Data supplement for De Kovel et al., No Alterations of Brain Structural Asymmetry in Major Depressive Disorder: An ENIGMA Consortium Analysis. Am J Psychiatry (doi: 10.1176/appi.ajp.2019.18101144)

Supplemental Tables

Supplemental Figures

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Supplemental Tables

TABLE S1. Demographics. Age (in years), sex, and MDD patients-control breakdown for participating sites, separately for adult and adolescent samples.

	ADULTS AGE > 21								YOUNG AGE ≤ 21								
STUDY-SITE	**Age Contr**	**sd**	**Age MDD**	**sd**	**Female Contr**	**Female MDD**	**N[a] Contr**	**N MDD**	**Age Contr**	**sd**	**Age MDD**	**sd**	**Female Contr**	**Female MDD**	**N Contr**	**N MDD**	**Country**
AFFDIS	33.9	11.8	41.4	14.5	0.47	0.48	17	25	19.3	0.6	20.3	1.0	0.67	0.25	3	4	Germany
BARCELONA	46.0	8.1	47.0	7.7	0.72	0.79	32	62									Spain
BIPOLAR FAMILY STUDY	24.2	1.6	24.2	2.3	0.65	0.64	48	14	19.7	0.9	18.9	0.7	0.79	0.50	14	4	UK
BRCDECC	51.7	7.9	47.9	8.9	0.52	0.68	61	69									UK
CALGARY	22.7	0.8	22.3	0.7	0.33	0.40	6	10	14.5	5.0	17.9	1.7	0.61	0.52	41	50	Canada
CALGARY									16.9	2.3	16.5	1.7	0.57	0.78	7	18	Canada
CLING	25.8	5.2	38.7	10.2	0.58	0.47	281	43	20.5	0.7	19.2	0.8	0.68	1.00	40	6	Germany
CODE	41.1	12.9	41.2	11.8	0.56	0.64	70	101	20.8	0.5	20.0		1.00	1.00	4	1	Germany
DUBLIN 3T	38.8	12.3	41.6	10.8	0.52	0.63	46	52	20.2	1.6			0.83		6		Ireland
DUBLIN 1.5T	30.8	8.1	34.8	7.9	0.44	0.41	89	32	20.0	0.7	18.3	1.3	0.60	0.50	5	4	Ireland
EPISCA									14.7	1.6	15.4	1.5	0.87	0.84	30	19	Netherlands
FOR2107	34.1	12.3	39.1	12.8	0.61	0.64	605	493	19.9	1.1	19.7	1.0	0.75	0.65	73	57	Germany
GRONINGEN SAMPLE (DIP)	42.8	14.4	43.1	13.8	0.74	0.73	23	22									Netherlands
MAGDEBURG (SFB - SEXPECT)	33.8	7.2	39.2	11.1	0.15	0.42	20	19			20.0			0.00		1	Germany
MCMASTER	32.8	11.0	38.9	12.0	0.63	0.57	40	42	18.5	1.5	18.5	1.6	0.63	0.33	8	9	Canada
MELBOURNE	23.2	1.1	23.1	1.0	0.52	0.53	33	17	17.8	1.8	18.1	2.0	0.54	0.57	69	67	Australia
MINNESOTA									15.7	2.0	15.4	1.8	0.65	0.76	40	70	USA
MÜNSTER NEUROIMAGING COHORT[B]	36.8	11.6	39.2	11.2	0.56	0.57	666	264	19.8	1.5	19.4	1.4	0.65	0.70	60	20	Germany

NOVOSIBIRSK	43.6	9.1	47.7	10.9	0.71	0.81	17	16			19.0			1.00		1	Russia
OXFORD	32.3	9.7	33.6	10.2	0.58	0.71	26	28	19.8	0.8	20.4	0.5	0.60	0.40	5	10	UK
PHARMO (AMC)			29.4	4.7	0.00	1.00	0.0	51									Netherlands
SAN FRANCISCO UCSF									15.3	1.3	15.6	1.3	0.48	0.65	90	75	USA
SAO PAULO (WELCOME)	32.7	7.1	30.6	8.2	0.51	0.70	71	20	19.8	1.1	20.8	0.5	0.24	0.75	17	4	Brazil
SHIP	55.5	12.8	53.7	11.7	0.44	0.71	448	138									Germany
SHIP-TREND	50.7	14.3	49.2	12.2	0.44	0.65	937	312	21.0				1.00		1		Germany
SINGAPORE	38.5	4.6	40.1	7.6	0.53	0.45	17	22									Singapore
STANFORD UNIVERSITY	38.2	10.0	37.8	9.8	0.63	0.57	56	54	20.0	1.0	19.6	1.4	0.33	1.00	3	2	USA
SYDNEY	50.6	22.4	49.0	20.0	0.54	0.63	92	122	20.1	1.0	17.3	2.4	0.77	0.70	13	90	Australia

[a] all numbers before central quality control and clean-up

[b] subcortical data only

TABLE S2. Instrument for diagnosing Major Depressive Disorder and exclusion criteria by site

STUDY-SITE	DIAGNOSIS MEASUREMENT	INCLUSION/EXCLUSION CRITERIA
AFFDIS	ICD 10/ DSM- 5 criteria[1]	All subjects inclusion criteria: Between the ages of 18-60 years old. All subjects exclusion criteria: current or history of neurological disorder or brain injury, substance dependence, pregnancy, MRI contraindications, inability to give consent. MDD specific inclusion criteria: currently experiencing depressive episode with a diagnosis of MDD, no comorbid psychiatric diagnosis. Healthy control specific inclusion criteria: No current or history of psychiatric illness or diagnosis.
BARCELONA	DSM-IV-TR acc. to CIDI-interview	The exclusion criteria for healthy participants were: lifetime psychiatric diagnoses, first-degree relatives with psychiatric diagnoses and clinically significant physical or neurological illnesses. Axis I comorbidity according to DSM-IV-TR criteria was an exclusion criteria for all participants.
BIPOLAR FAMILY STUDY	SCID interview[2]	(Note: despite the name of the study, the included patients suffered from MDD, not bipolar disorder). MDD subjects exclusion criteria: presence of other axis I diagnoses. Control subjects exclusion criteria: medical history, including neurological and psychiatric history, as well as previous or actual use of psychotropic medication All subjects exclusion criteria: any major neurological disorder, learning disability, or any history of head injury that included loss of consciousness and any contraindications to MRI.
BRCDECC	SCAN interview[3]	Exclusion criteria controls/cases: contraindications to MRI, diagnosis of neurological disorder, head injury leading to loss of consciousness or conditions known to affect brain structure or function (including alcohol or substance misuse), if they or a first-degree relative had ever fulfilled criteria for mania, hypomania, schizophrenia or mood-incongruent psychosis. There was no history of psychiatric illness in the healthy controls.
CALGARY	KSADS[4]	Dalhousie Sample exclusion critera: A history of neurological illness, medical illness, claustrophobia, >21 year of age, or the presence of a ferrous implant or pacemaker. University of Calgary sample exclusion criteria: Left handed; history of seizures, epilepsy or other neurological or psychiatric diagnoses (specifically bipolar disorder, psychosis, pervasive developmental disorder, eating disorders, PTSD); pregnancy. The controls had no current or past psychiatric diagnosis.
CLING	ICD-10 interview	MDD subjects exclusion criteria: 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 exclusion criteria: medical history, including neurological and psychiatric history, as well as previous or actual use of psychotropic medication
CODE	SCID interview	MDD exclusion criteria: 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 exclusion criteria: 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.

DUBLIN T3	SCID-1 interview	MDD subjects exclusion criteria: comorbid psychiatric disorders (Axis I or Axis II, other than MDD), Treatment with antipsychotics or mood stabilizers, age <18 or >65, Control subjects exclusion criteria: Axis-I diagnosis, 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. Controls had no history of psychiatric disorders (either axis I or axis II psychiatric disorders).
DUBLIN T1.5	SCID-1 interview	MDD subjects exclusion criteria: comorbid psychiatric disorders (Axis I or Axis II, other than MDD), Treatment with antipsychotics or mood stabilizers, age <18 or >65, Control subjects exclusion criteria: Axis-I diagnosis, 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. Controls had no history of psychiatric disorders (either axis I or axis II psychiatric disorders).
EPISCA	ADIS	All subject exclusion criteria: Primary DSM-IV clinical diagnosis of ADHD, ODD, CD, pervasive developmental disorders, post-traumatic stress disorder, Tourette's syndrome, obsessive–compulsive disorder, bipolar disorder, and psychotic disorders; current substance abuse; history of neurological disorders or severe head injury; age < 12 or > 21 years; pregnancy; left-handedness; IQ score < 80 as measured by the Wechsler Intelligence Scale for Children (WISC)[5] or Adults[6]; and general MRI contra-indications. The healthy control adolescents were recruited through local advertisement, with the following additional criteria: no clinical scores, meaning scores below cut-off points for clinical presentation of symptoms, on validated mood and behavioral questionnaires or past or current Anxiety Disorders Interview Schedule (ADIS C/P) DSM-IV classification, no history of traumatic experiences on ADIS C/P and Adult Attachment Interview and no current psychotherapeutic intervention of any kind.
FOR2107	SCID-1	Inclusion criteria: age 18-65 years; patients were diagnosed with major depressive disorder by SCID-Interview, currently depressed or remitted. Exclusion criteria all: any MRI contraindications; any neurological abnormalities. Exclusion criteria controls: any current or former psychiatric disorder; Exclusion criteria patients: substance dependence or current benzodiazepine treatment (wash out of at least three half-lives before study participation)"
GRONINGEN SAMPLE (DIP)	MINI-SCAN	Inclusion MDD: Outpatients treated in mental health care for depression, BDI-II>13 at screening, adults. Exclusion MDD: Comorbid axis-I disorders other than anxiety disorders or past substance abuse, other psychotropic medication than stable use of SSRI/SNRI/TCA, established cardiovascular disease, active and concrete suicidal plans, inadequate language proficiency, cognitive impairments or neurological disease that interferes with task performance. Exclusion controls: Same as MDD, lifetime history of MDD, BDI>8.
MAGDEBURG (SFB - SEXPECT)	ICD-10 interview	MDD subjects exclusion criteria: history of seizures, medication with glutamate modulating drugs (ketamine, riluzole, etc.) or benzodiazepines, prior electroconvulsive therapy (ECT) treatments and pregnancy, atypical forms of depression, any additional psychiatric disorder, and a history of substance abuse or dependence. Control subjects exclusion criteria: psychiatric illness including no psychiatric history. Both groups: contraindications against MRI, major medical and neurological illness.
MCMASTER	SCID	MDD exclusion criteria: presence of axis-I disorders other than MDD and anxiety disorders (DSM-IV)., including for example, psychosis, bipolar, PTSD substance dependence or current active eating disorder. Control subjects had to have no psychiatric history. Control subjects were also assessed on the 17-item Hamilton Depression Rating Scale (HDRS-17) and the Global Assessment of Functioning Scale (GAF) to rule out the presence of sub-threshold psychiatric illness. Exclusion criteria for both groups included: i) treatment with anti-cholinergic or typical (first generation) anti-psychotic medication; ii) electroconvulsive therapy (ECT) or transcranial magnetic stimulation (TMS) within the past year; iii) a history of substance dependence or significant and recent (< 1 year) substance abuse; iv) a history

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		(within the past 12 months) of an endocrine or other medical disorder known to adversely affect cognition (e.g., Cushing's, uncontrolled diabetes, seizure disorder); and v) English comprehension lower than a grade 6 reading level.
MELBOURNE	SCID interview	MDD subjects exclusion criteria: lifetime or current SCID-I diagnosis of psychotic disorder, or bipolar I or II disorder. Control subjects exclusion criteria: any SCID-I diagnosis or medication use. Both groups: Acute or unstable medical disorder; general MRI contraindications. Current as well as past psychiatric illness were exclusion criteria for the healthy controls.
MINNESOTA	Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version and the Children's Depression Rating Scale–Revised (CDRS-R).	Exclusion criteria for both groups included the presence of a neurologic or other chronic medical condition, mental retardation, pervasive developmental disorder, substance use disorder, bipolar disorder, or schizophrenia. For healthy controls, any current psychiatric disorder was an exclusion criterion. They could have a past psychiatric disorder, but it could not be a past mood disorder. In addition the family history could not be positive for parental depression or parental bipolar disorder.
MÜNSTER NEUROIMAGING COHORT	SCID interview	MDD subjects exclusion criteria: presence of bipolar disorder, schizoaffective disorders and schizophrenia; substance-related disorders or current benzodiazepine treatment (wash out of at least three half-lives before study participation), and former electroconvulsive therapy. Control subjects exclusion criteria: any current or former psychiatric disorder. Both groups: any neurological abnormalities, MRI contra-indications
NOVOSIBIRSK	MINI, SCID, ICD-10 interviews	MDD subjects exclusion criteria: 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; age 18 or below; alcohol or substance abuse/dependence within 6 months of study participation; current major medical problems. Control subjects exclusion criteria: age over 65; any current or former psychiatric disorder. Both groups: MRI contra-indications.
OXFORD	SCID interview	MDD exclusion criteria: psychosis or substance dependence (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); HC: current or past history of Axis I disorder as defined by DSM-IV; Both groups exclusion criteria: major somatic or neurological disorders, pregnancy or breast-feeding, contra-indications to MR imaging or concurrent medication which could alter emotional processing

PHARMO (AMC)	MINI Plus	MDD and control exclusion criteria: Less than three week medication-free interval before scanning, current psychotropic medication use, a history of chronic or neurological disorder, family history of sudden heart failure or epileptic attacks, pregnancy (tested via urine sampling prior to the assessment), breast feeding, alcohol dependence and contra-indications for an MRI scan (e.g., ferromagnetic fragments). Participants agreed to abstain from smoking, caffeine and alcohol use for 24 hours prior to the assessments. MINI Plus was used to exclude current or lifetime depression and/or anxiety in controls.
SAN FRANCISCO UCSF	KSADS (semi-structured interview based on DSM) for MDD, DISC/DPS for HCL[7]	Exclusion criteria for all participants included: 1) use of pharmacotherapeutics for treating psychiatric conditions within the past 6 months, 2) misuse of drugs within two months prior to MRI scanning; 3) two or more alcoholic drinks per week within the previous month (as assessed by the Customary Drinking and Drug Use Record; CDDR) [8]; 4) a full scale IQ score of less than 75 (as assessed by the Wechsler Abbreviated Scale of Intelligence; WASI)[9]; 5) contraindications for MRI including ferromagnetic implants and claustrophobia; 6) pregnancy or the possibility of pregnancy; 7) left-handedness; 8) prepubertal status (as assessed as Tanner stages of 1 or 2)[10]; 9) inability to understand and comply with procedures; 10) neurological disorder (including meningitis, migraine, or HIV); 11) head trauma; 12) learning disability; 13) serious health problems; and 14) complicated or premature birth (i.e., birth before 33 weeks of gestation). The MDD group was subject to the additional exclusion criterion of a primary psychiatric diagnosis other than MDD. The HCL group was subject to the additional exclusion criteria of: 1) history of mood or psychotic disorders in a first- or second-degree relative (as assessed by the Family Interview for Genetics; FIGS[11]); and 2) current or lifetime DSM-IV-TR Axis I psychiatric disorder.
SAO PAULO (WELCOME)	Hamilton Rating Scale for Depression (HRSD)	People with psychotic disorders due to a general medical condition or substance-induced psychosis were excluded. Additional exclusion criteria were: (a) history of head injury; (b) presence of neurological disorders or any organic disorders that could affect the central nervous system; and (c) contraindications for MRI. Exclusion criteria specific for the control group were personal history of psychosis or other Axis I disorders, except substance misuse or mild anxiety disorders.
SHIP	M-CIDI interview	MDD subjects exclusion criteria: presence of axis-I disorders other than MDD, anxiety disorders, conversion, somatization and eating disorder. Control subjects exclusion criteria: lifetime diagnosis of depression, antidepressiva, and severity index=0 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 artefacts or inhomogeneity of the magnetic field).
SHIP-TREND	M-CIDI interview	MDD subjects: no special exclusion criteria Control subjects exclusion criteria: lifetime diagnosis of depression, antidepressiva, and MDD severity index=0. 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 artefacts or inhomogeneity of the magnetic field).

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SINGAPORE	SCID interview	Inclusion: 1) DSM IV dx of MDD (Patients) 2) Age: 21-65 3) English speaking 4) Provision of informed written consent. Exclusion criteria 1) History of significant head injury 2)Neurological diseases such as epilepsy, cerebrovascular accident 3) Impaired thyroid function 4) Steroid use 5) DSM IV alcohol or substance use or dependence 6) Contraindications to MRI (e.g. pacemaker, orbital foreign body, recent surgery/procedure with metallic devices/implants deployed) using standard MRI Request Form from NNI 7)Pregnant women 8) Claustrophobia. A history of psychiatric illness was an exclusion criterion for healthy controls.
STANFORD UNIVERSITY	SCID interview	MDD subjects exclusion criteria: presence of axis-I disorders other than MDD, anxiety and eating disorders . Control subjects: control individuals did not meet diagnostic criteria for any current psychiatric. Both groups exclusion criteria: alcohol / substance abuse or dependence within six months prior to MRI scanning, history of head trauma with loss of consciousness > 5 min, aneurysm, or any neurological or metabolic disorders that require ongoing medication or that may affect the central nervous system (including thyroid disease, diabetes, epilepsy or other seizures, or multiple sclerosis), MRI contraindications, or bad MRI data (e.g., extreme movement). Healthy control participants had no current or past MDD.
SYDNEY	SCID interview	MDD subjects exclusion criteria: presence of axis-I disorders other than MDD, panic disorder, social anxiety disorder, or generalized anxiety disorder. Control subjects exclusion criteria: Axis-I diagnosis, medication use. 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. Controls did not have a history of psychiatric or neurological disorders.

TABLE S3. Patient characteristics per study site

		Recurrence (count)			Anti-depressant use (count)			Remission (count)			Age at onset (yr)			
Study-site	**Nr datasets**	**first episode**	**recurrent**	**NA**	**AD free**	**AD user**	**NA**	**remitted**	**acute**	**NA**	**Mean**	**N**	**Std. Deviation**	**Missing**
AFFDIS	1	2	27	0	0	29	0	0	29	0	30.5	29	15.5	0
Barcelona	1	22	40	0	4	58	0	23	39	0	33.2	62	11.4	0
Bipolar Family Study	1	0	0	18	15	3	0	0	0	18	21.6	13	3.3	5
BRCDECC	1	0	69	0	19	50	0	0	0	69	20.4	54	9.3	15
Calgary	1	0	60	0	23	37	0	0	60	0	14.2	46	2.1	14
Calgary	1	18	0	0	18	0	0	0	18	0	14.3	10	2.3	8
CLING	1	23	26	0	3	46	0	3	46	0	30.4	49	10.6	0
CODE	5	0	102	0	102	0	0	0	102	0	-			102
Dublin 3T	1	8	44	0	14	37	1	0	52	0	26.3	50	12.1	2
Dublin 1.5T	1	17	18	1	3	33	0	0	36	0	29.6	36	9.2	0
EPISCA	1	19	0	0	17	2	0	0	19	0	-			19
FOR2107	1	165	333	52	211	338	1	142	408	0	26.2	543	12.7	7
Groningen sample (DIP)	1	6	13	3	12	10	0	0	22	0	25.6	21	13.0	1
Magdeburg (SFB - Sexpect)	1	4	16	0	0	20	0	0	20	0	30.9	15	11.2	5
McMaster	1	22	29	0	22	29	0	0	51	0	22.5	49	11.0	2
Melbourne	1	28	50	6	62	22	0	0	84	0	16.6	73	2.8	11
Minnesota	1	16	22	32	52	16	2	6	0	64	12.4	65	2.4	5
Münster Neuroimaging Cohort[a]	1	66	216	2	23	256	5	22	262	0	29.6	281	11.9	3
Novosibirsk	1	2	15	0	7	10	0	7	10	0	39.4	17	12.7	0

Oxford	1	19	19	0	38	0	0	0	38	0	25.6	38	9.1	0
Pharmo (AMC)	1	20	23	8	51	0	0	13	37	1	21.3	49	7.0	2
San Francisco UCSF	1	24	42	9	75	0	0	7	59	9	13.3	60	2.3	15
Sao Paulo (Welcome)	1	5	11	8	11	13	0	0	18	6	-			24
SHIP	1	77	61	0	114	24	0	0	0	138	38.2	138	13.2	0
SHIP-trend	1	113	199	0	258	54	0	0	0	312	36.2	312	14.3	0
Singapore	1	8	14	0	22	0	0	0	0	22	33.8	21	8.4	1
Stanford University	1	6	48	2	27	20	9	0	56	0	19.5	54	9.2	2
Sydney	1	58	151	3	83	128	1	164	37	11	24.2	203	17.0	9

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TABLE S4. Image acquisition and processing by site

STUDY SITE	FIELD STRENGTH	SCANNER TYPE	SEQUENCE T1	FREESURFER VERSION
AFFDIS	3T	3T Siemens Magnetom TrioTim	Whole-brain 3D gradient-echo T1-weighted image, acquired with 176 slices; TR = 2250 ms; TE = 3.26 ms; TI = 900 ms; FOV 256 mm X 256 mm; Percent phase FOV 100 %; Phase encoding – A >> P; Phase encoding steps – 224; Sagittal slice orientation; Flip angle of 9°;voxel size 1x1x1mm; duration 8:26	5.3
BARCELONA	3T	3T Philips Achieva	3D MPRAGE images (Whole-brain T1-weighted); TR=6.7ms, TE=3.2ms; 170 slices, voxel size 0.89X0.89X1.2 mm. Image dimensions 288X288X170; field of view: 256X256X204; slice thickness: 1.2 mm; with a sagittal slice orientation, T1 contrast enhancement, flip angle: 8º, grey matter as a reference tissue, ACQ matrix MXP = 256X240 and turbo-field echo shots (TFE) = 218.	
BIPOLAR FAMILY STUDY	1.5T	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
BRCDECC	1.5T	1.5T GE Signa HDx	ADNI-1 MPRAGE pulse sequence (details at http://adni.loni.ucla.edu/research/protocols/mri-protocols/)	5.3
CALGARY	1.5T / 3T	1.5T Siemens Magnetom Vision. 3T GE Discovery MR750	1.5T: A sagittal scout series was acquired to test image quality. 3D fast low angle shot (FLASH) sequence was used to acquire data from 124 1.5 mm-thick contiguous coronal slices through the entire brain (echo time = 5ms, repetition time = 25ms, acquisition matrix = 256 x 256 pixels, field of view = 24 cm and flip angle = 40°). 3T: Anatomical imaging acquisition parameters: axial acquisition, repetition time (TR), 2200 milliseconds (ms); echo time (TE), 3.04 ms; TI, 766, 780; flip angle, 13 degrees; 208 partitions; 256 × 256 matrix; and field of view, 256.	
CLING	3T	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	5.3
CODE	3T	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
DUBLIN 3T	3T	3T Phillips Achieva	3T: 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: 256×256.	5.3
DUBLIN 1.5T	1.5T	1.5T Siemens Vision	1.5T: A coronal. 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.	
EPISCA	3T	3T Philips Achieva	a sagittal 3-dimensional gradient-echo T1-weighted image was acquired (repetition time = 9.8 ms; echo time = 4.6 ms; flip angle = 8°; 140	

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			sagittal slices; no slice gap; field of view =256 × 256 mm; 1.17 × 1.17 × 1.2 mm voxels; duration = 4:56 min)	
FOR2107	3T	Marburg: 3T Siemens Magnetom TiroTim syngo; Münster: 3T Siemens PRISMA	Marburg: - Sequence: 3D T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) - Sagittal Acquisition Direction, # of Slices 176, 0.5mm Slice Gap, 1.0x1.0x1.0 Voxel Size (mm3), TI 900 ms, TE 2.26 ms, TR 1900 ms, Flip Angle 9. Münster: - Sequence: 3D T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE). - Sagittal Acquisition Direction, # of Slices 192, 0mm Slice Gap, 1.0x1.0x1.0 Voxel Size (mm3), TI 900 ms, TE 2.28 ms, TR 1900 ms, Flip Angle 8	5.3
GRONINGEN SAMPLE (DIP)	3T	3T Philips	3D T1-weighted scan (170 slices; TR = 9ms; TE = 3.6ms; 256x231 matrix of 1×1×1 mm voxels)	
MAGDEBURG (SFB - SEXPECT)	3T	3 Tesla Siemens MAGNETOM Trio scanner (Siemens, Erlangen, Germany)	High resolution T1 -weighted structural MRI scans of the brain were acquired for structural reference using a 3D -MPRAGE sequence (TE = 4.77 ms, TR = 2500 ms, T1 = 1100 ms, flip angle = 7°, bandwidth = 140 Hz/pixel, acquisition matrix = 256 × 256 × 192, isometric voxel size = 1.0 mm3).	5.3
MCMASTER	1.5T / 3T	1.5T (GE); 3T(GE)	1.5-T. Sigma GE Genesis-based Echo-Speed scanner running version 5.7 software and using a standard 30-cm circularly polarized head coil. Sagittal anatomic images were acquired by using a 3D/FSPGR/20 sequence (flip angle=20; echo delay time in-phase (TE), minimum repetition time (TR)=300 ms; inversion recovery=300 ms; matrix=512x256; field of view (FOV)=24 cm; scan thickness=1.2 mm). 3-T MRI Sigma GE Genesis (General Electric Medical Systems, Milwaukee, WI). Sagittal T-1 weighted images were acquired using a 3D FSPGR-IR sequence, (TR/TE=10.3/2.1 ms; flip angle=20; inversion time=300; matrix=512x256; FOV=24; and slice thickness=1.2 mm.	
MELBOURNE	3T	3T GE Signa Excite	3D BRAVO sequence 140; TR=7900 ms; TE=3000 ms; flip angle=13º; FOV=256 mm; matrix=256 x 256	5.3
MINNESOTA	3T	3.0 Tesla Tim Trio scanner; Siemens Corp	A 5-minute structural scan was acquired using a T1-weighted, high-resolution, magnetization-prepared gradient-echo sequence: repetition time, 2530 milliseconds; echo time, 3.65 milliseconds; inversion time, 1100 milliseconds; flip angle, 7°; field of view, 256 × 176 mm; voxel size, 1-mm isotropic; 224 slices; and generalized, autocalibrating, partially parallel acquisition acceleration factor, 2.	5.3
MÜNSTER NEUROIMAGING COHORT[a]	3T	3T Philips Gyroscan Intera	3D fast gradient echo sequence (turbo field echo), repetition time = 7.4 milliseconds, echo time = 3.4 milliseconds, flip angle = 9°, two signal averages, inversion prepulse every 814.5 milliseconds, acquired over a field of view of 256 (feet -head [FH]) × 204 (anterior -posterior [AP]) × 160 (right -left [RL]) mm, phase encoding in AP and RL direction, reconstructed to cubic voxels of .5 mm × .5 mm × .5 mm	5.3
NOVOSIBIRSK	3T	3T GE Discovery™ MR750w	Whole-brain T1-weighted images - 3D fast spin gradient echo sequence (FSPGR BRAVO), repetition time = 9.5 ms, echo time = 3.7 ms, flip angle = 3°, acquired over a field of view of 256 (feet-head [FH]) × 256	5.3

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			(anterior-posterior [AP]) × 188 (rightleft [RL]) mm, reconstructed to cubic voxels of 1 mm × 1 mm × 1 mm	
OXFORD	3T	3T Siemens Tim Trio	Voxel resolution 0.78 x 0.8 x 0.78 mm on a 208 x 256 x 200 grid, TE/TI/TR= 4.8/1100/2040 ms	5.3
PHARMO (AMC)	3T	3T Philips	T1 sequence details: 3D-TFE sequence TR= 9.7 ms, TE=4.6ms, matrix 192x192, voxel size = 0.875 x 0.875 x 1.2 mm; 120 slices. Axial plane. Philips 3T Ingenia 16 channel coil	5.3
SAN FRANCISCO UCSF	3T	3T GE Discovery MR750	SPGR T1-weighted: TR=8.1 ms; TE=3.17 ms; TI=450 ms; flip angle=12°; 256x256 matrix; FOV=250x250 mm; 168 sagittal slices; slice thickness=1 mm; in-plane resolution=0.98x 0.98 mm	
SAO PAULO (WELCOME)	1.5T	1.5T General Eletric (GE)	Imaging data were acquired using two MRI scanners (at the Clinics Hospital of the University of Sa˜ o Paulo 1.5 T GE Signa scanner, General Electric, Milwaukee Wisconsin, USA). T1-SPGR sequence providing 124 contiguous slices, voxel size 0.8660.8661.5 mm, echo time 5.2 ms, resolution time 21.7 ms, flip angle 20, field of vision 22, matrix 256x192)	5.3
SHIP	1.5T	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	5.3 (cortical), 5.1 (subcortical)
SHIP-TREND	1.5T	1.5T Siemens Avanto	3D T1-weighted (MP-RAGE/ axial plane); TR=1900 msec; TE=3.4 msec; Flip 5.3 Axial Centos6_x86_64 angle=15°; voxel size 1 mm x 1 mm x 1 mm	5.3 (cortical), 5.1 (subcortical)
SINGAPORE	3T	Achieva 3T, Philips Medical Systems, Netherlands	Whole brain high resolution 3D MP-RAGE (magnetisation-prepared rapid acquisition with a gradient echo) volumetric scans (TR/TE/TI/flip angle 8.4/3.8/3000/8; matrix 256x204; FOV 240mm2) with axial orientation (reformatted to coronal)	5.3
STANFORD UNIVERSITY	1.5T	1.5T GE Signa Excite	Whole-brain T1-weighted images were collected using a spoiled gradient echo (SPGR) pulse sequence (116 sagittal slices; through-plane resolution = 1.5 mm; in-plane resolution = 0.86 x 0.86 mm; flip angle = 15 degrees; repetition time [TR] = 8.3-10.1 ms; echo time [TE] = 1.7-3.0; inversion time [TI] = 300 ms; matrix = 256 x 192).	5.3
SYDNEY	3T	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

[a] Site Münster: only subcortical data

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TABLE S5A. Linear model results for asymmetry indexes (AI) of volumes of subcortical structures and lateral ventricles.

Region	N	AI±sd controls	AI±sd cases	Effect diagx[a]	s.e.	t	P diagx	FDR[b]	Cohen's d[c]	Effect sex[d]	s.e. Sex	P sex	Effect age[e]	s.e. Age	P age
ACCUMBENS	3952/2424	-0.005±0.09	-0.020±0.10	0.0001	0.002	0.035	0.972	0.986	0.0009	0.005	0.002	0.011	-0.346	0.109	0.002
AMYGDALA	4053/2447	-0.028±0.05	-0.027±0.05	0.0008	0.001	0.639	0.523	0.899	0.0163	0.001	0.001	0.314	-0.151	0.062	0.015
CAUDATE	4049/2461	-0.007±0.03	-0.007±0.03	-0.0004	0.001	-0.622	0.534	0.899	-0.0159	0.002	0.001	0.001	0.068	0.033	0.039
HIPPOCAMPUS	4066/2466	-0.009±0.03	-0.010±0.03	-0.0012	0.001	-1.623	0.105	0.505	-0.0414	-0.001	0.001	0.436	-0.062	0.036	0.088
LATERAL VENTRICLES	4120/2497	0.038±0.13	0.045±0.12	0.0076	0.003	2.306	0.021	0.328	0.0584	0.000	0.003	0.937	-0.083	0.145	0.567
PALLIDUM	3884/2318	0.019±0.07	0.001±0.07	-0.0013	0.001	-0.859	0.391	0.894	-0.0224	-0.004	0.001	0.005	-0.381	0.071	1.00E-07
PUTAMEN	3909/2329	0.019±0.03	0.021±0.03	-0.0009	0.001	-1.068	0.286	0.744	-0.0278	0.000	0.001	0.706	0.266	0.041	8.25E-11
THALAMUS	4058/2457	0.020±0.04	0.030±0.04	0.0000	0.001	0.039	0.969	0.986	0.0010	0.005	0.001	4.41E-09	-0.042	0.043	0.337

[a] Unstandardized effect of diagnosis on AI in the model, i.e. the mean AI difference between cases and controls after adjustment for the other model effects. A positive effect means that cases are more leftwards/less rightwards asymmetrical than controls

[b] FDR (Benajmini-Hochberg) computed for eight subcortical volumes (seven plus the lateral ventricles).

[c] Computed as t*sqrt(1/n1 + 1/n2)

[d] Unstandardized effect of sex on AI in the model. A positive effect means that females are more leftwards/less rightwards asymmetrical

[e] Unstandardized effect of age on AI in the model. A positive effect means that older people are more leftwards/less rightwards asymmetrical

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TABLE S5B. Linear model results for asymmetry indexes of surface areas of cortical structures.

Region	N	AI±sd controls	AI±sd cases	Effect diagx[a]	s.e.	t	P diagx	FDR[b]	Cohen's d[c]	Effect sex[d]	se. Sex	P sex	Effect age[e]	s.e. Age	P age
TOTAL SURFACE AREA	3434/2234	-0.002±0.01	-0.002±0.01	0.00012	0.00019	0.608	0.543	0.899	0.017	0.000	0.000	0.009	0.029	0.009	0.001
BANKS STS	3124/1972	0.042±0.08	0.038±0.08	0.00036	0.00235	0.153	0.879	0.986	0.004	-0.002	0.002	0.431	0.211	0.104	0.042
CAUDAL ANTERIOR CINGULATE	3310/2193	-0.082±0.12	-0.086±0.12	-0.00271	0.00346	-0.783	0.434	0.894	-0.022	0.004	0.003	0.261	-0.072	0.146	0.622
CAUDAL MIDDLE FRONTAL	3338/2199	0.037±0.07	0.043±0.07	0.00439	0.00210	2.096	0.036	0.401	0.058	-0.003	0.002	0.145	-0.128	0.091	0.159
CUNEUS	3339/2168	-0.019±0.06	-0.023±0.06	-0.00472	0.00161	-2.922	0.003	0.104	-0.081	0.003	0.002	0.042	0.011	0.070	0.876
ENTORHINAL	2896/1931	0.084±0.10	0.082±0.11	-0.00056	0.00324	-0.171	0.864	0.986	-0.005	0.002	0.003	0.544	0.197	0.141	0.161
FRONTAL POLE	3423/2227	-0.143±0.09	-0.146±0.09	-0.00438	0.00268	-1.637	0.102	0.505	-0.045	0.003	0.003	0.196	-0.156	0.117	0.183
FUSIFORM	3193/2158	0.017±0.05	0.015±0.05	-0.00010	0.00146	-0.070	0.944	0.986	-0.002	0.011	0.001	2.93E-15	0.051	0.066	0.436
INFERIOR PARIETAL	3287/2167	-0.083±0.05	-0.084±0.05	-0.00164	0.00149	-1.097	0.273	0.734	-0.031	0.008	0.001	5.64E-08	0.148	0.067	0.028
INFERIOR TEMPORAL	3355/2174	0.027±0.05	0.026±0.05	0.00207	0.00156	1.325	0.185	0.601	0.037	0.001	0.001	0.329	0.151	0.070	0.031
INSULA	3306/2179	-0.015±0.04	-0.010±0.04	0.00206	0.00124	1.657	0.098	0.505	0.046	0.006	0.001	4.62E-08	-0.183	0.058	0.002
ISTHMUS CINGULATE	3393/2209	0.031±0.07	0.033±0.07	0.00021	0.00205	0.102	0.918	0.986	0.003	-0.009	0.002	6.86E-06	0.141	0.092	0.124
LATERAL OCCIPITAL	3394/2211	0.014±0.05	0.014±0.05	-0.00002	0.00131	-0.018	0.986	0.986	0.000	0.000	0.001	0.977	-0.019	0.049	0.694
LATERAL ORBITOFRONTAL	3426/2228	0.006±0.04	0.003±0.04	0.00015	0.00108	0.137	0.891	0.986	0.004	0.001	0.001	0.264	0.036	0.052	0.493
LINGUAL	3392/2200	-0.003±0.05	-0.005±0.05	0.00047	0.00137	0.345	0.730	0.986	0.010	-0.003	0.001	0.021	0.060	0.065	0.355
MEDIAL-ORBITOFRONTAL	3286/2174	0.014±0.06	0.009±0.06	-0.00108	0.00161	-0.669	0.503	0.899	-0.019	-0.005	0.002	5.29E-04	0.252	0.076	9.58E-04
MIDDLE TEMPORAL	3190/2053	-0.047±0.04	-0.050±0.04	-0.00191	0.00129	-1.476	0.140	0.575	-0.042	-0.002	0.001	0.199	0.224	0.055	4.83E-05
PARA-CENTRAL	3291/2189	-0.064±0.06	-0.060±0.06	0.00195	0.00173	1.123	0.261	0.734	0.031	0.006	0.002	1.16E-04	-0.249	0.070	3.91E-04
PARAHIPPOCAMPAL	3334/2182	0.018±0.06	0.017±0.06	-0.00017	0.00181	-0.094	0.925	0.986	-0.003	0.009	0.002	8.35E-08	0.044	0.078	0.571
PARS OPERCULARIS	3354/2201	0.086±0.08	0.088±0.08	0.00182	0.00220	0.826	0.409	0.894	0.023	-0.001	0.002	0.766	-0.144	0.080	0.071
PARS ORBITALIS	3408/2219	-0.105±0.06	-0.103±0.06	0.00137	0.00169	0.807	0.420	0.894	0.022	0.002	0.002	0.188	-0.054	0.075	0.473
PARS TRANGULARIS	3374/2212	-0.071±0.07	-0.070±0.07	0.00041	0.00204	0.200	0.841	0.986	0.006	0.006	0.002	0.005	-0.023	0.074	0.760
PERI-CALCARINE	3370/2171	-0.050±0.05	-0.051±0.05	-0.00166	0.00149	-1.116	0.265	0.734	-0.031	0.000	0.001	0.917	0.060	0.066	0.366
POST-CENTRAL	3277/2155	0.021±0.04	0.020±0.04	-0.00086	0.00114	-0.760	0.447	0.894	-0.021	0.002	0.001	0.146	-0.076	0.044	0.086
POSTERIOR CINGULATE	3402/2218	-0.008±0.07	-0.011±0.07	-0.00333	0.00209	-1.597	0.110	0.505	-0.044	0.004	0.002	0.070	0.162	0.080	0.043
PRE-CENTRAL	3286/2181	-0.005±0.03	-0.002±0.03	0.00136	0.00099	1.367	0.172	0.600	0.038	0.001	0.001	0.469	-0.021	0.042	0.620

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PRE-CUNEUS	3391/2214	-0.020±0.04	-0.020±0.04	0.00020	0.00106	0.188	0.851	0.986	0.005	0.002	0.001	0.048	0.200	0.044	5.9E-06
ROSTRAL ANTERIOR CINGULATE	3235/2159	0.098±0.10	0.102±0.10	0.00145	0.00298	0.488	0.626	0.957	0.014	0.001	0.003	0.758	0.214	0.133	0.106
ROSTRAL MIDDLE FRONTAL	3386/2218	-0.015±0.04	-0.016±0.04	-0.00254	0.00114	-2.232	0.026	0.338	-0.062	0.000	0.001	0.758	-0.034	0.051	0.506
SUPERIOR FRONTAL	3265/2185	0.014±0.03	0.016±0.03	0.00219	0.00095	2.303	0.021	0.328	0.064	-0.001	0.001	0.291	-0.021	0.038	0.579
SUPERIOR PARIETAL	3332/2183	0.002±0.04	0.001±0.04	-0.00085	0.00115	-0.734	0.463	0.899	-0.020	0.003	0.001	0.003	0.082	0.047	0.084
SUPERIOR TEMPORAL	3104/1958	0.024±0.04	0.023±0.04	0.00066	0.00115	0.575	0.565	0.899	0.017	-0.014	0.001	6.47E-36	0.068	0.049	0.161
SUPRA-MARGINAL	3164/2089	0.028±0.06	0.028±0.06	0.00240	0.00178	1.351	0.177	0.600	0.038	-0.008	0.002	2.04E-06	-0.091	0.079	0.245
TEMPORAL POLE	3325/2177	0.063±0.08	0.062±0.08	-0.00025	0.00220	-0.115	0.908	0.986	-0.003	-0.006	0.002	0.004	-0.392	0.097	5.72E-05
TRANVERSE TEMPORAL	3425/2227	0.142±0.08	0.142±0.08	0.00063	0.00214	0.292	0.770	0.986	0.008	-0.002	0.002	0.314	0.223	0.088	0.012

[a,c,d,e] as for table S5a

[b] FDR (Benajmini-Hochberg) computed for 35 cortical surfaces (34 regions plus whole hemisphere).

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TABLE S5C. Linear model results for asymmetry indexes of thicknesses of cortical structures.

Region	N	AI±sd controls	AI±sd cases	Effect diagx[a]	s.e.	t	P diagx	FDR[b]	Cohen's d[c]	Effect sex[d]	s.e. Sex	P sex	Effect age[e]	s.e. Age	P age
AVERAGE THICKNESS	3450/2237	0.001±0.01	0.001±0.01	0.00019	0.00019	1.022	0.307	0.772	0.028	0.000	0.000	0.037	-0.054	0.009	7.24E-09
BANKS STS	3251/2016	-0.022±0.04	-0.024±0.04	0.00063	0.00114	0.550	0.582	0.908	0.016	0.003	0.001	0.003	0.012	0.053	0.819
CAUDAL ANTERIOR CINGULATE	3419/2225	0.024±0.05	0.027±0.05	0.00410	0.00142	2.883	0.004	0.104	0.079	-0.004	0.001	0.004	0.077	0.068	0.256
CAUDAL MIDDLE FRONTAL	3423/2223	0.006±0.03	0.006±0.03	0.00045	0.00073	0.618	0.537	0.899	0.017	-0.002	0.001	0.017	-0.196	0.035	1.92E-08
CUNEUS	3392/2185	-0.009±0.03	-0.009±0.03	-0.00092	0.00094	-0.985	0.325	0.792	-0.027	-0.002	0.001	0.025	-0.088	0.043	0.040
ENTORHINAL	3221/2022	-0.021±0.05	-0.020±0.05	0.00055	0.00162	0.342	0.733	0.986	0.010	-0.003	0.002	0.049	-0.075	0.073	0.300
FRONTALPOLE	3442/2229	0.008±0.06	0.009±0.06	0.00102	0.00176	0.579	0.563	0.899	0.016	-0.007	0.002	1.06E-05	0.019	0.084	0.817
FUSIFORM	3425/2221	-0.003±0.02	-0.003±0.02	0.00004	0.00065	0.058	0.954	0.986	0.002	0.001	0.001	0.154	0.028	0.031	0.369
INFERIOR PARIETAL	3398/2200	-0.007±0.02	-0.009±0.02	-0.00119	0.00062	-1.906	0.057	0.491	-0.052	0.001	0.001	0.042	0.050	0.030	0.098
INFERIOR TEMPORAL	3388/2179	-0.007±0.03	-0.006±0.03	0.00131	0.00075	1.751	0.080	0.505	0.048	-0.002	0.001	0.002	-0.177	0.036	9.71E-07
INSULA	3341/2184	0.007±0.02	0.005±0.02	0.00013	0.00069	0.189	0.850	0.986	0.005	-0.001	0.001	0.033	-0.075	0.032	0.018
ISTHMUS CINGULATE	3428/2216	0.011±0.04	0.009±0.04	-0.00071	0.00112	-0.633	0.527	0.899	-0.017	0.000	0.001	0.717	-0.035	0.048	0.468
LATERAL OCCIPITAL	3423/2220	-0.016±0.02	-0.017±0.02	-0.00030	0.00065	-0.460	0.645	0.968	-0.013	0.002	0.001	0.009	0.139	0.032	1.16E-05
LATERAL ORBITOFRONTAL	3418/2229	0.004±0.03	0.007±0.03	0.00119	0.00074	1.607	0.108	0.505	0.044	-0.001	0.001	0.138	-0.072	0.035	0.041
LINGUAL	3401/2199	-0.012±0.03	-0.010±0.03	0.00052	0.00074	0.703	0.482	0.899	0.019	0.000	0.001	0.866	-0.089	0.035	0.012
MEDIAL ORBITOFRONTAL	3381/2205	0.012±0.03	0.007±0.04	-0.00187	0.00097	-1.925	0.054	0.491	-0.053	-0.006	0.001	7.83E-12	0.117	0.047	0.013
MIDDLE TEMPORAL	3312/2089	-0.005±0.03	-0.005±0.03	-0.00021	0.00072	-0.297	0.766	0.986	-0.008	0.000	0.001	0.725	-0.160	0.034	3.18E-06
PARA-CENTRAL	3427/2228	-0.008±0.03	-0.006±0.03	0.00002	0.00078	0.021	0.983	0.986	0.001	0.001	0.001	0.087	-0.091	0.037	0.014
PARA-HIPPOCAMPAL	3436/2213	0.005±0.05	0.006±0.05	0.00152	0.00131	1.163	0.245	0.734	0.032	-0.003	0.001	0.036	-0.026	0.058	0.649
PARS OPERCULARIS	3427/2218	0.001±0.03	0.000±0.03	-0.00127	0.00085	-1.496	0.135	0.575	-0.041	0.001	0.001	0.330	-0.104	0.040	0.009
PARS ORBITALIS	3433/2223	0.002±0.04	0.004±0.04	-0.00045	0.00122	-0.366	0.714	0.986	-0.010	-0.001	0.001	0.205	-0.252	0.058	1.41E-05
PARS TRIANGULARIS	3420/2223	0.002±0.03	0.002±0.03	-0.00013	0.00092	-0.137	0.891	0.986	-0.004	-0.002	0.001	0.005	-0.176	0.044	6.54E-05
PERI-CALCARINE	3370/2174	-0.003±0.04	0.001±0.04	0.00032	0.00108	0.295	0.768	0.986	0.008	0.001	0.001	0.193	-0.229	0.052	8.76E-06
POST-CENTRAL	3380/2203	0.007±0.02	0.008±0.02	0.00111	0.00065	1.692	0.091	0.505	0.047	0.001	0.001	0.211	-0.035	0.031	0.254
POSTERIOR CINGULATE	3434/2227	0.005±0.03	0.006±0.03	0.00122	0.00088	1.390	0.165	0.600	0.038	-0.001	0.001	0.352	-0.049	0.040	0.223

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PRE-CENTRAL	3398/2207	0.005±0.02	0.007±0.02	0.00055	0.00057	0.962	0.336	0.794	0.026	-0.001	0.001	0.010	-0.062	0.027	0.023
PRECUNEUS	3427/2219	-0.005±0.02	-0.005±0.02	-0.00108	0.00058	-1.863	0.063	0.491	-0.051	0.001	0.001	0.334	-0.055	0.028	0.050
ROSTRAL ANTERIOR CINGULATE	3408/2212	0.005±0.05	0.007±0.05	-0.00031	0.00128	-0.243	0.808	0.986	-0.007	0.002	0.001	0.056	-0.185	0.062	0.003
ROSTRAL MIDDLE FRONTAL	3427/2227	0.012±0.02	0.013±0.02	-0.00069	0.00063	-1.109	0.268	0.734	-0.030	-0.002	0.001	0.002	-0.285	0.031	1.90E-20
SUPERIOR FRONTAL	3420/2225	0.007±0.02	0.008±0.02	-0.00017	0.00043	-0.398	0.691	0.986	-0.011	-0.001	0.000	0.097	-0.104	0.021	7.31E-07
SUPERIOR PARIETAL	3413/2218	0.003±0.02	0.002±0.02	0.00008	0.00052	0.161	0.872	0.986	0.004	0.001	0.000	0.125	0.067	0.025	0.007
SUPERIOR TEMPORAL	3212/1996	-0.004±0.02	-0.002±0.02	0.00195	0.00066	2.963	0.003	0.104	0.085	0.001	0.001	0.304	-0.057	0.031	0.068
SUPRA-MARGINAL	3325/2137	-0.001±0.02	-0.001±0.02	0.00053	0.00070	0.764	0.445	0.894	0.021	0.001	0.001	0.107	0.040	0.033	0.221
TEMPORAL POLE	3395/2195	-0.018±0.05	-0.016±0.05	-0.00048	0.00140	-0.345	0.730	0.986	-0.010	0.000	0.001	0.769	-0.014	0.064	0.822
TRANSVERSE TEMPORAL	3406/2217	-0.005±0.05	-0.003±0.05	0.00184	0.00135	1.361	0.174	0.600	0.037	0.005	0.001	6.19E-05	-0.019	0.061	0.760

[a,c,d,e] as for table S5a

[b] FDR (Benajmini-Hochberg) computed for 35 cortical thicknesses (34 regions plus whole hemisphere).

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TABLE S6A. Linear model results for asymmetry indexes of volumes of subcortical structures in patients, effects of using antidepressants vs not (AD), having acute depression vs in remission (Rem) or having a first episode vs recurrent (Recur). FDR adjusted p-values adjusted for 8 structures.

Region	N AD free/user	p AD	Cohen's d AD	Padj AD	N Rem/acute	p Rem	Cohen's d Rem	Padj Rem	N first/recur	p Recur	Cohen's d Recur	Padj Recur
ACCUMBENS	860/1030	0.470	0.033	0.699	348/790	0.707	-0.025	0.707	630/1191	0.450	0.037	0.904
AMYGDALA	885/1032	0.035	-0.097	0.281	352/778	0.654	-0.030	0.707	644/1206	0.904	-0.006	0.904
CAUDATE	895/1041	0.169	-0.063	0.678	353/792	0.570	0.038	0.707	656/1211	0.812	-0.012	0.904
HIPPOCAMPUS	899/1044	0.328	0.045	0.699	357/793	0.704	0.025	0.707	651/1217	0.621	-0.024	0.904
LATERAL VENTRICLES	904/1053	0.469	-0.033	0.699	362/809	0.698	-0.026	0.707	658/1232	0.230	0.058	0.904
PALLIDUM	832/983	0.524	0.030	0.699	338/726	0.642	-0.032	0.707	614/1130	0.655	-0.023	0.904
PUTAMEN	832/1004	0.999	0.000	0.999	336/748	0.181	0.092	0.707	608/1133	0.678	0.021	0.904
THALAMUS	891/1038	0.813	0.011	0.929	357/788	0.007	0.182	0.052	641/1212	0.329	0.048	0.904

TABLE S6B. Linear model results for asymmetry indexes of surface areas of cortical structures in patients using antidepressants vs not (AD), having acute depression vs in remission (Rem) or having a first episode vs recurrent (Recur). FDR adjusted p-values adjusted for 35 cortical regions.

Region	N AD	p AD	Cohen's d AD	Padj AD	N Rem	p Rem	Cohen's d Rem	Padj Rem	N Recur	P Recur	Cohen's d Recur	Padj Recur
TOTAL SURFACE AREA	891/774	0.206	0.062	0.888	342/520	0.851	0.013	0.991	599/1000	0.196	0.072	0.494
BANKS STS	791/681	0.822	-0.012	0.917	281/437	0.721	0.027	0.991	527/883	0.110	0.084	0.473
CAUDAL ANTERIOR CINGULATE	866/762	0.249	-0.058	0.888	341/515	0.312	0.071	0.985	586/977	0.083	0.091	0.473
CAUDAL MIDDLE FRONTAL	868/764	0.136	0.074	0.888	341/515	0.855	-0.013	0.991	586/980	0.420	0.043	0.736
CUNEUS	858/755	0.776	-0.014	0.917	332/500	0.119	-0.111	0.603	577/971	0.319	0.056	0.620
ENTORHINAL	752/686	0.446	-0.040	0.888	290/417	0.686	-0.031	0.991	511/851	0.505	0.035	0.797
FRONTAL POLE	888/771	0.703	0.019	0.917	341/517	0.940	0.005	0.991	598/996	0.040	-0.110	0.465
FUSIFORM	832/759	0.384	-0.044	0.888	339/517	0.788	0.019	0.991	567/962	0.545	-0.032	0.797
INFERIOR PARIETAL	851/752	0.487	-0.035	0.888	340/497	0.254	0.081	0.942	578/963	0.118	-0.082	0.473
INFERIOR TEMPORAL	874/753	0.865	0.009	0.917	338/508	0.183	-0.094	0.802	591/986	0.033	0.112	0.465
INSULA	871/754	0.473	0.036	0.888	331/497	0.959	-0.004	0.991	589/976	0.973	0.002	0.987
ISTHMUS CINGULATE	879/767	0.716	0.018	0.917	336/516	0.068	-0.128	0.476	591/990	0.987	0.001	0.987
LATERAL OCCIPITAL	880/763	0.508	0.033	0.888	340/514	0.896	0.009	0.991	590/991	0.162	-0.073	0.473
LATERAL ORBITOFRONTAL	887/773	0.400	0.042	0.888	341/519	0.370	-0.063	0.985	595/998	0.675	0.022	0.844
LINGUAL	875/760	0.935	0.004	0.942	340/502	0.361	0.065	0.985	590/980	0.830	-0.011	0.937
MEDIAL-ORBITOFRONTAL	842/768	0.723	0.018	0.917	336/513	0.047	-0.140	0.476	575/970	0.287	0.058	0.592
MIDDLE TEMPORAL	810/717	0.333	-0.050	0.888	297/474	0.394	-0.063	0.985	551/911	0.730	0.018	0.882
PARA-CENTRAL	855/766	0.010	0.128	0.367	341/518	0.592	0.037	0.991	579/977	0.145	-0.077	0.473
PARA-HIPPOCAMPAL	862/761	0.165	0.069	0.888	339/514	0.121	0.109	0.603	586/971	0.127	0.080	0.473
PARS OPERCULARIS	866/770	0.327	0.049	0.888	339/517	0.026	0.156	0.476	582/989	0.279	-0.057	0.592
PARS ORBITALIS	885/768	0.031	0.107	0.547	340/516	0.719	-0.025	0.991	595/993	0.572	0.030	0.797
PARS TRANGULARIS	876/773	0.789	0.013	0.917	340/518	1.000	0.000	1.000	590/992	0.094	-0.089	0.473
PERI-CALCARINE	875/751	0.848	-0.010	0.917	332/496	0.877	-0.011	0.991	584/972	0.675	-0.022	0.844

POST-CENTRAL	841/751	0.272	0.055	0.888	338/506	0.036	-0.149	0.476	580/950	0.592	0.028	0.797
POSTERIOR CINGULATE	882/768	0.942	0.004	0.942	341/517	0.906	0.008	0.991	595/991	0.154	-0.075	0.473
PRE-CENTRAL	856/763	0.353	-0.046	0.888	337/511	0.269	-0.078	0.942	581/974	0.155	-0.074	0.473
PRE-CUNEUS	878/772	0.471	-0.036	0.888	339/519	0.460	0.052	0.991	592/992	0.198	0.069	0.494
ROSTRAL ANTERIOR CINGULATE	836/759	0.635	-0.024	0.917	337/508	0.847	0.014	0.991	570/960	0.362	0.048	0.666
ROSTRAL MIDDLE FRONTAL	880/770	0.295	0.052	0.888	342/517	0.598	-0.037	0.991	593/991	0.573	-0.030	0.797
SUPERIOR FRONTAL	858/762	0.749	0.016	0.917	342/516	0.499	-0.047	0.991	580/972	0.515	0.034	0.797
SUPERIOR PARIETAL	857/764	0.176	0.068	0.888	340/515	0.059	0.133	0.476	583/973	0.028	0.121	0.465
SUPERIOR TEMPORAL	779/676	0.414	-0.043	0.888	297/428	0.759	-0.023	0.991	532/896	0.919	0.005	0.975
SUPRA-MARGINAL	828/724	0.571	-0.029	0.917	326/477	0.643	0.034	0.991	560/944	0.249	0.060	0.581
TEMPORAL POLE	859/758	0.740	0.017	0.917	341/520	0.963	0.003	0.991	587/988	0.810	0.013	0.937
TRANVERSE TEMPORAL	888/772	0.700	-0.019	0.917	342/516	0.940	-0.005	0.991	597/997	0.911	0.006	0.975

TABLE S6C. Linear model results for asymmetry indexes of average thickness of cortical structures in patients using antidepressants vs not (AD), having acute depression vs in remission (Rem) or having a first episode vs recurrent (Recur). FDR adjusted p-values adjusted for 35 cortical regions.

Region	N AD free/user	p AD	Cohen's d AD	Padj AD	N Rem/acute	p Rem	Cohen's d Rem	Padj Rem	N first/recur	P Recur	Cohen's d Recur	Padj Recur
AVG THICKNESS	894/774	0.168	-0.068	0.589	342/520	0.211	0.096	0.618	603/999	0.173	0.074	0.675
BANKS STS	827/686	0.430	-0.041	0.783	281/437	0.406	-0.058	0.748	552/899	0.706	0.020	0.830
CAUDAL ANTERIOR CINGULATE	890/770	0.269	-0.055	0.673	341/515	0.089	0.119	0.591	601/993	0.363	-0.048	0.830
CAUDAL MIDDLE FRONTAL	887/768	0.516	0.032	0.783	341/515	0.240	-0.084	0.618	597/992	0.896	-0.007	0.924
CUNEUS	875/755	0.891	0.007	0.987	332/500	0.714	-0.028	0.918	590/975	0.691	0.022	0.830
ENTORHINAL	827/701	0.400	0.043	0.783	290/417	0.649	-0.032	0.918	550/902	0.506	0.035	0.830
FRONTAL POLE	889/772	0.308	0.050	0.719	341/517	0.589	-0.038	0.918	600/996	0.453	-0.039	0.830
FUSIFORM	884/770	0.001	-0.159	0.046	339/517	0.391	0.061	0.748	598/994	0.897	-0.007	0.924

INFERIOR PARIETAL	882/754	0.537	0.031	0.783	340/497	0.952	0.004	0.952	598/977	0.572	0.030	0.830
INFERIOR TEMPORAL	879/753	0.045	-0.100	0.441	338/508	0.048	0.141	0.562	595/987	0.491	-0.036	0.830
INSULA	877/753	0.919	-0.005	0.987	331/497	0.860	-0.012	0.918	595/976	0.169	-0.072	0.675
ISTHMUS CINGULATE	885/768	0.070	-0.090	0.489	336/516	0.498	0.048	0.872	595/993	0.287	-0.056	0.830
LATERAL OCCIPITAL	888/764	0.984	0.001	0.987	340/514	0.118	0.109	0.591	601/989	0.567	0.030	0.830
LATERAL ORBITOFRONTAL	890/771	0.935	-0.004	0.987	341/519	0.200	-0.091	0.618	599/995	0.641	-0.025	0.830
LINGUAL	874/760	0.774	-0.014	0.967	340/502	0.708	0.026	0.918	593/977	0.710	0.020	0.830
MEDIAL-ORBITOFRONTAL	875/766	0.242	0.058	0.651	336/513	0.056	0.141	0.562	592/984	0.159	0.076	0.675
MIDDLE TEMPORAL	843/720	0.101	0.084	0.503	297/474	0.853	-0.013	0.918	571/927	0.012	-0.131	0.207
PARA-CENTRAL	889/771	0.227	0.060	0.651	341/518	0.167	-0.097	0.618	600/995	0.352	0.049	0.830
PARA-HIPPOCAMPAL	886/768	0.128	-0.075	0.532	339/514	0.828	-0.015	0.918	597/991	0.065	-0.097	0.675
PARS OPERCULARIS	883/771	0.087	-0.085	0.503	339/517	0.109	0.112	0.591	595/994	0.356	0.048	0.830
PARS ORBITALIS	888/769	0.503	0.033	0.783	340/516	0.064	0.130	0.562	600/992	0.567	0.030	0.830
PARS TRANGULARIS	888/772	0.463	0.036	0.783	340/518	0.917	-0.007	0.944	600/993	0.234	0.063	0.821
PERI-CALCARINE	877/751	0.137	-0.074	0.532	332/496	0.207	-0.089	0.618	589/969	0.099	0.087	0.675
POST-CENTRAL	877/763	0.638	-0.023	0.893	338/506	0.745	0.023	0.918	596/982	0.807	0.013	0.883
POSTERIOR CINGULATE	889/771	0.050	0.097	0.441	341/517	0.406	0.059	0.748	602/993	0.634	-0.025	0.830
PRE-CENTRAL	878/767	0.422	0.040	0.783	337/511	0.772	-0.020	0.918	595/986	0.163	-0.073	0.675
PRE-CUNEUS	883/772	0.736	0.017	0.954	339/519	0.287	0.075	0.628	596/993	0.429	-0.041	0.830
ROSTRAL ANTERIOR CINGULATE	883/765	0.506	-0.033	0.783	337/508	0.691	0.028	0.918	596/987	0.735	-0.018	0.830
ROSTRAL MIDDLE FRONTAL	889/770	0.684	-0.020	0.921	342/517	0.788	0.019	0.918	601/993	0.296	-0.054	0.830
SUPERIOR FRONTAL	890/770	0.987	0.001	0.987	342/516	0.219	0.086	0.618	602/990	0.573	-0.029	0.830
SUPERIOR PARIETAL	885/771	0.895	-0.007	0.987	340/515	0.265	0.085	0.618	599/992	0.082	0.095	0.675
SUPERIOR TEMPORAL	807/680	0.349	-0.049	0.764	297/428	0.566	-0.042	0.918	547/913	0.733	-0.018	0.830
SUPRA-MARGINAL	860/734	0.023	-0.115	0.396	326/477	0.257	0.079	0.618	582/964	0.994	0.000	0.994
TEMPORAL POLE	874/761	0.914	-0.005	0.987	341/520	0.866	0.012	0.918	599/994	0.003	0.154	0.109
TRANVERSE TEMPORAL	882/768	0.235	0.059	0.651	342/516	0.008	0.185	0.293	595/989	0.446	-0.040	0.830

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TABLE S7A. Linear model results for asymmetry indexes of volumes of subcortical structures in patients, effects of age at onset. (Note Cohen's d per year later age at onset). FDR adjusted p-values adjusted for 8 structures.

Region	N AO	p AO	Cohen's d AO	Padj AO
ACCUMBENS	2147	0.512	-0.014	0.700
AMYGDALA	2169	0.561	0.012	0.700
CAUDATE	2182	0.736	-0.007	0.736
HIPPOCAMPUS	2191	0.235	0.025	0.700
LATERAL VENTRICLES	2218	0.613	0.011	0.700
PALLIDUM	2044	0.509	0.015	0.700
PUTAMEN	2058	0.432	-0.017	0.700
THALAMUS	2177	0.528	-0.014	0.700

TABLE S7B. Linear model results for asymmetry indexes of average thickness of cortical structures in patients, effects of age at onset. (Note Cohen's d per year later age at onset). FDR adjusted p-values adjusted for 35 cortical regions.

Region	N AO	p AO	Cohen's d AO	Padj AO
AVG THICKNESS	1962	0.822	-0.005	0.950
BANKS STS	1771	0.428	-0.019	0.950
CAUDAL ANTERIOR CINGULATE	1952	0.669	-0.010	0.950
CAUDAL MIDDLE FRONTAL	1949	0.629	0.011	0.950
CUNEUS	1912	0.923	0.002	0.951
ENTORHINAL	1760	0.988	0.000	0.988
FRONTAL POLE	1955	0.751	0.007	0.950
FUSIFORM	1947	0.303	-0.023	0.950
INFERIOR PARIETAL	1929	0.486	-0.016	0.950

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INFERIOR TEMPORAL	1911	0.217	-0.028	0.950
INSULA	1917	0.911	0.003	0.951
ISTHMUS CINGULATE	1944	0.018	0.054	0.311
LATERAL OCCIPITAL	1946	0.535	0.014	0.950
LATERAL ORBITOFRONTAL	1954	0.479	-0.016	0.950
LINGUAL	1926	0.793	-0.006	0.950
MEDIAL-ORBITOFRONTAL	1932	0.688	-0.009	0.950
MIDDLE TEMPORAL	1828	0.802	0.006	0.950
PARA-CENTRAL	1954	0.599	0.012	0.950
PARA-HIPPOCAMPAL	1942	0.257	-0.026	0.950
PARS OPERCULARIS	1945	0.612	-0.012	0.950
PARS ORBITALIS	1952	0.834	0.005	0.950
PARS TRANGULARIS	1950	0.231	-0.027	0.950
PERI-CALCARINE	1904	0.337	-0.022	0.950
POST-CENTRAL	1929	0.869	0.004	0.950
POSTERIOR CINGULATE	1953	0.185	0.030	0.950
PRE-CENTRAL	1937	0.821	0.005	0.950
PRE-CUNEUS	1949	0.013	0.056	0.311
ROSTRAL ANTERIOR CINGULATE	1940	0.869	0.004	0.950
ROSTRAL MIDDLE FRONTAL	1953	0.417	-0.018	0.950
SUPERIOR FRONTAL	1952	0.817	-0.005	0.950
SUPERIOR PARIETAL	1947	0.041	0.046	0.477
SUPERIOR TEMPORAL	1749	0.710	0.009	0.950
SUPRA-MARGINAL	1875	0.776	-0.007	0.950
TEMPORAL POLE	1925	0.541	-0.014	0.950
TRANVERSE TEMPORAL	1944	0.285	0.024	0.950

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TABLE S7C. Linear model results for asymmetry indexes of surface area of cortical structures in patients, effects of age at onset. (Note Cohen's d per year later age at onset). FDR adjusted p-values adjusted for 35 cortical regions.

Region	N AO	p AO	Cohen's d AO	Padj AO
TOTAL SURFACE AREA	1959	0.448	-0.017	0.863
BANKS STS	1729	0.930	0.002	0.958
CAUDAL ANTERIOR CINGULATE	1920	0.541	-0.014	0.863
CAUDAL MIDDLE FRONTAL	1925	0.537	-0.014	0.863
CUNEUS	1895	0.847	0.004	0.957
ENTORHINAL	1671	0.592	-0.013	0.863
FRONTAL POLE	1953	0.162	-0.032	0.863
FUSIFORM	1884	0.305	0.024	0.863
INFERIOR PARIETAL	1896	0.686	-0.009	0.957
INFERIOR TEMPORAL	1906	0.839	-0.005	0.957
INSULA	1912	0.894	-0.003	0.958
ISTHMUS CINGULATE	1937	0.340	-0.022	0.863
LATERAL OCCIPITAL	1937	0.532	-0.014	0.863
LATERAL ORBITOFRONTAL	1953	0.582	0.012	0.863
LINGUAL	1927	0.203	0.029	0.863
MEDIAL-ORBITOFRONTAL	1901	0.218	-0.028	0.863
MIDDLE TEMPORAL	1792	0.539	-0.015	0.863
PARA-CENTRAL	1915	0.733	0.008	0.957
PARA-HIPPOCAMPAL	1911	0.805	-0.006	0.957
PARS OPERCULARIS	1928	0.905	-0.003	0.958
PARS ORBITALIS	1948	0.780	0.006	0.957
PARS TRANGULARIS	1939	0.195	-0.029	0.863
PERI-CALCARINE	1901	0.274	0.025	0.863

POST-CENTRAL	1881	0.457	-0.017	0.863
POSTERIOR CINGULATE	1944	0.298	-0.024	0.863
PRE-CENTRAL	1911	0.078	0.040	0.863
PRE-CUNEUS	1944	0.493	0.016	0.863
ROSTRAL ANTERIOR CINGULATE	1887	0.825	0.005	0.957
ROSTRAL MIDDLE FRONTAL	1944	0.374	-0.020	0.863
SUPERIOR FRONTAL	1912	0.151	0.033	0.863
SUPERIOR PARIETAL	1912	0.212	-0.029	0.863
SUPERIOR TEMPORAL	1713	0.523	-0.015	0.863
SUPRA-MARGINAL	1828	0.583	-0.013	0.863
TEMPORAL POLE	1907	0.065	-0.042	0.863
TRANVERSE TEMPORAL	1954	0.991	0.000	0.991

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Supplemental Figures

See separate PDF file for Figure S1 (Frequency histograms for asymmetry indexes of all structures)

See below for Figure S2a-c

.

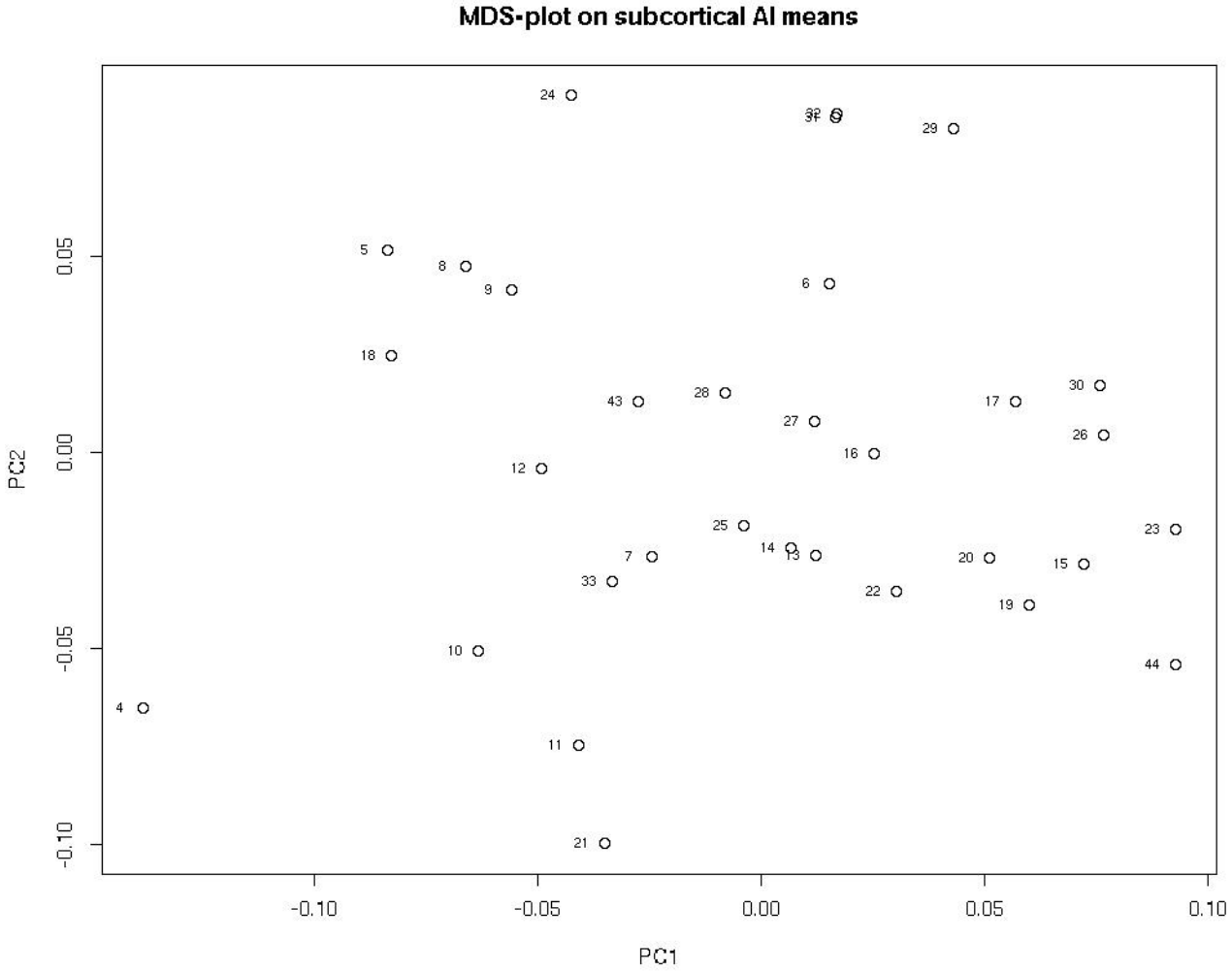

FIGURE S2A. MDS plot for the means of subcortical asymmetry index values per dataset

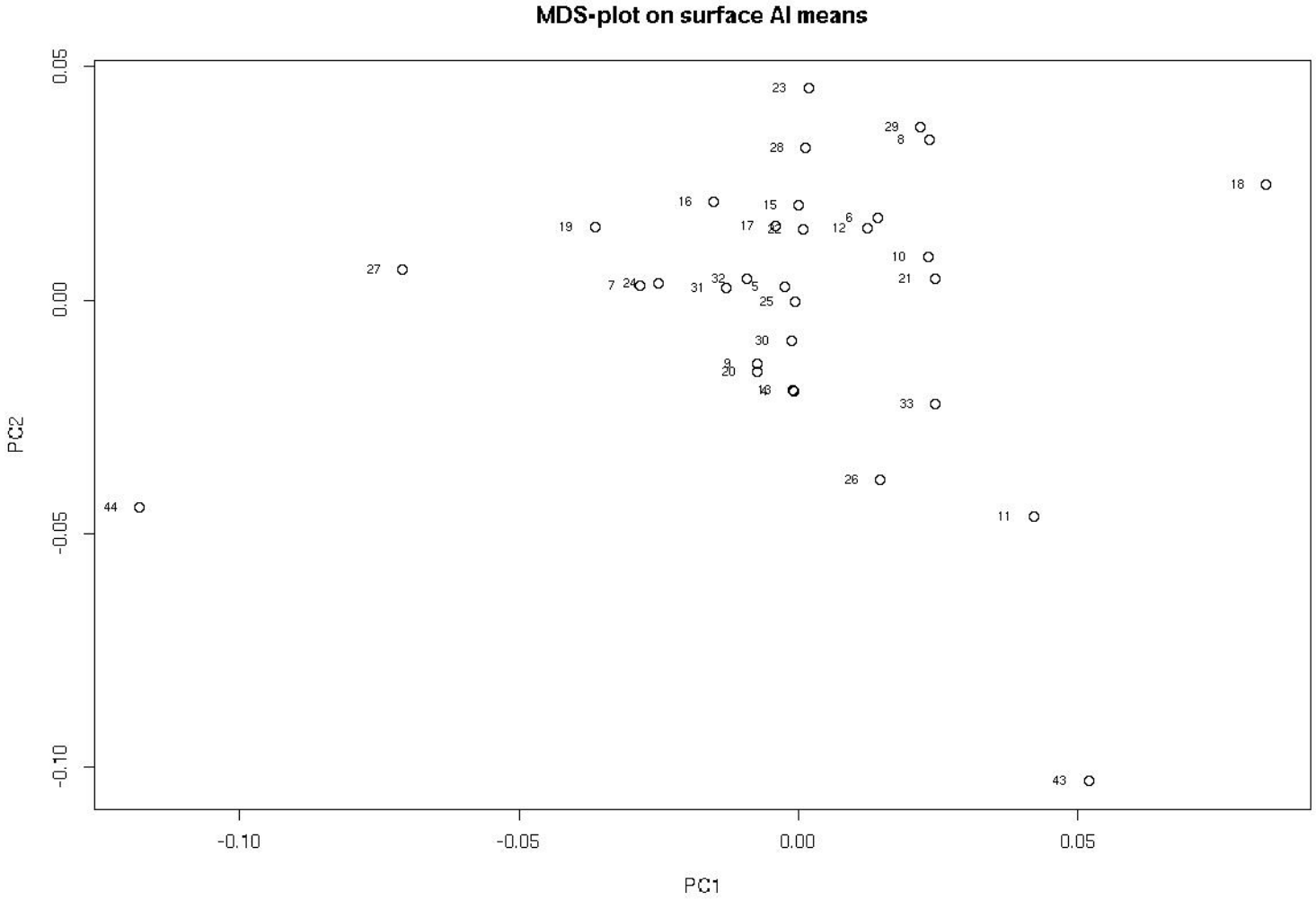

FIGURE S2B. MDS plot for the means of cortical surface area asymmetry index values per dataset

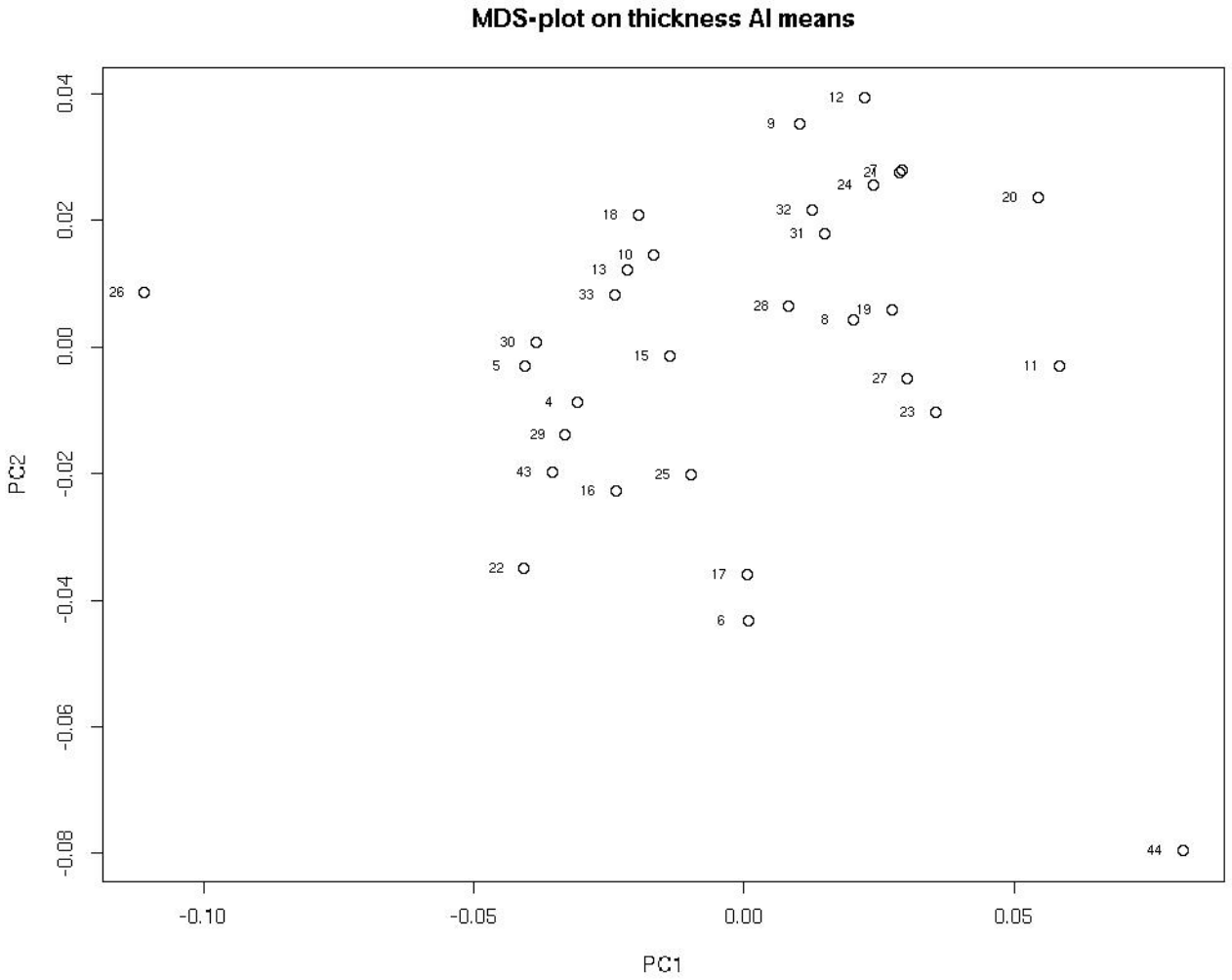

FIGURE S2C. MDS plot for the means of cortical thickness asymmetry index values per dataset