- Duran FL, Hoexter MQ, Valente AA, Jr., Miguel EC, Busatto GF (2009). Association between symptom severity and internal capsule volume in obsessive-compulsive disorder. *Neurosci Lett* **452**(1): 68-71.
- Fan Q, Yan X, Wang J, Chen Y, Wang X, Li C, et al (2012). Abnormalities of white matter microstructure in unmedicated obsessive-compulsive disorder and changes after medication. *PLoS One* **7**(4): e35889.
- Fontenelle LF, Bramati IE, Moll J, Medlowicz MV, de Oliveira-Souza R, Tovar-Moll F (2011). White Matter Changes in OCD Revealed by Diffusion Tensor Imaging. *CNS Spectr*.
- Garibotto V, Scifo P, Gorini A, Alonso CR, Brambati S, Bellodi L, et al (2010). Disorganization of anatomical connectivity in obsessive compulsive disorder: a multi-parameter diffusion tensor imaging study in a subpopulation of patients. *Neurobiol Dis* **37**(2): 468-476.
- Gruner P, Vo A, Ikuta T, Mahon K, Peters BD, Malhotra AK, et al (2012). White matter abnormalities in pediatric obsessive-compulsive disorder. *Neuropsychopharmacology* **37**(12): 2730-2739.
- Ha TH, Kang DH, Park JS, Jang JH, Jung WH, Choi JS, et al (2009). White matter alterations in male patients with obsessive-compulsive disorder. *Neuroreport* **20**(7): 735-739.

Huyser C, van den Heuvel OA, Wolters LH, de Haan E, Boer F, Veltman DJ (2012). Increased orbital frontal gray matter volume after cognitive behavioural therapy in paediatric obsessive compulsive disorder. *World J Biol Psychiatry* **14**(4): 319-331.

Jayarajan RN, Venkatasubramanian G, Viswanath B, Janardhan Reddy YC, Srinath S, Vasudev MK, et al (2012). White matter abnormalities in children and adolescents with obsessive-compulsive disorder: a diffusion tensor imaging study. *Depress Anxiety* **29**(9): 780-788.

Koprivova J, Horcek J, Tintera J, Prasko J, Raszka M, Ibrahim I, et al (2009). Medial frontal and dorsal cortical morphometric abnormalities are related to obsessive-compulsive disorder. *Neurosci Lett* **464**(1): 62-66.

Lazaro L, Bargallo N, Castro-Fornieles J, Falcon C, Andres S, Calvo R, et al (2009). Brain changes in children and adolescents with obsessive-compulsive disorder before and after treatment: a voxel-based morphometric MRI study. *Psychiatry Res* **172**(2): 140-146.

Lazaro L, Castro-Fornieles J, Cullell C, Andres S, Falcon C, Calvo R, et al (2011). A voxel-based morphometric MRI study of stabilized obsessive-compulsive adolescent patients. *Prog Neuropsychopharmacol Biol Psychiatry* **35**(8): 1863-1869.

Li F, Huang X, Yang Y, Li B, Wu Q, Zhang T, et al (2011). Microstructural brain abnormalities in patients with obsessive-compulsive disorder: diffusion-tensor MR imaging study at 3.0 T. *Radiology* **260**(1): 216-223.

Lochner C, Fouche JP, du Plessis S, Spottiswoode B, Seedat S, Fineberg N, et al (2012). Evidence for fractional anisotropy and mean diffusivity white matter abnormalities in the internal capsule and cingulum in patients with obsessive-compulsive disorder. *J Psychiatry Neurosci* **37**(3): 193-199.

Matsumoto R, Ito H, Takahashi H, Ando T, Fujimura Y, Nakayama K, et al (2010). Reduced gray matter volume of dorsal cingulate cortex in patients with obsessive-compulsive disorder: a voxel-based morphometric study. *Psychiatry Clin Neurosci* **64**(5): 541-547.

Menzies L, Williams GB, Chamberlain SR, Ooi C, Fineberg N, Suckling J, et al (2008). White matter abnormalities in patients with obsessive-compulsive disorder and their first-degree relatives. *Am J Psychiatry* **165**(10): 1308-1315.

Nakamae T, Narumoto J, Sakai Y, Nishida S, Yamada K, Nishimura T, et al (2011). Diffusion tensor imaging and tract-based spatial statistics in obsessive-compulsive disorder. *J Psychiatr Res* **45**(5): 687-690.

Nakamae T, Narumoto J, Shibata K, Matsumoto R, Kitabayashi Y, Yoshida T, et al (2008). Alteration of fractional anisotropy and apparent diffusion coefficient in obsessive-compulsive disorder: a diffusion tensor imaging study. *Prog Neuropsychopharmacol Biol Psychiatry* **32**(5): 1221-1226.

Oh JS, Jang JH, Jung WH, Kang DH, Choi JS, Choi CH, et al (2011). Reduced fronto-callosal fiber integrity in unmedicated OCD patients: a diffusion tractography study. *Hum Brain Mapp* **33**(10): 2441-2452.

Pujol J, Soriano-Mas C, Alonso P, Cardoner N, Menchon JM, Deus J, et al (2004). Mapping structural brain alterations in obsessive-compulsive disorder. *Arch Gen Psychiatry* **61**(7): 720-730.

Riffkin J, Yucel M, Maruff P, Wood SJ, Soulsby B, Olver J, et al (2005). A manual and automated MRI study of anterior cingulate and orbito-frontal cortices, and caudate nucleus in obsessive-compulsive disorder: comparison with healthy controls and patients with schizophrenia. *Psychiatry Res* **138**(2): 99-113.

Saito Y, Nobuhara K, Okugawa G, Takase K, Sugimoto T, Horiuchi M, et al (2008). Corpus callosum in patients with obsessive-compulsive disorder: diffusion-tensor imaging study. *Radiology* **246**(2): 536-542.

Szeszko PR, Ardekani BA, Ashtari M, Malhotra AK, Robinson DG, Bilder RM, et al (2005). White matter abnormalities in obsessive-compulsive disorder: a diffusion tensor imaging study. *Arch Gen Psychiatry* **62**(7): 782-790.

Togao O, Yoshiura T, Nakao T, Nabeyama M, Sanematsu H, Nakagawa A, et al (2010). Regional gray and white matter volume abnormalities in obsessive-compulsive disorder: a voxel-based morphometry study. *Psychiatry Res* **184**(1): 29-37.

van den Heuvel OA, Remijnse PL, Mataix-Cols D, Vrenken H, Groenewegen HJ, Uylings HB, et al (2009). The major symptom dimensions of obsessive-compulsive disorder are mediated by partially distinct neural systems. *Brain* **132**(Pt 4): 853-868.

Yoo SY, Jang JH, Shin YW, Kim DJ, Park HJ, Moon WJ, et al (2007). White matter abnormalities in drug-naive patients with obsessive-compulsive disorder: a diffusion tensor study before and after citalopram treatment. *Acta Psychiatr Scand* **116**(3): 211-219.

Yoo SY, Roh MS, Choi JS, Kang DH, Ha TH, Lee JM, et al (2008). Voxel-based morphometry study of gray matter abnormalities in obsessive-compulsive disorder. *J Korean Med Sci* **23**(1): 24-30.

Zarei M, Mataix-Cols D, Heyman I, Hough M, Doherty J, Burge L, et al (2011). Changes in gray matter volume and white matter microstructure in adolescents with obsessive-compulsive disorder. *Biol Psychiatry* **70**(11): 1083-1090.