

# Supplementary Tables

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**Supplementary Table S11:** Full meta-analytic results for each mean structure for the association between symptom severity and brain volumes within MDD patients based on the HDRS-17 questionnaire controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

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**Supplementary Table S13:** Full meta-analytic results for each mean structure for the MDD patients versus Controls comparison (excluding remitted patients) controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

**Supplementary Table 14:** Adjusted means and standard errors for each site including the total number of subjects (N) for each structure and split into MDD patients and controls (CTL). Means are adjusted for age, sex, scan center, and ICV using the *lsmeans* package in R.

**Supplementary Table 15:** Full results from the moderator analyses of mean age, field strength of scanner, percent of acute patients, FreeSurfer version used for processing, percent of patients taking antidepressants, and percent of patients taking antipsychotics. Effect sizes for the meta-regression models were available from all 15 sites (percent of patients taking antipsychotics was not available in MMDP 1.5T and MMDP 3T).

**Supplementary Table S16:** Meta-analytic results for each mean structure for the diagnosis \* sex interactive effect in the full sample of MDD patients and Controls while controlling for age, sex, diagnosis, scan center and ICV. Adjusted Cohen's d is reported.

**Table S1.** ENIGMA - Major Depressive Disorder Working Group Demographics. Age (in years), sex, and MDD patients-control breakdown for participating sites

Study #	Study name	Age Controls (Mean ± SD)	Age MDD (Mean ± SD)	% Female Controls	% Female MDD	Total N Controls	Total N MDD	Total N
1	NESDA	40.5 ± 9.8	37.2 ± 10.4	65	65	66	156	222
2	Imaging Genetics Dublin	36.7 ± 13.0	41.6 ± 10.8	56	63	52	52	104
3	Clinical Depression Dublin	30.2 ± 8.2	32.9 ± 9.1	45	42	94	36	130
4	CODE	40.0 ± 13.3	41.0 ± 12.0	58	65	74	102	176
5	CLING	25.1 ± 5.2	36.3 ± 11.6	60	53	321	49	370
6	SHIP	55.4 ± 12.8	53.5 ± 11.8	45	71	441	139	580
7	SHIP-trend	50.6 ± 14.3	49.4 ± 12.2	44	66	952	323	1275
8	Sydney	47.0 ± 23.2	35.8 ± 22.0	57	65	106	214	320
9	QTIM	22.9 ± 3.2	23.1 ± 2.7	69	82	262	38	300
10	Rotterdam study	64.6 ± 11.1	60.7 ± 9.8	53	72	4408	69	4477
11	Bipolar Family Study	23.2 ± 2.4	23.0 ± 3.1	68	61	62	18	80
12	DepOx	30.3 ± 10.0	30.1 ± 10.6	58	63	31	38	69
13	MPIP	49.1 ± 13.1	48.0 ± 13.8	58	56	222	368	590
14	MMDP 1.5T	27.4 ± 10.7	31.3 ± 12.2	64	51	44	53	97
15	MMDP 3T	30.2 ± 11.2	36.2 ± 14.5	63	55	64	73	137
	<b>Combined</b>					<b>7199</b>	<b>1728</b>	<b>8927</b>

**Table S2.** ENIGMA - Major Depressive Disorder Working Group Clinical characteristics of MDD patients. Percentage of MDD patients using antidepressant medication, percentage of first episode and recurrent episode MDD patients, percentage of acutely depressed and remitted MDD patients, percentage of patients with a co-occurring anxiety disorder, age of onset of MDD and severity of symptoms breakdown for participating sites

Study #	Sample	% Antidepressants users	% Antipsychotics users	% First episode MDD/Recurrent episode MDD	% Acute MDD/ Remitted MDD	Age of onset MDD (mean $\pm$ SD)	% co-occurring anxiety disorder	HDRS-17 <sup>a</sup> Severity MDD (mean $\pm$ SD)	BDI-II <sup>b</sup> Severity MDD (mean $\pm$ SD)	IDS-SR <sup>c</sup> Severity MDD (mean $\pm$ SD)
1	NESDA	37	0	44/56	100/0	24.3 $\pm$ 11.0	60			25.4 $\pm$ 12.0
2	Imaging Genetics Dublin	71	0	15/85	100/0	25.3 $\pm$ 12.8	0	23.6 $\pm$ 5.0	33.1 $\pm$ 11.7	
3	Clinical Depression Dublin	92	0	50/50	100/0	29.6 $\pm$ 9.2	0	20.8 $\pm$ 5.1		
4	CODE	0	0	0/100	100/0	NA	0			38.2 $\pm$ 11.6
5	CLING	94	12	45/55	94/6	30.4 $\pm$ 10.6	18	20.0 $\pm$ 4.3	21.9 $\pm$ 9.8	
6	SHIP	17	1	55/45	NA	38.1 $\pm$ 13.2	37		11.7 $\pm$ 10.3	
7	SHIP-trend	17	5	37/63	NA	36.2 $\pm$ 14.3	NA		12.4 $\pm$ 8.1	
8	Sydney	61	24	12/88	17/83	24.6 $\pm$ 17.2	19	12.2 $\pm$ 6.9		
9	QTIM	24	0	61/39	24/76	17.8 $\pm$ 3.5	29	NA	NA	
10	Rotterdam study	29	4	45/55	100/0	NA	11	NA	NA	
11	Bipolar Family Study	17	0	NA	NA	21.4 $\pm$ 3.3	0	5.4 $\pm$ 5.7		
12	DepOx	0	0	50/50	100/0	25.6 $\pm$ 9.1	3	22.9 $\pm$ 4.3		
13	MPIP	84	7	27/73	87/13	35.2 $\pm$ 14.0	14	24.9 $\pm$ 6.6	14.2 $\pm$ 10.9	
14	MMDP 1.5T	25	NA	75/25	100/0	23.6 $\pm$ 11.5	19	12.6 $\pm$ 7.2		
15	MMDP 3T	55	NA	45/55	100/0	23.4 $\pm$ 11.9	30	12.0 $\pm$ 7.0		

<sup>a</sup> Measured with the Hamilton Depression Rating Scale (HDRS-17; range: 0-52)

<sup>b</sup> Measured with the Beck Depression Inventory (BDI-II; range: 0-63)

<sup>c</sup> Measured with the Inventory of Depressive Symptomatology-Severity report (IDS-SR; range: 0-84)

**Table S3:** Instrument for diagnosing Major Depressive Disorder and exclusion criteria by site

Sample	Instrument for diagnosing MDD	Exclusion criteria
NESDA	CIDI interview	MDD subjects: presence of axis-I disorders other than MDD, panic disorder, social anxiety disorder, or generalized anxiety disorder and any use of psychotropic medication other than stable use of SSRIs or infrequent benzodiazepine use (i.e., equivalent to 2 doses of 10 mg of oxazepam 3 times per week or use within 48 hours prior to scanning). Control subjects: no Axis-I diagnosis, no medication use. All subjects: presence or history of major internal or neurological disorder, dependence on or recent abuse (past year) of alcohol and/or drugs, hypertension, and general MRI contraindications.
Imaging Genetics Dublin	SCID-1 interview	MDD subjects: comorbid psychiatric disorders (Axis I or Axis II, other than MDD), Treatment with antipsychotics or mood stabilizers, age <18 or >65, Control subjects: no Axis-I diagnosis, no medication use. All subjects: history of neurological or other severe medical illness, head injury or severe substance abuse in their lifetime history and general MRI contraindications.
Clinical Depression Dublin	SCID-1 interview	MDD subjects: comorbid psychiatric disorders (Axis I or Axis II, other than MDD), Treatment with antipsychotics or mood stabilizers, age <18 or >65, Control subjects: no Axis-I diagnosis, no medication use. All subjects: history of neurological or other severe medical illness, head injury or severe substance abuse in their lifetime history and general MRI contraindications.
CODE	SCID interview	MDD: Presence of any other Axis-1 diagnosis; Acute risk for suicide (in contrast to suicidal ideation); History of psychotic symptoms, bipolar disorder, or dementia; Schizotypal, antisocial or borderline personality disorder; Use of psychotropic medication within two weeks prior to the start of the study; No current psychotherapeutic treatment. Control subjects: No history of or current Axis-1 or 2 disorders. All subjects: History of or current neurological disorder or brain injury; Serious medical condition; Severe cognitive impairment; Substance-related abuse or dependence disorder; Use of psychotropic medication; Use of central-acting medication; Pregnancy; General MRI contraindications.
CLING	ICD-10 interview	MDD subjects: past or actual presence of other axis I diagnoses other than anxiety disorders, alcohol/cannabis abuse and tobacco dependence; neurological or other medical conditions that could be related to affective symptoms Control subjects: no medical history, including neurological and psychiatric history, as well as no previous or actual use of psychotropic medication

<b>SHIP</b>	M-CIDI interview	<p>MDD subjects: presence of axis-I disorders other than MDD, anxiety disorders, conversion, somatization and eating disorder.</p> <p>Control subjects: no lifetime diagnosis of depression, no antidepressiva, and severity index=0</p> <p>All subjects: We removed subjects with medical conditions (e.g. a history of cerebral tumor, stroke, Parkinson's diseases, multiple sclerosis, epilepsy, hydrocephalus, enlarged ventricles, pathological lesions) or due to technical reasons (e.g. severe movement artifacts or inhomogeneity of the magnetic field).</p>
<b>SHIP-trend</b>	M-CIDI interview	<p>MDD subjects: no special exclusion criteria</p> <p>Control subjects: no lifetime diagnosis of depression, no antidepressiva, and severity index=0</p> <p>All subjects: We removed subjects with due to medical conditions (e.g. a history of cerebral tumor, stroke, Parkinson's diseases, multiple sclerosis, epilepsy, hydrocephalus, enlarged ventricles, pathological lesions) or due to technical reasons (e.g. severe movement artifacts or inhomogeneity of the magnetic field).</p>
<b>Sydney</b>	SCID interview	<p>MDD subjects: presence of axis-I disorders other than MDD, panic disorder, social anxiety disorder, or generalized anxiety disorder.</p> <p>Control subjects: no Axis-I diagnosis, no medication use.</p> <p>Exclusion criteria for all subjects included medical instability (as determined by a psychiatrist), history of neurological disease (e.g. tumour, head trauma, epilepsy), medical illness known to impact cognitive and brain function (e.g. cancer), intellectual and/or developmental disability and insufficient English for neuropsychological assessment. All subjects were asked to abstain from drug or alcohol use for 48 hours prior to testing and informed about a drug screen protocol.</p>
<b>QTIM</b>	CIDI interview	<p>MDD subjects: presence of axis-I disorders other than MDD, anxiety disorders</p> <p>Control subjects: antidepressant use, psychiatric disorders</p> <p>All subjects: relatedness between subjects, left handedness, history of neurological or other severe medical illness, head injury or current or past diagnosis of substance abuse, use of cognition affecting medication and general MRI contraindications</p>
<b>Rotterdam study</b>	SCAN interview	<p>MDD subjects: Persons who screened positive for depressive symptoms on CESD but did not meet criteria for MDD from SCAN interview. Persons who screened positive for depressive symptoms on CESD and then did not undergo SCAN interview. Presence of axis-I disorders other than MDD and anxiety disorders (DSM-IV). Persons with MRI contraindications.</p> <p>Control subjects: use of psychoanaleptics, MRI contraindications.</p>
<b>Bipolar Family Study</b>	SCID interview	<p>MDD subjects: presence of other axis I diagnoses.</p> <p>Control subjects: no medical history, including neurological and psychiatric history, as well as no previous or actual use of psychotropic medication</p>

	<p>All subjects: any major neurological disorder, learning disability, or any history of head injury that included loss of consciousness and any contraindications to MRI.</p>
<p><b>DepOx</b></p>	<p>SCID interview</p> <p>MDD subjects: presence of axis-I disorders other than MDD and anxiety disorders (DSM-IV), clinically significant risk of suicidal behaviour, having contraindications to escitalopram treatment or being treated with psychotropic medication less than three weeks before the study (five weeks in the case of fluoxetine)</p> <p>Control subjects: current or past history of Axis I disorder as defined by DSM-IV</p> <p>Both groups: major somatic or neurological disorders, pregnancy or breast-feeding, contra-indications to MR imaging or concurrent medication which could alter emotional processing</p>
<p><b>MPIP</b></p>	<p>M-CIDI/SCAN interview</p> <p>1. Munich Antidepressant Response Signature (MARS) study</p> <p>MDD subjects (clinical consensus diagnosis or M-CIDI (since 2008)): depressive syndromes secondary to any medical or neurological condition (e. g., intoxication, drug abuse, stroke), the presence of manic, hypomanic or mixed affective symptoms, lifetime diagnosis of alcohol dependence, illicit drug abuse or the presence of severe medical conditions (e.g., ischemic heart disease). Patients with bipolar depression were excluded for the current MR study.</p> <p>Control subjects: age &gt; 65, MMSE&lt;27, presence of severe somatic diseases or lifetime history of the following axis I disorders as assessed by the M-CIDI interview: alcohol dependence, drug abuse or dependence, possible psychotic disorder, mood disorder, anxiety disorder including OCD and PTSD, somatoform disorder, dissociative disorder NOS, and eating disorder</p> <p>2. Recurrent unipolar depression (RUD) study</p> <p>MDD subjects (SCAN interview): presence of manic episodes, mood incongruent psychotic symptoms, the presence of a lifetime diagnosis of intravenous drug abuse and depressive symptoms only secondary to alcohol or substance abuse or to medical illness or medication.</p> <p>Control subjects: presence of severe somatic diseases or life-time history of anxiety and affective disorders according to the Composite International Diagnostic-Screener (CIDI-S)</p> <p>All subjects: gross incidental MR findings such as territorial infarction, tumor, hydrocephalus, malformations and anatomical deviations (e.g. enlarged ventricles) that prevent appropriate image processing were additional exclusion criteria.</p> <p>3. MR images of 9 additional controls acquired at the LMU, Munich, meeting equivalent criteria as the RUD control sample were included.</p>
<p><b>MMDP 3T</b></p>	<p>SCID interview</p> <p>MDD subjects: presence of axis-I disorders other than MDD and anxiety disorders (DSM-IV). Control subjects had to have no psychiatric history, as assessed with the SCID-I/P</p>

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Symptom severity was assessed using the 17-item Hamilton Depression Rating Scale (HDRS-17) and the Global Assessment of Functioning Scale (GAF). Control subjects also received these measures to rule out the presence of sub-threshold psychiatric illness.

Exclusion criteria for all groups were:

- (1) substance-use related disorder within the past 6 months as determined by the SCID;
- (2) lifetime history of substance dependence as measured by the SCID;
- (3) PTSD as determined by the SCID;
- (4) treatment with anti-cholinergic or typical (first generation) anti-psychotic medication;
- (5) use of alcohol or illicit psychoactive substance within 48 h of testing;
- (6) untreated medical illness such as uncontrolled diabetes or other endocrine disorders eg. Cushing's;
- (7) history of head injury with loss of consciousness;
- (8) history of neurological disease; and
- (9) past treatment with electroconvulsive therapy (ECT), transcranial magnetic stimulation, or psychotherapy within the past year.
- (10) English comprehension lower than a grade 6 reading level.

**MMDP 1.5T**

SCID interview

MDD subjects: presence of axis-I disorders other than MDD and anxiety disorders (DSM-IV),

Control subjects had to have no psychiatric history, as assessed with the SCID-I/P

Symptom severity was assessed using the 17-item Hamilton Depression Rating Scale (HDRS-17) and the Global Assessment of Functioning Scale (GAF). Control also received these measures to rule out the presence of sub-threshold psychiatric illness.

Exclusion criteria for all groups were:

- (1) substance-use related disorder within the past 6 months as determined by the SCID;
- (2) lifetime history of substance dependence as measured by the SCID;
- (3) PTSD as determined by the SCID;
- (4) treatment with anti-cholinergic or typical (first generation) anti-psychotic medication;
- (5) use of alcohol or illicit psychoactive substance within 48 h of testing;
- (6) untreated medical illness such as uncontrolled diabetes or other endocrine disorders eg. Cushing's;
- (7) history of head injury with loss of consciousness;
- (8) history of neurological disease; and
- (9) past treatment with electroconvulsive therapy (ECT), transcranial magnetic stimulation, or psychotherapy within the past year.
- (10) English comprehension lower than a grade 6 reading level.



MDD: Major Depressive Disorder; CIDI: the Composite International Diagnostic Interview; SCID: Structured Clinical Interview for DSM disorders; SCAN: Schedules for Clinical Assessment in Neuropsychiatry; CESD: Center for Epidemiologic Studies Depression scale; DSM: Diagnostic and Statistical Manual of Mental Disorders; MRI: Magnetic Resonance Imaging; OCD: Obsessive Compulsive Disorder; PTSD: Posttraumatic Stress Disorder.

**Table S4:** Image acquisition and processing by site

Sample	Scanner vendor and type	Acquisition parameters	Freesurfer version	Slice orientation	Operating system
<b>NESDA</b>	3T Phillips Achieva/Intera	3D gradient-echo T1-weighted sequence. TR=9 msec; TE=3.5 msec; flip angle 8°, FOV = 256 mm; matrix: 25x62x56; in plane voxel size = 1 mm x 1 mm x 1 mm; 170 slices.	5.0	Sagittal	Linux-centos4_x86_64
<b>Imaging Genetics Dublin</b>	3T Phillips Achieva	A sagittal T1 3D TFE was used to scan all participants. TR=8.5 msec; TE=3.9 msec; FOV = 256 mm, AP: 256 mm, RL: 160 mm; matrix: 256x256.	5.3	Sagittal	Mac OS
<b>Clinical Depression Dublin</b>	1.5T Siemens Vision	3D-MPRAGE T1-weighted sequence. TR=11.6 msec; TE=4.9 msec; FOV=230 mm; matrix 512 x 512, slice thickness: 1.5 mm.	5.3	Coronal	Mac OS
<b>CODE</b>	3T Siemens Trio (4 Sites), 3 T Philips Achieva (1 site)	Siemens: T1 mprage, voxel size 1 mm x 1 mm x 1 mm; TR=1900 msec; TE=2.52 msec; Sample 1: 192 slices, Sample 2: 176 slices (except 1 site: 192) Philips: T1 3D-TFE, voxel size 1 mm x 1 mm x 1 mm; TR=8.3 msec; TE=3.8 msec; 170 slices.	5.3	Sagittal	Ubuntu 12.04 LTS (Linux 64bit)
<b>CLING</b>	3T Siemens Tim Trio	Standard 3D T1-weighted turbo fast low angle shot (turbo FLASH); voxel size 1 mm x 1 mm x 1mm (based on the ADNI protocol (Jack et al. 2008); TR=225 msec; TE=3.26 msec, FOV=256 x 256 x 192	5.1	Sagittal	Linux
<b>SHIP</b>	1.5T Siemens Avanto	3D T1-weighted (MP-RAGE/ axial plane); TR=1900 msec; TE=3.4 msec; Flip angle=15°; voxel size 1 mm x 1 mm x 1 mm	5.1	Axial	Centos6_x86_64

<b>SHIP-trend</b>	1.5T Siemens Avanto	3D T1-weighted (MP-RAGE/ axial plane); TR=1900 msec; TE=3.4 msec; Flip angle=15°; voxel size 1 mm x 1 mm x 1 mm	5.1	Axial	Centos6_x86_64
<b>Sydney</b>	3T GE MR750	3D T1-weighted sequence. TR=7.2 msec; TE=2.78 msec; matrix =256; FOV=240; No. slices=196; thick=0.9mm; inplane resolution=0.9375	5.1	Coronal	Linux_Ubuntu12.04_64
<b>QTIM</b>	Bruker 4T Whole-body MRI	3D T1 weighted sequence. TR=1500 msec; TE=3.35 msec; flip angle=8°, 256 or 240 (coronal or sagittal) slices, FOV=240 mm, matrix 256x256x256 (or 256x256x240)	5.1	Coronal, then sagittal following software upgrade.	Linux-centos4_x86_64-stable-pub-v5.1.0
<b>Rotterdam study</b>	1.5T Signa Excite - General Electric Healthcare, Milwaukee, USA, software version 11x	3D GRE T1 weighted sequence. TR= 13.8 msec; TE=2.8 msec; TI=400 ms; Flip angle=20°; FOV=25cm <sup>2</sup> ; maxtrix 416 x 256; voxel size 1 mm x 1 mm x 1 mm.	4.5	Axial	
<b>Bipolar Family Study</b>	1.5T GE Signa	T1-weighted sequence. TR=500 msec; TE=4 msec; flip angle 8°; matrix 192 x 192; 180 slices; voxel size 1.25 mm x 1.25 mm x 1.20 mm; FOV=24, phase FOV 1	5.3	Coronal	linux 6, x86_64, kernel 2.6.32
<b>DepOx</b>	3T Siemens Tim Trio	T1 weighted sequence. TR=1100 msec; TE=4.8 msec; TI=2040 msec; voxel size 0.78 mm x 0.8 mm x 0.78 mm on a 208 x 256 x 200 grid,	5.3	Transversal	Suse Linux x86_64
<b>MPIP</b>	1.5T GE and Siemens (the latter: only few cases)	#1: T1-weighted SPGR sagittal 3D volume. TR=1030 msec; TE=3.4 msec; 124 slices; matrix=256x256; FOV=23.0x23.0 cm <sup>2</sup> ; voxel size=0.8975 mm x0.8975 mm x 1.2-1.4 mm; flip angle=90°; birdcage resonator.  #2: same scanner as #1, platform update Signa Excite, sagittal T1-weighted (spin echo sequence, TR=9.7 msec, TE=2.1	5.3	1.5 GE: sagittal 1.5 Siemens: axial	Linux 2.6.37.1-1.2-desktop x86_64

		<p>msec; FOV=25.0x25.0 cm<sup>2</sup>, voxel size=0.875 mm x0.875 mm x1.2 mm, 124-132 slices, flip angle=90°.</p> <p>#3: Siemens 1.5 Tesla, Vario, 3D MPRAGE, TR=11.6 msec; TE=4.9 msec; FOV 23x23 cm<sup>2</sup>; matrix 512x512; 126 axial slices; voxel size 0.45 mm x 0.45 mm x 1.5 mm. (only N=2 subjects)</p>		
<b>MMDP 3T</b>	3T MRI Signa GE Excite	<p>Axial T-1 weighted sequence; 3D SPGR pulse; fast IRP sequence; TR = 7.012 msec; TE = 2.1 msec; Ti=450 msec; flip angle= 12°; FOV = 240; slice thickness = 2 mm no skip; frequency matrix = 320; phase matrix = 192; frequency direction = A/P</p>	5.3	Axial
<b>MMDP 1.5T</b>	1.5-T. Signa GE Genesis-based Echo-Speed scanner	<p>Sagittal anatomic images were acquired by using a 3D/FSPGR/20 sequence. flip angle=20; TR=300 msec; inversion recovery=300 msec; matrix=512x256; FOV=24 cm; scan thickness=1.2 mm</p>	5.3	Sagittal

3D: three-dimensional; TR: repetition time; TE: echo time; FOV: field of view

**Supplementary Table S5:** Full meta-analytic results for each mean structure for the first episode MDD patients versus Controls comparison controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (First episode MDD - CTL)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# Controls	# Patients
<b>Lateral Ventricles</b>	0.034	0.049	[-0.061 - 0.129]	0.601	0.485	<0.001	6922	567
<b>Thalamus</b>	-0.047	0.049	[-0.142 - 0.049]	-0.575	0.339	<0.001	6910	566
<b>Caudate</b>	-0.009	0.088	[-0.181 - 0.164]	-0.542	0.923	65.118	6898	573
<b>Putamen</b>	-0.032	0.061	[-0.151 - 0.088]	-0.652	0.605	27.697	6821	557
<b>Pallidum</b>	-0.008	0.049	[-0.104 - 0.089]	-0.286	0.876	<0.001	6882	558
<b>Hippocampus</b>	-0.073	0.074	[-0.219 - 0.073]	-0.762	0.325	51.155	6904	572
<b>Amygdala</b>	-0.041	0.057	[-0.153 - 0.072]	-0.317	0.478	20.999	6924	570
<b>Accumbens</b>	0.012	0.066	[-0.117 - 0.142]	-0.117	0.853	37.094	6831	550
<b>ICV</b>	-0.005	0.055	[-0.113 - 0.103]	-0.071	0.930	17.697	7063	583

<sup>a</sup> Included Samples: NESDA, Clinical Depression Dublin, CLING, SHIP, SHIP-trend, Sydney, QTIM, Rotterdam study, DepOx, MPIP, MMDP 3T, MMDP 1.5T. ICV: Intracranial Volume; MDD: Major Depressive Disorder; CTL: Controls.

**Supplementary Table S6:** Full meta-analytic results for each mean structure for the recurrent MDD patients versus Controls comparison controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (Recurrent MDD - CTL)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# Controls	# Patients
<b>Lateral Ventricles</b>	0.067	0.040	[-0.01 - 0.145]	2.096	0.089	<0.001	6996	1096
<b>Thalamus</b>	0.001	0.040	[-0.078 - 0.079]	-0.042	0.990	<0.001	6984	1090
<b>Caudate</b>	0.015	0.052	[-0.086 - 0.117]	0.268	0.768	29.644	6972	1082
<b>Putamen</b>	0.045	0.043	[-0.039 - 0.128]	0.404	0.294	5.850	6895	1073
<b>Pallidum</b>	0.010	0.040	[-0.069 - 0.089]	0.114	0.799	<0.001	6956	1073
<b>Hippocampus</b>	-0.174	0.040	[-0.252 - -0.096]	-1.443	1.12E-05	<0.001	6978	1102
<b>Amygdala</b>	-0.070	0.040	[-0.148 - 0.008]	-0.814	0.077	<0.001	6998	1100
<b>Accumbens</b>	-0.043	0.040	[-0.121 - 0.036]	-0.612	0.288	<0.001	6905	1076
<b>ICV</b>	0.017	0.046	[-0.074 - 0.108]	0.135	0.712	18.621	7137	1119

<sup>a</sup> Included Samples: NESDA, Imaging Genetics Dublin, Clinical Depression Dublin, CODE, CLING, SHIP, SHIP-trend, Sydney, QTIM, Rotterdam study, DepOx, MPIP, MMDP 3T, MMDP 1.5T.

ICV: Intracranial Volume; MDD: Major Depressive Disorder; CTL: Controls.

**Supplementary Table S7:** Full meta-analytic results for each mean structure for the recurrent MDD patients versus first episode MDD patients comparison controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (Recurrent MDD - First episode MDD)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# First MDD	# Recur MDD
<b>Lateral Ventricles</b>	0.015	0.056	[-0.095 - 0.124]	1.262	0.795	<0.001	567	994
<b>Thalamus</b>	0.053	0.056	[-0.056 - 0.163]	0.488	0.341	<0.001	566	988
<b>Caudate</b>	-0.020	0.056	[-0.13 - 0.09]	-0.049	0.718	<0.001	573	980
<b>Putamen</b>	0.033	0.090	[-0.144 - 0.21]	0.980	0.715	52.590	557	971
<b>Pallidum</b>	-0.015	0.058	[-0.128 - 0.098]	0.026	0.795	1.968	558	971
<b>Hippocampus</b>	-0.069	0.079	[-0.223 - 0.085]	-0.701	0.379	39.712	572	1000
<b>Amygdala</b>	-0.035	0.056	[-0.145 - 0.075]	-0.528	0.531	<0.001	570	999
<b>Accumbens</b>	-0.093	0.066	[-0.222 - 0.037]	-0.865	0.160	17.638	550	975
<b>ICV</b>	0.030	0.055	[-0.079 - 0.138]	0.362	0.593	<0.001	583	1017

<sup>a</sup> Included Samples: NESDA, Clinical Depression Dublin, CLING, SHIP, SHIP-trend, Sydney, QTIM, Rotterdam study, DepOx, MPIP, MMDP 3T, MMDP 1.5T.  
 % Difference is difference between recurrent MDD patients and first episode MDD patients divided by the average volume in first episode MDD patients.  
 ICV: Intracranial Volume; MDD: Major Depressive Disorder; CTL: Controls.

**Supplementary Table S8:** Full meta-analytic results for each mean structure for the early age of onset ( $\leq 21$ ) MDD patients versus Controls comparison controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (EAO MDD - CTL)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# Controls	# Patients
<b>Lateral Ventricles</b>	0.145	0.055	[0.037 - 0.253]	5.107	8.50E-03	<0.001	2628	533
<b>Thalamus</b>	-0.067	0.055	[-0.175 - 0.042]	-0.678	0.228	0.003	2603	531
<b>Caudate</b>	0.020	0.073	[-0.123 - 0.163]	0.093	0.783	36.502	2597	529
<b>Putamen</b>	0.020	0.067	[-0.111 - 0.151]	0.075	0.763	24.492	2533	525
<b>Pallidum</b>	0.047	0.060	[-0.071 - 0.165]	0.538	0.434	10.892	2572	526
<b>Hippocampus</b>	-0.205	0.056	[-0.314 - -0.096]	-1.846	2.31E-04	0.579	2603	533
<b>Amygdala</b>	-0.117	0.055	[-0.225 - -0.01]	-1.228	0.033	<0.001	2612	537
<b>Accumbens</b>	-0.058	0.056	[-0.167 - 0.052]	-0.830	0.302	<0.001	2504	526
<b>ICV</b>	0.041	0.080	[-0.116 - 0.199]	-0.173	0.607	48.751	2717	541

<sup>a</sup> Included Samples: NESDA, Imaging Genetics Dublin, CLING, SHIP, SHIP-trend, Sydney, QTIM, DepOx, MPIP, MMDP 3T, MMDP 1.5T. ICV: Intracranial Volume; EAO: Early Age of Onset; MDD: Major Depressive Disorder; CTL: Controls.



**Supplementary Table S9:** Full meta-analytic results for each mean structure for the late age of onset (> 21) MDD patients versus Controls comparison controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (LAO MDD - CTL)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# Controls	# Patients
<b>Lateral Ventricles</b>	-0.005	0.041	[-0.085 - 0.075]	-0.314	0.911	<0.001	2628	967
<b>Thalamus</b>	0.034	0.044	[-0.053 - 0.12]	0.262	0.447	7.019	2603	962
<b>Caudate</b>	-0.051	0.052	[-0.153 - 0.052]	-0.683	0.332	24.946	2597	965
<b>Putamen</b>	0.013	0.045	[-0.074 - 0.101]	0.039	0.766	7.080	2533	943
<b>Pallidum</b>	-0.032	0.041	[-0.113 - 0.05]	-0.373	0.446	0.009	2572	942
<b>Hippocampus</b>	-0.103	0.053	[-0.207 - 0.001]	-0.818	0.052	27.690	2603	978
<b>Amygdala</b>	-0.028	0.048	[-0.123 - 0.067]	-0.343	0.568	17.350	2612	971
<b>Accumbens</b>	-0.030	0.042	[-0.112 - 0.052]	-0.278	0.471	<0.001	2504	938
<b>ICV</b>	0.003	0.074	[-0.142 - 0.148]	0.213	0.968	61.068	2717	997

<sup>a</sup> Included Samples: NESDA, Imaging Genetics Dublin, Clinical Depression Dublin, CLING, SHIP, SHIP-trend, Sydney, DepOx, MPIP, MMDP 3T, MMDP 1.5T. ICV: Intracranial Volume; MDD: LAO: Late Age of Onset; Major Depressive Disorder; CTL: Controls.

**Supplementary Table S10:** Full meta-analytic results for each mean structure for the late age of onset (> 21) MDD patients versus early age of onset ( $\leq$  21) MDD patients comparison controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (LAO MDD – EAO MDD)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# Controls	# Patients
<b>Lateral Ventricles</b>	-0.133	0.062	[-0.254 - -0.011]	-7.101	0.032	<0.001	533	967
<b>Thalamus</b>	0.096	0.070	[-0.042 - 0.234]	1.554	0.173	15.429	531	962
<b>Caudate</b>	-0.059	0.077	[-0.21 - 0.092]	-1.209	0.442	26.757	529	965
<b>Putamen</b>	-0.028	0.070	[-0.164 - 0.109]	-0.625	0.691	13.196	525	943
<b>Pallidum</b>	-0.082	0.090	[-0.258 - 0.094]	-2.064	0.359	43.465	526	942
<b>Hippocampus</b>	0.143	0.066	[0.013 - 0.272]	2.228	0.031	8.355	533	978
<b>Amygdala</b>	0.120	0.065	[-0.008 - 0.247]	1.940	0.066	5.954	537	971
<b>Accumbens</b>	0.074	0.063	[-0.049 - 0.198]	1.079	0.238	<0.001	526	938
<b>ICV</b>	-0.074	0.096	[-0.262 - 0.114]	-0.609	0.439	52.258	541	997

<sup>a</sup> Included Samples: NESDA, Imaging Genetics Dublin, CLING, SHIP, SHIP-trend, Sydney, DepOx, MPIP, MMDP 3T, MMDP 1.5T.

% Difference is difference between late age of onset (> 21) MDD patients and early age of onset ( $\leq$  21) MDD patients divided by the average volume in late age of onset (> 21) MDD patients.

ICV: Intracranial Volume; LAO: Late Age of Onset; EAO: Early Age of Onset; MDD: Major Depressive Disorder.

**Supplementary Table S11:** Full meta-analytic results for each mean structure for the association between symptom severity and brain volumes within MDD patients based on the HDRS-17 questionnaire controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Pearson's r <sup>a</sup>	Std. Err.	95% CI	P-value	I <sup>2</sup>	# Patients
<b>Lateral Ventricles</b>	-0.013	0.066	[-0.142 - 0.117]	0.847	59.501	659
<b>Thalamus</b>	0.018	0.039	[-0.058 - 0.094]	0.640	0.003	658
<b>Caudate</b>	0.076	0.039	[-0.001 - 0.152]	0.053	<0.001	654
<b>Putamen</b>	0.005	0.039	[-0.072 - 0.081]	0.900	<0.001	657
<b>Pallidum</b>	-0.018	0.039	[-0.095 - 0.058]	0.639	<0.001	656
<b>Hippocampus</b>	0.109	0.068	[-0.024 - 0.241]	0.109	62.572	664
<b>Amygdala</b>	0.022	0.050	[-0.075 - 0.119]	0.659	29.854	667
<b>Accumbens</b>	0.017	0.039	[-0.059 - 0.093]	0.663	0.020	658
<b>ICV</b>	0.002	0.039	[-0.073 - 0.078]	0.956	<0.001	667

<sup>a</sup> Included samples: Imaging Genetics Dublin, Clinical Depression Dublin, CLING, Sydney, Bipolar Family Study, DepOx, MPIP, MMDP 3T, MMDP 1.5T. HDRS-17: Hamilton Rating Scale for Depression 17 items; ICV: Intracranial Volume; MDD: Major Depressive Disorder.

**Supplementary Table S12:** Full meta-analytic results for each mean structure for the association between symptom severity and brain volumes within MDD patients based on the BDI-2 questionnaire controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Pearson's r <sup>a</sup>	Std. Err.	95% CI	P-value	I <sup>2</sup>	# Patients
<b>Lateral Ventricles</b>	-0.020	0.076	[-0.168 - 0.128]	0.791	66.343	634
<b>Thalamus</b>	-0.048	0.056	[-0.157 - 0.062]	0.391	38.219	624
<b>Caudate</b>	-0.062	0.040	[-0.14 - 0.016]	0.120	<0.001	628
<b>Putamen</b>	-0.034	0.041	[-0.114 - 0.046]	0.408	<0.001	603
<b>Pallidum</b>	0.028	0.041	[-0.053 - 0.108]	0.500	<0.001	599
<b>Hippocampus</b>	-0.058	0.053	[-0.161 - 0.045]	0.271	34.161	646
<b>Amygdala</b>	-0.016	0.040	[-0.094 - 0.061]	0.677	0.059	639
<b>Accumbens</b>	-0.061	0.041	[-0.141 - 0.018]	0.130	0.008	599
<b>ICV</b>	-0.080	0.039	[-0.156 - -0.005]	0.037	0.496	667

<sup>a</sup> Included samples: Imaging Genetics Dublin, CLING, SHIP, SHIP-trend, MPIP.

BDI-2: Beck Depression Inventory second edition; ICV: Intracranial Volume; MDD: Major Depressive Disorder.

**Supplementary Table S13:** Full meta-analytic results for each mean structure for the MDD patients versus Controls comparison (excluding remitted patients) controlling for age, sex, scan center and ICV. Adjusted Cohen's d is reported.

	Cohen's d <sup>a</sup> (MDD - CTL)	Std. Err.	95% CI	% Difference	P-value	I <sup>2</sup>	# Controls	# Patients
<b>Lateral Ventricles</b>	0.081	0.060	[-0.036 - 0.198]	1.179	0.175	<0.001	4779	570
<b>Thalamus</b>	-0.108	0.075	[-0.256 - 0.04]	-1.040	0.152	33.014	4780	569
<b>Caudate</b>	-0.015	0.061	[-0.135 - 0.106]	-0.258	0.808	3.435	4782	563
<b>Putamen</b>	0.022	0.066	[-0.108 - 0.153]	0.146	0.737	15.933	4766	568
<b>Pallidum</b>	-0.011	0.060	[-0.128 - 0.107]	-0.174	0.855	<0.001	4788	567
<b>Hippocampus</b>	-0.189	0.060	[-0.306 - -0.072]	-1.534	0.002	<0.001	4787	575
<b>Amygdala</b>	-0.036	0.064	[-0.162 - 0.09]	-0.373	0.577	12.667	4798	576
<b>Accumbens</b>	-0.034	0.060	[-0.151 - 0.083]	-0.538	0.569	<0.001	4812	572
<b>ICV</b>	-0.046	0.061	[-0.165 - 0.073]	-0.446	0.449	3.571	4833	579

<sup>a</sup> Included samples: NESDA, Imaging Genetics Dublin, Clinical Depression Dublin, CODE, Rotterdam study, DepOx, MMDP 1.5T and MMDP 3T  
 ICV: Intracranial Volume; MDD: Major Depressive Disorder; CTL: Controls.

**Supplementary Table 14:** Adjusted means and standard errors for each site including the total number of subjects (N) for each structure and split into MDD patients and controls (CTL). Means are adjusted for age, sex, scan center, and ICV using the *lsmeans* package in R.

		Lateral Ventricles		Thalamus		Caudate		Putamen		Pallidum		Hippocampus		Amygdala		Accumbens		ICV	
		Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N	Mean (Std Err)	N
<b>Bipolar Family Study</b>	CTL	5889.994 (310.279)	62	6598.157 (61.08)	62	3761.069 (54.768)	62	5891.301 (76.594)	62	1893.376 (27.259)	62	3570.397 (42.926)	62	1878.994 (28.872)	62	709.989 (17.126)	62	1478595.321 (15147.359)	62
	MDD	5564.152 (565.765)	19	6407.857 (111.373)	19	3549.248 (99.865)	19	5635.256 (139.662)	19	1905.38 (49.703)	19	3454.205 (78.272)	19	1826.493 (52.646)	19	742.377 (31.227)	19	1429565.795 (27391.122)	19
<b>CLING</b>	CTL	6942.48 (211.514)	321	8169.268 (36.942)	321	4038.22 (23.439)	321	5694.382 (30.049)	321	1830.209 (10.654)	321	4320.772 (18.88)	321	1511.964 (7.769)	321	600.179 (4.461)	321	1591240.917 (8643.52)	321
	MDD	7237.454 (608.396)	49	8076.854 (106.259)	49	4037.733 (67.419)	49	5744.305 (86.431)	49	1828.344 (30.646)	49	4228.621 (54.308)	49	1545.63 (22.348)	49	585.005 (12.832)	49	1528713.378 (24731.27)	49
<b>Clinical Depression Dublin</b>	CTL	6988.118 (353.937)	93	8016.539 (53.974)	92	3811.332 (38.635)	94	5441.171 (48.265)	92	1660.76 (15.822)	94	4356.998 (31.401)	94	1579.756 (14.264)	94	549.138 (6.435)	94	1589222.261 (13006.95)	94
	MDD	6941.056 (572.299)	36	7899.126 (88.14)	35	3745.882 (62.793)	36	5371.409 (77.645)	36	1628.905 (25.715)	36	4353.172 (51.036)	36	1586.111 (23.183)	36	533.528 (10.458)	36	1607308.54 (21120.33)	36
<b>CODE</b>	CTL	7976.951 (344.051)	74	8184.291 (64.931)	74	3677.004 (43.3)	74	5090.771 (56.463)	74	1461.715 (19.857)	74	4504.577 (40.154)	74	1612.084 (18.493)	74	483.598 (8.869)	74	1548828.284 (15376.579)	74
	MDD	7739.908 (292.603)	102	8042.78 (55.221)	102	3661.025 (36.825)	102	5171.045 (48.019)	102	1466.824 (16.888)	102	4432.727 (34.149)	102	1599.804 (15.802)	101	496.076 (7.58)	101	1540359.872 (13078.319)	102
<b>DepOx</b>	CTL	6664.878 (534.892)	31	8675.676 (132.515)	30	4048.715 (81.239)	31	5478.909 (105.135)	31	1746.877 (32.757)	31	4124.748 (56.534)	31	1385.321 (25.847)	31	526.116 (15.71)	31	1362278.954 (29042.624)	31
	MDD	6999.747 (488.697)	37	8398.466 (117.587)	38	4144.386 (73.267)	38	5424.366 (94.818)	38	1741.563 (29.542)	38	4156.386 (51.682)	37	1396.384 (23.311)	38	527.716 (14.169)	38	1310535.09 (26227.952)	38
<b>Imaging Genetics Dublin</b>	CTL	6679.671 (332.052)	52	7813.388 (109.202)	41	3736.322 (53.219)	46	5615.651 (80.859)	46	1592.106 (22.241)	43	4442.311 (44.762)	51	1702.007 (24.781)	52	585.418 (12.733)	51	1474215.129 (27484.837)	52
	MDD	6445.497 (346.033)	48	7699.211 (105.262)	44	3767.299 (57.183)	40	5759.584 (81.777)	45	1595.575 (22.513)	42	4385.849 (44.762)	51	1734.793 (24.781)	52	581.516 (12.996)	49	1443020.948 (27484.837)	52
<b>MMDP 1.5T</b>	CTL	6791.453	44	7022.211	44	3695.889	44	5583.459	44	1641.016	44	3284.799	44	1218.104	44	566.467	44	1324071.785	44

		(410.328)		(92.464)		(62.307)		(96.093)		(31.318)		(57.458)		(33.778)		(14.881)		(16810.368)	
	MDD	6956.363 (376.762)	52	7170.824 (84.073)	53	3642.837 (56.653)	53	5768.374 (87.373)	53	1595.806 (28.476)	53	3309.866 (52.244)	53	1274.021 (30.713)	53	580.716 (13.531)	53	1318317.763 (15285.375)	53
<b>MMDP 3T</b>	CTL	6896.163 (551.065)	63	7190.513 (84.787)	64	3773.774 (63.633)	64	5701.727 (97.508)	63	1586.822 (34.388)	64	4101.055 (74.291)	64	1552.397 (31.698)	63	687.643 (24.293)	63	1334270.65 (20454.624)	64
	MDD	7094.725 (518.085)	71	7287.834 (79.224)	73	3676.387 (59.89)	72	5799.168 (91.698)	71	1621.507 (32.365)	72	3915.255 (69.416)	73	1489.517 (29.377)	73	672.536 (22.841)	71	1317098.334 (19114.304)	73
<b>MPIP</b>	CTL	8818.892 (307.642)	222	7073.492 (38.931)	222	3523.561 (24.625)	222	4799.981 (35.187)	222	1424.726 (12.855)	222	4157.692 (24.707)	222	1300.625 (9.879)	222	536.087 (5.525)	222	1488615.256 (9114.622)	222
	MDD	9038.434 (233.636)	368	7134.62 (29.566)	368	3566.813 (18.701)	368	4854.76 (26.723)	368	1435.139 (9.762)	368	4069.651 (18.793)	367	1304.765 (7.502)	368	534.338 (4.196)	368	1519925.444 (6932.068)	368
<b>NESDA</b>	CTL	7603.141 (424.098)	66	7128.616 (77.535)	66	3726.262 (46.938)	66	5427.6 (59.58)	66	1656.268 (20.11)	66	3977.239 (43.535)	66	1671.812 (20.174)	66	534.181 (10.025)	66	1403332.576 (21205.533)	66
	MDD	7737.325 (272.951)	156	7140.999 (49.902)	156	3645.383 (30.21)	156	5314.881 (38.346)	156	1663.002 (12.943)	156	3869.517 (28.118)	155	1623.787 (13.03)	155	515.112 (6.452)	156	1447890.846 (13687.025)	156
<b>QTIM</b>	CTL	5953.172 (162.994)	262	7369.803 (44.326)	259	3998.126 (25.534)	260	6304.493 (33.373)	258	1706.745 (12.131)	258	4064.651 (20.285)	259	1767.142 (13.887)	260	771.597 (6.508)	260	1250942.494 (12205.945)	262
	MDD	6156.33 (430.333)	38	7296.289 (116.389)	38	3883.602 (68.022)	37	6244.967 (87.457)	38	1686.245 (31.779)	38	4034.612 (54.739)	36	1742.808 (36.519)	38	770.1 (17.118)	38	1208587.409 (32164.565)	38
<b>Rotterdam study</b>	CTL	12852.092 (91.357)	4356	6410.049 (6.77)	4369	3444.598 (6.641)	4363	4740.189 (7.24)	4350	1540.048 (2.721)	4372	4067.812 (5.103)	4363	1403.836 (2.045)	4374	548.964 (1.117)	4389	1489885.576 (1945.914)	4408
	MDD	14864.288 (732.799)	68	6300.27 (54.405)	68	3557.156 (54.109)	66	4717.23 (58.48)	67	1540.473 (21.865)	68	3977.368 (40.966)	68	1405.81 (16.436)	68	549.663 (8.994)	68	1467863.014 (15585.051)	69
<b>SHIP</b>	CTL	9728.093 (209.644)	422	7102.279 (24.194)	411	3578.507 (16.767)	408	4855.628 (21.313)	384	1552.076 (7.773)	397	3904.607 (16.157)	408	1480.362 (6.219)	408	457.687 (2.855)	386	1571014.869 (6143.991)	441
	MDD	9768.208 (385.635)	129	7091.613 (44.867)	123	3538.137 (30.413)	128	4901.653 (39.029)	117	1542.359 (14.463)	119	3922.065 (28.503)	135	1466.248 (11.229)	129	459.48 (5.312)	115	1590808.94 (11103.52)	139
<b>SHIP-trend</b>	CTL	8821.668 (139.014)	884	7254.004 (18.827)	885	3622.718 (12.413)	873	4929.271 (15.066)	838	1576.587 (5.581)	865	3979.707 (10.353)	875	1498.57 (4.288)	883	472.71 (2.086)	798	1586377.419 (3941.202)	952
	MDD	8701.92 (239.646)	303	7252.366 (32.491)	303	3599.847 (21.191)	305	4907.621 (26.098)	285	1575.163 (9.843)	284	3973.491 (17.664)	306	1480.291 (7.372)	304	473.698 (3.54)	282	1586590.378 (6829.382)	323

<b>Sydney</b>	CTL	7747.358 (463.926)	106	7146.326 (61.633)	106	4168.19 (58.437)	106	6393.662 (72.337)	106	1635.336 (18.616)	105	4208.748 (39.453)	106	1577.017 (17.808)	106	532.778 (8.548)	106	1499287.583 (12294.367)	106
	MDD	9079.575 (323.319)	214	7173.986 (42.953)	214	4332.366 (40.806)	213	6379.102 (50.525)	213	1649.354 (12.911)	214	4110.809 (27.496)	214	1549.776 (12.41)	214	524.398 (6.006)	210	1500726.805 (8568.216)	214



**Supplementary Table 15:** Full results from the moderator analyses of mean age, field strength of scanner, percent of acute patients, percent of patients with anxiety, FreeSurfer version used for processing, percent of patients taking antidepressants, and percent of patients taking antipsychotics. Effect sizes for the meta-regression models were available from all 15 sites (percent of patients taking antipsychotics was not available in MMDP 1.5T and MMDP 3T). Table is split into two parts to fit on a single page for easier comparison.

A)

	Mean Age			Field Strength			Percent Acute			Percent with Anxiety		
	Beta	Std Err	P-value	Beta	Std Err	P-value	Beta	Std Err	P-value	Beta	Std Err	P-value
<b>Lateral Ventricles</b>	2.62E-03	3.41E-03	0.441	-3.01E-02	7.72E-02	0.697	-1.79E-03	1.42E-03	0.206	1.07E-04	2.59E-03	0.967
<b>Thalamus</b>	6.67E-04	3.51E-03	0.849	4.34E-02	8.01E-02	0.587	-1.10E-03	1.75E-03	0.530	5.05E-03	2.85E-03	0.076
<b>Caudate</b>	7.46E-03	4.07E-03	0.067	-8.47E-03	1.04E-01	0.935	-1.00E-03	2.00E-03	0.616	-3.92E-03	3.26E-03	0.229
<b>Putamen</b>	1.28E-03	3.20E-03	0.690	1.80E-03	7.35E-02	0.981	1.01E-03	1.40E-03	0.469	-2.01E-03	2.48E-03	0.417
<b>Pallidum</b>	8.92E-04	3.09E-03	0.773	-4.59E-02	7.07E-02	0.516	-2.91E-04	1.40E-03	0.835	-5.66E-04	2.48E-03	0.819
<b>Hippocampus</b>	1.36E-03	3.61E-03	0.707	1.19E-01	7.87E-02	0.130	-4.43E-06	1.40E-03	0.997	1.25E-03	2.64E-03	0.638
<b>Amygdala</b>	-1.52E-03	3.33E-03	0.647	2.81E-02	7.88E-02	0.722	1.59E-03	1.44E-03	0.270	-4.45E-03	2.45E-03	0.070
<b>Accumbens</b>	2.41E-03	3.10E-03	0.436	7.70E-02	7.06E-02	0.276	3.47E-04	1.40E-03	0.804	-2.41E-03	2.48E-03	0.330
<b>ICV</b>	6.63E-03	4.24E-03	0.118	1.28E-01	1.00E-01	0.201	2.08E-04	2.15E-03	0.923	5.72E-03	3.35E-03	0.088

B)

	FreeSurfer Version			Percent on Antidepressants			Percent on Antipsychotics		
	Beta	Std Err	P-value	Beta	Std Err	P-value	Beta	Std Err	P-value
<b>Lateral Ventricles</b>	-0.294	0.194	0.128	7.02E-04	1.24E-03	0.571	1.06E-02	5.52E-03	0.055
<b>Thalamus</b>	0.265	0.197	0.366	1.42E-03	1.24E-03	0.253	8.30E-03	6.05E-03	0.170
<b>Caudate</b>	-0.470	0.257	0.285	1.48E-03	1.60E-03	0.355	1.61E-02	5.95E-03	6.71E-03
<b>Putamen</b>	-0.187	0.192	0.135	9.53E-04	1.11E-03	0.392	1.67E-03	5.54E-03	0.763
<b>Pallidum</b>	0.039	0.191	0.979	5.70E-04	1.11E-03	0.608	4.57E-03	5.40E-03	0.397
<b>Hippocampus</b>	-0.039	0.192	0.054	-2.31E-03	1.12E-03	0.038	-6.13E-03	6.25E-03	0.327
<b>Amygdala</b>	-0.310	0.192	0.049	2.07E-03	1.10E-03	0.061	6.64E-04	5.78E-03	0.909
<b>Accumbens</b>	-0.246	0.191	0.505	-1.96E-03	1.11E-03	0.078	-4.19E-03	5.39E-03	0.438
<b>ICV</b>	0.043	0.245	0.862	9.11E-04	1.75E-03	0.603	-2.96E-04	8.71E-03	0.973

**Supplementary Table S16:** Meta-analytic results for each mean structure for the diagnosis \* sex interactive effect in the full sample of MDD patients and Controls while controlling for age, sex, diagnosis, scan center and ICV. Adjusted Cohen's d is reported.

	<b>Cohen's d (Diagnosis * Sex)</b>	<b>Std. Err.</b>	<b>95% CI</b>	<b>P-value</b>	<b><i>f</i><sup>2</sup></b>	<b># Controls</b>	<b># Patients</b>
<b>Lateral Ventricles</b>	-0.029	0.0378	[-0.103 - 0.045]	0.437	14.275	7058	1689
<b>Thalamus</b>	-0.002	0.0463	[-0.093 - 0.088]	0.962	37.700	7046	1682
<b>Caudate</b>	0.029	0.0361	[-0.042 - 0.099]	0.428	8.460	7034	1681
<b>Putamen</b>	-0.005	0.0338	[-0.071 - 0.062]	0.891	0.033	6957	1656
<b>Pallidum</b>	0.023	0.0484	[-0.071 - 0.118]	0.627	42.117	7018	1657
<b>Hippocampus</b>	-0.008	0.0332	[-0.073 - 0.057]	0.809	<0.001	7040	1700
<b>Amygdala</b>	0.027	0.0333	[-0.038 - 0.092]	0.413	0.017	7060	1696
<b>Accumbens</b>	0.029	0.0338	[-0.037 - 0.095]	0.394	<0.001	6967	1652
<b>ICV</b>	0.002	0.0579	[-0.111 - 0.116]	0.971	61.128	7199	1728

