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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)

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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 | Fema le Contr | Fema le MDD | N ^a Contr | N MDD | Age Contr | sd | Age MDD | sd | Fema le Contr | Fema le 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 NEUROIMAGIN | 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 |

| G COHORT ^B | | | | | | | | | | | | | | | | | | |
|--------------------------|------|------|------|------|------|------|-----|-----|------|------|------|-----|------|------|----|----|-------------|---------|
| 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) SHIP | 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 criteria: 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. |
| MCMMASTER | 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 (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. |

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| 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). |
| 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 |

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: 8°, 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 | 1.5T: A sagittal scout series was acquired to test image quality. 3D fast low | |

| | | | | |
|----------------------------------|-----------|--|---|-----|
| | | Vision. 3T GE Discovery MR750 | 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 x 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: 256x256. | 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 sagittal slices; no slice gap; field of view =256 x 256 mm; 1.17 x 1.17 x 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 1x1x1 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 x 256 x 192, isometric voxel size = 1.0 mm3). | 5.3 |
| MCMMASTER | 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=13°; 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 x 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]) x 204 (anterior -posterior [AP]) x 160 (right -left [RL]) mm, phase encoding in AP and RL direction, reconstructed to cubic voxels of .5 mm x .5 mm x .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]) x 256 (anterior-posterior [AP]) x 188 (rightleft [RL]) mm, reconstructed to cubic voxels of 1 mm x 1 mm x 1 mm | 5.3 |
| 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 São 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, | Whole brain high resolution 3D MP-RAGE (magnetisation-prepared rapid acquisition with a gradient echo) volumetric scans (TR/TE/TI/flip angle | 5.3 |

| | | | | |
|----------------------------|------|----------------------|--|-----|
| | | Netherlands | 8.4/3.8/3000/8; matrix 256x204; FOV 240mm2) with axial orientation (reformatted to coronal) | |
| 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

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 | se. 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 $t \cdot \sqrt{1/n_1 + 1/n_2}$

^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

Table S5b. Linear model results for asymmetry indexes of surface areas of cortical structures.

| Region | N | Al±sd controls | Al±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 |
| 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).

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 | se. 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 |
| 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 |

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|--------------------------------|-----------|-------------|-------------|----------|---------|--------|-------|-------|--------|-------|-------|----------|--------|-------|-------|
| 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).

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 |

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|----------------------------|---------|-------|--------|-------|---------|-------|--------|-------|---------|-------|--------|-------|
| 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 |

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|---------------------------|---------|-------|--------|-------|---------|-------|--------|-------|---------|-------|-------|-------|
| 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 |

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 |
| 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 |

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

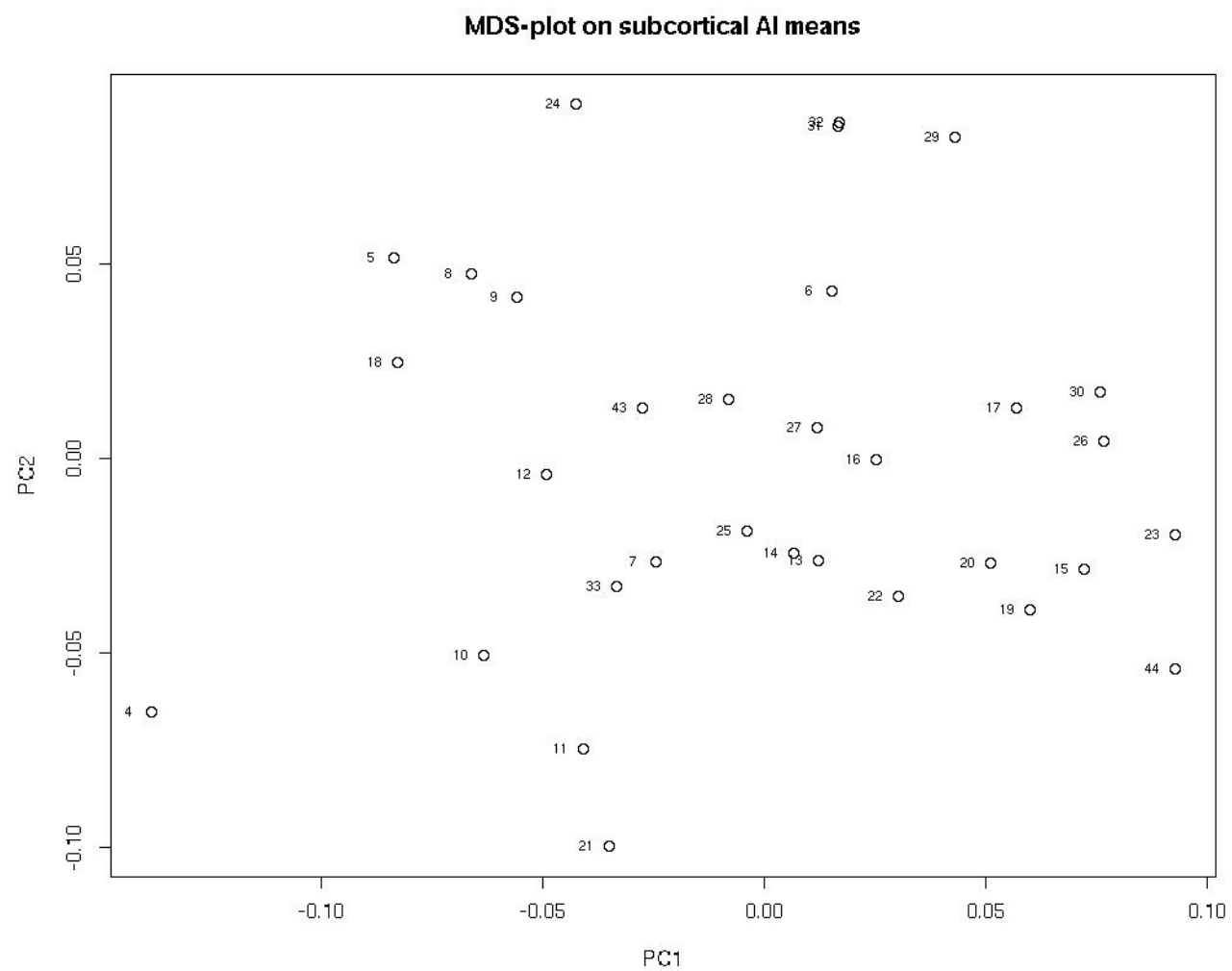


FIGURE S2A MDS PLOT FOR THE MEANS OF SUBCORTICAL ASYMMETRY INDEX VALUES PER DATASET

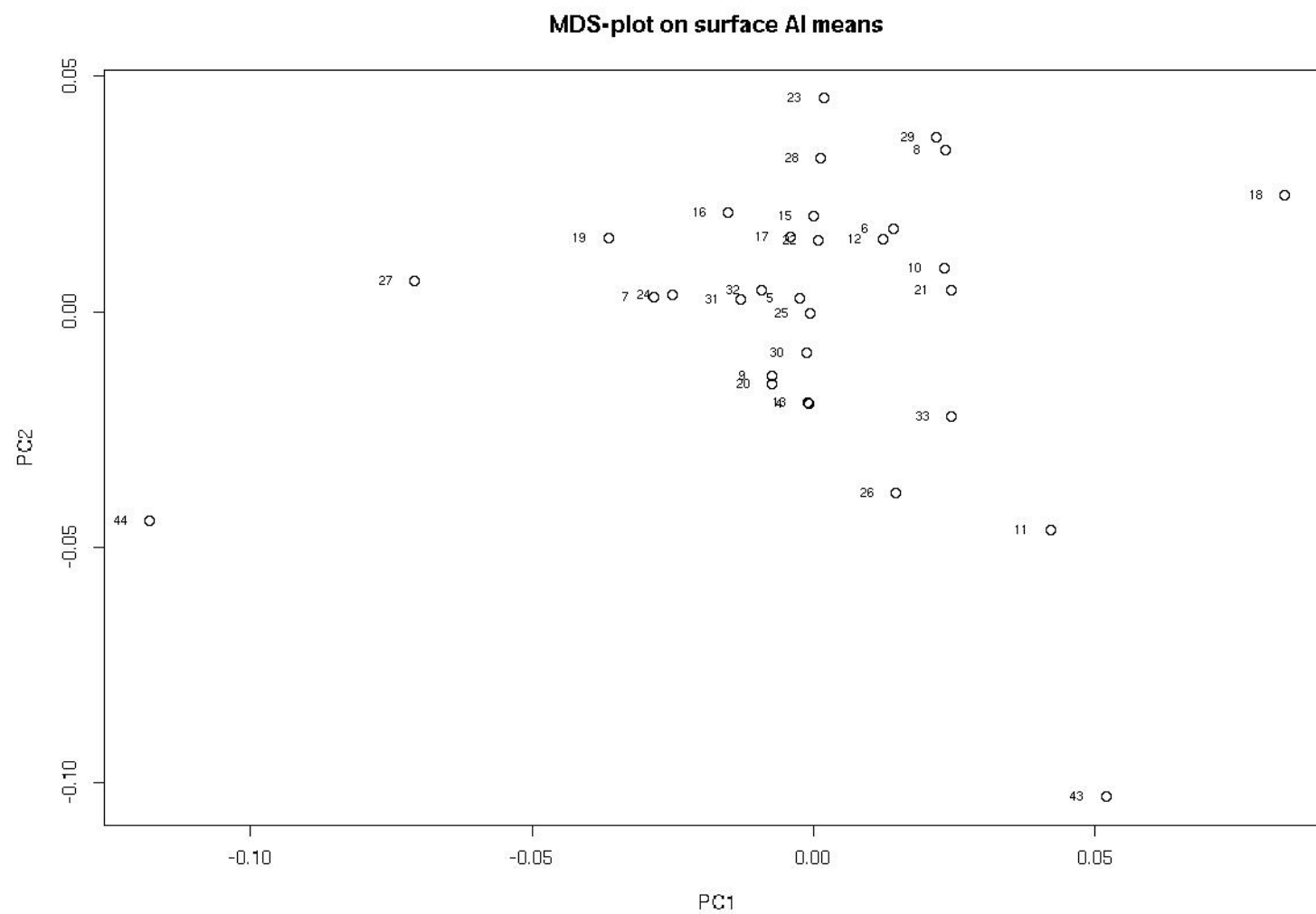


FIGURE S2B MDS PLOT FOR THE MEANS OF CORTICAL SURFACE AREA ASYMMETRY INDEX VALUES PER DATASET

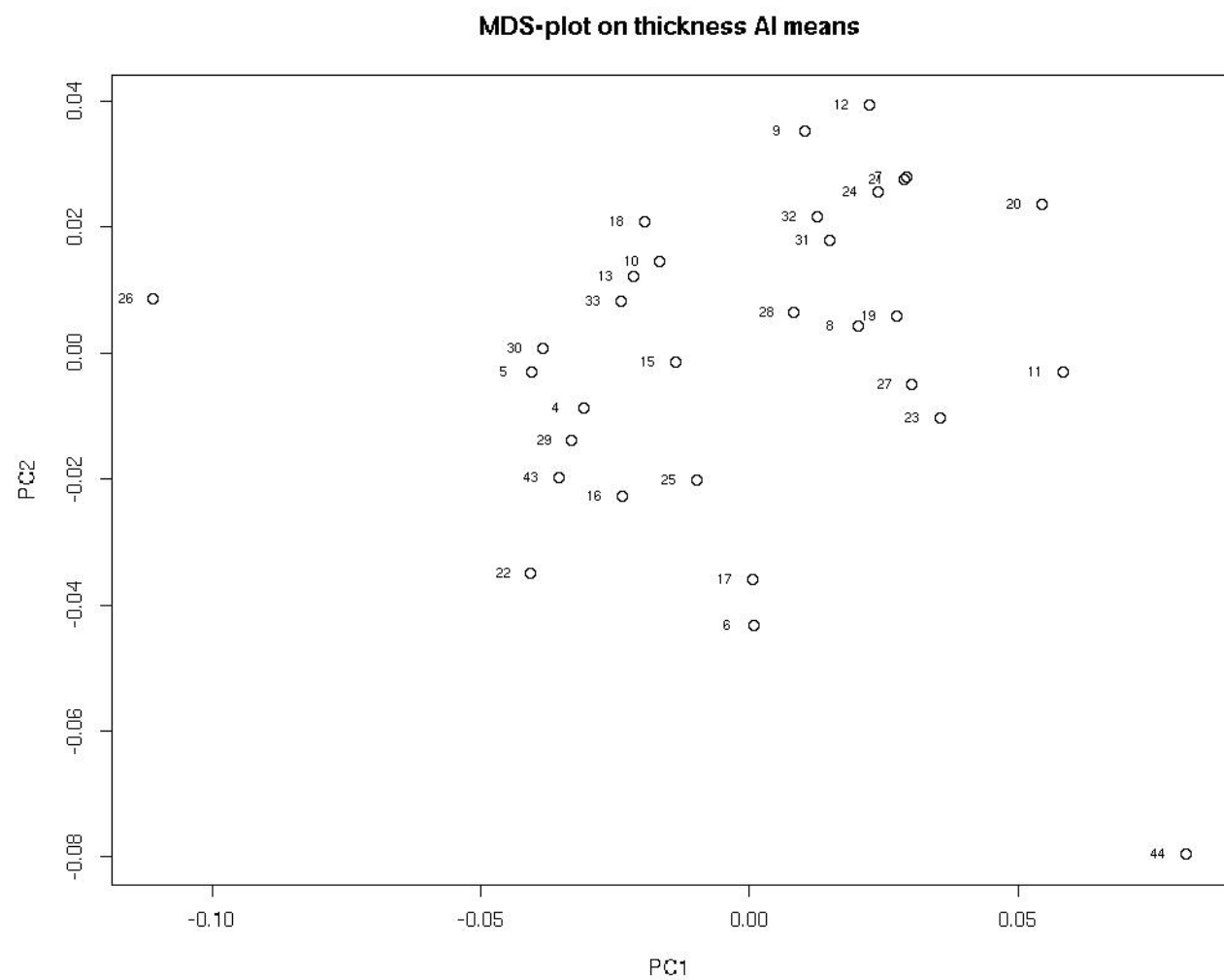


FIGURE S2c MDS PLOT FOR THE MEANS OF CORTICAL THICKNESS ASYMMETRY INDEX VALUES PER DATASET