Common Gray Matter Reductions in Alcohol Use and Obsessive-Compulsive Disorders: A Meta-analysis

Supplemental Information

Figure S1. Flow Diagram for Article Selection for Alcohol Use Disorder.

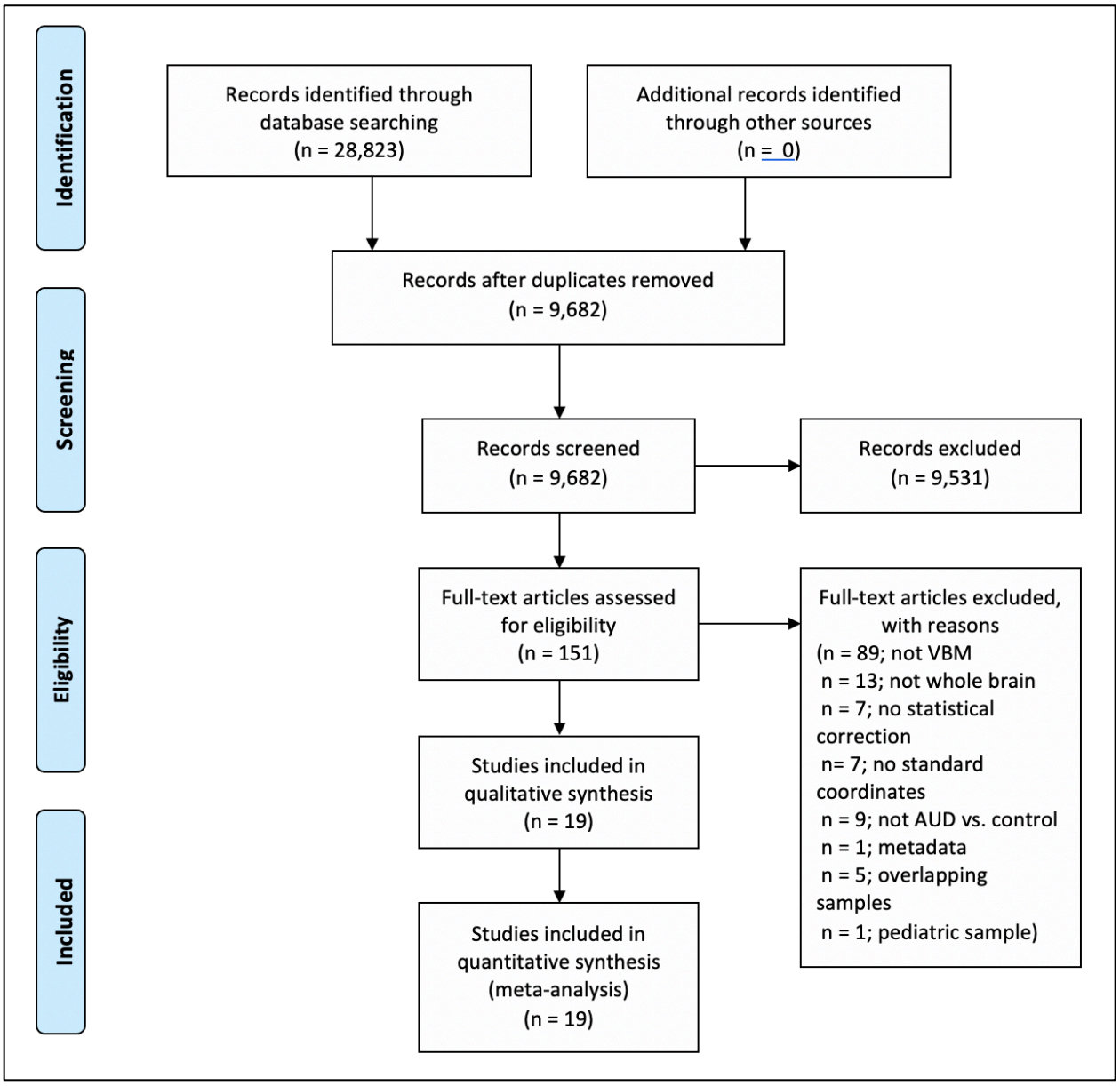

Figure S1. AUD = alcohol use disorder; VBM = voxel-based morphometry.

Figure S2. Flow Diagram for Article Selection for Obsessive-Compulsive Disorder.

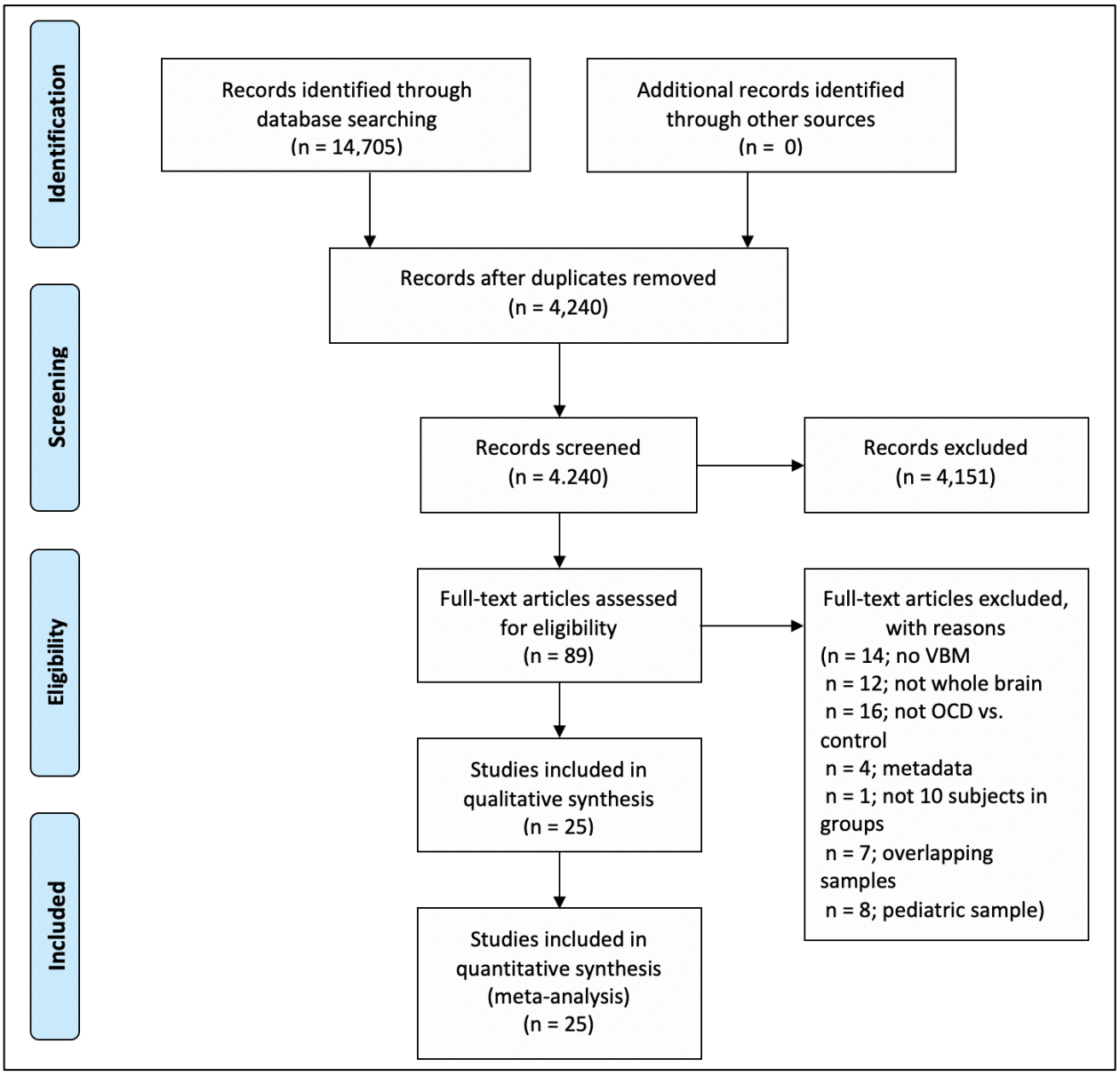

Figure S2. OCD = Obsessive-Compulsive Disorder; VBM = voxel-based morphometry.

Figure S3. Negative Regression Between GM Differences in OCD Studies and Compulsive Subscale of the YBOT.

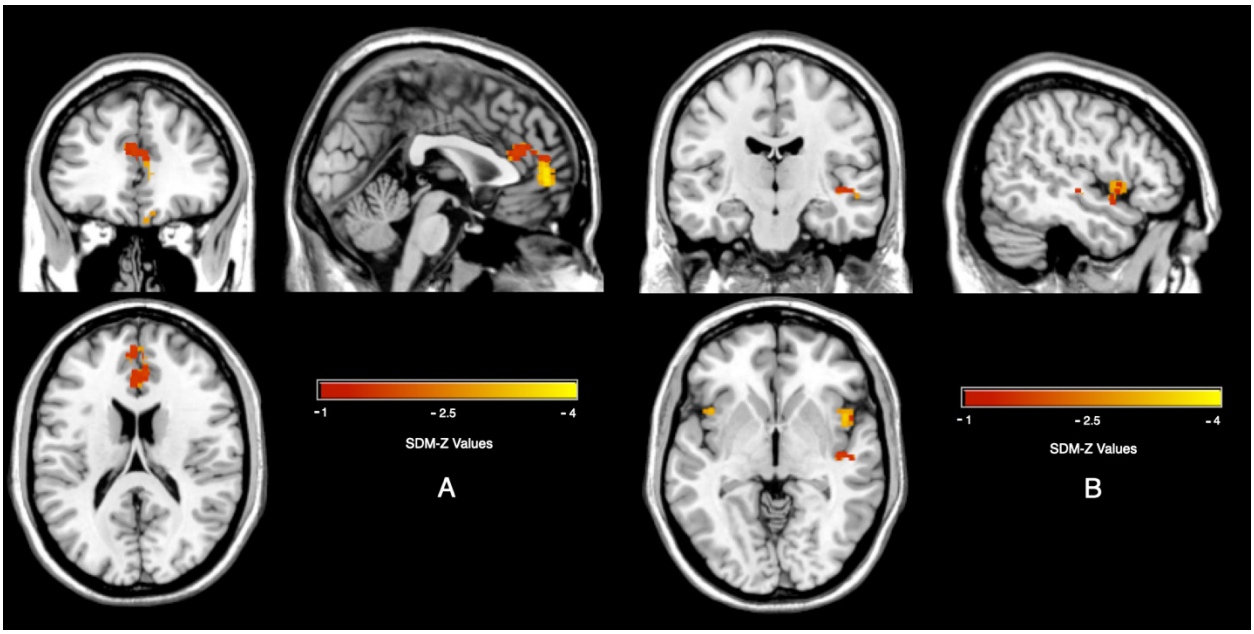

Figure S3. A) Negative correction between GM volume in the anterior cingulate and compulsive subscale of YBOT; B) Negative correction between GM volume in the insula and compulsive subscale of YBOT. In both cases lower volume in OCD patients related to higher YBOT scores.

Figure S4. OCD Metanalysis Controlling for if Studies Were Medication Naïve or Not.

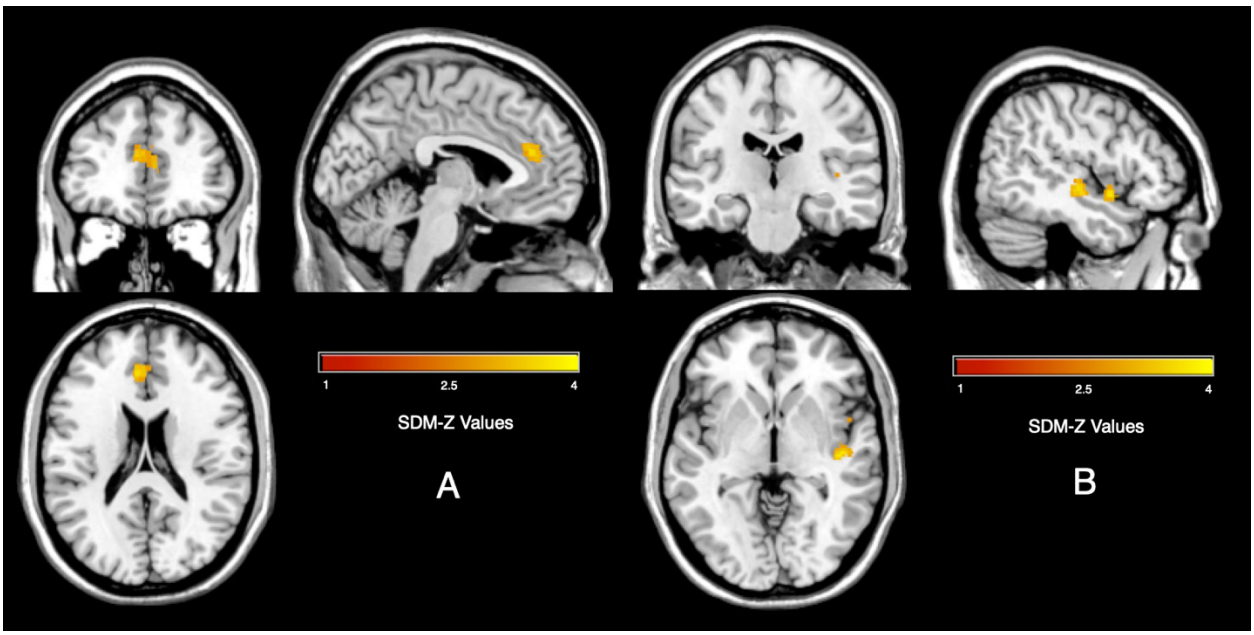

Figure S4. A) Decreased GM in OCD compared to controls in the anterior cingulate B) Decreased GM in OCD compared to controls in the right insula.

Table S1. Regression Between GM Differences in OCD Studies and Compulsive Subscale of the YBOT.

Clusters ≥ 10 Voxels and SDM-Z ≤ -1 and all peak SDM-Z ≤ -1: Negative Regression						
Peak MNI Coordinates						
X	**Y**	**Z**	**SDM-Z**	**Uncorrected P-Value**	**Voxels**	**Brain Region**
4	54	4	-4.1	0.00002	181	Right medial superior frontal gyrus
46	12	-2	-3.5	0.0003	148	Right insula
8	46	-20	-3.2	0.0006	81	Right gyrus rectus
8	36	6	-3.2	0.0006	45	Right median cingulum
-42	14	-4	-3.0	0.001	20	Left insula
32	-6	0	-2.9	0.002	10	Right putamen
Clusters ≥ 10 Voxels and SDM-Z ≥ 1 and all peak SDM-Z ≥ 1: Positive Regression						
N/A						

Table S2. OCD Metanalysis Controlling for if Studies Were Medication Naïve or Not.

Clusters ≥ 10 Voxels and SDM-Z ≤ -1 and all peak SDM-Z ≤ -1 (OCD > HC)						
Peak MNI Coordinates						
X	**Y**	**Z**	**SDM-Z**	**Uncorrected P-Value**	**Voxels**	**Brain Region**
-8	-22	8	-3	0.0015	7	Left thalamus
0	-28	-20	-3	0.0012	11	Bilateral cortico-spinal projections
Clusters ≥ 10 Voxels and SDM-Z ≥ 1 and all peak SDM-Z ≥ 1 (OCD < HC)						
-4	40	20	3.6	0.0002	200	Bilateral anterior cingulate
46	-16	-6	4.1	0.00002	167	Right posterior insula
50	6	-10	3.8	0.00008	102	Right middle insula

Table S3. Additional Information for Studies Included in the AUD Analysis.

Study	**Software Used for VBM**	**Length of Diagnosis - years (SD)**	**Psychiatric/Neurological Exclusions**
Asenio et al,(1) 2016	SPM5	4.71 (2.93)	Any other Axis I psychiatric disorder including dependence of alcohol or other substance (except for nicotine), presence of structural brain abnormalities, any systemic or neurological disease.
Chanraud et al,(2) 2007	SPM2	8 (6.3)	Drug abuse (other than nicotine), anxiety or depressive disorders and neurological, somatic or other psychiatric symptoms, including a history of head injury with loss of consciousness, stroke.
Charlet et al,(3) 2014	SPM8	11.6 (8.4)	Axis I disorders except for alcohol/nicotine abuse/dependence, epilepsy, other neurological illnesses.
Demirakca et al,(4) 2011	SPM8	12.4 (7.4)	Axis I lifetime psychiatric disorder, any lifetime substance dependence (other than alcohol or nicotine), antisocial personality disorder, neurological illness.

Fein et al,(5) 2006	SPM2	N/A	History or presence of an axis I diagnosis, history of drug dependence other than nicotine or caffeine, significant neurological disease, current substance abuse other than caffeine or nicotine.
Galandra et al,(6) 2018	SPM12	10.8 (7.21)	Presence/history of neurological/psychiatric disorders other than AUDs, or any comorbid disorder except for nicotine dependence.
Grodin et al,(7) 2013	FSL-VBM v.1.1	10.3 (7.5)	Neurological abnormalities, or who had a history of psychotic symptoms.
Guggenmos et al,(8) 2017	SPM12	11.7 (9.9)	History of or current neurological or mental disorders (excluding nicotine dependence and alcohol abuse in AD, but including abuse of other drugs).
Jang et al,(9) 2007	SPM2	10.2 (6.9)	Current or past psychiatric disorders, traumatic brain injury, neurological illness, and other substance use disorder except for caffeine or nicotine,
Mechtcheriakov et al,(10) 2007	SPM2	N/A	History of illicit drug misuse or dependency, major psychiatric disorders (other than alcohol addiction), history of severe brain injury.
Nurmedov et al,(11) 2016	SPM8	7.7 (4.75)	Another psychiatric disorder, a past or current substance use disorder other than nicotine, neurological disease, dementia, history of head trauma.
Rando et al,(12) 2011	SPM8	N/A	Current dependence on psychoactive substances other than nicotine or any other axis I disorder.
Segobin et al,(13) 2014	SPM5	8.22 (8.79)	Substance dependence (except tobacco), psychiatric problems, or had a history of neurologic pathology.
van Holst et al,(14) 2012	SPM8	11.69 (9.7)	Lifetime diagnosis of schizophrenia or psychotic episodes, 12-month diagnosis of manic disorder, OCD, and post-traumatic stress disorder, substance use disorders (except for nicotine), treatment for mental disorders other than those under study.
J. Wang et al,(15) 2018 *	SPM8	N/A	No previous substance dependence or current substance abuse other than alcohol and nicotine, A history of head trauma, past or current neurological disease.
J. Wang et al,(15) 2018 *	SPM8	N/A	No previous substance dependence or current substance abuse other than alcohol and nicotine, A history of head trauma, past or current neurological disease.
Wiers et al,(16) 2015	SPM8	14.82 (7.4)	Axis I psychiatric disorders, history of neurological diseases.
Wu et al,(17) 2018 *	SPM12	13.9 (10.1)	Current psychotic episode or delirium, history of epilepsy, neurosurgery.
Wu et al,(17) 2018 *	SPM12	8.9 (8)	Current psychotic episode or delirium, history of epilepsy, neurosurgery.
Yoon et al,(18) 2017	SPM8	5.4 (2.7)	History of significant head injury, seizure disorder, mental retardation, other substance abuse (except smoking) or psychotic disorder.
Zois et al,(19) 2017	SPM8	10.9 (8.9)	An Axis-I disorder within the previous 12 months (aside alcohol and nicotine dependence), epilepsy, neurological illness.

Table S3. SPM = Statistical Parametric Mapping; FSL = FMRIB's Software Library; VBM = voxel-based morphometry. * = two subsamples in the study not directly combined and compared to control, so the subsamples were entered as separate studies.

Table S4. Additional Information for Studies Included in the OCD Analysis.

Study	Software Used for VBM	Length of Diagnosis-years (SD)	Psychiatric/Neurological Exclusions	Compulsive Subscale Score from YBOT
Christian et al,(20) 2008	SPM2	N/A	Gilles de la Tourette's, Huntington's Disease, Parkinson's Disease, encephalitis, strokes, aneurysms, tumors, CNS infections, degenerative brain diseases, trauma, dementia, delirium, schizophrenia, schizoaffective disorder, delusional disorder, brief reactive psychosis, psychotic disorder NOS, and mental retardation.	13.9
Gilbert, Mataix-Cols et al,(21) 2008	SPM5	8 (10.75)	Brain injury, any neurological condition, psychosis, substance abuse.	N/A
Gonçalves et al,(22) 2017	SPM12	N/A	No comorbid conditions.	N/A
Hashimoto et al,(23) 2014 *	SPM8	6.3 (3.2)	Axis I disorders besides OCD, neurological disease and other psychiatric disorders.	16.5
Hashimoto et al,(23) 2014*	SPM8	5.2 (2.5)	Axis I disorders besides OCD, neurological disease and other psychiatric disorders.	16.2
Hoexter et al,(24) 2012	SPM5	18.2 (10.4)	History of head injury with loss of consciousness, past/current substance abuse or dependence, lifetime history of psychosis, suicide risk, any organic disorders that could affect the central nervous system.	12.9
Hou et al,(25) 2013	SPM8	6.3 (9.9)	A history of other psychiatric or neurological illness, a history of drug or alcohol abuse, Comorbid depressive and anxious symptoms were not considered as an exclusion criterion.	9.8
Ikari et al,(26) 2017	SPM12	15.6 (11.4)	Comorbid axis I diagnoses (except for major depression), neurological disorders, head injuries, histories of clinically significant substance or alcohol addiction.	N/A
Kobayashi et al,(27) 2015	SPM8	11.5 (7.5)	Past or current diagnosis of comorbid schizophrenia or substance-related disorders, a clinically significant neurological disease that might influence the structural brain image.	N/A
Kopřivová et al,(28) 2009	SPM5	15.6 (8.3)	N/A	8.2
Lv et al,(29) 2017	SPM8	7.39 (8.54)	Any neurological disorders, psychosurgery, current or past substance abuse or dependence, or any substantial physical illness such as brain tumor, brain injury, stroke, or epilepsy.	12.33
Matsumoto et al,(30) 2010	SPM5	N/A	Patients with psychiatric disorders other than OCD, such as current major depressive disorder, schizophrenia, bipolar disorders, and substance abuse.	N/A
Moon et al,(31) 2018	SPM8	6.5 (5.3)	N/A	N/A

Moreira et al,(32) 2017	FSL VBM v.1.1	6.87 (6.45)	History of neurological or comorbid disorders, additional Axis I psychiatric disorders besides OCD.	11.45
Pujol et al,(33) 2004	SPM99	13 (10.5)	Relevant medical, neurological, and other major psychiatric diseases. Specifically, no patient met the criteria for Tourette syndrome or showed psychoactive substance abuse. Comorbidity with anxiety and depression symptoms was not considered an exclusion criterion.	13
Real et al,(34) 2016	SPM8	13.6 (8.89)	Lifetime history of psychotic disorders, mental retardation, a neurological disease other than tic disorder, lifetime history of substance abuse/dependence, Comorbidity with other DSM Axis I disorders was not considered an exclusion criterion.	13.2
Riffkin et al,(35) 2005	SPM99	N/A	History of significant head injury, neurological disorders, seizures, or alcohol and substance abuse or dependence.	11.2
Spalletta et al,(36) 2014	SPM8	13.52 (10.84)	Comorbid psychiatric disorders, a lifetime history of substance dependence or abuse, history of neurologic illness or brain injury, or dementia.	N/A
Subirà et al,(37) 2013 *	SPM8	14.86 (7.85)	Present or past history of psychoactive substance abuse or dependence, mental retardation, neurological disease comorbidity except tic disorder, present or past history of psychotic disorders, Comorbidity with other Axis I disorders was not considered an exclusion criterion.	N/A
Subirà et al,(37) 2013 *	SPM8	11.68 (8.68)	Present or past history of psychoactive substance abuse or dependence, mental retardation, neurological disease comorbidity except tic disorder, present or past history of psychotic disorders, Comorbidity with other Axis I disorders was not considered an exclusion criterion.	N/A
Tan et al,(38) 2013	SPM5	4.5 (4.1)	All patients with comorbid Axis I psychiatric disorders or a history of neurologic disorders.	N/A
Wanjie Tang et al,(39) 2015	SPM8	4.8 (2.55)	History of head injury, neurologic disorders. No patients had major depressive disorder, generalized anxiety disorder, Tourette syndrome or other tic-related disorder.	N/A
Wenxin Tang et al,(40) 2016	SPM8	N/A	Organic brain diseases, alcohol or drug addiction, other mental disorders in DSM-IV.	N/A
Togao et al,(41) 2010	SPM2	12.9 (8.5)	Comorbid Axis I diagnosis, neurological disorder, head injury, or history of drug or alcohol addiction.	14.6
Valente et al,(42) 2005	SPM2	18.3 (10.6)	Alcohol or drug abuse, presence of psychotic symptoms, chronic neurological illness.	N/A
Y. Wang et al,(43) 2018	SPM12	4.09 (5.05)	Serious neurological disorders, nicotine, alcohol or substance dependence.	12.68
Yoo et al,(44) 2008	SPM2	8.02 (6.1)	N/A	10.49

Table S4. SPM = Statistical Parametric Mapping; FSL = FMRIB's Software Library; VBM = voxel-based morphometry. * = two subsamples in the study not directly combined and compared to control, so the subsamples were entered as separate studies.

Table S5. Jackknife Analysis for Alcohol Use Disorder.

Brain Cluster ->	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**
Total from the 21 studies	**19**	**19**	**19**	**19**	**19**	**19**	**19**	**19**	**19**	**19**	**19**	**17**	**16**
Study Excluded													
Asensio et al,(1) 2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Chanraud et al,(2) 2007	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Charlet et al,(3) 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Demirakca et al,(4) 2011	N	N	N	N	N	N	N	N	N	N	N	N	N
Fein et al,(5) 2006	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Galandra et al,(6) 2018	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	N
Grodin et al,(7) 2013	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
Guggenmos et al,(8) 2017	N	N	N	N	N	N	N	N	N	N	N	N	N
Jang et al,(9) 2007	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Mechtcheriakov et al,(10) 2007	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Nurmedov et al,(11) 2016	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Rando et al,(12) 2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Segobin et al,(13) 2014	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N
van Holst et al,(14) 2012	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
J. Wang et al,(15) 2018 *	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
J. Wang et al,(15) 2018 *	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wiers et al,(16) 2015	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wu et al,(17) 2018 *	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wu et al,(17) 2018 *	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Yoon et al,(18) 2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Zois et al,(19) 2017	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y

Table S5. Brain cluster number meanings: 1) Right median cingulate gyrus; 2) Right insula; 3) Left Heschl's gyrus 4) Left postcentral gyrus; 5) Right precentral gyrus; 6) Left precuneus; 7) Left cerebellum lobule VIII; 8) Right cerebellum lobule VIII; 9) Left middle frontal gyrus; 10) Left thalamus; 11) Right parahippocampal gyrus; 12) Right parahippocampal gyrus; 13) Left hippocampus. * = two subsamples in the study not directly combined and compared to control, so the subsamples were entered as separate studies.

Table S6. Jackknife Analysis for Obsessive-Compulsive Disorder.

Brain Cluster ->	**1**	**2**	**3**	**4**	**5**
Total from the 27 studies	21	19	24	22	24
Study Excluded					
Christian et al,(20) 2008	Y	Y	Y	Y	Y
Gilbert, Mataix-Cols et al,(21) 2008	Y	Y	Y	Y	Y
Gonçalves et al,(22) 2017	Y	Y	Y	Y	Y
Hashimoto et al,(23) 2014 *	Y	Y	Y	Y	Y
Hashimoto et al,(23) 2014 *	Y	N	Y	Y	Y
Hoexter et al,(24) 2012	Y	Y	Y	Y	Y
Hou et al,(25) 2013	N	N	N	N	N
Ikari et al,(26) 2017	Y	Y	Y	Y	Y
Kobayashi et al,(27) 2015	Y	Y	Y	Y	Y
Kopřivová et al,(28) 2009	Y	Y	Y	Y	Y
Lv et al,(29) 2017	N	N	Y	Y	Y
Matsumoto et al,(30) 2010	Y	Y	Y	Y	Y
Moon et al,(31) 2018	Y	Y	Y	Y	Y
Moreira et al,(32) 2017	Y	Y	Y	N	Y
Pujol et al,(33) 2004	Y	Y	Y	Y	Y
Real et al,(34) 2016	Y	N	Y	Y	Y
Riffkin et al,(35) 2005	Y	Y	Y	Y	Y
Spalletta et al,(36) 2014	Y	Y	Y	Y	Y
Subirà et al,(37) 2013*	N	N	Y	Y	Y
Subirà et al,(37) 2013*	N	N	Y	N	Y
Tan et al,(38) 2013	N	N	N	N	N
Wanjie Tang et al,(39) 2015	Y	Y	Y	Y	Y
Wenxin Tang et al,(40) 2016	Y	Y	Y	Y	Y
Togao et al,(41) 2010	Y	Y	Y	Y	Y

Valente et al,(42) 2005	Y	Y	Y	Y	Y
Y. Wang et al,(43) 2018	Y	Y	Y	Y	Y
Yoo et al,(44) 2008	N	N	N	N	N

Table S6. Brain cluster number meanings: 1) Left thalamus; 2) Bilateral cortico-spinal projections; 3) Bilateral anterior cingulate; 4) Right posterior insula; 5) Right middle insula. * = two subsamples in the study not directly combined and compared to control, so the subsamples were entered as separate studies.

Supplemental References

1. Asensio S, Morales JL, Senabre I, Romero MJ, Beltran MA, Flores-Bellver M, *et al.* (2016): Magnetic resonance imaging structural alterations in brain of alcohol abusers and its association with impulsivity. *Addict Biol* 21: 962–971.
2. Chanraud S, Martelli C, Delain F, Kostogianni N, Douaud G, Aubin H-J, *et al.* (2007): Brain morphometry and cognitive performance in detoxified alcohol-dependents with preserved psychosocial functioning. *Neuropsychopharmacology* 32: 429–438.
3. Charlet K, Schlagenhauf F, Richter A, Naundorf K, Dornhof L, Weinfurtner CEJ, *et al.* (2014): Neural activation during processing of aversive faces predicts treatment outcome in alcoholism. *Addict Biol* 19: 439–451.
4. Demirakca T, Ende G, Kämmerer N, Welzel-Marquez H, Hermann D, Heinz A, Mann K (2011): Effects of alcoholism and continued abstinence on brain volumes in both genders. *Alcohol Clin Exp Res* 35: 1678–1685.
5. Fein G, Landman B, Tran H, McGillivray S, Finn P, Barakos J, Moon K (2006): Brain atrophy in long-term abstinent alcoholics who demonstrate impairment on a simulated gambling task. *Neuroimage* 32: 1465–1471.
6. Galandra C, Basso G, Manera M, Crespi C, Giorgi I, Vittadini G, *et al.* (2018): Salience network structural integrity predicts executive impairment in alcohol use disorders. *Sci Rep* 8: 1–13.
7. Grodin EN, Lin H, Durkee CA, Hommer DW, Momenan R (2013): Deficits in cortical, diencephalic and midbrain gray matter in alcoholism measured by VBM: Effects of co-morbid substance abuse. *NeuroImage Clin* 2: 469–476.
8. Guggenmos M, Schmack K, Sekutowicz M, Garbusow M, Sebold M, Sommer C, *et al.* (2017): Quantitative neurobiological evidence for accelerated brain aging in alcohol dependence. *Transl Psychiatry* 7: 1–7.
9. Jang D-P, Namkoong K, Kim J-J, Park S, Kim I-Y, Kim SI, *et al.* (2007): The relationship between brain morphometry and neuropsychological performance in alcohol dependence. *Neurosci Lett* 428: 21–26.
10. Mechtcheriakov S, Brenneis C, Egger K, Koppelstaetter F, Schocke M, Marksteiner J (2007): A widespread distinct pattern of cerebral atrophy in patients with alcohol addiction revealed by voxel-based morphometry. *J Neurol Neurosurg Psychiatry* 78: 610–614.
11. Nurmedov S, Noyan O, Metin B, Ekmen S, Avcil C, Kose S (2016): Extensive gray matter volume reduction and correlations with neuropsychological performance in alcohol use disorder patients. *Klin Psikofarmakol Bülteni-Bulletin Clin Psychopharmacol* 26: 355–363.
12. Rando K, Hong K, Bhagwagar Z, Li CR, Bergquist K, Guarnaccia J, Sinha R (2011): Association of frontal and posterior cortical gray matter volume with time to alcohol relapse: a prospective study. *Am J Psychiatry* 168: 183–192.
13. Segobin SH, Chételat G, Le Berre A-P, Lannuzel C, Boudehent C, Vabret F, *et al.* (2014): Relationship between brain volumetric changes and interim drinking at six months in alcohol-dependent patients. *Alcohol Clin Exp Res* 38: 739–748.
14. van Holst RJ, de Ruiter MB, van den Brink W, Veltman DJ, Goudriaan AE (2012): A voxel-based morphometry study comparing problem gamblers, alcohol abusers, and healthy controls. *Drug Alcohol Depend* 124: 142–148.
15. Wang J, Fan Y, Dong Y, Ma M, Dong Y, Niu Y, *et al.* (2018): Combining gray matter volume in the cuneus and the cuneus-prefrontal connectivity may predict early relapse in abstinent alcohol-dependent patients. *PLoS One* 13: 1–18.
16. Wiers CE, Gawron CK, Gröpper S, Spengler S, Stuke H, Lindenmeyer J, *et al.* (2015): Decreased gray matter volume in inferior frontal gyrus is related to stop-signal task performance in alcohol-dependent patients.

Psychiatry Res - Neuroimaging 233: 125–130.
17. Wu G-R, Baeken C, Van Schuerbeek P, De Mey J, Bi M, Herremans SC (2018): Accelerated repetitive transcranial magnetic stimulation does not influence grey matter volumes in regions related to alcohol relapse: An open-label exploratory study. *Drug Alcohol Depend* 191: 210–214.
18. Yoon EJ, Choi J-S, Kim H, Sohn BK, Jung HY, Lee J-Y, *et al.* (2017): Altered hippocampal volume and functional connectivity in males with Internet gaming disorder comparing to those with alcohol use disorder. *Sci Rep* 7: 1–12.
19. Zois E, Vollstädt-Klein S, Hoffmann S, Reinhard I, Charlet K, Beck A, *et al.* (2017): Orbitofrontal structural markers of negative affect in alcohol dependence and their associations with heavy relapse-risk at 6 months post-treatment. *Eur Psychiatry* 46: 16–22.
20. Christian CJ, Lencz T, Robinson DG, Burdick KE, Ashtari M, Malhotra AK, *et al.* (2008): Gray matter structural alterations in obsessive-compulsive disorder: Relationship to neuropsychological functions. *Psychiatry Res - Neuroimaging* 164: 123–131.
21. Gilbert AR, Mataix-Cols D, Almeida JRC, Lawrence N, Nutche J, Diwadkar V, *et al.* (2008): Brain structure and symptom dimension relationships in obsessive-compulsive disorder: A voxel-based morphometry study. *J Affect Disord* 109: 117–126.
22. Gonçalves OF, Sousa S, Carvalho S, Leite J, Ganho A, Fernandes-Gonçalves A, *et al.* (2017): Alterations of gray and white matter morphology in obsessive compulsive disorder. *Psicothema* 29: 35–42.
23. Hashimoto N, Nakaaki S, Kawaguchi A, Sato J, Kasai H, Nakamae T, *et al.* (2014): Brain structural abnormalities in behavior therapy-resistant obsessive-compulsive disorder revealed by voxel-based morphometry. *Neuropsychiatr Dis Treat* 10: 1987–1996.
24. Hoexter MQ, De Souza Duran FL, D'Alcante CC, Dougherty DD, Shavitt RG, Lopes AC, *et al.* (2012): Gray matter volumes in obsessive-compulsive disorder before and after fluoxetine or cognitive-behavior therapy: A randomized clinical trial. *Neuropsychopharmacology* 37: 734–745.
25. Hou J, Song L, Zhang W, Wu W, Wang J, Zhou D, *et al.* (2013): Morphologic and functional connectivity alterations of corticostriatal and default mode network in treatment-naïve patients with obsessive-compulsive disorder. *PLoS One* 8: 1–11.
26. Ikari K, Nakao T, Nemoto K, Okada K, Murayama K, Honda S, *et al.* (2017): Morphologic and clinical differences between early- and late-onset obsessive-compulsive disorder: Voxel-based Morphometric study. *J Obsessive Compuls Relat Disord* 13: 35–41.
27. Kobayashi T, Hirano Y, Nemoto K, Sutoh C, Ishikawa K, Miyata H, *et al.* (2015): Correlation between morphologic changes and autism spectrum tendency in obsessive-compulsive disorder. *Magn Reson Med Sci* 14: 329–335.
28. Kopřivová J, Horáček J, Tintěra J, Praško J, Raszka M, Ibrahim I, Höschl C (2009): Medial frontal and dorsal cortical morphometric abnormalities are related to obsessive-compulsive disorder. *Neurosci Lett* 464: 62–66.
29. Lv Q, Wang Z, Zhang C, Fan Q, Zhao Q, Zeljic K, *et al.* (2017): Divergent structural responses to pharmacological interventions in orbitofronto-striato-thalamic and premotor circuits in obsessive-compulsive disorder. *EBioMedicine* 22: 242–248.
30. 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: 541–547.
31. Moon C-M, Jeong G-W (2018): Associations of neurofunctional, morphometric and metabolic abnormalities with clinical symptom severity and recognition deficit in obsessive–compulsive disorder. *J Affect Disord* 227: 603–612.
32. Moreira PS, Marques P, Soriano-Mas C, Magalhães R, Sousa N, Soares JM, Morgado P (2017): The neural correlates of obsessive-compulsive disorder: a multimodal perspective. *Transl Psychiatry* 7: e1224.
33. Pujol J, Soriano-Mas C, Alonso P, Cardoner N, Menchón JM, Deus J, Vallejo J (2004): Mapping structural brain alterations in obsessive-compulsive disorder. *Arch Gen Psychiatry* 61: 720–730.
34. Real E, Subirà M, Alonso P, Segalàs C, Labad J, Orfila C, *et al.* (2016): Brain structural correlates of obsessive–compulsive disorder with and without preceding stressful life events. *World J Biol Psychiatry* 17: 366–377.
35. Riffkin J, Yücel 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 - Neuroimaging* 138: 99–113.
36. Spalletta G, Piras F, Fagioli S, Caltagirone C, Piras F (2014): Brain microstructural changes and cognitive correlates in patients with pure obsessive compulsive disorder. *Brain Behav* 4: 261–277.

37. Subirà M, Alonso P, Segalàs C, Real E, López-Solà C, Pujol J, *et al.* (2013): Brain structural alterations in obsessive-compulsive disorder patients with autogenous and reactive obsessions. *PLoS One* 8: e75273.
38. Tan L, Fan Q, You C, Wang J, Dong Z, Wang X, *et al.* (2013): Structural changes in the gray matter of unmedicated patients with obsessive-compulsive disorder: A voxel-based morphometric study. *Neurosci Bull* 29: 642–648.
39. Tang W, Huang X, Li B, Jiang X, Li F, Xu J, *et al.* (2015): Structural brain abnormalities correlate with clinical features in patients with drug-naïve OCD: A DARTEL-enhanced voxel-based morphometry study. *Behav Brain Res* 294: 72–80.
40. Tang W, Zhu Q, Gong X, Zhu C, Wang Y, Chen S (2016): Cortico-striato-thalamo-cortical circuit abnormalities in obsessive-compulsive disorder: A voxel-based morphometric and fMRI study of the whole brain. *Behav Brain Res* 313: 17–22.
41. 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 - Neuroimaging* 184: 29–37.
42. Valente AA, Miguel EC, Castro CC, Amaro E, Duran FLS, Buchpiguel CA, *et al.* (2005): Regional gray matter abnormalities in obsessive-compulsive disorder: A voxel-based morphometry study. *Biol Psychiatry* 58: 479–487.
43. Wang Y, Zou L, Xie W, Yang Z, Zhu X, Cheung EFC, *et al.* (2018): Altered grey matter volume and cortical thickness in patients with schizo-obsessive comorbidity. *Psychiatry Res - Neuroimaging* 276: 65–72.
44. Yoo SY, Roh M-S, Choi J-S, Kang D-H, Tae HH, Lee J-M, *et al.* (2008): Voxel-based morphometry study of gray matter abnormalities in obsessive-compulsive disorder. *J Korean Med Sci* 23: 24–30.